

Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks

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Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks

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Key Messages

Purpose of Review

To synthesize the evidence regarding the effects of dietary sodium reduction and increased potassium intake on blood pressure and risk for cardiovascular diseases (CVD) and renal disease outcomes and related risk factors.

Key Messages

- Decreasing dietary sodium intake most likely reduces blood pressure in normotensive adults and more so in those with hypertension.
- Higher sodium intake may be associated with greater risk for developing hypertension.
- Use of potassium-containing salt substitutes in the diet to reduce sodium intake most likely reduces blood pressure in adults.
- Increasing potassium intake most likely decreases blood pressure in adults with hypertension.
- All-cause mortality may be associated with sodium intake.
- Reduced sodium intake may decrease the risk for combined CVD morbidity and mortality.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks

Structured Abstract

Objectives. This systematic review synthesized the evidence regarding the effects of interventions to decrease sodium intake or increase potassium intake on cardiovascular and renal disease outcomes and related risk factors, as well as evidence from prospective cohort studies on the associations between sodium, potassium, or sodium to potassium ratio and these outcomes. The purpose of the review is to provide a future Dietary Reference Intakes (DRI) Committee with the evidence on chronic disease endpoints for consideration in reviewing the DRIs for sodium and potassium.

Data sources. PubMed[®], Embase[®], the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, CINAHL[®], Web of Science, references of prior reviews, hand searches of gray literature, and expert recommendations.

Review methods. Two reviewers independently screened citations and full-text publications. Eligible studies included randomized controlled trials (RCTs), nonrandomized controlled trials, and prospective observational studies published through 2017 that enrolled healthy populations or those with pre-existing hypertension, cardiovascular disease (CVD), diabetes, or obesity and that assessed blood pressure (BP), incident hypertension, achievement of prespecified blood pressure goals, all-cause mortality, CVD morbidity and mortality, coronary heart disease morbidity and mortality, stroke, myocardial infarction, renal morbidity and mortality, kidney stones, and adverse events. We extracted data, assessed risk of bias (RoB, or study quality), summarized and synthesized results, and evaluated the strength of the evidence (SoE) supporting the conclusions separately for conclusions based on controlled trials and those based on prospective cohort studies.

Results. We identified 15,912 unique citations, of which 257 publications reporting on 171 studies were deemed eligible for the review.

Moderate-strength evidence from 48 RCTs supports a significant BP-lowering effect of dietary sodium reduction in adults (e.g., a decrease of 3.23 mm Hg [95% confidence interval 2.41 to 4.06] in systolic blood pressure with a 42 mmol weighted mean decrease in sodium intake), but sodium reduction interventions do not appear to show statistically significant effects on BP in children (low SoE). Comparing the findings of studies of adults with hypertension with those in adults with normal BP showed that sodium reduction has a greater BP-lowering effect in adults with hypertension than in normotensive adults (moderate SoE). Sodium reduction may also increase the proportion of study participants who achieve a prespecified BP goal (low SoE), but the evidence is unclear regarding the effect of reducing sodium intake on the incidence of hypertension (because of the small number of trials). Prospective cohort studies suggest an association between lower urinary sodium excretion and reduced risk for hypertension (low SoE because of high RoB and lack of consistency).

Only a small number of RCTs assessed the effects of sodium reduction on longer term chronic disease outcomes: Sodium reduction decreased the risk for the combined outcome of CVD mortality/morbidity and a composite outcome of any CVD events (low SoE). Although sodium levels appear to be associated with all-cause mortality (low SoE), the shape of this relationship could not be determined (insufficient SoE), and evidence from prospective cohort studies was insufficient to draw conclusions regarding associations with combined CVD morbidity/mortality and stroke risk.

Use of potassium salt substitutes in place of sodium chloride and increasing potassium intake itself through the use of supplements significantly decrease BP (moderate SoE), but evidence is insufficient to assess their effect on risk for hypertension, kidney stones, or longer term outcomes, including all-cause mortality or CVD, stroke, or renal morbidity or mortality, or the potential moderating effects of other factors, and whether these effects are moderated by changes in sodium intake. Evidence from prospective cohort studies suggests potassium intake may be associated with decreased risk for kidney stones but is insufficient to assess associations of potassium intake with other outcomes of interest.

Conclusions. Reducing sodium intake, increasing potassium intake, and use of potassium-containing salt substitutes in the diet significantly decrease BP, particularly among those with hypertension. Limited evidence also suggests that sodium intake is associated with risk for all-cause mortality, and that reducing sodium intake may decrease the risk for CVD morbidity and mortality.

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Evidence Summary

Background and Objectives

Cardiovascular disease (CVD) and kidney disease¹ are responsible for the majority of deaths worldwide. A primary risk factor for CVD (cardiovascular disease), stroke, and other circulatory diseases is hypertension (HTN). In November 2017, the American Heart Association and the American College of Cardiology modified the definition of hypertension to a systolic blood pressure of 130 or higher and a diastolic blood pressure of 80 or higher. Before issue of the 2017 report on which these changes were based, health organizations worldwide defined hypertension as a systolic blood pressure (BP) of 140 or higher or a diastolic BP of 90 or higher; however, for the purpose of this review, the definition of HTN is that used by the individual included studies.

Sodium and potassium are vital for life. However, the role of excess dietary sodium as a major risk factor for HTN has been supported by large bodies of evidence.^{2, 3} Evidence has also suggested a protective role for dietary potassium, independently or through its influence on the body's management of sodium.⁴ The aim of the current report is to assess the evidence that interventions to decrease sodium intake or increase potassium intake on blood pressure, total mortality, and risk for CVD and kidney disease as well as evidence from prospective cohort studies on the associations between sodium, potassium, or sodium to potassium ratio and these outcomes.

Dietary Reference Intakes

The Governments of the United States and Canada have jointly undertaken the development of the Dietary Reference Intakes (DRIs) since the mid-1990s. Federal DRI committees from each country work collaboratively to identify DRI needs, prioritize nutrient reviews, and advance work to resolve any methodological issues that could impede new reviews. DRIs are a set of reference values that provide guidance on adequate and safe intakes of nutrients across the life span, by sex, and during pregnancy and lactation in apparently healthy individuals. They are based on an expert consensus process in which ad hoc committees convened by the Food and Nutrition Board of the National Academies of Sciences, Engineering, and Medicine Health and Medicine Division (HMD) used scientific evidence, augmented by scientific judgment when dealing with uncertainties, to derive the reference values. The default reference values for adequate intakes are Estimated Average Requirements (EARs), from which a Recommended Dietary Allowance (RDA) is derived, “the average daily intake level sufficient to meet the nutrient requirement of nearly all healthy individuals” (97.5 percent) in a particular age and sex (life stage) group. If the available data are inadequate to identify an RDA requirement for nutrient sufficiency, an Adequate Intake (AI) reference value may be used in place of an EAR/RDA. The AI is a recommended intake level thought to meet or exceed the nutrient requirements of almost all individuals in a particular life stage and sex group.⁵ The reference value that represents an intake above which the risk of potential adverse effects due to excessive intakes may increase is called the Tolerable Upper Intake Level (UL).

The DRIs are for dietary intakes only (i.e., foods and dietary supplements) and are intended to cover the needs of almost all healthy persons. These values serve multiple purposes, including guidance for (a) health professionals for use in dietary counseling and for developing educational materials for consumers and patients, (b) scientists in designing and interpreting research, (c)

users of national nutrition monitoring, and (d) policy for a number of applications such as the Dietary Guidelines for Americans, nutrition labeling, and federal nutrition programs.

In 2005, the Dietary Reference Intakes: Water, Potassium, Sodium, Chloride, and Sulfate report was released by the Institute of Medicine Food and Nutrition Board.⁶ The report established nutrient reference values for water, potassium, sodium, chloride and sulfate to maintain health and reduce chronic disease risk.

Sodium Dietary Reference Intakes

The 2005 IOM report set the AI for sodium for the population aged 19-50 years at 1500 mg (65 mmol) per day based on three criteria: (1) the amount of sodium that would likely need to be ingested in order to meet the needs of all other essential nutrients through food (2) the amount of sodium that would need to be replenished due to sweat losses in un-acclimatized individuals who are exposed to high temperatures or who are moderately physically active (as recommended in other DRI reports) and (3) the level of sodium intake that had shown an association in some studies with adverse effects on blood lipids and insulin resistance. The AI does not apply to highly active populations such as competitive athletes and workers exposed to extreme heat stress, such as fire fighters.⁶

The critical endpoint selected for determination of the UL was blood pressure.⁵ The IOM concluded that the relationship between sodium intake and blood pressure was continuous without an apparent threshold; thus it was difficult to precisely set a UL, especially because other factors (weight, exercise, potassium intake, dietary pattern, alcohol intake, and genetic factors) also affect blood pressure. The IOM set the UL for sodium at 2,300 mg per day for people aged 14 years and over, with lower values for those 1-13 years of age. The ULs for children were extrapolated from the adult UL based on median energy intakes.

Since 2005, two related IOM reports, Strategies to Reduce Sodium Intake in the United States,⁷ and Sodium Intake in Populations: Assessment of Evidence⁸ have been published. The literature summarized in these reports as well as a number of subsequent evidence reviews, which include both observational studies and randomized controlled trials, support the relationship between sodium intake and blood pressure. In addition, some recent reviews of randomized controlled trials and observational studies have shown that reducing sodium leads to reductions in blood pressure among people with and without high blood pressure.⁹⁻¹³

Additional evidence, largely from observational studies, has shown that higher dietary sodium intake is associated with greater risk for hypertension, fatal and nonfatal stroke, and cardiovascular disease.^{8, 13-15} Hypertension is strongly associated with a higher risk for CVD, stroke, congestive heart failure, and kidney disease.¹⁶ Lowering blood pressure lowers these risks, and some evidence supports an indirect relationship between sodium intake and CVD has been proposed.¹⁷ Assessing the relationship between sodium intake and chronic disease outcomes (i.e., CVD, Stroke, myocardial infarction (MI), coronary heart disease (CHD), and kidney disease), and more importantly, whether reducing dietary intakes of sodium lowers the risk of these diseases, requires that the findings from observational studies be subjected to greater scrutiny and that they be supported by the findings of randomized controlled trials.

The limitations of the observational studies assessing the relationship between sodium intake and CVD outcomes have been carefully reviewed and critiqued.¹⁸ Limitations may include methods used for sodium intake assessment, residual confounding, and possible reverse causality. Assessment of sodium intake in observational studies as well as in older randomized controlled trials has typically relied on the use of food frequency questionnaires or spot urine

assays of urinary sodium excretion. However, these methods have repeatedly been shown to be highly prone to both random and systematic error. More accurate but still error prone methods include 24- to 72-hour food diaries or recall assessment or 8-hour (overnight) urine assays. The most accurate method of assessing sodium intake in observational studies, particularly decreases in sodium intake, is the repeated 24-hour urinary sodium excretion with validation.^{19,20} In light of the limitations of the existing observational studies, the current state of knowledge needs to be reconsidered.

Potassium DRIs

The 2005 IOM committee also set an AI level for potassium at 4,700 milligrams (120 mmol) per day, based on levels that blunt the sodium-related increase in blood pressure as well as the reduction in risk of kidney stones.⁶ The DRI report noted the need for dose-response studies on potassium related to cardiovascular disease and blood pressure. The IOM Sodium Intake in Populations report listed “analyses examining the effects of dietary sodium in combination with other electrolytes, particularly potassium” on health outcomes as a research gap.⁸ Understanding the health effects of potassium added to the diet and the interaction of potassium with sodium are essential. The latter is particularly important in monitoring the health impact of the use of potassium chloride (KCl) as a salt substitute in reformulating foods to reduce the amount of sodium, as KCl is already in use as a salt substitute in foods, including selected restaurant and packaged foods.

Use of Chronic Disease Endpoints in Setting DRIs

The DRI steering committees jointly decided that prior to undertaking a nutrient review, whether—and how—data on chronic disease risk reduction could be used in setting future DRI values need to be determined. Thus, a scientific expert panel was convened to review and critically evaluate evidentiary, dose response, and process issues related to the use of chronic disease endpoints and develop options for their incorporation into future DRI reviews.²¹ The panel report identified the challenges that would need to be overcome in using chronic disease endpoints, namely systematically identifying and evaluating the strength of the evidence underlying proposed relationships. Because chronic disease endpoints were essential to development of the current UL for sodium, 2,300 milligrams per day, and may be used to set other DRI values, the US and Canadian steering committees commissioned the HMD to develop an authoritative report on the feasibility and practicality of using chronic disease endpoints in setting DRI values, and to develop an appropriate framework for use by future DRI panels. The commission of a systematic review for nutrients under review is now an integral part of the DRI process. The current review was undertaken at the recommendation of the DRI Working Group and its federal partners to inform the update of the sodium and potassium DRIs by the Institute of Medicine (Health and Medicine Division [HMD] of the National Academies of Sciences, Engineering, and Medicine).

Scope and Key Questions

Scope of Review

This report focuses on sodium and potassium intake, blood pressure, incident hypertension, and risk for all-cause mortality, chronic diseases, and related outcomes in all populations, including those with hypertension, Type 2 Diabetes, renal disease, CVD, and obesity.

The goal of this review is to provide a future DRI sodium and potassium panel with a systematic review of the evidence, including the general body of evidence reviewed by the 2005 DRI panel⁶ (through 2002) and updated evidence, regarding sodium and potassium intakes, blood pressure, and the risks for hypertension, CVD, coronary heart disease, stroke, renal disease, and kidney stones.

This report does not include a review of studies that assess the levels of dietary sodium and potassium required to prevent deficiencies.

The protocol has been published on the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Web site (<http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=2428>). In addition, the protocol was registered in PROSPERO (CRD42017056126).

Key Questions

The Key Questions (KQs) for sodium and potassium are as follows.

Sodium

- KQ1. Among adults and children of all age groups (including both sexes and pregnant and lactating women), what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on blood pressure at the time of the study and in later life?
- Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?
 - Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).
 - Among subpopulations defined by hypertension, diabetes, and obesity health status.
- KQ2. Among adults and children, what is the association between dietary sodium intake and blood pressure?
- Among subpopulations defined by sex, race/ethnicity, and age (children, adolescents, young adults, older adults, elderly).
 - Among subpopulations defined by hypertension, diabetes, and obesity health status.

KQ3. Among adults, what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on CVD and kidney disease morbidity and mortality and on total mortality?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

KQ4. Among adults, what is the association between dietary sodium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary sodium intake and total mortality?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the association with sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

Potassium

KQ5. Among children and adults what is the effect of interventions to increase potassium intake on blood pressure and kidney stone formation?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the effect of potassium?

b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity and renal health status.

KQ6. Among children and adults, what is the association between potassium intake and blood pressure and kidney stone formation?

a. Among subpopulations defined by sex, race/ethnicity, and age (children, adolescents, young adults, older adults, elderly).

b. Among subpopulations defined by hypertension, diabetes, and obesity health status.

KQ7. Among adults, what is the effect of interventions aimed at increasing potassium intake on CVD and kidney disease morbidity and mortality, and on total mortality?

a. Do other minerals modify the effect of potassium (e.g., sodium, calcium, magnesium)?

b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

KQ8. Among adults, what is the association between dietary potassium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary potassium and total mortality?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the association with potassium?

b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Methods

The Evidence-based Practice Center conducted this review following established methods as outlined in the AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Reviews.²² A complete description of the methods appears in the full report.

Literature Search Strategy

We searched PubMed[®], CINAHL[®], Embase[®], the Cochrane Database of Systematic Reviews (CDSR), CENTRAL, and Web of Science for English-language publications, commencing with 2003. In addition, reference lists of existing systematic reviews on the outcomes of interest as well as the 2005 DRI report were screened to identify all relevant studies from inception.

Criteria for Inclusion/Exclusion of Studies in the Review

We included randomized and nonrandomized controlled trials and observational studies published in English that examined interventions to restrict sodium intake or increase potassium intake, used a comparator group, and reported outcomes of interest in participants at least 4 weeks or more after the initiation of the intervention (longer minimum followup times were established for some outcomes, as described in the full report). Observational studies were included if they were prospective cohort studies with followup times and baseline participant conditions that met prespecified criteria.

Pairs of investigators independently determined study eligibility and resolved disagreements through discussions; if needed, the project leader was consulted until consensus was achieved.

Quality (Risk of Bias) Assessment of Individual Studies

Risk of bias (RoB) of eligible studies was assessed by two independent investigators using an instrument based on AHRQ guidance.²² The investigators consulted to reconcile any discrepancies in overall RoB assessments. Overall summary RoB assessments for each study were classified as low, moderate, or high based on a composite of the individual items.

Data Synthesis

The results for each study are described in evidence tables as well as in figures and summary tables in the full report. For both sodium and potassium, evidence is synthesized by study design (odd-numbered vs. even-numbered questions), outcome, types of intervention or intake assessment), and, where possible, separately by subgroups of interest.

Where possible, we pooled results of studies with similar study designs and interventions and report these summary findings. We also conducted meta-regressions on the findings of trials that assessed the effects of sodium reduction, to compare the outcomes relative to mean differences in 24-hour urinary sodium excretion.

A draft version of the report was posted for peer review and for public comment and the report was revised in response to comments. However, the findings and conclusions are those of the authors, who are responsible for the contents of the report.

Strength of the Body of Evidence

We evaluated the overall strength of evidence for each outcome and subgroup based on five domains: (1) study limitations (study design, number of studies, study size, and overall RoB [low, moderate, high, or unclear]); (2) directness (the degree to which the assessed outcome represented the true outcome of interest, the findings were based on randomized controlled trials, or, in the case of subgroup analyses, whether subgroups were compared within the same intervention); (3) consistency (similarity of effect direction and size); (4) precision (degree of certainty around an estimate); and (5) reporting bias (evidence that reported outcomes were prespecified by the study protocol).²² Four strength of evidence grades were possible:

- **High:** High confidence that the evidence reflects the true effect. Further research is unlikely to change the estimates.
- **Moderate:** Moderate confidence that the estimate reflects the true effect. Further research may change estimates and our confidence in the estimates.
- **Low:** Limited confidence that the estimate of effect lies close to true effect. Further research is likely to change confidence in the estimate of effect, and may change the estimate.
- **Insufficient:** Evidence is either unavailable or does not permit a conclusion to be drawn.

Results

We identified 15,912 unique titles, of which 257 publications (reporting on 171 studies) were deemed eligible for review. A flow diagram appears in the main text of the report.

The bodies of evidence varied greatly in size by outcome and sodium or potassium intake. No conclusions were deemed to have a high strength of evidence. The strength of evidence of

conclusions that depended on associations (observational studies) were assessed separately from those based on interventions.

The key findings (primarily those for which the strength of evidence was high or moderate) are summarized by KQ below, along with the strength of evidence. The findings for healthy adults are presented first, followed by the findings for subpopulations of interest. Additional findings are provided in the main report.

Odd-numbered KQs are addressed with randomized controlled trials (RCTs) and controlled clinical trials, whereas even-numbered questions are addressed with prospective cohort studies. The conclusions are based primarily on data from controlled trials.

KQ1. Among adults and children of all age groups (including both sexes and pregnant and lactating women), what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on blood pressure at the time of the study and in later life?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

- Sodium reduction decreases systolic (mean difference [MD] -3.23 millimeters [mm] mercury [Hg], 95% confidence intervals [CI] $-4.07, -2.38$; I^2 77%; 47 RCTs) and diastolic (MD -2.24 mm Hg, 95% CI $-2.96, -1.61$; I^2 75%; 48 RCTs) blood pressure significantly in adults (weighted mean difference in sodium intake 42 mmol/d) (moderate strength of evidence [SoE]).
- Sodium reduction in adults may increase the likelihood of achieving a prespecified blood pressure goal (low SoE; 6 RCTs).
- Sodium reduction lowers BP in both men and women (moderate SoE); the evidence does not support a moderating effect of sex on BP in adults (low SoE).
- Short term sodium reduction interventions do not appear to show statistically significant effects on BP in children (low SoE based on eight RCTs); however, a sensitivity analysis that excluded high or unclear RoB studies resulted in a small difference in systolic blood pressure and a statistically significant decrease in diastolic BP with sodium reduction for children (MD -1.54 , 95% CI $-2.57, -0.51$; I^2 0%; 4 RCTs)
- Sodium reduction decreases systolic BP in both those with hypertension (MD -4.14 , 95% CI $-5.21, -3.07$; I^2 75%) and those with normal BP (MD -1.51 , 95% CI $-2.76, -0.26$; I^2 42%); the effect is greater in adults with HTN than in those with normal BP ($p < 0.001$, moderate SoE; 45 RCTs). Sodium reduction decreases diastolic BP in those with hypertension (moderate SoE; 37 RCTs).

- Evidence may not support a moderating effect of increasing dietary potassium via food or supplements on the blood pressure-lowering effect of sodium reduction (low SoE; 5 RCTs).
- Potassium-containing salt substitutes decrease systolic and diastolic BP (moderate SoE; 13 RCTs).

KQ2. Among adults and children, what is the association between dietary sodium intake and blood pressure?

a. Among subpopulations defined by sex, race/ethnicity, and age (children, adolescents, young adults, older adults, elderly).

b. Among subpopulations defined by hypertension, diabetes, and obesity health status.

- Sodium intake may be associated with systolic BP in adults based on prospective observational studies (low SoE, 5 studies). Most studies had high RoB for the methods used to assess sodium intake, and findings were inconsistent across studies.
- Sodium intake may be associated with risk of incident hypertension in prospective cohort studies of adults (low SoE, 5 studies). Most studies had high RoB for the methods used to assess sodium intake, and the number of studies was small).

KQ3. Among adults, what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on CVD and kidney disease morbidity and mortality and on total mortality?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the association with sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

- In adults, evidence was insufficient to draw a conclusion regarding the effect of sodium reduction on the risk for all-cause mortality or CVD mortality, alone.
- Sodium reduction may significantly decrease the risk for combined CVD morbidity and mortality (8 RCTs; low SoE).
- Evidence from a small number of RCTs does not support an effect of sodium reduction on the risk for stroke. (3 RCTs; low SoE)
- Sodium reduction may significantly decrease the risk for a composite measure of any CVD outcomes as reported by study authors (7 RCTs; low SoE).

KQ4. Among adults, what is the association between dietary sodium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary sodium intake and total mortality?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the association with sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

- Although sodium levels appear to be associated with risk for all-cause mortality (low SoE, based on 11 studies), the shape of the relationship could not be determined (insufficient SoE).
- Evidence is insufficient to assess the possible association of sodium intake level and risk for CVD, CHD, or stroke morbidity or mortality.

KQ5. Among children and adults, what is the effect of interventions to increase potassium intake on blood pressure and kidney stone formation?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the effect of potassium?

b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

- Increased potassium intake from dietary supplements reduces blood pressure in adults (moderate SoE based on 10 parallel RCTs and 8 crossover RCTs). However the effect is limited to studies of adults with prehypertension or hypertension (moderate SoE). Studies of adults with normal BP did not show evidence that increased potassium intake decreases blood pressure in this group (3 RCTs; low SoE)
- Evidence does not support an effect of increasing potassium intake through changes in food intake alone on BP in adults (low SoE based on four RCTs).
- Evidence is insufficient to support a conclusion regarding the effect of increasing potassium intake on kidney stone formation (1 RCT).

KQ6. Among children and adults, what is the association between potassium intake and blood pressure and kidney stone formation?

a. Among subpopulations defined by sex, race/ethnicity, and age (children,

adolescents, young adults, older adults, elderly).

b. Among subpopulations defined by hypertension, diabetes, and obesity health status.

- Evidence from prospective cohort studies does not support a consistent association of higher potassium intake with lower adjusted BP in cohort studies of adults (6 prospective cohort studies; low SoE based on inconsistent findings and studies with high RoB).
- Higher potassium intake appears to be associated with a lower risk for kidney stones in cohort studies of adults (low SoE, based on 4 prospective cohorts [reported in 2 publications] with high RoB).

KQ7. Among adults, what is the effect of interventions aimed at increasing potassium intake on CVD and kidney disease morbidity and mortality, and on total mortality?

a. Do other minerals modify the effect of potassium (e.g., sodium, calcium, magnesium)?

b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

- Evidence was insufficient, based on only one RCT, to address this question.

KQ8. Among adults, what is the association between dietary potassium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary potassium and total mortality?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the association with potassium?

b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

- Evidence is insufficient to identify associations of potassium intake with long-term chronic disease outcomes of interest, primarily due to the limitations in the potassium intake assessments.

Discussion

Summary of Findings in Relation to What Is Already Known

Since the *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* was published in 2005, a number of systematic reviews have been conducted on the effects of sodium intake and sodium reduction on BP, as well as CVD and CHD outcomes. We briefly review our findings in light of the findings of the most recent reviews. Aburto and colleagues conducted reviews on the relationship between sodium and potassium intake and BP, CVD, CHD, and stroke from observational studies and the effects of sodium reduction and increased potassium intake as reported in RCTs; these reviews were sponsored by the World Health Organization (WHO) in support of their current guidelines. The WHO review on sodium and BP, which included 37 RCTs, found significant beneficial effects of interventions to reduce sodium on blood pressure in adults and children but no difference between very low- (defined as a target of 50mmol/d) and low-sodium (defined as a target of 100mmol/d) interventions.^{4,23} Our report found similar effects of sodium reduction on BP in adults, but only statistically non-significant beneficial effects in children. A sensitivity analysis that omitted high- and unclear RoB studies showed that when only low- and moderate-RoB studies were pooled, sodium reduction resulted in a statistically significant decrease in diastolic BP in children (the decrease in systolic BP remained non-significant). The WHO report did not assess effects of sodium reduction on incident hypertension or achievement of specific BP goals. The inclusion criteria for our report and those of the WHO report differed in several ways. Our review included sodium reduction RCTs regardless of achieved sodium excretion, whereas the WHO review excluded RCTs with a mean difference in achieved sodium excretion of less than 40 mmol/d.

More recently, Graudal and colleagues systematically reviewed the trial literature on sodium reduction and BP and reached similar conclusions to those of Aburto and our current review; the Graudal review excluded only trials with a duration of less than 4 days, resulting in a larger number of included trials.²⁴ Our review also corroborates the findings of the Graudal review regarding a larger effect of sodium reduction on individuals with HTN than on normotensive individuals.

The WHO report found no effect of sodium reduction on plasma epinephrine, norepinephrine, blood lipids, or kidney function, as measured by serum creatinine and creatinine clearance; four studies that met our inclusion criteria corroborated the apparent absence of effect of sodium reduction on blood lipids (reported as adverse effects or primary outcomes), but no studies met our inclusion criteria for assessing changes in kidney function or catecholamines. In contrast, the Graudal review reported significant increases in cholesterol and triglycerides, possibly due to the shorter followup of some included studies and the larger number of studies that met inclusion criteria.²⁴

Several recent systematic reviews also appraised the evidence linking sodium with all-cause mortality, CVD, CHD, or stroke. A 2014 systematic review by Adler and colleagues that reviewed eight RCTs assessing effects of sodium reduction on these longer-term outcomes reported no effect on all-cause mortality.¹⁵

Graudal and colleagues (2014) conducted a meta-analysis of prospective cohort studies that assessed the association between sodium intakes and mortality: They reported an increased mortality risk at both low- and high intakes of sodium (which they referred to as a “U-shaped curve”).²⁵ The review include only observational studies, and the findings could be explained by errors in estimation of sodium intake at the lower or the upper end as well as reverse causality.

Our review of RCTs that reported on the effects of sodium reduction on all-cause mortality found a non-statistically significant decrease in the risk for all-cause mortality but evidence was insufficient on which to base a conclusion. Our review of prospective cohort studies found that sodium intake may be associated with increased risk but evidence was insufficient to draw any conclusions regarding the shape of the curve. The methods used to estimate sodium intake varied across the observational studies, and only a small number used multiple 24-hour sodium excretion measures with validation to ensure complete collection; in addition, these studies could not rule out reverse causation: In sodium studies, reverse causality arises when study participants with medical morbidity have reduced their sodium intake on medical advice or because their illness has resulted in decreased food consumption.

Our current review also adds to the evidence by identifying an effect of sodium reduction on reducing combined CVD morbidity and mortality across RCTs. The review by Adler found similar effects on CVD mortality and morbidity; they largely attributed the observed effect on mortality to one study that implemented use of a potassium salt substitute to reduce sodium intake.²⁶ We also reported statistically significant effects of sodium reduction on a composite of any CVD outcomes. The Adler review included one RCT²⁷ that we excluded, as it was a multicomponent intervention that did not control for other dietary changes (the remaining RCTs were included in our review).¹⁵ The WHO also reviewed the evidence linking sodium with CVD, CHD, and stroke; that report, which included 14 prospective cohort studies and five RCTs, found sufficient evidence only to conclude (based on the evidence from cohort studies) that increased sodium intake was linked to increased risk for stroke, stroke mortality, and CHD mortality.⁴

We identified few studies on individuals with chronic kidney disease, and no studies that met our inclusion criteria addressed renal endpoints. A Cochrane review by McMahon and colleagues appraised the evidence on effects of sodium reduction on cardiovascular outcomes in persons with kidney disease.²⁸ However like our review, they identified no studies with long enough follow up to assess long term chronic disease outcomes. Instead they reported only on studies that assessed effects of sodium reduction on BP outcomes in persons with kidney disease, reporting that sodium reduction decreased systolic BP and diastolic BP in these studies. Across the studies that met our inclusion criteria, we also noted that sodium reduction generally decreased BP; however, we determined that the populations were too dissimilar (based on comorbidities) to permit studies to be pooled.

Aburto and colleagues subsequently reviewed the evidence for an association of potassium intake with BP, HTN, and CVD for the WHO, concluding that higher potassium intake was associated with reduced BP in individuals with HTN but not in normotensive persons.²⁹ That report found insufficient evidence to draw conclusions regarding the association of potassium intake with risk for CVD or CHD morbidity or mortality. Our current review confirmed the association of potassium with BP lowering, by identifying RCTs that assessed the effects of increased potassium intake and also extended their finding to healthy populations. We found insufficient evidence to draw any conclusions on the effects of increased potassium intake on incident HTN, and like the WHO review, we identified insufficient evidence to draw conclusions regarding the effects of increased potassium intake on CVD/CHD morbidity or mortality. In

addition, the beneficial effects of increased potassium intake on BP were not reflected in any association between (urinary or dietary) potassium intake and BP.

Limitations of the Evidence Base

The purpose of this review was to assess the evidence for the intermediate and clinical health effects of reduced sodium intake, mainly as reflected in reduced 24-hour urinary sodium excretion. We did not assess the evidence regarding the most effective intervention design(s).

Most RCTs demonstrated an overall low or moderate RoB. However, a number of studies omitted many details of study design and conflict of interest, so actual RoB was unclear for some items. Nearly all observational (prospective cohort) studies that met inclusion criteria relied on single 24-hour urinary excretion measures, single or 2-day dietary recall without 24-hour urinary excretion, estimated sodium excretion to assess status, or food frequency questionnaires. The implications of assessment of sodium and potassium intake are discussed further below. Additional limitations are listed here, organized by a PICOTSS (populations, interventions, comparators, outcomes, timings, settings, study design) framework (see Table 1 in full report report).

Populations

- Few to no studies conducted subgroup analyses by sex, age, race/ethnicity, or comorbidities.
- RCTs may enroll individuals who are more motivated than average, although compliance across studies (usually based on 24-hour sodium excretion) does not necessarily support this possibility.
- Studies defined prehypertension and mild-to-moderate HTN differently or not at all, and some studies included individuals with pre- or mild HTN along with individuals with more advanced HTN.
- Although most RCTs either prohibited or required use of antihypertensive medications or withdrew participants from medications at baseline and assessed need to resume their use, at least 25 percent of studies did not consider use of these medications, or allowed participants to remain on medications but did not account for their use. Studies that enrolled only participants taking antihypertensive medications usually did not control for the class of medication, thus potentially introducing a confounding factor. Concurrent use of some antihypertensive medications could have masked the potential effects of a reduced sodium diet.
- Few studies of individuals with chronic kidney disease met the inclusion criteria for the review, and no studies that assessed renal outcomes met inclusion criteria.
- Observational studies had limited ability to control for pre-existing health conditions at study baseline, that might have resulted in decreased sodium intake, contributing to potentially spurious associations of lower sodium intakes with morbidity or mortality outcomes of interest.
- Observational studies may have residual confounding, as they could not adjust for all factors that may increase risk for HTN, CVD, CHD outcomes.

Interventions/Intakes

- RCTs use widely varying methods to achieve different sodium intake levels, and most RCTs actually employ multicomponent lifestyle interventions or at least multicomponent dietary interventions; thus not all changes in outcomes of interest might be attributable to reduced sodium or increased potassium intake. The potential implication of this variation in background diet for study findings is highlighted by the findings of the Dietary Approaches to Stop Hypertension (DASH) Sodium trial, which showed that at each dietary sodium level, mean BP was higher (2.2 to 5.9 mm Hg) among control diet participants than among the DASH diet groups, that the decreases in BP achieved with decreasing sodium intake were greater for those on the control diet than for those on the DASH diet, but that nevertheless, the low-sodium DASH participants achieved the greatest reduction in BP overall.³⁰ Thus a diet that includes more fruits and vegetables (and, as a result, more vitamins, minerals, and fiber, and less saturated fat), as well as whole grains and low-fat dairy, has effects on BP that are independent of sodium intake.
- Only a small number of studies assessed effects of natural experiments, community- or government-level interventions.
- Many RCTs failed to report intended goals of the intervention (e.g., achieving 70 mmol/d urinary sodium excretion or a difference between the intervention group and the control group of 40 mmol/d or more).
- Effectiveness of behavioral/lifestyle interventions in reducing sodium intake may be affected by unmeasured or unreported factors, such as intensity of counseling.
- Few prospective cohort studies used multiple 24-hour urinary excretion analyses, although increasing evidence demonstrates that multiple, non-consecutive 24-hour urinary sodium excretion measurements need to be used as the indicator of intake in observational studies.^{19, 31, 32} Thus nearly all included prospective cohort studies had high risk for both systematic (24-h urine collections without evidence of quality control measures, spot or overnight urine collections, food frequency questionnaire (FFQ), 24-hour recalls, and food records) and random error (e.g., single 24-hour or spot urine collections or single-day food recalls).
- Both RCTs and prospective cohort studies varied widely in baseline sodium intake. Most RCTs employed 24-hour urinary sodium excretion as a measure of compliance with the intervention. However, differences in baseline intake could affect the potential to achieve sodium reduction goals through dietary interventions and introduces a source of heterogeneity among prospective cohort studies. Evidence in support of this idea is presented by a recent post hoc assessment of data from the DASH Sodium trial found that reducing sodium intakes in the context of the control or the DASH diet were associated with progressively greater reductions in BP with higher baseline BP (through baseline systolic BP of 150 mm Hg or higher).³³
- Wide variation in achieved intake across RCTs introduces another potential source of heterogeneity and calls into question whether differences in achieved sodium intake can accurately predict changes in outcomes of interest.
- Few RCTs reported sodium/potassium ratios. Potentially related to this observation, studies that employed potassium-containing salt substitutes to reduce sodium intake or tested the effects of potassium supplements tended to find no consistent effects on sodium excretion.

- Few studies employ food-based interventions to assess the effects of increasing potassium intake. Those that do use dietary interventions do not consistently control for differences in other micronutrients, carbohydrates, and fiber.
- Potassium supplementation studies range from about 15 to 120 mmol/d in the amounts provided (average intakes from food range from 50 to 150 mmol/d and the current AI for adults is 120 mmol/d), introducing a potential source of heterogeneity across studies.

Comparators

- Confounding in dietary intervention studies (for example, adoption of use of salt substitutes or other salt reduction practices by control groups) was difficult to control or measure, and blinding had limited effectiveness when the comparison group consumed their usual diet (most dietary intervention studies that relied on counseling reported that participants were not blinded).
- Studies with usual diet as the control may not be comparable with studies that impose a low-sodium diet on all participants and then achieve differences in sodium intake using sodium tablets to mimic usual sodium intake.

Outcomes

- Studies defined HTN, CVD, and CHD outcomes differently.
- Few RCTs assessed the effect of sodium reduction or increased potassium intake on the risk for incident HTN as an outcome.
- Of the small number of studies that assessed long term CVD outcomes, few assessed these as primary or even prespecified outcomes, were not powered to assess them as prespecified outcomes, and reported them instead as adverse events.
- Little research assesses effects of sodium reduction on CHD outcomes.

Timing/Duration

- Few to no RCTs were identified that assessed longer-term clinical outcomes of most interest: RCTs seldom had adequate duration of interventions or followup to assess longer-term outcomes.
- Renal outcomes, including kidney stones, require longer followups to observe potential effects of interventions than were employed in any of the studies identified.
- Long-term outcomes resulting from brief interventions may not show effects.

Setting

- RCTs in clinical research settings are resource intensive and may have limited practical application. RCTs in populations confined to residential settings such as long-term care facilities, schools, or prisons may provide more useful results in terms of assessing outcomes but still fail to address the potential effects of voluntary efforts (individual or community) to reduce dietary sodium intake.

Study Design

- Observational studies predominated for long term chronic disease outcomes.
- As described, RCTs with parallel arm designs present challenges that are difficult to overcome regarding blinding, allocation concealment, and contamination.

- RCTs with crossover designs may provide some advantages, but existing crossover trials seldom describe washout periods or assess potential carryover effects of short (or no) washouts.

Limitations of This Review

Since the inclusion of participants with pre-existing conditions could confound attempts to link the outcomes of interest with changes in sodium intake, studies that enrolled sick participants were excluded from the affected analyses. For example, studies of patients with CVD were excluded from analysis of risk for CVD morbidity, but not analysis of CVD mortality, and studies of patients with cancer, HIV/AIDS, and end stage renal disease were excluded from all analyses.

We did not take use of antihypertensive medications into account in our analyses of RCT data, primarily because studies did not consistently report or adjust for such use. As a result, we could not eliminate the possibility that potential effects of reduced sodium might be masked by the effects of such medications.

Similarly, we did not conduct sensitivity analyses to assess the effects of the methods used to measure blood pressure, which may strongly affect outcomes.

Because of the small number of studies that assessed moderating effects of demographic factors or comorbidities (and were powered to do so), we conducted meta-regressions to try to shed light on potential moderators, realizing these are indirect comparisons.

The duration of interventions or followup is likely critical. For that reason, we set strict lower limits on the durations of studies we included, especially for long term clinical outcomes. However, we did not attempt to assess the effects of intervention or followup duration on outcomes, mainly because we identified too few studies to enable realistic comparisons.

We excluded crossover studies that did not describe the use of washout or duration of washout and did not describe a process to assess the possible effects of carryover. As a result, we excluded one dose-response study, the findings of which supported the conclusion that decreasing sodium intake decreases blood pressure.³⁴ However, some evidence suggests potential carryover may need to be considered.³⁵

Research Gaps Identified by This Review

In light of the large body of evidence on the effects of sodium reduction on blood pressure in healthy adults and those with hypertension, the determination that the effect of reducing sodium intake on blood pressure is supported by moderate but not high strength evidence is attributable to inconsistency in the direction of study findings and to study heterogeneity. Sensitivity analyses that omitted high- and unclear RoB studies did not appreciably alter consistency, heterogeneity, or effect sizes; thus, other factors—such as differing participant comorbidities, intervention design, or blood pressure measurement methods—may contribute to the variation.

Studies to assess whether those with HTN may benefit more or less from reduced dietary sodium than those with normal blood pressure showed greater benefits for those with HTN, but at least one fourth of studies that enroll adults with HTN do not report controlling for use of antihypertensive medication.

Among studies that met inclusion criteria, only a small number directly compared effects of sodium reduction on participants with normal blood pressure with those on participants with HTN. Studies to assess the benefits of reducing dietary sodium for those with normal blood

pressure were fewer in number than studies of populations with HTN, and some studies of normotensive populations included individuals with high normal blood pressure.

Few studies that met inclusion criteria directly compared the effects of sodium reduction on men with those on women, the effects on one racial/ethnic group with those on other racial/ethnic groups, and the effects among different age groups. Few studies designed to determine whether dietary interventions reduce blood pressure among younger individuals—both children, adolescents, and young adult—met inclusion criteria.

Most dietary intervention studies to reduce sodium (or increase potassium) from food sources involved counseling, making it difficult to isolate the effects of sodium reduction, either because of poor adherence or because of the challenge of ruling out alterations in intake of other nutrients.

Few trials that met inclusion criteria assessed the effects of sodium reduction or increased potassium intake on CVD, CHD, stroke, or renal outcomes, including the effect of increasing potassium intake on the incidence of kidney stones.

Conclusions

We undertook this systematic review to appraise the evidence from trials regarding the effects of dietary sodium reduction and/or increased potassium intake on blood pressure and risk for cardiovascular diseases—as well as the evidence on associations of dietary sodium and potassium with blood pressure and cardiovascular diseases. This review finds that interventions that reduce sodium intake (including those that use potassium-containing salt substitutes in the diet) reduce blood pressure in both normotensive adults and to a greater extent in those with hypertension. Interventions to reduce sodium intake increase the likelihood of reaching a prespecified blood pressure goal and may decrease the incidence of hypertension in adults, in agreement with prospective cohort studies, which show that higher sodium intakes may be associated with greater risk for hypertension.

Increasing potassium intake via potassium supplements significantly decreases blood pressure, but the effects of increasing potassium intake through food alone remain unclear.

Interventions to assess the effects of reducing sodium intake on the risk for all-cause mortality are small in number and provide an insufficient basis on which to draw a conclusion. Prospective cohort studies suggest sodium intake may be associated with all-cause mortality. Findings from randomized controlled trials also suggest that interventions to reduce sodium intake may decrease the risk for composite measures of cardiovascular disease outcomes.

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Introduction

Background and Objectives

Circulatory diseases, including coronary heart disease (such as myocardial infarction and heart failure), coronary artery disease (such as stroke), and kidney disease,¹ are responsible for the majority of deaths worldwide. A primary risk factor for cardiovascular diseases (CVD), stroke, and other circulatory diseases is hypertension (HTN). Prior to November 2017, when the American Heart Association and the American College of Cardiology modified the definition of hypertension to include a systolic blood pressure of 120 or higher and a diastolic blood pressure of 80 or higher, health organizations worldwide define hypertension as a systolic blood pressure (BP) of 140 or higher or a diastolic BP of 90 or higher; however, for the purpose of this review, the definition of HTN is that used by the individual included studies.

Sodium and potassium are vital for life. However, the role of excess dietary sodium as a major risk factor for HTN has been supported by large bodies of evidence.^{2, 3} Evidence has also suggested a protective role for dietary potassium, independently or through its influence on the body's management of sodium.⁴ The aim of the current report is to review the evidence regarding the effects of interventions to decrease sodium intake or increase potassium intake on blood pressure, total mortality, and risk for CVD and kidney disease as well as evidence from prospective cohort studies on the associations between sodium, potassium, or sodium to potassium ratio and these outcomes.

Dietary Reference Intakes

The Governments of the United States and Canada have jointly undertaken the development of the Dietary Reference Intakes (DRIs) since the mid-1990s. Federal DRI committees from each country work collaboratively to identify DRI needs, prioritize nutrient reviews, and advance work to resolve any methodological issues that could impede new reviews. DRIs are a set of reference values that provide guidance on adequate and safe intakes of nutrients across the life span, by sex, and during pregnancy and lactation in apparently healthy individuals. They are based on an expert consensus process in which ad hoc committees convened by the Food and Nutrition Board of the National Academies of Sciences, Engineering, and Medicine Health and Medicine Division (HMD) used scientific evidence, augmented by scientific judgment when dealing with uncertainties, to derive the reference values. The default reference values for adequate intakes are Estimated Average Requirements (EARs), from which a Recommended Dietary Allowance (RDA) is derived, "the average daily intake level sufficient to meet the nutrient requirement of nearly all healthy individuals" (97.5 percent) in a particular age- and sex (life stage) group. If the available data are inadequate to identify an RDA requirement for nutrient sufficiency, an Adequate Intake (AI) reference value may be used in place of an EAR/RDA. The AI is a recommended intake level thought to meet or exceed the nutrient requirements of almost all individuals in a particular life stage and sex group.⁵ The reference value that represents an intake above which the risk of potential adverse effects due to excessive intakes may increase is called the Tolerable Upper Intake Level (UL).

The DRIs are for dietary intakes only (i.e., foods and dietary supplements) and are intended to cover the needs of almost all healthy persons. These values serve multiple purposes, including guidance for a) health professionals for use in dietary counseling and for developing educational materials for consumers and patients, b) scientists in designing and interpreting research, c) users

of national nutrition monitoring, and d) policy for a number of applications such as the Dietary Guidelines for Americans, nutrition labeling, and federal nutrition programs.

In 2005, the Dietary Reference Intakes: Water, Potassium, Sodium, Chloride, and Sulfate report was released by the Institute of Medicine Food and Nutrition Board.⁶ The report established nutrient reference values for water, potassium, sodium, chloride and sulfate to maintain health and reduce chronic disease risk.

Sodium Dietary Reference Intakes

The 2005 Institute of Medicine (IOM) report set the AI for sodium for the population aged 19-50 years at 1500 mg (65 mmol) per day based on three criteria: (1) the amount of sodium that would likely need to be ingested in order to meet the needs of all other essential nutrients through food (2) the amount of sodium that would need to be replenished due to sweat losses in un-acclimatized individuals who are exposed to high temperatures or who are moderately physically active (as recommended in other DRI reports) and (3) the level of sodium intake that had shown an association in some studies with adverse effects on blood lipids and insulin resistance. The AI does not apply to highly active populations such as competitive athletes and workers exposed to extreme heat stress, such as firefighters.⁶

The critical endpoint selected for determination of the Tolerable Upper Intake Level (UL) was blood pressure.⁵ The IOM concluded that the relationship between sodium intake and blood pressure was continuous without an apparent threshold; thus it was difficult to precisely set a UL, especially because other factors (weight, exercise, potassium intake, dietary pattern, alcohol intake, and genetic factors) also affect blood pressure. The IOM set the UL for sodium at 2,300 mg per day for people aged 14 years and over, with lower values for those 1-13 years of age. The ULs for children were extrapolated from the adult UL based on median energy intakes.

Since 2005, two related IOM reports, Strategies to Reduce Sodium Intake in the United States,⁷ and Sodium Intake in Populations: Assessment of Evidence⁸ have been published. The literature summarized in these reports as well as a number of additional evidence reviews, which include both observational studies and randomized controlled trials, support the relationship between sodium intake and blood pressure. In addition, some recent reviews of randomized controlled trials and observational studies have shown that reducing sodium leads to reductions in blood pressure among people with and without high blood pressure.⁹⁻¹³

Additional evidence, largely from observational studies, has shown that higher dietary sodium intake is associated with greater risk for fatal and nonfatal stroke and cardiovascular disease.^{8, 13-15} High blood pressure is strongly associated with a higher risk for CVD, stroke, congestive heart failure, and kidney disease.¹⁶ Lowering blood pressure lowers these risks, and some evidence supports an indirect relationship between sodium intake and CVD.¹⁷ Assessing the relationship between sodium intake and chronic disease outcomes (i.e., CVD, Stroke, coronary heart disease [CHD], myocardial infarction [MI], and kidney disease), and in particular whether reducing dietary intakes of sodium lowers the risk of these diseases, would benefit from a critical appraisal of the findings of both observational studies and long-term trials.

The limitations of the observational studies assessing the relationship between sodium intake and CVD outcomes have been carefully reviewed and critiqued.¹⁸ Limitations may include methods used for sodium intake assessment, residual confounding, and possible reverse causality.

Assessment of sodium intake in observational studies has typically relied on the use of food frequency questionnaires or spot urine assays of urinary sodium excretion. However, these

methods have repeatedly been shown to be highly prone to both random and systematic error. More accurate but still error prone methods include 24- to 72-hour food diaries or recall assessment or 8-hour (overnight) urine assays. The most accurate method of assessing sodium intake, particularly decreases in sodium intake, is the repeated 24-hour urinary sodium excretion with validation.^{19, 20} Realization of the limitations of the existing observational studies requires reconsideration of the current state of knowledge.

Potassium DRIs

The 2005 IOM committee also set an AI level for potassium at 4,700 milligrams per day, based on levels that blunt the sodium-related increase in blood pressure as well as the reduction in risk of kidney stones.⁶ The DRI report noted the need for dose-response studies on potassium related to cardiovascular disease and blood pressure. The IOM Sodium Intake in Populations report listed “analyses examining the effects of dietary sodium in combination with other electrolytes, particularly potassium” on health outcomes as a research gap.⁸ Understanding the health effects of potassium added to the diet and the interaction of potassium with sodium are essential. The latter is particularly important in monitoring the health impact of the use of potassium chloride (KCl) as a salt substitute in reformulating foods to reduce the amount of sodium, as KCl is already in use as a salt substitute in foods, including selected restaurant and packaged foods.

Use of Chronic Disease Endpoints in Setting DRIs

The DRI steering committees jointly decided that prior to undertaking a nutrient review, whether—and how—data on chronic disease risk reduction could be used in setting future DRI values need to be determined. Thus, a scientific expert panel was convened to review and critically evaluate evidentiary, dose response, and process issues related to the use of chronic disease endpoints and develop options for their incorporation into future DRI reviews.²¹ The panel report identified the challenges that would need to be overcome in using chronic disease endpoints, namely systematically identifying and evaluating the strength of the evidence underlying proposed relationships. Because chronic disease endpoints were essential to development of the current UL for sodium, 2,300 milligrams per day, and may be used to set other DRI values, the US and Canadian steering committees commissioned the HMD to develop an authoritative report on the feasibility and practicality of using chronic disease endpoints in setting DRI values, and to develop an appropriate framework for use by future DRI panels. The commission of a systematic review for nutrients under review is now an integral part of the DRI process. The current review was undertaken at the recommendation of the DRI Working Group and its federal partners to inform the update of the sodium and potassium DRIs by the Institute of Medicine (HMD of the National Academies of Sciences, Engineering, and Medicine).

Scope and Key Questions

Scope of Review

This report focuses on sodium and potassium intake, blood pressure, incident hypertension, and risk for all-cause mortality, chronic disease risk reduction, and related outcomes in all populations, including those with hypertension, Type 2 Diabetes, renal disease, CVD, and obesity.

The goal of this review is to provide a future DRI sodium and potassium panel with a systematic review of the evidence, including the general body of evidence reviewed by the 2005 DRI panel⁶ (through 2002) and updated evidence, regarding sodium and potassium intakes, blood pressure and the risk for hypertension, and the risk for CVD, coronary heart disease, stroke, renal disease, and kidney stones.

This report does not include a review of studies that assess the levels of dietary sodium and potassium required to prevent deficiencies.

Key Questions

Sodium

Key Question 1. Among adults and children of all age groups (including both sexes and pregnant and lactating women), what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on blood pressure at the time of the study and in later life?

- a. Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?
- b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).
- c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Key Question 2. Among adults and children, what is the association between dietary sodium intake and blood pressure?

- a. Among subpopulations defined by sex, race/ethnicity, and age (children, adolescents, young adults, older adults, elderly).
- b. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Key Question 3. Among adults, what is the effect (benefits and harms) of interventions to reduce dietary sodium intake on CVD and kidney disease morbidity and mortality and on total mortality?

- a. Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?
- b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).
- c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

Key Question 4. Among adults, what is the association between dietary sodium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary sodium intake and total mortality?

a. Do other minerals (e.g., potassium, calcium, magnesium) modify the association with sodium?

b. Among subpopulations defined by sex, race/ethnicity, age (adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity and renal health status.

Potassium

Key Question 5. Among children and adults, what is the effect of interventions to increase potassium intake on blood pressure and kidney stone formation?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the effect of potassium?

b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

Key Question 6. Among children and adults, what is the association between potassium intake and blood pressure and kidney stone formation?

a. Among subpopulations defined by sex, race/ethnicity, and age (children, adolescents, young adults, older adults, elderly).

b. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Key Question 7. Among adults, what is the effect of interventions aimed at increasing potassium intake on CVD and kidney disease morbidity and mortality, and on total mortality?

a. Do other minerals modify the effect of potassium (e.g., sodium, calcium, magnesium)?

b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, obesity, and renal health status.

Key Question 8. Among adults, what is the association between dietary potassium intake and CVD, CHD, stroke, and kidney disease morbidity and mortality, and between dietary potassium and total mortality?

a. Do other minerals (e.g., sodium, calcium, magnesium) modify the association with potassium?

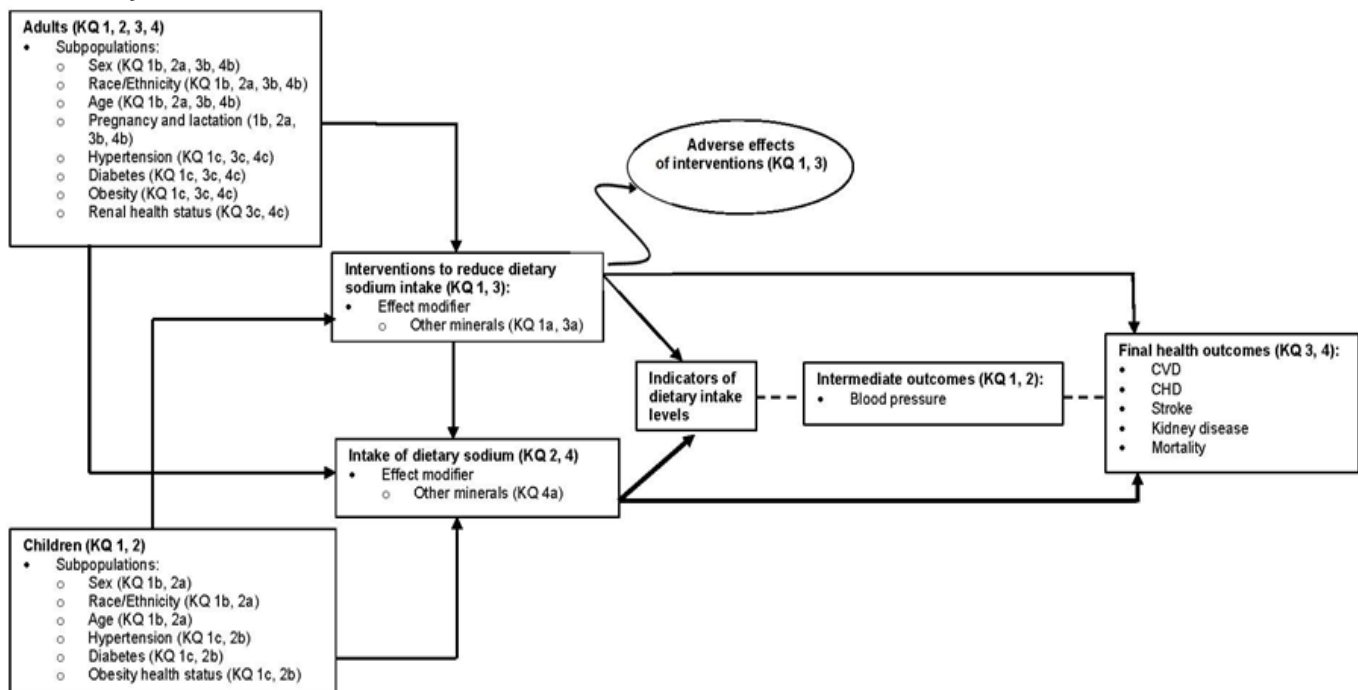
b. Among subpopulations defined by sex, race/ethnicity, age (young adults, older adults, elderly), and for women (pregnancy and lactation).

c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Analytic Frameworks

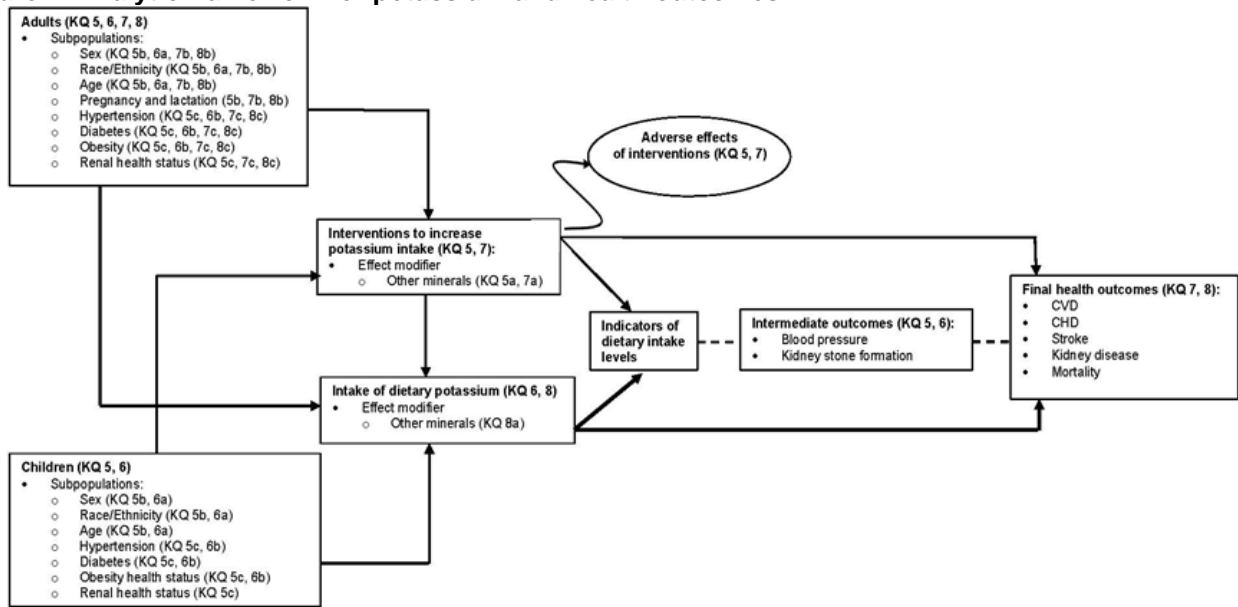
The review was guided by the analytic frameworks shown in Figures 1 and 2.

Figure 1. Analytic framework for sodium and health outcomes



CHD = Coronary Heart Disease; CVD = Cardiovascular Disease; KQ = Key Question

Figure 2. Analytic framework for potassium and health outcomes



CHD = Coronary Heart Disease; CVD = Cardiovascular Disease; KQ = Key Question

Organization of This Report

The remainder of this report presents the methods used to conduct the literature searches, data abstraction, and analysis for this review; the results of the literature searches, organized by Key Question and intervention; the conclusions; and a discussion of the findings within the context of what is already known, the limitations of the review and the literature, and suggestions for future research.

Methods

The methods used to conduct this systematic review are based on the Agency for Healthcare Research and Quality (AHRQ) Methods Guide.²² The Key Questions were developed by the federal sponsors prior to the start of the review and refined by the research team in collaboration with the technical expert panel (TEP) and the Federal sponsors during development of the protocol.

Criteria for Inclusion/Exclusion of Studies in the Review

Inclusion and exclusion criteria are described below according to the PICOTSS (population, intervention/intake, comparison group, outcome, time, setting, and study design) framework (Table 1). The criteria are based on the 2005 Institute of Medicine (IOM) report and on discussions with and recommendations of federal sponsors and the TEP for the current review. Studies that were considered for addressing Key Questions intended to assess the effect of interventions on the outcomes of interest (KQ 1, 3, 5, and 7) were limited to randomized controlled trials (RCTs) and controlled clinical trials (CCTs). Both parallel and crossover trials were included; however, based on concerns about possible carryover effects,²³ crossover trials that did not incorporate a minimum 2-week washout phase between treatment phases and did not explicitly describe the procedure used to ensure lack of carryover were excluded. If an article did not mention washout period duration or an effort to assess the potential for carryover, we searched for a separately published study protocol. If washout or a method to assess carryover were not mentioned in the protocol, the study was excluded.

Studies that were considered in addressing Key Questions pertaining to the association between sodium and/or potassium intake and health effects included both prospective observational studies and multivariate analyses of results of RCTs in which randomization was not maintained. Included observational studies were limited to those studies that measured and quantified intake of sodium and/or potassium with valid indicators. Valid assessment measures were selected together with input from the Technical Expert Panel (TEP) and content expert and are described below in the section on assessment of risk of bias (RoB).

The Key Questions pertaining to associations excluded studies that exclusively followed participants with preexisting disease specific to the clinical outcome of interest. To use valid samples to determine associations, the cohort would need to include participants with and without the condition of interest at followup. Because the pool of association studies included observational studies where the exposure to a specific dietary strategy was self-selected and compared groups might differ in more characteristics than simply dietary sodium or potassium intake, eligible studies were limited to those reporting baseline data for the outcomes of interest.

The intervention or followup durations required for study inclusion (e.g., two years for studies on kidney disease) were determined by the federal sponsors, the TEP, and other clinical experts to ensure we included only studies with sufficient followup durations to detect the incident outcome of interest.

Other Exclusions Applying to All Key Questions

Only full-text peer-reviewed English-language publications were included. These decisions were made to ensure that sufficient study detail was provided and accessible to assess study quality fairly.

Table 1. PICOTSS

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
KQ1	Studies in human participants will be eligible for inclusion in the review, with the exception of studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer.	Studies evaluating interventions to reduce dietary sodium intake that specify the oral consumption from food or supplements of quantified amounts of sodium and sodium chloride (salt) or sodium-to-potassium ratio will be eligible, with the exception of trial arms in which participants demonstrate a weight change of +/- 3% or more. Interventions simultaneously addressing sodium and potassium intake that document sodium/potassium ratio are eligible; all other multicomponent interventions in which the effect of sodium reduction cannot be disaggregated from other intervention components will be excluded.	Studies comparing interventions to placebo or control diets will be eligible. Studies comparing an experimental diet to usual diet, studies comparing levels of sodium intake, or studies that alter sodium/potassium ratio in other ways will be included if they control for other nutrient levels.	Studies reporting on blood pressure outcomes (e.g., systolic blood pressure, diastolic blood pressure, rate of hypertensive/non-hypertensive participants, incident hypertension, percent participants at blood pressure goal, and change in blood pressure) will be eligible.	Studies reporting on an intervention period of at least four weeks will be eligible.	Studies in outpatient settings will be eligible.	Parallel RCTs and cross-over RCTs with a washout period of two weeks or more will be eligible.
KQ2	Studies in community-dwelling (non-institutionalized) human participants will be eligible for inclusion in the review with the exception of studies exclusively reporting on patients with pre-existing conditions specific to the clinical outcome of interest, as well as studies exclusively reporting on patients	Studies that measure the intake (oral consumption from food or supplements of quantified amounts of sodium and sodium chloride [salt] or sodium-to-potassium ratio) with validated measures or that use biomarker values to assess sodium level ((at least one 24-hour urinary analysis with or without reported quality control measure, chemical analysis of diet with intervention/intake adherence measure, composition of salt	Studies comparing groups with different documented sodium intake or biomarker values for sodium will be eligible. Studies where differences in sodium intake or values are confounded with alteration of other nutrient levels will be excluded.	Studies reporting on blood pressure outcomes (e.g., systolic blood pressure, diastolic blood pressure, rate of hypertensive/non-hypertensive participants, incident hypertension, percent participants at blood pressure goal, change in blood pressure) will be eligible. Studies that do not report baseline blood	Studies reporting on an intervention period of at least four weeks will be eligible.	Studies in community-dwelling participants will be eligible.	Prospective cohort studies and nested case-control studies, where at least two groups are compared based on measured sodium intake or biomarker values will be eligible. Retrospective studies, case series, cross-sectional studies

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
	with end stage renal disease, heart failure, HIV, or cancer.	<p>substitute with intervention/intake adherence measure, and food diaries with reported validation [adherence check, electronic prompts]) will be eligible. Observational studies that report a weight change of +/- 3% or more (in any intake group) among adults; multicomponent studies that do not properly control for confounders; and studies relying only on serum sodium levels, composition of salt substitute without intervention/intake adherence measure, food diaries without reported validation, use of a published food frequency questionnaire, or partial or spot urine without validated prediction equation will be excluded.</p>		pressure status will be excluded.			or surveys, and case reports will be excluded.
KQ3	Studies in human adults will be eligible for inclusion in the review. Studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer will be excluded.	Studies evaluating interventions to reduce dietary sodium intake that specify the oral consumption from food or supplements of quantified amounts of sodium and sodium chloride (salt) or sodium-to-potassium ratio will be eligible. Studies with trial arms in which participants demonstrate a weight change of +/- 3% or more will be excluded. Interventions simultaneously addressing sodium and potassium intake with documents sodium/potassium ratio are	Studies comparing interventions to placebo or control diets will be eligible. Studies comparing an experimental diet to usual diet, studies comparing levels of sodium intake, or studies that alter sodium/potassium ratio in other ways will be included if they control for	Studies reporting on mortality (all-cause, CVD, CHD, or renal); cardiovascular disease morbidity, including acute coronary syndrome (unstable angina and myocardial infarction), stroke, myocardial infarction (STEMI and non-NSTEMI), requiring coronary revascularization procedures (angioplasty, coronary stent placement, coronary	Only interventions of two years or longer will be included for kidney disease outcomes; only interventions of three months or longer will be included for cardiovascular disease outcomes; all other studies need to report on an	Studies in outpatient settings will be eligible.	Parallel RCTs and cross-over RCTs with a washout period of two weeks or more will be eligible.

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
		eligible. All other multicomponent interventions in which the effect of sodium reduction cannot be disaggregated from other intervention components will be excluded.	other nutrient levels.	artery bypass), other atherosclerotic revascularization procedures (carotid endarterectomy), left ventricular hypertrophy, hospitalization for heart failure, hospitalization for any cause of coronary heart disease or cardiovascular disease, or combined CVD morbidity and mortality; or reporting on renal function intermediary and clinical outcomes including creatinine clearance (CrCl), serum creatinine (SCr), glomerular filtration rate (GFR), end stage renal disease, chronic kidney disease (CKD), albuminuria or proteinuria (including urine albumin-to-creatinine ratio, urine albumin dipstick level, urine protein-to-creatinine ratio, albumin excretion rate), kidney stone incidence, or acute kidney injury will be eligible.	intervention period of at least four weeks to be eligible.		
KQ4	Studies in community-dwelling (non-institutionalized) adults will be eligible for inclusion in the review with the exception of studies exclusively reporting	Studies that measure the intake (oral consumption from food or supplements of quantified amounts of sodium and sodium chloride [salt] or sodium-to-potassium ratio) with validated measures or use biomarker values to	Studies comparing groups with different documented sodium intake or biomarker values for sodium will be eligible. Studies	Studies reporting on mortality (all-cause, CVD, CHD, or renal); cardiovascular mortality; cardiovascular disease morbidity, including coronary heart disease (CHD), acute coronary	Studies reporting exclusively on kidney disease outcomes need to report follow up periods of at least two years,	Studies in community-dwelling participants will be eligible.	Prospective cohort studies and nested case-control studies, where at least two groups are compared based on measured

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
	<p>on patients with pre-existing conditions specific to the clinical outcomes of interest, as well as studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer.</p>	<p>assess sodium level (at least one 24-hour urinary analysis with or without reported quality control measure, chemical analysis of diet with intervention/intake adherence measure, composition of salt substitute with intervention/intake adherence measure, and food diaries with reported validation [adherence check, electronic prompts]) will be eligible. Observational studies that report a weight change of +/- 3% or more (in any intake group) among adults; multicomponent studies that do not properly control for confounders; and studies relying only on serum sodium levels, composition of salt substitute without intervention/intake adherence measure, food diaries without reported validation, use of a published food frequency questionnaire, or partial or spot urine without validated prediction equation will be excluded.</p>	<p>where differences in sodium intake or values are confounded with alteration of other nutrient levels will be excluded.</p>	<p>syndrome (unstable angina and myocardial infarction), stroke, myocardial infarction (STEMI and NSTEMI), requiring coronary revascularization procedures (angioplasty, coronary stent placement, coronary artery bypass), other atherosclerotic revascularization procedures (carotid endarterectomy), left ventricular hypertrophy, hospitalization for heart failure, or hospitalization for any cause of coronary heart disease or cardiovascular disease, or combined CVD morbidity and mortality; or reporting on renal function intermediary and clinical outcomes including creatinine clearance (CrCl), serum creatinine (SCr), glomerular filtration rate (GFR), end stage renal disease, chronic kidney disease (CKD), albuminuria/proteinuria (including, urine albumin-to-creatinine ratio, urine albumin dipstick level, urine protein-to-creatinine ratio, albumin excretion rate), acute kidney injury will be</p>	<p>studies reporting exclusively on cardiovascular disease outcomes or stroke need to report on follow up periods of at least 12 months duration; studies reporting on other outcomes need to evaluate intake lasting at least four weeks to be eligible.</p>		<p>sodium intake or biomarker values will be eligible. Retrospective studies, case series, cross-sectional studies or surveys, and case reports will be excluded.</p>

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
				eligible. Studies that do not report baseline data for the outcomes of interest will be excluded.			
KQ5	Studies in human participants will be eligible for inclusion in the review; studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer will be excluded.	Studies evaluating interventions to increase dietary potassium intake that specify the oral consumption from food or supplements of quantified amounts of potassium, potassium supplements, salt substitutes such as potassium chloride, or sodium-to-potassium ratio will be eligible, with the exception of trial arms in which participants demonstrate a weight change of +/- 3% or more among adults. Interventions simultaneously addressing sodium and potassium intake with documents sodium/potassium ratio are eligible; all other multicomponent interventions in which the effect of sodium reduction cannot be disaggregated from other intervention components will be excluded.	Studies comparing interventions to placebo or control diets will be eligible. Studies comparing an experimental diet to usual diet, studies comparing levels of potassium intake, or studies that alter sodium/potassium ratio in other ways will be included if they control for other nutrient levels.	Studies reporting on blood pressure outcomes (e.g., systolic blood pressure, diastolic blood pressure, rate of hypertensive/non-hypertensive participants, hypertension incidence, percent participants at blood pressure goal, change in blood pressure) and incident kidney stones or kidney stone regrowth will be eligible.	Studies reporting exclusively on kidney stone formation need to report on an intervention period of two years; all other studies need to report on an intervention period of at least four weeks to be eligible.	Studies in outpatient settings will be eligible.	Parallel RCTs and cross-over RCTs with a washout period of two weeks or more will be eligible.
KQ5	Studies in human participants will be eligible for inclusion in the review; studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer will be excluded.	Studies evaluating interventions to increase dietary potassium intake that specify the oral consumption from food or supplements of quantified amounts of potassium, potassium supplements, salt substitutes such as potassium chloride, or sodium-to-potassium ratio will be eligible, with the	Studies comparing interventions to placebo or control diets will be eligible. Studies comparing an experimental diet to usual diet, studies comparing levels of potassium intake,	Studies reporting on blood pressure outcomes (e.g., systolic blood pressure, diastolic blood pressure, rate of hypertensive/non-hypertensive participants, hypertension incidence, percent participants at blood pressure goal,	Studies reporting exclusively on kidney stone formation need to report on an intervention period of two years; all other studies need to report on an	Studies in outpatient settings will be eligible.	Parallel RCTs and cross-over RCTs with a washout period of two weeks or more will be eligible.

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
		<p>exception of trial arms in which participants demonstrate a weight change of +/- 3% or more among adults. Interventions simultaneously addressing sodium and potassium intake with documents sodium/potassium ratio are eligible; all other multicomponent interventions in which the effect of sodium reduction cannot be disaggregated from other intervention components will be excluded.</p>	<p>or studies that alter sodium/potassium ratio in other ways will be included if they control for other nutrient levels.</p>	<p>change in blood pressure) and incident kidney stones or kidney stone regrowth will be eligible.</p>	<p>intervention period of at least four weeks to be eligible.</p>		
KQ6	<p>Studies in community-dwelling (non-institutionalized) human participants will be eligible for inclusion in the review; studies reporting exclusively on patients with pre-existing conditions specific to the clinical outcomes of interest, as well as studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer will be excluded.</p>	<p>Studies that measure intake (oral consumption from food or supplements of quantified amounts of potassium, potassium supplements, salt substitutes such as potassium chloride, or sodium-to-potassium ratio) with validated measures or use biomarkers values to assess potassium level (at least one 24-hour urinary analysis with or without reported quality control measure, chemical analysis of diet with intervention/intake adherence measure, composition of potassium supplement with intervention/intake adherence measure, use of a published food frequency questionnaire, and food diaries) will be eligible. Observational studies that report a weight change of +/- 3% or more (in any intake</p>	<p>Studies comparing groups with different documented potassium intake, serum potassium levels, or urinary potassium excretion will be eligible. Studies where differences in potassium intake or values are confounded with alteration of other nutrient levels will be excluded.</p>	<p>Studies reporting on blood pressure outcomes (e.g., systolic blood pressure, diastolic blood pressure, rate of hypertensive/non-hypertensive participants, hypertension incidence, percent participants at blood pressure goal, change in blood pressure), and kidney stone incident or kidney stone regrowth will be eligible. Studies that do not report baseline blood pressure status and the presence or absence of kidney stones will be excluded.</p>	<p>Studies exclusively reporting on kidney stone formation need to follow participants for at least five years; all other studies need to report on intake of at least four weeks to be eligible.</p>	<p>Studies in community-dwelling participants will be eligible.</p>	<p>Prospective cohort studies and nested case-control studies, where at least two groups are compared based on measured potassium intake or biomarker values will be eligible. Retrospective studies, case series, cross-sectional studies or surveys, and case reports will be excluded.</p>

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
		group) among adults; multicomponent studies that do not properly control for confounders; and studies measuring potassium intake by reporting chemical analysis of diet without intervention/intake adherence measures, composition of potassium supplement without intervention/intake measure, or serum potassium will be excluded.					
KQ7	Studies in adults will be eligible for inclusion in the review; studies reporting exclusively on patients with heart failure, end stage renal disease, HIV, or cancer will be excluded.	Studies evaluating interventions to increase dietary potassium intake that specify the oral consumption from food or supplements of quantified amounts of potassium, potassium supplements, salt substitutes such as potassium chloride, or sodium-to-potassium ratio will be eligible, with the exception of trial arms in which participants demonstrate a weight change of +/- 3% or more. Interventions simultaneously addressing sodium and potassium intake with documents sodium/potassium ratio are eligible; all other multicomponent interventions in which the effect of sodium reduction cannot be disaggregated from other intervention components will be excluded.	Studies comparing interventions to placebo or control diets will be eligible. Studies comparing an experimental diet to usual diet, studies comparing levels of potassium intake, or studies that alter sodium/potassium ratio in other ways will be included if they control for other nutrient levels.	Studies reporting on mortality (all-cause, CVD, CHD, or renal); cardiovascular disease morbidity, including acute coronary syndrome (unstable angina and myocardial infarction), stroke, myocardial infarction (STEMI and NSTEMI), requiring coronary revascularization procedures (angioplasty, coronary stent placement, coronary artery bypass), other atherosclerotic revascularization procedures (carotid endarterectomy), left ventricular hypertrophy, hospitalization for heart failure, or hospitalization for any cause of coronary heart disease or cardiovascular disease, or combined CVD morbidity and	Studies reporting exclusively on kidney disease outcomes need to report on an intervention period of two years, studies reporting on cardiovascular disease or stroke need to report on an intervention period of three months; all other studies need to report on an intervention period of at least four weeks to be eligible.	Studies in outpatient settings will be eligible.	Parallel RCTs and cross-over RCTs with a washout period of two weeks or more will be eligible.

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
				mortality; or reporting on renal function intermediary and clinical outcomes including creatinine clearance (CrCl), serum creatinine (SCr), glomerular filtration rate (GFR), end stage renal disease, chronic kidney disease (CKD), albuminuria or proteinuria (including urine albumin-to-creatinine ratio, urine albumin dipstick level, urine protein-to-creatinine ratio, albumin excretion rate), kidney stone incidence, or acute kidney injury will be eligible.			
KQ8	Studies in community-dwelling (non-institutionalized) adults will be eligible for inclusion in the review with the exception of studies exclusively reporting on patients with pre-existing conditions specific to the clinical outcomes of interest, as well as studies exclusively reporting on patients with end stage renal disease, heart failure, HIV, or cancer.	Studies that measure intake (oral consumption from food or supplements of quantified amounts of potassium, potassium supplements, salt substitutes such as potassium chloride, or sodium-to-potassium ratio) with validated measures or use biomarkers values to assess potassium level (at least one 24-hour urinary analysis with or without reported quality control measure, chemical analysis of diet with intervention/intake adherence measure, composition of potassium supplement with intervention/exposure adherence measure, use of a	Studies comparing groups with different documented potassium intake, serum potassium levels, or urinary potassium excretion will be eligible. Studies where differences in potassium intake or values are confounded with alteration of other nutrient levels will be excluded.	Studies reporting on mortality (all-cause, CVD, CHD, or renal); cardiovascular disease morbidity, including coronary heart disease (CHD), acute coronary syndrome (unstable angina and myocardial infarction), stroke, myocardial infarction (ST-segment elevation myocardial infarction [STEMI] and non-ST elevation myocardial infarction [NSTEMI]), requiring coronary revascularization procedures (angioplasty, coronary stent placement, coronary	Studies reporting exclusively on kidney stone formation need to follow participants for at least five years, studies reporting exclusively on kidney disease need to follow participants for at least two years, studies reporting exclusively on cardiovascular disease or stroke need to	Studies in community-dwelling participants will be eligible.	Prospective cohort studies and nested case-control studies, where at least two groups are compared based on measured potassium intake or biomarker values will be eligible. Retrospective studies, case series, cross-sectional studies or surveys, and case reports will be excluded.

KQ	Population	Intervention/Intake	Comparators	Outcomes	Timing	Setting	Study Design
		<p>published food frequency questionnaire, and food diaries) will be eligible. Observational studies that report a weight change of +/- 3% or more (in any exposure group) among adults; multicomponent studies that do not properly control for confounders; and studies measuring potassium intake by reporting chemical analysis of diet without intervention/intake adherence measures, composition of potassium supplement without intervention/intake measure, or serum potassium will be excluded.</p>		<p>artery bypass), other atherosclerotic revascularization procedures (carotid endarterectomy), left ventricular hypertrophy, hospitalization for heart failure, or hospitalization for any cause of coronary heart disease or cardiovascular disease, or combined CVD morbidity and mortality; or reporting on renal function intermediary and clinical outcomes including creatinine clearance (CrCl), serum creatinine (SCr), glomerular filtration rate (GFR), end stage renal disease, chronic kidney disease (CKD), albuminuria/proteinuria (including urine albumin-to-creatinine ratio, urine albumin dipstick level, urine protein-to-creatinine ratio, albumin excretion rate), kidney stone incidence, or acute kidney injury will be eligible. Studies that do not report baseline data on the outcomes of interest will be excluded.</p>	<p>follow patients for at least 12 months; all other studies need to report on a follow up period of at least four weeks to be eligible.</p>		

Table Notes: CrCl = Creatinine Clearance; CHD = Coronary Heart Disease; CVD = Cardiovascular Vascular Disorder; GFR = Glomerular Filtration Rate; NSTEMI = Non-ST Elevation Myocardial Infarction; RCT(s) = Randomized Controlled Trial(s); STEMI = ST-Segment Elevation Myocardial Infarction; SCr = Serum Creatinine

Searching for the Evidence

This section describes the literature search strategies, and screening protocols used.

Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions

We first conducted a scoping review of the existing systematic reviews and evidence reports on sodium and potassium intake, including the 2005 DRI report to identify critical sources of collated research evidence relevant to this evidence report. We screened all studies of sodium and potassium cited in those reviews as well as the 2005 DRI report for inclusion based on our inclusion/exclusion criteria.

Additional searches were conducted for more recent literature in PubMed®, CINAHL®, Embase®, the Cochrane Database of Systematic Reviews (CDSR), CENTRAL, and Web of Science for English-language publications. Searches were conducted for each Key Question, commencing in 2003, the year the original DRI report assembled study material, through December 12, 2017. Search strategies were developed for each Key Question (see Appendix A), and searches were conducted in accordance with the latest edition of the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.²² In addition, reference lists of the existing systematic reviews on the outcomes of interest were screened to identify any relevant studies; all relevant studies were included, regardless of publication date.

Pairs of reviewers, including at least one senior, experienced reviewer, independently screened all citations found by the literature searches using Distiller^{SR} online systematic review management software, after a training session. For all citations that were deemed potentially relevant by at least one reviewer, full-text publications were retrieved.

Full-text publications were independently screened by two reviewers, applying the inclusion and exclusion criteria. Reasons for exclusion were recorded. Disagreements about inclusion were resolved through discussion in the review team. A complete list of publications excluded after reviewing the full text appears in Appendix B.

Data Abstraction and Data Management

A detailed and standardized web-based data extraction form was used to record study-level information (see Protocol²⁴ for list of study-level variables) and RoB assessments for all studies that met inclusion criteria (Appendix B). The form was pilot-tested and refined within the review team. Data were extracted by one reviewer and checked by a second, senior systematic reviewer to ensure accuracy.

A number of studies had study-level details and/or outcomes reported in more than one publication. For those articles, abstractors ensured that the records were linked so that the correct study level data (e.g., baseline conditions for subgroups) were matched with outcome data and so that data were not abstracted in duplicate.

Outcome data, including confounders and effect modifiers, were abstracted into Excel spreadsheets and prepared for analysis by two members of the research team (one member extracted data from trials and one extracted data from observational studies) and were reviewed for accuracy by one of the PIs and the biostatistician. Data from studies that met inclusion criteria that were included in the 2005 DRI report or other systematic reviews were re-extracted.

All included studies are described in evidence tables (Appendix C). At the end of the project, all data will be uploaded to customized forms in Systematic Review Data Repository (SRDR) online system (<http://srdp.ahrq.gov>) for full public access.

Assessment of Methodological Risk of Bias of Individual Studies

We assessed the methodological RoB of each original study included in the review, based on predefined criteria.

We implemented the Cochrane Risk of Bias tool to assess RoB of RCTs, with criteria modified to cover concerns in the types of nutrition trials considered for this review. These modifications included considering bias that could arise if participants in parallel randomized controlled trials (RCTs) were not matched for (or were not at least similar regarding) body mass index (BMI), sodium excretion, age, gender, race/ethnicity, and hypertensive status; sodium intake assessment; adherence/compliance; absence of the outcome of interest at baseline; and use of appropriate statistical methods for assessing crossover trial outcomes (see Appendix E).

To assess RoB among observational studies, we used questions from the Newcastle Ottawa tool that are relevant for prospective studies (see Appendix E).^{25, 26} The RoB from the method used to assess sodium and potassium intakes was determined according to criteria described in Appendix E.²⁰ Other items assessed included similarity at baseline across treatment groups or quantiles regarding age, BMI, ethnicity, hypertensive status, and urinary sodium excretion.

An overall RoB was determined for each RCT by tabulating the numbers of individual “low,” “high,” “moderate,” and “unclear” scores. RCTs earned a low overall risk-of-bias rating if their total “low” scores were 8 or higher (out of 11) and their “high” scores were 1 or fewer and did not include intake assessment method; overall moderate ratings included 5 to 7 “low” scores and 2 or fewer “high” scores; overall high ratings included fewer than 4 “low” scores or more than 2 “high” scores; and overall unclear scores included 5 or more “unclear” ratings.

An overall RoB was determined for each observational study by giving the RoB of the method used to assess sodium or potassium intake the most weight and adjusting the grade down by tabulating the numbers of other individual “high,” “moderate” or “unclear” risk-of-bias domains. Observational studies earned a low overall risk-of-bias rating if the RoB of the method used to assess sodium or potassium intake was rated “low” and all other individual risk-of-bias domains were rated “low.” Observational studies earned a high overall risk-of-bias rating if their RoB of the method used to assess sodium or potassium intake was rated “high” or if the RoB of the method used to assess sodium or potassium intake was rated “moderate” and more than one other individual risk-of-bias domains were rated “high” or unclear.” The RoB of the method used to assess sodium or potassium intake was rated separately. As such, an observational study could receive different overall ratings for sodium- and potassium-outcome pairs.

One reviewer assessed the methodological RoB for all included studies and one other reviewer confirmed or refuted the RoB assessments. Disagreements were reconciled among the systematic review team and resolved via group consensus. When determining the overall strength of evidence, we considered any quality issues pertinent to the specific outcomes of interest.

Original studies whose references were reference mined from existing systematic reviews were screened, assessed for risk-of-bias, and data abstracted along with studies identified in literature searches.

Data Synthesis/Analysis

All included studies are presented in evidence tables (Appendix C and D). Continuous outcomes are reported as mean differences (MD), dichotomous incidence outcomes are reported as relative risks (RR), together with the 95% confidence interval (CI). Unless otherwise noted, the continuous outcomes are always mean differences in BP, expressed as mm Hg

In describing interventions and reporting the findings of pooled analyses, we did not attempt to define “reduced dietary sodium,” “low sodium,” or “increased potassium,” as definitions and target goals differed across studies, and some provided no definition or goal. However, for each sodium reduction RCT included in a pooled analysis, we report sodium or potassium intakes in terms of achieved 24-hour sodium excretion in the figures that accompany the text, and we report the weighted mean differences in sodium intakes in figure legends. For studies aimed at increasing potassium, we reported the levels of potassium provided and/or the 24-hour potassium excretion when reported.

Random effects meta-analyses using the Hartung-Knapp-Sidik-Jonkman method were conducted on RCTs of similar populations or subpopulations²⁷⁻³⁰ (based on baseline comorbidities and nutrient status), implementation of similar interventions or use of similar intake measures, and use of compatible outcome measures. Each study is weighted by the inverse of its variance. In a random effects model, the variance includes the within-study variance along with the between-study variance. Studies including patients with pre-existing conditions specific to the clinical outcome of interest were excluded from analyses for the respective outcome of interest in this review, unless they report subgroup data where patients with pre-existing conditions were excluded. The findings are presented in forest plots.

To assess the possible effect of study quality on findings, we conducted sensitivity analyses for all meta-analyses of RCTs that had included studies with high or unclear RoB, omitting those studies. The findings are described along with the findings for the full analyses, and the resulting forest plots and lists of omitted studies appear in Appendix I.

To assess the possible effect of achieved sodium excretion by individual interventions, we did not conduct sensitivity analysis, but arranged the studies in each forest plot in the order of decreasing difference in sodium excretion between the intervention and control groups at followup. For selected comparisons, we describe the relationships between achieved sodium status and effect sizes.

Meta-regressions were conducted to assess whether other minerals affected outcomes of interest, if sufficient numbers of studies assessed these effects (KQ1a, 3a, 5a, 7a) and to compare differences between subgroups. Subgroup analyses were conducted when sufficient data were available to answer the subquestions on subpopulations of interest, i.e., sex, race/ethnicity, DRI age group(s) (1-3 y, 4-8y, 9-13y, 14-18y, 19-30y, 31-50y, 51-70y, and ≥ 71 y), reproductive status (pregnant and lactating women), as well as hypertensive status, diabetes, obesity (i.e., BMI ≥ 30), and renal health status for individual Key Questions.

The data for subgroups are reported in separate evidence tables (Appendix D).

Statistical heterogeneity was assessed and expressed as the I^2 statistic and considered in interpreting and weighing the results of meta-analyses.

If data from observational studies were sufficient (3 or more studies using 24-hour urinary excretion measures for each outcome), we would have performed both linear and non-linear dose-response meta-regressions to examine the associations between dietary intake levels and the risks of clinical outcomes using a two-stage hierarchical regression model.^{31, 32} It is important to note that this dose-response meta-regression model requires categorical exposure data (at least

three exposure categories, including the reference category, within each study). No dose-response meta-regression could be performed for this report, due to lack of sufficient quantitative data. Thus, standard random effects meta-analysis was performed to pool reported linear trend estimates from the adjusted model assessing the association between 24-hour urinary excretion levels (continuous measure) and all-cause mortality outcomes (the only clinical outcome with sufficient data for pooling).

Summary of findings tables organized by Key Question, interventions or intakes, and key outcomes summarize the available evidence.

Grading the Strength of Evidence (SoE) for Major Comparisons and Outcomes

The project leaders assessed the strength of evidence (SoE) for the key outcomes listed in Table 2, based on guidance provided in the AHRQ Methods Guide. These outcomes were also used to answer the subquestions.

Table 2. Outcomes for determination of strength of evidence

Key Question	Key Outcomes
KQ1.	Mean difference in systolic BP Mean difference in diastolic BP Percent participants at blood pressure goal Hypertension incidence Adverse events associated with sodium intake
KQ2.	Mean difference in systolic BP Mean difference in diastolic BP Percent participants at blood pressure goal Hypertension incidence
KQ3.	All-cause mortality CVD mortality CHD mortality Renal disease mortality Stroke Coronary heart disease Myocardial infarction Number of patients with any CVD event as reported by the study authors Combined CHD morbidity/mortality Combined CVD morbidity/mortality Mean difference between groups in eGFR Number of patients with end stage renal disease Adverse events associated with sodium intake
KQ4.	All-cause mortality CVD mortality CHD mortality Renal disease mortality Stroke Coronary heart disease Myocardial infarction Number of patients with any CVD event as reported by the study authors Combined CHD morbidity/mortality Combined CVD morbidity/mortality Mean difference between groups in eGFR Number of patients with end stage renal disease

Key Question	Key Outcomes
KQ5.	Mean difference systolic BP Mean difference in diastolic BP Percent participants at blood pressure goal Hypertension incidence Number of patients with kidney stones (occurrence and recurrence, symptomatic and asymptomatic) Kidney stone incidence Number of kidney stones Symptomatic kidney stone incidence Hyperkalemia
KQ6.	Mean difference systolic BP Mean difference in diastolic BP Percent participants at blood pressure goal Hypertension incidence Number of patients with kidney stones (occurrence and recurrence, symptomatic and asymptomatic) Kidney stone incidence Number of kidney stones Symptomatic kidney stone incidence
KQ7.	All-cause mortality CVD mortality CHD mortality Renal disease mortality Stroke Coronary heart disease Myocardial infarction Number of patients with any CVD event as reported by the study authors Combined CHD morbidity/mortality Combined CVD morbidity/mortality Mean difference between groups in eGFR Number of patients with end stage renal disease Hyperkalemia
KQ8.	All-cause mortality CVD mortality CHD mortality Renal disease mortality Stroke Coronary heart disease Myocardial infarction Number of patients with any CVD event as reported by the study authors Combined CHD morbidity/mortality Combined CVD morbidity/mortality Mean difference between groups in eGFR Number of patients with end stage renal disease

Table Note: BP=blood pressure; CHD=coronary heart disease; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; KQ=Key Question

The SoE approach we used assesses the body of evidence for each conclusion based on five dimensions: study limitations (the RoB of the individual studies and the study designs), consistency (the degree to which included studies find the same direction of effect, within study designs), directness (for this report, we used directness to mean two things: whether the outcome in question is intermediary or clinical, but mainly, whether the assessment of moderating factors was based on a direct or indirect comparison, for example men compared with women), precision (the degree of certainty surrounding an effect estimate), and reporting bias (the likelihood that some findings were omitted from publication).

Four strength-of-evidence ratings were used—high, moderate, low, or insufficient—as defined below (Table 3). Bodies of evidence based entirely on pooled RCTs are considered to have a high strength of evidence, which can be down-graded for major concerns in each of the domains (study limitations, indirectness, inconsistency, imprecision, or suspected reporting bias). For example, a high strength of evidence conclusion would be based on a pooled analysis of (e.g.,) five or more RCTs sufficiently powered to assess the outcome of interest and with overall low RoB, with consistent findings across studies, relatively tight confidence intervals, and assessing a direct comparison. If overall RoB was high, if results were inconsistent, if confidence intervals were wide compared with the effect size (for mean differences), if the effect size was of borderline significance, *or* if the comparison of interest was indirect, we would downgrade one level for any one of those factors to moderate RoB or to low RoB for two or more of those factors. If the number of studies was insufficient to allow pooling or if only three or four small (particularly underpowered or inconsistent) studies could be included, we would downgrade to low strength of evidence. An insufficient strength of evidence was reserved for questions for which no more than two inconsistent RCTs were identified that addressed the question.

We used a similar approach for rating the strength of evidence based on observational studies (which were used to answer association questions), with several modifications detailed as follows. Bodies of evidence based on more than two large, population-based prospective cohort studies are considered to have a high strength of evidence, which can be down-graded for major concerns in each of the domains (study limitations, indirectness, inconsistency, imprecision, or suspected reporting bias). For each outcome, observational studies were first synthesized separately for each type of intake measurement method (i.e., 24-hour urinary excretions, estimated 24-hour urinary excretions, and self-report dietary assessment methods), and then synthesized across different types of intake measurement methods at the strength-of-evidence rating level. Almost all observational studies were synthesized qualitatively (within each type of intake measurement method). When assessing consistency or inconsistency across studies, the ranges of intake were taken into account, given that nutrient-outcome relationships may vary according to the ranges of intake. Thus, the consistency or inconsistency across studies can be assessed only within the same ranges of intakes. Overlapping in study populations was carefully considered in the qualitative synthesis to avoid double counting data from the same study cohort. Multiple publications from the same study cohort were retained in the review if they differed in study characteristics, outcome definitions, followup durations or statistical analyses.

For this review, we did not assess strengths of a body of evidence that included both RCTs and observational studies. However, if the RCT evidence is robust, observational studies may not contribute to strengthening the evidence unless they are high quality studies with large, precise effect sizes. Similarly, because of challenges in accounting for confounding, a body of evidence comprising only observational studies usually can provide only a low strength of evidence unless the studies demonstrate a very large effect, a strong dose-response association, or the observed effect cannot be accounted for by uncontrolled confounding.

Table 3. Definitions of the levels of strength of evidence³³

Grade	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion

Assessing Applicability

Applicability was assessed at the level of the total body of evidence for each conclusion. We considered the similarity of the population to the North American population in terms of mean baseline intakes/status of sodium and potassium, weight status, and baseline comorbidities, as well as age.

Peer Review and Public Commentary

Experts in the fields of nutrition, epidemiology and statistics, and medicine and individuals representing stakeholder and user communities were invited to provide external peer review of this draft systematic review; AHRQ and an associate editor provided comments. The draft report was posted on the AHRQ website for 4 weeks to elicit public comment. We addressed all reviewer comments, revised the text as appropriate, and will document everything in a disposition of comments report that will be made available 3 months after the Agency posts the final systematic review on the Effective Health Care Web site.

Results

Introduction

This section first describes the results of the literature searches, followed by descriptions of the studies that met inclusion criteria for each of the Key Questions and the key points (conclusions).

Key Questions 1 through 4 pertain to interventions and intake that focus primarily on assessing effects of sodium or sodium to potassium ratios. Key Questions 5 through 8 pertain to interventions and intakes that focus primarily on potassium. Studies that assess relationships of the sodium-to-potassium ratio with outcomes of interest are described in Key Questions 1 through 4.

Results of Literature Searches

Our searches identified 15,468 references. An additional search via reference mining of systematic reviews resulted in 444 titles, which yielded 15,912 citations that underwent dual screening, of which 14,305 citations were rejected because they did not meet inclusion criteria. We identified 1,607 full text articles to be screened, of which 1,224 were excluded for the following reasons: population not of interest (44), interventions not of interest (443), comparators not of interest (6), outcomes not of interest (151), timing not of interest (176), setting not of interest (6), study design (344), language (4), protocol (7), duplicate data (32). We could not retrieve eleven articles. We identified and reference-mined 97 systematic reviews and identified numerous research reports as well as 29 citations that were helpful for the background on the topic.

We include 171 studies reported in 257 publications.³⁴⁻²⁹⁰ A breakdown per Key Question is shown in Figure 3 below.

Figure 3. Literature flow diagram

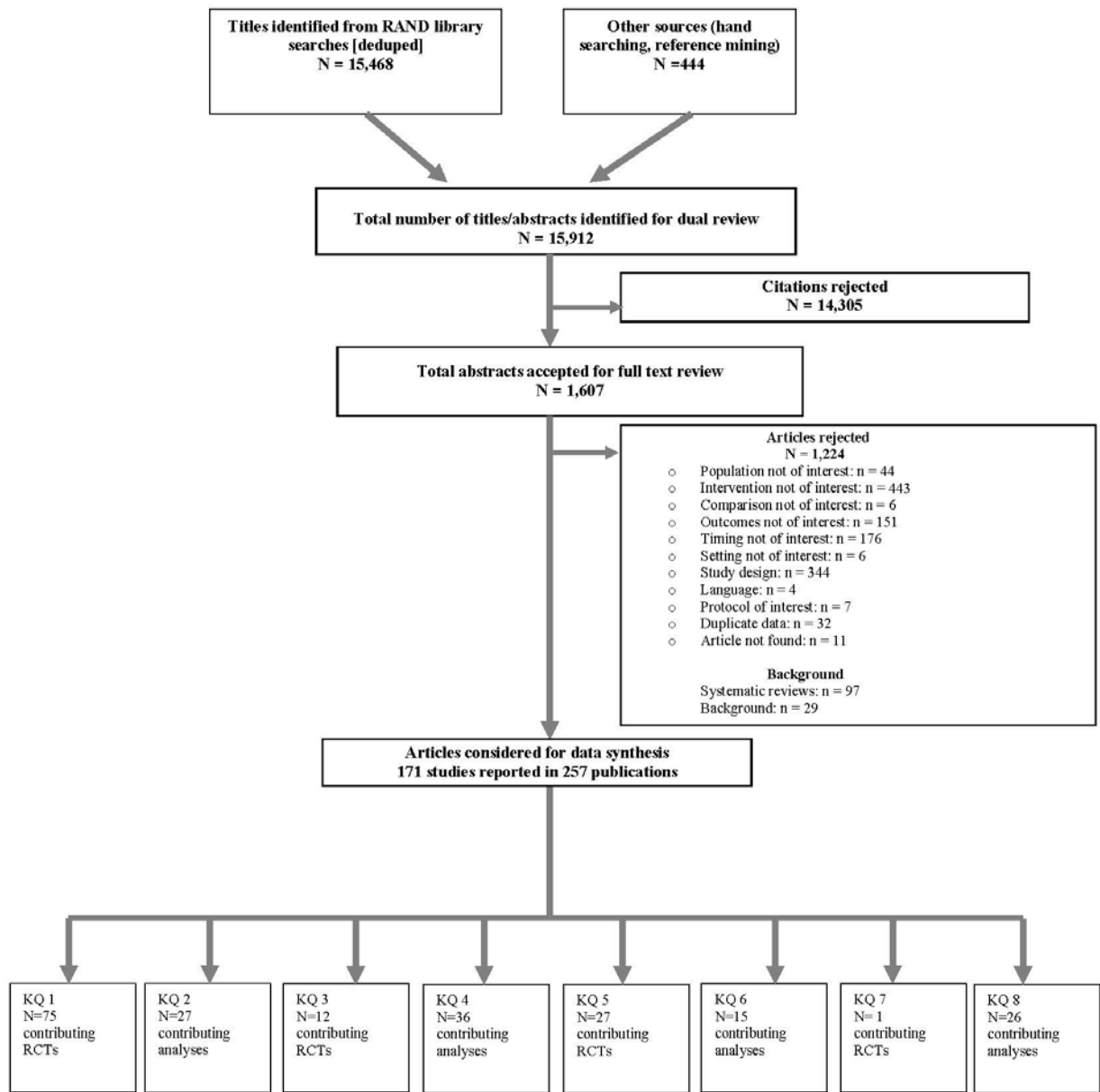


Figure notes: KQ = Key Question; RCT = Randomized Controlled Trial(s); Duplicate Data = Reported in more than one publication

For each of the following questions, we describe first the key points, followed by detailed results for each of the subquestions. Results for healthy adults precede those for subpopulations of interest.

Key Question 1. Effect of Interventions To Reduce Sodium Intake on Blood Pressure

Key Points

- Sodium reduction decreases systolic and diastolic blood pressure (BP) significantly in adults (moderate strength of evidence [SoE] based on 47 and 48 randomized controlled trials [RCTs], respectively). Findings were inconsistent across studies.
- Short term sodium reduction interventions do not appear to show statistically significant effects on systolic BP in children (low SoE based on eight RCTs). A sensitivity analysis that excluded high or unclear RoB studies suggests that sodium reduction may result in a statistically significant decrease in diastolic BP with sodium reduction for children (six RCTs).
- Sodium reduction may decrease BP in both men and women (moderate SoE based on eight RCTs), and sex does not appear to moderate the effect of sodium reduction on BP in adults (low SoE, based on only three direct comparisons).
- Sodium reduction in adults may increase the likelihood of achieving a prespecified blood pressure goal (low SoE based on six RCTs).
- Evidence is insufficient to draw a conclusion on the potential for sodium reduction to modify the risk for incident HTN in adults (three RCTs).
- Sodium reduction decreases systolic BP in both those with hypertension and those with normal BP; the effect is greater in adults with HTN than in those with normal BP (moderate SoE based on 45 RCTs; only two direct comparisons).
- Sodium reduction decreases diastolic BP in those with hypertension (moderate SoE) but may not decrease diastolic BP in those with normal BP (low SoE based on 47 RCTs).
- Evidence is insufficient to support conclusions on potential moderating effects of race/ethnicity.
- Evidence is insufficient to support conclusions on potential moderating effects of diabetes, renal disease, or obesity.
- Based on a low strength of evidence, sodium reduction does not appear to affect blood lipids (triglycerides, total cholesterol, low density lipoprotein [LDL] cholesterol, and HDL cholesterol; based on three RCTs); however, evidence is insufficient to draw a conclusion regarding the effects of sodium reduction on dizziness, headache, insulin sensitivity, and muscle cramping (based on one to two studies per outcome).
- Evidence may not support a moderating effect of increasing dietary potassium via food or supplements on the blood pressure-lowering effect of sodium reduction compared with sodium reduction alone (low SoE, based on five RCTs).
- Potassium-containing salt substitutes decrease systolic and diastolic BP; however, studies do not make it possible to ascertain whether the effects are due to decreased sodium intake, independent effects of potassium, or effects of other minerals contained therein (moderate SoE, based on 13 RCTs).

Description of Included Studies

This question addresses the effects of reduced sodium intakes on outcomes related to blood pressure. We do not define reduced dietary sodium or low sodium in this review, as definitions and target goals differed across studies, and some provided no definition or goal; however, we report sodium intakes in terms of achieved 24-hour sodium excretion for each RCT included in a pooled analysis.

We identified 73 RCTs (reported in 76 publications) that met inclusion criteria to answer this question and related subquestions: 62 parallel RCTs and 11 crossover RCTs. Of the total, 56 address the question of whether sodium reduction interventions implemented through counseling or provision of food lowers blood pressure and whether these effects are modified by demographic effects or chronic health conditions (KQ1b and c), and 17 address the question of whether the effects of sodium reduction are moderated by other minerals, including the effects of potassium-containing salt substitutes (KQ1a). Four controlled clinical trials (CCTs) also addressed these questions (three parallel and one crossover). The study-level details are described below and in the evidence tables (Appendix C): The findings for KQ1a are described after the findings for KQ1b and 1c.

All studies that address this Key Question were designed to assess the effects of lower intakes of sodium relative to usual diet. Most studies randomized participants to a low sodium diet (via counseling and/or provision of food products) or to usual diet. Some imposed a low-sodium diet on all participants and then randomized them to receive sodium chloride tablets (to restore usual sodium intake) or placebo tablets (to maintain a low sodium intake). Studies designed to assess the added effects of other minerals, addressed in subquestion 1a, either combined a low-sodium diet with supplementation of other minerals or placebo, or they provided a potassium-containing salt substitute. For each study (or groups of studies), urinary sodium excretion is noted, if reported.

Outcomes addressed for this question include mean differences (MD) in blood pressure across intervention and control groups, incident hypertension, proportion of participants who meet a prespecified blood pressure goal, and adverse events associated with treatments.

Intervention durations ranged from 4 weeks (shorter duration studies were excluded) to three years. Follow ups were as long as 8 years: For most studies, we report only the longest followup for a specific outcome.

Parallel RCTs are described separately from crossover RCTs.

Key Question 1b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

Description of Included Studies

No RCTs that met inclusion criteria compared outcomes among Dietary Reference Intakes (DRI) age groups. Thirty-seven parallel RCTs and twelve crossover RCTs reported on the effects of sodium reduction on systolic BP in adults only.^{171, 230 39, 42, 45-51, 53, 86, 90, 92, 93, 95, 114, 157, 159-164, 169, 170, 200, 205, 206, 208-210, 212, 213, 216, 217, 231, 232, 236, 238, 260, 262, 263, 266, 276, 282-284} Thirty-nine parallel RCTs and thirteen crossover RCTs reported on the effects of sodium reduction on diastolic BP in adults.^{171, 230 39, 42, 45-47, 50, 51, 53, 57, 76, 86, 90, 92, 93, 114, 157, 159-164, 170, 200, 203, 205, 206, 208, 210, 212, 213, 215, 217, 231, 232, 236, 238, 240, 260, 262, 266, 276, 282-284} Three CCTs reported on the effects of sodium reduction on BP in adults.^{38, 84, 268}

Eight RCTs reported on effects of sodium reduction on systolic BP in children.^{114, 131, 173-175, 207, 234, 237} Seven RCTs reported on effects on diastolic BP in children.^{114, 131, 173-175, 207, 237} Two of the trials assessed effects in newborns.^{234, 237} Two reported outcomes separately for boys and girls,^{131, 174} and one included only adolescent girls.²⁰⁷ In addition, one CCT reported on the effects of sodium reduction in male and female high school students.¹⁷²

Five parallel RCTs reported on the effects of sodium reduction on systolic BP,^{171 53, 131, 161, 170, 208} and five reported on diastolic BP, for adult males only.^{53, 131, 161, 170, 171, 203} Five parallel RCTs reported on the effects of sodium reduction on systolic BP for adult non-pregnant females,^{53, 131, 161, 171, 214, 217} and six parallel RCTs reported on the effects on diastolic BP.^{171 53, 131, 161, 203, 214, 215, 217} Three RCTs assessed effects of sodium reduction on pregnant women.^{214, 215, 238} One crossover RCT compared the effects of dietary sodium reduction between adult males and females,²¹⁸ and one reported the effects of three different dietary sodium levels on men and women.⁵⁷

Three parallel RCTs reported on the effects of sodium reduction on systolic and diastolic BP separately in US whites and blacks.^{51, 53, 171} One crossover RCT compared the effects of three dietary sodium levels between whites and blacks.⁵⁷

Detailed Synthesis

Age

Only two RCTs that met inclusion criteria compared the effects of sodium reduction on BP, achievement of a prespecified goal blood pressure, or incident HTN across different age groups. Therefore, this section mainly reports the results of studies of adults, followed by those for children, for each outcome of interest.

Mean Difference in Systolic Blood Pressure

Adults

Thirty-five parallel RCTs and 12 crossover RCTs reported on the effects of sodium reduction on systolic BP in adult men and (nonpregnant) women (Figure 4a). Of those, 25 reported a MD in urinary sodium excretion of 40 mmol/d or more. Parallel RCTs were pooled separately from crossover RCTs as well as together. The weighted mean difference for sodium intake at followup was -37 mmol for parallel RCTs, -74 mmol for crossover RCTs, and -42 mmol for all RCTs combined. Random effects meta-analyses showed that reducing sodium significantly decreased systolic BP for parallel RCTs (MD -2.68 mm Hg, 95% CI -3.59, -1.77; I^2 39%), crossover RCTs (MD -3.77 mm Hg, 95% CI -5.45, -2.08; I^2 89%), and all RCTs combined (MD -3.23 mm Hg, 95% CI -4.07, -2.38; I^2 77%) (moderate RoB overall: 20 RCTs with low RoB, 20 with moderate/unclear RoB, 3 with high RoB, and four with unclear RoB). Throughout the remainder of the report, all pooled continuous outcomes are reported as MD in mm Hg unless otherwise specified.

Sensitivity analysis to eliminate studies with high or unclear RoB resulted in no appreciable difference in the pooled effect size or the heterogeneity (MD -3.33, 95% CI -4.24, -2.42; I^2 79%) (forest plot for this and all sensitivity analyses are shown in Appendix I).

A moderate SoE supports a beneficial effect of sodium reduction on decreasing systolic BP in adults (the moderate rating is due primarily to inconsistency in the direction of study outcomes along with high heterogeneity as well as moderate RoB).

Pregnant Women

Three RCTs enrolled only pregnant women;^{214, 215, 238} however, in one RCT, the women had HTN.²¹⁵ These studies were not included in the pooled analysis of the effects of reducing dietary sodium on blood pressure in adults. A 6-month RCT conducted in the Netherlands randomized 42 pregnant normotensive women at 14 weeks gestation to a sodium restricted diet or usual care; urinary sodium excretion fell by two thirds in the sodium-restricted group compared with the control group, however term systolic blood pressure did not differ between groups.²³⁸ An 8-month RCT conducted in the Netherlands by the same group randomized 270 normotensive first trimester pregnant women (mean age 28) to dietary counseling aimed at restricting sodium or to usual care; urinary sodium excretion was expressed as sodium to creatinine ratio, and no inter-group differences were shown in systolic BP.²¹⁴ A multisite RCT in the Netherlands randomized 361 first trimester pregnant women with high blood pressure readings in the first trimester to a low or normal sodium diet; the mean sodium excretion differed by 40 mmol/d across groups, however, no difference was seen in systolic BP at term.²¹⁵ Thus across these three studies, sodium reduction did not decrease systolic BP in pregnant women at term (RoB moderate); however evidence is insufficient to draw a conclusion regarding the effect of sodium reduction on systolic BP in pregnant women, because of the small study size and heterogeneity of the study population.

Dose Response Trials

Three RCTs assessed the dose-response effects of decreasing levels of dietary sodium on blood pressure by including three intervention arms: one in adults with normal BP,²⁶⁰ one in adults with HTN,⁸⁶ and one in a mixed group of adults.⁴⁹

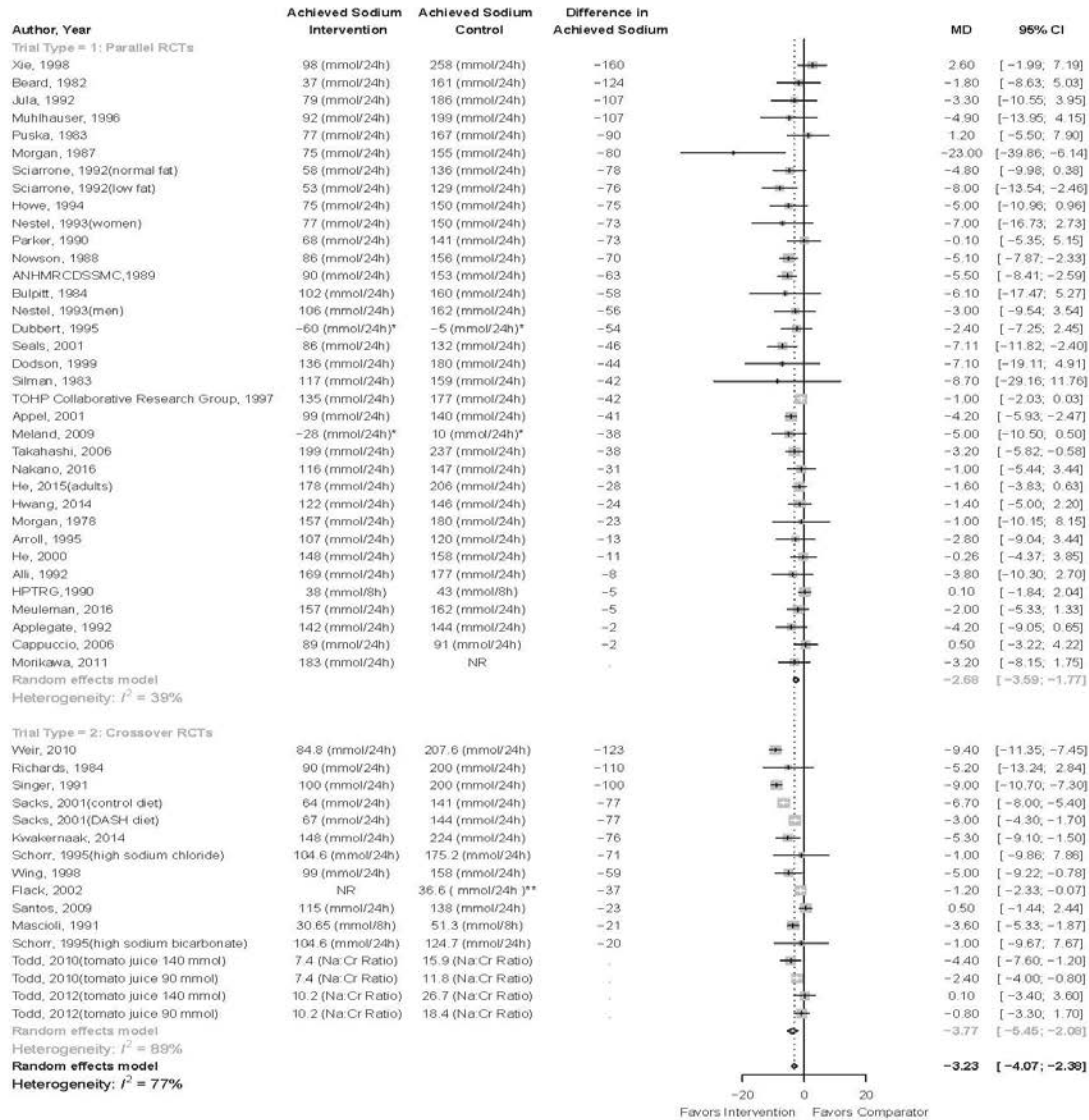
Two of the studies achieved decreasing sodium intakes by instructing all participants to follow a low sodium diet and, following a run-in period, randomizing them to receive one of three different beverages (tomato juice), differing in sodium content.^{86, 260} These two studies did not observe a significant dose-response effect of the stepwise decreases in sodium.

The third dose-response study, the DASH Sodium Trial, randomized 412 adults with high normal BP or HTN in parallel fashion to one of two diets: a typical Western (control) diet and a diet enriched in fruits and vegetables, whole grains, and low-fat dairy, and low in saturated fat (the DASH diet). Within each of these two groups, after an initial run-in period, participants were then further randomized to one of three sodium intake levels (150 mmol, 100 mmol, and 50 mmol/d, with the highest approximating typical intake) and consumed each of the three sodium levels for 30 days. The researchers maintained relatively close control of food intake by providing most meals at the research sites and providing additional foods for offsite eating. Double blinding was strictly maintained, and repeated multiple 24-hour urine samples were obtained. The largest difference in blood pressure was seen between those on the control diet at the highest sodium level and those on the DASH diet at the lowest sodium level (MD -8.9 mm Hg, 95% CI -6.7, -11.1, $p < 0.001$). The study also showed significant decreases in systolic blood pressure between the highest and the lowest sodium intake levels for the control diet (MD -6.7, 95% CI -5.4, -8.0, $p < 0.001$) and for the DASH diet (MD -3.0, 95% CI -1.7, -4.3, $p < 0.001$) as well as smaller but still significant differences between the high and the intermediate and the intermediate and the low sodium intakes for both diets.⁴⁹ To prevent double counting of the participants, we included only the comparisons of the highest to the lowest sodium intakes for each of the two diets in the pooled analysis (Figure 4a).

The DASH Diet Trial assessed the moderating effects of age by comparing the outcomes of participants age 45 and under with those of adults over 45. In unadjusted analyses, reducing

sodium produced greater decreases in systolic BP in those older than 45 than in those 45 and under.⁵⁷

Figure 4a. Systolic blood pressure in sodium reduction trials: adults



* change from baseline
** difference between intervention and control
ANHMRCDSSMC=Australian National Health and Medical Research Council Dietary Salt Study Management Committee
HPTRG=Hypertension Prevention Trial Research Group

Figure Notes: Weighted mean differences for sodium excretion: -37 mmol (parallel RCTs); -74 mmol (crossover RCTs); -42 mmol all RCTs combined; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Children

Eight parallel RCTs reported on effects on systolic BP in children (Figure 4b).^{114, 131, 173-175, 207, 234, 237} Of the eight, 1 RCT showed a difference in 24-hour sodium excretion of 40 mmol/d or more.¹⁷⁵ A random effects meta-analysis showed a non-significant decrease in systolic BP among children in sodium reduction interventions compared with those given usual diets (MD - 0.73, 95% CI -1.83, 0.36; I^2 48%) (moderate RoB). Sensitivity analysis that omitted studies of

high or unclear RoB resulted in no appreciable difference in the pooled effect size (MD -0.80, 95% CI -1.79, 0.20; I² 35%), which was still statistically non-significant.

The effects on systolic BP in studies of adults compared with those of children differed significantly (p=0.002).

One RCT reported on the effects of a sodium reduction intervention on both children and their parents.¹¹⁴ This study, in northern China, enrolled 293 children and 553 family members in a 3 ½ month cluster-randomized trial. At followup, the difference between intervention and control 24-hour sodium excretion exceeded 40 mmol/d for adults but not for children. Both adults and children had a non-statistically significant decrease in systolic BP compared with controls (MD -1.6, 95% CI -3.83, 0.63 for adults vs. MD -0.60, CI -2.83, 1.63 for children) (low RoB).

One crossover CCT compared the effects of 15 to 20 percent reductions in sodium intakes among 649 high school students at two US boarding schools over two academic years with 3-month washout period.¹⁷² The study found that sodium reduction significantly decreased systolic BP across the intervention groups compared with the control groups (MD -1.7, 95% CI -0.6, -2.9), but outcome measurements were self reported and no pairwise comparisons were performed. Differences were significant for females (MD -2.6, 95% CI -4.3, -0.8) but not for males (MD -0.9, 95% CI -2.7, 0.8) (high RoB).

The findings across studies suggest sodium reduction may not significantly lower systolic BP in children (low SoE). Given the lack of direct comparisons, the evidence is insufficient to assess whether children and adults respond differently to interventions aimed at reducing sodium intake.

Figure 4b. Systolic blood pressure in sodium reduction trials: children

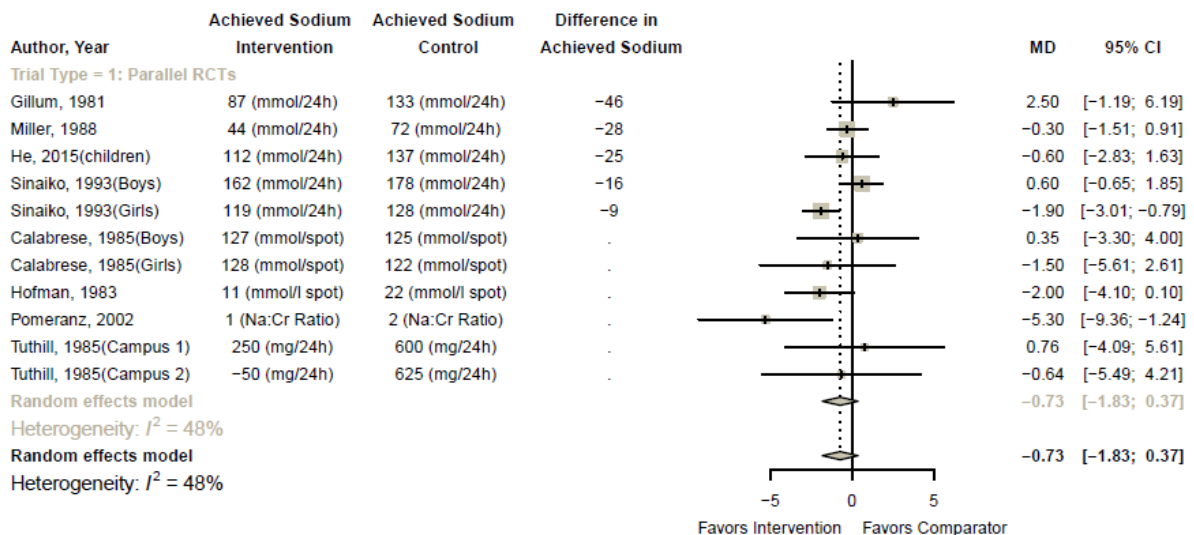


Figure notes: Weighted mean differences for sodium excretion: -25 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Mean Difference in Diastolic Blood Pressure

Adults

Thirty-five parallel RCTs and 13 crossover RCTs reported on the effects of sodium reduction on diastolic BP in adult men and non-pregnant women (Figure 5a). Of those, 25 reported a MD in urinary sodium excretion of 40 mmol/d or more. Parallel RCTs were pooled separately from crossover RCTs as well as together. The weighted mean difference for sodium intake at followup was -37 mmol for parallel RCTs, -74 mmol for crossover RCTs, and -42 mmol for all RCTs combined. Random effects meta-analyses showed a significant beneficial effect of sodium reduction on diastolic BP for parallel RCTs (MD -2.04, 95% CI -2.71, -1.36; I² 50%), crossover RCTs (MD -2.51, 95% CI -4.07, -0.95; I² 86%), and all RCTs combined (MD -2.26, 95% CI -2.91, -1.60; I² 72%) (moderate RoB overall: 20 low, 19 moderate, 5 unclear; 3 high). A sensitivity analysis that omitted studies of high or unclear RoB resulted in no appreciable change in the pooled effect size or heterogeneity (MD -2.24, 95% CI -2.96, -1.51; I² 75%).

A moderate SoE supports a beneficial effect of sodium reduction on diastolic BP in adults.

Among the three RCTs that enrolled only pregnant women,^{214, 215, 238} none of the three showed inter-group differences in diastolic BP.²¹⁴

Children

Of the seven RCTs that reported on effects on diastolic BP in children (Figure 5b),^{114, 131, 173-175, 207, 237} one reported a mean difference in 24-hour urinary sodium excretion 40 mmol/d or greater.¹⁷⁵ The weighted mean difference for sodium intake at followup was -25 mmol. A random effects meta-analysis showed a non-significant decrease in diastolic BP with sodium reduction (MD -2.10, 95% CI -4.75, 0.55; I² 79%) (moderate overall RoB). A sensitivity analysis that omitted three studies of high or unclear RoB resulted in a decrease in the pooled effect size that now reached significance and a decrease in heterogeneity to zero (MD -1.54, 95% CI -2.57, -0.51; I² 0%).

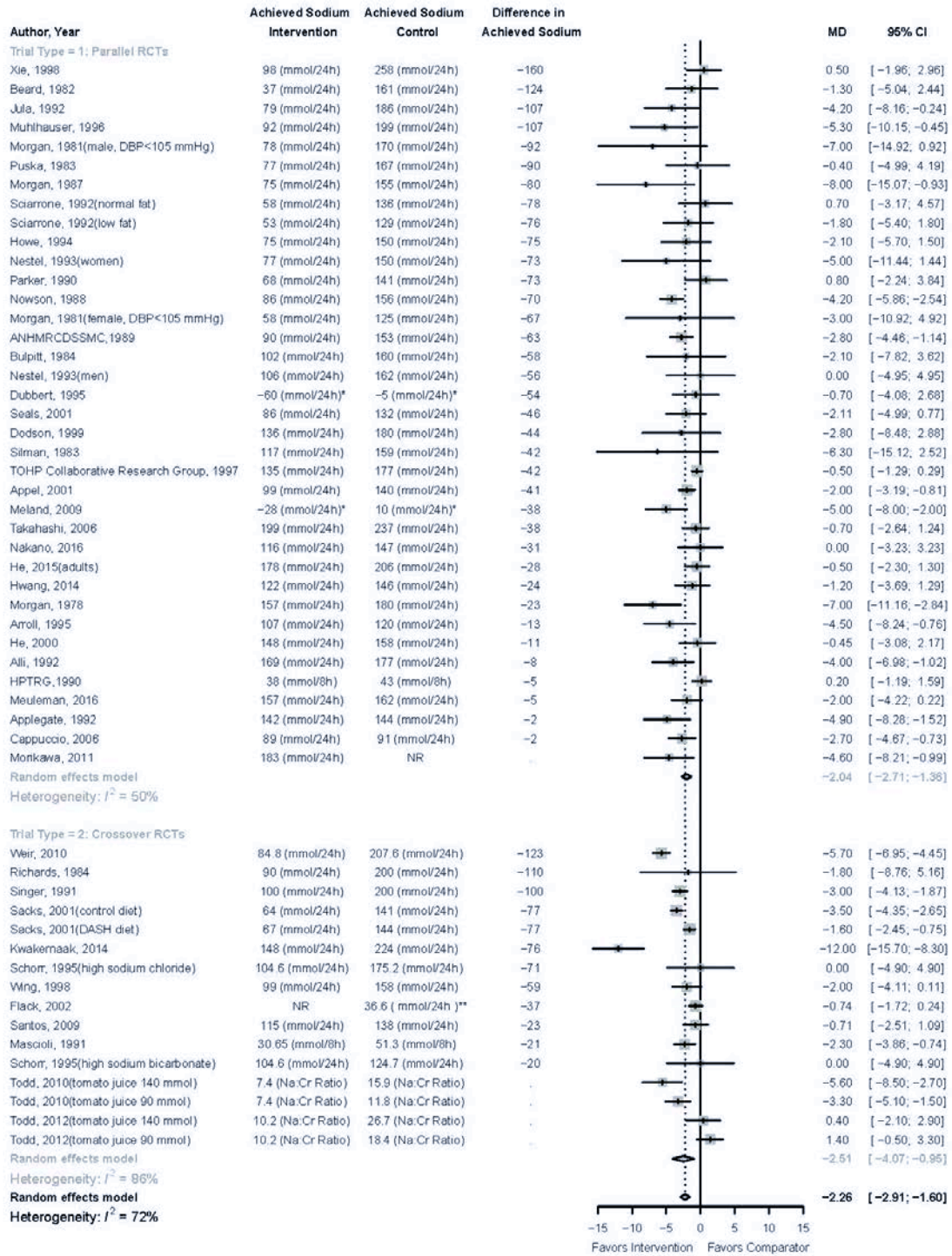
Adults did not differ significantly from children in the effect of sodium reduction on diastolic BP (p=0.845).

In the one RCT that compared children with their families, sodium reduction had no significant effect on diastolic BP in either adults or children.¹¹⁴

The crossover CCT described above found that sodium reduction significantly decreased diastolic BP across the intervention groups compared with the control groups (MD -1.5, 95% CI -0.6, -2.5) (high RoB).¹⁷²

Although the beneficial effect of sodium reduction among children was statistically non-significant when all eligible studies were included, omission of high or unclear RoB studies resulted in a statistically significant decrease in diastolic BP (MD -1.54, 95% CI -2.57, -0.51) with sodium reduction for children (low SoE). Evidence is insufficient to compare the effects of sodium reduction on diastolic BP in adults and children.

Figure 5a. Diastolic blood pressure in sodium reduction trials: adults



* change from baseline

** difference between intervention and control

ANHMRCDSSMC=Australian National Health and Medical Research Council Dietary Salt Study Management Committee

HPTRG=Hypertension Prevention Trial Research Group

Figure notes: Weighted mean differences for sodium excretion: -37 mmol (parallel RCTs); -74 mmol (crossover RCTs); -42 mmol all RCTs combined; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Figure 5b. Diastolic blood pressure in sodium reduction trials: children

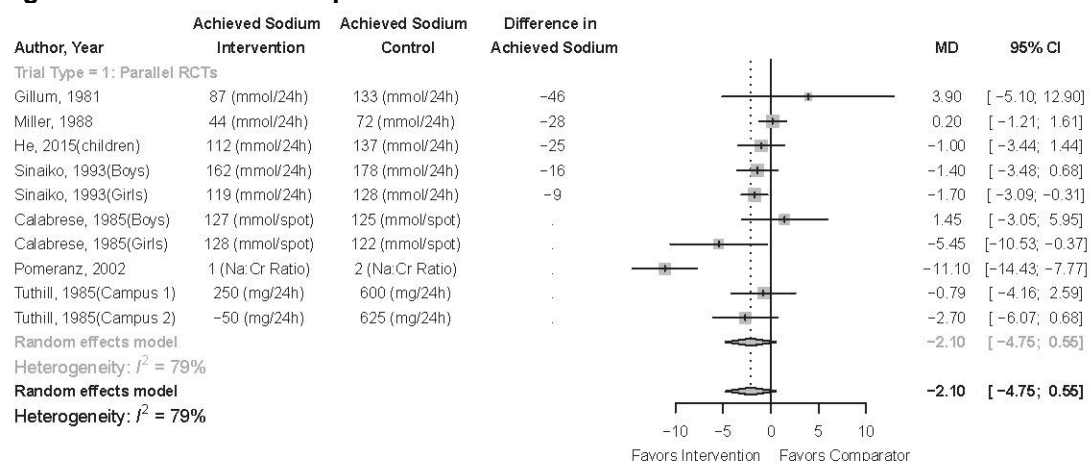


Figure notes: Weighted mean differences for sodium excretion: -25 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Percent Participants at Blood Pressure Goal

Five parallel and one crossover RCTs reported on the effect of sodium reduction on the likelihood of adult study participants reaching a prespecified blood pressure goal (Figure 6).^{49, 170, 171, 205, 206, 284} Five of the trials reported a difference in 24-hour sodium excretion of 40 mmol/d or more. The goals varied, with three RCTs reporting on likelihood of reducing need for antihypertensive medications,^{170, 205, 206} one reporting on likelihood of not needing to resume medication after withdrawal,¹⁷¹ and two reporting on the likelihood of achieving a prespecified BP goal.^{49, 284}

The DASH Sodium Trial compared the likelihood of participants with high normal or stage 1 hypertension at baseline achieving the prespecified goal of blood pressure control (defined as less than 140/90) between two diets at three sodium levels.⁴⁹ Seventy seven percent of those consuming the DASH lower sodium diet and 71 percent of those on the control lower sodium diet achieved blood pressure control. Among those with stage 1 hypertension, 63, 65, and 84 percent achieved blood pressure control on the high, intermediate, and low sodium DASH diets; and 32, 51, and 74 percent achieved blood pressure control on the high, intermediate, and low sodium control diets.²⁶¹

The random effects pooled estimated relative risk (RR) for all RCTs favored reduced sodium (1.73, 95% CI 1.24, 2.40) but studies were somewhat heterogeneous (overall I^2 65%) (2 low RoB, 1 moderate RoB, 1 high RoB, 2 unclear RoB). A sensitivity analysis that omitted studies with high and unclear RoB decreased the pooled relative risk, although it remained statistically significant (RR 1.68, 95% CI 1.12, 2.54; I^2 61%).

The findings show a low SoE for achieving a prespecified blood pressure goal, based on inconsistency and lack of precision.

Figure 6. Likelihood of achieving prespecified blood pressure goal in trials of sodium reduction

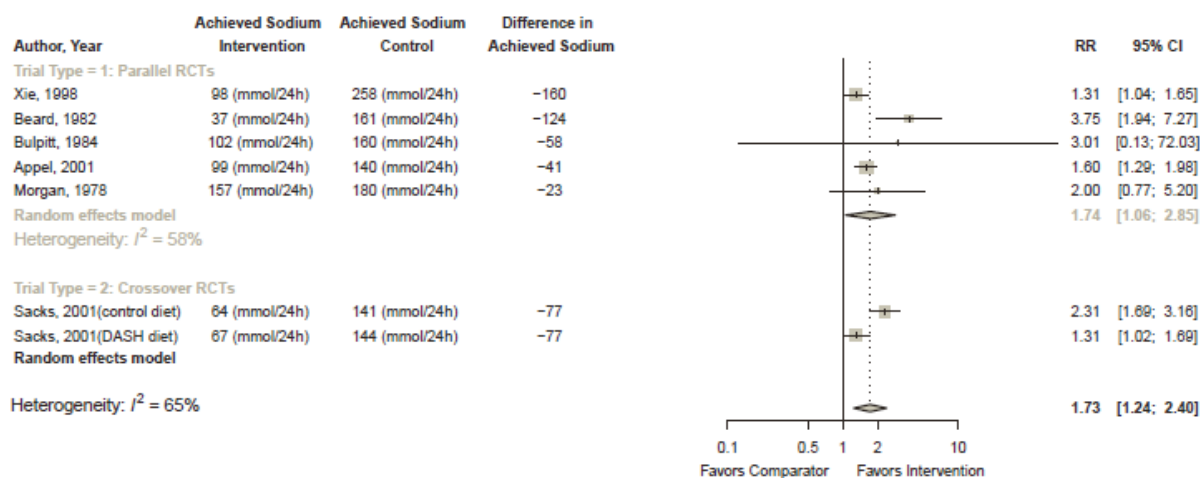


Figure notes: Weighted mean differences for sodium excretion: -67 mmol (parallel RCTs); -77 mmol (crossover RCTs); -68 mmol (all RCTs combined); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Hypertension Incidence in Adults

Three RCTs reported on the effects of sodium reduction on the risk for incident HTN in adult men and nonpregnant women (Figure 7), and one reported on the incidence of gestational HTN in pregnant women.^{42, 51, 53, 214}

The Trial of Hypertension Prevention (Phase I) (TOHP I) was a multisite trial conducted from 1987 through 1990 that was designed to test the efficacy of seven nonpharmacologic interventions in persons with high normal BP. The interventions included the lifestyle interventions of weight loss, sodium reduction, and stress management, and the nutritional supplement interventions of calcium, magnesium, potassium and fish oil, and collected multiple 24-hour urine samples to track adherence through sodium excretion. In the current report, we consider only the sodium reduction, potassium supplementation (Key Question 5), and usual care arms. For this trial, 327 individuals were randomized to a 6-month sodium reduction intervention and 589 were randomized to usual care.⁵¹ TOHP II (Phase II) was also a multisite trial conducted from 1990 to 1995 and designed to test the efficacy of interventions to promote weight loss, sodium reduction, and their combination (in a factorial design) in decreasing BP and the incidence of hypertension during a 3- to 4-year followup in overweight adults with high normal diastolic BP. The study randomized 594 adults to sodium reduction and 596 to usual care.⁵³ Followup for some outcomes was as long as 20 years.

TOHP I defined incident HTN as attaining a diastolic BP of 90 mm Hg or higher on nine separate measurements and/or treatment with an antihypertensive (follow up was as long as 7 years).⁵¹ TOHP II defined incident HTN as systolic BP of 140 or higher or diastolic BP of 90 or higher, or use of antihypertensive drugs (at 4 years).⁵³ The HPTRG defined incident HTN using the same criteria as TOHP II (at 3 years).

Two of the RCTs reported that differences in sodium excretion across intervention arms exceeded 40 mmol/d (however, in TOHP-II, the difference in sodium excretion exceeded 40 mmol/d or more only for men).

The random effects estimate for RR of incident HTN across the three studies showed a statistically non-significant decrease with sodium reduction (RR 0.83, 95% CI 0.67, 1.03; I^2 0%) (low overall RoB) (Figure 7).

A fourth RCT assessed the effect of sodium reduction on the risk for gestational hypertension: This study found no difference between groups on the rate of incident hypertension.²¹⁴

Based on imprecision, small number of studies, and differing definitions of hypertension, these findings suggest that sodium reduction might decrease the risk for incident HTN in non-pregnant adults but the strength of evidence is insufficient to make a definitive determination. No studies reported on this outcome in subgroups defined by age, gender, or race.

Adverse Events Associated With Sodium Intake

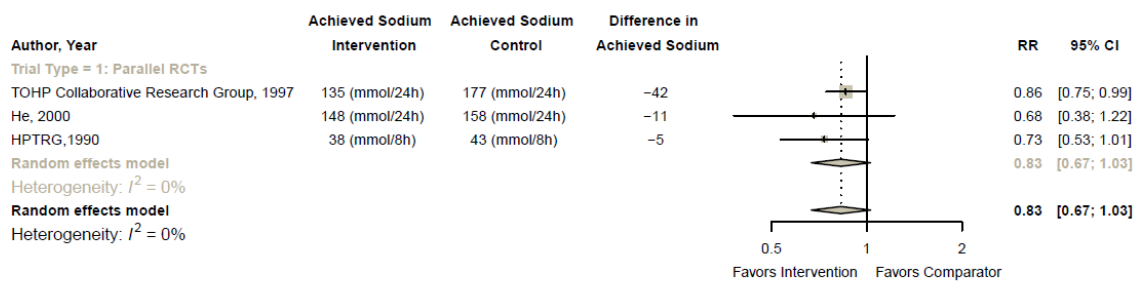
Mortality and CVD/CHD morbidity outcomes reported for sodium reduction interventions are described in the response to KQ3.

Eight RCTs described other adverse events reported in RCTs of sodium reduction. Two studies reported no significant between-group differences in the risk for dizziness or unsteadiness.^{171, 206} Across three studies that reported on headache, one reported no difference, and two reported significantly higher rates in the usual sodium group: the DASH Sodium trial reported a significant decrease in the rate of headaches in the low sodium control diet group and the low sodium DASH diet group compared with the high sodium control diet group, $p < 0.05$.^{49, 93, 206}

Three studies (reported in four publications) reported no between-group differences in blood lipids (total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides).^{49, 158, 160, 163} One study reported no difference in fasting or post-oral glucose challenge serum glucose or insulin,¹⁶⁰ and one study reported no difference in insulin sensitivity across three levels of sodium intake.²⁶⁰ One study reported improvements in muscle cramps across both groups.²⁰⁵

We did not find evidence to support an effect of reduced sodium on blood lipids (low SoE), but evidence is insufficient from studies that met inclusion criteria to assess other adverse effects of sodium reduction.

Figure 7. Risk for incident hypertension in trials of sodium reduction



HPTRG=Hypertension Prevention Trial Research Group

Figure notes: Weighted mean differences for sodium excretion: -31 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Sex

Mean Difference in Systolic Blood Pressure

Eight parallel RCTs reported on the effects of sodium reduction on systolic BP in adult males,^{171,53, 131, 161, 170, 208} and seven parallel RCTs also reported on the effects of sodium reduction on systolic BP for non-pregnant females.^{49, 51, 53, 131, 161, 169, 171, 214, 217} Two crossover RCTs reported on adult males and females;^{49, 169} one, the DASH-sodium Trial reported on the effects of three different dietary sodium levels on men and women.⁵⁷ A crossover CCT compared changes in systolic BP between male and female high school students.¹⁷² RoB was low overall for the eight RCTs.^{49, 53, 161, 169-171, 208, 214}

Eight RCTs reported differences in 24-hour sodium excretion of 40 mmol or more between the high and low sodium groups for at least some subgroups.^{51, 53, 49, 161, 169, 171, 208, 214, 217}

The random effects pooled estimate for the change in systolic BP for adult males showed a statistically significant improvement in favor of reduced sodium (MD -2.38 (95% CI $-4.22, -0.53$; I^2 69%). For adult females, the improvement was also statistically significant (MD -4.39 (95% CI $-6.18, -2.61$; I^2 42%) (Figure 8). Of note, the difference between males and females was not significant, and none of the studies reported significant differences between men and women.

The DASH-Sodium Trial⁴⁹ reported significant decreases in systolic BP from the highest to the lowest concentration of dietary sodium for both men and women who consumed the control diet and the DASH diet, with no significant differences between the sexes at any sodium concentration (low RoB).⁵⁷

Evidence suggests that both men and women experience significant decreases in systolic blood pressure with sodium reduction interventions and that sex may not influence the effects of sodium reduction on systolic BP (low SoE based on inconsistency and imprecision).

Figure 8. Systolic blood pressure in sodium reduction trials: sex effects

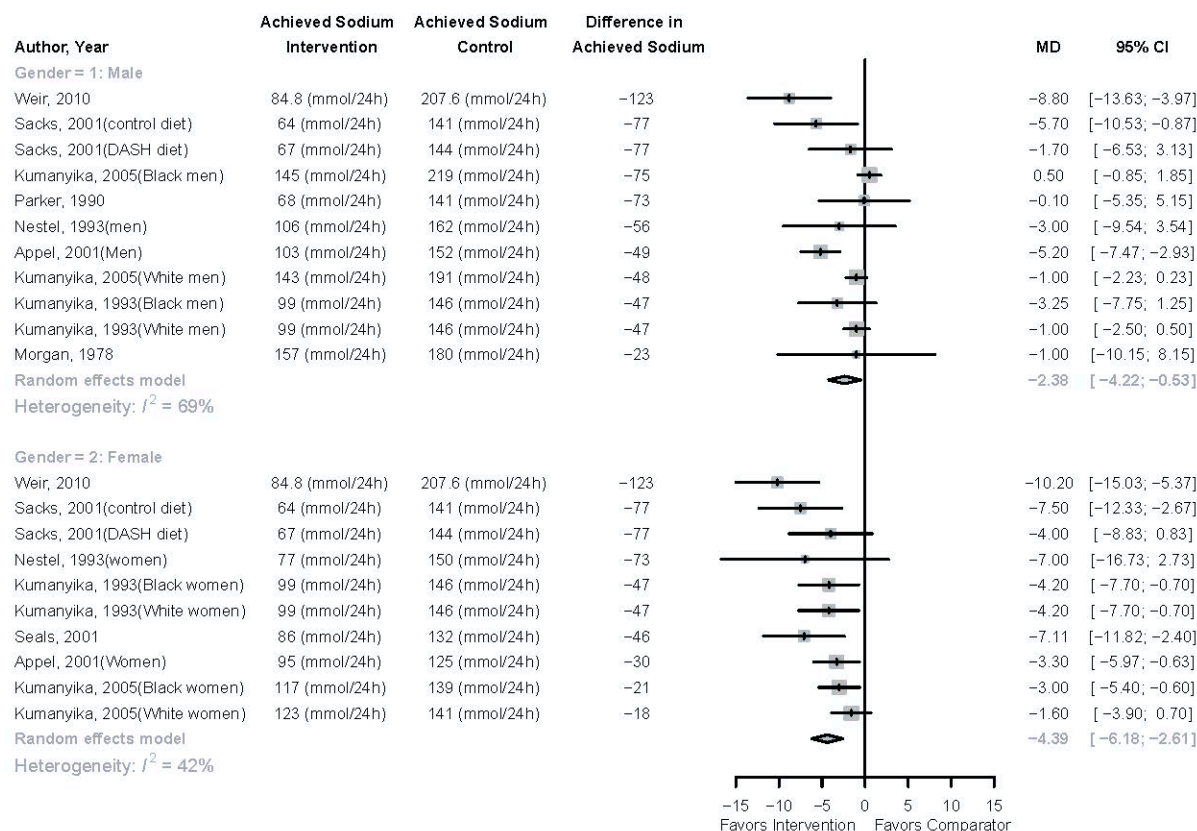


Figure note: Weighted mean differences for sodium excretion: -59 mmol (men); -41 mmol (women); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Mean Difference in Diastolic Blood Pressure

Eight parallel RCTs reported on diastolic BP for males only,^{49, 51, 171, 208 53, 131, 161, 170, 203} and seven RCTs reported on the effects on diastolic BP in females.^{49, 51, 53, 131, 161, 171, 203, 214, 215, 217} One crossover study (described in two publications) reported the effects of three different dietary sodium levels on men and women.^{49, 57} RoB was low overall for the eight RCTs.

Eight RCTs had a difference in urinary excretion of 40 mmol/d or more for at least some subgroups.^{53, 217 49, 161, 169, 171, 208, 214, 215}

The random effects pooled estimate showed a non-statistically significant beneficial effect of sodium reduction on diastolic BP in men (MD -1.29 [95% CI -2.79, 0.22]; I^2 71%) and a significant effect among women (MD -1.84 [95% CI -2.37, -1.31]; I^2 0%). No significant difference was observed between men and women (Figure 9).

The DASH-Sodium Trial^{57, 278} reported significant dose-dependent decreases in DBP for both men and women who consumed the control diet at the low sodium level compared with the high sodium, with no significant differences between them (low RoB). No significant differences were seen between the high and low sodium DASH diet groups for either men or women.

Evidence suggests that both men and women may experience decreases in diastolic blood pressure with sodium reduction interventions and that sex may not influence the effects of sodium reduction on diastolic BP (but the SoE is low based on inconsistency and imprecision).

Figure 9. Diastolic blood pressure in sodium reduction trials: sex effects

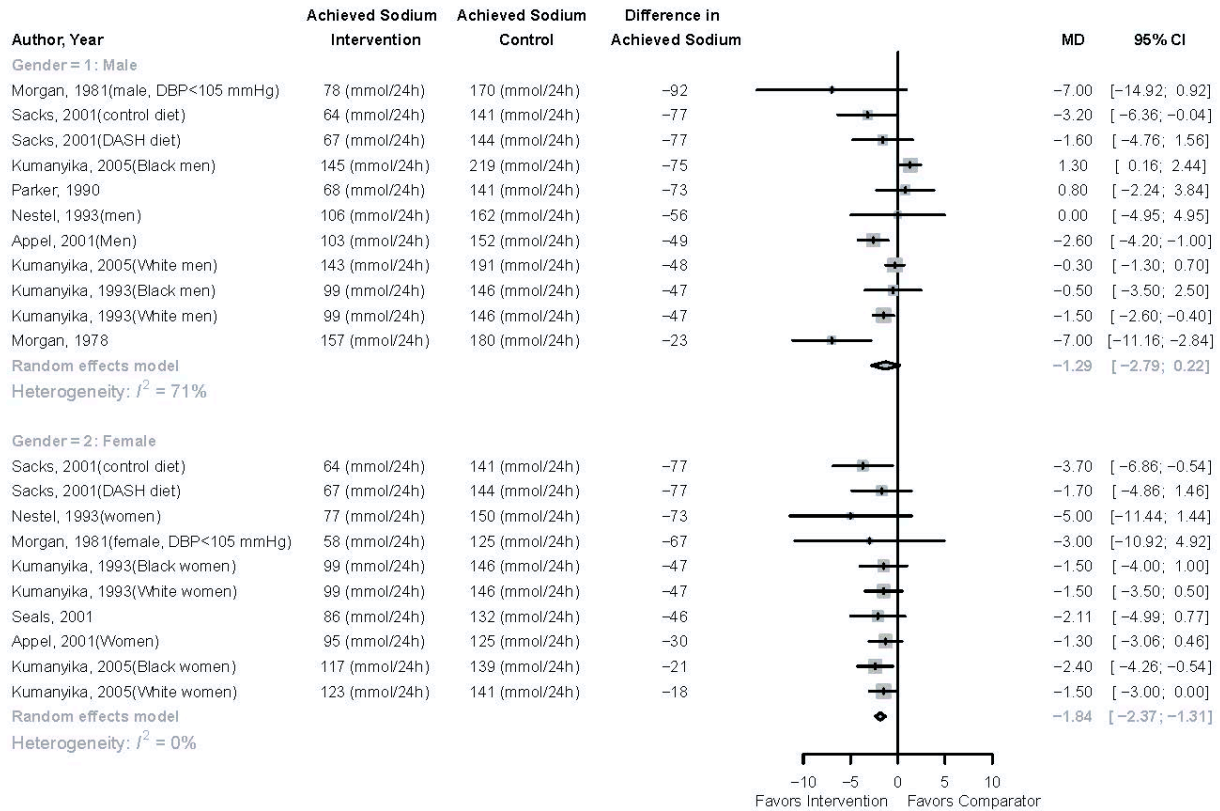


Figure notes: Weighted mean differences for sodium excretion: -57 mmol (men); -38 mmol (women); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Hypertension Incidence

One RCT assessed differences in the effects of sodium reduction on relative risk for incident hypertension by sex (criteria are described above in the description of findings for all adults) (low RoB).⁵³ One RCT assessed incidence of gestational hypertension (shown in Figure 10 only for comparison) (moderate RoB).^{53, 214} The study that compared differences by sex also assessed white and black men and women separately.⁵³ No significant difference was seen across sexes, (Figure 10) but evidence is insufficient to draw a conclusion regarding moderating effects of sex on the effects of reducing sodium on this outcome because the findings were based almost entirely on indirect evidence from heterogeneous studies .

Figure 10. Hypertension incidence in sodium reduction trials: sex effects

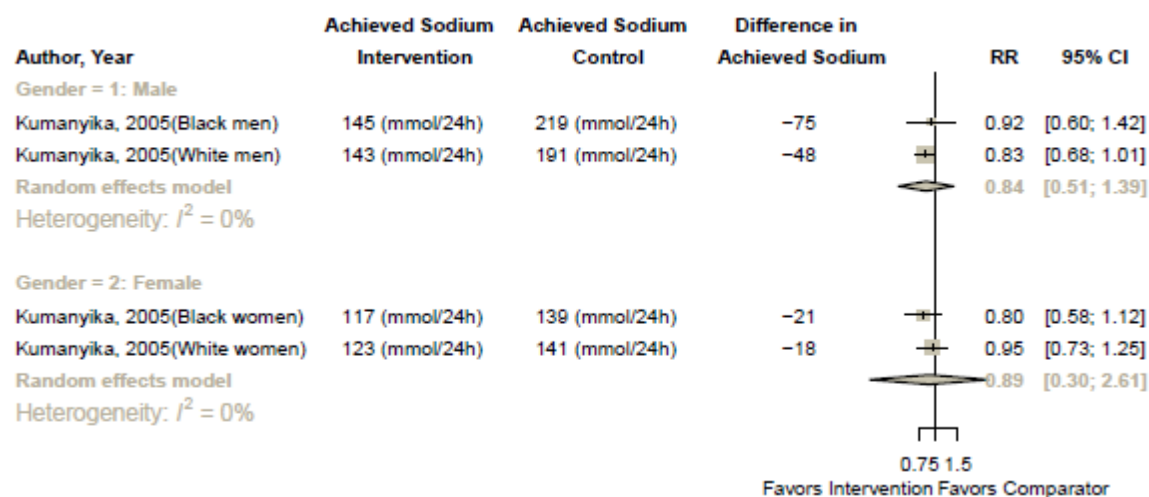


Figure notes: Weighted mean differences for sodium excretion: -51 mmol (men); -19 mmol (women); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Race/Ethnicity

Mean Difference in Systolic Blood Pressure

Three parallel RCTs and one crossover RCT reported on the effects of sodium reduction on systolic BP separately by race.^{51, 53, 57, 171} Mean differences in 24-hour sodium excretion reached 40 mmol/d or more among Blacks in three of four RCTs,^{49, 51, 53} and among whites or non-Blacks in the same studies; however the difference was smaller for white women in the TOHP II study.⁵³ Sodium reduction had a statistically significant beneficial effect on systolic blood pressure among both black participants (MD -3.76, 95% CI -6.22, -1.31; I^2 92%) and non-black participants (MD -2.69, 95% CI -4.17, -1.02; I^2 73%) (low RoB; high heterogeneity). Non-blacks and blacks did not differ significantly in MD in systolic BP (confidence intervals were wide) (Figure 11). Evidence was insufficient based on the small number of direct comparisons, inconsistency, and imprecision to draw a conclusion regarding the moderating effect of race/ethnicity on the effects of reducing sodium on systolic BP.

Figure 11. Systolic blood pressure in sodium reduction trials: effects of race and ethnicity

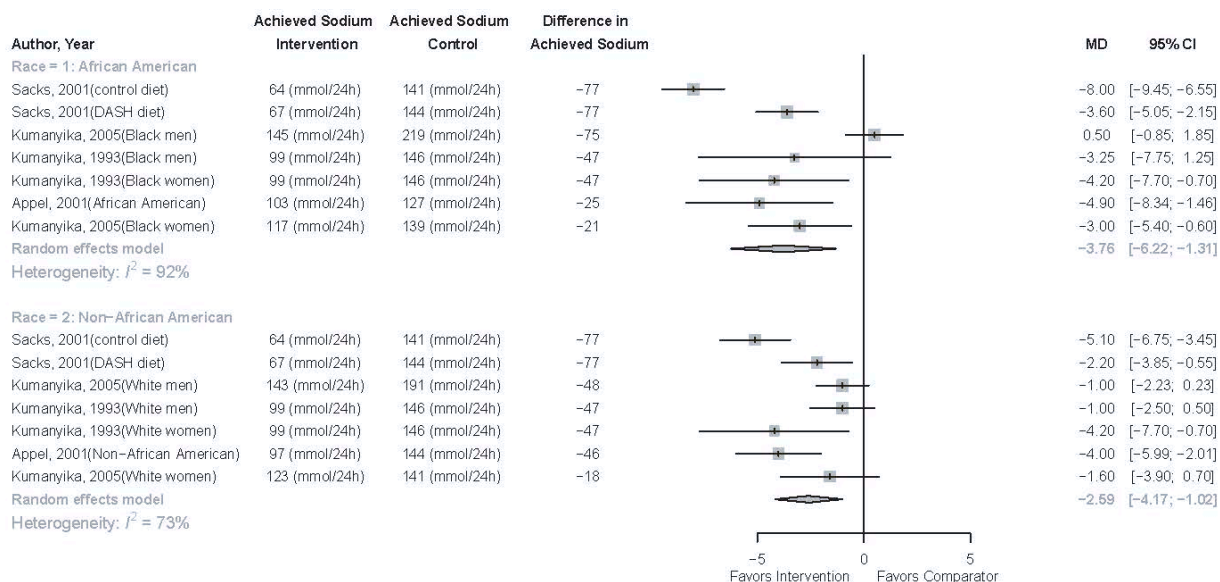


Figure notes: Weighted mean differences for sodium excretion: -58 mmol (African American); -46 mmol (non-African American); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Mean Difference in Diastolic Blood Pressure

Four RCTs reported on the effects of sodium reduction on diastolic BP separately by race.^{49, 51, 53, 171} Mean differences in 24-hour sodium excretion reached 40 mmol/d or more among Blacks in three of the four RCTs,^{49, 51, 53} and among whites or non-Blacks in the same studies; however the difference was smaller for white women in the TOHP II study.⁵³ Sodium reduction had a small statistically significant beneficial effect on diastolic blood pressure among black participants (MD -1.82, 95% CI -3.59, -0.04, I^2 0%) (low RoB). Among non-Black participants, sodium reduction decreased diastolic BP slightly but significantly (MD -1.37, 95% CI -1.97, -0.76, I^2 15%). Non-blacks and blacks did not differ significantly in MD in diastolic BP (Figure 12). Evidence was insufficient based on the small number of direct comparisons, inconsistency, and imprecision to draw a conclusion regarding the moderating effect of race/ethnicity on the effects of reducing sodium on diastolic BP.

Figure 12. Diastolic blood pressure in sodium reduction trials: effects of race and ethnicity

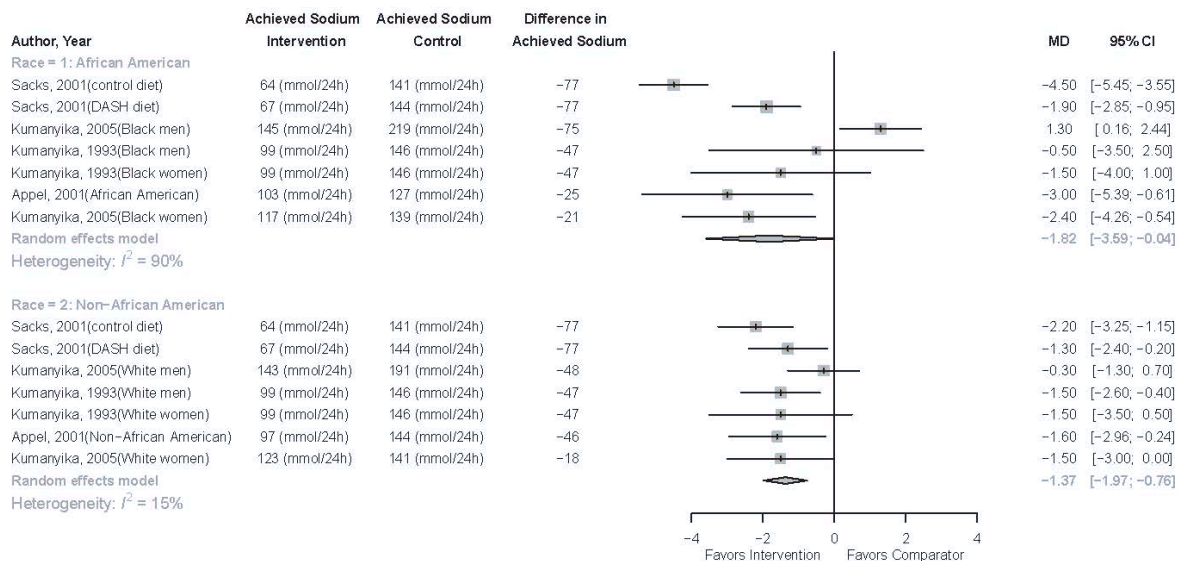


Figure notes: Weighted mean differences for sodium excretion: -58 mmol (African American); -46 mmol (non-African American); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Hypertension Incidence

One RCT compared incident hypertension (see criteria below) rates between Whites and Blacks (both stratified by sex)(low RoB).⁵³ This study found no significant effect of sodium reduction on incident hypertension and no difference between Blacks and Whites (Figure 13).

Figure 13. Hypertension incidence in sodium reduction trials: effects of race and ethnicity

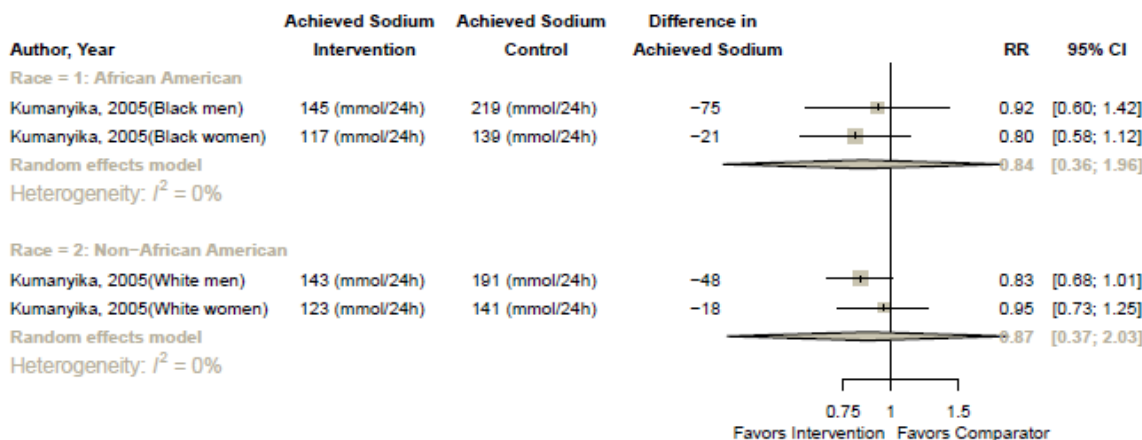


Figure notes: Weighted mean differences for sodium excretion: -44 mmol (African American); -39 mmol (non-African American); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Key Question 1c. Subpopulations Defined by Hypertension, Diabetes, and Obesity Health Status

Description of Included Studies

Forty-three RCTs enrolled participants with high-normal BP or HTN (see below). In categorizing studies regarding participants' baseline blood pressure status, we relied on the terms and definitions used by the authors, realizing that these terms and definitions have changed over time.

Six RCTs enrolled participants with DM and /or kidney disease.^{39, 47, 95, 113, 266, 282}

One RCT compared obese and non-obese participants,⁵⁷ and one compared overweight and non-overweight participants.¹⁷¹ The remainder enrolled participants with mean BMIs in the slightly overweight range.

Detailed Synthesis

Hypertensive Status

Among the RCTs that compared sodium reduction to usual diet or usual sodium intake in adults, 3 parallel RCTs^{42, 161, 200} and six crossover RCTs^{45, 49, 50, 86, 263, 283} enrolled participants with normal BP. The remaining parallel and crossover RCTs in adults enrolled participants with high-normal BP, or mild, moderate or more severe (Figures 14 and 15).^{36, 39, 41, 46-49, 51, 90, 92, 93, 96, 113, 157, 159, 160, 163, 164, 169, 170, 205, 206, 208-213, 216, 217, 230, 231, 236, 260, 266, 284} One RCT compared BP responses in mild vs. more severe HTN,²⁰³ and one RCT compared responses in normotensive adults to those of adults with HTN.⁴⁹

In addition, one CCT enrolled healthy normotensive adults,³⁸ and two enrolled adults with hypertension.^{84, 268}

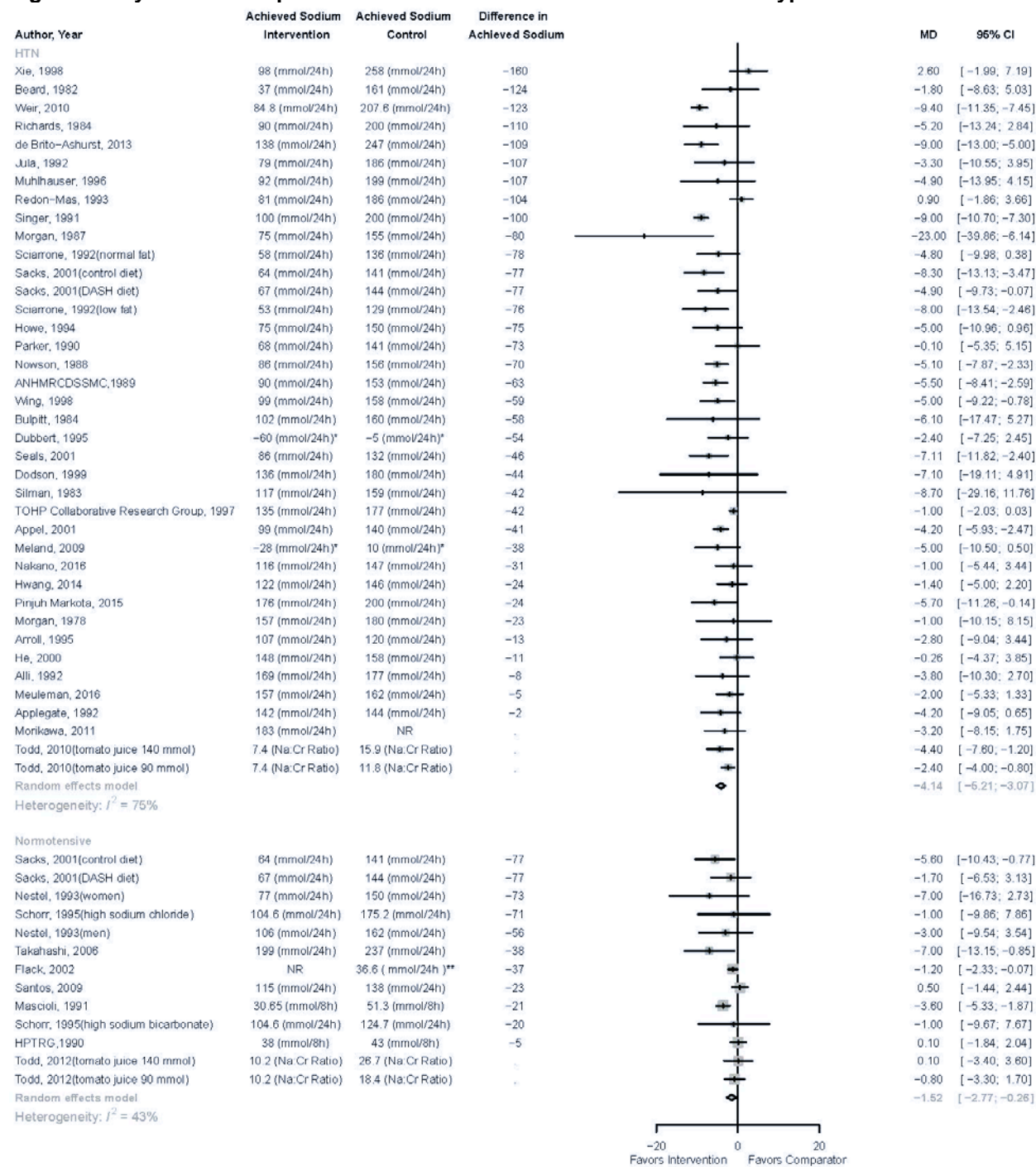
Mean Difference in Systolic Blood Pressure

One study directly compared effects of sodium reduction on systolic BP between normotensive and hypertensive groups of adults.⁴⁹ The DASH Sodium Trial found that sodium reduction had a greater effect on BP in hypertensive than in normotensive adults for both the control diet (Hypertensives: MD -8.30, [95% CI -13.22, -3.38] vs. normotensives: MD -5.60, [95% CI -10.52, 0.68] p=0.01) and the DASH diet (Hypertensives MD -4.90, [95% CI -9.82, 0.02] vs. normotensives MD -1.70, 95% CI -6.62, 3.22] p=0.003).

Random effects meta-analyses of trials that enrolled only participants with normal BP and those that enrolled only participants with HTN showed that sodium reduction lowered systolic BP both in studies of normotensive individuals (9 RCTs; MD -1.52, 95% CI -2.77, -0.26; I² 43%; RoB) as well as in studies of those with prehypertension, mild HTN, and more severe HTN (36 RCTs; MD -4.14, 95% CI -5.21, -3.07; I² 75%; low RoB). The effect in studies that enrolled participants with HTN was significantly greater than that in studies of normotensives (p<0.001) (Figure 14). The weighted mean difference for sodium intake at followup was -56 mmol for studies of populations with hypertension and -37 mmol for studies of normotensives. Sensitivity analysis that omitted high- or unclear- RoB RCTs showed a modest increase in the effect size for decreased systolic BP (but no change in heterogeneity) with sodium reduction in studies of people with HTN (MD -4.67, 95% CI -5.85, -3.49; I² 77%).

A moderate SoE supports a beneficial effect of sodium reduction on (lowering) systolic BP in adults with HTN, a beneficial effect in those with normal BP, and a significantly greater effect in those with HTN than in normotensive participants. The strength of evidence was rated as moderate because of inconsistency across study findings.

Figure 14. Systolic blood pressure in sodium reduction trials: effects of hypertension



* change from baseline
 ANHRCDSMCM=Australian National Health and Medical Research Council Dietary Salt Study Management Committee
 HPTRC=Hypertension Prevention Trial Research Group

Figure notes: Weighted mean differences for sodium excretion: -56 mmol (Hypertensives); -37 mmol (normotensives); CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Mean Difference in Diastolic Blood Pressure

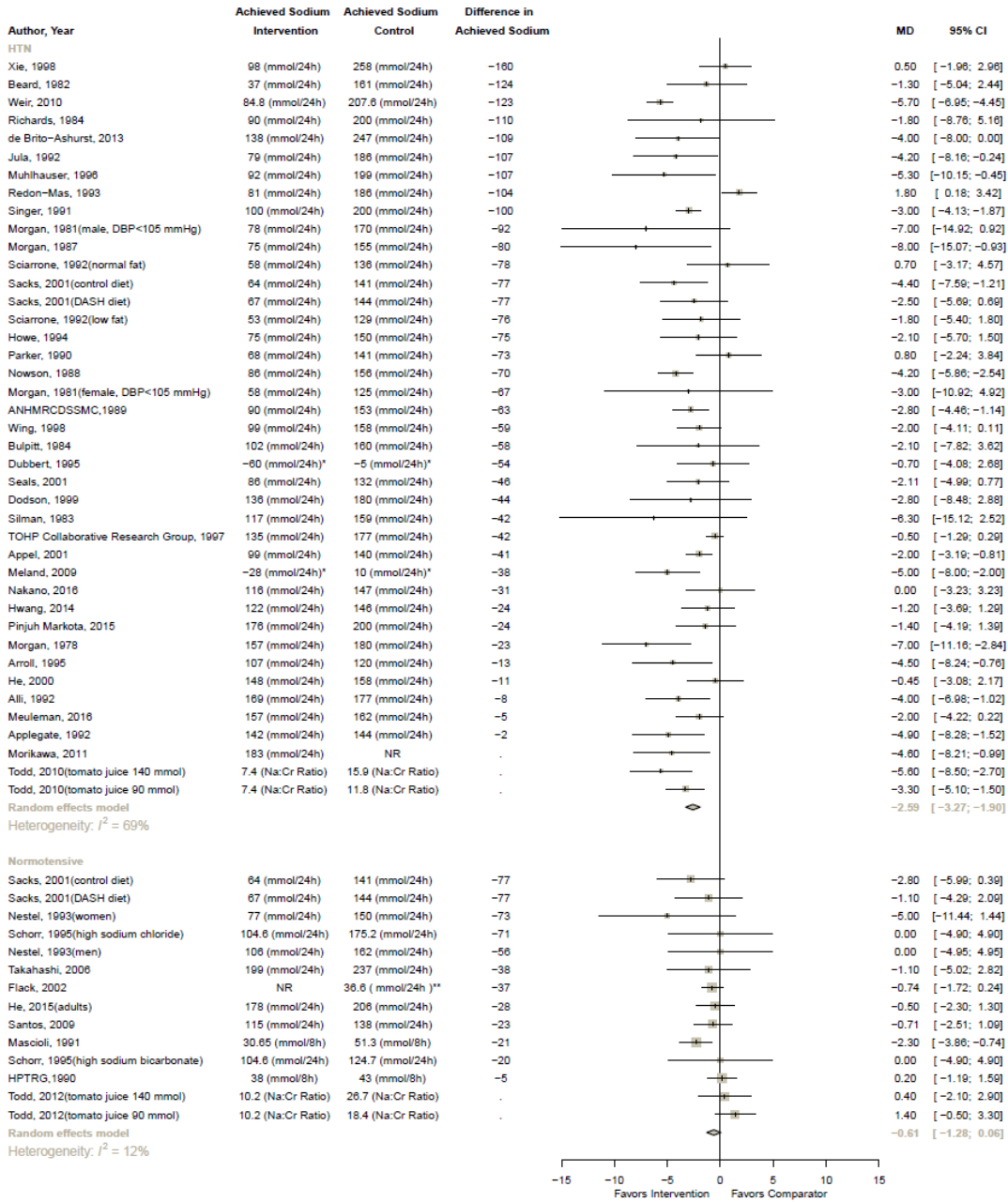
One small RCT stratified their description of the effects of sodium reduction on diastolic BP between individuals with mild and those with more advanced HTN.²⁰³ The effects were comparable in both groups; however, they did not do a statistical comparison, and they did not account for the use of medication among those with more advanced HTN.

One study directly compared effects of sodium reduction on systolic BP between normotensive and hypertensive groups of adults.⁴⁹ The DASH-Sodium Trial found that sodium reduction had a greater effect on BP in hypertensive than in normotensive adults for both the control diet (Hypertensives: MD -4.40, [95% CI -7.59, -1.21] vs. normotensives: MD -2.80, [95% CI -5.99, 0.39] p=0.01) and the DASH diet (MD -2.50, [95% CI -5.69, 0.69] vs. MD -1.01, 95% CI -4.29, 2.09] p=0.003).

Random effects meta-analyses of studies that assessed the effects of sodium reduction among normotensives and those that assessed effects in those with HTN showed that sodium reduction did not significantly lower diastolic BP in studies of normotensive individuals (10 RCTs; MD -0.61 95% CI -1.28, 0.06; I² 12%; moderate RoB) but significantly lowered diastolic BP in studies of those with prehypertension and HTN (37 RCTs; MD -2.59, 95% CI -3.27, -1.90; I² 69%; low RoB) (p<0.002 for the difference between those with HTN and those with normal BP) (Figure 15). Sensitivity analysis that omitted high- and unclear-RoB RCTs showed a modest increase in the effect size for studies of individuals with HTN (MD -2.86, 95% CI -3.59, -2.13).

Thus, sodium reduction significantly decreases diastolic BP in adults with HTN (moderate SoE), but we did not find evidence that sodium reduction reduces diastolic BP significantly in those with normal BP (low SoE) (Figure 15). Sensitivity analysis that omitted high- and unclear-RoB RCTs showed a modest increase in the effect size for studies of individuals with HTN (MD -2.86, 95% CI -3.59, -2.13; I² 66%).

Figure 15. Diastolic blood pressure in sodium reduction trials: effects of hypertension



* change from baseline
 ANHMRCDSSMC-Australian National Health and Medical Research Council Dietary Salt Study Management Committee
 HPTRG-Hypertension Prevention Trial Research Group

Figure notes: Weighted mean differences for sodium excretion: -56 mmol (hypertensives); -34 mmol (normotensives); CI=confidence interval; HTN=hypertension; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Diabetic Status and/or Kidney Disease

Mean Difference in Blood Pressure

Six RCTs that met inclusion criteria enrolled participants with DM and/or chronic kidney disease. Five were parallel RCTs,^{39, 47, 95, 266, 282, 291} and one was a crossover RCT that enrolled adults with DM and nephropathy.⁹⁵ No studies compared the effects of sodium reduction by diabetic status and none compared individuals with kidney disease to healthy individuals.

One small UK study randomized 34 participants with mild hypertension and Type 2 DM and without nephropathy to 3 months of moderately sodium restricted- or usual diabetic diet. Sodium reduction resulted in a significant difference in urinary sodium excretion across groups (60mM) but a non-statistically significant decrease in systolic BP and diastolic BP (low RoB).³⁹

A small study in Germany imposed a sodium-restricted diet on 16 participants with mild hypertension and Type 1 DM with nephropathy. After a 2-week run-in period, participants were randomized to receive sodium tablets to normalize sodium intake or placebo tablets to maintain sodium reduction.⁴⁷ After four weeks, 24-hour urinary sodium excretion differed across groups by over 100mM; systolic BP was not significantly different between groups but diastolic BP was significantly lower BP (MD -5.30 mm Hg, 95% CI $-10.15, -0.45$) (low RoB).

A UK trial randomized 40 individuals with HTN and Type 2 DM to 9 months of a salt substitute or usual diet.²⁸² At the end of the intervention period, urinary sodium excretion did not differ across treatment groups. Systolic BP was significantly reduced in the intervention group, compared with the control group (MD -21.50 mm Hg, 95% CI $-39.38, -3.62$), however diastolic BP was not significantly reduced (low RoB). A crossover trial in the Netherlands randomized individuals with diabetic nephropathy on angiotensin converting enzyme inhibitors (lisinopril) to sodium reduction via dietary counseling with or without hydrochlorothiazide (HCTZ).⁹⁵ This study found that sodium reduction decreased systolic and diastolic BP (although less than that of HCTZ) and that the effects were additive with those of HCTZ (low RoB).

A parallel RCT in the Netherlands randomized 138 individuals with chronic kidney disease to a 3-month self-management intervention aimed at reducing sodium intake or to usual care.²⁶⁶ At the end of 3 months, both sodium excretion and diastolic BP (-5.2 mm Hg [95% CI, -8.4 to -2.1]) were significantly decreased in the intervention group, compared with the control group; at 6 months, systolic and diastolic BP were significantly lower in the intervention group (MD -7.3 mm Hg [95% CI, -12.7 to -1.9] and -3.8 [95% CI, -6.9 to -0.6], respectively), although sodium excretion was no longer significantly lower than the control group (moderate RoB).

A parallel RCT in the UK randomized 56 adults with chronic kidney disease to a 6-month intervention consisting of tailored dietary advice to lower sodium intake or usual care.²⁹¹ The low sodium intervention significantly reduced urinary sodium excretion and decreased both systolic (MD -8 mm Hg [95% CI $-11, -5$]) and diastolic BP (MD -2 mm Hg [95% CI $-4, -2$]) (low RoB).

Sodium reduction appears to decrease blood pressure in those with diabetes and in those with kidney disease, although the trials were too dissimilar to pool.

Thus, five of six RCTs found that sodium reduction decreased BP in individuals with DM and/or kidney disease compared with usual diet. However, evidence was insufficient, based on heterogeneity of the trials, to draw a conclusion regarding the effects of sodium reduction on BP in adults with DM.

Obesity

Mean Difference in Blood Pressure

One included study addressed the potential moderating effect of obesity and one addressed the effect of overweight on the effects of sodium reduction on systolic blood pressure.

The DASH Sodium trial compared the effects of the six dietary interventions among obese (BMI \geq 30) and non-obese (BMI<30) adults and found no differences in the effects of the diets by weight status.⁵⁷

The multisite US Trial of Nonpharmacologic Interventions on the Elderly (TONE) randomized 681 individuals, 60-80 years, with HTN to 3.5 months of sodium and/or calorie reduction and compared the effects of sodium reduction between overweight or obese and non-overweight participants.³⁶ Among non-overweight participants, mean differences in urinary sodium excretion between the sodium restricted and usual treatment groups exceeded 40 mmol/d, whereas among the overweight participants, mean differences in urinary sodium excretion were significant but did not reach 40 mmol/d. Sodium reduction significantly reduced systolic BP in both overweight (MD -4.9, 95% CI -7.2, -2.6) and non-overweight (MD -3.9, 95% CI -6.2, -1.5) participants. Diastolic BP decreased significantly among non-overweight participants (MD -2.2, 95% CI -3.7, -0.7) but non-significantly among overweight participants.³⁶

Key Question 1a. Effect of Other Minerals on Effect of Sodium (Reduction)

The evidence we present in the response to this subquestion describes the modulatory effects of potassium and other minerals on the effects of reduced dietary sodium. Five studies (reported in seven publications) compare the effects of a low sodium diet with and without potassium enrichment (direct comparison).^{42, 61, 64, 233, 235, 236, 275} Four studies assessed the effects of modifying potassium intake via foods;^{42, 61, 235, 275} the remaining trial administered potassium supplements.⁶⁴

Thirteen studies assess the effects of using potassium salt substitutes in place of sodium chloride table salt (indirect comparison).^{99, 101, 102, 124, 196, 199, 232, 239, 241, 265, 267, 275, 282} One of the studies reports on an intervention that included both low sodium foods and potassium salt substitute.²⁷⁵ These studies are analyzed separately from those that assessed the effects of sodium reduction with or without supplemental potassium.

We identified no RCTs that assessed the modifying effects of divalent cationic minerals (e.g., calcium or magnesium) alone on the effect of dietary interventions to lower sodium.

Moderating Effects of Potassium Intake

As described above in the introduction to this section, five RCTs compared the effects of a low-sodium diet alone with the effects of combining a low-sodium diet with a high potassium diet or potassium supplement (some containing divalent cations).^{42, 61, 64, 233, 235, 236, 275}

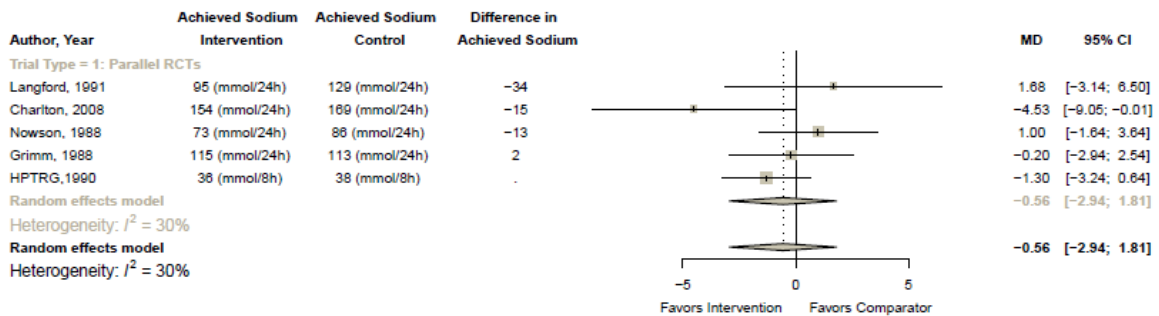
The five RCTs enrolled 80-529 participants; three were conducted in the US, one was conducted in Australia, and the remaining study was conducted in South Africa. Mean ages ranged from 39 to 61. The proportion of males ranged from 15 percent to 100 percent. One study enrolled healthy adults,⁴² and the remaining studies enrolled individuals with mild-to-moderate or more advanced hypertension. Follow-up times ranged from 2 months to 36 months.

Mean Difference in Systolic Blood Pressure

Among the five RCTs, the difference in urinary sodium excretion between the intervention and control groups did not reach 40 mmol/day in any study (Figure 16). Only one study, the one trial that administered potassium supplements, showed a substantial increase in potassium excretion in the potassium-enriched group.²³³ RoB was unclear for one trial,²³⁶ low for two trials,^{235, 275} and moderate for two trials^{42, 292} for an overall moderate RoB across studies. Random effects meta-analysis of the five RCTs showed no significant effect of low sodium diet combined with increased potassium intake on systolic BP (MD -0.56 mm Hg, 95% CI -2.94, 1.81; I² 30%). The study that employed a potassium supplement did not achieve findings that differed from those of the food-based studies.²³³

These findings suggest raising dietary potassium via food or supplements has no significant moderating effect on the systolic BP-lowering effect of sodium reduction (low SoE based on inconsistency and imprecision).

Figure 16. Systolic blood pressure in combination interventions to restrict sodium



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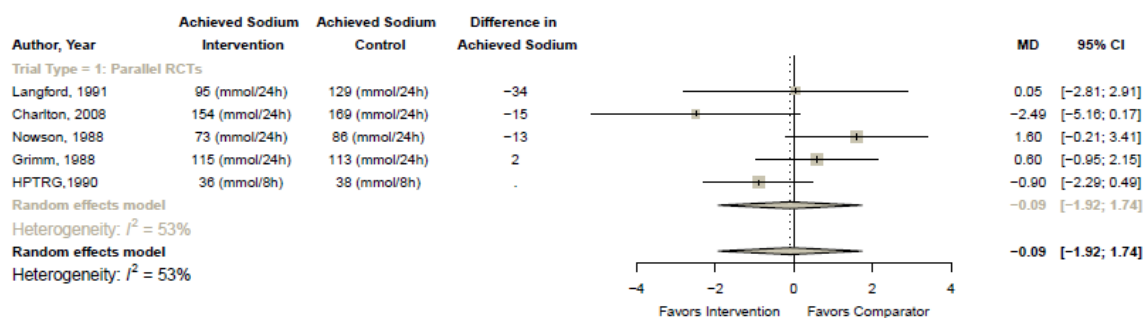
Figure notes: Weighted mean difference for sodium intake: -12 mmol; ; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Mean Difference in Diastolic Blood Pressure

Random effects meta-analysis of the five RCTs showed no significant effect of low sodium diet combined with increased potassium intake on diastolic BP (MD -0.09 mm Hg, 95% CI -1.92, 1.74; I² 53%) (Figure 17).

These findings suggest raising dietary potassium via food or supplements has no significant moderating effect on the DBP lowering effect of sodium reduction (low SoE based on inconsistency and imprecision).

Figure 17. Diastolic blood pressure in combination interventions to restrict sodium



HPTRG=Hypertension Prevention Trial Research Group

Figure notes: Weighted mean differences for sodium excretion: -12 mmol

Percent Participants at Blood Pressure Goal

No studies that met inclusion criteria for this intervention reported directly on this outcome. Two RCTs reported on the effects of increasing potassium intake on the need to increase or resume use of HTN medication.

The Trial of Antihypertensive Interventions and Management (TAIM) randomized individuals with HTN to a low sodium, high potassium diet or the usual diet. No effect was seen on the primary outcome, change in diastolic BP (see above). At the end of 6 months, 16.5 percent of those in the low sodium plus potassium group required additional HTN medication, compared with 20 percent of those in the usual diet group (no significant difference) (low RoB).²³⁵

The Minnesota Mount Sinai Hypertension Trial (MMSHT), in which men were withdrawn from their antihypertensive medication at baseline and randomized to a low sodium diet with or without potassium chloride supplements, found that at 6 months, 55 percent of each group—those in the low sodium, potassium supplement group as well as those in the low sodium only group—had to resume their antihypertensive medication (low RoB).^{64, 233}

The findings of these two RCTs provide insufficient evidence on which to base a conclusion regarding the effects of increasing potassium intake on the likelihood of meeting a blood pressure goal (or, in this case, better BP control).

Incidence of Hypertension

The Hypertension Prevention Trial, the only study that met inclusion criteria for this intervention and enrolled healthy participants, reported no differences between the effect of low-sodium diet with and without increased potassium intake on incident hypertension, as indicated by initiation of anti-hypertensive drugs (low RoB).⁴²

Evidence is insufficient to draw a conclusion on the moderating effect of potassium on sodium reduction.

Adverse Events Associated With Use of Potassium Supplements in a Low Sodium Diet

One RCT that met inclusion criteria for this intervention reported on adverse events.²³³ The MSHHT reported no statistically significant differences between the potassium-supplemented and placebo-treated groups over two years' followup in six indicators of gastrointestinal function or in need to change medication because of side effects (low RoB).

Conclusions regarding adverse events associated with increasing potassium intake are presented in the response to KQ5.

Effects of Potassium-Containing Salt Substitutes

Thirteen RCTs compared the effects of a salt substitute containing some combination of potassium and sodium vs. a regular diet including sodium chloride (indirect comparison).^{99, 101, 102, 124, 196, 199, 232, 239, 241, 265, 267, 275, 282} One of the studies reported on an intervention that included both low sodium foods and potassium salt substitute.²⁷⁵

The thirteen RCTs enrolled 35 to 2566 participants; five were conducted in China, two were conducted in the UK, and one each was conducted in Finland, Tibet, the Netherlands, Italy, South Africa, and Brazil. Mean ages ranged from 21 to 67. The proportion of males ranged from 15 percent to 62 percent. Nine studies enrolled only individuals with mild-to-moderate or more advanced hypertension, and four enrolled mostly participants with hypertension. Follow-up times ranged from 1 month to 36 months. Four trials had a low RoB^{99, 232, 275, 282} six had a moderate RoB^{102, 124, 196, 199, 241, 267}, and two had unclear RoB^{239, 265} for an overall moderate RoB.

Mean Difference in Systolic Blood Pressure

Of the 13 RCTs that met inclusion criteria for this question, only three showed a difference in urinary sodium excretion of 40 mmol or more, indicating that any reductions in sodium intake were not necessarily being reflected by decreasing sodium excretion.^{99, 101, 241} Random effects meta-analysis showed a statistically significant effect of the salt substitute on systolic BP (MD – 5.58, 95% CI –7.08, –4.09; I² 74%) (Figure 18).

Figure 18. Systolic blood pressure in trials of salt substitutes

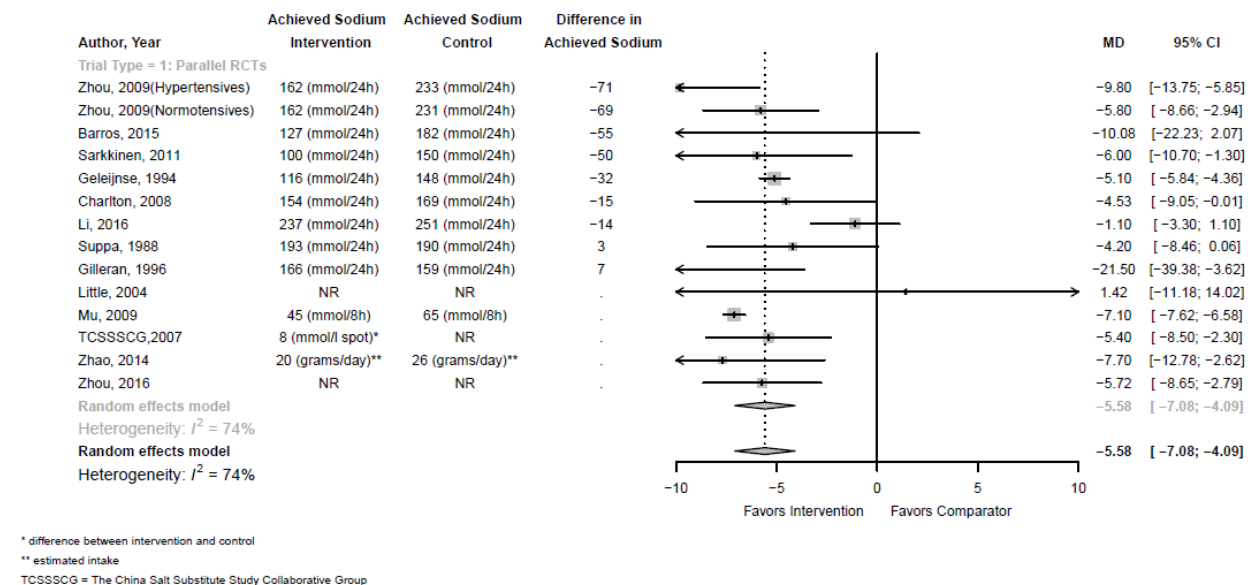


Figure notes: Weighted mean differences for sodium excretion: –18 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Subgroup analyses by sex in the 3-year RCT found that the beneficial effect of the salt substitute was similar for both men and women.¹⁰²

Subgroup analyses by age group in the 3-year RCT found that the beneficial effect of the salt substitute was limited to those between 40 and 70 years of age, compared with those younger than 40 or over 70.¹⁰²

One RCT analyzed the effect of the intervention separately for participants with hypertension and those with normal blood pressure.²⁴¹ At 6 months, urinary sodium excretion was identical in hypertensives and normotensives in the same intervention groups. The mean difference in systolic BP at 6 months was significant for both hypertensives and normotensives but greater for hypertensives than for normotensives.

These findings suggest use of potassium-containing salt substitutes in the diet to reduce sodium intake has a significant beneficial effect on systolic BP (moderate SoE due to imprecision of estimate and slight inconsistency).

Evidence is insufficient to draw conclusions regarding the moderating effects of sex, age, or blood pressure status on the effects of salt substitutes on systolic BP.

Mean Difference in Diastolic Blood Pressure

Random effects meta-analysis of 13 studies showed a significant effect of the salt substitute on diastolic BP (MD -2.88 , 95% CI -3.93 , -1.83 ; I^2 78%) (Figure 19).

These findings suggest use of potassium-containing salt substitutes has a significant beneficial effect on DBP (moderate SoE based on imprecision).

Figure 19. Diastolic blood pressure in trials of salt substitutes

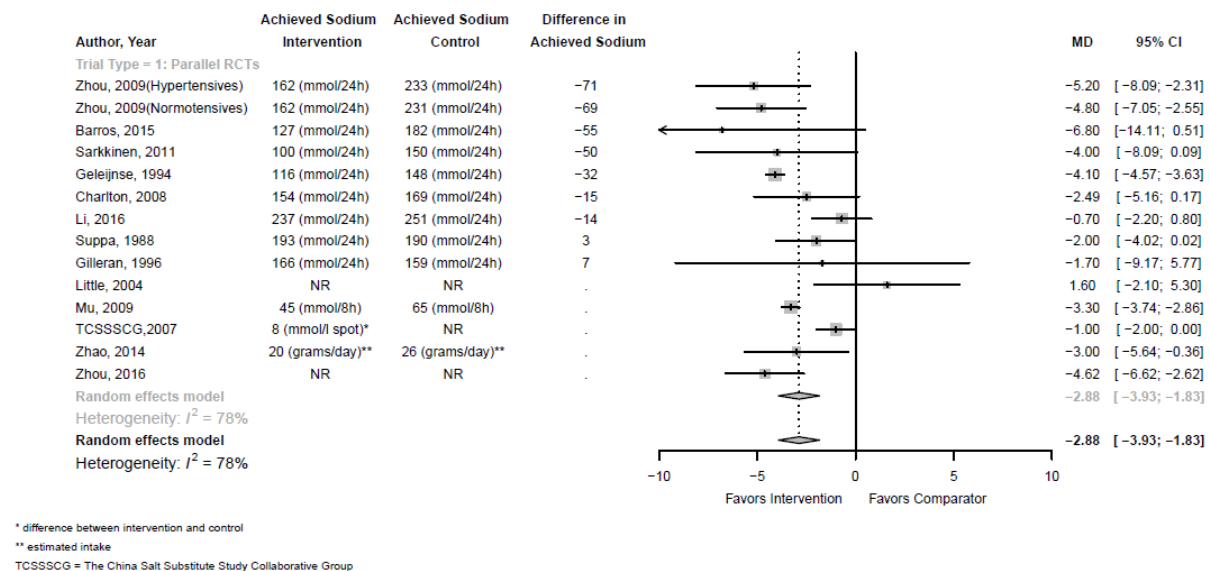


Figure notes: Weighted mean differences for sodium excretion: -18 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RCT=randomized controlled trial

Percent Participants at Blood Pressure Goal

One study assessed the effects of potassium-containing salt substitutes on blood pressure control. After 3 months, Zhao (2014) reported a non-statistically significant increase in the proportion of participants with good blood pressure control (SBP/DBP $<140/90$) with the use of the salt substitutes (RR 0.57, 95% CI 0.28, 1.17) (moderate RoB).¹²⁴

The findings of this RCT provide insufficient evidence on which to base a conclusion regarding the effects of salt substitutes on the likelihood of meeting a blood pressure goal (in this case, better BP control).

Incidence of Hypertension

Although no studies that met inclusion criteria for this intervention assessed hypertension incidence, two studies reported on the effects of potassium-containing salt substitutes on use of antihypertensive medications.^{102, 124} Both studies used the 25% potassium chloride salt substitute, and neither study withdrew participants from antihypertensive medications at baseline. Participants in one study were all hypertensive; after 3 months, salt substitutes resulted in a small, non-significant reduction in use of antihypertensive medications (moderate RoB).¹²⁴ At 3 years, the study by Zhou, in which half of participants had HTN at baseline, showed that use of the salt substitute resulted in a significant decrease in use of antihypertensive medications (moderate RoB).¹⁰²

The findings of these two RCTs provide insufficient evidence on which to base a conclusion regarding the effects of salt substitutes on incident hypertension because of the small number of studies, indirect assessment of the question, and RoB.

Adverse Events Associated With Use of Salt Substitutes

Three studies of salt substitutes assessed the risk for adverse events.^{99, 124, 196} Deaths and cardiovascular events are described in the response to KQ3a.

The China Salt Substitute Study Collaborative Group¹⁹⁶ compared the risk for hyperkalemia between the salt substitute group and the control group. No incidents of hyperkalemia were reported (moderate RoB).

Zhao reported that two intervention group participants discontinued because of gastrointestinal complaints, and one control group participant discontinued due to poor taste of the salt (moderate RoB).¹²⁴

Sarkkinen reported 7 instances of respiratory symptoms (five in the intervention group and two in the control group); 17 reports of GI symptoms (12 in the intervention group); and three reports of CV symptoms (one in the intervention group) (low RoB).⁹⁹

The findings of these studies suggest that use of potassium-containing salt substitutes in the diet may be associated with a small increase in the risk for minor respiratory and GI adverse events (low SoE, based on number of studies and lack of ability to pool findings across studies).

Key Question 2. Association Between Sodium Intake and Blood Pressure

Key Points

- Based on a low strength of evidence from prospective observational studies, sodium intake may be associated with systolic but not diastolic BP in adults. All studies had high or moderate RoB based on the methods used to assess sodium intake (single 24-hour urine excretion without validation or estimated excretion) (five studies).
- Sodium intake may be associated with the risk for incident hypertension in adults (low strength of evidence; five studies). Most studies had high RoB based on the methods used to assess sodium intake.

- Evidence is insufficient based on prospective cohort studies to draw conclusions about the association between sodium intake and BP in children. Three studies had high RoB, based on methods used to assess sodium intake.
- Evidence is insufficient based on lack of direct comparisons to draw conclusions regarding a moderating effect of sex on the association between lower sodium intake and blood pressure, incident hypertension, or achievement or a prespecified goal.
- Evidence is insufficient based on lack of direct comparisons to draw conclusions regarding a moderating effect of race/ethnicity on the association between lower sodium intake and blood pressure, incident hypertension, or achievement or a prespecified goal.
- Evidence is insufficient based on prospective cohort studies to draw conclusions about the moderating effects of age on the association between sodium intake and BP.
- Evidence is insufficient based on prospective cohort studies to draw conclusions regarding the moderating effect of hypertension on the association between sodium intake and BP.
- Evidence is insufficient based on prospective cohort studies to draw conclusions regarding the moderating effect of renal health status on the association between sodium intake and BP.
- Evidence is insufficient based on prospective cohort studies to draw conclusions regarding the moderating effect of weight status on the association between sodium intake and BP.

Overview

To address the question of the association between sodium intakes and BP outcomes, we examined prospective cohort studies as well as post hoc observational assessments of the association between dietary sodium excretion and outcomes of interest from a small number of studies. Key Question 2a reviews the associations between sodium intake and blood pressure and HTN outcomes and the moderating effects of sex, race/ethnicity, and age (adults vs. children). Key Question 2b reviews the moderating effects of HTN, diabetes, obesity, and renal disease on these associations.

Key Question 2a. Subpopulations Defined by Sex, Race/Ethnicity, and Age

Description of Included Studies

We identified 13 observational studies, described in 15 publications, that prospectively followed groups of adults or children to assess the association between baseline sodium intake and blood pressure or associated outcomes at followup and assessed sodium intake using a validated measure.^{104, 109, 146, 269 51, 79, 111, 112, 120, 132, 135, 139, 145, 171, 274}

Detailed Synthesis

Age

No studies directly compared adults with children. Therefore, we describe the results of adult studies and then the results of studies of children.

Adult Studies

Mean Systolic and Diastolic Blood Pressure

24-Hour Urinary Excretion

Singer and colleagues followed a cohort of 3,505 hypertensive adults, mean age 52, who participated in a worksite hypertension program in the US, over an average of 18.6 years.¹³⁹ After 6.5 years' in-program time, they found a small but statistically significant inverse association between 24-hour urinary sodium excretion and systolic BP by quartile, where the mean systolic BP was the highest in quartile (Q1) (lowest sodium excretion) and lowest in Q4 (Adjustment factors unclear). No association was seen for diastolic BP. (high RoB: single 24-hour urinary sodium with validation, but participants advised to begin sodium reduction prior to assessment.).

Phase 1 of the Trials of Hypertension Prevention (TOHP-1), randomly assigned 327 healthy adults with a diastolic BP 80-89 mmHg to receive counseling for dietary sodium reduction, and 417 healthy adults to maintain their usual diet over 18 months.⁵¹ After adjustment for age, sex, race, baseline BP, and baseline sodium excretion, the pooled dose-response analysis indicated a significant association between 24-hour urinary sodium excretion and systolic BP for the usual diet group, where a 100 mmol decrease in urinary sodium corresponds to a 1.4 mmHg decrease in systolic BP (low RoB: multiple 24-hour urinary excretion with validation).

Estimation of 24-Hour Urinary Sodium Excretion From Spot or Overnight Urine

The Circulatory Risk in the Community Study (CIRCS) conducted in a rural Japanese city followed a cohort of 889 normotensive adults (mean age 57.3) for a mean followup period of 6 years.¹³⁵ After adjusting for age, sex, BMI, drinking status, current smoking and eGFR, they found no association between sodium concentrations in spot urine and systolic BP or diastolic BP (moderate RoB based on assessment method).

Chien and colleagues followed a cohort of 1,520 healthy men and women (mean age 52) in a Taiwan village over a median of 8 years (the Chin-Shan Community Cardiovascular Cohort Study [CCCC]).²⁷⁴ They found that after adjusting for age and sex, higher 24-hour urinary sodium excretion was significantly correlated with higher systolic BP and diastolic BP (high RoB). The main outcome for this study was incident hypertension, reported below.

The Renal Risk in Derby (RRID) study followed a cohort of 1607 adults with stage-3 chronic kidney disease (mean age 72.6) in the UK over 1 year.¹¹¹ At followup, they found a significant association between reduced sodium intake, measured by estimating 24-hour urinary excretion, and reduced systolic and diastolic BP (Adjustment factors unclear; high RoB).

Thus, sodium intake may be associated with systolic but not diastolic BP in adults. All studies had high or moderate RoB based on the methods used to assess sodium intake (single 24-hour urine excretion without validation or estimated excretion).

Hypertension Incidence

Urinary Sodium Excretion

The Prevention of Renal and Vascular End-Stage Disease (PREVEND) Study has followed 8,592 men and women since the late 1990s. At a median followup of 6.4 years, they assessed incident hypertension in a subgroup of 5,556 normotensive adults (mean age 43).⁷⁹ They found that the association between urinary sodium excretion and incident hypertension was

significantly modified by serum uric acid and urine albumin excretion. Among individuals in the highest tertiles of serum uric acid and urine albumin, higher sodium intake was significantly associated with higher incidence of hypertension (HR=1.09 and 1.18 respectively; $p<0.05$), adjusting for age, BMI, sex, alcohol intake, smoking status, family history of hypertension, eGFR, plasma glucose and cholesterol, and urinary potassium, calcium, and creatinine (moderate RoB).

At a median followup of 7.6 years, the PREVEND researchers assessed the association between urinary sodium-to-potassium ratio and risk for HTN. After adjustment for age, sex, BMI, smoking status, alcohol consumption, parental history of HTN, education, and urinary magnesium and calcium excretion, multivariate analysis found no association between sodium-potassium excretion ratio and the risk of hypertension (moderate RoB).¹²⁰

The CCCC described above found a significant J-shape relationship between urinary sodium excretion and the risk of hypertension across quartiles. Controlling for BMI, lifestyle, socioeconomic status, baseline diabetes status, and systolic BP, the multivariate analysis showed that, compared with individuals in the second quartile, those in the highest quartile had a significantly higher risk of developing hypertension (RR=1.26; $p=0.043$) while those in the first quartile had a non-significantly higher risk of hypertension (RR=1.24; $P=0.07$) (high RoB).²⁷⁴

Inoue and colleagues found no association between urinary salt (sodium chloride) excretion and the incidence of pregnancy-induced hypertension in the multivariate analysis, further controlling for pregnancy >40 years, chronic hypertension, BUN, creatinine, and baseline blood pressure (high RoB).²⁶⁹

The Trial Of Nonpharmacological interventions in the Elderly (TONE), which randomly assigned 681 elderly US men and women (mean age 65.8) with hypertension to a reduced sodium intervention (dietary counseling with the goal of achieving 80 mmol/d urinary sodium excretion) or control group, assessed the association between urinary sodium excretion and need to resume use of antihypertensives across intervention groups.¹⁷¹ At an average of 27.8 months' followup, dose-response analyses found that greater reduction in urinary sodium excretion was significantly associated with reduced risk of an end point defined by the occurrence of systolic BP \geq 150 mmHg, diastolic BP \geq 90mmHg, resumption of anti-hypertensives, or a CVD event (low overall RoB).

Dietary Sodium Intake

The China Health and Nutrition Survey (CHNS) followed a cohort of 16,869 Chinese adults, aged 20 to 60, over 10 years.¹⁴⁵ After adjusting for energy intake, age, sex, education, income, region, BMI, physical activity, smoking status, and alcohol consumption, flexible parametric models showed a significant dose-response association between sodium intake (from multiple 24-hour dietary recalls) in the third to fifth quintiles and incident hypertension (HR=1.20, 1.37, and 1.84, respectively [95% CI not reported]; $p<0.05$) (moderate RoB).

In summary, a low strength of evidence supports an association of sodium intake with incident hypertension in adults. Most studies had high RoB, largely based on the methods used to assess sodium intake.

Child Studies

Mean Systolic and Diastolic Blood Pressure

Three prospective cohort studies, described in five publications, followed children 17 and younger.^{104, 109, 112, 132, 146}

24-Hour Urinary Sodium Excretion

Shi and colleagues followed a sub-cohort of 6-year old healthy children from the DONALD study, described above, for 10 years.¹⁴⁶ Using two adjustment models, they found no statistically significant association between 24-hour urinary sodium excretion and systolic or diastolic BP either in the pre-pubertal or in the pubertal stage (moderate RoB: single 24-hour sample with validation).

Estimated Urinary Sodium Excretion From Spot Urine

Geleijnse and colleagues followed a cohort of 233 healthy children, aged 5 to 17, who resided in a small Netherlands town.¹³² At a median of 7 years' followup, no significant association was observed between estimated 24-hour urinary sodium excretion (from overnight collection) and systolic or diastolic BP (low RoB).¹³²

Dietary Assessment of Sodium Intake

Vitolo and colleagues followed a cohort of 331 full-term healthy infants from low-income families in Brazil for 3 to 4 years from birth and reported a significant association between sodium intake and high systolic BP at 3-4 years.¹¹² The multivariate analysis showed that children consuming more than 1,200 mg of sodium per day presented a significantly greater risk for having high systolic BP, adjusting for exclusively breastfeeding for at least 4 months, child overweight, waist-to-height ratio greater than 0.5 and change in body mass index z score greater than 0.67 (high RoB based on dietary assessment method).

Evidence is insufficient to draw conclusions about the association between sodium intake and BP in children. Two of three studies had high RoB, based on methods used to assess sodium intake.

Sex

Associations were reported by sex only for BP outcomes. No associations were reported for incident HTN or achievement of prespecified blood pressure goals.

24-Hour Urinary Excretion

The Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study followed a cohort of healthy children in Germany from infancy to young adulthood. Krupp et al followed a sub-cohort of adolescents from the DONALD study, from the age of 12 until they reached adult age (18-25).¹⁰⁹ The multivariate analysis, adjusted for adult age, adult BMI, adolescent BP, adolescent height, maternal BP, maternal education, energy intake, intake of saturated fat, as well as fruit and vegetables (including 100% juice), indicated a significantly positive association between 24-hour salt (sodium chloride) excretion and systolic BP in males but not in females. Systolic BP was on average 7.5 mmHg higher in males in the highest quartile compared to those in the lowest quartile of salt excretion. No association was found for DBP in either males or females (moderate RoB: single 24-hour urinary excretion with validation and 3-day food records).

One study that met inclusion criteria assessed the association of sodium excretion with risk for gestational hypertension. Inoue and colleagues followed a cohort of 184 pregnant women in Japan from their 20th to 30th gestational week.²⁶⁹ After adjusting for age, parity, multiple pregnancy, family history of hypertension, BMI, serum uric acid, eGFR, and hematocrit, they

found no association between urinary salt (sodium chloride) excretion and BP (high RoB: single 24-hour urinary excretion with validation).

In their assessments of the association between sodium intake and BP in the DONALD cohort during childhood, the researchers found no differences between boys and girls in the association of sodium intake and BP (in both prepubertal and pubertal age groups) (moderate RoB).¹⁴⁶

Assessment of Dietary Sodium

The NHLBI Growth and Health Study (NGHS) followed a cohort of 10-year old girls in the U.S. over 10 years (to the age of 20).¹⁰⁴ Adjusting for race, height, activity levels, screen time, energy intake (and percentage of calories from solid fats and added sugar), and dietary fiber, they found no association between sodium intake (from multiple 3-day diet records) and systolic or diastolic BP (high RoB: dietary assessment method).

Thus, evidence is insufficient based on lack of direct comparisons to draw conclusions regarding a moderating effect of sex on the association between lower sodium intake and blood pressure, incident hypertension, or achievement of a prespecified goal.

Race/Ethnicity

Only one cohort study assessed associations by race. In race-stratified analyses, the NGHS study, which relied on 3-day diet records to assess sodium intake) reported no association between sodium intake and BP either among black or among white women.¹⁰⁴

Thus, evidence is insufficient based on lack of direct comparisons to draw conclusions regarding a moderating effect of race/ethnicity on the association of lower sodium intake on blood pressure, incident hypertension, or achievement of a prespecified goal.

Key Question 2b. Subpopulations Defined by Hypertension, Diabetes, and Obesity Health Status

Description of Included Studies

One prospective cohort study¹³⁹ that met inclusion criteria enrolled men and women with hypertension. One study included only people with stage 3 chronic kidney disease.¹¹¹ The remaining studies enrolled entirely or mostly healthy people.

One study compared the association between sodium concentrations in spot urine and BP in overweight (BMI>25) with that in non-overweight (BMI≤25) individuals.¹³⁵

No studies that met inclusion criteria assessed the moderating role of diabetes.

Detailed Synthesis

Hypertension

No studies compared outcomes between normotensive and hypertensive individuals.

In a study described above that followed a cohort of adults with hypertension in a worksite-based program, Singer and colleagues reported that at 6.5 years, a higher quartile of sodium intake was slightly but significantly associated with lower systolic BP among hypertensive men and women, while no association was found with diastolic BP (high RoB for assessment of sodium intake).¹³⁹

TONE, which assessed the effect of a sodium reduction intervention among hypertensive older adults, found that greater reduction in sodium intake was associated with lower risk of having elevated BP, resumption of anti-hypertensive medication, or a CVD event in dose-response analyses (low RoB).¹⁷¹

Thus, evidence is insufficient, based on number of studies and indirect comparisons, to draw conclusions regarding the moderating effect of hypertension on the association between sodium intake and BP.

Renal Health Status

No studies directly compared groups with kidney disease and those with healthy individuals.

One study assessed associations between sodium excretion and BP among those with impaired renal health (high RoB: estimated urinary sodium).¹¹¹ The RRID study, which followed men and women with stage 3 chronic kidney disease, reported that decreased sodium intake was significantly associated with reduced systolic and diastolic BP (high RoB).

Thus, evidence is insufficient, based on only one prospective cohort study, to draw conclusions regarding the moderating effect of renal health status on the association between sodium intake and BP.

Obesity

Only one study assessed the potential moderating effect of overweight or obesity on the association between sodium intake and outcomes of interest.¹³⁵

Among non-overweight individuals (BMI<25), the CIRCUS found a significant association between multivariable-adjusted sodium concentration in spot urine and systolic BP, where a 53mmol/l increase in sodium concentration increases systolic BP by 1.1 mmHg. Nonetheless, the relationship slightly attenuated when further adjusting for baseline systolic BP (p=0.078). Among overweight individuals, no significant association was observed between sodium concentration and systolic BP. For both overweight and non-overweight people, no association was found between sodium concentration and diastolic BP (moderate RoB).¹³⁵

Thus, evidence is insufficient, based on one prospective cohort study, to draw conclusions regarding the moderating effect of weight status on the association between sodium intake and BP.

Key Question 3. Effects of Interventions To Reduce Sodium Intake on CVD and Kidney Disease Morbidity and Mortality, and on Total Mortality, in Adults

Key Points

- In adults, evidence is insufficient to draw a conclusion regarding the effect of sodium reduction on the risk for all-cause mortality (seven RCTs; moderate RoB).
- In adults, evidence is insufficient to draw a conclusion regarding the effect of sodium reduction on the risk for CVD mortality (two RCTs; low RoB).
- In adults, a low strength of evidence suggests that sodium reduction decreases risk for combined CVD morbidity and mortality (eight RCTs; low RoB).

- In adults, a low strength of evidence suggests that sodium reduction may not affect risk for stroke (three RCTs; low RoB overall).
- In adults, evidence is insufficient to assess the effect of sodium reduction on the risk for myocardial infarction (one RCT; low RoB).
- In adults, a low strength of evidence suggests that sodium reduction decreases risk for a composite measure of any CVD outcomes as reported by study authors (seven RCTs; low RoB).
- Evidence is insufficient to draw conclusions about the moderating effects of sex, race/ethnicity, age, or reproductive status on the effects of sodium reduction on CVD or CHD outcomes.
- Evidence is insufficient to draw conclusions on the moderating effects of hypertension, diabetes, or renal disease on the effects of sodium reduction interventions on all-cause, CVD, or CHD mortality, CVD- or CHD morbidity, or other longer term CVD outcomes.
- Conflicting evidence from two RCTs is insufficient to draw conclusions regarding the moderating impact of overweight or obesity on the effect of sodium reduction on composite CVD outcomes (low RoB).
- Evidence was insufficient, based on one RCT, to draw conclusions on whether the effects of sodium reduction on clinical CVD, CHD, and renal outcomes as well as all-cause mortality are affected by higher dietary potassium.
- Evidence was insufficient, based on two RCTs, to draw conclusions on the moderating effects of potassium-containing salt substitutes on the effects of sodium reduction on clinical CVD, CHD, and renal outcomes and all-cause mortality.

Overview

This question addresses three subquestions: a) the moderating effects of other minerals on the effects of reduced sodium on all-cause mortality and CVD/CHD mortality and morbidity; b) the effects of reduced sodium on those outcomes in adults, and moderating effects of sex and race/ethnicity; and c) moderating effects of comorbidities on those outcomes. We begin by addressing subquestion b.

Key Question 3b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

Description of Included Studies

A total of ten RCTs (reported in 14 publications) that met inclusion criteria reported on the effects of reduced sodium intake on all-cause mortality, CVD, CHD, or renal morbidity (including stroke) or mortality.^{36, 42, 113, 130, 148, 170, 171, 192, 196, 234, 273, 275, 284}

All studies randomized participants to receive counseling/ education about reducing dietary sodium or no counseling; two studies also used a potassium-containing salt substitute.^{196, 275}

One study enrolled newborn infants with normal blood pressure;²³⁴ one enrolled adults with normal blood pressure;⁴² one study, the TOHP Follow Up Study, which combined the populations of two earlier studies, TOHP I and TOHP II, enrolled individuals with prehypertension (high normal blood pressure);^{130, 148, 273} and six studies enrolled only participants with hypertension.^{113, 171, 192, 196, 275, 284}

Follow-up times ranged from 3 months to 240 months. Three studies occurred in the US, one in Australia, one in Taiwan, one in China, two in the UK, and one in South Africa.

Nine studies had a low RoB and one had a moderate RoB.

Three RCTs stratified analyses of the effects of interventions to decrease sodium by one of the demographic subgroups of interest. Outcomes for which stratified analyses were reported included all-cause mortality¹⁹² and composite CVD outcomes.^{36, 148} Two RCTs reported outcomes by sex,^{36, 148} two reported outcomes by race/ethnicity; and three reported outcomes by age.^{36, 148, 192} No studies stratified outcomes exactly by the DRI age categories, and no studies stratified outcomes by reproductive status (pregnant or breastfeeding).

Detailed Synthesis

Of nine RCTs that reported on all-cause mortality or CVD outcomes,^{36, 42, 113, 130, 148, 170, 171, 192, 196, 234, 273, 275, 284} none stratified by DRI age categories. Three RCTs stratified CVD outcomes by age group.^{36, 148, 192}

The TONE study reported that individuals with hypertension in the 60-69 age group had a significant beneficial effect of reduced sodium on the risk for a cardiovascular event during a mean followup of 28 months (HR 0.66, 95% CI 0.54, 0.82), whereas individuals in the 70-80 age group had a non-significant benefit (HR 0.75, 95% CI 0.50, 1.14).³⁶

The combined TOHP I and TOHP II followup study showed similar non-significant benefits of sodium reduction for composite cardiovascular disease outcomes (myocardial infarction, stroke, coronary revascularization, or cardiovascular death) for age groups 30-44 and 45-54.¹⁴⁸

The remainder of this section describes the findings of studies in adult populations by outcomes of interest.

All-Cause Mortality

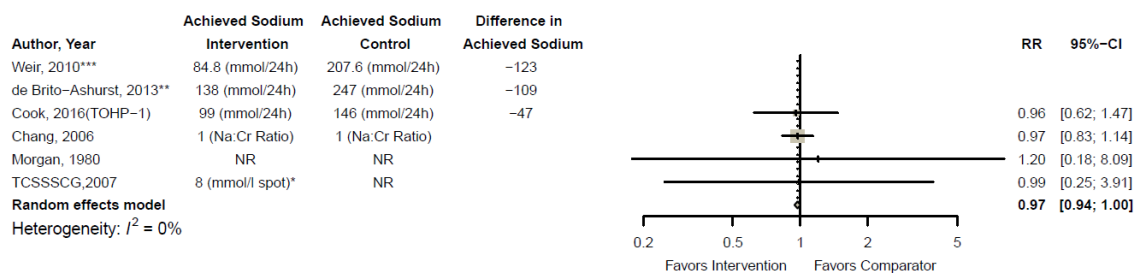
Seven studies (described in six publications) reported on the effects of sodium reduction on deaths from any cause,^{113, 169, 196, 273}

Three of the studies reported the deaths as reasons for withdrawal or as serious adverse events, rather than as prespecified outcomes.^{113, 169, 196}

Two studies, described in one publication, reported a non-significant intervention-related decrease in all-cause mortality.²⁷³ In a study designated the Trials of Hypertension Prevention Follow-up Study, Cook and colleagues (2016) followed up participants from the TOHP I⁵¹ and TOHP II⁵³ trials to assess the effects of dietary sodium reduction on all-cause mortality (a secondary outcome to CVD) over 20 years using ITT analysis. Net 24-hour urinary sodium decreased in the intervention groups by 44mmol and 33 mmol, respectively (absolute levels achieved were not reported). Within each study and in the combined studies, adjusted all-cause mortality was slightly but not significantly lower in the reduced sodium group (HR 0.85, CI 0.66, 1.09). We included TOHP I and TOHP II separately in our analysis.

A random-effects meta-analysis of the studies^{51, 53, 113, 169, 170, 182, 196} that assessed the effects of interventions to reduce sodium on all-cause mortality found a non-significant effect of sodium reduction on decreasing the risk for all-cause mortality (RR 0.97, 95% CI 0.94, 1.00, I² 0%; n=4,328; moderate RoB) (Figure 20). The findings suggest that sodium reduction might slightly decrease the risk for all-cause mortality in adults but the evidence is insufficient to draw a conclusion based on inconsistency in the direction of findings, considerable imprecision, and the fact that most studies were not powered to assess mortality as an outcome).

Figure 20. Relative risk for all-cause mortality in sodium reduction trials



* difference between intervention and control

** unable to calculate RR due to 0 deaths in control (1 death in intervention)

*** unable to calculate RR due to 0 deaths in control & 0 deaths in intervention

TCSSSCG = The China Salt Substitute Study Collaborative Group

Figure notes: Weighted mean differences for sodium excretion: -61 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RR=relative risk

CVD Mortality

Two RCTs reported on the effects of reduced dietary sodium on CVD mortality in adults.^{170, 182, 273} One trial enrolled adults with HTN,¹⁷⁰ and the other enrolled a mixture of hypertensive and normotensive older men.¹⁸² The mean follow up time for the two RCTs was only 3 years.^{170, 182}

Morgan reported no difference in rates of mortality due to CVD between the low sodium and usual care groups (moderate RoB).¹⁷⁰ The study by Chang reported a significant decrease in age-adjusted risk for CVD mortality in the group that received potassium-enriched salt (RR 0.59, 95% CI: 0.37, 0.95).¹⁸² These findings present insufficient evidence, based on the identification of only two studies that met inclusion criteria, with inconsistent findings, to assess whether sodium reduction affects the risk for CVD mortality in adults.

Stroke

Three RCTs reported on incidence of stroke in adults.^{36, 275, 282} The TONE study, with a followup of 33 months, reported it as a prespecified adverse event (Figure 21).³⁶ A feeding study with a duration of 8 weeks reported stroke as a reason for loss of one participant to follow up.²⁷⁵ No significant difference was seen in the incidence of stroke in any study (all low RoB) or in a pooled analysis of the studies. We also assessed the association between mean differences in 24-hour urinary sodium excretion and relative risk for stroke. The weighted mean difference in sodium intake at followup was -35 mmol, and of the three studies, only one reported a mean difference of 40 mmol/d or more:³⁶ Only this RCT reported a (non-significant) decrease in the RR for stroke with sodium reduction. Nevertheless, the findings suggest sodium reduction may not affect the risk for stroke in adults (low strength of evidence).

Figure 21. Relative risk for stroke in sodium reduction trials

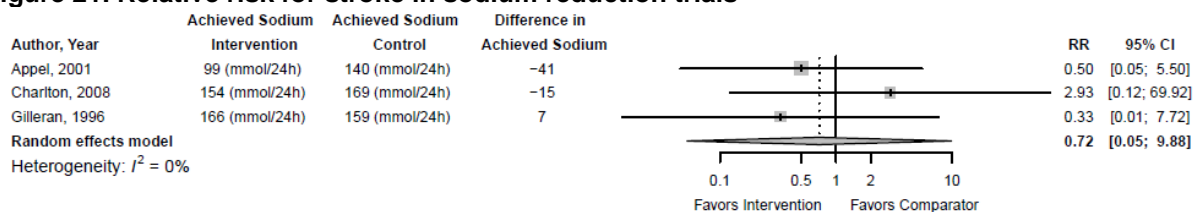


Figure notes: Weighted mean differences for sodium excretion: -35 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RR relative risk

Myocardial Infarction

The TONE study reported on the incidence of MI as an adverse event in older adults.³⁶ During the 30-month period following medication withdrawal, no significant difference was found in the incidence of MI: Two instances of MI were reported in the reduced sodium group, compared with four such events in the control group (effect size not calculated). The evidence based on this one study was insufficient to draw a conclusion regarding the effects of sodium reduction on risk for MI.

Number of Patients With Any CVD Event as Reported by Study Authors

Seven RCTs, described in six publications, reported on some CVD morbidity or mortality endpoint that could be considered for this outcome.^{36, 99, 148, 170, 182, 196}

The TONE study, as described above, reported a composite outcome of blood pressure control (need to begin or resume medication) or CVD/CHD measures over a follow up of 30 months.^{36, 171} They also reported any cardiovascular event as an adverse event outcome: In the reduced sodium group, 36 participants were diagnosed with 44 CV events, compared with 57 events among 46 participants in the control group, a non-significant difference. Reduced sodium resulted in a non-significantly lower risk for experiencing an endpoint (RR 0.81, CI 0.54, 1.21).

The primary outcome for the TOHP I and II followup was a composite of CVD outcomes that included MI, stroke, coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), or CVD mortality at 10 to 15 years followup. Followup information was obtained for 77 percent of participants. The sodium reduction intervention significantly decreased adjusted relative risk for this composite CVD outcome by 25 percent (RR 0.75, 95% CI 0.57, 0.99, $p=0.04$).¹⁴⁸

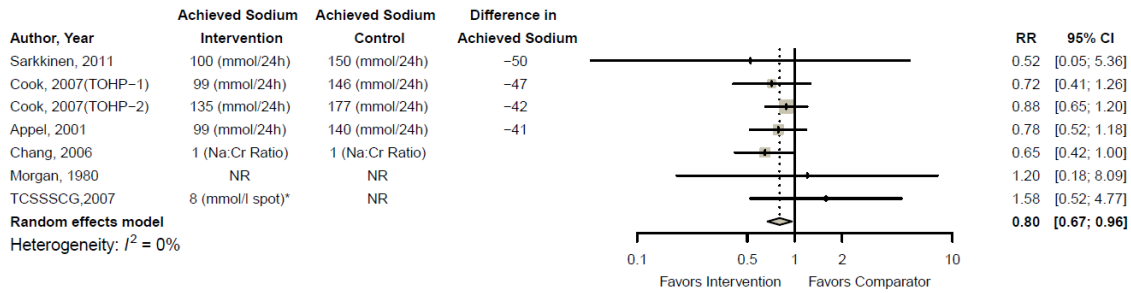
Sarkkinen randomized 45 adults in Finland with mildly elevated BP to use of a salt substitute or to sodium chloride for 8 weeks. The primary outcome was change in BP, but cardiovascular events were reported as adverse events. Intervention participants had a non-significantly decreased risk for these events (RR 0.52, 95% CI 0.05, 5.36).⁹⁹

The China Salt Substitute Study randomized 608 adults to use salt substitute or sodium chloride for 13 months. The primary outcome was blood pressure. At followup, the authors reported 13 serious cardiovascular adverse events—5 in the intervention group and eight in the control group.¹⁹⁶

A random effects pooled analysis that included the TOHP-I and TOHP-II composite outcomes, CVD morbidity outcomes from TONE, the outcomes of the China Salt Substitute Study, the Finnish study,⁹⁹ and two additional trials described above^{148, 170, 171, 182, 196} showed a statistically significant beneficial effect of sodium reduction on this study-specific outcome (RR

0.80, 95% CI 0.67, 0.96, I^2 0%; $n=4,328$; RoB low for four RCTs and moderate for three (Figure 22). These findings provide evidence for an effect of sodium reduction on risk for the composite outcome of any CVD event (low strength of evidence due to inconsistency in direction of effects and imprecision).

Figure 22. Relative risk for any cardiovascular disease event in sodium reduction trials (as reported by the study authors)



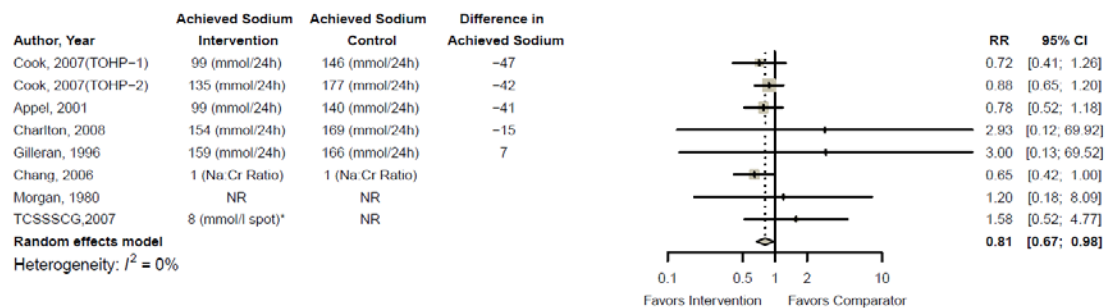
* difference between intervention and control
TCSSSCG = The China Salt Substitute Study Collaborative Group

Figure notes: Weighted mean differences for sodium excretion: -43 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RR=relative risk

Combined CVD Morbidity and Mortality

Eight RCTs that met inclusion criteria reported on the effects in adults of reduced sodium on endpoints that contributed to an outcome of combined morbidity and mortality due to CVD (low RoB).^{51, 53, 170, 171, 182, 196, 275, 282} Reduced sodium significantly decreased the relative risk for this outcome (RR 0.81, 95% CI 0.67, 0.98) (Figure 23). Among three RCTs that reported differences of 40 mmol/d or more in achieved 24-hour sodium excretion, none reported a statistically significant decrease in the RR. These findings provide low strength evidence to support an effect of reduced sodium on this composite outcome (low, based on the inconsistency in direction of effects, imprecision among effect sizes, and reliance on only one study with borderline significance).

Figure 23. Relative risk for combined CVD morbidity and mortality



* difference between intervention and control
TCSSSCG = The China Salt Substitute Study Collaborative Group

Figure notes: Weighted mean differences for sodium excretion: -42 mmol; CI=confidence interval; MD=mean difference; mmol=millimoles per day; RR=relative risk

Other CVD Outcomes

The Hypertension Prevention Trial (HPT) assessed differences in gross morbidity (hypertension) between intervention groups (all adults) and reported no differences.⁴²

A study conducted in China assessed the effects of sodium reduction on left ventricular mass (hypertrophy). Xie (the Chinese PEP investigators) cluster-randomized seven hypertension clinics (169 adults patients) to a manualized educational intervention or to routine care for up to 3 years.²⁸⁴ The intervention included counseling on non-pharmacologic approaches to lower blood pressure. Because randomization was at the clinic level, results were reported as changes from baseline for each group. No significant differences were seen in 24-hour urinary sodium excretion at the end of years 1 or 2. Likewise, left ventricular hypertrophy did not differ significantly between groups. These findings provide an insufficient basis for drawing conclusions regarding the effects of sodium reduction on any other outcomes of interest.

Sex

Two RCTs stratified reports of any CVD outcomes by sex.^{36, 148}

The TONE study reported that men experienced a greater decrease in urinary sodium excretion than did women in response to the intervention (-27 mmol [95% CI $-16, -39$] vs. -53 mmol [95% CI $-41, -64$], $p < 0.001$). Both men and women showed a decreased incidence in the composite CVD outcome measure compared with the control group, similar to that of the overall intervention population (men: HR 0.72, 95% CI 0.56, 0.94, $p = 0.01$; women: HR 0.64, 95% CI 0.49, 0.83, $p = 0.001$).³⁶

Likewise, the combined 12-17-year followup of TOHP I and TOHP II showed similar findings for men and women and for the overall study population, although the effect size was statistically significant only for men (men: HR 0.71, 95% CI 0.51, 0.97, $p = 0.032$; women: HR 0.71, 95% CI 0.35, 1.43, $p = 0.33$).¹⁴⁸

Evidence was insufficient, based on only two RCTs, to draw a conclusion regarding a moderating effect of sex on the effect of sodium reduction on CVD outcomes.

Race/Ethnicity

Two RCTs stratified CVD outcomes by race/ethnicity.^{36, 148}

The TONE study reported that urinary sodium excretion was similar between blacks and whites although within racial groups, sex differences persisted. The relative HR for the composite CVD outcome for blacks associated with the reduced dietary sodium intervention showed a significant beneficial effect, similar to that of non-blacks (HR 0.56, 95% CI, 0.37, 0.84, $p = 0.005$ vs. HR 0.72, 95% CI 0.58, 0.68 [as reported]).³⁶

The combined TOHP I and TOHP II followup study reported that only white participants had a statistically significant composite CVD response to the sodium reduction intervention (HR 0.71, 95% CI 0.52, 0.98; $p = 0.034$), whereas the responses of blacks and individuals of “other” racial/ethnic groups were not significant (blacks: HR 0.86, 95% CI 0.33, 2.26; other: HR 0.08, 95% CI 0.00, 22.90).¹⁴⁸

Evidence was insufficient, based on only two RCTs, to draw a conclusion regarding a moderating effect of race/ethnicity on the effect of sodium reduction on other CVD outcomes.

Key Question 3c. Subpopulations Defined by Hypertension, Diabetes, Obesity, and Renal Health Status

Description of Included Studies

Two RCTs stratified analyses of the effects of interventions to decrease sodium by comorbidity subgroups: the two RCTs reported composite CVD outcomes (combined MI, stroke, CABG, PTCA, and CVD mortality events) by BMI status.^{36, 148} No studies stratified analyses by hypertensive status, diabetes status, or renal health status.

Detailed Synthesis

No RCTs that met inclusion criteria assessed the potential moderating effects of HTN, DM, or renal disease on the effects of sodium reduction on CVD outcomes. Therefore no conclusions can be drawn.

Obesity

The TONE trial reported no significant difference in the effect of sodium reduction on overweight participants compared with those who were not overweight, where overweight was defined as BMI 27.8 or higher for men and 27.3 or higher for women.³⁶

The combined analysis of TOHP I and TOHP II reported that for individuals with BMI of 25 or more, the sodium reduction intervention significantly decreased the risk for the composite CVD outcome (HR 0.72, 95% CI 0.53, 0.96), whereas for those with BMI less than 25, the decrease in risk was not statistically significant (HR 0.24, 95% CI 0.05, 1.16).¹⁴⁸

Thus, conflicting evidence from two RCTs is insufficient to draw conclusions regarding the impact of overweight or obesity on the effect of sodium reduction on composite CVD outcomes. The two RCTs had overall low RoB but high RoB for assessment of sodium intake.

Key Question 3a. Effect of Other Minerals on Effect of Sodium

Description of Included Studies

One RCT, the HPT, compared the effect of counseling to achieve a low sodium/high potassium diet to that of a low sodium diet alone on gross morbidity (defined as hospitalization) and death.⁴² This study was described above in the response to KQ1a. No studies assessed the potential moderating effects of magnesium, calcium, or other minerals.

Detailed Synthesis

Effects of Potassium

All-Cause Mortality

The HPT reported one death each in both the low dietary sodium and low dietary sodium plus high dietary potassium groups (low RoB).⁴² Evidence was insufficient from this one RCT to

draw conclusions on whether the effects of sodium reduction on all-cause mortality are affected by higher dietary potassium.

Other CVD Outcomes

The HPT reported no difference between groups on the outcome of gross morbidity, that is, hospitalization for any reason.⁴² Evidence was insufficient from this one RCT to draw conclusions on whether the effects of sodium reduction on other CVD outcomes are affected by higher dietary potassium.

Key Question 4. Association Between Sodium Intake and CVD, CHD, Stroke, and Kidney Disease Morbidity and Mortality, and Between Sodium Intake and Total Mortality, Among Adults

Key Points

- Although sodium levels appear to be associated with all-cause mortality (low SOE, based on 11 unique observational studies), the shape of this relationship could not be determined (insufficient SOE).
- Evidence is insufficient to draw conclusions regarding associations of sodium intake levels and risk for CVD, CHD, or stroke morbidity and mortality.
- Evidence is insufficient to assess effects of sex, race/ethnicity, age, or comorbidities on associations between sodium intake status and outcomes of interest.

Overview

For this question, for each outcome of interest, we first describe the studies that assess associations for sodium intake of generally healthy populations. Findings are described separately for sodium intake assessed by urinary sodium excretion (24-hour excretion and estimated excretion, separately) and sodium intake assessed by dietary sodium intake. We then describe the studies that assess associations between sodium to potassium ratios and the outcomes of interest: urinary sodium to potassium followed by dietary sodium to potassium.

Detailed Synthesis

Total Mortality

Sodium Intake and Total Mortality

A total of 13 prospective cohort studies^{35, 40, 55, 56, 80, 98, 100, 116, 134, 136, 137, 141, 273} and one nested case-cohort study¹²⁹ that examined the associations between sodium intake levels and total mortality outcomes among generally healthy adult populations were included. These studies included 13 cohorts, which are the combined FLEMENGHO and EPOGH cohort,⁹⁸ the TOHP (I and II) cohort,²⁷³ the Scottish Heart Health study,⁵⁵ PREVEND,¹³⁷ a population-based cohort in south-western Finland,⁵⁶ a pooled analysis of four cohorts (PURE, EPIDREAM, ONTARGET and TRANSCEND),⁸⁰ PURE cohort,¹⁴¹ PURE South America cohort,¹³⁶ the Rotterdam study,¹²⁹ NHANES I,^{35, 40} NHANES II Mortality study,¹³⁴ NHANES III,¹¹⁶ and MONICA.¹⁰⁰ The pooled

analysis of four cohorts⁸⁰ had overlapping study populations with the PURE cohort¹⁴¹ and PURE South America cohort.¹³⁶ The other 10 studies analyzed data from nine non-overlapping cohorts (two studies analyzed data from NHANES I)^{35, 40} across European countries and the U.S. All studies included both adult men and women at baseline (mean ages ranged from 40.9 to 69.2 years). Mean or median followup time ranged from 3.7 to 19 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in five studies,^{55, 56, 98, 137, 273} by spot-urine samples in four studies,^{80, 129, 136, 141} by 24-hour dietary recall in four studies,^{35, 40, 116, 134} and by 3-day dietary records in one study.¹⁰⁰ The sodium intake ranged from 68 mmol/d (1564 mg/d) to 365 mmol/d (8395 mg/d); the wide range might be attributable to the variety of methods used to assess intake. Individual study results are shown in Figure 24 (studies with low or moderate RoB), Table 4 (all studies), and Appendix H (studies with high RoB). The effects are examined separately by sodium intake measurement method.

Overall Summary of Results for Sodium and All-Cause Mortality

Among the nine studies that examined urinary sodium levels and total mortality, the relationships between sodium intake levels and total mortality outcomes are inconsistent.^{55, 56, 80, 98, 129, 136, 137, 141, 273} Five studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risk of total mortality and showed inconsistent results,^{55, 56, 98, 137, 273} although random-effects meta-analysis of three of the studies^{56, 137, 273} showed that a 50 mmol increase in 24-hour urinary excretion level was associated with an average 9 percent increase in the risk of total mortality (pooled RR = 1.09; 95% CI 1.00, 1.19; $I^2 = 22.6\%$). The other two studies could not be included in the pooled analysis: one because it reported only population means, which could not be converted to effect sizes, and one because it did not report confidence intervals (Figure 25).^{55, 98} However, the meta-analysis pooled estimate would have been smaller with wider confidence intervals if all five studies were included, because the two excluded studies both reported non-significant relationships between levels of 24-hour urinary sodium excretion and total mortality outcomes.

Of the four studies that estimated urinary sodium excretion by the Kawasaki equation, three multi-country studies had overlapping study populations: Their results consistently showed a U-shaped association between estimated 24-hour urinary sodium excretion and total mortality outcome.^{80, 136, 141} Overlapping cohorts were grouped together, as they had consistent findings (Figure 24). The fourth study showed no significant linear relationship between estimated 24-hour urinary excretion based on an overnight urine sample and total mortality.¹²⁹

Finally, five studies analyzed data from four cohorts (NHANES I,^{35, 40} NHANES II,¹³⁴ NHANES III,¹¹⁶ and MONICA¹⁰⁰) using dietary sodium intake assessment. Most showed that higher dietary sodium intake levels were associated with an increased risk of total mortality.^{35, 40, 100, 116, 134} Two of the studies (NHANES III,¹¹⁶ and MONICA¹⁰⁰) were rated moderate RoB (Figure 24) and the other three studies were rated high RoB (Appendix H).

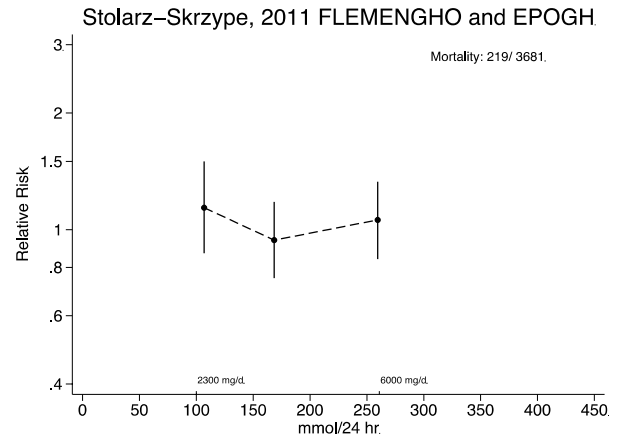
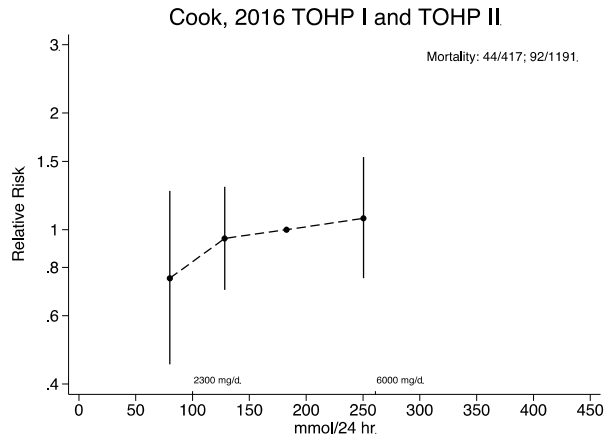
All studies, except for the Scottish Heart Health study, controlled for various demographics, lifestyle factors, and medical history or medications. Among these, PREVEND,¹³⁷ FLEMENGHO, the EPOGH cohort study,⁹⁸ and the Rotterdam study¹²⁹ also adjusted for urinary potassium excretion in their analyses. The Scottish Heart Health study adjusted only for age in their analyses, so the results may be at increased risk for confounding.

The strength of evidence was rated low for the association between higher sodium levels and higher risks for all-cause mortality, primarily because the overall risk of bias was rated moderate and findings were consistent at the higher ranges of sodium intake levels across studies, regardless of methods for assessing sodium intake levels.

We now describe the findings of individual studies in more detail, according to the method of sodium intake assessment.

Figure 24. Categorical analysis of the association between urinary sodium levels and total mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

Panel a. 24-hour urinary excretion measures



Panel b. Dietary sodium intake measures

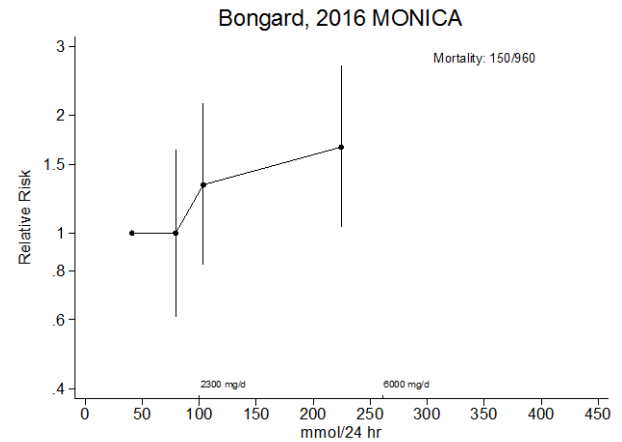
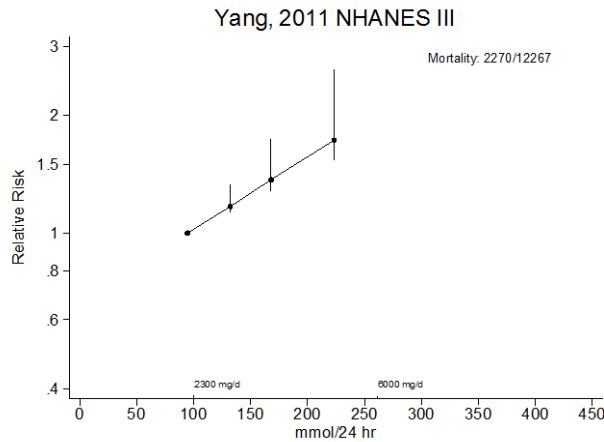


Table 4. Continuous analyses of the association between sodium levels and total mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Cook, 2016 ²⁷³ TOHP I & II	Overweight and pre-HTN	Both	median 25.7 y (TOHP I); 22.4 y (TOHP II)	44/417 (TOHP I); 92/1191 (TOHP II)	0.106 (TOHP I); 0.077 (TOHP II)	24-hour urinary sodium excretion	TOHP I: 3839 mg/d* in men & 2948 mg/d in women; TOHP II: 4576 mg/d in men & 3541 mg/d in women	per 1 mg/d increase	HR	1.12	1	1.26
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	493/7795	0.063	24-hour urinary sodium excretion	Median 155 mmol/24 hr in men & 122 mmol/24 hr in women	per 50-mmol/d increase	HR	1.02	0.9	1.16
Tuomilehto, 2001 ⁵⁶	All	Both	up to 13 years	180/2436	0.074	24-hour urinary sodium excretion	Mean 216 (SD 83) in men & 162 (SD 62) mmol/d in women	per 100 mmol/d increase	HR	1.22	1.02	1.47
	Male	Male	up to 13 years	136/1173	0.116	24-hour urinary sodium excretion	Mean 216 (SD 83)	per 100 mmol/d increase	HR	1.3	1.06	1.59
	Female	Female	up to 13 years	44/1263	0.035	24-hour urinary sodium excretion	Mean 162 (SD 62)	per 100 mmol/d increase	HR	0.91	0.56	1.47
	Normal weight	Male	up to 13 years	60/659	0.091	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	HR	0.98	0.7	1.36

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Overweight	Male	up to 13 years	76/514	0.148	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	HR	1.56	1.21	2.00
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.144	Estimated 24-hour urinary sodium excretion (spot urine)	117 (SD 69) mmol/d in a random sample	per SD increase	RR	0.95	0.81	1.12
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary sodium excretion (spot urine)	NR	per SD increase	RR	1.12	0.86	1.46
He, 1999 ⁴⁰ NHANES I	Non-overweight	Both	mean 19 y	ND/6797	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	0.98	0.88	1.09
	Overweight	Both	mean 19 y	ND/2688	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	1.32	1.16	1.50
Alderman, 1998 ³⁵ NHANES I	All	Both	ND	ND/11346	ND	Dietary sodium intake	Mean 2515 mg/d in men and 1701 mg/d in women	per SD (1313 mg) increase	HR	0.88	0.80	0.96
Cohen, 2006 ¹³⁴ NHANES II	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 (SD 23) mg/d	per 1000 mg/d increase	HR	0.93	0.87	1.00
	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 mg/d	<2300 mg/d vs. ≥2300 mg/d	HR	1.20	1.10	1.40
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary sodium intake	Median 3434 (IQR 2641-4384) mg/d	per 1000 mg/d increase	HR	1.20	1.03	1.41

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Male	Male	median 14.8 y	1267/5899	0.215	Dietary sodium intake	Median 4165 (IQR 3390-5043) mg/d	per 1000 mg/d increase	HR	1.34	1.12	1.6
	Female	Female	median 14.8 y	1003/6368	0.158	Dietary sodium intake	Median 2838 (IQR 2252-3521) mg/d	per 1000 mg/d increase	HR	1.07	0.75	1.53
	Non-Hispanic White	Both	median 14.8 y	1253/2269	0.552	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.23	1.01	1.49
	Non-Hispanic Black	Both	median 14.8 y	527/1540	0.342	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.16	0.93	1.45
	Mexican American	Both	median 14.8 y	449/1859	0.241	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.20	0.91	1.58
	Hypertensive	Both	median 14.8 y	1155/NR	--	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.18	0.88	1.57
	Non-hypertensive	Both	median 14.8 y	1115/NR	--	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.22	1.02	1.46

Table Notes: CI = confidence interval; CVD=cardiovascular disease; HTN=hypertension; HR = hazard ratio; IQR = interquartile range; mg/d=milligrams per day; mmol=millimoles; ND=not determined; NR = not reported; RR = relative risk; SD = standard deviation; y = years; *1000 mg/d ~40 mmol/d

24-Hour Urinary Sodium Excretion and Total Mortality: Individual Studies

Five studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of total mortality and showed inconsistent results.^{55, 56, 98, 137, 273} Specifically, the FLEMENGHO and EPOGH cohort study (moderate RoB),⁹⁸ PREVEND study (moderate RoB)¹³⁷ and the Scottish Heart Health study (high RoB)⁵⁵ found that baseline 24-hour urinary sodium excretion levels were not associated with risks of total mortality, while the TOHP cohort (low RoB) of overweight and pre-hypertensive adults²⁷³ and a Finnish cohort study (high RoB) by Tuomilehto and colleagues (2001)⁵⁶ showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of total mortality at the followups. All studies, except for the Scottish Heart Health study, controlled for various demographics, lifestyle factors, and cardiovascular disease risk factors. The FLEMENGHO and EPOGH cohort and PREVEND studies further controlled for urinary potassium excretion in their analyses. The Scottish Heart Health study adjusted only for age in their analyses so the results may be at higher risk for confounding.

Although five studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risk of total mortality and showed inconsistent results, random-effects model meta-analysis of three of the five prospective cohort studies^{56, 137, 273} showed that a 50 mmol increase in 24-hour urinary excretion level was associated with an average 9 percent increase in the risk of total mortality (pooled RR = 1.09; 95% CI 1.00, 1.19; $I^2 = 22.6\%$) (Figure 25). The other two studies could not be included in this meta-analysis, one because it reported only population means, which could not be converted to effect sizes, and the other because it did not report confidence intervals. Had these two studies been included in the meta-analysis, the pooled estimate would have been smaller and had wider confidence intervals, because both reported non-significant relationships between levels of 24-hour urinary sodium excretion and total mortality outcomes.^{55, 98} Specifically, the FLEMENGHO and EPOGH cohort study showed that low (median = 95 mmol/d in women; 120 mmol/d in men), medium (median = 150 mmol/d in women; 189 mmol/d in men), and high (median = 291 mmol/d in women; 232 mmol/d in men) tertiles of 24-hour urinary sodium excretion were not significantly associated with the risks for total mortality (adjusted HR = 1.14, 95% CI 0.87, 1.50; 0.94, 95% CI 0.75, 1.18; and 1.06, 95% CI 0.84, 1.33, respectively; n=3681).⁹⁸ These analyses compared the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This approach allows computation of CIs for the hazard ratio (HR) in each tertile without definition of an arbitrary reference group.

The Scottish Heart Health study showed a borderline significant inverse relationship between quintiles of 24-hour urinary sodium excretion levels (range from 46.8 to 416.7 mmol/d) and total mortality outcome in men (age-adjusted HR = 0.99, 0.65, 0.86, 0.71 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754), and no significant association in women (age-adjusted HR = 0.61, 0.82, 0.67, 0.85 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875).⁵⁵ Again, because the Scottish Heart Health study adjusted only for age in their analyses, these results are at higher risk for confounding.

Figure 25. Random-effects model meta-analysis of adjusted relative risks of total mortality per 50 mmol/d (1,150 mg/d) increase in urinary sodium excretion in generally healthy populations

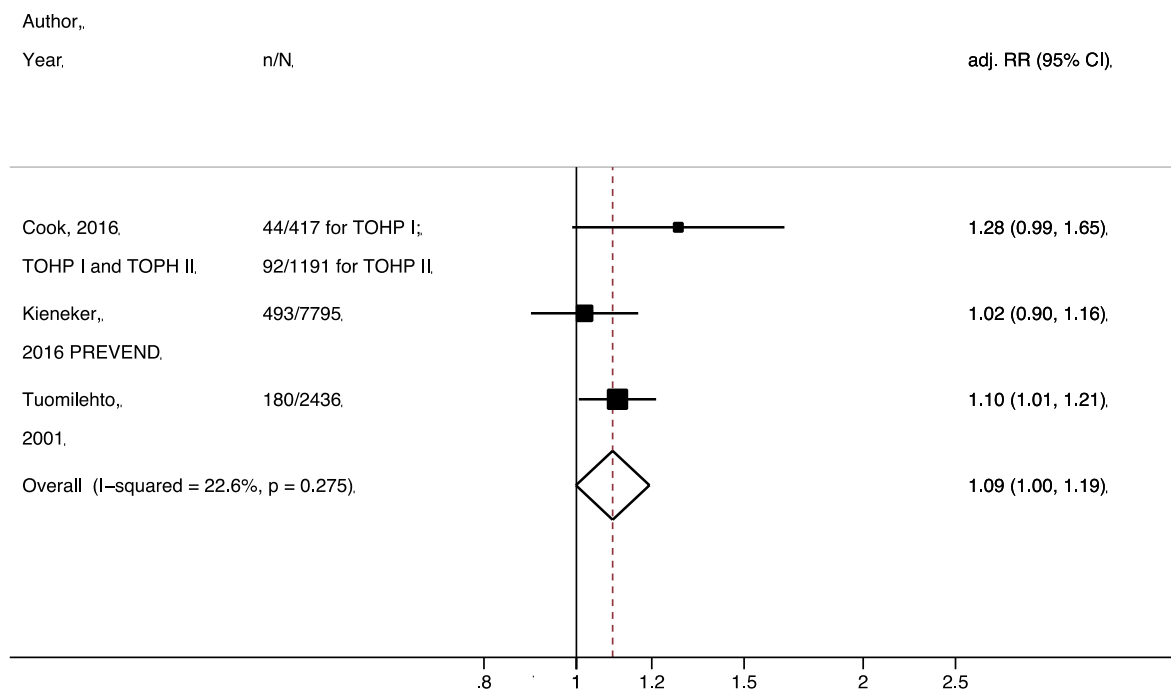


Figure notes: CI = confidence interval; d = day; mg = milligram; n = number of cases; N = total sample number; RR = relative risk

Estimated 24-Hour Urinary Sodium Excretion

The association between *estimated* 24-hour urinary sodium excretion and total mortality was examined in four studies.^{80, 129, 136, 141} Among these four studies, three studies had overlapping study populations, and results consistently showed a U-shaped association between 24-hour urinary sodium excretion estimated by Kawasaki equation and total mortality. The fourth study showed no significant linear relationship between estimated 24-hour urinary excretion based on an overnight urine sample and total mortality.¹²⁹ All four studies were rated high RoB due to sodium exposure assessment methods.^{80, 136, 141}

The pooled analysis of four cohorts (PURE, EPIDREAM, ONTARGET and TRANSCEND) from 49 countries showed a U-shaped relationship between baseline levels of 24-hour urinary sodium excretion (estimated by Kawasaki equation) and risks of total mortality (n=133118), using the median quintile of urinary excretion (195 mmol/d) as the reference group.⁸⁰ That is, compared with urinary sodium excretion of 4 (172 mmol) to 5 (215 mmol) g/day (median = 195 mmol/d), urinary sodium excretion of 7 (300mmol) g/day or more (adjusted HR 1.31, 95% CI 1.17, 1.47]) and less than 3 g/day (adjusted HR 1.41, 95% CI 1.28, 1.54) were both associated with increased risk of total mortality. Similar U-shape relationships were found in subgroup analyses by hypertension status (n=63559 with hypertension and n=69559 without hypertension).⁸⁰ Not surprisingly, the analyses using the PURE cohort (n=101945)¹⁴¹ and PURE South America cohort (n=16549)¹³⁶ also showed U-shaped associations, but the level of urinary sodium excretion used as the reference group was different in the PURE cohort (4 to 5.99 g/day; median = 217 mmol/d), and some comparisons were not statistically significant due to smaller sample sizes. The fourth study, the Rotterdam study, showed no significant linear relationship between estimated 24-hour urinary excretion based on an overnight urine sample and total

mortality (adjusted RR 0.95 per SD increase; 95% CI 0.81, 1.12; n=5531).¹²⁹ Thus, three of these four prospective cohort studies, all with high RoB, showed non-linear associations estimated sodium intake and all-cause mortality risk, and the fourth showed no relationship.

Dietary Sodium Intake and Total Mortality

Five studies examined the relationship between dietary sodium intake and total mortality, analyzing data from four cohorts (NHANES I,^{35,40} NHANES II,¹³⁴ NHANES III,¹¹⁶ and MONICA¹⁰⁰). The studies that analyzed data from NHANES I and II followup cohorts (all rated high RoB), which enrolled a representative US sample from 1971 to 1975 and from 1976 to 1980 respectively, showed an inverse relationship between dietary sodium intake and total mortality.^{35,40,134} In contrast, the studies that analyzed data from the NHANES III followup cohort and MONICA (both rated moderate RoB), which enrolled a representative US sample from 1988 to 1994 and adults living in France between 1995 and 1997, respectively, found a positive relationship between dietary sodium intake and total mortality.^{100,116} These studies mostly showed higher dietary sodium intake levels were associated with an increased risk of total mortality.^{35,40,100,116,134}

The ranges of dietary sodium intake levels differed across studies. In the NHANES I followup study, the mean dietary sodium intake was 2515 mg/day (109 mmol/d) in men and 1701 mg/day (74 mmol/d) in women, and higher dietary sodium intake levels were associated with lower risks of total mortality (adjusted HR 0.88 per SD [1313 mg or 57 mmol] increase; 95% CI 0.80, 0.96; n=11346).³⁵ However, subgroup analyses by overweight status (albeit using different methods) showed a significant positive association among overweight adults. The interaction between sodium intake and body weight (non-overweight vs. overweight) was significant (p for interaction =0.002). In the NHANES II followup study, the mean dietary sodium intake was 2719 mg/day (118 mmol/d), and higher dietary sodium intake levels were associated with lower risks of total mortality (adjusted HR = 0.93 per 1000 mg increase; 95% CI 0.87, 1.00; n=7154).¹³⁴ Furthermore, when compared to dietary sodium intake levels of 2300 mg/day or more, sodium intakes less than 2300 mg/d were significantly associated with an increased risk of total mortality (adjusted HR = 1.20; 95% CI 1.10, 1.40).

In contrast, in the NHANES III followup study, the median dietary sodium intake was 3434 mg/day (149 mmol/d), and higher dietary sodium intake levels were associated with an increased risk of total mortality for both categorical and continuous analyses (adjusted HR = 1.20 per 1000 mg increase; 95% CI 1.03, 1.41; n=12267).¹¹⁶ There were no significant interactions by sex, race/ethnicity, or presence of hypertension. Finally, in the MONICA cohort, the median dietary sodium intake was 2061 mg/day (149 mmol/d), and higher dietary sodium intake levels were associated with an increased risk of total mortality (adjusted HR 1.00, 95% CI 0.61, 1.64, 1.33, 95% CI 0.83, 2.15; 1.66, 95% CI 1.04, 2.68 comparing quartiles 2, 3, and 4 to the lowest quartile, respectively; p=0.023 for trend; n=960) (no figures available).¹⁰⁰

Thus of the five studies that used dietary intake data, the three older studies observed non-linear associations between sodium intake and all-cause mortality risk, whereas the newer studies, with higher median sodium intakes and more refined data collection methods, showed linear associations.

Sodium/Potassium Ratio and All-Cause Mortality

A total of six studies^{87, 98, 116, 129, 137, 273} that reported analyses examining the associations between sodium-to-potassium ratio (Na-K ratio) and total mortality outcome were included. These studies analyzed data from six non-overlapping cohorts among generally healthy adult populations.

Five prospective cohort studies^{87, 98, 116, 137, 273} and one case-cohort study¹²⁹ examined the associations between levels of Na-K ratio and total mortality among generally healthy adult populations. The cohorts included in these studies are the combined FLEMENGHO and EPOGH cohort,⁹⁸ NHANES III,¹¹⁶ PREVEND,¹³⁷ NIPPON DATA80,⁸⁷ TOHP,²⁷³ and the Rotterdam Study.¹²⁹ All studies included both adult men and women. Mean age was reported to be in the 40s for most studies, except for one study that had a mean age of 76.9 years (the Rotterdam Study), and one study that did not report mean age but included participants over 20 years of age (NHANES III). Mean or median followup times ranged from 5 years to 24 years.

Na-K ratios were assessed by 24-hour urinary excretion in three studies,^{98, 137, 273} by spot urine (estimated 24-hour urinary excretion) in one study,¹²⁹ by 24-hour dietary recall in one study,¹¹⁶ and by 3-day weighed food records for each household in one study.⁸⁷ No syntheses were conducted for these studies. Individual study results are shown in Figure 26, Table 5, and Appendix H.

Overall Summary of Results for Sodium/Potassium Ratio and All-Cause Mortality

Among the four studies that examined urinary Na-K ratios and total mortality, the relationships are inconsistent.^{98, 129, 137, 273} However, both studies that assessed dietary Na-K intake showed significant and positive linear associations with total mortality.^{87, 116} All studies controlled for various demographic, clinical, and lifestyle factors. The overall RoB was rated as low to moderate.

Urinary Sodium/Potassium Ratio and Total Mortality

Four studies that examined urinary Na-K ratios and total mortality reported inconsistent results (Figure 26). The TOHP cohort study (low RoB) showed a significant linear association between continuous Na-K ratio and total mortality (adjusted HR = 1.13; 95% CI 1.01, 1.27; n=1608). However, using categories of Na-K ratio, no significant linear trend was detected.²⁷³ In the FLEMENGHO and EPOGH study (moderate RoB), a slight but nonsignificant inverse linear trend (p=.063; n=3681) was detected using tertiles of Na-K ratio, with higher risk of total mortality occurring in the lower tertiles of Na-K ratio.⁹⁸ The Rotterdam study found no relationship between Na-K ratio and total mortality in the full case-cohort or in participants free of CVD and hypertension at baseline.¹²⁹ The PREVEND study (moderate RoB) found no linear association between Na-K ratio and total mortality (adjusted HR = 1.00; 95% CI 0.90, 1.12; n=7795).¹³⁷

Evidence was determined to be insufficient to support any conclusion regarding the association between Na-K ratio and total mortality, because of inconsistency and study quality.

Dietary Sodium/Potassium Ratio and Total Mortality

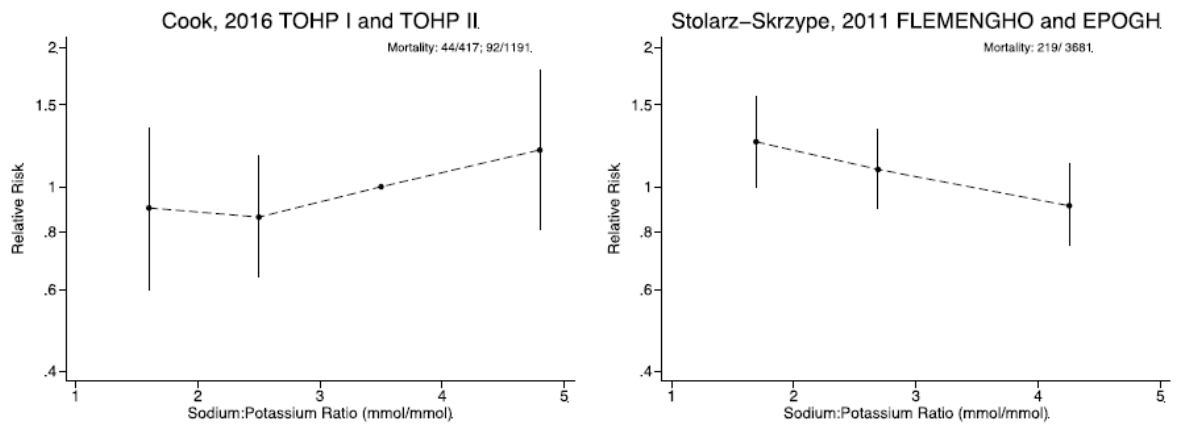
The two studies that assessed dietary Na-K ratio reported consistent significant associations with total mortality.^{87, 116} In NHANES III (moderate RoB, Figure 26), the risk of total mortality increased with increasing quartile of Na-K ratio (p for trend <.001; n=12267).¹¹⁶ In addition, significant linear associations between continuous Na-K ratio and total mortality were reported

among the entire cohort and in all the subgroups examined (sex, race/ethnicity, and hypertension). In the NIPPON DATA80 cohort (high RoB), significant linear (age-adjusted model: $p=.005$; $n=8283$) and quadratic non-linear (fully adjusted model: $p=.001$) trends were found between quintiles of Na-K ratio and total mortality.⁸⁷ Those in the highest quintile of Na-K ratio had a significantly increased risk of total mortality compared to those in the lowest quintile (adjusted HR = 1.16; 95% CI 1.06, 1.27).

Based on the numbers of studies and study quality, evidence was insufficient to support a conclusion regarding the association between Na-K ratio and total mortality.

Figure 26. Categorical analysis of the association between levels of sodium to potassium ratio and total mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

Panel a. 24-hour urinary excretion measures



Panel b. Dietary sodium intake measures

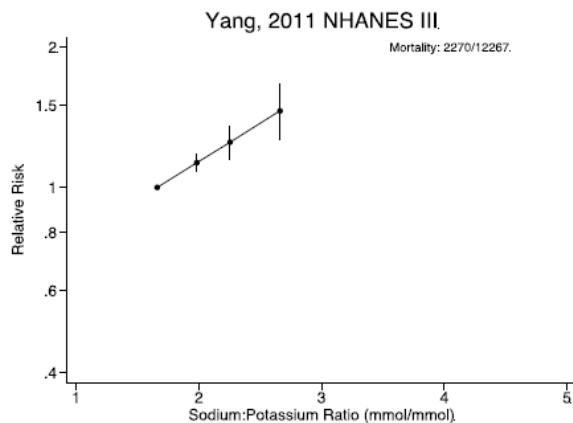


Figure notes: mmol = millimoles

Table 5. Continuous analyses of the association between sodium to potassium ratio and total mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Kieneker, 2016 ¹³⁷ PREVED	All	Both	median 10.5y (IQR 9.9 - 10.8y)	493/7795	0.063	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.00	0.90	1.12
Cook, 2016 ²⁷³ TOHP I & II	Overweight and pre-HTN	Both	median 25.7 y (TOHP I) 22.4 y (TOHP II)	44/417 (TOHP I); 92/1191 (TOHP II)	0.106 (TOHP I); 0.077 (TOHP II)	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.13	1.01	1.27
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.144	Estimated 24-Hour Urinary Excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	1.01	0.91	1.12
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	1.13	0.93	1.36
	CVD free and BMI ≥25 kg/m ²	Both	median 5.5 y	NR/NR	--	Estimated 24-hour urinary potassium excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	1.19	1.02	1.39
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.89	1.5	2.37
	Male	Male	median 14.8 y	1267/5899	0.215	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.84	1.21	2.82
	Female	Female	median 14.8 y	1003/6368	0.158	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.24	1.28	3.91
	Non-Hispanic White	Both	median 14.8 y	1253/2269	0.552	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.91	1.45	2.52

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Non-Hispanic Black	Both	median 14.8 y	527/1540	0.342	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.74	1.08	2.8
	Mexican American	Both	median 14.8 y	449/1859	0.241	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.28	1.05	4.97
	Hypertensive	Both	median 14.8 y	1155/NR	--	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.09	1.17	3.72
	Non-hypertensive	Both	median 14.8 y	1115/NR	--	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.00	1.37	2.91

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; mg = milligram; N = number; NR = not reported; RR = relative risk; SD = standard deviation; y = years

CVD Mortality

Sodium Intake and CVD Mortality

A total eight prospective cohort studies,^{35, 40, 56, 98, 116, 134, 136, 141} and one case-cohort study¹²⁹ examined the associations between sodium intake levels and CVD mortality among generally healthy adult populations were included. These studies included eight cohorts, which are the combined FLEMENGHO and EPOGH cohort,⁹⁸ a population-based cohort in southwestern Finland,⁵⁶ PURE cohort,¹⁴¹ PURE South America cohort,¹³⁶ the Rotterdam study,¹²⁹ NHANES I,^{35, 40} NHANES II Mortality study,¹³⁴ and NHANES III.¹¹⁶ Study populations overlap between the PURE and PURE South America cohorts.^{136, 141} The other 10 studies analyzed data from nine non-overlapping cohorts (two studies analyzed data from NHANES I^{35, 40}) across European countries and the U.S. All studies included adult men and women at baseline (mean ages ranged from 40.9 to 69.2 years). Mean or median followup time ranged from 3.7 to 19 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in two studies,^{56, 98} by spot-urine samples in three studies,^{129, 136, 141} by 24-hour dietary recalls in four studies.^{35, 40, 116, 134} The sodium intake ranged from 95 mmol/d (2176 mg/d) to 365 mmol/d (8395 mg/day). Individual study results are shown in Figure 27, Table 6 and Appendix H.

Overall Summary of Results for Sodium and CVD Mortality

Among the five studies that examined the association between urinary sodium levels and CVD mortality, the relationships are inconsistent.^{56, 98, 129, 136, 141} Of these five, two studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of CVD mortality and showed conflicting results.^{56, 98} Of the remaining three studies, which used 24-hour urinary sodium excretion estimated by Kawasaki equation, two multi-country studies with overlapping study populations showed a U- or J-shaped association between sodium excretion and CVD mortality,^{136, 141} and the third study showed no significant linear relationship.¹²⁹

Four studies that analyzed the association between sodium (assessed by dietary intake assessment) and CVD mortality in NHANES I, II, and III also showed inconsistent results.^{35, 40, 116, 134}

All studies controlled for various demographics, lifestyle factors, and medical history or medications. Among these, the FLEMENGHO and EPOGH cohort study,⁹⁸ and the Rotterdam study¹²⁹ also adjusted for urinary potassium excretion in their analyses.

The strength of evidence was rated insufficient for both linear and non-linear associations between sodium intake levels and CVD mortality, primarily because the findings are inconsistent and the overall RoB was rated high. Indirect (qualitative) comparisons across studies with wide ranges of sodium intake levels (as opposed to analyses within single studies with wide ranges of intake) suggest a non-linear association between sodium intake levels and CVD mortality, but quantitative analyses were not possible. Data are insufficient to determine the inflection point or the shape of this apparent non-linear association, due to limitations and heterogeneity in the sodium exposure assessment methods across studies.

The details of the individual studies are described below, by method of sodium intake assessment.

Description of Individual Studies Using 24-Hour Urinary Sodium Excretion and CVD Mortality

Two studies that examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of CVD mortality showed conflicting results.^{56,98} Specifically, the FLEMENGHO and EPOGH cohort study (moderate RoB)⁹⁸ found a significant inverse association between CVD mortality and tertiles of baseline 24-hour urinary sodium excretion levels ($p=0.02$; $n=3681$), and the low tertile (median = 95 mmol/d in women; 120 mmol/d in men) was associated with a significantly increased risk of CVD mortality (adjusted HR = 1.56; 95% CI 1.02, 2.36) (Figure 27). The medium (median = 150 mmol/d in women; 189 mmol/d in men) and high (median = 291 mmol/d in women; 232 mmol/d in men) tertiles of 24-hour urinary sodium excretion were not significantly associated with risk for CVD mortality (adjusted HR [95% CI] = 1.05 [0.72, 1.53] and 0.95 [0.66, 1.38], respectively). These analyses compared the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This approach allows computation of CIs for the hazard ratio (HR) in each tertile without definition of an arbitrary reference group.

On the contrary, a Finnish cohort study (high RoB) by Tuomilehto et al. (2001)⁵⁶ showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of CVD mortality at followup (adjusted HR per 100 mmol/d increase = 1.36; 95% CI 1.05, 1.76; $n=2436$). The results were similar in subgroup analyses (by sex or by overweight status [normal vs. overweight] status although not statistically significant in women and in normal weight subgroups).

Thus, results of studies that assessed 24-hour urinary sodium excretion were inconsistent.

Description of Individual Studies Using Estimated 24-Hour Urinary Sodium Excretion and CVD Mortality

The association between estimated 24-hour urinary sodium excretion and CVD mortality was examined in three studies.^{129, 136, 141} Two of the studies had overlapping study populations.^{136, 141} All three studies were rated high RoB due to sodium exposure assessment methods. The analyses using the PURE cohort ($n=101945$)¹⁴¹ and PURE South America cohort ($n=16549$)¹³⁶ both showed that highest quintile of urinary sodium excretion (>365 mmol/d) was associated with a significantly increased risk of CVD mortality (adjusted HR [95% CI] = 1.54 [1.21, 1.95] and 1.72 [1.24, 2.4], respectively), but the level of urinary sodium excretion used as the reference group was 4 to 5.99 g/day (median = 217 mmol/d) in the PURE cohort and 5 to 5.99 g/day (median = 239 mmol/d) in the PURE South America cohort. The lowest quintile of urinary sodium excretion (<104 mmol/d) was also associated with a significantly increased risk of CVD mortality in the PURE cohort (adjusted HR = 1.77; 95% CI 1.36, 2.13) but an increase that was not statistically significant in the PURE South America cohort (adjusted HR = 1.2; 95% CI 0.86, 1.65), possibly due to smaller sample sizes.

The third study is the Rotterdam study, which showed a non-significant relationship between estimated 24-hour urinary excretion based on an overnight urine sample and CVD mortality (adjusted RR = 0.77 per SD increase; 95% CI 0.60, 1.01; $n=5531$).¹²⁹

Thus, the findings of the studies that estimated urinary sodium excretion are inconsistent.

Description of Individual Studies Using Dietary Sodium Intake and CVD Mortality

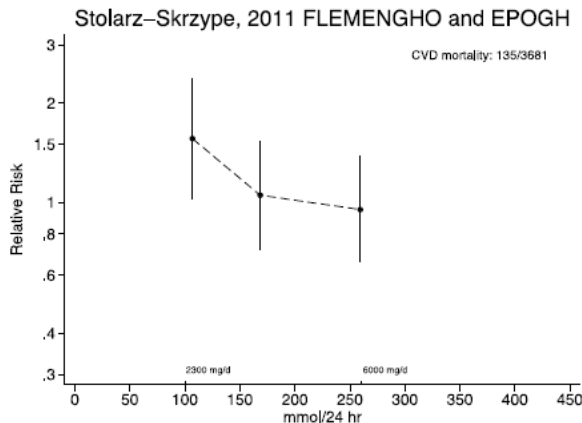
Four studies analyzed data from three cohorts (NHANES I,^{35, 40} NHANES II,¹³⁴ and NHANES III¹¹⁶) to examine the relationship between dietary sodium intake and CVD mortality. Results were inconsistent across studies. The studies that analyzed data from NHANES I and II

followup cohorts (both rated high RoB), which enrolled a US representative sample from 1971 to 1975 and from 1976 to 1980 respectively, showed an inverse relationship between dietary sodium intake and CVD mortality.^{35, 40, 134} In contrast, the studies that analyzed data from the NHANES III followup cohort (moderate RoB), which enrolled a US representative sample from 1988 to 1994, did not find a significant relationship between dietary sodium intake and CVD mortality (Figure 27).¹¹⁶

In the NHANES I followup study, the mean dietary sodium intake was 2515 mg/day (109 mmol/d) in men and 1701 mg/day (74 mmol/d) in women, and higher dietary sodium intake levels were associated with lower risks of CVD mortality (adjusted HR = 0.89 per SD [1313 mg or 57 mM] increase; 95% CI 0.77, 1.02; n=11346).³⁵ However, subgroup analyses by overweight status showed a significant positive association between sodium intake and CVD mortality risk among overweight adults (adjusted RR 1.32 per 100mmol increase; 95% CI 1.16, 1.50; n=2688), but not among normal weight adults (adjusted RR 0.98 per 100mmol increase; 95% CI 0.88, 1.09; n=6797).⁴⁰ In the NHANES II followup study, the mean dietary sodium intake was 2719 mg/day (118 mmol/d), and higher dietary sodium intake levels were associated with lower risks of CVD mortality (adjusted HR = 0.89 per 1000 mg increase; 95% CI 0.80, 0.99; n=7154).¹³⁴ Furthermore, when compared to dietary sodium intake level ≥ 2300 mg/day, sodium intake < 2300 mg/d was associated with a significantly increased risk of CVD mortality (adjusted HR = 1.40; 95% CI 1.10, 1.70). In the NHANES III followup study, the median dietary sodium intake was 3434 mg/day (149 mmol/d), and dietary sodium intake levels were not significantly associated with risks of CVD mortality for both categorical and continuous analyses (adjusted HR = 0.94 per 1000 mg increase; 95% CI 0.67, 1.32; n=12267).¹¹⁶ There were no significant interactions by sex, race/ethnicity, or presence of hypertension.

Figure 27. Categorical analysis of the association between sodium levels and cardiovascular disease mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

Panel A. 24-hour urinary excretion measures



Panel B. Dietary sodium intake measures

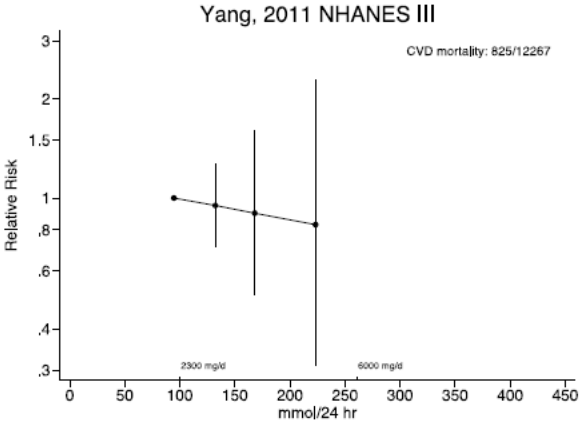


Figure notes: CVD = cardiovascular disease; hr = hours; mmol = millimoles

Table 6. Continuous analyses of the association between sodium levels and CVD mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Tuomilehto, 2001 ⁵⁶	All	Both	up to 13 years	180/2436	0.034	24-hour urinary sodium excretion	Mean 216 (SD 83) in men & 162 (SD 62) mmol/d in women	per 100 mmol/d increase	HR	1.36	1.05	1.76
	Male	Male	up to 13 years	136/1173	0.061	24-hour urinary sodium excretion	Mean 216 (SD 83)	per 100 mmol/d increase	HR	1.38	1.04	1.82
	Female	Female	up to 13 years	44/1263	0.012	24-hour urinary sodium excretion	Mean 162 (SD 62)	per 100 mmol/d increase	HR	1.43	0.73	2.78
	Normal weight	Male	up to 13 years	60/659	0.044	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	HR	1.23	0.76	1.98
	Overweight	Male	up to 13 years	76/514	0.0837	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	HR	1.44	1.02	2.04
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.039	Estimated 24-hour urinary sodium excretion (spot urine)	117 (SD 69) mmol/d in a random sample	per SD increase	RR	0.77	0.60	1.01
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary sodium excretion (spot urine)	NR	per SD increase	RR	0.83	0.47	1.44
He, 1999 ⁴⁰ NHANES I	Non-overweight	Both	mean 19 y	ND/6797	ND	Dietary sodium intake	NR	per 100-mmol/d increase	RR	1.00	0.84	1.19

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Overweight	Both	mean 19 y	ND/2688	ND	Dietary sodium intake	NR	per 100-mmol/d increase	RR	1.45	1.2	1.75
Alderman, 1998 ³⁵ NHANES I	All	Both	ND	ND/11346	ND	Dietary sodium intake	Mean 2515 mg/d in men and 1701 mg/d in women	per SD (1313 mg) increase	HR	0.89	0.77	1.02
Cohen, 2006 ¹³⁴ NHANES II	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 (SD 23) mg/d	per 1000 mg/d increase	HR	0.89	0.80	0.99
	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 mg/d	<2300 mg/d vs. ≥2300 mg/d	HR	1.4	1.1	1.7
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary sodium intake	Median 3434 (IQR 2641-4384) mg/d	per 1000 mg/d increase	HR	0.94	0.67	1.32
	Male	Male	median 14.8 y	1267/5899	0.215	Dietary sodium intake	Median 4165 (IQR 3390-5043) mg/d	per 1000 mg/d increase	HR	1.17	0.81	1.7
	Female	Female	median 14.8 y	1003/6368	0.158	Dietary sodium intake	Median 2838 (IQR 2252-3521) mg/d	per 1000 mg/d increase	HR	0.69	0.38	1.25
	Non-Hispanic White	Both	median 14.8 y	1253/2269	0.552	Dietary sodium intake	NR	per 1000 mg/d increase	HR	0.89	0.58	1.37
	Non-Hispanic Black	Both	median 14.8 y	527/1540	0.342	Dietary sodium intake	NR	per 1000 mg/d increase	HR	0.81	0.51	1.28

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Mexican American	Both	median 14.8 y	449/1859	0.241	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.33	0.75	2.35
	Hypertensive	Both	median 14.8 y	1155/NR	--	Dietary sodium intake	NR	per 1000 mg/d increase	HR	0.86	0.56	1.31
	Non-hypertensive	Both	median 14.8 y	1115/NR	--	Dietary sodium intake	NR	per 1000 mg/d increase	HR	1.05	0.69	1.59

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; mg=milligrams; mmol/d=millimoles per day; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium/Potassium Ratio and CVD Mortality

A total of four studies^{87, 98, 116, 129} that reported analyses examining the associations between Na-K ratio and CVD mortality were identified. These studies analyzed data from four non-overlapping cohorts among generally healthy adult populations.

Three prospective cohort studies^{87, 98, 116} and one case-cohort study¹²⁹ examined the associations between levels of Na-K ratio and CVD mortality among generally healthy adult populations. The cohorts included in these studies are the combined FLEMENGHO and EPOGH cohort,⁹⁸ NHANES III,¹¹⁶ NIPPON DATA80,⁸⁷ and the Rotterdam Study.¹²⁹ All studies included both adult men and women. Mean age was reported to be in the 40s for two of the studies (FLEMENGHO/EPOGH and NIPPON DATA80), and 76.8 years for the cases in the Rotterdam Study; the NHANES III study did not report mean age but included participants >20 years of age. Mean or median followup time ranged from 5 years to 24 years.

Na-K ratios were assessed by 24-hour urinary excretion in one study,⁹⁸ by spot urine (estimated 24-hour urinary excretion) in one study,¹²⁹ by 24-hour dietary recall in one study,¹¹⁶ and by 3-day weighed food records for each household in one study.⁸⁷ Individual study results are reported below and shown in Figure 28, Table 7, and Appendix H.

Overall Summary of Results for Sodium to Potassium Ratio and CVD Mortality

The relationships between levels of Na-K ratio and CVD mortality outcome are inconsistent among the two studies that examined urinary Na-K ratios and CVD mortality.^{98, 129} However, both studies that assessed dietary Na-K intake showed significant and positive linear associations of the Na-K ratio with CVD mortality.^{87, 116} All studies controlled for various demographic, clinical, and lifestyle factors. The overall RoB was rated as low to moderate.

Description of Individual Studies Assessing Urinary Sodium/Potassium Ratio and CVD Mortality

Two studies that examined urinary Na-K ratios and CVD mortality reported inconsistent results. The FLEMENGHO/EPOGH study (moderate RoB) reported a significant inverse linear trend ($p=.0069$; $n=3681$) using tertiles of Na-K ratio, with higher risk of CVD mortality occurring in the lower tertiles of Na-K ratio when each tertile was compared to the overall risk in the whole cohort (Figure 28).⁹⁸ However, in the Rotterdam study (high RoB), no relationship was observed between Na-K ratio and CVD mortality in the full case-cohort, in healthy participants, or in CVD-free participants with a BMI ≥ 25 kg/m².¹²⁹ Thus, findings were inconsistent between the two studies that assessed urinary Na-K ratio.

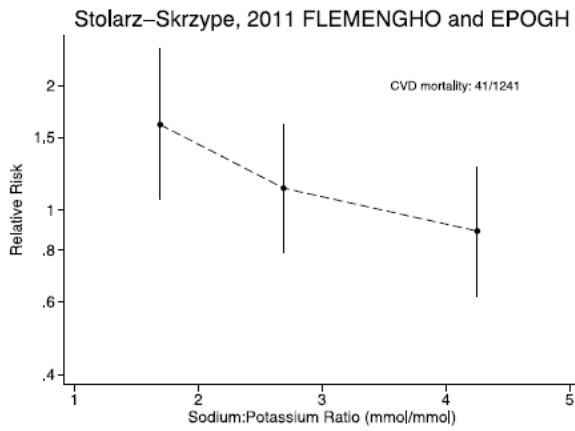
Description of Individual Studies Assessing Dietary Sodium/Potassium Ratio and CVD Mortality

The two studies that assessed dietary Na-K ratio reported consistent significant associations with CVD mortality.^{87, 116} In NHANES III (moderate RoB), the risk of CVD mortality increased with increasing quartile of Na-K ratio among the whole cohort (p for trend =.01; $n=12267$) (Figure 28).¹¹⁶ In addition, a significant linear association between continuous Na-K ratio and CVD mortality was reported among the whole cohort (HR = 1.90; 95% CI 1.20, 3.03). In subgroup analyses, significant linear associations were found in men, but not in women; in non-Hispanic Blacks and Mexican-Americans, but not in non-Hispanic Whites; and in both hypertensives and non-hypertensives. In the NIPPON DATA80 cohort (high RoB), significant linear (age-adjusted model: $p=.032$; $n=8283$) and quadratic non-linear (fully adjusted model: $p=.005$) trends were found between quintiles of Na-K ratio and CVD mortality.⁸⁷ Those in the

highest quintile of Na-K ratio had a significantly increased risk of CVD mortality compared to those in the lowest quintile (adjusted HR = 1.39; 95% CI 1.20, 1.61).

Figure 28. Categorical analysis of the association between sodium levels and cardiovascular disease mortality outcome in generally healthy populations (data from studies rated low or moderate risk of biasRoB)

Panel a. 24-hour urinary excretion measures



Panel b. Dietary sodium intake measures

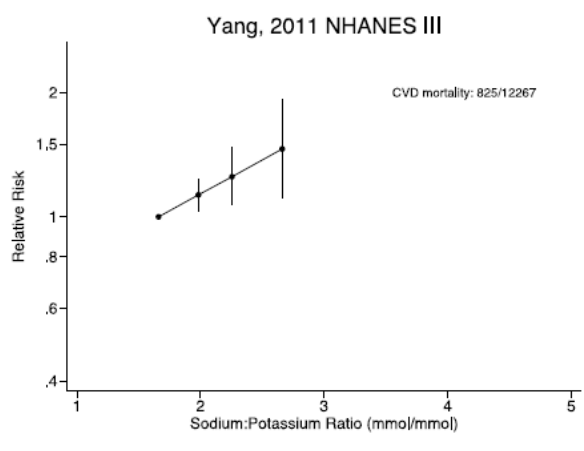


Table 7. Continuous analyses of the association between sodium to potassium ratio and CVD in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	217/5531	0.039	Estimated 24-Hour Urinary Excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	0.92	0.80	1.07
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	0.91	0.65	1.27
	CVD free and BMI \geq 25 kg/m ²	Both	median 5.5 y	NR/NR	--	Estimated 24-hour urinary potassium excretion (spot urine)	NR	per 1-unit increase (mmol/m mol)	RR	0.86	0.60	1.25
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	825/12267	0.067	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.90	1.20	3.03
	Male	Male	median 14.8 y	437/5899	0.074	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.24	1.11	4.52
	Female	Female	median 14.8 y	388/6368	0.061	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.74	0.73	4.14
	Non-Hispanic White	Both	median 14.8 y	498/2269	0.219	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.66	0.93	2.95
	Non-Hispanic Black	Both	median 14.8 y	163/1540	0.106	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.93	1.05	3.57
	Mexican American	Both	median 14.8 y	147/1859	0.079	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	5.88	1.67	20.68
	Hypertensive	Both	median 14.8 y	490/NR	--	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	2.40	1.09	5.31
	Non-hypertensive	Both	median 14.8 y	335/NR	--	Dietary sodium/potassium intake	NR	per 1-unit increase (mg/mg)	HR	1.95	1.00	3.80

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; mg=milligrams; mmol/d=millimoles per day; NR = not reported; RR = relative risk; SD = standard deviation; y = year

Other CVD Outcomes

Sodium Intake and Other CVD Outcomes

Two publications^{97, 151} reported analyses examining the associations between sodium intake levels and other CVD outcomes among generally healthy adult populations. The two studies are the EPIC-Norfolk prospective cohort study⁹⁷ and the NHANES I followup study.¹⁵¹ Both studies included both adult men and women at baseline and reported heart failure outcomes, and were rated high RoB. Mean or median followup times were 12.9 and 19 years. Sodium intake levels were assessed by spot-urine samples in one study,⁹⁷ and by 24-hour dietary recall in another.¹⁵¹ The sodium intake ranged from 33.7 mmol/d (775 mg/d) to 229 mmol/d (5272 mg/d). Individual study results are described below and shown in Appendix H.

Overall Summary of Results for Sodium and Other CVD Outcomes

Two studies that met inclusion criteria and assessed the association between sodium intake and other CVD outcomes reached partly consistent conclusions. The EPIC-Norfolk prospective cohort study⁹⁷ reported a U-shaped association between estimated urinary sodium and risk for heart failure. The NHANES I followup study reported a significant association between dietary sodium intake and risk for congestive heart failure (CHF).

Description of Individual Studies Using Estimated 24-Hour Urinary Sodium Excretion and Other CVD Outcomes

The EPIC-Norfolk prospective cohort study (n=19857)⁹⁷ showed a U-shaped relationship between estimated 24-hour urinary sodium excretion levels (estimated by Tanaka equation) and risks of heart failure, using the second quintile level of urinary sodium excretion as the reference group (128 to 148 mmol/d). Specifically, both lowest (≤ 127 mmol/d) and highest (≥ 191 mmol/d) quintiles of estimated urinary sodium excretion levels were associated with a significant increased risk of heart failure (adjusted HR [95% CI] = 1.30 [1.08, 1.55] and 1.22 [1.06, 1.46] in the multivariable model including blood pressure as covariates. Similar U-shaped relationships were shown in men and in women.

Description of Individual Studies Using Dietary Sodium Intake and Other CVD Outcomes

NHANES I followup study showed no associations between dietary sodium intake levels and risks of congestive heart failure (CHF) among non-overweight adults (n=5233), but showed that highest quartile of dietary sodium intake level (mean = 167.6 mmol/d) was significantly associated with an increased risk of CHF (adjusted HR = 1.43; 95% CI 1.01, 1.91) compared to the lowest intake level (mean = 33.7 mmol/d) among overweight adults (n=5129).¹⁵¹ In continuous analyses, relative risk of CHF for a 100-mmol/d higher intake of sodium was 0.90 (95% CI, 0.67, 1.20) among non-overweight adults, and 1.26 (95% CI, 1.03, 1.53) among overweight adults.

Coronary Heart Disease Mortality

Sodium Intake and Coronary Heart Disease Mortality

A total of five publications^{40, 55, 56, 116, 134} that analyzed the associations between sodium intake levels and coronary heart disease (CHD) or ischemic heart disease (IHD) mortality met inclusion criteria. These publications analyzed data from five non-overlapping studies among generally healthy adult populations.

Five prospective cohort studies^{40, 55, 56, 116, 134} examined the associations between sodium intake levels and CHD or IHD mortality outcomes among generally healthy adult populations. These cohorts are the Scottish Heart Health study,⁵⁵ a population-based cohort study set in south-western Finland,⁵⁶ NHANES I,⁴⁰ the NHANES II Mortality study,¹³⁴ and NHANES III.¹¹⁶ All studies included both adult men and women at baseline (mean ages ranged from 43 to 48 years). Mean or median followup times ranged from 7.6 to 19 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in two studies,^{55, 56} and by 24-hour dietary recall in three studies.^{40, 116, 134} The sodium intake ranged from 68 mmol/d (1564 mg/d) to 253 mmol/d (5826 mg/d).

Overall Summary of Results for Coronary Heart Disease Mortality

The relationships between sodium intake levels and CHD or IHD mortality outcomes are inconsistent between the two studies that examined urinary sodium levels and CHD mortality.^{55, 56} Both studies were rated high RoB. The other three studies, which assessed dietary sodium intake, mostly showed non-significant associations with CHD or IHD mortality outcome.^{40, 116, 134} Except for the Scottish Heart Health study, all studies controlled for various demographics, lifestyle factors, and medical history or medications. The Scottish Heart Health study adjusted only for age in their analyses, so the results may be at increased risk for confounding. The overall risk of bias was rated high. The strength of evidence was rated insufficient, primarily because of high RoB and inconsistent findings across studies. Individual study results are shown in Figure 29, Table 8, and Appendix H.

Description of Individual Studies Using 24-Hour Urinary Sodium Excretion and CHD Mortality

Two studies that examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of CHD mortality showed inconsistent results.^{55, 56} Both studies were rated high RoB. The Scottish Heart Health study adjusted only for age in their analyses so the results may be at higher risk for confounding. Specifically, the study⁵⁵ reported that baseline 24-hour urinary sodium excretion levels were positively associated with risks of CHD mortality in women (age-adjusted HR 0.36, 0.41, 0.85, 2.05 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875), but not in men (age-adjusted HR 0.96, 0.62, 0.97, 10.92, comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754). A Finnish cohort study by Tuomilehto and colleagues (2001)⁵⁶ showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of CHD mortality at follow up (adjusted HR 1.56; 95% CI 1.15, 2.12; n=2436). The positive association between 24-hour urinary sodium excretion and CHD mortality was significant only in men (adjusted HR = 1.55; 95% 1.12, 2.13; n=1263), but not in women (adjusted HR 2.07; 95% 0.80, 5.36; n=1263). Thus, the two studies showed conflicting findings.

Description of Individual Studies Using Dietary Sodium Intake and CHD Mortality

Three studies analyzed data from the NHANES I,⁴⁰ NHANES II,¹³⁴ and NHANES III¹¹⁶ cohorts to examine the relationship between dietary sodium intake and CHD or IHD mortality. A subgroup analysis of the NHANES I cohort found that higher dietary sodium intake levels were significantly associated with higher risks of CHD mortality (see response to Key Question 4c).⁴⁰ No other significant associations were identified.

In the NHANES I followup study (high RoB), subgroup analyses by overweight status showed that the association between dietary sodium intake levels and CHD mortality was

significant among overweight adults (adjusted RR 1.29 per 100 mmol increase; 95% CI 1.01, 1.64; n=2688), but not among non-overweight adults (adjusted RR 1.07 per 100 mmol increase; 95% CI 0.89, 1.28; n=6797).⁴⁰ The interaction between sodium intake and body weight (non-overweight vs. overweight) was not statistically significant (p for interaction = 0.22). In the NHANES II followup study (high RoB), the mean dietary sodium intake was 2719 mg/day (118 mmol/d), and higher dietary sodium intake levels were not significantly associated with risks of CHD mortality (adjusted HR 0.91 per 1000 mg increase; 95% CI 0.79, 1.05; n=7154).¹³⁴ Additionally, when compared to dietary sodium intake levels of 2300 mg/day or more, sodium intakes less than 2300 mg/d were not significantly associated with CHD mortality (adjusted HR 1.21; 95% CI 0.87, 1.68). In the NHANES III followup study (moderate RoB), the median dietary sodium intake was 3434 mg/day (149 mmol/d), and dietary sodium intake levels were not significantly associated with risk of IHD mortality for either categorical or continuous analyses (adjusted HR 1.20 per 1000 mg increase; 95% CI 0.80, 1.77; n=12267) (Figure 29).¹¹⁶

Figure 29. Categorical analysis of the association between dietary sodium levels and CHD mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

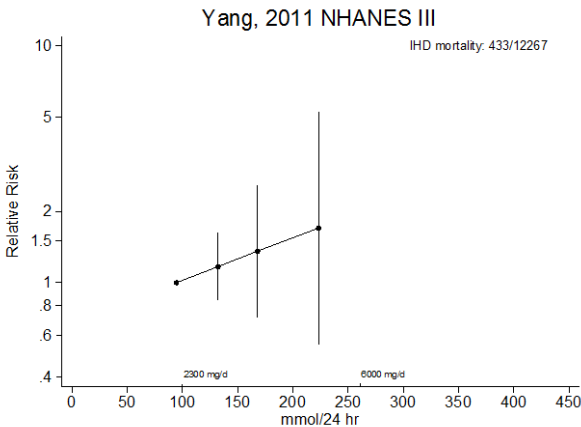


Figure notes: d = day; hr = hour; IHD = ischemic heart disease; mg = milligrams; mmol = millimole

Table 8. Continuous analyses of the association between sodium levels and CHD mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Tuomilehto, 2001 ⁵⁶	All	Both	up to 13 years	61/2436	0.025	24-hour urinary sodium excretion	Mean 216 (SD 83) in men & 162 (SD 62) mmol/d in women	per 100 mmol/d increase	HR	1.56	1.15	2.12
	Male	Male	up to 13 years	54/1173	0.046	24-hour urinary sodium excretion	Mean 216 (SD 83)	per 100 mmol/d increase	HR	1.55	1.12	2.13
	Female	Female	up to 13 years	7/1263	0.006	24-hour urinary sodium excretion	Mean 162 (SD 62)	per 100 mmol/d increase	HR	2.07	0.8	5.36
He, 1999 ⁴⁰ NHANES I	Non-overweight	Both	mean 19 y	ND/6797	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	1.07	0.89	1.28
	Overweight	Both	mean 19 y	ND/2688	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	1.29	1.01	1.64
Cohen, 2006 ¹³⁴ NHANES II	All	Both	mean 13.7 y	282/7154	0.039	Dietary sodium intake	Mean 2719 (SD 23) mg/d	per 1000 mg/d increase	HR	0.91	0.79	1.05
	All	Both	mean 13.7 y	282/7154	0.039	Dietary sodium intake	Mean 2719 mg/d	<2300 mg/d vs. ≥2300 mg/d	HR	1.21	.87	1.68
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary sodium intake	Median 3434 (IQR 2641-4384) mg/d	per 1000 mg/d increase	HR	1.20	0.81	1.77

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; mg=milligrams; mmol/d=millimoles per day; NR = not reported; RR = relative risk; SD = standard deviation; y = year

Sodium/Potassium Ratio and CHD Mortality

One study¹¹⁶ that examined the association between Na-K ratio and IHD mortality was identified. This study analyzed data from the NHANES III cohort, a generally healthy adult population. The overall RoB was rated moderate.

Overall Summary of Results for Sodium to Potassium Ratio and CHD Mortality

The only study that assessed the association between Na-K ratio and CHD or IHD mortality, the NHANES III followup study, found a significant association between categorical and continuous dietary Na-K ratio and risk for IHD mortality. Details appear below.

Description of Individual Studies Using Dietary Assessment of Sodium/Potassium Ratio and CHD/IHD Mortality

The NHANES III cohort included both adult men and women. Mean age was not reported, but the cohort included participants over 20 years of age. Median followup time was 14.8 years in this study. Na-K ratios were assessed by 24-hour dietary recall. The study results are shown in Figure 30. The risk of IHD mortality increased with increasing quartile of Na-K ratio among the whole cohort (p for trend <.001; n=12267). In addition, a significant linear association between continuous Na-K ratio and IHD mortality was reported among the whole cohort (HR = 3.66; 95% CI 1.94, 6.90).

Figure 30. Categorical analysis of the association between sodium to potassium ratio and IHD mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

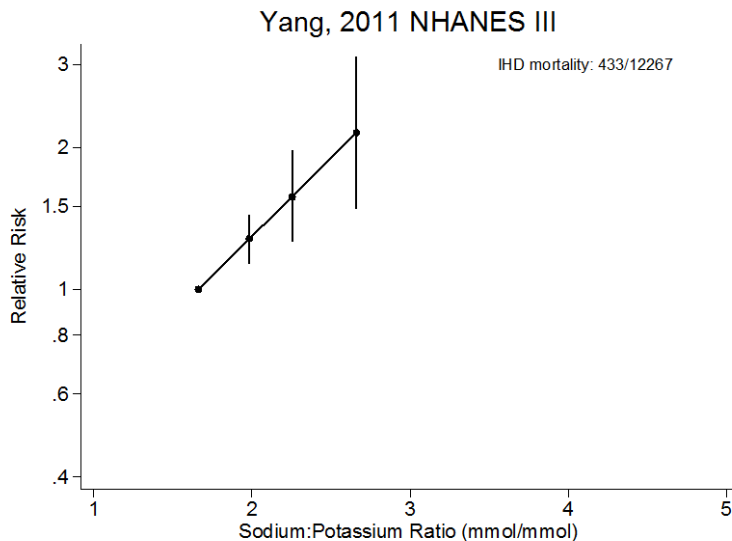


Figure notes: IHD = ischemic heart disease; mmol = millimole

Risk for Stroke

Sodium Intake and Risk for Stroke

A total of six prospective cohort studies,^{40, 43, 56, 98, 134, 141} and one case-cohort study¹²⁹ examined the associations between sodium intake levels and risk for stroke among generally healthy adult populations. These studies included seven non-overlapping cohorts, which are the combined FLEMENGHO and EPOGH cohort,⁹⁸ a population-based cohort in south-western Finland,⁵⁶ the PURE cohort,¹⁴¹ the Rotterdam study,¹²⁹ the Hawaiian study cohort,⁴³ NHANES I,⁴⁰ and the NHANES II Mortality study.¹³⁴ Except for the Hawaiian study cohort, all studies included both adult men and women at baseline (mean ages ranged from 40.9 to 69.2 years). The Hawaiian study cohort enrolled men of Japanese ancestry (mean age = 54.3 years). Mean or median followup times ranged from 3.7 to 19 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in two studies,^{56, 98} by spot-urine samples in two studies,^{129, 141} and by 24-hour dietary recalls in three studies.^{40, 43, 134} The sodium intake ranged from 62 mmol/d (1424 mg/d) to 365 mmol/d (8395 mg/day).

Overall Summary of Results for Sodium and Risk for Stroke

The relationships between sodium intake levels and stroke were mostly not significant among the four studies that examined urinary sodium levels and stroke,^{56, 98, 129, 141} except for one large multi-country study that showed that the lowest quintile (<2 g/d) of 24-hour urinary sodium excretion (estimated by Kawasaki equation) was associated with an increased risk of stroke, but the second quintile of urinary sodium excretion (3.0-3.99 g/d or median = 152 mmol/d) was associated with a reduced risk of stroke. However, this study was rated high RoB for sodium exposure assessment method. The associations between dietary sodium intake and stroke were also non-significant in two studies;^{43, 134} a third study showed that higher sodium intake levels were significantly associated with higher risks of stroke among overweight adults, but not among non-overweight adults.⁴⁰ Except for the Hawaiian study, all studies controlled for various demographics, lifestyle factors, and medical history or medications. Among these, the FLEMENGHO and EPOGH cohort studies⁹⁸ and the Rotterdam study¹²⁹ also adjusted for urinary potassium excretion in their analyses. The Hawaiian study adjusted only for age in their analyses.⁴³ The overall risk of bias was rated high. The strength of evidence was rated insufficient for the association between sodium intake levels and risks for stroke due to the limitations in sodium exposure assessment methods across studies.

Individual study results are shown in Figure 31 (low and moderate RoB studies), Table 9, and Appendix H.

Description of Individual Studies Using 24-Hour Urinary Sodium Excretion and Risk for Stroke

Two studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of stroke:^{56, 98} Specifically, the FLEMENGHO and EPOGH cohort (moderate RoB)⁹⁸ did not find significant associations between risks of fatal and nonfatal stroke and tertiles of baseline 24-hour urinary sodium excretion levels (adjusted HR 1.07, 95% CI 0.58, 2.0, 1.29 [0.74, 2.2], and 0.78 [0.45, 1.33] in the low, median, and high sodium excretion tertiles; n=3681) (Figure 31). These analyses compared the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This approach allows computation of CIs for the HR in each tertile without definition of an arbitrary reference group. Furthermore, a Finnish cohort study (high RoB) by Tuomilehto et al. (2001)⁵⁶ also did not

find a significant relationship between baseline 24-hour urinary sodium excretion and stroke at followup (adjusted HR per 100 mmol/d increase = 1.13; 95% CI 0.84, 1.51; n=2436). The results were similar in subgroup analyses by sex. Thus, both showed no significant associations.

Description of Individual Studies Using Estimated 24-Hour Urinary Sodium Excretion and Risk for Stroke

The association between estimated 24-hour urinary sodium excretion and stroke outcome was examined in two studies.^{129, 141} Both were rated high RoB. The PURE cohort (n=101945) found that the lowest quintile of urinary sodium excretion (<3 g/d) was associated with an increased risk of stroke but the second quintile of urinary sodium excretion (3.0-3.99 g/d or median = 152 mmol/d) was associated with a reduced risk of stroke (adjusted HR 1.39, 95% CI 1.21, 1.95 and 1.72, 1.24, 2.4, respectively), compared to the third quintile level (4 to 5.99 g/day or median 217 mmol/d).¹⁴¹ No significant associations were observed between the fourth and the highest quintiles of urinary sodium excretion (6-6.99 g/d and >7 g/d) and risks of stroke compared to the third quintile level as the reference group. The Rotterdam study showed no significant linear relationship between levels of estimated 24-hour urinary excretion (based on an overnight urine sample) and risks of stroke (adjusted RR 1.08 per SD increase; 95% CI 0.80, 1.46; n=5531).¹²⁹ Thus, these two studies essentially showed no significant associations.

Description of Individual Studies Using Dietary Sodium Intake and Risk for Stroke

Three studies analyzed data from three cohorts (NHANES I,⁴⁰ NHANES II,¹³⁴ and the Hawaiian study cohort of men of Japanese ancestry⁴³) to examine the relationship between dietary sodium intake and stroke. All three studies were rated high RoB due to limitations in sodium exposure assessment methods (high random errors, which would biased the results toward the null).

In NHANES I (n=6797), a subgroup analysis by overweight status showed that higher sodium intake levels were significantly associated with higher risks of stroke among overweight adults (adjusted RR 1.39 per 100 mmol increase; 95% CI 1.09, 1.77; n=2688), but not among non-overweight adults (adjusted RR 0.99 per 100 mmol increase; 95% CI 0.81, 1.21).⁴⁰ The interaction between sodium intake and body weight (non-overweight vs. overweight) was significant (p for interaction =0.03). In the NHANES II followup study, the mean dietary sodium intake was 2719 mg/day (118 mM/day). This study showed no significant associations between dietary sodium intake levels and risks of stroke (adjusted HR 0.95 per 1000 mg increase; 95% CI 0.75, 1.21; n=7154).¹³⁴ Compared to dietary sodium intake levels \geq 2300 mg/day, sodium intake <2300 mg/d was associated with a non-significant increased risk of stroke (adjusted HR 1.78, 95% CI 0.89, 3.66). In the Hawaiian study cohort of men of Japanese ancestry (n=8006), the age-adjusted stroke incidences were similar across quartiles of dietary sodium intake levels (median = 2.39-3.01 g/d).⁴³ Thus with the exception of the association shown among overweight individuals between dietary sodium intake and risk for stroke in the NHANES I study, none of the studies showed significant associations. However, RoB was moderate or high for all studies.

Figure 31. Categorical analysis of the association between urinary sodium levels and stroke outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

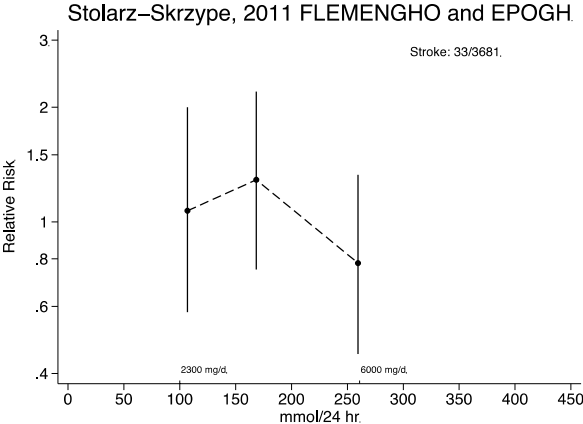


Figure notes: d = day; hr = hour; mg = milligrams; mmol = millimoles

Table 9. Continuous analyses of the association between sodium levels and stroke outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Tuomilehto, 2001 ⁵⁶	All	Both	up to 13 years	84/2420	0.035	24-hour urinary sodium excretion	Mean 216 (SD 83) in men & 162 (SD 62) mmol/d in women	per 100 mmol/d increase	HR	1.13	0.84	1.51
	Male	Male	up to 13 years	43/1161	0.038	24-hour urinary sodium excretion	Mean 216 (SD 83)	per 100 mmol/d increase	HR	1.00	0.68	1.47
	Female	Female	up to 13 years	41/1259	0.033	24-hour urinary sodium excretion	Mean 162 (SD 62)	per 100 mmol/d increase	HR	1.34	0.87	2.07
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.039	Estimated 24-hour urinary sodium excretion (spot urine)	117 (SD 69) mmol/d in a random sample	per SD increase	RR	1.08	0.80	1.46
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary sodium excretion (spot urine)	NR	per SD increase	RR	1.02	0.66	1.58
Kagan, 1985 ⁴³ Hawaiian study cohort	Japanese ancestry	Male	10 y	238/8006	0.030	Dietary sodium intake	2.39-3.01 g	Chi-squared for trend across quintiles of sodium intake levels	Age-adjusted incidence/1000 people	29.9 (Q1), 31.3 (Q2), 23.9 (Q3), 32.0 (Q4), 28.4 (Q5)	NR	NR
He, 1999 ⁴⁰ NHANES I	Non-overweight	Both	mean 19 y	NR/6797	NR	Dietary sodium intake	NR	per 100-mmol increase	RR	0.99	0.81	1.21

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Overweight	Both	mean 19 y	NR/2688	NR	Dietary sodium intake	NR	per 100-mmol increase	RR	1.39	1.09	1.77
Cohen, 2006 ¹³⁴ NHANES II	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 (SD 23) mg/d	per 1000 mg/d increase	HR	0.95	0.75	1.21
	All	Both	mean 13.7 y	1343/7154	0.188	Dietary sodium intake	Mean 2719 mg/d	<2300 mg/d vs. ≥2300 mg/d	HR	1.78	0.89	3.55

Table Notes: CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; HTN = hypertension; IQR = interquartile range; mmol/d = millimoles per day; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium/Potassium Ratio and Risk for Stroke

A total of four studies^{87, 98, 129, 137} that reported analyses examining the association between Na-K ratio and fatal or nonfatal stroke events were included. These studies analyzed data from four non-overlapping cohorts among generally healthy adult populations.

Three prospective cohort studies^{87, 98, 137} and one case-cohort study¹²⁹ examined the associations between levels of Na-K ratio and stroke among generally healthy adult populations. The cohorts included in these studies are the combined FLEMENGHO and EPOGH cohort,⁹⁸ PREVEND,¹³⁷ NIPPON DATA80,⁸⁷ and the Rotterdam Study.¹²⁹ All studies included both adult men and women. Mean age was reported to be in the 40s for all studies, except for the Rotterdam Study, which reported a mean age of 74 years for cases and 69.2 years for controls who were randomly sampled from the cohort. Mean or median followup times ranged from 5 years to 24 years.

Na-K ratios were assessed by 24-hour urinary excretion in two studies,^{98, 137} by spot urine (estimated 24-hour urinary excretion) in one study,¹²⁹ and by 3-day weighed food records in one study.⁸⁷

Overall Summary of Results for Sodium-Potassium Ratio and Risk for Stroke

The three studies that examined urinary Na-K ratios found no association with risk for stroke.^{98, 129, 137} However, these results were not consistent with the results from the study that examined the association of dietary Na-K intake and stroke mortality risk.⁸⁷ All studies controlled for various demographic, clinical, and lifestyle factors. The overall RoB was rated as low to moderate. Individual study results are described below and shown in Figure 32 (low and moderate RoB studies), Table 10, and Appendix H.

Description of Individual Studies Using 24-Hour Urinary Sodium/Potassium Ratio and Risk for Stroke Events (Fatal and Non-Fatal)

Three studies that examined urinary Na-K ratios and stroke outcomes reported consistent lack of association between Na-K ratios and stroke events. In the combined FLEMENGHO and EPOGH cohort (moderate RoB), no association was detected between tertiles of Na-K ratio and risk of fatal and non-fatal events due to stroke (Figure 32).⁹⁸ In the Rotterdam study (high RoB), no relationship was observed between Na-K ratio and incidence of fatal or non-fatal stroke events, either in the full case-cohort or in participants who were free of CVD and hypertension at baseline.¹²⁹ Finally, in the PREVEND study (moderate RoB), no association was observed between continuous or quintiles of Na-K ratio and fatal and non-fatal stroke events.¹³⁷

Description of Individual Studies Using Dietary Sodium/Potassium Ratio and Risk for Stroke Mortality

One study, the NIPPON DATA80 cohort study (high RoB), assessed the association between quintiles of dietary Na-K ratio and risk of mortality from stroke and found significant linear (age-adjusted model: $p=.009$; $n=8283$) and quadratic non-linear (fully adjusted model: $p=.002$) trends.⁸⁷ Those in the highest quintile of Na-K ratio had a significantly increased risk of total stroke mortality compared to those in the lowest quintile (adjusted HR = 1.43; 95% CI 1.17, 1.76).

Figure 32. Categorical analysis of the association between levels of sodium to potassium ratio and stroke outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

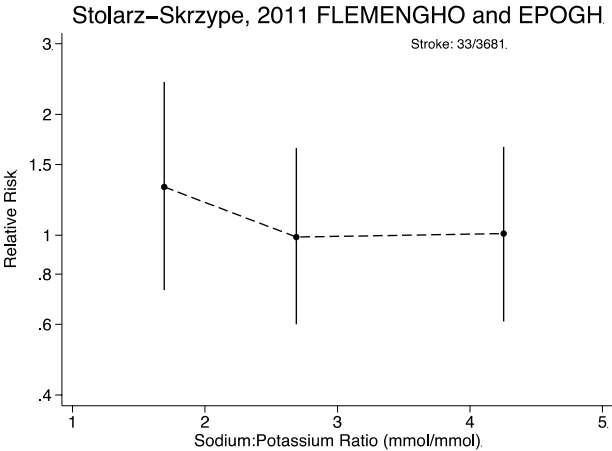


Figure notes: mmol = millimoles

Table 10. Continuous analyses of the association between sodium to potassium ratio and stroke outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	1172/7795	0.022	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/mmol)	HR	0.81	0.64	1.02
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	181/5531	0.033	Estimated 24-Hour Urinary Excretion (spot urine)	NR	per 1-unit increase (mmol/mmol)	RR	0.99	0.83	1.18
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	NR	per 1-unit increase (mmol/mmol)	RR	0.90	0.66	1.22

Table Notes: CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; HTN = hypertension; IQR = interquartile range; mmol = millimoles; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium and Risk for Myocardial Infarction

Sodium Intake and Risk for Myocardial Infarction

A total of two publications^{129, 141} reported analyses examining the associations between sodium intake levels and myocardial infarction (MI) outcome among generally healthy adult populations.

The two studies are the PURE prospective cohort study¹⁴¹ and the Rotterdam case-cohort study.¹²⁹ Both studies included both adult men and women at baseline (mean ages were 51 and 69.2 years, respectively). Mean or median followup time were 3.7 and 5.5 years. Sodium intake levels were assessed by spot-urine samples in both studies, ranging from 104 mmol/d (2392 mg/d) to 365 mmol/d (8395 mg/d).

Overall Summary of Results for Sodium and Risk for Myocardial Infarction

The two studies both showed non-significant results for the relationship between estimated 24-hour urinary sodium excretion and MI.^{129, 141} Both studies controlled for various demographics, lifestyle factors, and medical history or medications. One study¹²⁹ also adjusted for urinary potassium excretion in their analyses. The strength of evidence was rated insufficient, primarily because the overall RoB was rated high due to the limitations for exposure assessment. Individual study results are described below and shown in Appendix H.

Description of Individual Studies Using Estimated 24-hour Urinary Sodium Excretion and Risk for Myocardial Infarction The analyses of the PURE cohort (n=101,945)¹⁴¹ showed no significant associations between 24-hour urinary sodium excretion levels (estimated by Kawasaki equation) and risks of MI, using the third quintile level of urinary sodium excretion as the reference group (4 to 5.99 g/day; median = 217 mmol/d. The Rotterdam study also showed no significant linear relationship between estimated 24-hour urinary excretion based on an overnight urine sample and MI (adjusted RR = 1.19 per SD increase; 95% CI 0.97, 1.46; n=5531).¹²⁹ Both studies were rated high RoB due to the limitations for exposure assessment.

Sodium to Potassium Ratio and Risk for Myocardial Infarction

One study¹²⁹ that examined the association between Na-K ratio and fatal and non-fatal MI was included. This was a case-cohort analysis from the Rotterdam Study, a population-based study that included men and women aged 55 years of age or older. The mean age was 71 years for the cases of incident MI and 69.2 years for the controls, who were randomly sampled from the entire cohort. The median followup time was 5.5 years. Na-K ratios were assessed by spot urine.

Overall Summary of Results for Sodium to Potassium Ratio and Risk for Myocardial Infarction

No significant linear association was found between estimated 24-hour urinary excretion and incidence of fatal and non-fatal MI among all the subjects (RR = 1.04; 95% CI = 0.93, 1.17) or among subjects free of CVD and hypertension at baseline (RR = 0.91; 95% CI = 0.72, 1.16). The overall RoB for this study was rated as high.

Sodium and Combined CVD Morbidity and Mortality

Sodium Intake and Combined CVD Morbidity and Mortality

A total of seven publications^{80, 98, 107, 130, 136, 137, 141} reported analyses examining the associations between sodium intake levels and combined CVD morbidity and mortality outcomes among generally healthy adult populations. These studies included six cohorts: the combined FLEMENGHO and EPOGH cohort,⁹⁸ the TOHP (I and II) cohort,^{107, 130} PREVEND,¹³⁷ a pooled analysis of four cohorts (PURE, EPIDREAM, ONTARGET and TRANSCEND),⁸⁰ the PURE cohort,¹⁴¹ and the PURE South America cohort.¹³⁶ The pooled analysis of four cohorts⁸⁰ had overlapping study populations with the PURE cohort¹⁴¹ and PURE South America cohort.¹³⁶ All studies included both adult men and women at baseline (mean ages ranged from 40.9 to 58 years). Mean or median followup time ranged from 3.7 to 10.5 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in four studies,^{98, 107, 130, 137} and by spot-urine samples in three studies.^{80, 136, 141} The sodium intake ranged from 80 mmol/d (1840 mg/d) to 365 mmol/d (8395 mg/d). Individual study results are shown in Figure 33 and Table 11 and Appendix H.

Overall Summary of Results for Combined CVD Morbidity and Mortality

The relationships between urinary sodium levels and combined CVD morbidity and mortality outcomes were inconsistent across the studies,^{80, 98, 107, 130, 136, 137, 141} as were the definitions of CVD morbidity and mortality outcomes. Of the seven publications, two publications analyzed data from the same studies (the TOHP I and II followup study^{107, 130}). Three multi-country studies had overlapping study populations, and results consistently showed a U-shaped association between 24-hour urinary sodium excretion estimated by Kawasaki equation and major CVD outcomes.^{80, 136, 141} All studies controlled for various demographics, lifestyle factors, and medical history or medications. Among these, the TOHP I and II followup study,¹⁰⁷ PREVEND,¹³⁷ and the FLEMENGHO and EPOGH cohort study⁹⁸ also adjusted for urinary potassium excretion in their analyses. The overall RoB was rated moderate. The SoE was rated insufficient, primarily due to inconsistent findings and heterogeneity in outcome definitions.

Description of Individual Studies Using 24-Hour Urinary Sodium Excretion and Risk for Combined CVD Morbidity and Mortality

Three studies (in 4 publications)^{98, 107, 130, 137} examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of combined CVD morbidity and mortality outcomes. The results were inconsistent across studies.^{98, 107, 130, 137} Specifically, the TOHP (I and II) followup study (low RoB), which enrolled the control groups from the original sodium reduction trials, showed a trend in increasing 24-hour urinary sodium excretion levels with higher risks of total cardiovascular events in categorical analyses^{130, 293} or in continuous analyses (adjusted RR per 100 mmol/d increase = 1.42; 95% CI 0.99, 2.04) (Figure 33).¹³⁰ Although no significant interactions were observed between sex (men vs. women), race (White vs. Black), or obesity (BMI \geq 30 vs. BMI $<$ 30) and 24-hour sodium excretion levels, the subgroup results showed statistically significantly increased risks of total cardiovascular events in men (adjusted RR per 100 mmol/d increase = 1.26; 95% CI 1.04, 1.53), in whites (adjusted RR per 100 mmol/d increase = 1.21; 95% CI 1.04, 1.49), and in obese individuals (adjusted RR per 100 mmol/d increase = 1.33; 95% CI 1.05, 1.63).¹³⁰

In contrast, both the FLEMENGHO and EPOGH cohort study (moderate RoB) (Figure 33)⁹⁸ and PREVEND study (moderate RoB)¹³⁷ showed no significant associations between the

baseline 24-hour urinary sodium excretion levels and risks of total cardiovascular events. Specifically, the FLEMENGHO and EPOGH cohort study showed that low (median = 95 mmol/d in women; 120 mmol/d in men), medium (median = 150 mmol/d in women; 189 mmol/d in men), and high (median = 291 mmol/d in women; 232 mmol/d in men) tertiles of 24-hour urinary sodium excretion were not significantly associated with the risks for total fatal and nonfatal cardiovascular events (adjusted HR [95% CI] = 1.13 [0.90, 1.42], 1.11 [0.90, 1.42], and 0.90 [0.73, 1.11], respectively; n=3681).⁹⁸ These analyses compared the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This approach allows computation of CIs for the hazard ratio (HR) in each tertile without definition of an arbitrary reference group. The PREVEND study did not find a significant linear relationship between 24-hour urinary sodium excretion levels and risks of composite cardiovascular outcome (adjusted RR per 50 mmol/d increase = 0.97; 95% CI 0.87, 1.08).

Description of Individual Studies Using Estimated 24-Hour Urinary Sodium Excretion and Risk for Combined CVD Morbidity and Mortality

The association between estimated 24-hour urinary sodium excretion and combined CVD morbidity and mortality outcome was examined in three studies.^{80, 136, 141} However, these studies (all rated high RoB) had overlapping study populations, and showed consistent results. The pooled analysis of four cohorts (PURE, EPIDREAM, ONTARGET and TRANSCEND) from 49 countries showed a U-shaped relationship between baseline levels of 24-hour urinary sodium excretion (estimated by Kawasaki equation) and risks of major CVD events (n=133118), using the median quintile of urinary excretion (195 mmol/d) as the reference group.⁸⁰ That is, compared with urinary sodium excretion of 4 (172 mM) to 5 (215 mM) g/day (median = 195 mmol/d), urinary sodium excretion of 7 (300mM) g/day or more (adjusted HR = 1.21; 95% CI 1.10, 1.34) and less than 3 g/day (adjusted HR = 1.34; 95% CI 1.23, 1.47) were both associated with increased risk of major CVD events. Similar U-shape relationships were found in subgroup analyses by hypertension status (n=63559 with hypertension and n=69559 without hypertension) although higher urinary sodium excretion levels (5 to 5.99 g/day, 6 to 6.99 g/day, or ≥7 g/day) were not significantly associated with risks of major CVD events among non-hypertensive individuals.⁸⁰ Not surprisingly, the analyses using the PURE cohort (n=101945)¹⁴¹ and PURE South America cohort (n=16549)¹³⁶ also showed U-shaped associations, but the level of urinary sodium excretion used as the reference group was different in the PURE cohort (4 to 5.99 g/day; median = 217 mmol/d), and some comparisons were not statically significant due to smaller sample sizes.

Figure 33. Categorical analysis of the association between urinary sodium levels and combined cardiovascular disease morbidity and mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

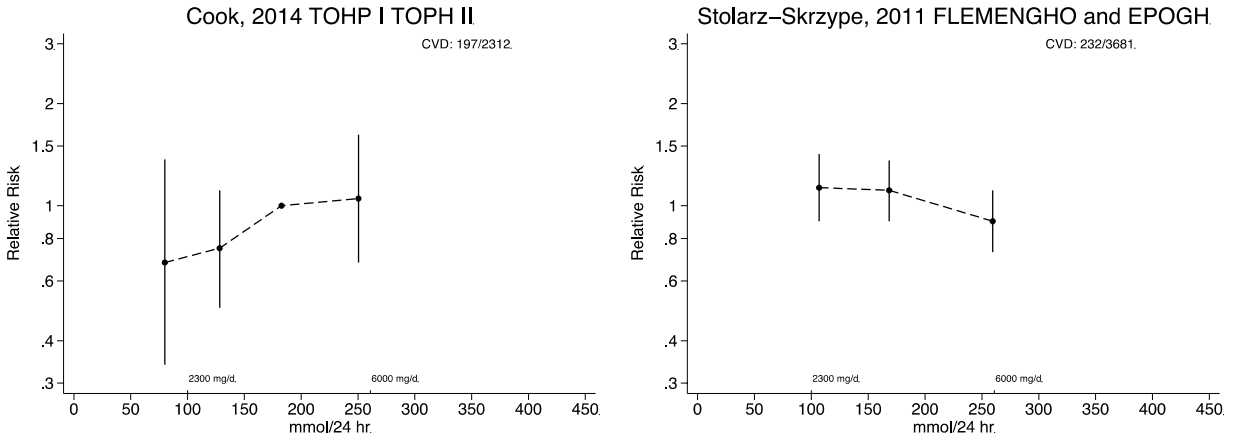


Figure notes: CVD = cardiovascular disease; hr = hour; mmol = millimole

Table 11. Continuous analyses of the association between sodium levels and combined morbidity and mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Cook, 2009 ¹³⁰ TOHP I & II control groups	All	Both	median 5 y (TOHPI) 4 y (TOHP II)	166/2084	0.080	24-hour urinary sodium excretion	Median 158 (IQR 127-194) mmol/24 hr	per 100 mmol/d increase	RR	1.42	0.99	2.04
	Men	Male	Median 4-5 y	141/1459	0.097	24-hour urinary sodium excretion	Median 171 mmol/24 hr	per 100 mmol/d increase	RR	1.26	1.04	1.53
	Women	Female	Median 4-5 y	25/625	0.040	24-hour urinary sodium excretion	Median 134 mmol/24 hr	per 100 mmol/d increase	RR	1.21	0.79	1.85
	White	Both	Median 4-5 y	141/1743	0.081	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	RR	1.21	1.04	1.49
	Black	Both	Median 4-5 y	19/284	0.067	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	RR	1.86	0.94	3.63
	BMI<30	Both	Median 4-5 y	100/1284	0.078	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	RR	1.16	0.9	1.49
	BMI≥30	Both	Median 4-5 y	66/798	0.083	24-hour urinary sodium excretion	NR	per 100 mmol/d increase	RR	1.33	1.05	1.68
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	785/7795	0.101	24-hour urinary sodium excretion	Median 155 mmol/24 hr in men & 122 mmol/24 hr in women	per 50-mmol/d increase	HR	0.97	0.87	1.08

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium to Potassium Ratio and Risk for Combined CVD Morbidity and Mortality

Three studies^{98, 130, 137} examined the association between Na-K ratio and combined CVD morbidity and mortality (cohorts included in these studies are the FLEMENGHO and EPOGH cohort,⁹⁸ the PREVEND study,¹³⁷ and the combined TOHP I/II cohort study).¹³⁰ All studies included generally healthy adult men and women. Median followup time ranged from 4 to 10.5 years. Na-K ratios were assessed by 24-hour urinary excretion in all three studies.

Overall Summary of Results for Sodium to Potassium Ratio and Risk for Combined CVD Morbidity and Mortality

The relationships between urinary sodium-to-potassium ratios and combined CVD morbidity and mortality outcomes are inconsistent across studies.^{98, 130, 137} All studies controlled for various demographics, lifestyle factors, and medical history or medications. The overall RoB was rated as low to moderate. The SoE was considered insufficient to draw any conclusions. Individual study results are shown in Figure 34 and Table 12.

Description of Individual Studies Using 24-hour Urinary Sodium to Potassium Ratio and Risk for Combined CVD Morbidity and Mortality In the combined FLEMENGHO and EPOGH cohort (moderate RoB), an elevated risk of CVD fatal and nonfatal events was detected in the lowest tertile of Na-K ratio when compared with the overall risk in the whole outcome cohort (adjusted HR = 1.26; 95% CI 1.00, 1.52) (Figure 34).⁹⁸ No associations were observed in the middle or highest tertiles of Na-K ratio. In the PREVEND study (moderate RoB), no association was seen between continuous or quintiles of Na-K ratio and risk of combined CVD morbidity and mortality (adjusted HR = 0.98; 95% CI 0.89, 1.08).¹³⁷ In the TOHP I/II cohorts (low RoB), no association was found between quartiles of sodium-to-potassium ratio and cardiovascular events, although a significant and positive linear trend was detected (p for trend = 0.04). When Na-K ratio was analyzed as a continuous variable, a significant association was found after adjusting for several sociodemographic and lifestyle factors (adjusted HR = 1.24; 95% CI 1.05, 1.46). In subgroup analyses, significant linear associations were found in men (adjusted HR = 1.26; 95% CI = 1.04, 1.53), but not in women (adjusted HR = 1.21; 95% CI = 0.79, 1.85); in whites (adjusted HR = 1.24; 95% CI 1.04, 1.49), but not in blacks (adjusted HR = 1.85; 95% CI 0.94, 3.63); and in those with BMI \geq 30 (adjusted HR = 1.33; 95% CI 1.05, 1.68), but not in those with BMI $<$ 30 (adjusted HR = 1.16; 95% CI 0.90, 1.49).

Figure 34. Categorical analysis of the association between levels of sodium to potassium ratio and combined morbidity and mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

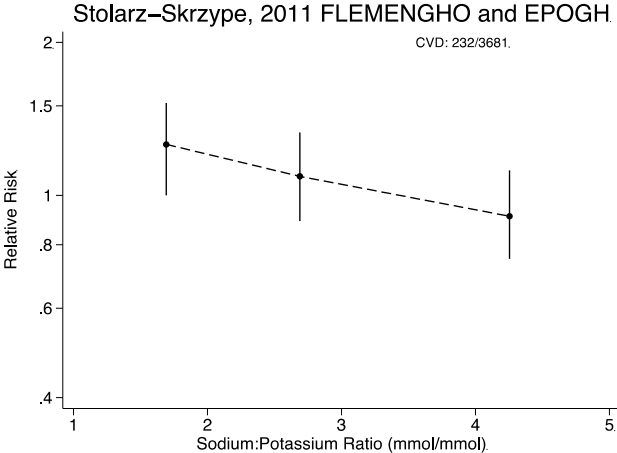


Figure notes: CVD = cardiovascular disease; mmol = millimoles

Table 12. Continuous analyses of the association between sodium to potassium ratio and combined cardiovascular disease morbidity and mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	785/7795	0.101	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	0.98	0.89	1.08
Cook, 2009 ¹³⁰ TOHP I/II control groups	All	Both	median 5y (TOHP I) 4y (TOHP II)	166/2084	0.080	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.24	1.05	1.46
	Men	Male	median 5y (TOHP I) 4y (TOHP II)	141/1459	.112	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.26	1.04	1.53
	Women	Female	median 5y (TOHP I) 4y (TOHP II)	25/625	.04	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.21	0.79	1.85
	White	Both	median 5y (TOHP I) 4y (TOHP II)	141/1743	.081	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.24	1.04	1.49
	Black	Both	median 5y (TOHP I) 4y (TOHP II)	19/284	.067	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.85	0.94	3.63
	BMI <30	Both	median 5y (TOHP I) 4y (TOHP II)	100/1286	.078	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.16	0.90	1.49
	BMI ≥30	Both	median 5y (TOHP I) 4y (TOHP II)	66/798	.083	24-hour urinary potassium excretion	NR	per 1-unit increase (mmol/m mol)	HR	1.33	1.05	1.68

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; mmol = millimole; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium and Risk for Combined CHD Morbidity and Mortality

Sodium Intake and Risk for Combined CHD Morbidity and Mortality

A total of five publications^{40, 55, 56, 98, 117} that reported analyses examining the associations between sodium intake levels and combined CHD morbidity and mortality met inclusion criteria. These publications analyzed data from five non-overlapping prospective cohort studies among generally healthy adult populations. These cohorts are the combined FLEMENGHO and EPOGH cohort,⁹⁸ the Scottish Heart Health study,⁵⁵ PREVEND,¹¹⁷ a population-based cohort in southwestern Finland,⁵⁶ and NHANES I.⁴⁰ All studies included both adult men and women at baseline (mean ages ranged from 40.9 to 50 years). Mean or median followup time ranged from 7.6 to 19 years.

Sodium intake levels were assessed by 24-hour urinary sodium excretion in four studies,^{55, 56, 98, 117} and by 24-hour dietary recall in one study.⁴⁰ The sodium intake ranged from 68 mmol/d (1564 mg/d) to 334 mmol/d (7682 mg/d).

Overall Summary of Results for Sodium Intake and Risk for Combined CHD Morbidity and Mortality

The relationships between sodium intake levels and combined CHD morbidity and mortality outcomes are inconsistent among the four studies that examined urinary sodium levels and combined CHD morbidity and mortality outcome.^{55, 56, 98, 117} The definitions of CVD morbidity and mortality outcomes are heterogeneous. Only one study assessed the associations between dietary sodium intake levels and risks of CHD among overweight vs. non-overweight adults, and the results showed no significant associations.⁴⁰ With the exception of the Scottish Heart Health study, all studies controlled for various demographics, lifestyle factors, and medical history or medications. Among these, PREVEND¹¹⁷ and FLEMENGHO, the EPOGH cohort study⁹⁸ also adjusted for urinary potassium excretion in their analyses. The Scottish Heart Health study adjusted only for age in their analyses, so the results may be at increased risk for confounding. The overall risk of bias was rated moderate. The strength of evidence was rated insufficient primarily due to inconsistent findings and heterogeneity in outcome definitions. Individual study results are described below and shown in Figure 35 (low and moderate RoB studies), Table 13, and Appendix H (high RoB studies).

Description of Individual Studies Using Estimated 24-Hour Urinary Sodium Excretion and Risk for Combined CHD Morbidity and Mortality

Four studies examined the relationships between baseline 24-hour urinary sodium excretion levels and risks of CHD morbidity and mortality and showed inconsistent results.^{55, 56, 98, 117} Specifically, the FLEMENGHO and EPOGH cohort study (moderate RoB) showed that low (median = 95 mmol/d in women; 120 mmol/d in men), medium (median = 150 mmol/d in women; 189 mmol/d in men), and high (median = 291 mmol/d in women; 232 mmol/d in men) tertiles of 24-hour urinary sodium excretion were not significantly associated with the risks for fatal and coronary events (adjusted HR [95% CI] = 1.42 [0.99, 2.04], 1.17 [0.89, 1.54], and 0.86 [0.65, 1.13], respectively; n=3681) although there was a trend in decreasing risks with higher tertiles of 24-hour urinary sodium excretion (p=0.10) (Figure 35).⁹⁸ These analyses compared the risk in each tertile with the overall risk in the whole study population. This approach allows computation of CIs for the hazard ratio (HR) in each tertile without definition of an arbitrary reference group. On the contrary, a Finnish cohort study (high RoB) by Tuomilehto and

colleagues (2001)⁵⁶ showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of CHD at followup (adjusted HR = 1.34; 1.08, 1.67). The PREVEND study (moderate RoB)¹¹⁷ did not find a significant linear association between baseline 24-hour urinary sodium excretion and CHD events (adjusted HR = 1.07; 95% CI 0.98, 1.18; n=7543). Subgroup analyses by hypertension status showed a significant positive linear relationship between levels of 24-hour urinary sodium excretion and risks of CHD in hypertensive individuals (adjusted HR = 1.14; 95% CI 1.01, 1.28), but no significant relationship in normotensive individuals (adjusted HR = 0.97; 95% CI 0.82, 1.15).¹¹⁷ The Scottish Heart Health study (high RoB) showed a positive relationship between quintiles of 24-hour urinary sodium excretion levels and all CHD outcomes in women (age-adjusted HR = 0.93, 1.97, 1.09, 1.76 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875), but no significant association in men (age-adjusted HR = 1.18, 1.11, 1.26, 1.23 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754).⁵⁵ Again, because the Scottish Heart Health study adjusted only for age in their analyses, these results are at higher risk for confounding.

Description of Individual Studies Using Dietary Sodium Intake and Risk for Combined CHD Morbidity and Mortality

One study (high RoB) performed subgroup analyses by overweight status using data from NHANES I⁴⁰ to examine the relationship between dietary sodium intake and CHD outcome. Results showed no significant associations among overweight adults (adjusted RR = 1.06 per 100 mmol increase; 95% CI 0.88, 1.29; n=2688), or among non-overweight adults (adjusted RR = 0.95 per 100 mmol increase; 95% CI 0.83, 1.10; n=6797).⁴⁰ The interaction between sodium intake and body weight (non-overweight vs. overweight) was not significant (p for interaction =0.39).

Figure 35. Categorical analysis of the association between urinary sodium levels and combined CHD morbidity and mortality outcome in generally healthy populations (data from studies rated low or moderate risk of bias)

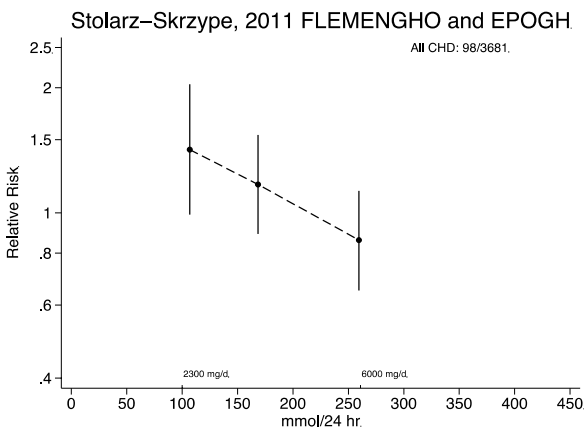


Figure notes: CHD = coronary heart disease; hr = hours; mmol = millimoles

Table 13. Continuous analyses of the association between sodium levels and combined CHD morbidity and mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Joosten, 2014 ¹¹⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	452/7543	.060	24-hour urinary sodium excretion	Median 137 mmol/24 hr	per 1 g/d increase	HR	1.07	0.98	1.18
	Normotensive	Both	median 10.5y (IQR 9.9 - 10.8y)	162/NR	.021	24-hour urinary sodium excretion	Median 137 mmol/24 hr	per 1 g/d increase	HR	0.97	0.82	1.15
	Hypertension	Both	median 10.5y (IQR 9.9 - 10.8y)	290/NR	.038	24-hour urinary sodium excretion	Median 137 mmol/24 hr	per 1 g/d increase	HR	1.14	1.01	1.28
Tuomilehto, 2001 ⁵⁶	All	Both	up to 13 years	180/2436	0.074	24-hour urinary sodium excretion	Mean 216 (SD 83) in men & 162 (SD 62) mmol/d in women	per 100 mmol/d increase	HR	1.34	1.08	1.67
He, 1999 ⁴⁰ NHANES I	Non-overweight	Both	mean 19 y	ND/6797	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	0.96	.86	1.08
	Overweight	Both	mean 19 y	ND/2688	ND	Dietary sodium intake	NR	per 100-mmol increase	RR	0.94	.76	1.17

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Sodium to Potassium Ratio and Risk for Combined CHD Morbidity and Mortality

Two studies that examined the association between Na-K ratio and risk of morbidity and mortality from CHD were included.^{98, 137} Na-K ratios were assessed by 24-hour urinary excretion among generally healthy populations in both studies.

Overall Summary of Results for Sodium to Potassium Ratio and Risk for Combined CHD Morbidity and Mortality

The two studies that examined urinary Na-K ratios and risk of morbidity and mortality from CHD reported a consistent lack of associations. Both studies controlled for various demographic, clinical, and lifestyle factors. The overall RoB was rated as moderate. Study findings are described in detail below.

Description of Individual Studies Using Urinary Sodium/Potassium Ratio and Risk of Morbidity and Mortality From CHD

The analysis from the PREVEND cohort (moderate RoB) included subjects free of cardiovascular events at baseline. The cohort included both men and women, with an average age of 49.1 years. The median followup time was 10.5 years. No significant association was found with risk of ischemic heart disease when Na-K ratio was analyzed either as a continuous variable (HR = 1.05; 95% CI = 0.95, 1.15) or in quintiles.¹³⁷ The analysis from the combined FLEMENGHO and EPOGH cohort (moderate RoB) was a population-based cohort that included both men and women, with an average age of 40.9 years. The median followup time was 7.9 years. No significant associations to risks of coronary fatal and nonfatal events were found when tertiles of Na-K ratio were compared with the overall risk in the whole outcome cohort. (HR (95% CI) = 1.31 (0.94, 1.84); 0.97 (0.73, 1.3); and 1.03 (0.77, 1.37) for the low, medium and high tertiles of Na-K ratio, respectively).

Sodium and Kidney Disease Morbidity and Mortality Outcomes

One study, the PREVEND study (moderate RoB) assessed the association between sodium intake and mean difference between groups in estimated glomerular filtration rate (eGFR). This study followed 5315 healthy Dutch adults (free of CKD), aged 28 to 75 years, for a median of 10.3 years. Using a multi-variable adjusted model, this study found no association between 24-hour urinary sodium excretion and risk of developing CKD, defined as an eGFR < 60 ml/min per 1.73 m², or urinary albumin excretion of >30 mg/24 h, or both (adjusted HR per 50 mmol/d increase = 0.97; 95% CI 0.89, 1.07).¹⁵²

No studies were identified that assessed other renal outcomes, i.e., number of patients with end-stage renal disease.

Key Question 4a. Effect of Other Minerals on Association With Sodium

No studies were identified that addressed this question.

Key Question 4b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

Sex

Among the studies described in the overview for this question, five reported subgroup analyses by sex.

All-Cause Mortality

The Scottish Heart Health study (high RoB) showed a borderline significant inverse relationship between quintiles of 24-hour urinary sodium excretion levels (range from 46.8 to 416.7 mmol/day) and total mortality outcome in men (age-adjusted HR = 0.99, 0.65, 0.86, 0.71 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754), and no significant association in women (age-adjusted HR = 0.61, 0.82, 0.67, 0.85 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875).⁵⁵

In the NHANES I followup study (high RoB), the mean dietary sodium intake was 2515 mg/day (109 mmol/day) in men and 1701 mg/day (74 mmol/day) in women. Higher dietary sodium intake levels were associated with lower risks of total mortality (adjusted HR 0.88 per SD [1313 mg or 57 mmol] increase; 95% CI 0.80, 0.96; n=11346).³⁵

In the NHANES III followup study (moderate RoB), where higher dietary sodium intake levels were associated with an increased risk of total mortality, no significant interactions were seen by sex. In addition, significant linear associations between continuous Na-K ratio and total mortality were reported for both men and women.¹¹⁶

CVD Mortality

In the 2001 Finnish cohort study (high RoB),⁵⁶ higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of CVD mortality for both men and women, although the association was not statistically significant in women.

In the NHANES I followup study (high RoB), where the mean dietary sodium intake was 50 percent higher in men than in women, higher dietary sodium intake levels were associated with lower risks of CVD mortality.³⁵

In the NHANES III followup study (moderate RoB), no significant interactions by sex were seen for CVD mortality. The risk of CVD mortality increased with increasing quartile of Na-K ratio among the whole cohort (p for trend =.01; n=12267).¹¹⁶ In addition, a significant linear association between continuous Na-K ratio and CVD mortality was reported among the whole cohort (HR = 1.90; 95% CI 1.20, 3.03). In subgroup analyses assessing the moderating effect of sex on the association of Na-K ratio to CVD mortality, significant linear associations were found in men, but not in women.

CHD Mortality

The Scottish Heart Health study (high RoB)⁵⁵ reported that baseline 24-hour urinary sodium excretion levels were positively associated with risks of CHD mortality in women (age-adjusted HR 0.36, 0.41, 0.85, 2.05 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875), but not in men (age-adjusted HR 0.96, 0.62, 0.97, 10.92, comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754)

The Finnish cohort study (high RoB) showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of CHD mortality at followup. However, the association was significant only in men (adjusted HR = 1.55; 95% 1.12, 2.13; n=1263), but not in women (adjusted HR 2.07; 95% 0.80, 5.36; n=1263).⁵⁶

Stroke

The Finnish cohort study (high RoB)⁵⁶ found no significant relationship between baseline 24-hour urinary sodium excretion and stroke at followup and no differences by sex.

Combined CVD Morbidity and Mortality

In the TOHP (I and II) followup study (low RoB), which enrolled the control groups from the original sodium reduction trials, no significant interactions were observed by sex, for the association between 24-hour sodium excretion levels and total cardiovascular events. But the subgroup results showed statistically significantly increased risks of total cardiovascular events in men (adjusted RR per 100 mmol/d increase = 1.26; 95% CI 1.04, 1.53) compared with women.¹³⁰

No studies reported analyses stratified by sex for other outcomes of interest.

Race/Ethnicity

Total Mortality

In the NHANES III followup study (moderate RoB), where higher dietary sodium intake levels were associated with an increased risk of total mortality, no significant interactions were seen by race/ethnicity.¹¹⁶

CVD Mortality

In the NHANES III followup study (moderate RoB), subgroup analyses assessing the moderating effect of race/ethnicity on the association of sodium to CVD mortality found no significant linear associations.

In another NHANES III (moderate RoB) study, the risk of CVD mortality increased with increasing quartile of Na-K ratio among the whole cohort.¹¹⁶ In addition, a significant linear association between continuous Na-K ratio and CVD mortality was reported in non-Hispanic Blacks and Mexican-Americans, but not in non-Hispanic Whites.

Total CVD Events

The TOHP (I and II) followup study (low RoB) found no significant interactions between race (White vs. Black) and 24-hour sodium excretion levels. However, the subgroup results showed statistically significantly increased risks of total cardiovascular events in Whites (adjusted RR per 100 mmol/d increase = 1.21; 95% CI 1.04, 1.49).¹³⁰

Age

No studies that met inclusion criteria for this question conducted subgroup analysis by age.

Key Question 4c. Subpopulations Defined by Hypertension, Diabetes, Obesity, and Renal Health Status

Twelve publications examined the associations between sodium intake and total mortality, CVD, CHD, stroke, or kidney disease morbidity and mortality exclusively among people with existing diseases such as hypertension,^{34, 139, 155} primary aldosteronism,¹³⁸ history of CVD,¹²² Type 2 DM,^{81, 85, 154} Type 1 DM⁷⁷, and CKD.^{118, 121, 142} The individual study results are shown in Figures 36 and 37 and in Table 14.

The results from these studies are described together with subgroup analyses of generally healthy population defined by hypertension,^{80, 116, 117} and by weight status^{40, 56, 130} below. The sections are categorized according to comorbidity, rather than outcome.

Effects of Hypertension

All-Cause Mortality

In a subgroup analysis of the pooled analysis of four cohorts (PURE, EPIDREAM, ONTARGET and TRANSCEND) from 49 countries (high RoB), a U-shape relationship between baseline levels of 24-hour urinary sodium excretion (estimated by Kawasaki equation) and risk of total mortality was found among individuals with hypertension (n=63559) at baseline.⁸⁰ However, no significant linear relationship was observed between baseline dietary sodium intake levels and risks of total mortality or CVD mortality (adjusted HR [95% CI] = 1.18 [0.8, 1.57] and 0.86 [0.56, 1.31], respectively) among adults with HTN in a subgroup analysis of NHANES III (moderate RoB).¹¹⁶

Two publications analyzed data from the same prospective cohort study of adult hypertensive patients in a worksite HTN program in New York City (high RoB; in addition, participants were advised to reduce sodium intake several days prior to urinary sodium assessment).^{34, 139} The later publication reported all-cause mortality outcomes after an average of 6.5 years of followup. This study found that lower baseline 24-hour urinary sodium excretion levels were associated with borderline lower risks of total mortality (adjusted HR [95% CI] = 0.81 [0.66, 1.00], 0.90 [0.73, 1.10], 0.88 [0.71, 1.09], comparing the first, second, and third quartiles to the highest quartile; n=3505).

CVD, CHD, and Stroke

Five publications examined the associations between sodium intake and CVD, CHD, or stroke outcomes among hypertensive adults.^{34, 80, 116, 117, 139} Of these, two publications analyzed data from the same prospective cohort study,^{34, 139} and three publications reported subgroup analyses of three non-overlapping prospective cohort studies among generally healthy populations by hypertension status.^{80, 116, 117} The sodium intake levels were measured by 24-hour urinary excretion in two studies (in three publications^{34, 117, 139}), by estimated urinary excretion in one study,⁸⁰ and by 24-hour dietary recall in one study.¹¹⁶ Results are not consistent across studies. Overall RoB was rated moderate.

One publication pooled the findings from four drug trials (PURE, TRANSCEND, EPIDREAM, and ONTARGET) to assess the association between sodium intake and CVD outcomes.⁸⁰ One publication analyzed outcome data for NHANES III.¹¹⁶ Findings are not described here.

Two publications analyzed data from the same prospective cohort study of adult hypertensive patients in a worksite HTN program in New York City (high RoB).^{34, 139} The earlier publication reported CVD incidence, MI incidence, and stroke incidence after an average of 3.8 years of followup, and no significant associations were observed between quartiles of baseline 24-hour urinary sodium excretion levels and risks of CVD, MI, and stroke.³⁴ However, only unadjusted analyses were performed in the earlier publication. A later publication reported CVD mortality and all-cause mortality outcomes after an average of 6.5 years of followup. This study found no significant associations between baseline 24-hour urinary sodium excretion levels and risks of CVD mortality (adjusted HR [95% CI] = 1.00 [0.71, 1.42], 0.96 [0.68, 1.36], 1.06 [0.75, 1.49] comparing the 1st, 2nd, and 3rd quartile to the highest quartile; n=3505)¹³⁹ On the contrary, a subgroup analysis of the PREVEND study (moderate RoB) showed a significant positive linear relationship between levels of 24-hour urinary sodium excretion and risks of CHD in hypertensive individuals (adjusted HR = 1.14; 95% CI 1.01, 1.28).¹¹⁷

Kidney Disease Morbidity and Mortality Outcomes

A study in Fukuoka, Japan, followed 133 hypertensive outpatients for an average of 10.5 years.¹⁵⁵ This study reported on outcomes including eGFR and change in eGFR. Both males and females showed a significantly slower decline in renal function (as measured by change in eGFR) with lower average urinary sodium excretion (<9.5 g/day for men and <8 g/day for women) compared to those with higher average urinary sodium excretion.¹⁵⁵ The association was independent of blood pressure change or increase in number of antihypertensive drugs. The overall RoB was rated moderate.

Effects of Cardiovascular Disease

One study (high RoB) examined the associations between estimated urinary sodium excretion levels and total mortality, CVD, CHD, or stroke outcomes among adults with a history of CVD (including HTN).¹²² ONTARGET and TRANSCEND were two large, multi-center, multi-country cohorts of people at high risk of CVD; and analyses of the combined cohorts reported on all-cause mortality, CVD mortality, MI incidence, and stroke incidence.¹²²

This study found a U-shaped relationship between baseline levels of 24-hour urinary sodium excretion (estimated by Kawasaki equation) and risk of total mortality (n=26880), using the median quintile of urinary excretion (4-5.99 g/day or median 217 mmol/d) as the reference group. Both the lowest quintile (<2 g/day) and highest quintile (>8 g/day) of the urinary sodium excretion levels were associated with an increased risk of total mortality (adjusted HR [95% CI] = 1.19 [0.99, 1.45] and 1.56 [1.30, 1.89]).

Similar U-shaped relationships were found between baseline levels of 24-hour urinary sodium excretion and risks of CVD mortality. Both lowest quintile (<2 g/day) and highest quintile (>8 g/day) of the urinary sodium excretion levels were associated with an increased risk of CVD mortality (adjusted HR [95% CI] = 1.37 [1.09, 1.73] and 1.66 [1.31, 2.1]).

This study also found that the highest quintile (>8 g/day) of the urinary sodium excretion (estimated by Kawasaki equation) was significantly associated with an increased risk of stroke (adjusted HR = 1.48; 95% CI 1.09, 2.01) and MI (adjusted HR = 1.48; 95% CI 1.11, 1.98) compared to the reference quintile level (4-5.99 g/day or median 217 mmol/d) but the comparisons between other quintiles to the median quintile of urinary sodium excretion were not statistically significant.

Other CVD Outcomes

One study followed 65 patients with primary hyperaldosteronism who were referred to a hypertension clinic in Italy.¹³⁸ This study found that the percentage decrease in LV mass index was significantly greater in patients who had more than 10 percent reduction in urinary sodium excretion (15 ± 12.5 [SD] %) than in the remaining patients (5.5 ± 9.3 [SD] %) after 1 year followup. The overall RoB was rated high.

Effects of Diabetes

Four publications examined the associations between 24-hour urinary sodium excretion levels and total mortality, CVD, CHD, stroke, or kidney disease morbidity and mortality outcomes among patients with type 2 diabetes^{81, 85, 154} or type 1 diabetes.⁷⁷ Among these, two studies had overlapping study populations.^{81, 154} The overall RoB was rated high.

A subsample of ONTARGET participants who were diagnosed with vascular disease or type 2 diabetes with end-organ damage reported on CKD incidence and total mortality (high RoB).¹⁵⁴ No significant relationship was seen between urinary sodium excretion levels and total mortality (adjusted OR [95% CI] = 1.03 [0.93, 1.15] and 1.07 [0.86, 1.13] comparing the second and third tertiles to the lowest tertile; n=3088). This study did not find a significant association between estimated sodium excretion and risk of CKD in type 2 diabetes patients.

Another prospective observational study followed a subsample of ONTARGET participants (high RoB), who were diagnosed with type 2 DM but without macroalbuminuria, for 5.5 years.⁸¹ This study found no association between sodium intake and CKD, defined as new microalbuminuria or macroalbuminuria or more than 5% decline in glomerular filtration rate per year.

A cohort study followed adult patients with type 2 diabetes attending a single diabetes clinic in Australia (high RoB), and found an inverse association between baseline 24-hour urinary sodium excretion levels and total mortality outcome (adjusted HR = 0.72 per 100 mmol increase; 95% CI 0.55, 0.94; n=620). It also found an inverse association between baseline 24-hour urinary sodium excretion levels and CVD mortality (adjusted HR = 0.65 per 100 mmol increase; 95% CI 0.44, 0.95; n=620)⁸⁵

The FinnDiane study prospectively followed Finnish adult patients with Type 1 diabetes without end-stage renal disease for a median of 10 years (high RoB). This study found a U-shaped relationship between baseline levels of 24-hour urinary sodium excretion and risks of total mortality and ESRD (n=2807), setting 150 mmol/d (3450 mg/day) urinary excretion as the reference level (data reported in the figures only).⁷⁷

Effects of Chronic Kidney Disease

Three publications examined the associations between 24-hour urinary sodium excretion levels and total mortality, CVD, CHD, stroke, or kidney disease morbidity and mortality outcomes among patients with CKD.^{118, 121, 142} Of these, two publications analyzed data from the CRIC study (moderate RoB) and reported on all-cause mortality,¹²¹ composite CVD incidence, MI incidence, and stroke incidence.¹¹⁸ The third publication was an analysis of the MDRD study on risk of kidney failure and risk of a composite outcome defined as kidney failure or all-cause mortality.¹⁴²

In the CRIC study of patients with CKD in the U.S. (n=3757), the highest quartile of 24-hour urinary sodium excretion (≥ 194.6 mmol/24 hours or ≥ 4476 mg/day) was significantly associated

with an increased risk of total mortality (adjusted HR = 1.42; 95% CI 1.05, 1.91), compared to the lowest quartile (<116.8 mmol/24 hours or <2686 mg/day).¹²¹ The second and third quartiles of 24-hour urinary sodium excretion were not significantly associated with the risks of total mortality compared to the lowest quartile (adjusted HR [95% CI] = 1.14 [0.89, 1.46] and 1.13 [0.86, 1.49], respectively).¹²¹ Another publication from the CRIC cohort study reported a significantly increased risk of stroke (adjusted HR = 1.81; 95% CI 1.08, 3.02), comparing the highest quartile of 24-hour urinary sodium excretion (≥ 4548 mg/d) to the lowest quartile (<2894 mg/d).¹¹⁸ There was also a significant continuous linear association between baseline 24-hour urinary sodium excretion levels and stroke outcome (adjusted HR = 1.16 per 1000 mg increase; 95% CI 1.05, 1.28; n=3542).¹¹⁸ No significant interactions were observed between 24-hour urinary sodium excretion and sex, race (black vs. nonblack), older age (≥ 60 vs. <60 years), or diabetes (diabetes vs. no diabetes) among CKD patients.

An analysis of 840 CKD patients enrolled in the MDRD study reported on risk of kidney failure and risk of a composite outcome defined as kidney failure or all-cause mortality (moderate RoB).¹⁴² This study found no association between 24 hour urinary sodium excretion and kidney failure (HR = 0.99; 95% Ci=0.91-1.08).

Effects of Obesity

Three subgroup analyses of a generally healthy population defined by obesity status were included.^{40, 56, 130} All three studies reported a positive relationship between sodium intake levels and risks of total and CVD mortality among overweight adults. The overall RoB was rated moderate.

Specifically, a 2001 Finnish cohort study showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of total mortality (adjusted HR per 100 mmol/d increase = 1.56; 95% CI 1.21, 2.00; n=514) and CVD mortality (adjusted HR per 100 mmol/d increase = 1.44; 95% CI 1.02, 2.04; n=514) among overweight adults. Furthermore, a subgroup analysis of the TOHP (I & II) study participants who were obese (BMI ≥ 30) at baseline showed that higher levels of baseline 24-hour urinary sodium excretion were significantly associated with higher risks of total cardiovascular events (adjusted HR 1.33 per 100 mmol/d increase; 95% CI 1.05, 1.68; n=798).⁵⁶

In subgroup analyses of the NHANES I followup study, higher dietary sodium intake levels were associated with higher risks of total mortality (adjusted RR = 1.32 per 100 mmol increase; 95% CI 1.16, 1.50; n=2688) CVD mortality (adjusted RR = 1.45 per 100 mmol increase; 95% CI 1.20, 1.75), CHD mortality (adjusted RR = 1.29 per 100 mmol increase; 95% CI 1.01, 1.64), and stroke (adjusted RR 1.39 per 100 mmol increase; 95% CI 1.09, 1.77) among overweight adults.⁴⁰ This study showed no associations between dietary sodium intake levels and risks of congestive heart failure (CHF) among non-overweight adults, but showed that the highest quartile of dietary sodium intake level (mean = 167.6 mmol/d) was significantly associated with an increased risk of CHF (adjusted HR = 1.43; 95% CI 1.01, 1.91) compared to the lowest intake level (mean = 33.7 mmol/d).¹⁵¹ In continuous analyses, relative risk of CHF for a 100-mmol/d higher intake of sodium was 0.90 (95% CI, 0.67, 1.20) among non-overweight adults, and 1.26 (95% CI, 1.03, 1.53) among overweight adults.

Figure 36. Categorical analyses of the association between sodium levels and total mortality, cardiovascular disease outcomes in non-healthy populations

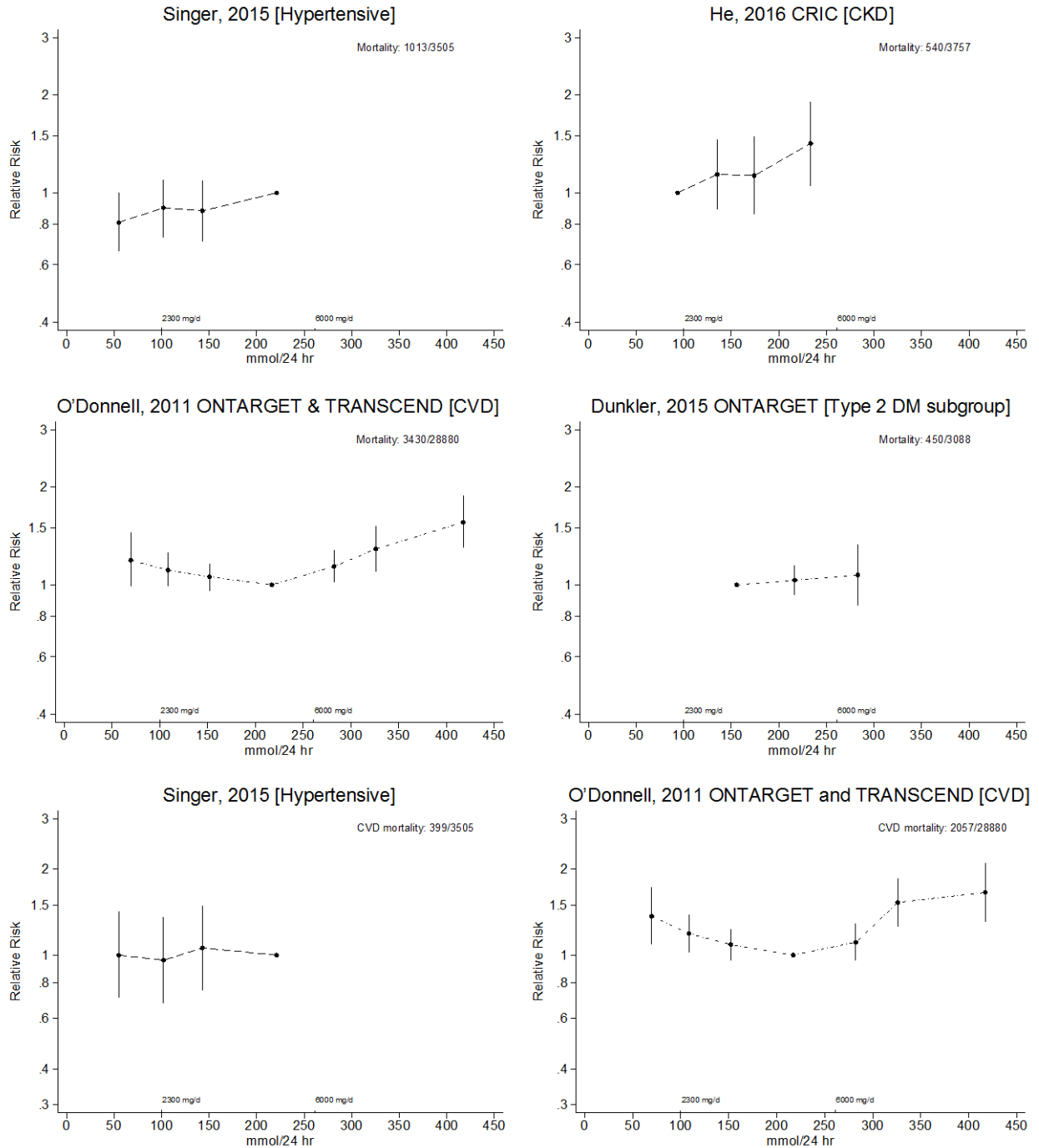


Figure notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dash line connects different levels of 24-hour urinary excretion; Dotted-dash line connects different levels of estimated 24-hour urinary excretion; CVD = cardiovascular disease; CKD = chronic kidney disease; DM = diabetes mellitus; hr = hours; mmol = millimoles

Figure 37. Categorical analyses of the association between sodium levels and stroke outcome in non-healthy populations

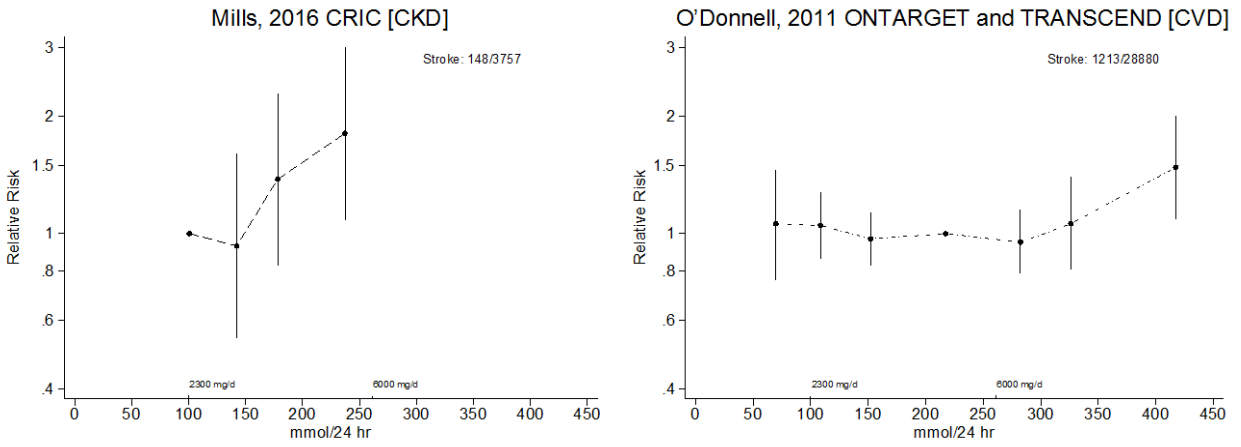


Figure notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dash line connects different levels of 24-hour urinary excretion; Dotted-dash line connects different levels of estimated 24-hour urinary excretion; CVD = cardiovascular disease; CKD = chronic kidney disease; hr = hours; mmol = millimoles

Table 14. Continuous analyses of the association between sodium levels and total mortality outcome in non-healthy populations

Author, Year Cohort Name	Population	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Total mortality outcome												
Ekinci, 2011 ⁸⁵	Type 2 diabetes	Both	median 9.9 y	175/620	0.282	24-hour urinary sodium excretion	Mean 184 mmol/d	per 100 mmol/d increase	HR	0.72	0.55	0.94
Thomas, 2011 ⁷⁷ FinnDiane Study	Type 1 diabetes	Both	Median 10 y	217/2807	0.077	24-hour urinary sodium excretion	Median	non-linear relationships established by fractional polynomials	NR	NR	NR	NR
CVD mortality outcome												
Ekinci, 2011 ⁸⁵	Type 2 diabetes	Both	median 9.9 y	175/620	0.282	24-hour urinary sodium excretion	Mean 184 mmol/d	per 100 mmol/d increase	HR	0.65	0.44	0.95
Stroke outcome												
Alderman, 1997 ³⁴	HTN	Both	median 3.8 y	23/2937	0.008	24-hour urinary sodium excretion	NR	<89 vs. ≥175 mmol/d	RR	1.2	0.30	4.0
	HTN: Male	Male	median 3.8 y	17/1900	0.009	24-hour urinary sodium excretion	NR	<89 vs. ≥175 mmol/d	RR	1.6	0.40	6.5
	HTN: Female	Female	median 3.8 y	6/1037	0.006	24-hour urinary sodium excretion	NR	<89 vs. ≥175 mmol/d	RR	0.5	0.05	5.6
Mills, 2016 ¹¹⁸ CRIC	CKD	Both	median 6.8 y	148/3542	0.042	24-hour urinary sodium excretion	mean 3701 (SD 1443) mg/d	per 1000 mg/d increase	HR	1.16	1.05	1.28
	CKD: Male	Male	median 6.8 y	NR/1950	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.15	1.02	1.3

Author, Year Cohort Name	Population	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	CKD: Female	Female	median 6.8 y	NR/1592	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.2	0.98	1.47
	CKD: Black	Both	median 6.8 y	NR/1472	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.22	1.05	1.42
	CKD: Non-black	Both	median 6.8 y	NR/2070	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.1	0.94	1.29
	CKD: Age <60	Both	median 6.8 y	NR/1767	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.17	1.02	1.34
	CKD: Age ≥60	Both	median 6.8 y	NR/1775	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.15	0.98	1.34
	CKD: DM	Both	median 6.8 y	NR/1684	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.17	1.05	1.32
	CKD: No DM	Both	median 6.8 y	NR/1858	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.13	0.93	1.36
	CKD: No DM	Both	median 6.8 y	NR/1858	NR	24-hour urinary sodium excretion	NR	per 1000 mg/d increase	HR	1.13	0.93	1.36

Table Notes: CKD = chronic kidney disease; CI = confidence interval; DM = diabetes mellitus; HR = hazard ratio; IQR = interquartile range; MDRD = Modification of Diet in Renal Disease; NR = not reported; SD = standard deviation; y = year

Key Question 5. Effect of Interventions To Increase Potassium Intake on Blood Pressure and Kidney Stone Formation

Key Points

- Increased potassium intake from dietary supplements reduces blood pressure in adults (moderate SoE based on 10 parallel RCTs and 8 crossover RCTs). However the effect is limited to studies of adults with prehypertension or hypertension (moderate SoE based on 18 RCTs with low RoB, some with inconsistent findings). Studies of adults with normal BP did not show evidence that increased potassium intake decreases blood pressure in this group (low SoE).
- We did not find evidence to support an effect of increasing potassium through changes in food intake alone on BP in adults, based on four RCTs (low SoE).
- Evidence is insufficient to draw any conclusions regarding superiority of one form of potassium supplement over another for lowering BP in adults, based on single studies.
- Evidence is insufficient to draw a conclusion regarding a beneficial effect of increased potassium intake on BP in children, based on two conflicting studies.
- Evidence from three studies is insufficient to draw conclusions regarding the modifying effect of other minerals (one study each on calcium, magnesium, and reduced sodium) on the effects of dietary or supplemental potassium.
- Evidence is insufficient (based on single RCTs) to draw conclusions regarding the moderating effect of age, sex, or race/ethnicity on the effects of increased potassium intake on BP in adults.
- Evidence is insufficient based on one study to draw conclusions regarding effects of increased potassium intake on achievement of a prespecified blood pressure goal or risk for HTN.
- Evidence is insufficient based on one study to draw conclusions regarding effects of increased potassium intake on risk for kidney stones.
- A low strength of evidence based on six RCTs suggests potassium supplements may be associated with minor gastrointestinal discomfort.
- Evidence is insufficient to draw conclusions regarding the moderating effects of diabetes, kidney disease, or obesity on the effects of potassium supplementation or increased dietary potassium from food on blood pressure.

Overview and Description of Included Studies

This question addresses three subquestions: a) the moderating effects of other minerals on the effects of increasing potassium intake on blood pressure related outcomes and kidney stone formation; b) the effects of increasing potassium on those outcomes in adults, and moderating effects of sex and race/ethnicity; and c) moderating effects of comorbidities on those outcomes. We begin by addressing subquestion b.

We identified 26 trials, described in 28 publications, that assessed the effects of potassium supplementation on blood pressure and related outcomes and kidney stone formation (described in detail in the Evidence Table in Appendix C).^{51, 60, 70, 73-75, 83, 110, 125, 127, 131, 277 61, 72, 89, 176, 236, 280 91 48, 65, 71, 94, 126, 133, 218, 264, 271}

Among the 26 studies, one enrolled adolescents in the upper 15th percentile of blood pressure for their age group,¹³¹ one controlled non-randomized trial enrolled both adults and children,¹³³ and the remaining 24 enrolled adults only (the results for these studies are described in the response to Key Question 5b).

Two parallel RCTs and one crossover RCT assessed the effects of potassium on blood pressure in healthy adult participants.^{70, 91, 277} Eleven parallel RCTs^{51, 60, 61, 65, 71, 73, 74, 83, 264, 280, 294} and seven crossover RCTs^{48, 72, 89, 94, 110, 126, 127} reported on the effects of increased potassium intake or increased dietary potassium on BP in participants with prehypertension, or mild-, moderate-, or more advanced hypertension (findings reported in the response to Key Question 5c).^{60, 83, 91, 110, 125, 280}

Three studies reported the moderating effect of other minerals on the effect of increased dietary or supplemental potassium, described in the response to Key Question 5a.^{72, 218, 264} Five additional studies that compared the effect of increased potassium intake and low sodium diet with that of low sodium diet alone^{42, 61, 64, 233, 235, 236, 275} and thirteen additional studies that assessed the effects of potassium-containing salt substitutes)^{99, 101, 102, 124, 196, 199, 232, 239, 241, 265, 267, 275, 282} are described and analyzed in KQ1a.

Six studies were conducted in the UK,^{60, 70, 110, 126, 127, 277} four were conducted in Italy,^{73, 125, 131, 271} five in the US,^{51, 74, 75, 83, 94, 133} two each were conducted in Spain,^{89, 176} India,^{72, 280} and Australia,^{61, 236} and one each was conducted in Denmark,⁹¹ Iran,²⁶⁴ Kenya,⁷¹ China,⁶⁵ and New Zealand.⁴⁸

Most studies administered potassium in the form of potassium chloride, in amounts ranging from 20 to 120mmol/d (the Adequate Intake for potassium for individuals age 14 years and over is 120 mmol). However, three studies assessed a diet intervention to increase potassium intake,^{83, 127, 218} one study administered potassium citrate (480mg/d) in the form of a low sodium bread,⁸⁹ several studies administered potassium citrate as a supplement,^{127, 176, 277} one study administered potassium gluconate and citrate,¹³³ one compared potassium bicarbonate and chloride,¹²⁶ one administered potassium aspartate,²⁷¹ one administered potassium magnesium citrate,⁹⁴ and three studies did not specify the form of potassium.^{48, 71, 264} Durations of supplementation ranged from 1 month (4 weeks) to 36 months.

Comparators in most studies were placebo; however, comparators also included other salts of potassium or a diet high in fruits and vegetables.

Many but not all studies assessed urinary potassium excretion to monitor status and compliance. Of the studies that reported actual levels or comparisons between interventions and controls, most showed significantly higher levels for the intervention groups compared with the controls.

All but one study assessed the effects of increased potassium intake on changes in blood pressure and related outcomes; that remaining study assessed the effects of potassium citrate on the risk for kidney stones in individuals with idiopathic hypercitraturia.¹⁷⁶

Fifteen RCTs had a parallel design,^{51, 60, 61, 65, 70, 71, 73, 74, 83, 125, 131, 176, 264, 277, 280} nine RCTs had a crossover design,^{48, 72, 89, 91, 94, 110, 126, 127, 218} and two were CCTs.^{133, 271} The results of these three study designs are described separately.

Key Question 5b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

Detailed Synthesis

Age

Only two trials reported results of studies of increasing potassium intake for children: one RCT and one CCT. The remainder report results in adults. Descriptions of the included studies and pooled effect sizes for parallel and crossover RCTs of adults are described below and shown in the figures, separately from those for children. Parallel RCTs were pooled separately from crossover RCTs that reported on adults. Results are also described separately by type of intervention for adults.

Mean Difference in Systolic Blood Pressure

Adults

Potassium Supplements Versus Placebo

Parallel RCTs. Ten parallel RCTs (results reported in 11 publications) that met inclusion criteria reported on the effects of potassium supplements, typically potassium chloride, to increase potassium status compared with placebo controls in adults.^{51, 60, 65, 70, 71, 73-75, 236, 264, 277, 280} Of the eight RCTs that reported urinary potassium excretion, all reported increases in the intervention groups compared with controls. Two RCTs did not report the levels but reported that they were increased and correlated with supplementation. The random effects pooled estimate for the effects of increased potassium on systolic BP showed a significant beneficial effect (MD -9.44 (95% CI -17.76 -1.13 I^2 97%). The studies were highly heterogeneous with respect to intervention type (Figure 38a).

Crossover RCTs. Eight crossover RCTs that met inclusion criteria reported on the effects of potassium supplements vs. placebo on systolic blood pressure.^{48, 72, 89, 91, 94, 110, 126, 127} Six RCTs reported increased urinary potassium excretion compared with the control groups;^{48, 72, 91, 94, 126, 127} one RCT reported no significant difference,¹¹⁰ and one trial did not report on urinary potassium but provided foods with defined amounts of potassium.⁸⁹ The random effects pooled estimate of the mean difference in systolic BP showed a non-significant beneficial effect of increased potassium intake on systolic BP (MD -2.44 , 95% CI -5.27 , 0.39 ; I^2 55%) (Figure 38a).

Pooled parallel and crossover RCTs. Eighteen RCTs could be pooled. The random effects pooled effect estimate for both parallel and crossover RCTs showed a significant beneficial effect of increased potassium intake but very high heterogeneity (MD -6.43 , 95% CI -11.06 , -1.80 ; I^2 94%). A sensitivity analysis that omitted high- and unclear-RoB studies had no appreciable effect on the pooled effect size or heterogeneity (MD -6.43 , 95% CI -11.37 , -1.49 ; I^2 94% [Appendix I]).

Controlled clinical trials. Two non-randomized placebo controlled trials assessed the effects of increased potassium intake on systolic blood pressure.

A UK study that provided daily potassium gluconate/potassium citrate supplements to half of a group of healthy adults and placebo to the remainder reported increases in urinary potassium excretion but no significant change in systolic blood pressure (high RoB based on study design and other factors).¹³³

A study conducted in Italy administered 30mmol potassium aspartate daily to half of a group of adults with mild HTN and placebo to the remainder. At 4 weeks, systolic BP was significantly decreased in the potassium supplemented group (154.4 ± 8.2 vs. 142.2 ± 7.6 mmHg, $p < 0.001$) (high RoB based on study design and other factors).²⁷¹

Potassium From Foods Versus Usual Diet

Parallel RCTs. A 1-year RCT conducted in Italy randomized 47 adults with HTN to receive dietary counseling to increase potassium intake through dietary changes or to remain on their usual diet.¹²⁵ Potassium intake was assessed via food records and urinary excretion. At the end of one year, no difference was seen in blood pressure between the two groups but the group that received the dietary intervention was able to decrease their use of antihypertensive medication.¹²⁵

A 12-week RCT conducted in Australia randomized 107 participants with mild HTN to a dietary intervention aimed at increasing potassium intake through food or to a control group.²³⁶ At follow up, systolic (and diastolic) BP were significantly decreased in the group that received dietary coaching, in proportion to the decrease in sodium-to-potassium intake ratio.

A 2-month RCT that used coaching about dietary choices and food vouchers to increase potassium intake among urban blacks in Baltimore with controlled hypertension found increases in urinary potassium excretion in the intervention group (compared with baseline and the control group) but no change in systolic BP (high RoB).⁸³

Crossover RCTs. A 1.5 month crossover RCT conducted in the UK compared the use of a diet enriched with fruits and vegetables to raise potassium levels to that of potassium citrate supplements and placebo controls among individuals with mild (early) hypertension (low RoB).¹²⁷ This study reported no effects of increased potassium on systolic BP.

Potassium Salts Compared

Parallel RCTs. A 1.5-month parallel RCT conducted in the UK randomized 85 healthy participants to 30mmol potassium chloride, 30mmol potassium citrate, or placebo.²⁷⁷ Both potassium chloride and citrate significantly reduced systolic BP compared with placebo (MD – 5.24, CI –7.43, –3.06 and – 6.69, CI –8.85, –4.43, respectively) urinary potassium excretion was significantly increased in both intervention groups compared with the placebo group (low RoB).

Crossover RCTs. He and colleagues reported no difference in the effects of potassium bicarbonate, potassium chloride, and placebo on systolic BP (low RoB).¹²⁶ Vongpatanasin reported that 4 weeks of KCl supplementation decreased systolic BP but potassium magnesium citrate and potassium citrate did not (moderate RoB).⁹⁴

Children

Sinaiko and colleagues assessed the feasibility of reducing dietary sodium or supplementing with potassium in 5th to 8th grade youth in the US, mean age 13.¹³¹ The findings for sodium reduction were reported in the response to KQ1. They randomized 140 boys and girls in the upper 15th percentile of blood pressure distribution for their age group to 3 years of increased potassium intake (1mmol per kg body weight per day) or placebo while maintaining usual diet.

They reported a small, statistically insignificant mean difference in systolic BP (MD -0.30, 95% CI -7.92, 7.32; I^2 56%; moderate RoB) (Figure 38b).

A CCT supplemented one member each of 38 pairs of normotensive twin children with a mixture of potassium gluconate and potassium citrate (approximately 40 mmol; daily doses were based on caloric needs calculated by weight and sex); the other members of the twin pairs received placebo.¹³³ After 4 weeks, 24-hour urinary excretion increased significantly, but systolic BP did not change (high RoB).

Figure 38a. Effect of increased potassium intake from supplements on mean difference in systolic BP for adults

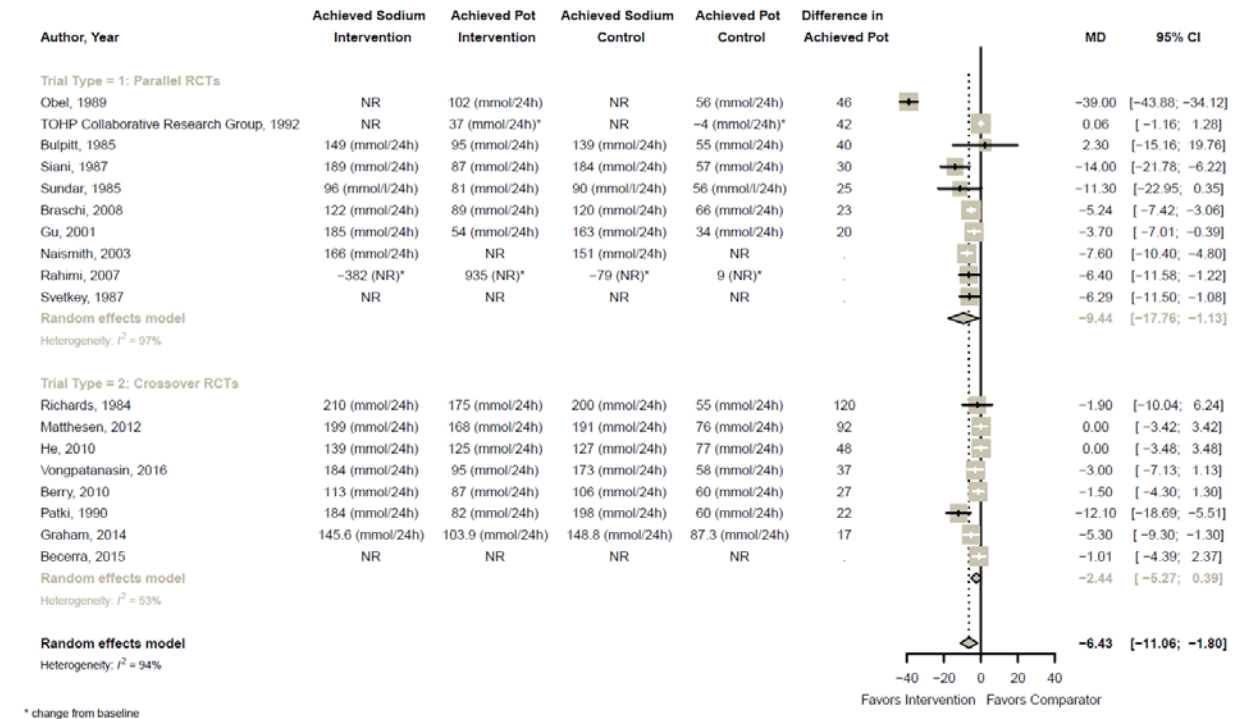


Figure 38b. Effect of increased potassium intake from supplements on mean difference in systolic BP for children

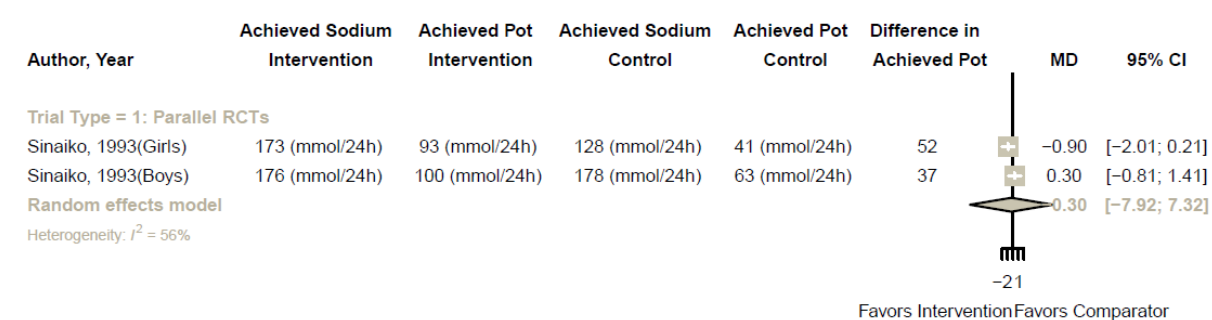


Figure notes: CI = confidence interval; h = hours; MD = mean difference; mmol = millimoles; RCT = randomized controlled trial

Mean Difference in Diastolic Blood Pressure

Adults

Potassium Supplements Versus Placebo

Parallel RCTs. Ten parallel RCTs that met inclusion criteria reported on the effects of potassium supplements, typically potassium chloride, to increase potassium status compared with placebo controls on diastolic BP in adults (overall RoB low),^{51, 60, 65, 70, 71, 73, 74, 125, 131, 236, 264, 277,}

²⁸⁰ Of the seven RCTs that reported urinary potassium excretion, all reported increases in the intervention groups compared with controls. Two RCTs did not report the levels but reported that they were increased and correlated with supplementation. The random effects pooled estimate of the mean difference in diastolic BP showed a significant beneficial effect of potassium supplements (MD -4.71 , 95% CI -8.92 , -0.51 ; I^2 96%) (Figure 39a).

Crossover RCTs. Eight crossover RCTs that met inclusion criteria reported on the effects of potassium supplements vs. placebo on diastolic BP.^{48, 72, 89, 91, 94, 110, 126, 127} Five RCTs reported increased urinary potassium excretion compared with the control groups, and one trial did not report on urinary potassium. The random effects pooled estimate of the mean difference in diastolic BP for the eight studies showed a non-significant beneficial effect of increased potassium intake on decreasing diastolic BP (MD -1.24 , 95% CI -3.91 1.42 , I^2 57%).

Pooled parallel and crossover RCTs. Eighteen parallel and crossover RCTs were pooled. The random effects pooled effect estimate for both parallel and crossover RCTs showed a significant beneficial effect of increased potassium intake on diastolic BP but high heterogeneity (MD -3.50 , 95% CI -6.10 , -0.89 ; I^2 93%) (low RoB). Sensitivity analysis omitting high- or unclear RoB RCTs had no appreciable effect on the pooled effect size or heterogeneity (MD -3.37 , 95% CI -6.14 , -0.61 ; I^2 93% [Appendix I]).

Controlled clinical trials. Two non-randomized placebo controlled trials assessed the effects of increased potassium intake on diastolic BP.

The UK study that provided daily potassium gluconate/potassium citrate supplements to half of a group of healthy adults and placebo to the remainder reported increases in urinary potassium excretion but no significant change in diastolic BP (high RoB).¹³³

The study conducted in Italy administered 30mmol potassium aspartate daily to half of a group of adults with mild HTN and placebo to the remainder. At 4 weeks, diastolic BP was significantly decreased in the potassium supplemented group (95.0 ± 5.6 vs. 87.2 ± 4.3 mmHg, $P < 0.001$).²⁷¹

Potassium From Foods Versus Usual Diet

Parallel RCTs. Three parallel RCTs assessed the effect of increasing potassium intake through diet alone on BP (described above).^{83, 125, 127, 236}

A 2-month RCT that used coaching about dietary choices and food vouchers to increase potassium intake among urban blacks in Baltimore with controlled hypertension found increases in urinary potassium excretion in the intervention group (compared with baseline and the control group) but no change in diastolic BP (high RoB).⁸³

A second study, which randomized 106 adults with mild HTN to a diet calculated to provide 120 mmol potassium daily or a control diet, significantly reduced BP (unclear RoB).²³⁶

The third study, which randomized 47 adults on antihypertensive medications to receive advice to increase potassium-rich foods or to usual care, reported a significant decrease in the

need for antihypertensive medications among individuals in the high-potassium diet group (moderate RoB).¹²⁵

Crossover RCTs. A 1.5 month crossover RCT conducted in the UK compared the use of a diet enriched with fruits and vegetables to raise potassium levels to that of potassium citrate supplements and placebo controls among individuals with mild (early) hypertension.¹²⁷ This study reported no effects of increased dietary potassium intake on diastolic BP (low RoB).

Potassium Salts Compared

Parallel RCTs. A 1.5-month parallel RCT conducted in the UK randomized 85 healthy participants to 30mmol potassium chloride, 30mmol potassium citrate, or placebo.²⁷⁷ Both potassium chloride and citrate significantly reduced diastolic BP compared with placebo (MD – 4.30, CI –6.39, –2.20 and – 4.26, CI –6.31, –2.21, respectively); urinary potassium excretion was significantly increased in both intervention groups compared with the placebo group.²⁷⁷

Crossover RCTs. He and colleagues reported no difference in the effects of potassium bicarbonate, potassium chloride, and placebo on diastolic BP (low RoB).¹²⁶ Vongpatanasin reported that 4 weeks of KCl supplementation decreased diastolic BP but potassium magnesium citrate and potassium citrate did not (moderate RoB).⁹⁴

Children

Sinaiko and colleagues reported a small, statistically insignificant mean difference in diastolic BP with increasing potassium intake (–1.14, 95% CI –5.34, 3.07) (moderate RoB) (Figure 39b).¹³¹

The CCT that enrolled twins found no difference in diastolic BP between the potassium gluconate and potassium citrate mixture and placebo (high RoB).¹³³

Figure 39a. Effect of increased potassium intake from dietary supplements on mean difference in diastolic BP for adults

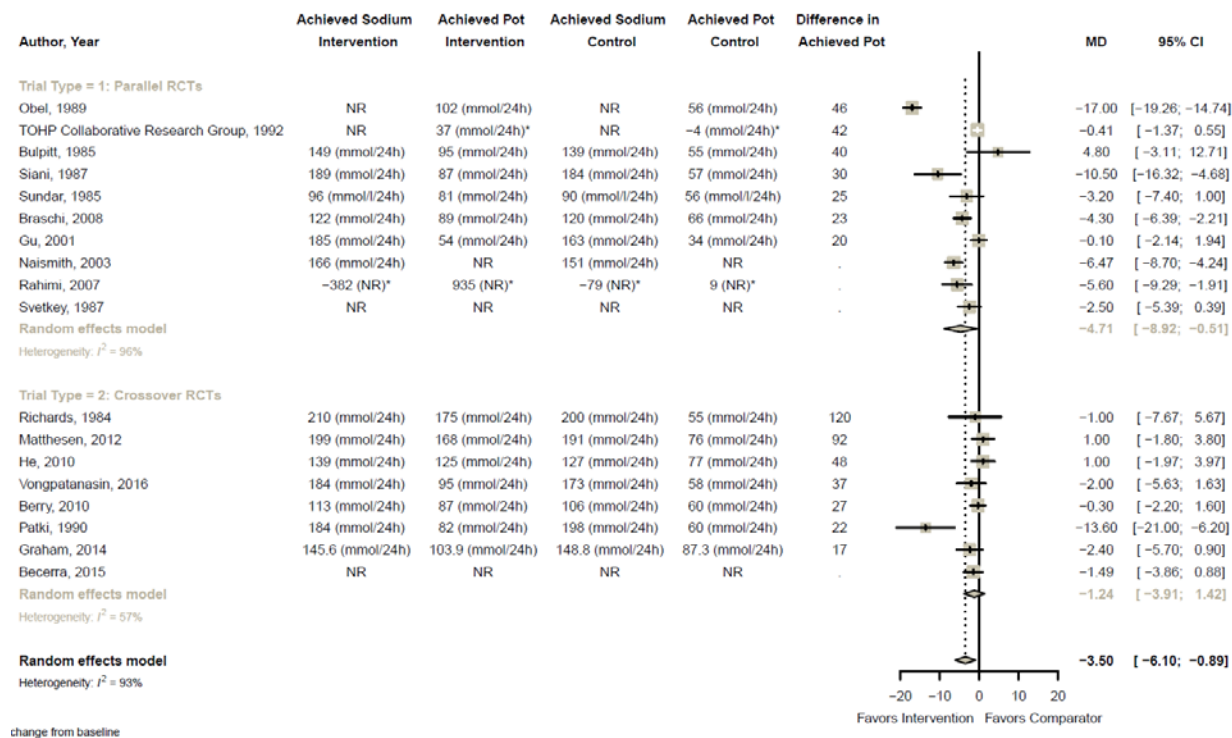


Figure 39b. Effect of increased potassium intake on mean difference in diastolic BP for children

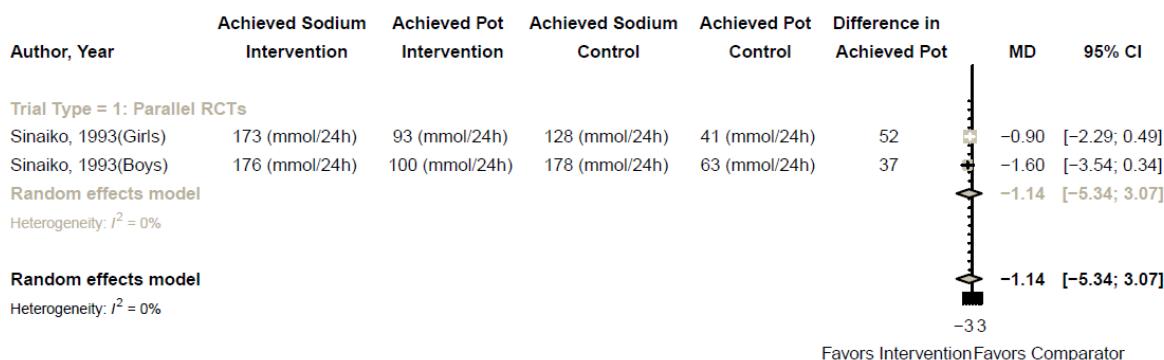


Figure notes: BP = blood pressure; CI = confidence interval; hr = hours; MD = mean difference; mmol = millimoles; RCT = randomized controlled trial

Percent Participants at Blood Pressure Goal

No studies that met inclusion criteria reported on the actual proportion of participants who achieved a prespecified blood pressure goal. However, one study assessed the effect of increased potassium on the continued need for antihypertensive medication. A study conducted in Italy randomized 54 patients with hypertension to receive advice to improve dietary potassium intake or to usual diet for 1 year.¹²⁵ Urinary potassium excretion increased significantly in the potassium-rich diet group compared with the usual diet group. At the end of the year, the average number of antihypertensive medications used per day decreased by 76 percent in the intervention

group, compared with a 40 percent decrease in the usual diet group. Some 81 percent of intervention patients had their HTN managed on less than half of their baseline dosage, compared with 29 percent of the usual diet group.

Evidence is insufficient based on one study to draw conclusions regarding effects of increased potassium intake on achievement of a prespecified blood pressure goal.

Kidney Stones

Only one RCT that assessed the effect of increased potassium intake on kidney stone incidence or recurrence met inclusion criteria. A US RCT, reported by Barcelo and colleagues, randomized 57 patients with active idiopathic hypocitraturic calcium nephrolithiasis to 30-60 mmol/d potassium citrate supplementation for 3 years to assess the effect on the risk for kidney stone recurrence.¹⁷⁶ Potassium citrate significantly decreased the incidence of kidney stone recurrence (MD -1.00, CI -1.16, -0.84) in the supplemented group.

Evidence is insufficient based on one study to draw conclusions regarding effects of increased potassium intake on risk for kidney stones.

Adverse Events

Six RCTs reported on adverse events associated with potassium supplement interventions (low RoB).^{60, 70, 74 72, 110, 176}

All six described minor gastrointestinal discomfort, but in at least one study (low RoB),⁷⁰ no difference was seen between active intervention and control groups.

One study reported no increase in LDL cholesterol with increased potassium intake (moderate RoB).⁶⁰

A low strength of evidence based on six RCTs suggests minor gastrointestinal discomfort associated with use of potassium supplements.

Sex

One RCT reported outcomes of increased potassium intake on BP by sex in adults⁵¹ and one in adolescents.¹³¹ The study on children is reported above. No RCTs reported on outcomes of increased potassium intake on incidence of HTN, percent of participants who achieve a prespecified goal, incidence of kidney stones, or AEs, by sex.

The TOHP-I trial randomized 353 US men and women to 6 months' 60mmol potassium chloride supplementation or placebo. Women constituted 23 percent of the intervention group and 30 percent of the controls.^{51, 75}

Mean Difference in Blood Pressure

The TOHP-I found no significant differences between men and women in the apparent absence of effect of increased potassium intake on systolic or diastolic blood pressure at 6 months (low RoB).^{51, 75}

A study that compared the effects of potassium supplementation on the developmental trajectory of blood pressure over 4 years in male and female adolescents found that among girls, potassium supplementation lowered the increase in systolic blood pressure, whereas potassium had no effect on boys (moderate RoB).¹³¹ No difference was seen in the effects of potassium on diastolic pressure between boys and girls.

Evidence is insufficient (based on one RCT in adults and one in teens) to draw a conclusion regarding the moderating effect of sex on the effects of increased potassium intake on BP in adults or youth.

Race/Ethnicity

Description of Included Studies

Two RCTs assessed effects of increased potassium intake on BP separately for black adults and the adult study population as a whole or for white and black adults,^{51,74,75} and two additional studies included only black adult participants.^{71,83} No RCTs reported on outcomes of increased potassium intake on incidence of HTN, percent of participants who achieve a prespecified goal, incidence of kidney stones, or AEs, by race/ethnicity.

Svetkey randomized 101 US adults with mild hypertension to 120mmol potassium chloride or placebo for 2 months; 11 percent of the intervention group and 17 percent of the placebo control group identified as black.⁷⁴

As just described, the TOHP-I randomized 353 adults with high-normal BP to 6 months' increased potassium intake. Seven percent of the intervention group and 11 percent of the control group identified themselves as black.^{51,75}

Obel assigned 48 black adult patients with mild hypertension in Kenya to a daily supplement of 64 mmol potassium (salt not identified) or placebo for 4 months.⁷¹

Miller and colleagues conducted a 2-month parallel RCT (the "Five Plus Nuts and Beans" trial) among US urban blacks to assess the effect of increasing dietary potassium through counseling and consumption of specific foods.⁸³

Mean Difference in Systolic Blood Pressure

In their study of the effects of 2 months of oral potassium chloride supplementation (120 mEq/d), Svetkey found a significant decrease in systolic BP in response to increased potassium intake among the small number of black participants (MD -20.00, 95% CI -41.67, -1.67), larger than that for the overall group (MD -6.29, 95% CI -11.50, -1.08) (moderate RoB).⁷⁴

In a study of 48 black patients with mild hypertension, Obel reported that 4 months of oral supplementation with 64mmol potassium decreased systolic BP significantly (MD -39.00, CI -43.88, -34.12) (low RoB).⁷¹

A 2-month RCT that used coaching about dietary choices and food vouchers to increase potassium intake among urban blacks in Baltimore with controlled hypertension found increases in urinary potassium excretion in the intervention group (compared with baseline and the control group) but no change in systolic BP (high RoB for potassium exposure determination).⁸³

The TOHP-I found no significant differences between white and black participants in the lack of effect of increased potassium intake on systolic blood pressure at 6 months (low RoB for potassium exposure determination).^{51,75}

Mean Difference in Diastolic Blood Pressure

Svetkey found a significant decrease in diastolic BP in response to increased potassium intake among black participants (MD -13.00, 95% CI -22.83, -3.17), higher than the overall response of the group (MD -2.50, 95% CI -5.39, 0.39).⁷⁴

The TOHP-I found no significant differences between white and black participants in the lack of effect of increased potassium intake on diastolic blood pressure at 6 months.^{51,75}

Among 48 black patients, Obel reported a significant decrease in diastolic BP with 2 months of increased potassium intake, compared with placebo (MD−17.00, CI −19.26, −14.74).⁷¹

The dietary intervention among hypertensive urban black patients reported no improvement in diastolic blood pressure.⁸³

Evidence is insufficient to draw a conclusion regarding a moderating effect of race/ethnicity on the effect of dietary or supplemental potassium on BP-related outcomes (four RCTs, two with low RoB, one with moderate, and one with high RoB, only one of which directly compared blacks with the total population).

Key Question 5c. Subpopulations Defined by Hypertension, Diabetes, Obesity, and Renal Health Status

Description of Included Studies

No studies that met inclusion criteria compared the effects of potassium supplementation or increased dietary potassium on blood pressure between healthy individuals and those with hypertension or other chronic conditions within the same study. However, two parallel RCTs and one crossover RCT assessed the effects of potassium supplementation on blood pressure in healthy participants.^{70, 91, 277} Ten parallel RCTs^{51, 60, 65, 71, 73, 74, 83, 125, 264, 280} and eight crossover RCTs^{48, 72, 89, 94, 110, 126, 127, 236} reported on the effects of increased potassium intake from food, supplements, or both, on BP in participants with prehypertension, or mild-, moderate-, or more advanced hypertension. No studies that met inclusion criteria assessed the impact of diabetes, obesity, or renal health status on the effects of potassium interventions.

Detailed Synthesis

Mean Difference in Systolic Blood Pressure

Healthy People

Three small RCTs that enrolled only normotensive participants and assessed effects of potassium interventions on systolic BP were eligible for pooling.^{70, 91, 277} The random effects pooled estimate for the studies showed that potassium lowered systolic BP but the effect was not statistically significant (MD −4.42, 95% CI−13.85, 5.02; I² 83%; n=173; low RoB) (Figure 40).

People With Prehypertension or Hypertension

The random effects pooled estimate for the parallel and crossover studies that enrolled participants with prehypertension or hypertension and increased potassium intake through use of potassium supplements showed a statistically significant beneficial effect of potassium supplementation on lowering systolic BP, but studies were highly heterogeneous (MD −6.95, 95% CI −12.59; −1.30; I² 95%; n=1,051; low RoB) (Figure 40).

As described above, four RCTs assessed the effects of increasing potassium intake through dietary modification on blood pressure among adults with hypertension.^{83, 125, 127, 236} Two of the RCTs showed no effects of increased dietary potassium on BP among participants (low and high RoB).^{83, 127} A third study, which randomized 106 adults with mild HTN to a diet calculated to provide 120 mmol potassium daily or a control diet, significantly reduced BP (unclear RoB).²³⁶ The fourth study, which randomized 47 adults on antihypertensive medications to receive advice

to increase potassium-rich foods or to usual care, reported a significant decrease in the need for antihypertensive medications among individuals in the high-potassium diet group (moderate RoB).¹²⁵

Figure 40. Effects of increased potassium intake from supplements on mean difference in systolic BP for populations with hypertension and those with normal blood pressure

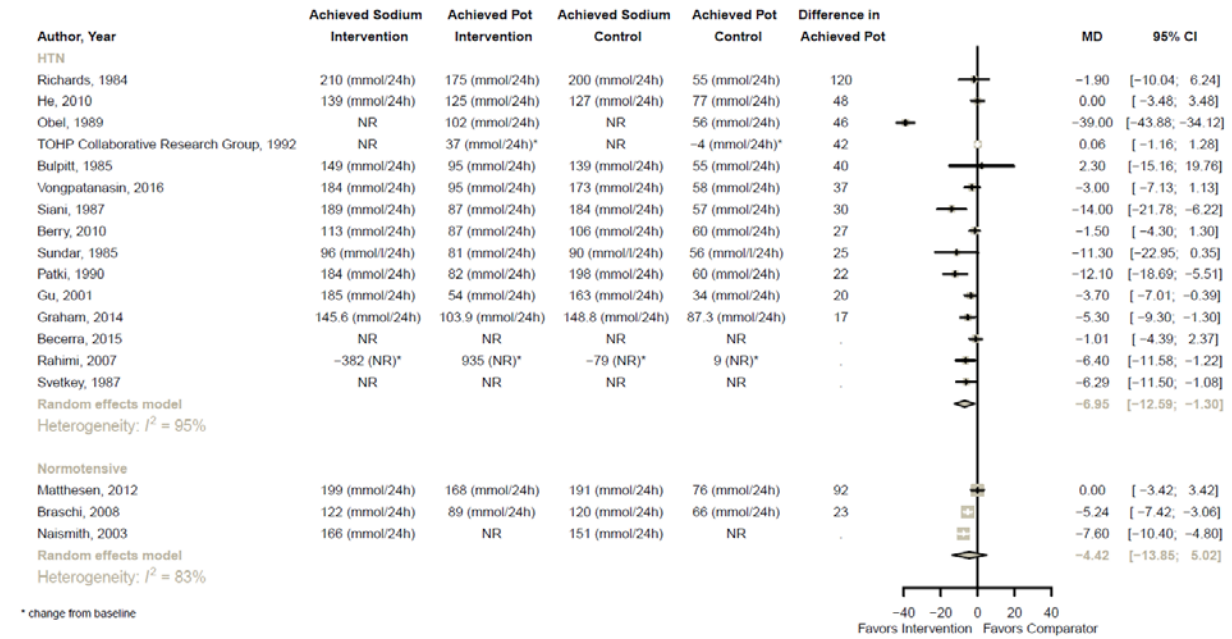


Figure notes: BP = blood pressure; CI = confidence interval; h = hour; HTN = hypertension; mmo l= millimole; MD = mean difference

Mean Difference in Diastolic Blood Pressure

Healthy People

The random effects pooled effect size for the RCTs that assessed the effect of increased potassium intake on diastolic BP in normotensive individuals showed a non-significant beneficial effect (MD -3.35, -12.79, 6.10; I^2 88%; low RoB) (Figure 41).

People With Prehypertension or Hypertension

The random effects pooled estimate for the parallel RCTs that enrolled populations with prehypertension or HTN and assessed effects of potassium interventions on diastolic BP showed that potassium had a small but statistically significant beneficial effect on diastolic BP; studies were highly heterogeneous (MD -3.55, 95% CI -6.68, -0.42; I^2 93%; n=1,051; low RoB for assessment of potassium exposure) (Figure 41).

Figure 41. Effects of increased potassium intake from supplements on mean difference in diastolic BP for populations with hypertension and those with normal blood pressure

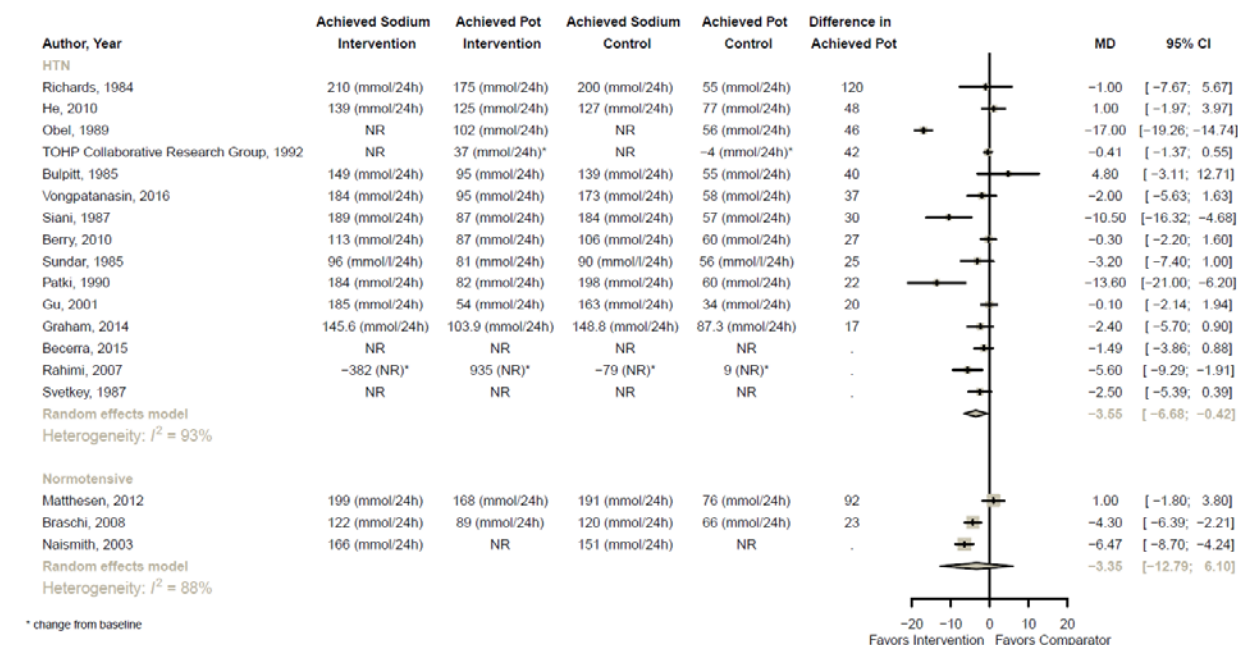


Figure notes: BP = blood pressure; CI = confidence interval; h = hour; HTN = hypertension; MD = mean difference; mmol = millimole; NR = not reported

Evidence is insufficient to draw conclusions regarding the moderating effect of hypertension on the effects of increased potassium intake or increased dietary potassium on blood pressure (no studies directly compared findings in normotensive populations and those with hypertension).

We did not find evidence that increasing potassium decreases BP in healthy populations (low SoE based on three RCTs).

A moderate strength of evidence supports a beneficial effect of potassium supplements on blood pressure in populations with prehypertension or hypertension (based on 15 RCTs, some with inconsistent findings).

Key Question 5a. Effect of Other Minerals on Effect of Potassium

Description of Included Studies

Three RCTs, one parallel and two crossover, assessed the potential moderating effects of calcium, magnesium, or reduced sodium on the effects of increased potassium intake on blood pressure.^{72, 218, 264} Rahimi and colleagues²⁶⁴ randomized 103 patients in Iran with hypertension or high-normal blood pressure to one of four interventions for 1 month: an 800mg (20 mmol) calcium diet, a 4000mg (100mmol) potassium diet, a combination of high calcium and high potassium diet, or a control (usual) diet. The sources of the minerals were foods; no description was provided regarding whether the intervention included instruction, provision of menus, or provision of foods, and it was not possible to estimate. Urinary potassium excretion increased significantly compared with the controls (units were not reported). Patki and colleagues⁷² randomized 37 Indian adults with mild hypertension to potassium chloride (30mmol/d) or

potassium chloride and magnesium (15mmol) for 2 months, followed by a 2-week crossover and 2 months on the other regimen.

No studies assessed the influence of other minerals on the effects of potassium on other outcomes of interest for this Key Question (i.e., incident hypertension, percentage at goal, or incident kidney stones)

Detailed Synthesis

Calcium

Rahimi's study found significant decreases in systolic blood pressure for the intervention groups receiving potassium (MD -6.40, CI -11.58, -1.22) and calcium plus potassium (MD -11.00, CI -17.80, -4.20) but not calcium alone, compared with the control group.²⁶⁴ Systolic blood pressure decreased slightly but not significantly more in the group that increased both calcium and potassium compared to those who consumed diets enriched in one or the other.

The study found significant decreases in diastolic blood pressure for the intervention groups receiving potassium (-4.40, CI -8.01, -0.79) and calcium (MD -5.60, CI -9.29, -1.91) but the decrease in diastolic blood pressure for calcium plus potassium just missed significance (MD -4.20, CI -8.44, 0.04), compared with the control group.²⁶⁴ Systolic blood pressure decreased slightly but not significantly more in the group that increased both calcium and potassium compared to those who consumed diets enriched in one or the other.

Magnesium

The crossover study conducted by Patki reported that supplementation with potassium alone and potassium plus magnesium reduced systolic blood pressure, with no significant difference between them (MD -8.90, CI -13.75, -4.05 compared with placebo vs. -12.10, CI -18.69, -5.51).⁷²

This study reported that supplementation with potassium alone and potassium plus magnesium reduced diastolic blood pressure, with no significant difference between them (MD -10.10, CI -15.60, -4.60 compared with placebo vs. -13.60, CI -21.00, -6.20).⁷²

Sodium Reduction

A crossover RCT conducted in Australia randomized adult twins with or without HTN who were consuming a low-sodium, high-potassium diet to receive sodium pills, aimed at returning sodium intake to usual levels, or placebo pills to assess the effects of low vs. usual sodium intake on the effects of higher potassium intake (low RoB).²¹⁸ The combination of low sodium and high potassium resulted in significantly lower systolic BP than did usual sodium and high potassium when measured at home but no difference when measured in the clinic. In addition, the study did not report whether the higher potassium, usual sodium diet lowered BP from that of usual diet. Thus, evidence from three studies is insufficient to draw conclusions regarding the modifying effect of other minerals (one study each on calcium, magnesium, and reduced sodium) on the effects of dietary or supplemental potassium (high RoB based on assessment of potassium and sodium exposure).

Key Question 6. Association Between Potassium Intake and Blood Pressure and Kidney Stone Formation

Key Points

- Higher potassium intake is not consistently associated with lower adjusted BP in adults (low SoE). Across six studies (four with high RoB), three studies observed associations only for diastolic BP, and one study observed an association only with systolic BP.
- Evidence is insufficient, based on lack of direct comparisons, to draw conclusions regarding sex, age, or racial/ethnic differences in the association between potassium intake and BP, risk for incident HTN, or risk for kidney stones.
- We did not find evidence for an association between potassium intake and decreased risk for incident hypertension in adults. Across five studies (four with high RoB), two studies observed an association between increased potassium intake and increased risk (low SoE).
- Higher potassium exposure may be associated with lower risk for kidney stones in adults (low SoE). Among four cohorts (analyzed in two publications), all had high RoB.
- Evidence is insufficient, based on lack of direct comparisons and only one study, to draw conclusions regarding a moderating effect of hypertension on the association between potassium exposure and BP, achievement of a prespecified blood pressure goal, or incidence of kidney stones.
- Evidence is insufficient, based on lack of direct comparisons and only one study, to draw conclusions regarding a moderating effect of obesity on the association between potassium exposure and BP, risk for incident HTN, achievement of a prespecified blood pressure goal, or risk for kidney stones.

Key Question 6a. Subpopulations Defined by Sex, Race/Ethnicity, and Age

Description of Included Studies

We identified 12 prospective cohort studies^{65, 75, 37, 67, 69, 76, 104, 120, 132, 145, 153, 274} that addressed the association of potassium status with blood pressure, hypertension, or the incidence of kidney stones in adults or children. One study included only young people (age 17 or less).^{104, 132} The rest followed adults. One study compared changes in BP and incidence hypertension between men under 50 and those 50 and over.³⁷

Of the studies that met the inclusion criteria for this Key Question, two studies included only females,^{76, 104} and reported on BP and incident HTN, respectively; two included only males^{37, 67} and reported on BP and incident HTN³⁷ and kidney stones.⁶⁷ Three studies compared the findings for males with those for females (on BP and kidney stones, respectively).^{69, 133, 153}

No studies compared findings by race/ethnicity.

Detailed Synthesis

Age

Blood Pressure

Adults

24-Hour or Estimated 24-Hour Urinary Potassium Excretion

Chien and colleagues followed a cohort of 1,520 healthy men and women (mean age 52) in a Taiwan village over a median of 8 years (the Chin-Shan Community Cardiovascular Cohort Study [CCCC]). They found no association between estimated 24-hour urinary potassium (based on overnight urine) and systolic BP but a small inverse correlation with age- and sex-adjusted diastolic BP (high RoB).²⁷⁴

Multivariate analysis of the results of the TOHP-I (which randomized 353 men and women with high-normal BP to 60mmol/d potassium or placebo),⁷⁵ adjusted for age, race, sex, baseline BP, 24-hour urinary sodium, post-randomization z, and changes in body weight, showed no association between urinary potassium and systolic BP (the mean of the 3- and 6-month change in systolic BP from baseline). Compared to those in the lowest quartile, change in 24-hour urinary potassium excretion for the highest quartile of excretion was associated with a 1.49-mm Hg larger reduction in diastolic BP. Multiple linear regression with a continuous term for urinary potassium excretion showed a p coefficient of change in diastolic BP (-0.015, P = 0.021) for each unit change in 24-hour urinary potassium excretion (low RoB).

Multivariate analysis of the results of the PAPSS, which supplemented Chinese adults with mild HTN with potassium (60mmol/d) found a significant association of 24-hour urinary potassium excretion (single measurement) with reduction in systolic BP after adjustment for sex, baseline diastolic BP, baseline body weight, and changes in sodium during the intervention. The study found no association of urinary potassium excretion with reduction in diastolic BP (low RoB).⁶⁵

Potassium Intake Assessment via Dietary Records

The association of dietary potassium and other nutritional factors (determined via FFQ) with self-reported blood pressure was assessed at 4 years' followup in the Health Professionals' Follow-Up Study.³⁷ Multivariate analysis adjusted for age, BMI, alcohol consumption, and intakes of calcium, magnesium, and fiber showed no association of potassium intake with systolic BP or diastolic BP. However, controlling for four nutrients (magnesium, calcium, sodium, and fiber) simultaneously showed a significant inverse association between potassium intake and diastolic BP (high RoB based on dietary assessment method).

As described above, the NHLBI Study found that the highest quartile of potassium intakes (from multiple 3-day diet records) was associated with lower adjusted systolic and diastolic BP (high RoB).¹⁰⁴

At 12 years' followup, potassium intake in the Rancho Bernardo Study, determined from 24-hour dietary recall, was inversely correlated with systolic BP (high RoB).⁶⁹

Children

One cohort study assessed the association of potassium exposure with blood pressure in children 17 and younger after an average of 7 years' follow up.^{104, 132} Geleijnse and coworkers

followed a cohort of children 5 to 17 who resided in a small Netherlands town and found a small association of potassium, assessed via overnight urine samples, with systolic but not diastolic BP (low RoB).

Thus, findings from six prospective cohort studies in adults and one study among children suggest potassium intake is not consistently associated with BP in adults (low strength of evidence). Evidence is insufficient to assess association in children or to compare associations in children with those in adults.

Incident Hypertension

Adults

24-Hour Urinary Potassium Excretion

The Prevention of Renal and Vascular End-Stage Disease (PREVEND) Study has followed 8,592 men and women since the late 1990s.¹²⁰ At a median followup of 7.6 years, they assessed factors associated with risk for incident HTN (Systolic BP of ≥ 140 mm Hg, a diastolic BP of ≥ 90 mmHg, or the use of antihypertensive drugs). Adjusting for age, sex, BMI, smoking status, alcohol consumption, parental history of HTN, urinary sodium excretion, education, and urinary magnesium and calcium excretion, multivariate analysis showed that the lowest tertile of 24-hour potassium excretion was associated with a significant increase in HTN risk, which they reported as a non-linear inverse association between urinary potassium excretion and risk for HTN (moderate RoB).

At a median followup of 7.9 years, the CCCC, described above, reported no significant difference in incidence rates for HTN across quartiles of potassium intake and no difference in relative risk using four different adjustment models (high RoB).²⁷⁴

Potassium Intake Assessment via Dietary Records

The Health Professionals' Followup Study assessed self-reported incident HTN at 4 years. Adjusting for age, BMI, alcohol consumption, and intakes of three other nutrients (magnesium, sodium, and fiber), they found a stronger association between dietary potassium and risk for HTN in men under 50 than in men 50 and over; but the overall effect disappeared in multivariate analysis. Thus, they found no significant association between potassium intake and risk for HTN (high RoB).³⁷

At 4 years' followup, the Nurses' Health Study assessed the association between self-reported HTN and various dietary factors among some 6,930 participants, ages 34 to 59.⁷⁶ Adjusting for age, BMI, alcohol consumption, and energy intakes, they found that increased potassium intake was associated with a slight decrease in relative risk for HTN (RR 0.77 at ≥ 3200 mg/d, $p < 0.001$). However, further adjustment for magnesium and calcium intakes eliminated the effect of potassium (high RoB).

The Chinese Health and Nutrition Survey (CHNS) has followed 16,869 healthy adults over 10 years. Dietary potassium intake was assessed using three 3-day food diaries. Results were adjusted for sodium intake, energy intake, age, sex, education, income, region, BMI, physical activity, smoking status, and alcohol consumption. At a median followup of 10 years, the second (1.2-1.4 g/d) through fifth quintiles (≥ 2.2 g/d) of potassium intake were associated with lower risk for incident HTN compared with the lowest quintile (< 1.2 g/d) (HR for highest potassium intake 0.66, CI .56, 0.78) (low RoB).¹⁴⁵

No studies assessed the association of potassium exposure and incident HTN among younger persons.

Thus, a low strength of evidence suggests potassium intake, by itself, does not appear to be associated with risk for HTN among adults.

Incidence of Kidney Stones

Adults

Two studies assessed the association between potassium exposure and first incidence of kidney stones in adults.^{67, 153} The Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention Study (ATBC) assessed the association between intakes of potassium (and other nutrients, based on baseline FFQ) and first-time physician diagnosis of a kidney stone over 5 to 8 (median 6) years (high RoB).⁶⁷ Before adjustment for magnesium intake, higher potassium intake was significantly associated with a lower incidence of kidney stones but after adjusting for magnesium, the association with potassium became nonsignificant.

The association between potassium intake and risk for incident kidney stones was examined across three large prospective cohort studies at approximately 25 years followup as part of an assessment of the role of dietary protein and potassium.¹⁵³ The cohorts included the HPFUS (42,919 enrolled), the Nurses' Health Study I (60,128 enrolled), and the Nurses' Health Study II (90,629 enrolled). Higher potassium intake was associated with lower risk for kidney stones in all 3 cohort studies assessed together and separately, adjusted for age alone or for age, BMI, history of DM, history of HTN, use of diuretics, supplemental calcium, and dietary intakes of fluids, calcium, sodium, fructose, oxalates, phytates, alcohol, and protein. Multivariate adjusted hazard ratios ranged from 0.44 (CI 0.36, 0.53) for the HPFS to 0.67 (CI 0.57, 0.78) for the NHS II (high RoB).

We did not find evidence for an association between high potassium intake and decreased risk for incident hypertension in adults. Across five studies (four with high RoB), two studies observed an inverse association.

A low strength of evidence suggests higher potassium exposure may be associated with lower risk for kidney stones in adults. Among four cohorts (analyzed in two publications), all had high RoB.

Sex

Blood Pressure

The NHLBI Growth and Health study followed a cohort of 10-year old girls in the U.S. over 10 years. After adjusting for race, height, activity levels, screen time, energy intake (and percentage of calories from solid fats and added sugar), and dietary fiber, they reported a small association between the highest quartile of potassium intake and decreased systolic and diastolic BP among the young women at 10 years' followup (ages 17 to 21 years) (high RoB).¹⁰⁴

The Health Professionals' Followup Study (HPFUS) followed a cohort of male physicians. At 4 years, they found no association of dietary potassium (assessed using a semi-quantitative food frequency questionnaire [FFQ]) with BP (high RoB).³⁷

The Rancho Bernardo Study was a prospective cohort study of 859 men and women, 50 to 79. At 12 years' follow up, this study found comparably small associations between potassium

intakes (assessed via 24-hour dietary recall) and systolic and diastolic BP for men and women (high RoB).⁶⁹

Incident Hypertension

At 4 years' followup, the Nurses' Health Study (NHS) assessed the association between self-reported HTN and various dietary factors among some 6,930 participants, ages 34 to 59 (high RoB).

Neither the Nurses' Health Study (all women) nor the HPFUS (all men) found an association between potassium and HTN incidence (both high RoB).^{37, 76}

Incidence of Kidney Stones

One study assessed findings from three large cohorts: the HPFUS, Nurses' Health Study (NHS)-I, and NHS-II. The cohorts included the HPFUS (42,919 enrolled), the NHS-I (60,128 enrolled), and the NHS-II (90,629 enrolled). They reported comparable decreases in the risk for incident kidney stones among men and women with increasing dietary potassium: Men experienced a nonsignificantly lower risk than did women in the highest quintile (high RoB).¹⁵³

Thus, evidence is insufficient, based on lack of direct comparisons, to draw conclusions regarding sex differences in the association between potassium exposure and BP, risk for incident HTN, or risk for kidney stones.

Key Question 6b. Subpopulations Defined by Hypertension, Diabetes, and Obesity Health Status

Description of Included Studies

Only one study that met inclusion criteria to respond to this Key Question enrolled a population all of whom had HTN.^{65, 271} The remainder enrolled entirely or mostly healthy people.

One study compared the association of potassium status and incident hypertension in obese participants (BMI \geq 29) with that in men with BMI less than 29.³⁷

No studies that met inclusion criteria assessed the potential moderating role of DM or kidney disease.

Detailed Synthesis

Hypertension

No studies assessed the modifying effects of hypertension on the association of potassium status with achievement of a prespecified goal or with incidence of kidney stones.

Blood Pressure

No studies assessed the modifying effects of hypertension on associations of potassium status with BP by comparing participants with HTN and normotensives within the same study.

Multivariate analysis of the PAPSS cohort (Chinese adults with mild HTN, half of whom were supplemented with potassium [60mmol/d]) found a significant association of urinary potassium excretion with reduction in systolic and diastolic BP after adjustment for sex, baseline DBP, baseline body weight, and changes in sodium during the intervention (low RoB).⁶⁵ Thus, evidence is insufficient, based on lack of direct comparisons and only one study, to draw

conclusions regarding a moderating effect of hypertension on the association between potassium exposure and BP, achievement of a prespecified blood pressure goal.

Obesity

No studies assessed the modifying effects of weight status on associations of potassium status with BP, achievement of a prespecified goal, or kidney stones.

Incident Hypertension

The HPFUS compared the association of potassium and risk for HTN in obese and non-obese adults. In bivariate analysis, the lowest tertile of potassium intake among overweight and normal weight men—but not obese men—was associated with increased HTN risk. In multivariate analysis, this relationship did not hold (high RoB).³⁷ Thus, evidence is insufficient to support a conclusion regarding the moderating effect of weight status on the association between potassium intake and the risk for hypertension.

Key Question 7. Effect of Interventions To Increase Potassium Intake on CVD and Kidney Disease Morbidity and Mortality, and on Total Mortality, Among Adults

Key Point

- Evidence was insufficient to assess the effect of potassium supplementation on the risk for all-cause mortality, CVD/CHD morbidity or mortality, or renal morbidity or mortality (one RCT).

Description of Included Studies

One RCT met inclusion criteria for this question. Chang and colleagues block-randomized 1,981 male veterans in a retirement home in northern Taiwan by the kitchen in which they had their meals to receive potassium-enriched salt substitute (49% sodium chloride, 49% potassium chloride, 2% other) or sodium chloride and followed them for approximately 2 to 3 years.¹⁸² Forty percent of the veterans had HTN. This study reported only on all-cause, CVD-, CHD- and other causes of mortality and had moderate RoB.

Detailed Synthesis

All-Cause Mortality

At three months, the urinary sodium to creatinine ratio (available for approximately one fourth of participants) decreased in the salt substitute group and increased in the control group; urinary sodium and sodium/potassium were not reported. At 31 months, the potassium salt-supplemented group showed a significant decrease in cumulative age-adjusted all-cause mortality compared with the control group (RR 0.68, 95% CI 0.58, 0.80).¹⁸²

CVD Mortality

Chang reported a significantly lower age-adjusted rate of CVD-related mortality among men who received the potassium-enriched salt substitute (RR 0.42, 95% CI 0.27, 0.66), which translated to an additional 4 to 11 months of life).¹⁸²

CHD Mortality

Chang also reported a significantly lower age-adjusted rate of CHD-related mortality among men who received the potassium-enriched salt substitute (RR 0.45, 95% CI 0.21, 0.99).¹⁸²

Key Question 7a. Effect of Other Minerals on Effect of Potassium

We identified no studies other than the one reported above.

Key Question 7b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

No studies that met inclusion criteria stratified by subpopulations.

Key Question 7c. Subpopulations Defined by Hypertension, Diabetes, Obesity, and Renal Health Status

No studies that met inclusion criteria stratified by the populations of interest.

Key Question 8. Association Between Dietary Potassium Intake and CVD, CHD, Stroke, and Kidney Disease Morbidity and Mortality, and Between Dietary Potassium and Total Mortality, Among Adults

Key Points

- Evidence is insufficient to identify associations of potassium intake with long term chronic disease outcomes of interest.

Detailed Synthesis

Total Mortality

A total of 10 studies^{55, 116, 121-123, 129, 137, 140, 141, 154} that reported analyses examining the associations between potassium intake levels and total mortality outcome were included. These studies included six among generally healthy adult populations,^{55, 116, 129, 137, 140, 141} and four studies among people with existing diseases such as CVD,¹²² type 2 diabetes¹⁵⁴ and CKD.^{121, 123} The latter are described in the response to Subquestion 8c.

Five prospective cohort studies^{55, 116, 137, 140, 141} and one case-cohort study¹²⁹ examined the associations between potassium intake levels and total mortality outcomes among generally healthy adult populations. These cohorts are PREVENT,¹³⁷ the Scottish Heart Health study,⁵⁵ WHI Observational Study (WHI-OS),¹⁴⁰ NHANES III,¹¹⁶ PURE,¹⁴¹ and the Rotterdam study.¹²⁹

Except for the WHI Observational Study, all studies included both adult men and women at baseline (mean ages ranged from 50 to 69.2 years old). The WHI OS enrolled only postmenopausal women (mean age = 63.6 years old). Mean or median followup times ranged from 3.7 to 14.8 years.

Potassium intake levels were assessed by 24-hour urinary potassium excretion in the PREVEND and the Scottish Heart Health studies,^{55, 137} by spot-urine samples in the PURE and the Rotterdam studies,^{129, 141} by food frequency questionnaire in the WHI OS and the Rotterdam study,^{129, 140} and by 24-hour dietary recalls in NHANES III.¹¹⁶ The potassium intake ranged from 27.5 mmol/d (1075 mg/d) to 116.4 mmol/d (4551 mg/day). Individual study results are shown in Figure 42 and Table 15.

Overall Results

The relationships between potassium intake levels and total mortality are inconsistent among the four studies that examined urinary potassium levels and total mortality.^{55, 129, 137, 141} On the contrary, three studies consistently showed an inverse relationship between dietary potassium intake and total mortality.^{116, 129, 140} In the Rotterdam study, levels of both urinary potassium (by spot-urine estimated 24-hour urinary potassium excretion) and dietary potassium were assessed.¹²⁹ All studies, except for the Scottish Heart Health study, controlled for various demographics, lifestyle factors, and medical history or medications. Among these, the PREVEND,¹³⁷ ONTARGET and TRANSCEND cohort studies,¹²² and the Rotterdam study¹²⁹ also adjusted for urinary sodium excretion in their analyses. The Scottish Heart Health study adjusted only for age in their analyses so the results are at high risk for confounding. The overall RoB was rated moderate.

Urinary Potassium Excretion and Total Mortality

Four studies that examined urinary potassium levels and total mortality showed inconsistent results.^{55, 129, 137, 141} Among these, PREVEND¹³⁷ and the Scottish Heart Health study⁵⁵ measured 24-hour urinary potassium excretion. The PREVEND cohort (moderate RoB), which oversampled individuals with albuminuria (n=7795), did not find significant associations between 24-hour urinary potassium excretion (examined as a continuous measure and in quartiles) and total mortality in multivariable adjusted models that included urinary sodium excretion as a covariate (adjusted hazard ratio = 1.02; 95% CI 0.88, 1.19).¹³⁷ In contrast, the Scottish Heart Health study showed a significant inverse relationships between 24-hour urinary potassium excretion and total mortality among both men (n=5754) and women (n=5875).⁵⁵ However, because the Scottish Heart Health study adjusted only for age in their analyses, the results are at high risk for confounding.

The association between estimated 24-hour urinary potassium excretion and total mortality was examined in PURE and the Rotterdam study (both were rated high RoB).^{129, 141} The PURE cohort study was a large, multi-center, multi-country study, and the Rotterdam study is a population-based study of men and women living in the Netherlands. The PURE study showed significantly decreasing risk of total mortality with increasing levels of 24-hour urinary potassium excretion estimated by Kawasaki equation in the primary multivariable model (adjusted OR 0.76, 95% CI 0.65, 0.89; 0.72 [0.62, 0.85], 0.71 [0.60, 0.85], and 0.60 [0.48, 0.74] comparing quintile 2, 3, 4, and 5 to the lowest quintile, respectively, n=101945),¹⁴¹ whereas no significant linear relationship was found between estimated 24-hour urinary excretion based on an overnight urine sample and total mortality in a multivariable adjusted model that included

urinary sodium as a covariate in the Rotterdam study (adjusted RR 1.08 per SD increase; 95% CI 0.91, 1.28; n=5531).¹²⁹

Dietary Potassium Intake and Total Mortality

Three studies consistently showed an inverse relationship between dietary potassium intake and total mortality outcome.^{116, 129, 140} Using 24-hour dietary recall data with NCI methods for estimating usual intake, both categorical and continuous analyses of NHANES III (moderate RoB) showed that higher potassium intake was significantly associated with lower total mortality in the general US population (adjusted HR 0.8 per 1000 mg/d increase; 95% CI 0.67, 0.94; n=12267).¹¹⁶ There were no significant interactions by sex, race/ethnicity, or presence of hypertension. Similar to NHANES III, the WHI OS (moderate RoB), which enrolled postmenopausal women living in the U.S. (n=90137), also showed that the second, third, and fourth quartiles of potassium intake were significantly associated with a decreased risk of total mortality when compared to the lowest quartile of potassium intake in fully adjusted models (adjusted HR 0.91, 95% CI 0.86, 0.96, 0.84 [0.79, 0.89], and 0.90 [0.85, 0.95], respectively).^{116, 140} Unlike the analyses using urinary potassium levels, the analyses using dietary potassium intake measured by a semi-quantitative food frequency questionnaire found an inverse relationship between dietary potassium intake and total mortality in the Rotterdam study (high RoB) (adjusted RR = 0.78 per SD increase; 95% CI 0.65, 0.94; n=5531) (Figure 42).¹²⁹

Figure 42. Categorical analysis of the association between potassium levels and total mortality outcome in generally healthy populations

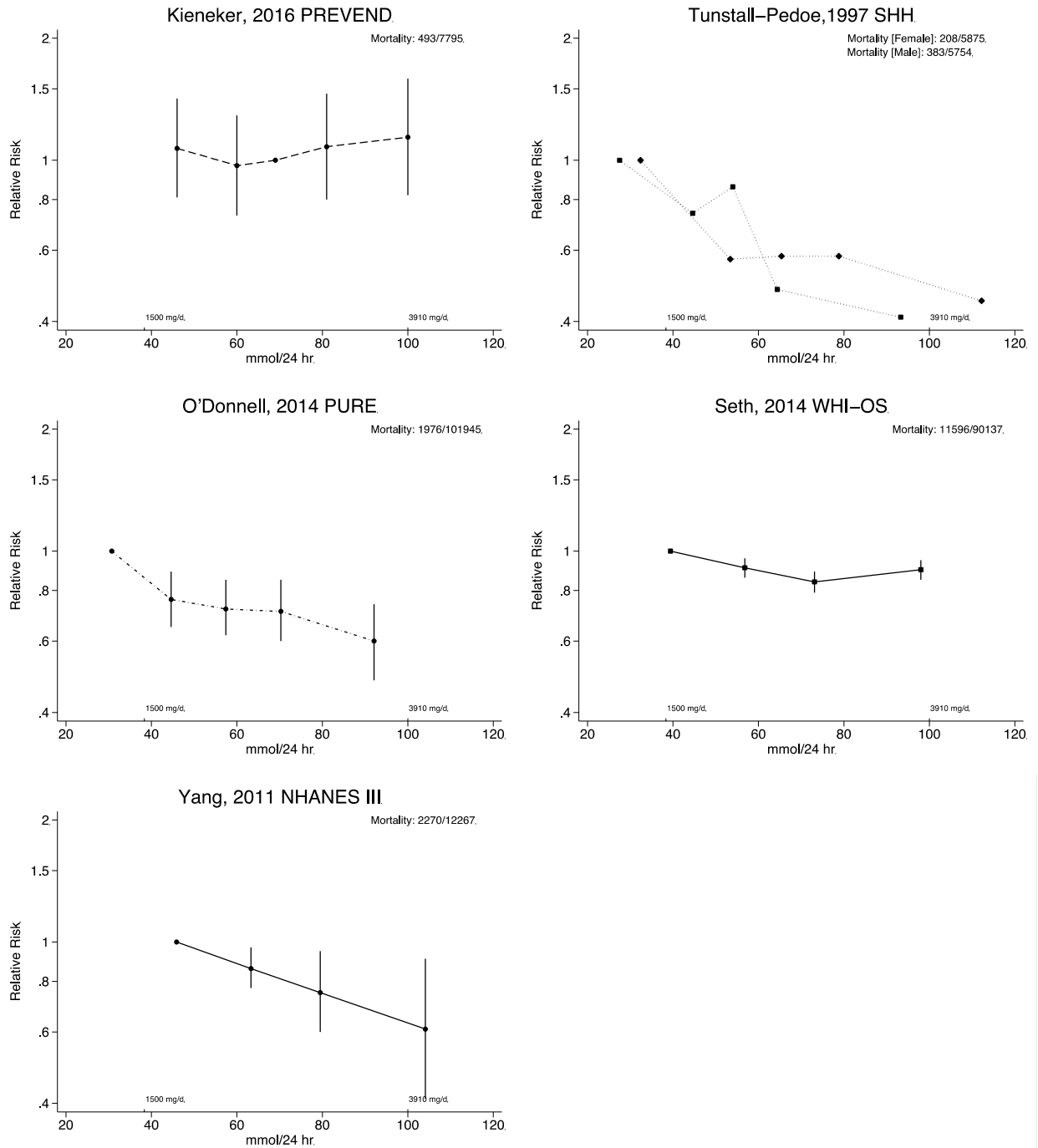


Figure notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dashed lines connect different levels of 24-hour urinary excretion; Dotted-dash lines connect different levels of estimated 24-hour urinary excretion; Solid lines connect different levels of dietary intake. hr = hour; mmol = millimoles; NHANES = National Health and Nutrition Examination Survey; PREVEND = Prevention of Renal and Vascular End-Stage Disease; PURE = Prospective Urban Rural Epidemiology Study; SHH = Scottish Heart Health [Study]; WHI-OS = Women’s Health Initiative – Observational Study

Table 15. Continuous analyses of the association between potassium levels and total mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	493/7795	0.063	24-hour urinary potassium excretion	Median 70 mmol/24h (IQR: 56–84 mmol/24h)	per 26-mmol/24-h increase	HR	1.02	0.88	1.19
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.144	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	0.78	0.65	0.94
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	0.71	0.51	1.00
	All	Both	median 5.5 y	795/5531	0.144	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	1.08	0.91	1.28
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	0.95	0.71	1.26
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary potassium intake	median 2780 (IQR 2164-3502; range 609-8839) mg/d	per 1000 mg/d increase	HR	0.8	0.67	0.94
	Male	Male	median 14.8 y	1267/5899	0.215	Dietary potassium intake	median 3272 (IQR 2660-3964) mg/d	per 1000 mg/d increase	HR	0.89	0.73	1.09
	Female	Female	median 14.8 y	1003/6368	0.158	Dietary potassium intake	median 2367 (IQR 1177-2932) mg/d	per 1000 mg/d increase	HR	0.55	0.4	0.78
	Non-Hispanic White	Both	median 14.8 y	1253/2269	0.552	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.8	0.66	0.97

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Non-Hispanic Black	Both	median 14.8 y	527/1540	0.342	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.73	0.54	0.99
	Mexican American	Both	median 14.8 y	449/1859	0.241	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.65	0.43	0.96
	Hypertensive	Both	median 14.8 y	1155/NR	--	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.83	0.66	1.06
	Non-hypertensive	Both	median 14.8 y	1115/NR	--	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.74	0.61	0.91

Table Notes: CI = confidence interval; CVD = cardiovascular disease; HTN = hypertension; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

CVD Mortality

A total of four studies^{116, 122, 129, 141} that reported analyses examining the associations between potassium intake levels and CVD mortality outcome were included. These studies analyzed data from three studies among generally healthy adult populations,^{116, 129, 141} and one study among people at high risk of CVD (previous medical history of myocardial infarction, stroke/TIA, hypertension, or diabetes), which is described in subquestion 8c.¹²²

Two prospective cohort studies^{116, 141} and one case-cohort study¹²⁹ examined the associations between potassium intake levels and CVD mortality outcome among generally healthy adult populations. These cohorts are PURE,¹⁴¹ the Rotterdam study,¹²⁹ and NHANES III.¹¹⁶ All studies included both adult men and women at baseline (mean ages ranged from 51 to 69.2 years old). Mean or median followup time ranged from 3.7 to 14.8 years.

Potassium intake levels were assessed by spot-urine samples in PURE and the Rotterdam study,^{129, 141} by food frequency questionnaire in the Rotterdam study,¹²⁹ and by 24-hour dietary recalls in NHANES III.¹¹⁶ The potassium intake ranged from 30.7 mmol/d (1197 mg/d) to 104 mmol/d (4069 mg/day). Individual study results are shown in Figure 43 and Table 16.

Overall Results for Potassium and CVD Mortality

Inverse relationships were observed between potassium intake levels and CVD mortality in two studies,^{116, 141} but no significant associations were shown between urinary potassium (by spot-urine estimated 24-hour urinary potassium excretion) or dietary potassium and CVD mortality in the Rotterdam study.¹²⁹ All three studies controlled for various demographics, lifestyle factors, and medical history or medications. The Rotterdam study¹²⁹ also adjusted for urinary sodium excretion in their analyses. The overall RoB was rated high.

Urinary Potassium Excretion and CVD Mortality

The association between estimated 24-hour urinary potassium excretion and total mortality was examined in the PURE and the Rotterdam studies (both were rated high RoB).^{129, 141} The PURE cohort study was a large, multi-center, multi-country study, and the Rotterdam study is a population-based study of men and women living in the Netherlands. The PURE study showed significantly decreasing risk of CVD mortality with increasing levels of 24-hour urinary potassium excretion estimated by Kawasaki equation in the primary multivariable model (adjusted OR 0.64, 95% CI 0.51, 0.80, 0.57 [0.44, 0.75], 0.45 [0.32, 0.64], and 0.48 [0.32, 0.71] comparing quintile 2, 3, 4, and 5 to the lowest quintile, respectively, n=101945),¹⁴¹ whereas no significant linear relationship was found between estimated 24-hour urinary excretion based on an overnight urine sample and CVD mortality in a multivariable adjusted model including urinary sodium as a covariate in the Rotterdam study (adjusted RR 1.23 per SD increase; 95% CI 0.94, 1.6; n=5531).¹²⁹

Dietary Potassium Intake and CVD Mortality

The association between estimated dietary potassium intake and CVD mortality was examined in the NHANES III (moderate RoB) and the Rotterdam study (high RoB).^{116, 129} Using 24-hour dietary recall data with NCI methods for estimating usual intake, both categorical and continuous analyses of NHANES III found that higher potassium intake was significantly associated with lower CVD mortality in the general US population (adjusted HR 0.63 per 1000 mg/d increase; 95% CI 0.46, 0.87; n=12267).¹¹⁶ There were no significant interactions by sex,

race/ethnicity, or presence of hypertension. Similar to the analyses using urinary potassium levels, the analyses using dietary potassium intake (measured by a semi-quantitative food frequency questionnaire) did not find a significant association between dietary potassium intake and CVD mortality in the Rotterdam study (adjusted RR = 0.97 per SD increase; 95% CI 0.72, 1.31; n=5531).¹²⁹

Figure 43. Categorical analysis of the association between dietary potassium intake and cardiovascular disease mortality outcome in generally healthy populations

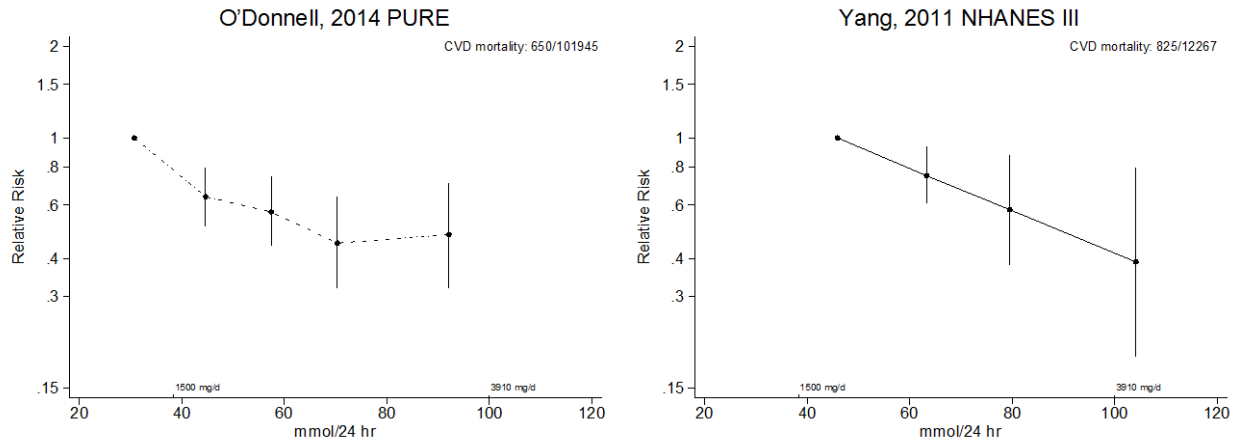


Figure notes: CVD = cardiovascular disease; d = day; hr = hour; mg = milligrams; mmol = millimoles

Table 16. Continuous analyses of the association between dietary potassium intake and CVD mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.144	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	0.97	0.72	1.31
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	1.43	0.67	3.03
	All	Both	median 5.5 y	795/5531	0.144	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	1.23	0.94	1.6
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	1.45	0.84	2.54
Yang, 2011 ¹¹⁶ NHANES III	All	Both	median 14.8 y	2270/12267	0.185	Dietary potassium intake	median 2780 (IQR 2164-3502; range 609-8839) mg/d	per 1000 mg/d increase	HR	0.63	0.46	0.87
	Male	Male	median 14.8 y	1267/5899	0.215	Dietary potassium intake	median 3272 (IQR 2660-3964) mg/d	per 1000 mg/d increase	HR	0.73	0.51	.103
	Female	Female	median 14.8 y	1003/6368	0.158	Dietary potassium intake	median 2367 (IQR 1177-2932) mg/d	per 1000 mg/d increase	HR	0.69	0.38	1.25
	Non-Hispanic White	Both	median 14.8 y	1253/2269	0.552	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.68	0.48	0.96
	Non-Hispanic Black	Both	median 14.8 y	527/1540	0.342	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.52	0.33	0.82
	Mexican American	Both	median 14.8 y	449/1859	0.241	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.36	0.18	0.72

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Hypertensive	Both	median 14.8 y	1155/NR	--	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.64	0.38	1.06
	Non-hypertensive	Both	median 14.8 y	1115/NR	--	Dietary potassium intake	NR	per 1000 mg/d increase	HR	0.66	0.46	0.95

Table Notes: CI = confidence interval; CVD = cardiovascular disease; HTN = hypertension; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

CHD Mortality

A total of two prospective cohort studies^{55, 116} examined the associations between potassium intake levels and CHD or IHD mortality outcomes among generally healthy adult populations. These cohorts are the Scottish Heart Health study⁵⁵ and NHANES III.¹¹⁶ Mean or median followup time were 7.6 and 14.7 years, respectively.

Potassium intake levels were assessed by 24-hour urinary excretion in one study,⁵⁵ and by 24-hour dietary recall in another.¹¹⁶ The potassium intakes ranged from 27.5 mmol/d (1075 mg/d) to 104 mmol/d (4069 mg/d). Individual study results are shown in Figure 44.

Overall Results for CHD Mortality

Both cohort studies showed inverse relationships between potassium intake levels and risks of CHD or IHD mortality.^{55, 116} However, one study (the Scottish Heart Health study) adjusted only for age in their analyses, so the results may be at increased risk for confounding. The overall RoB was rated as moderate.

Urinary Potassium Excretion and Total CHD Mortality

24-Hour Urinary Potassium

The Scottish Heart Health Study⁵⁵ reported that baseline 24-hour urinary potassium excretion levels were inversely associated with risks of CHD mortality in men (age-adjusted HR 0.57, 0.76, 0.59, 0.60 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875), but not in women (age-adjusted HR 0.73, 0.51, 0.62, 0.45 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754). The overall RoB was rated as high.

Dietary Potassium Intake and CHD Mortality

The NHANES III followup study showed that higher dietary potassium intake levels were associated with lower risks of CHD mortality for both categorical and continuous analyses (adjusted HR 0.51 per 1000 mg increase; 95% CI 0.32, 0.81; n=12267).¹¹⁶ The overall RoB was rated as low.

Figure 44. Categorical analysis of the association between urinary or dietary potassium levels and CHD mortality outcome in generally healthy populations

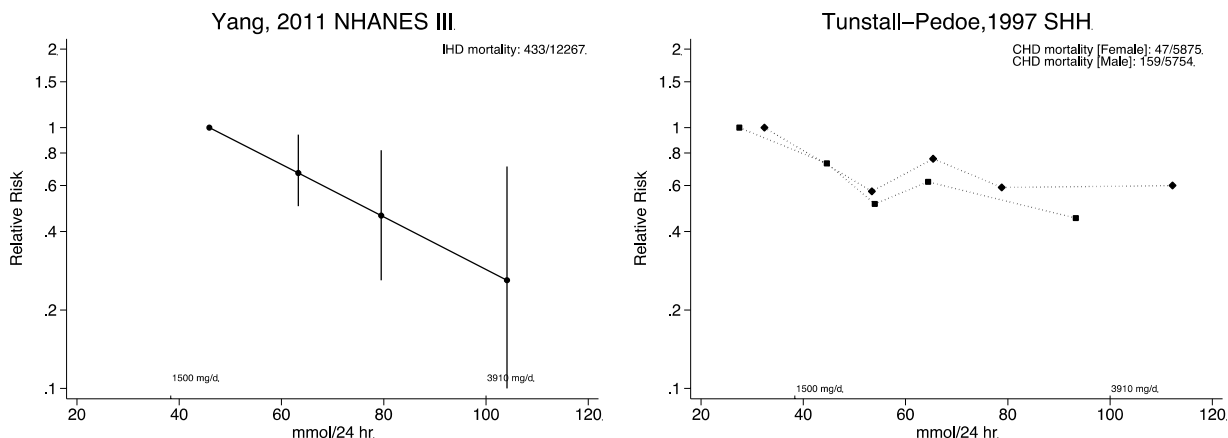


Figure Notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dashed lines connect different levels of 24-hour urinary excretion; Solid lines connect different levels of dietary intake; hr = hour; mmol = millimoles; NHANES = National Health and Nutrition Examination Survey; SHH = Scottish Heart Health [Study]

Stroke

A total of 15 studies^{58, 59, 62, 69, 129, 137, 140, 141, 63, 78, 103, 108, 118, 122, 128} that analyzed the associations between potassium intake levels and stroke were included. These studies analyzed data from 13 studies among generally healthy adult populations,^{69, 58, 129, 137, 140, 141, 59, 62, 63, 78, 103, 108, 128} and two studies among people with existing diseases such as CKD¹¹⁸ and CVD (described in subquestion 8c).¹²²

Twelve prospective cohort studies,^{58, 59, 62, 69, 137, 140, 141, 63, 78, 103, 108, 128} and one case-cohort study¹²⁹ examined the associations between potassium intake levels and stroke among generally healthy adult populations. These studies included 12 non-overlapping cohorts: the PREVEND cohort,¹³⁷ the Rancho Bernardo California cohort,⁶⁹ the PURE cohort,¹⁴¹ the Rotterdam study,¹²⁹ NHANES I,^{59, 62} EPIC-Netherland cohort,¹⁰³ a pooled analysis of NHS I and II,⁷⁸ Swedish Mammography cohort,¹⁰⁸ WHI-OS,¹⁴⁰ HPFS,⁵⁸ Cardiovascular Health Study,⁶³ and the ATBC cohort.¹²⁸ Among these, six cohorts (PREVEND,¹³⁷ the Rancho Bernardo California cohort,⁶⁹ PURE,¹⁴¹ the Rotterdam study,¹²⁹ the EPIC-Netherland cohort,¹⁰³ and NHANES I^{59, 62}) included both adult men and women (mean ages ranged from 48.6 to 69.2 years). The Cardiovascular Health Study enrolled older men and women (>65 years) living in four US communities.⁶³ Three studies (a pooled analysis of NHS I and II,⁷⁸ the Swedish Mammography cohort,¹⁰⁸ and WHI-OS¹⁴⁰) exclusively enrolled adult women (mean ages ranged from 60.7 to 63.6 years), and two studies (HPFS⁵⁸ and the ATBC cohort¹²⁸) exclusively enrolled adult men (mean ages ranged from 57.3 to 57.8 years). Mean or median followup times ranged from 3.7 to 19 years.

Potassium intake levels were assessed by 24-hour urinary potassium excretion in one study,¹³⁷ by spot-urine samples in two studies,^{129, 141} by food frequency questionnaires in eight studies,^{58, 63, 78, 103, 108, 128, 129, 140} and by 24-hour dietary recalls in three studies.^{59, 62, 69} Among these, the Rotterdam study assessed both urinary and dietary potassium intake levels.¹²⁹ The potassium intake ranged from 28 mmol/d (1424 mg/d) to 149 mmol/d (5859 mg/day). Individual study results are shown in Figures 45 and 46, and Table 17.

Overall Results for Stroke

The relationships between potassium intake levels and stroke are inconsistent among the three studies that examined urinary potassium levels and stroke outcome.^{137, 141, 294} Five of the 11 studies showed an inverse relationship between dietary potassium intake levels and risks of stroke,^{59, 62, 63, 69, 140} while the other six found no significant associations.^{58, 78, 103, 108, 128, 129}

Except for the Rancho Bernardo California study, all studies controlled for various demographics, lifestyle factors, and medical history or medications. Among these, the PREVEND cohort¹³⁷ and the Rotterdam study¹²⁹ also adjusted for urinary sodium excretion in their analyses. One of the NHANES I analyses adjusted only for age and race.⁶² The overall RoB was rated moderate.

Urinary Potassium Excretion and Stroke

Only one study examined the relationships between baseline 24-hour potassium excretion levels and risks of stroke.¹³⁷ Specifically, the PREVEND cohort (moderate RoB) found no significant associations between baseline 24-hour potassium excretion levels and risks of stroke in both categorical and continuous analyses (adjusted HR 1.13; 95% CI 0.88, 1.46; n=7795).

The association between estimated 24-hour urinary potassium excretion and stroke outcome was examined in two studies (both were rated high RoB).^{129, 141} The PURE cohort (n=101945) found that the second quintile of urinary potassium excretion (<1.5-1.99 g/d; median = 44.6 mmol/d) was associated with a reduced risk of stroke compared to the lowest quintile (<1.5 g/d) of urinary potassium excretion (adjusted OR = 0.82; 95% CI 0.68, 0.99). The risks of stroke were not statistically significant when comparing the third (2.0-2.49 g/d; median = 57.4 mmol/d), fourth (2.5-3.5 g/d; median = 70.3 mmol/d), and the highest quintile (>3 g/d) levels) to the lowest quintile (adjusted OR [95% CI] = 0.85 [0.70, 1.03], 0.81 [0.63, 1.05], and 0.97 [0.72, 1.31], respectively.¹⁴¹ The other study is the Rotterdam study, which showed no significant linear relationships between levels of estimated 24-hour urinary excretion (based on an overnight urine sample) and risks of stroke (adjusted RR = 1.17 per SD increase; 95% CI 0.86, 1.58; n=5531).¹²⁹

Dietary Potassium Intake and Stroke

Eleven studies examined the relationship between dietary potassium intake and stroke outcome.^{58, 59, 62, 63, 69, 78, 103, 108, 128, 129, 140} Among these, the Rancho Bernardo California cohort (high RoB),⁶⁹ the Rotterdam study (high RoB),¹²⁹ the EPIC-Netherlands cohort (high RoB),¹⁰³ and the NHANES I cohort (high RoB)^{59, 62} included both adult men and women. The Cardiovascular Health Study enrolled older men and women (>65 years) living in four U.S. communities (high RoB).⁶³ Three studies (a pooled analysis of NHS I and II,⁷⁸ the Swedish Mammography cohort,¹⁰⁸ and WHI-OS¹⁴⁰) exclusively enrolled adult women, and two studies (HPFS⁵⁸ and the ATBC cohort¹²⁸) exclusively enrolled adult men. All five studies were rated moderate risk-of-bias.

Assessment of the Rancho Bernardo California cohort found that higher baseline dietary potassium excretion levels were significantly associated with lower risks of stroke mortality (adjusted HR 0.60; 95% CI 0.44, 0.81; n=859). The associations were similar in men (adjusted RR = 0.65; 95% CI 0.41, 1.00; n=356) and in women (adjusted RR = 0.56; 95% CI 0.03, 0.82; n=503).⁶⁹ Furthermore, categorical analyses of the NHANES I followup study showed that higher potassium intake levels were associated with lower risks of stroke (adjusted HR 0.75 95% CI 0.63, 0.88, 0.85 [0.71, 1.01], and 0.76 [0.58, 1.01] comparing the second, third, and the highest quartile to the lowest quartile, respectively; n=9805)⁵⁹ Subgroup analyses of NHANES I

showed increased risk of stroke mortality (comparing the lowest to highest tertile of dietary potassium intake) in black men (age-adjusted RR = 4.27; 95% CI 1.88, 9.19) compared with white men (age-adjusted RR = 1.66; 95% CI 1.32, 2.14), but risk was higher in white women (age-adjusted RR 1.13, 95% CI 0.84, 1.66) than in black women (age-adjusted RR 0.80, 95% CI 0.21, 2.01).⁶² On the contrary, both the Rotterdam study (adjusted RR 1.02 per SD increase; 95% CI 0.71, 1.46; n=5531)¹²⁹ and the EPIC-Netherlands cohort study (adjusted HR 0.97 per 1 g increase; 95% CI 0.83, 1.13; n=36094)¹⁰³ showed no significant linear relationships between dietary potassium intake and stroke outcome.

The Cardiovascular Health Study found that lower potassium intake (≤ 2.34 g/d), compared to higher potassium intake (> 2.34 g/d) was associated with an increased risk of stroke among older men and women (> 65 years).⁶³

Three studies examined the associations between dietary potassium intake levels and risks of stroke among adult women.^{108, 140, 295} Only the WHI-OS study showed statistically significant results, that is, compared to the lowest potassium intake quartile (< 1925.5 mg/d), the second, third, and highest potassium intake quartiles were associated with lower risks of stroke (adjusted HR 0.88, 95% CI 0.79, 0.98, 0.85 [0.76, 0.94], and 0.88 [0.79, 0.98], respectively; n=90137) among postmenopausal women.¹⁴⁰ The analyses of the Swedish Mammography Cohort showed similar but smaller, non-significant associations (adjusted HR [95% CI] 0.90 [0.77, 1.06], 0.94 [0.79, 1.11], 0.85 [0.71, 1.03], and 0.89 [0.72, 1.10] comparing the second, third, fourth, and highest quintile to the lowest quintile, respectively; n=34670)¹⁰⁸ The pooled analysis of NHS I and II did not find significant associations (adjusted HR [95% CI] = 1.0 [0.89, 1.12], 0.92 [0.81, 1.05], 0.91 [0.79, 1.05], and 0.91 [0.78, 1.06] comparing the second, third, fourth, and highest quintile to the lowest quintile, respectively; n=34670).⁷⁸

The ranges of dietary potassium intake levels were greater in the two studies in adult men: the HPFS study (2400 to 4300 mg/d)⁵⁸ and the ATBC study¹²⁸ of adult male smokers (3919 to 5859 mg/d). The higher potassium intake levels were associated with small, but not statistically significant, reduced risks of stroke in the HPFS study (adjusted HR [95% CI] 0.86 [0.61, 1.18], 0.82 [0.56, 1.2], 0.83 [0.56, 1.24], and 0.69 [0.45, 1.07] comparing the second, third, fourth, and highest quintile to the lowest quintile, respectively; n=43738).⁵⁸ In the ATCB study, no significant associations were shown (adjusted HR [95% CI] = 1.07 [0.96, 1.21], 0.94 [0.83, 1.06], 0.95 [0.84, 1.08], and 0.92 [0.81, 1.04], respectively; n=26556).¹²⁸

Figure 45. Categorical analysis of the association between urinary or dietary potassium levels and stroke outcome in generally healthy populations

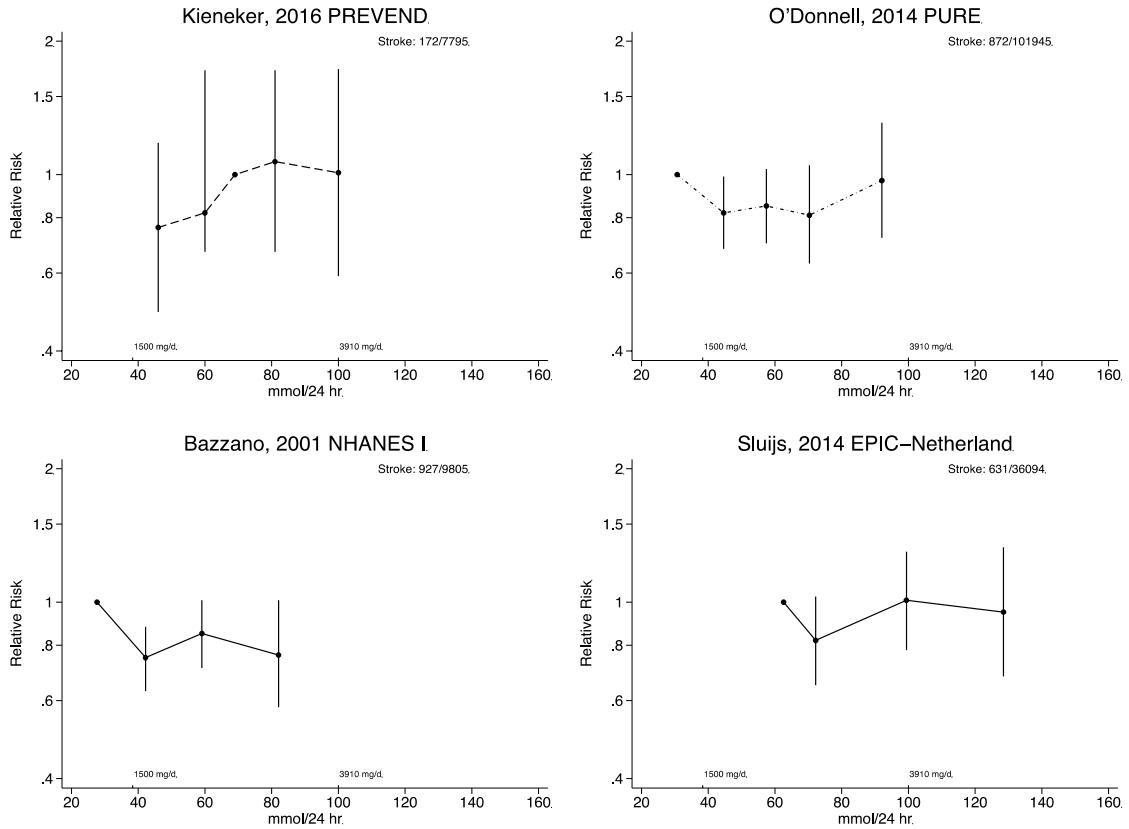


Figure Notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dashed lines connect different levels of 24-hour urinary excretion; Dotted-dash lines connect different levels of estimated 24-hour urinary excretion; Solid lines connect different levels of dietary intake; EPIC = European Prospective Investigation into Cancer and Nutrition; hr = hour; mmol = millimoles; NHANES = National Health and Nutrition Examination Survey; PREVENT = Prevention of Renal and Vascular End-Stage Disease; PURE = Prospective Urban Rural Epidemiology Study

Figure 46. Categorical analysis of the association between dietary potassium levels and stroke outcome in generally healthy adult women or men

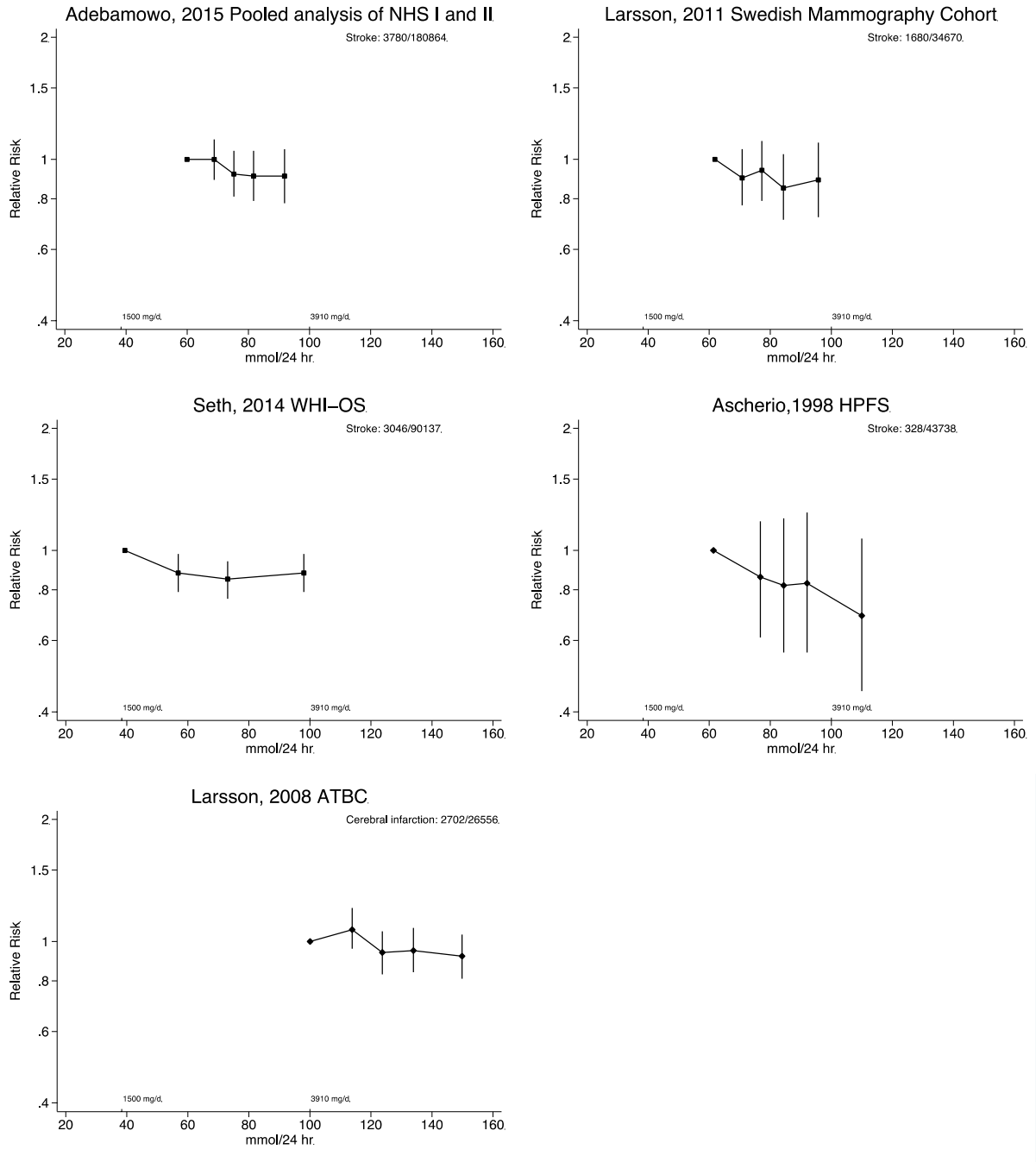


Figure Notes: Vertical solid lines represent the 95% confidence interval of the relative risk. Dashed line connects different levels of 24-hour urinary excretion; ATBC = Alpha Tocopherol Beta Carotene Cancer Prevention Study; HPFS = Health Professionals Followup Study; hr = hour; mmol = millimoles; NHS = Nurses' Health Study; WHI-OS = Women's Health Initiative – Observational Study

Table 17. Continuous analyses of the association between potassium levels and stroke outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	493/7795	0.063	24-hour urinary potassium excretion	Median 70 mmol/24h (IQR: 56–84 mmol/24h)	per 26-mmol/24-h increase	HR	1.13	0.88	1.46
Geleijnse, 2007 ¹²⁹ Rotterdam Study	All	Both	median 5.5 y	795/5531	0.144	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	1.17	0.86	1.58
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Dietary potassium intake	Random subsample mean 3.6 (SD 0.8) g/d	per SD increase	RR	1.11	0.61	2.04
	All	Both	median 5.5 y	795/5531	0.144	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	1.02	0.71	1.46
	Initially free of CVD and HTN	Both	median 5.5 y	NR/783	--	Estimated 24-hour urinary potassium excretion (spot urine)	Random subsample mean 45 (SD 22) mmol/24h	per SD increase	RR	1.06	0.50	2.29
Khaw, 1987 ⁶⁹	All	Both	12 y	24/859	0.028	Dietary potassium intake	mean 64 (range 17-154) mmol/d	per 10 mmol/d increase	RR	0.60	0.44	0.81
	Male	Male	12 y	9/356	0.026	Dietary potassium intake	NR	per 100 mmol/d increase	RR	0.65	0.41	1.0
	Female	Female	12 y	15/503	0.030	Dietary potassium intake	NR	per 10 mmol/d increase	RR	0.56	0.38	0.82

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Sluijs, 2014 ¹⁰³ EPIC-Netherland	All	Both	12 y	631/36094	0.017	Dietary potassium intake	mean 3672 (SD 903) mg/d	Per 1 g/d increase	HR	0.97	0.83	1.13
Green, 2002 ⁶³ Cardiovascular Health Study	>65 years	Both	Median 7.3 y	NR	NR	Dietary potassium intake	NR	≤2.34 g/d vs. >2.34 (reference)	RR	1.3	1.0	1.6
Fan, 2000 ⁶² NHANES I	White	Male	mean 16.7 y	93/3169	0.029	Dietary potassium intake	mean 2557 mg/d	<2003 mg/d vs. >2879 mg/d	RR	1.66	1.32	2.14
	Black	Male	mean 16.7 y	28/595	0.047	Dietary potassium intake	mean 1884 mg/d	<1260 mg/d vs. >2206 mg/d	RR	4.27	1.88	9.19
	White	Female	mean 16.7 y	136/5073	0.027	Dietary potassium intake	mean 1942 mg/d	<1508 mg/d vs. >2207 mg/d	RR	1.13	0.84	1.66
	Black	Female	mean 16.7 y	47/1029	0.046	Dietary potassium intake	mean 1469 mg/d	<1017 mg/d vs. >1641 mg/d	RR	0.8	0.21	2.01
	HTN	Male	mean 16.7 y	45/NR	-	Dietary potassium intake	NR	<2003 mg/d vs. >2879 mg/d	RR	2.13	1.09	6.78
	HTN	Female	mean 16.7 y	93/NR	-	Dietary potassium intake	NR	<1260 mg/d vs. >2206 mg/d	RR	1.16	0.86	3.59
	Non- HTN	Male	mean 16.7 y	76/NR	-	Dietary potassium intake	NR	<1508 mg/d vs. >2207 mg/d	RR	1.23	0.84	3.89

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
	Non- HTN	Female	mean 16.7 y	90/NR	-	Dietary potassium intake	NR	<1017 mg/d vs. >1641 mg/d	RR	1.11	0.85	3.54

Table Notes: CI = confidence interval; CVD = cardiovascular disease; HTN = hypertension; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Myocardial Infarction

A total of two publications^{129, 141} that reported analyses examining the associations between potassium intake levels and myocardial infarction (MI) among generally healthy adult populations.

The two studies are the PURE prospective cohort study¹⁴¹ and the Rotterdam case-cohort study.¹²⁹ Both studies included both adult men and women at baseline (mean ages were 51 and 69.2 years, respectively). Mean or median followup times were 3.7 and 5.5 years. Potassium intake levels were assessed by spot-urine samples in both studies, ranging from 104 mmol/d (2392 mg/d) to 365 mmol/d (8395 mg/d). In addition to urinary potassium measures, the Rotterdam study also assessed dietary potassium intake using a food frequency questionnaire. Individual study results are shown in Figure 47.

Overall Results

The two studies both showed non-significant results for relationship between estimated 24-hour urinary potassium excretion and MI.^{129, 141} One study also showed no significant linear relationship between dietary potassium intake and MI.¹²⁹ Both studies controlled for various demographics, lifestyle factors, and medical history or medications. One study¹²⁹ also adjusted for urinary potassium excretion in their analyses. The overall RoB was rated high based on exposure assessment and low to moderate for the other criteria.

Urinary Potassium Excretion and MI

Estimated 24-Hour Urinary Potassium Excretion

The analyses that used the PURE cohort (n=101945) showed no significant associations between 24-hour urinary potassium excretion levels (estimated by Kawasaki equation) and risks of MI (adjusted HR [95% CI] = 1.03 [0.83, 1.27], 0.85 [0.67, 1.07], 0.93 [0.72, 1.19], and 0.89 [0.66, 1.2] comparing the second, third, fourth, and highest quintile levels of urinary potassium excretion to the lowest quintile [<1.5 g/day], respectively).¹⁴¹

The Rotterdam study also showed no significant linear relationship between estimated 24-hour urinary excretion based on an overnight urine sample and MI (adjusted RR = 1.11 per SD increase; 95% CI 0.87, 1.43; n=5531).¹²⁹

Dietary Potassium Intake and MI

The Rotterdam study showed no significant linear relationship between dietary potassium intake and MI outcome (adjusted RR = 0.90 per SD increase; 95% CI 0.65, 1.24; n=5531).¹²⁹

Figure 47. Categorical analysis of the association between urinary potassium levels and MI outcome in generally healthy populations

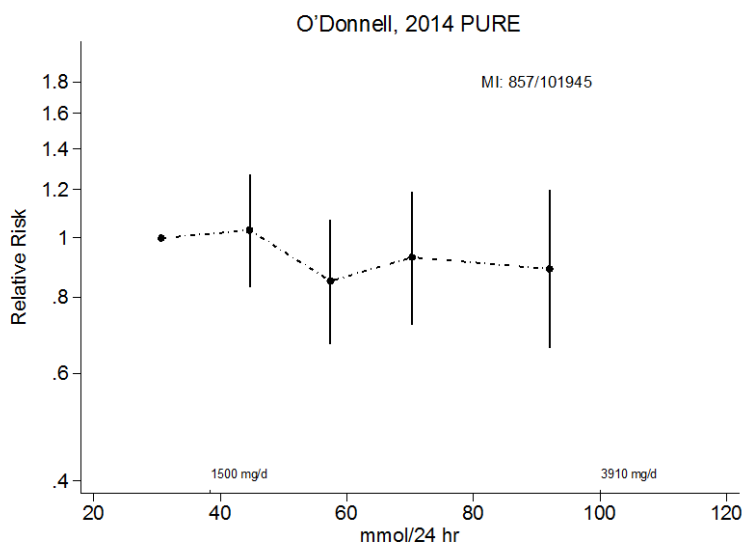


Figure Notes: Vertical solid lines represent the 95% confidence interval of the relative risk. Dashed line connects different levels of 24-hour urinary excretion; hr = hour; MI = myocardial infarction; mmol = millimoles; PURE = Prospective Urban Rural Epidemiology Study;

Combined CHD Morbidity and Mortality

A total of two prospective cohort studies^{55, 137} reported analyses examining the associations between potassium intake levels and combined CHD morbidity and mortality outcome among generally healthy adult populations. These cohorts are the Scottish Heart Health study⁵⁵ and PREVEND.¹³⁷ Both studies included both adult men and women at baseline. Mean or median followup times were 7.6 and 10.5 years, respectively. Potassium intake levels were assessed by 24-hour urinary potassium excretion in both studies, ranging from 27.5 mmol/d (1075 mg/d) to 112 mmol/d (4379 mg/d). Individual study results are shown in Figure 48.

Overall Results

The two studies showed inconsistent associations between urinary potassium levels and combined CHD mortality outcomes.^{55, 137} However, one controlled for various demographics, lifestyle factors, medical history or medications, and urinary sodium excretion,¹³⁷ whereas the other adjusted only for age in their analyses.⁵⁵ The latter study may be at increased risk for confounding. The overall risk of bias was moderate.

Urinary Potassium Excretion and Combined CHD Morbidity and Mortality

24-Hour Urinary Potassium

The two studies showed inconsistent associations between urinary potassium levels and combined CHD mortality outcomes.^{55, 137} Specifically, the PREVEND study (moderate RoB) did not find a significant association between baseline 24-hour potassium excretion and CHD events for either categorical or continuous analyses (adjusted HR = 0.9; 95% CI 0.77, 1.04; n=7795). The Scottish Heart Health study (high RoB) showed a positive relationship between quintiles of

24-hour urinary potassium excretion levels and all CHD outcome in men (age-adjusted HR = 0.62, 0.87, 0.58, 0.66 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754), but no significant association in women (age-adjusted HR = 0.91, 0.57, 0.79, 0.67 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875).⁵⁵ Again, because the Scottish Heart Health study adjusted only for age in their analyses, these results are at higher risk for confounding.

Figure 48. Categorical analysis of the association between urinary potassium levels and combined CHD morbidity and mortality outcome in generally healthy populations

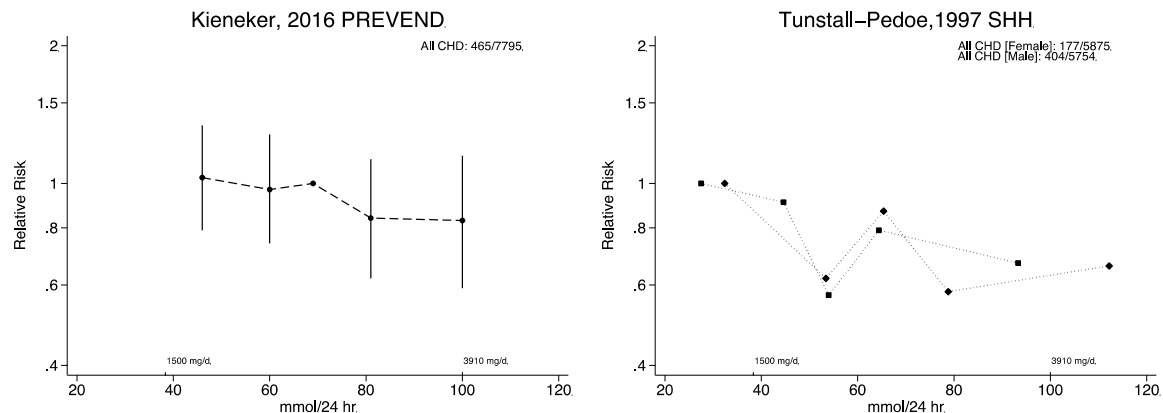


Figure notes: Vertical solid lines represent the 95% confidence interval of the relative risk. Dashed line connects different levels of 24-hour urinary excretion; CHD = coronary heart disease; hr = hour; mmol = millimoles; PREVEND = Prevention of Renal and Vascular End-Stage Disease; SHH = Scottish Heart Health [Study]

Combined CVD Morbidity and Mortality

A total of three publications^{130, 137, 141} were identified that reported on the associations between potassium intake levels and combined CVD morbidity and mortality outcome among generally healthy adult populations. These studies included three non-overlapping cohorts: the TOHP (I and II) cohort,¹³⁰ PREVEND,¹³⁷ and PURE cohort.¹⁴¹ All studies included both adult men and women at baseline. Mean or median followup time ranged from 3.7 to 10.5 years.

Potassium intake levels were assessed by 24-hour urinary potassium excretion in two studies,^{130, 137} and by spot-urine samples in one study.¹⁴¹ The potassium intake ranged from 30.7 mmol/d (1200 mg/d) to 100 mmol/d (3910 mg/d). Individual study results are shown in Figure 49 and Table 18.

Overall Results

No significant associations were found between urinary potassium levels and combined CVD morbidity and mortality outcomes.^{130, 137, 141} All studies controlled for various demographics, lifestyle factors, and medical history. Among these, the TOHP I and II followup study¹³⁰ and PREVEND,¹³⁷ also adjusted for urinary sodium excretion in their analyses. The overall RoB was rated low to moderate.

Urinary Potassium Excretion and Combined CVD Morbidity and Mortality

24-Hour Urinary Potassium

Two studies examined the relationships between baseline 24-hour urinary potassium excretion levels and risks of combined CVD morbidity and mortality outcomes. Both showed non-significant results.^{130, 137} Specifically, the TOHP (I and II) followup study (low RoB), which enrolled the control groups from the original sodium reduction trials, showed no significant associations between baseline 24-hour urinary potassium excretion levels and risks of total cardiovascular events in both categorical and continuous analyses (adjusted RR per 50 mmol/d increase = 0.67; 95% CI 0.41, 1.10).¹³⁰ The PREVEND study (moderate RoB)¹³⁷ also did not show significant associations between the baseline 24-hour urinary potassium excretion levels and risks of composite cardiovascular outcomes in both categorical and continuous analyses (adjusted RR per 26 mmol/d increase = 0.99; 95% CI 0.88, 1.13)

Estimated 24-Hour Urinary Potassium Excretion

The association between estimated 24-hour urinary sodium excretion and combined CVD morbidity and mortality outcomes was examined in one study.¹⁴¹ The PURE cohort (high RoB) showed that higher levels of urinary potassium excretion were associated with mostly non-significant, reduced risks of major cardiovascular events compared to the lowest quintile (adjusted OR [95% CI] = 0.9 [0.79, 1.03], 0.84 [0.73, 0.97], 0.87 [0.74, 1.03], and 0.87 [0.72, 1.06] compared second, third, fourth, and fifth quintile to the lowest quintile, respectively; n=101945).¹⁴¹

Figure 49. Categorical analysis of the association between urinary potassium levels and combined CVD morbidity and mortality outcome in generally healthy populations

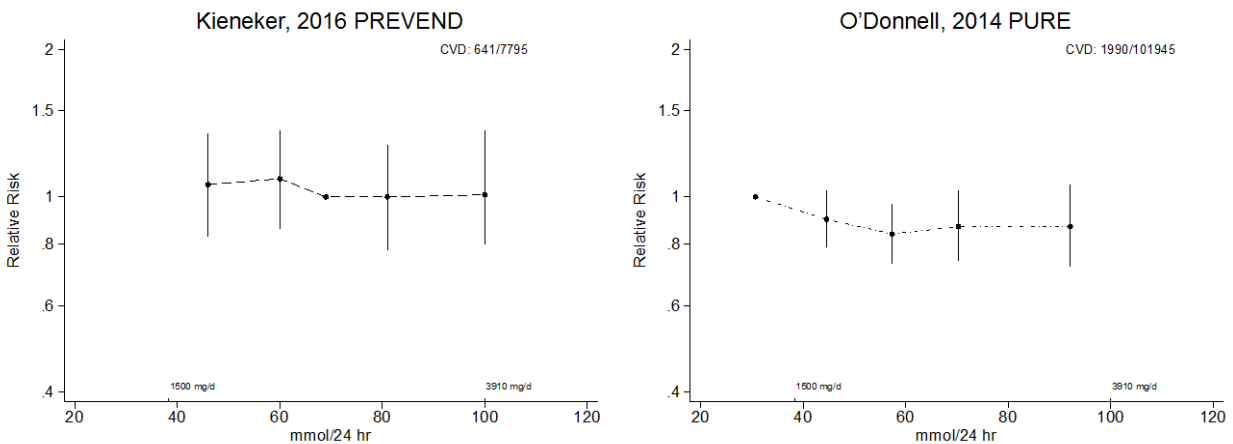


Figure notes: Vertical solid lines represent the 95% confidence interval of the relative risk. Dashed line connects different levels of 24-hour urinary excretion; Dotted-dash line connects different levels of estimated 24-hour urinary excretion; hr = hour; mmol = millimoles; PREVEND = Prevention of Renal and Vascular End-Stage Disease; PURE = Prospective Urban Rural Epidemiology Study

Other CVD Outcomes

Overview of Included Studies

One study⁸⁸ that examined the association between dietary potassium intake and other CVD outcomes was included. The Strong Heart Study (SHS) is a longitudinal population-based survey of cardiovascular risk factors and disease in young adult American Indians.⁸⁸ The mean age in the SHS was 28.4 years and followup time was 4 years.

Overall Results

The SHS study (high RoB) found that potassium intake (assessed by a food frequency questionnaire) was not associated with changes in left atrium diameter, LV diameter, or LV mass. The overall risk of bias of this study was rated high.

Table 18. Continuous analyses of the association between potassium levels and combined CVD morbidity and mortality outcome in generally healthy populations

Author, Year Cohort Name	Subgroup	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Cook, 2009 ¹³⁰ TOHP I & II control groups	All	Both	median 5 y (TOHPI) 4 y (TOHP II)	166/2084	0.080	24-hour urinary potassium excretion	NR	per 50 mmol/d increase	RR	0.67	0.41	1.1
Kieneker, 2016 ¹³⁷ PREVEND	All	Both	median 10.5y (IQR 9.9 - 10.8y)	785/7795	0.101	24-hour urinary potassium excretion	Median 70 (IQR 56–84) mmol/24h	per 26-mmol/d increase	HR	0.99	0.88	1.13

Table Notes: CI = confidence interval; HR = hazard ratio; IQR = interquartile range; NR = not reported; RR = relative risk; SD = standard deviation; y = years

Mean Difference Between Groups in Estimated Glomerular Filtration Rate

The PREVEND study followed 5315 Dutch adults free of CKD, aged 28 to 75 years, for a median of 10.3 years. Using a multi-variable adjusted model, this study found that a 1 SD (21 mmol/24hr) decrease in urinary potassium excretion was associated with a 16% higher risk of developing CKD, with risk of CKD defined as eGFR < 60 ml/min per 1.73 m², or urinary albumin excretion of >30 mg/24 h, or both (adjusted HR per 21 mmol/d increase = 1.16; 95% CI 1.06, 1.28).¹⁵² The overall RoB was rated low.

Number of Patients With End Stage Renal Disease

The U.S. National Institutes of Health–American Association of Retired Persons Diet and Health Study followed US adults, ages 51 to 70 years, for an average of 14.3 years. This study found that being in the highest quintile of potassium intake (assessed by a food frequency questionnaire) was associated with a decreased risk of dying from a renal cause (adjusted HR = 0.78; 95% CI 0.67, 0.90), and with an increased risk of self-reported dialysis (adjusted HR = 1.27; 95% CI 1.02, 1.57).⁸² The overall RoB was rated high.

Key Question 8a. Effect of Other Minerals on Potassium

No studies were identified that addressed this question.

Key Question 8b. Subpopulations Defined by Sex, Race/Ethnicity, Age, and Reproductive Status (for Women)

Description of Included Studies

Sex

All-Cause Mortality

Using 24-hour dietary recall data with NCI methods for estimating usual intake, both categorical and continuous analyses of NHANES III showed that higher potassium intake was significantly associated with lower total mortality in the general US population (adjusted HR 0.8 per 1000 mg/d increase; 95% CI 0.67, 0.94; n=12267),¹¹⁶ but no significant interactions by sex.

Similarly, the WHI OS also showed that the second, third, and fourth quartiles of potassium intake were significantly associated with a decreased risk of total mortality when compared to the lowest quartile of potassium intake in fully adjusted models (adjusted HR 0.91, 95% CI 0.86, 0.96, 0.84 [0.79, 0.89], and 0.90 [0.85, 0.95], respectively).¹⁴⁰

Stroke

Subgroup analyses of NHANES I showed increased risk of stroke mortality (comparing the lowest to highest tertile of dietary potassium intake) in black men (age-adjusted RR = 4.27; 95% CI 1.88, 9.19) compared with white men (age-adjusted RR = 1.66; 95% CI 1.32, 2.14), but risk was higher in white women (age-adjusted RR 1.13, 95% CI 0.84, 1.66) than in black women (age-adjusted RR 0.80, 95% CI 0.21, 2.01).⁶²

Total CHD Mortality

The Scottish Heart Health Study⁵⁵ reported that baseline 24-hour urinary potassium excretion levels were inversely associated with risks of CHD mortality in men (age-adjusted HR 0.57, 0.76, 0.59, 0.60 comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5875), but not in women (age-adjusted HR 0.73, 0.51, 0.62, 0.45 [CIs were not reported] comparing quintiles 2, 3, 4, and 5 to the lowest quintile; n=5754). The overall RoB was rated as high.

Assessment of the Rancho Bernardo California cohort found that higher baseline dietary potassium excretion levels were significantly associated with lower risks of stroke mortality and that the associations were similar in men (adjusted RR = 0.65; 95% CI 0.41, 1.00; n=356) and in women (adjusted RR = 0.56; 95% CI 0.03, 0.82; n=503).⁶⁹

Race/Ethnicity

Stroke

Subgroup analyses of NHANES I showed increased risk of stroke mortality (comparing the lowest to highest tertile of dietary potassium intake) in black men (age-adjusted RR = 4.27; 95% CI 1.88, 9.19) compared with white men (age-adjusted RR = 1.66; 95% CI 1.32, 2.14), but risk was higher in white women (age-adjusted RR 1.13, 95% CI 0.84, 1.66) than in black women (age-adjusted RR 0.80, 95% CI 0.21, 2.01).⁶²

Age

No studies that met inclusion criteria conducted subgroup analyses by age.

Key Question 8c. Subpopulations Defined by Hypertension, Diabetes, and Obesity Health Status

Description of Included Studies

Eight publications examined the associations between potassium intake and total mortality, CVD, CHD, stroke, or kidney disease morbidity and mortality exclusively among people with existing diseases such as hypertension,³⁴ history of CVD,¹²² Type 2 DM,^{81, 119, 154} and CKD.^{118, 121, 123} Individual study results are shown in Figure 50, Figure 51 and Table 19.

The results from these studies are described together with subgroup analyses^{62, 116} in this section. The findings are categorized by comorbidity, rather than by outcome.

Detailed Synthesis

Hypertension

One study examined the associations between 24-hour urinary potassium levels and risk for MI among hypertensive men in a worksite HTN program in New York City.³⁴ After an average of 3.8 years of followup, no significant linear associations were observed between baseline 24-hour urinary potassium excretion levels and risk of MI (adjusted HR per SD [26.4 mmol/d] increase = 1.29; 95% CI 0.93, 1.79; n=1900).³⁴

Two subgroup analyses of two population-based cohort studies in the U.S. examined the associations between dietary potassium levels and total mortality, CVD mortality, or stroke outcome among hypertensive adults.^{62, 116} Subgroup analyses of NHANES I showed an inverse

relationship between dietary potassium intake levels and risks of stroke among men and women adjusting for age and race. Comparing the lowest to highest tertile of dietary potassium intake, the age-adjusted risk of stroke mortality was 2.13 (95% CI 1.09, 6.78) in hypertensive men, and 1.16 (95% CI 0.86, 3.59) in hypertensive women.⁶² Significant inverse linear relationships also were observed between baseline dietary potassium take levels and risks of total mortality or CVD mortality (adjusted HR [95% CI] = 0.83 [0.66, 1.06] and 0.64 [0.38, 1.06], respectively) among adults with HNT in subgroup analyses of NHANES III.¹¹⁶

Effects of Cardiovascular Disease

One study examined the associations between estimated urinary potassium excretion levels and total mortality, CVD, CHD, or stroke outcomes among adults with history of CVD (including HTN).¹²² ONTARGET and TRANSCEND were two large, multi-center, multi-country cohorts of people at high risk of CVD; both cohorts reported on all-cause mortality, CVD mortality, MI incidence, and stroke incidence. This study found no significant associations between higher levels of 24-hour urinary potassium excretion (estimated by Kawasaki equation) and total mortality (adjusted HR was 1.06 [0.92, 1.21], 1.09 [0.95, 1.26], 1.07 [0.90, 1.25], and 1.01 [0.83, 1.24] comparing quintiles 2, 3, 4, and 5 to the lowest quintile, respectively; n=28880), CVD mortality (adjusted HR was 0.97 [0.82, 1.16], 0.99 [0.83, 1.19], 1.01 [0.82, 1.23], and 1.05 [0.81, 1.34] comparing quintile 2, 3, 4, and 5 to lowest quintile, respectively), and MI (adjusted HR was 1.18 [0.93, 1.50], 1.11 [0.87, 1.42], 1.10 [0.84, 1.43], and 1.07 [0.78, 1.47] comparing quintile 2, 3, 4, and 5 to lowest quintile, respectively). However, inverse relationships were found between estimated urinary potassium excretion levels and risks of stroke (adjusted HR was 0.77 [0.63, 0.94], 0.73 [0.59, 0.90], 0.71 [0.56, 0.91], and 0.68 [0.49, 0.92] comparing quintiles 2, 3, 4, and 5 to the lowest quintile, respectively).¹²²

Effects of Diabetes

Three publications examined the associations between 24-hour potassium excretion levels and total mortality or kidney disease morbidity and mortality outcomes among patients with type 2 diabetes.^{81, 119, 154} Among these, two studies had overlapping study populations.^{81, 154}

Among a subsample of ONTARGET participants who were diagnosed with vascular disease or Type 2 diabetes with end-organ damage, the second and third tertiles of 24-hour urinary potassium excretion were significantly associated with a decreased risk of total mortality (adjusted odds ratio [95% CI] was 0.89 [0.81, 0.99] and 0.77 [0.71, 0.98], respectively; n=3088).¹⁵⁴ This study did not find a significant association between potassium excretion and risk of CKD. Comparing the second and third tertiles to the lowest tertile, risk of CKD was 0.94 (95% CI=0.87 - 1.01) and 0.87 (95% CI=0.73 - 1.03), respectively.¹⁵⁴

However, another prospective observational study followed a subsample of ONTARGET participants who were diagnosed with Type 2 diabetes but without macroalbuminuria, for 5.5 years.⁸¹ This study reported on the incidence or progression of CKD and found that the 2nd and 3rd tertiles of potassium excretion were significantly associated with reduced risk of CKD compared to the lowest tertile (adjusted OR=.90 [0.85, 0.95] and 0.78 [0.69, 0.88], respectively).⁸¹

The Shiga Prospective Observational Followup Study followed patients with Type 2 diabetes and eGFR>=60 ml/min per 1.73 m² in Japan for a median of 11 years.¹¹⁹ This study reported on three outcomes related to renal function: incidence of a 50% decline in eGFR, progression to stage 4 CKD, and the rate of annual decline in eGFR. The highest quartile of urinary potassium

excretion was significantly associated with a lower incidence of 50% decline in eGFR (adjusted HR=0.24 [0.08, 0.70] and slower progression to CKD stage 4 (adjusted HR=0.08 [0.01, 0.50] when compared to the lowest quartile. The 2nd and 3rd quartiles were not significantly different from the lowest quartile for these outcomes. The annual rate of decline in eGFR was significantly lower in the highest quartile (-1.3 [-1.4, -1.0] when compared to the 1st (-2.2 [-2.4, -1.8] and 2nd (-1.9 [-2.0, -1.8]) quartiles, but not when compared to the 3rd quartile (-1.7 [-2.0, -1.5]).

Effects of Chronic Kidney Disease

Three publications examined the associations between 24-hour urinary potassium excretion levels and total mortality or kidney disease morbidity and mortality outcomes among patients with CKD.^{118, 121, 123} Of these, two publications analyzed data from the CRIC study and reported on all-cause mortality outcome,¹²¹ composite CVD incidence, MI incidence, and stroke incidence outcomes.¹¹⁸ The third publication was an analysis of the MDRD study on risk of kidney failure and all-cause mortality.¹²³

The CRIC study followed patients with CKD and reported on all-cause mortality.¹²¹ In the CRIC study of patients with CKD in the U.S., no significant association was found between levels of 24-hour urinary potassium excretion and total mortality (adjusted HR [95% CI] 0.92 [0.72, 1.18], 0.81 [0.61, 1.08], and 0.89 [0.64, 1.23] comparing quartile 2, 3, and 4 to the lowest quartile, respectively; n=3757).¹²¹ Another publication from the CRIC cohort study also reported no significant associations between levels of 24-hour urinary potassium excretion and composite CVD outcomes (adjusted HR [95% CI] 1.04 [0.84, 1.29], 1.02 [0.81, 1.30], and 1.26 [0.98, 1.63] comparing quartile 2, 3, and 4 to lowest quartile, respectively), MI (adjusted HR [95% CI] was 1.08 [0.75, 1.56], 0.98 [0.66, 1.45], and 1.04 [0.68, 1.583] comparing quartile 2, 3, and 4 to lowest quartile, respectively), and stroke (adjusted HR [95% CI] was 1.03 [0.64, 1.66], 1.04 [0.61, 1.77], and 1.41 [0.80, 2.48] comparing quartiles 2, 3, and 4 to the lowest quartile, respectively).¹¹⁸

The MDRD study followed patients with CKD and reported on all-cause mortality and risk of kidney failure.¹²³ This study identified a non-significant trend of increased kidney failure events in lower quartiles of baseline urinary potassium excretion. However, lower quartiles of potassium excretion were significantly associated with increased risk of all-cause mortality compared to the highest quartile of urinary potassium excretion (adjusted HR [95% CI] was 1.71 [1.23, 2.38], 1.70 [1.25, 2.31], and 1.53 [1.15, 2.02] comparing quartile 1, 2, and 3 to highest quartile, respectively n=812).¹²³ Furthermore, continuous analyses also showed that both baseline 24-hour urinary potassium excretion levels (adjusted HR = 0.83 per 1 SD increase; 95% CI 0.74, 0.94) and a time-updated average of 24-hour urinary excretion levels (adjusted HR = 0.83 per 1 SD increase; 95% CI 0.71, 0.97) were significantly associated with a decreased risk for total mortality.¹²³

Effects of Obesity

No studies were identified that assessed associations of potassium intake with risks of total mortality, CVD, CHD, stroke, or kidney disease morbidity and mortality in this population.

Figure 50. Categorical analyses of the association between potassium levels and total mortality and CVD mortality outcomes in non-healthy populations

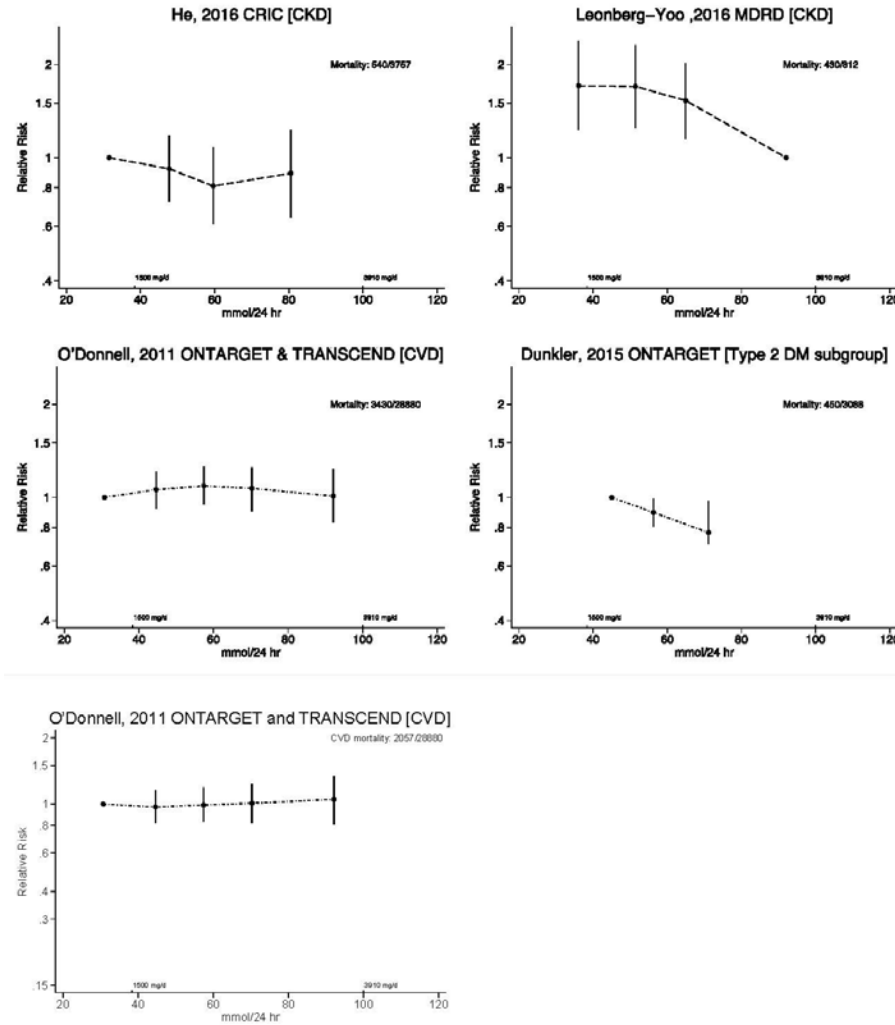


Figure notes: Vertical solid line represents the 95% confidence interval of the relative risk. Dash line connects different levels of 24-hour urinary excretion; Dotted-dash line connects different levels of estimated 24-hour urinary excretion; Solid line connect different levels of dietary intake

Figure 51. Categorical analyses of the association between potassium levels and stroke outcome in non-healthy populations

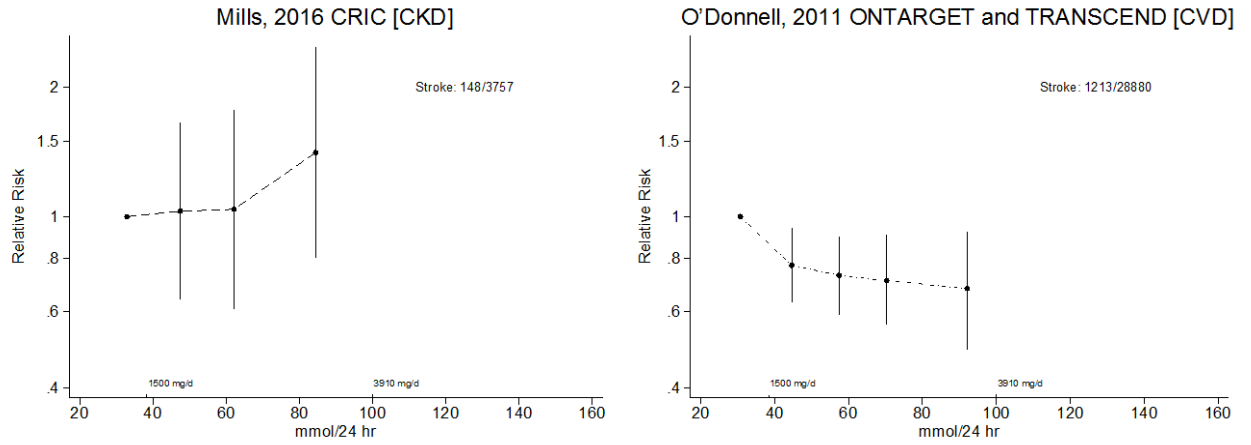


Figure note: Vertical solid line represents the 95% confidence interval of the relative risk. Dash line connects different levels of 24-hour urinary excretion; Dotted-dash line connects different levels of estimated 24-hour urinary excretion

Table 19. Continuous analyses of the association between potassium levels and total mortality and stroke outcomes in non-healthy populations

Author, Year Cohort Name	Population	Sex	Followup Duration	Number of Events / Total N	Cumulative Incidence	Exposure Assessment	Exposure Ranges	Analysis Unit	Metric	Estimate	Lower 95% CI	Upper 95% CI
Total mortality												
Leonberg-Yoo, 2016 ¹²³ MDRD	CKD	Both	median 19.2 (IQR 10.8-20.6) y	430/812	0.529	Baseline 24-hour urine potassium excretion	mean 2.39 (SD 0.89) g/d	per SD increase	HR	0.83	0.74	0.94
	CKD	Both	median 19.2 (IQR 10.8-20.6) y	390/812	0.480	Time-updated average 24-hour urine potassium excretion	NR	per SD increase	HR	0.83	0.71	0.97
Stroke outcome												
Fan, 2000 ⁶² NHANES I	HTN	Male	mean 16.7 y	45/NR	-	Dietary potassium intake	NR	<2003 mg/d vs. >2879 mg/d	RR	2.13	1.09	6.78
	HTN	Female	mean 16.7 y	93/NR	-	Dietary potassium intake	NR	<1260 mg/d vs. >2206 mg/d	RR	1.16	0.86	3.59
	Non- HTN	Male	mean 16.7 y	76/NR	-	Dietary potassium intake	NR	<1508 mg/d vs. >2207 mg/d	RR	1.23	0.84	3.89
	Non- HTN	Female	mean 16.7 y	90/NR	-	Dietary potassium intake	NR	<1017 mg/d vs. >1641 mg/d	RR	1.11	0.85	3.54

Table Notes: CKD = chronic kidney disease; CI = confidence interval; CKD = chronic kidney; disease; HTN = hypertension; HR = hazard ratio; IQR = interquartile range; MDRD = Modification of Diet in Renal Disease; NR = not reported; SD = standard deviation; y = years

Discussion

Summary of Key Findings and Strength of Evidence

The key points for each outcome appear in the Results section, organized by Key Question. Key points (primarily those for which the strength of evidence is moderate or higher are summarized below, along with the strength of evidence (SOE) ratings (the factors that contributed to the ratings are reported in full in Appendix F). In general, the Key Questions were organized, first, by exposure: Key Questions 1 through 4 considered sodium exposure and sodium to potassium ratio, whereas Key Questions 5 through 8 considered potassium exposures. The questions were then further organized by study design: Key Questions 1, 3, 5, and 7 assessed the findings of RCTs on the effects of studies intended to reduce sodium or increase potassium intake for the outcomes of interest, whereas the even-numbered questions assessed the associations between sodium or potassium exposures and the outcomes of interest in prospective cohort studies. The questions are then further organized by outcomes:

Key Questions 1 and 2 address the relationships between sodium intake and BP, achievement of a prespecified BP goal, incident HTN, and adverse effects.

Key Questions 3 and 4 address the relationships between sodium intake and all-cause mortality, CVD mortality, CHD mortality, stroke, MI, combined CVD morbidity and mortality, combined CHD morbidity and mortality, renal outcomes, any reported combination of CVD events, other CVD events, and adverse events.

Key Questions 5 and 6 address the relationships between potassium status and BP, achievement of a prespecified BP goal, incident HTN, kidney stones, and adverse effects.

Key Questions 7 and 8 address the relationships between potassium status and all-cause mortality, CVD mortality, CHD mortality, stroke, MI, combined CVD morbidity and mortality, combined CHD morbidity and mortality, renal outcomes, any reported combination of CVD events, other CVD events, and adverse events.

In this chapter, we discuss the overall findings for each outcome, considering all study designs together.

Key Question 1. Effect of Interventions To Reduce Dietary Sodium Intake on Blood Pressure

Conclusions

- Sodium reduction decreases systolic and diastolic blood pressure significantly in adults (moderate SoE).
- Sodium reduction in adults may increase the likelihood of achieving a prespecified blood pressure goal (low SoE).
- Sodium reduction lowers BP in both men and women (moderate SoE), and sex does not appear to moderate the effect of sodium reduction on BP in adults (low SoE).
- Short term sodium reduction interventions do not appear to show statistically significant effects on BP in children; however, a sensitivity analysis that excluded high or unclear RoB studies resulted in a statistically significant decrease in diastolic BP with sodium reduction for children.

- Sodium reduction decreases systolic BP in both those with hypertension and those with normal BP; the effect is greater in adults with HTN than in those with normal BP (moderate SoE).
- Sodium reduction decreases diastolic BP in those with hypertension (moderate SoE).
- Potassium-containing salt substitutes decrease systolic and diastolic BP (moderate SoE).

Key Question 2. Association Between Dietary Sodium Intake and Blood Pressure

Conclusions

- Prospective cohort studies suggest that sodium intake may be associated with systolic BP but not with diastolic BP in adults (low SoE). Most studies had high RoB based on the methods used to assess sodium intake (typically single 24-hour urine excretion with or without validation or estimated based on overnight urinary excretion), and findings were inconsistent across studies.
- Evidence from a small number of prospective cohort studies suggests that sodium intake may be associated with incident hypertension in adults (low SoE: Most studies had high RoB based on the methods used to assess sodium intake).

Sodium and Blood Pressure

Key Questions 1 and 2 considered the relationship between sodium intake and systolic and diastolic blood pressure. We limited inclusion to RCTs with a minimum four-week intervention (Key Question 1) and prospective observational studies with a minimum 4-week follow up (Key Question 2) to increase the applicability of the study findings to individual patient- and community interventions.

RCTs designed to assess the effects of interventions to restrict sodium intakes had significant, although somewhat inconsistent, beneficial effects on reducing both systolic BP and diastolic blood pressure, compared with usual sodium intakes in adults; follow up times were as long as 8 years, but most studies limited intervention duration and follow up to a year or less. Pooled analyses showed high heterogeneity across studies.^{39, 42, 45-51, 53, 86, 90, 92, 93, 95, 114, 157, 159-164, 169-171, 200, 203, 205, 206, 208-210, 212, 213, 216, 217, 230-232, 236, 260, 263, 266, 276, 282-284} Assessment of dose-response relationships between interventions, 24-hour urinary sodium excretion, and blood pressure showed significant positive effects in the DASH-Sodium trial⁴⁹ but findings were inconsistent in smaller dose-response studies. Prospective observational studies generally reported inconsistent associations of sodium exposure with blood pressure at follow up, however assessments of exposure often relied on high RoB methods such as single 24-hour urinary excretion without validation, estimated urinary excretion, or dietary assessments.^{51, 111, 135, 139, 274}

Few studies assessed the effects of sodium reduction on blood pressure in subgroups of interest, and even fewer studies conducted subgroup analyses within the same study. Evidence was insufficient to determine whether race/ethnicity moderate the effect of sodium reduction on blood pressure.

Evidence suggests that sodium reduction may not lower systolic BP in children (low strength of evidence), but evidence based on a sensitivity analysis that omitted high or unclear RoB studies suggests a significant effect on diastolic BP.^{114, 131, 173-175, 207, 237} Prospective observational

studies suggested stronger associations of sodium intake with BP in adults than in children.^{104, 109, 112, 132, 146}

Adults with HTN^{39, 46-49, 51, 53, 90, 92, 93, 96, 113, 157, 159, 160, 163, 164, 169-171, 205, 206, 208-213, 216, 217, 230, 231, 236, 260, 266, 284} showed greater improvements in BP with sodium excretion interventions than did those with normal blood pressure,^{42, 45, 49, 50, 86, 161, 200, 263, 283} (moderate strength of evidence for systolic BP; low strength of evidence for diastolic BP). The lower heterogeneity across studies included in these pooled analyses compared with that of the pooled analysis of studies of all adults suggests the higher heterogeneity in the latter analyses might be attributable to the inclusion of studies of both those with HTN and those with normal BP. Evidence was insufficient from prospective observational studies to determine whether the association between sodium intake and blood pressure differs between those with HTN and those with normal BP.

A small number of RCTs assessed the impact of alteration of other minerals (potassium) on the effect of sodium reduction. Those that compared the effects of combining sodium reduction and increased potassium intake with that of sodium reduction alone suggested potassium has no moderating effect on that of sodium reduction for BP.^{42, 233, 235, 236, 275} Another group of studies, which compared the effects of using potassium-rich salt substitutes to limit sodium intake to usual diet, found that these salt substitutes significantly lower blood pressure (moderate strength of evidence);^{99, 101, 102, 124, 196, 199, 232, 239, 241, 265, 267, 275, 282} however 24-hour sodium excretion levels reported in these studies do not suggest that sodium intakes were consistently decreased in the groups assigned to potassium-containing salt substitutes. No studies assessed the impact of other minerals on the effects of sodium reduction. No observational studies assessed these associations.

Sodium and Achievement of a Prespecified Goal

Few studies assessed the effects of interventions on the likelihood of reaching a prespecified BP goal. Across six RCTs, sodium reduction interventions had a significant beneficial effect on the proportion of adult study participants achieving a prespecified blood pressure goal, although goals differed among the studies (low strength of evidence).^{49, 170, 171, 205, 206, 284}

No RCTs assessed the potential moderating impact of subgroup status on this outcome. No observational studies assessed the association between sodium exposure and achievement of a prespecified BP goal.

Sodium and Incident Hypertension

RCTs showed a small, non-statistically significant beneficial effect of sodium reduction on the relative risk for incident HTN in adults (low SoE, because of the small number of studies and inconsistency). Observational studies suggested an association between urinary sodium excretion and risk for HTN (low strength of evidence due in part to high RoB and inconsistency: The small number of observational studies show mixed findings regarding the association between urinary sodium excretion and risk for HTN, ranging from no association to an association at higher exposure levels).^{42, 51, 53}

No studies of the moderating effects of potassium or potassium salt substitutes assessed effects on incident HTN.

No RCTs assessed the potential moderating effects of sex, race/ethnicity, age, or comorbidities on the effects of sodium reduction on incident hypertension. Sodium reduction during pregnancy had no effects on incident gestational hypertension, and urinary salt excretion was not associated with risk for gestational hypertension in one cohort study.

Sodium and Adverse Events

Few RCTs reported specific adverse events associated with sodium reduction to lower BP. Three studies, including the DASH-Sodium Trial, found no effects of sodium reduction on blood lipids (low strength of evidence). Evidence was insufficient regarding other adverse effects.^{49, 160, 163, 171, 206}

Key Question 3. Effect of Interventions To Reduce Dietary Sodium on CVD and Kidney Disease Morbidity and Mortality, and on Total Mortality

Conclusions

- In adults, evidence is insufficient to determine the effects of sodium reduction on the risk for all-cause mortality (based on seven RCTs with moderate RoB).
- In adults, evidence is insufficient to determine the effects of sodium reduction on the risk for CVD mortality (two RCTs).
- In adults, a low strength of evidence suggests that sodium reduction decreases the risk for combined CVD morbidity and mortality (eight RCTs; low RoB)
- In adults, sodium reduction does not appear to affect the risk for stroke (low SoE based on three RCTs with low RoB)
- In adults, evidence is insufficient to assess the effect of sodium reduction on the risk for myocardial infarction (one RCT; low RoB).
- In adults, a low strength of evidence suggests that sodium reduction significantly decreases the risk for a composite measure of “any CVD outcome” as reported by study authors (based on seven RCTs; low RoB).
- Evidence is insufficient to draw conclusions about the moderating effects of sex, race/ethnicity, age, or reproductive status on the effects of sodium reduction on CVD or CHD outcomes.
- Evidence is insufficient to draw conclusions on the moderating effects of hypertension, diabetes, or renal disease on the effects of sodium reduction interventions on all-cause, CVD, or CHD mortality, CVD- or CHD morbidity, or other longer term CVD outcomes.
- Conflicting evidence from two RCTs is insufficient to allow conclusions to be drawn regarding the moderating impact of overweight or obesity on the effect of sodium reduction on composite CVD outcomes (low RoB).
- Evidence is insufficient, based on one RCT, to allow conclusions to be drawn on whether the effects of sodium reduction on long-term outcomes are moderated by higher dietary potassium.
- Evidence is insufficient, based on two RCTs, to draw conclusions on the moderating effects of potassium-containing salt substitutes on the effects of sodium reduction on long-term outcomes.

Key Question 4. Association Between Dietary Sodium and CVD, CHD, Stroke, and Kidney Disease Morbidity and Mortality, and Between Dietary Sodium Intake and Total Mortality

Conclusions

- Although sodium levels appear to be directly associated with all-cause mortality (low SOE), the shape of this relationship could not be determined (insufficient SOE).
- Evidence is insufficient to assess possible associations of sodium intake levels and risk for CVD, CHD, or stroke morbidity or mortality.
- Evidence is insufficient to assess effects of sex, race/ethnicity, age, or comorbidities on associations between sodium intake status and outcomes of interest.

Sodium and All-Cause Mortality

Key Questions 3 and 4 consider the relationship between sodium intake and all-cause mortality. Only RCTs with follow up of 6 months or longer and observational studies of 1 year or longer were included.

Decreasing dietary sodium reduced the risk for all-cause mortality non-significantly in RCTs, and evidence was considered insufficient to draw a conclusion about this relationship.^{51, 53, 113, 169, 170, 182, 196} The number and size of studies was relatively small, outcomes were inconsistent and imprecise, and not all studies included mortality as a prespecified outcome and sometimes reported it as an adverse event. Differences in 24-hour urinary sodium excretion of 40 mmol or more showed a trend toward being associated with greater decreases in risk.

Data from prospective cohort studies with follow up times of 1 year or longer support an association between sodium intake based on 24-hour sodium excretion and all-cause mortality, but evidence was insufficient to assess the shape of this relationship or associations.^{55, 56, 98, 137, 273} At 20 years' follow up, multivariate analysis of TOHP-I and TOHP-II data showed trends toward a linear dose-response relationship between 24-hour urinary sodium excretion and mortality (for <100 mmol, 100 mmol to <150 mmol, 150 mmol to <200 mmol, and >200 mmol/24 h).²⁸¹

Too few RCTs assessed the potential moderating effects of sex, race/ethnicity, age, or comorbidities to draw any conclusions. Evidence was insufficient from prospective cohort studies that assessed sodium exposure using 24-hour urinary excretion to assess the potential moderating effects of sex, race/ethnicity, age, or comorbidities of interest.

Sodium and Cardiovascular Disease Mortality

Only two RCTs that met inclusion criteria assessed the effect of sodium reduction on CVD mortality. One small RCT with only 3 years' follow up found no effect.¹⁷⁰ However, a block-randomized institutional trial that assessed the effect of a potassium-containing salt substitute to lower sodium intake found a significant effect of reduced sodium intake on decreasing risk for CVD mortality.¹⁸² Evidence from prospective cohort studies was determined to be insufficient on which to base a conclusion regarding CVD mortality. Two cohort studies that conducted 24-hour urinary sodium excretion analyses^{56, 98} (but had moderate RoB) found inconsistent effects of lower sodium intake and lower sodium-to-potassium ratios, as did studies that estimated 24-hour excretion or conducted dietary intake assessments.^{35, 40, 116, 129, 134, 136, 141}

Sodium and CHD Mortality

No RCTs that met inclusion criteria assessed the effects of sodium reduction on CHD mortality. Two prospective cohort studies that assessed 24-hour urinary sodium excretion reported inconsistent associations of CHD mortality with sodium intake (insufficient evidence on which to base a conclusion).^{55, 56}

Sodium and Stroke

Three RCTs that met inclusion criteria reported on the incidence of stroke, although only one of the studies included stroke risk as a prespecified outcome. None of the studies reported significant differences in stroke risk (low strength of evidence).^{171, 275, 282} Across prospective cohort studies, insufficient evidence was identified to draw a conclusion on an association with stroke risk for normotensives or those with HTN .^{40, 43, 56, 98, 129, 134, 141}

Sodium and Myocardial Infarction

One RCT that reported on the incidence of MI reported no effect of sodium reduction on risk for MI (insufficient strength of evidence)¹⁷¹ . No observational studies that measured 24-hour sodium excretion assessed the association with MI risk.

Sodium and Combined CVD Morbidity and Mortality

Among eight RCTs that met inclusion criteria, sodium reduction had a statistically significant effect on reducing the relative risk for the combined outcome of CVD morbidity and mortality.^{51, 53, 170, 171, 182, 196, 275, 282} Four prospective cohort studies found no consistent associations between 24-hour urinary sodium excretion and this outcome^{98, 107, 130, 137} (insufficient evidence to draw a conclusion based on cohort studies).

Sodium and CHD Morbidity and Mortality

No RCTs that met inclusion criteria assessed the effect of sodium reduction on the combined outcomes of CHD morbidity and mortality. Four studies that assessed non-overlapping cohorts found inconsistent associations between 24-hour urinary sodium excretion and this outcome (insufficient evidence).

Sodium and Patients With Any CVD Event

Seven RCTs reported on endpoints that included a CVD outcome or a composite of CVD outcomes. A pooled analysis showed a statistically significant decrease in the relative risk for this outcome with sodium reduction (low strength of evidence because of inconsistent outcomes and extreme imprecision).^{51, 53, 99, 170, 171, 182, 196} Four prospective cohort studies with moderate RoB included a comparable outcome but evidence was considered insufficient to draw a conclusion.^{98, 107, 130, 137}

Stratified analysis by sex found no differences between males and females in RCTs.

Stratified analysis by race/ethnicity in the two TOHP trials combined found that only the response for white participants was statistically significant (evidence insufficient on which to draw a conclusion).

Stratified analysis by age in one large RCT found a greater benefit of sodium reduction among adults in the 60 to 69 age group than among older adults. None of these findings have sufficient strength of evidence to permit conclusions.

Sodium and Mean Difference in eGFR and Number of Patients With End Stage Renal Disease

No RCTs that met inclusion criteria reported on these outcomes. One cohort study found no association between sodium excretion and mean difference in eGFR. Another cohort study found that lower sodium excretion was associated with a slower decline in kidney function among individuals with HTN. Evidence was considered insufficient to draw any conclusions on sodium intake and renal outcomes.

Sodium and Left Ventricular Hypertrophy

Two RCTs reported no effect of sodium reduction on this outcome. No prospective cohort studies that met inclusion criteria reported on this outcome. Evidence is insufficient to draw conclusions from either RCTs or prospective cohort studies.

Key Question 5. Effect of Interventions To Increase Potassium Intake on Blood Pressure and Kidney Stones

Conclusions

- Increased potassium intake from dietary supplements reduces blood pressure in adults (moderate SoE based on 10 parallel RCTs and 8 crossover RCTs). However the effect is limited to studies of adults with prehypertension or hypertension (moderate SoE). Studies of adults with normal BP did not show evidence that increased potassium intake decreases blood pressure in this group (3 RCTs; low SoE)
- Evidence does not support an effect of increasing potassium intake through changes in food intake alone on BP in adults (low SoE, based on 4 RCTs).
- Evidence is insufficient to support a conclusion regarding the effect of increasing potassium intake on kidney stone formation (one RCT).

Key Question 6. Association Between Potassium Intake and Blood Pressure and Kidney Stones

Conclusions

- Higher potassium intake is not consistently associated with lower adjusted BP in cohort studies of adults (six RCTs; low SoE based on inconsistent findings and studies with high RoB).
- Higher potassium intake appears to be associated with a lower risk for kidney stones in cohort studies of adults (low SoE, based on four prospective cohorts reported in two publications with high RoB).

Potassium and Blood Pressure

Increased potassium intake significantly decreased systolic (by more than 5 mm Hg) and diastolic BP (by more than 3 mm Hg) in pooled analyses of 18 RCTs (moderate strength of evidence) but the evidence is based predominantly on studies that employed dietary supplements.^{48, 51, 60, 65, 70-74, 89, 94, 110, 125, 126, 236, 264, 277, 280} Prospective cohort studies and multivariate

analyses found inconsistent associations between urinary potassium excretion and BP, and three additional prospective cohort studies found inconsistent associations with potassium intake based on dietary assessment.^{48, 51, 60, 65, 70-74, 89, 94, 110, 125, 126, 236, 264, 277, 280}

Evidence was insufficient to determine whether the effect of potassium was moderated by sex, race/ethnicity, or age, or by baseline hypertensive status.

Potassium and Incident Hypertension

No RCTs that met inclusion criteria assessed the effect of increased potassium intake on incident HTN compared with placebo. Among five prospective cohort studies, one study found a significant association between the lowest quantile of potassium excretion and higher risk for HTN, whereas four studies found inconsistent associations with dietary potassium; this evidence was considered insufficient on which to base a conclusion.^{37, 76, 120, 145, 274}

Potassium and Percent Participants at Blood Pressure Goal

No RCTs that met inclusion criteria assessed the effect of increased potassium intake on potassium compared with placebo. No prospective cohort studies assessed this outcome.

Potassium and Kidney Stones

One RCT that met inclusion criteria reported that potassium (citrate) supplementation for 3 years significantly decreased the risk for kidney stone recurrence compared with placebo (insufficient strength of evidence).¹⁷⁶ Multivariate analysis of a large RCT dataset found only a nonsignificant association between dietary potassium and kidney stone risk. Across three large prospective cohort studies assessed together, dietary potassium intake was inversely associated with risk for incidence kidney stones (low strength of evidence; high RoB based on intake assessment).^{67, 153}

Potassium and Adverse Events

Six RCTs reported greater risk for minor gastrointestinal discomfort associated with increased potassium intake from supplements (low strength of evidence).^{60, 70, 72, 74, 110, 176}

Key Question 7. Effect of Interventions To Increase Potassium Intake on CVD and Kidney Disease Morbidity and Mortality, and on Total Mortality

- Evidence was insufficient to address this question (one RCT).¹⁸²

Key Question 8. Association Between Dietary Potassium Intake and CVD, CHD, Stroke, and Kidney Disease Morbidity and Mortality, and Between Dietary Potassium and Total Mortality

- Evidence is insufficient to identify associations of potassium intake with long-term chronic disease outcomes of interest, primarily due to the limitations in the potassium intake assessments.

Potassium and All-Cause Mortality

One RCT reported that the use of a potassium-containing salt substitute in place of sodium chloride significantly reduced all-cause mortality at 2 ½ years (insufficient evidence).

Prospective cohort studies were inconsistent in their assessments of potassium status and all-cause mortality: four studies showed inconsistent associations between urinary potassium excretion and all-cause mortality, whereas three studies showed consistent associations between dietary potassium intake and adjusted all-cause mortality.^{55, 100, 116, 129, 137, 140, 141}

Potassium and CVD Mortality

The RCT described above reported that the potassium-containing salt substitute produced a significant decrease in age-adjusted CVD mortality compared with usual diet (insufficient evidence).

Prospective cohort studies reported no consistent association between potassium status and CVD mortality. Two of three cohort studies reported inverse associations between dietary potassium intake and CVD mortality, whereas two studies found no association between estimated 24-hour urinary excretion and CVD mortality.^{116, 129, 141}

Potassium and CHD Mortality

The salt substitute study also reported a significant decrease in age-adjusted CHD mortality at 2 ½ years (insufficient evidence).

Potassium status was inversely associated with CHD mortality risk across two cohort studies, one of which assessed 24-hour urinary potassium excretion (insufficient evidence).^{55, 116}

Potassium and Stroke

No RCTs assessed the effect of increased potassium intake on the risk for stroke.

Among thirteen prospective cohort studies that assessed associations of potassium status with stroke risk among healthy cohorts, findings were inconsistent and could not be predicted by method used to assess potassium status (insufficient evidence).^{58, 59, 62, 63, 69, 78, 103, 108, 128, 129, 137, 140, 141}

Potassium and Myocardial Infarction

No RCTs assessed the effect of increased potassium intake on the risk for MI.

Two prospective cohort studies found no association between potassium status and risk for MI (insufficient evidence).^{129, 141}

Potassium and Combined CVD Morbidity and Mortality

No RCTs assessed the effect of potassium supplementation on the combined outcome of CVD morbidity and mortality.

No significant associations were found between urinary potassium levels and combined CVD morbidity and mortality outcomes across three prospective cohort studies (insufficient evidence).

Potassium and Combined CHD Morbidity and Mortality

No RCTs assessed the effect of increased potassium intake on the combined outcome of CHD morbidity and mortality.

Two prospective cohort studies showed inconsistent associations between 24-hour urinary potassium excretion and combined CHD morbidity and mortality outcomes (insufficient evidence).^{55, 137}

Potassium and Any CVD Outcomes

No RCTs assessed the effect of increased potassium intake on “any CVD outcomes” as reported by authors.

One cohort study reported no association between potassium intake and a combination of outcomes that included left ventricular hypertrophy (insufficient evidence).

Potassium and Renal Disease

No RCTs assessed the effect of increased potassium intake on risk for renal disease.

One prospective cohort study assessed the association between potassium status and renal outcomes. The study found that lower urinary potassium excretion was associated with an increased risk of developing chronic kidney disease (lower eGFR), but evidence is insufficient to draw a conclusion.

Summary of Findings in Relation to What Is Already Known

Since the *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* was published in 2005, a number of systematic reviews have been conducted on the effects of sodium intake and sodium reduction on BP, as well as CVD and CHD outcomes. We briefly review our findings in light of the findings of the most recent reviews. Aburto and colleagues conducted reviews on the relationship between sodium and potassium intake and BP, CVD, CHD, and stroke from observational studies and the effects of sodium reduction and increased potassium intake as reported in RCTs; these reviews were sponsored by the WHO in support of their current guidelines. The WHO review on sodium and BP, which included 37 RCTs, found significant beneficial effects of interventions to reduce sodium on blood pressure in adults and children but no difference between very low- (defined as a target of 50mmol/d) and low- (defined as a target of 100mmol/d) sodium interventions.^{4, 296} Our report found similar effects of sodium reduction on BP in adults, but only statistically non-significant beneficial effects in children. When we conducted a sensitivity analysis that omitted high- and unclear RoB studies, we found that when only low- and moderate-RoB studies were pooled, sodium reduction resulted in a statistically significant decrease in diastolic BP in children (the decrease in systolic BP remained non-significant). The WHO report did not assess effects of sodium reduction on incident hypertension or achievement of specific BP goals. The inclusion criteria for our report and those of the WHO report differed in several ways. Our review included sodium reduction RCTs regardless of achieved sodium excretion, whereas the WHO review excluded RCTs with a mean difference in achieved sodium excretion of less than 40 mmol/d; although excluding such studies might be expected to increase pooled effect sizes, visual inspection of the forest plots for our analyses does not appear to show strong associations between sodium intake and BP outcomes across all RCTs. The WHO review also included abstracts, whereas our report included only full, peer-reviewed publications.

More recently, Graudal and colleagues systematically reviewed the trial literature on sodium reduction and BP and reached similar conclusions to those of Aburto and our review; the Graudal review excluded only trials with a duration of less than 4 days, resulting in a larger

number of included trials.²⁹⁷ Our current review also corroborates the findings of the Graudal review regarding a larger effect of sodium reduction on individuals with HTN than on normotensive individuals.

The WHO report found no effect of sodium reduction on plasma epinephrine, norepinephrine, blood lipids, or kidney function, as measured by serum creatinine and creatinine clearance; four studies that met our inclusion criteria corroborated the apparent absence of effect of sodium reduction on blood lipids (reported as adverse effects or primary outcomes), but no studies met our inclusion criteria for assessing changes in kidney function or catecholamines. In contrast, the Graudal review reported significant increases in cholesterol and triglycerides, possibly due to the much shorter followup of some included studies.²⁹⁷

Several recent systematic reviews also appraised the evidence linking sodium with all-cause mortality, CVD, CHD, or stroke.

A 2014 systematic review by Adler and colleagues that reviewed eight RCTs assessing effects of sodium reduction on these longer-term outcomes reported no effect on all-cause mortality.

Graudal and colleagues (2014) conducted a meta-analysis of cohort studies that assessed the association between sodium exposures and all-cause mortality: They reported an increased mortality risk at both low- and high intakes of sodium (which they referred to as a “U-shaped curve”).²⁹⁸ The review included only observational studies, and the findings could be explained by errors in estimation of sodium intake at the lower- or the upper end as well as reverse causality. .

Our review of RCTs that reported on the effects of sodium reduction on all-cause mortality found a non-statistically significant decrease in the risk for all-cause mortality. Our review of prospective cohort studies found an association between higher intakes of sodium and increased risk but insufficient evidence to draw any conclusions regarding the shape of the curve. The methods used to estimate sodium intake varied across the prospective cohort studies, and few used multiple 24-hour sodium excretion measures with validation to ensure complete collection; in addition, these studies could not rule out reverse causation: In sodium studies, reverse causality arises when study participants with medical morbidity have reduced their sodium intake on medical advice or because their illness has resulted in decreased food consumption.

Our current review also adds to the evidence by identifying an effect of sodium reduction on reducing combined CVD morbidity and mortality across RCTs. The review by Adler found similar effects on CVD mortality and morbidity; they largely attributed the observed effect on mortality to one study that implemented use of a potassium salt substitute to reduce sodium intake.¹⁸² We also reported statistically significant effects of sodium reduction on a composite of any CVD outcomes. The Adler review included one RCT²⁹⁹ that we excluded, as it was a multicomponent intervention that did not control for other dietary changes (the remaining RCTs were included in our review).¹⁵ The WHO also reviewed the evidence linking sodium with CVD, CHD, and stroke; that report, which included 14 prospective cohort studies and five RCTs, found sufficient evidence only to conclude (based on the evidence from cohort studies) that increased sodium intake was linked to increased risk for stroke, stroke mortality, and CHD mortality.⁴

We identified few studies on individuals with chronic kidney disease, and no studies that met our inclusion criteria addressed renal endpoints. A Cochrane review by McMahon and colleagues appraised the evidence on effects of sodium reduction on cardiovascular outcomes in persons with kidney disease.³⁰⁰ However like our review, they identified no studies with long enough follow up to assess long term chronic disease outcomes. Instead they reported only on

studies that assessed effects of sodium reduction on BP outcomes in persons with kidney disease, reporting that sodium reduction decreased systolic BP and diastolic BP in these studies. . Across the studies that met our inclusion criteria, we also noted that sodium reduction generally decreased BP; however, we determined that the populations were too dissimilar (based on comorbidities) to permit studies to be pooled.

Aburto and colleagues subsequently reviewed the evidence for an association of potassium intake with BP, HTN, and CVD, for the WHO, concluding that higher potassium intake was associated with reduced BP in individuals with HTN but not in normotensive persons.³⁰¹ That report found insufficient evidence to draw conclusions regarding the association of potassium intake with risk for CVD or CHD morbidity or mortality. Our current review confirmed the association of potassium with BP lowering, by identifying RCTs that assessed the effects of increased potassium intake and also extended their finding to healthy populations. We found insufficient evidence to draw any conclusions on the effects of increased potassium intake on incident HTN, and like the WHO review, we identified insufficient evidence to draw conclusions regarding the effects of increased potassium intake on CVD/CHD morbidity or mortality. In addition, the beneficial effects of increased potassium intake on BP were not reflected in any association between (urinary or dietary) potassium intake and BP.

Limitations of the Evidence Base

The purpose of this review was to assess the evidence for the intermediate and clinical health effects of reduced sodium intake, mainly as reflected in reduced 24-hour urinary sodium excretion. We did not assess the evidence regarding the most effective intervention design(s).

Most RCTs demonstrated an overall low or moderate RoB. However, a number of studies omitted many details of study design and conflict of interest, so actual RoB was unclear for some items. Nearly all observational (prospective cohort) studies that met inclusion criteria relied on single 24-hour urinary excretion measures, single or 2-day dietary recall without 24-hour urinary excretion, estimated sodium excretion to assess status, or food frequency questionnaires. The implications of assessment of sodium and potassium status in observational studies are discussed further below. Additional limitations are listed here, organized by a PICOTSS framework.

Populations

- Few to no studies conducted subgroup analyses by sex, age, race/ethnicity, or comorbidities such as HTN.
- RCTs may enroll individuals who are more motivated than average, although compliance across studies (usually based on 24-hour sodium excretion) does not necessarily support this possibility.
- Studies defined prehypertension and mild-moderate HTN differently or not at all, and some studies included individuals with pre- or mild HTN along with individuals with more advanced HTN.
- Although most RCTs either prohibited or required use of antihypertensive medications or withdrew participants from medications at baseline and assessed need to resume their use, at least 25 percent of studies did not consider use of these medications or allowed participants to remain on medications but did not account for their use. Studies that enrolled only participants taking antihypertensive medications usually did not control for the class of medication, thus potentially introducing a confounding factor. Concurrent use

of some antihypertensive medications could have masked the potential effects of a reduced sodium diet.

- Observational studies had limited ability to control for pre-existing health conditions at study baseline that might have resulted in decreased sodium intakes, contributing to potentially spurious associations of lower sodium intakes with morbidity or mortality outcomes of interest.
- Observational studies may have residual confounding, as they could not adjust for all factors that may increase risk for HTN, CVD, CHD outcomes.

Interventions/Exposures

- RCTs used widely varying methods to achieve different sodium intake levels, and most RCTs actually employ multicomponent lifestyle interventions or at least multicomponent dietary interventions; thus not all changes in outcomes of interest might be attributable to reduced sodium or increased potassium intake. The potential implication of this variation in background diet for study findings is highlighted by the findings of the DASH Sodium trial, which showed that at each dietary sodium level, mean BP was higher (2.2 to 5.9 mm Hg) among control diet participants than among the DASH diet groups, that the decreases in BP achieved with decreasing sodium intake were greater for those on the control diet than for those on the DASH diet, but that nevertheless, the low-sodium DASH participants achieved the greatest reduction in BP overall ⁴⁹ Thus a diet that includes more fruits and vegetables (and, as a result, more vitamins, minerals, and fiber, and less saturated fat), as well as whole grains, and low-fat dairy has effects on BP that are independent of sodium intake ^{49, 302} Thus, a diet that includes more fruits and vegetables (and, as a result, more vitamins, minerals, and fiber, and less saturated fat) has effects on BP that are independent of sodium intake.
- .Only a small number of studies assessed effects of natural experiments, or community- or government-level interventions.
- Many RCTs failed to report intended goals of the intervention (e.g., achieving 70 mmol/d urinary sodium excretion or a difference between the intervention group and the control group of 40 mmol/d or more).
- Effectiveness of behavioral/lifestyle interventions in reducing sodium intake may be affected by unmeasured or unreported factors, such as intensity of counseling.
- Few prospective cohort studies used multiple 24-hour urinary excretion analyses, although increasing evidence demonstrates that multiple, non-consecutive 24-hour urinary sodium excretion measurements needs to be used as the indicator of exposure in observational studies.^{19, 303} Thus nearly all included prospective cohort studies had high risk for both systematic (24-h urine collections without evidence of quality control measures, spot or overnight urine collections, FFQ, 24-h recalls, and food records) and random error (e.g., single 24-hour or spot urine collections or single-day food recalls).
- Inconsistencies in apparent sodium intakes in studies over time may be attributable to changes in assessment methods used.
- Both RCTs and prospective cohort studies vary widely in baseline sodium intake. Most RCTs employed 24-hour urinary sodium excretion as a measure of compliance with the intervention. However, differences in baseline intake could affect the potential to achieve sodium reduction goals through dietary interventions and introduce a source of

heterogeneity among prospective cohort studies. Evidence in support of this idea is presented by a recent post hoc assessment of data from the DASH Sodium trial found that reducing sodium intakes in the context of the control or the DASH diet were associated with progressively greater reductions in BP with higher baseline BP (through baseline systolic BP of 150 mm Hg or higher).²⁹⁰

- Wide variation in achieved intakes across RCTs introduces another potential source of heterogeneity and calls into question whether differences in achieved sodium intake can accurately predict changes in outcomes of interest.
- Few RCTs reported sodium-to-potassium ratios. Potentially related to this observation, studies that employed potassium-containing salt substitutes to reduce sodium intake or tested the effects of potassium supplements tended to find no consistent effects on sodium excretion.
- Few studies employ food-based interventions to assess the effects of increasing potassium intake. Those that do use dietary interventions do not consistently control for differences in other micronutrients, carbohydrates, and fiber.
- Potassium supplementation studies range from about 15 to 120 mmol/d in the amounts provided (average intakes from food range from 50 to 150 mmol/d and the current AI for adults is 120 mmol/d), introducing a potential source of heterogeneity across studies.

Comparators

- Confounding in dietary intervention studies (for example, adoption of use of salt substitutes or other salt reduction practices by control groups) was difficult to control or measure, and blinding had limited effectiveness when the comparison group consumed their usual diet (most dietary intervention studies that relied on counseling reported that participants were not blinded).
- Studies with usual diet as the control may not be comparable with studies that impose a low-sodium diet on all participants and then achieve differences in sodium intake using sodium tablets to mimic usual sodium intake.

Outcomes

- Studies defined HTN, CVD, and CHD outcomes differently.
- Few RCTs assessed the effect of sodium reduction or increased potassium intake on the risk for incident HTN as an outcome.
- Of the small number of studies that assessed long term CVD outcomes, few assessed these as primary or even prespecified outcomes, were not powered to assess them as prespecified outcomes, and reported them instead as adverse events.
- Little research assesses effects of sodium reduction on CHD outcomes.

Timing/Duration

- Few to no RCTs were identified that assessed longer-term clinical outcomes of most interest: RCTs seldom had adequate duration of interventions or follow up to assess longer-term outcomes.
- Renal outcomes, including kidney stones, require longer follow ups to observe potential effects of interventions than were employed in any of the studies identified.

- Long-term outcomes resulting from brief interventions may not show any effects.

Setting

- RCTs in clinical research settings are resource intensive and may have limited practical application. RCTs in populations confined to residential settings such as long-term care facilities, schools, or prisons may provide more useful results in terms of assessing outcomes but still fail to address the potential effects of voluntary efforts (individual or community) to reduce dietary sodium intake.

Study Design

- Observational studies predominated for long term chronic disease outcomes.
- As described, RCTs with parallel arm designs present challenges that are difficult to overcome regarding blinding, allocation concealment, and contamination.
- RCTs with crossover designs may provide some advantages, but existing crossover trials seldom describe washout periods or assess potential carryover effects of short (or no) washouts.

Limitations of This Review

Since the inclusion of participants with pre-existing conditions could confound attempts to link the outcomes of interest with changes in sodium intake, studies that enrolled sick participants were excluded from the affected analyses. For example, studies of patients with CVD were excluded from analysis of risk for CVD morbidity, but not analysis of CVD mortality, and studies of patients with cancer, HIV/AIDS, and end stage renal disease were excluded from all analyses.

We did not take use of antihypertensive medications into account in our analyses of RCT data, primarily because studies did not consistently report or adjust for such use. Thus, we could not eliminate the possibility that potential effects of reduced sodium might be masked by the effects of such medications.

Similarly, we did not conduct sensitivity analyses to assess the effects of the methods used to measure blood pressure, which may strongly affect outcomes. The duration of interventions or exposures is likely critical. For that reason, we set strict lower limits on the durations of studies we included, especially for long term clinical outcomes. However, we did not attempt to assess the effects of intervention or exposure duration on outcomes, mainly because we identified too few studies to enable realistic comparisons.

We excluded crossover studies that did not describe the use of washout or duration of washout and did not describe a process to assess the possible effects of carryover. As a result, we excluded one dose-response study, the findings of which supported the conclusion that decreasing sodium intake decreases blood pressure.³⁰⁴ However, some evidence suggests potential carryover may need to be considered.²³

Research Gaps Identified by This Review

In light of the large body of evidence on the effects of sodium reduction on blood pressure in healthy adults and those with hypertension, the determination that the effect of reducing sodium intake on blood pressure is supported by moderate but not high strength evidence is attributable to inconsistency in the direction of study findings and to study heterogeneity. Sensitivity

analyses that omitted high- and unclear RoB studies did not appreciably alter consistency, heterogeneity, or effect sizes; thus, other factors—such as differing participant comorbidities, intervention design or blood pressure measurement methods—may be contributing to the variation.

Studies to assess whether those with HTN may benefit more or less from reduced dietary sodium than those with normal blood pressure showed greater benefits for those with HTN, but at least one fourth of studies that enroll adults with HTN do not report controlling for use of antihypertensive medication.

Among studies that met inclusion criteria, only a small number directly compared effects of sodium reduction on participants with normal blood pressure with those on participants with HTN. Studies to assess the benefits of reducing dietary sodium for those with normal blood pressure were fewer in number than studies of populations with HTN, and some studies of normotensive populations included individuals with high normal blood pressure.

Few studies that met inclusion criteria directly compared the effects of sodium reduction on men with those on women, the effects on one racial/ethnic group with those on other racial/ethnic groups, and the effects among different age groups. Few studies designed to determine whether dietary interventions reduce blood pressure among younger individuals—both children, adolescents, and young adult—met inclusion criteria.

Few trials that met inclusion criteria assessed the effects of sodium reduction or increased potassium intake on CVD, CHD, stroke, or renal outcomes, including the effect of increasing potassium intake on the incidence of kidney stones. Most dietary intervention studies to reduce sodium (or increase potassium) from food sources involved counseling, making it difficult to isolate the effects of sodium reduction or increased potassium intake, either because of poor adherence or because of the challenge of ruling out alterations in intake of other nutrients.

Few trials that met inclusion criteria assessed the effects of sodium reduction or increased potassium intake on CVD, CHD, stroke, or renal outcomes, including the effect of increasing potassium intake on the incidence of kidney stones.

Conclusions

We undertook this systematic review to appraise the evidence from trials regarding the effects of dietary sodium reduction and/or increased potassium intake on blood pressure and risk for cardiovascular diseases—as well as the evidence on associations of dietary sodium and potassium with blood pressure and cardiovascular diseases. This review finds that interventions that reduce dietary sodium intake (including those that use potassium-containing salt substitutes in the diet) reduce blood pressure in both normotensive adults and, to a greater extent, those with hypertension. Interventions to reduce sodium intake increase the likelihood of reaching a prespecified blood pressure goal and may decrease the incidence of hypertension in adults, in agreement with prospective cohort studies, which show that higher sodium intakes may be associated with greater risk for hypertension.

Increasing potassium intake via potassium supplements significantly decreases blood pressure, but the effects of increasing potassium intake through food alone remain unclear.

Interventions to assess the effects of reducing sodium intake on the risk for all-cause mortality are small in number and provide an insufficient basis on which to draw a conclusion. Prospective cohort studies suggest sodium intake may be associated with all-cause mortality. Findings from randomized controlled trials also suggest that interventions to reduce sodium intake may decrease the risk for composite measures of cardiovascular disease outcomes.

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Abbreviations/Acronyms

Acronym/Abbreviation	Definition
AE	Adverse effect
AI	Adequate Intake
ANHMRCDSMC	Australian National Health and Medical Research Council Dietary Salt Study Management Committee
ATBC	Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention Study
BMI	Body mass index
BP	Blood pressure
CABG	Coronary artery bypass graft
CCCC	Chin-Shan Community Cardiovascular Cohort Study
CCT	Controlled clinical trial
CDSR	Cochrane Database of Systematic Reviews
CHD	Coronary heart disease
CHNS	Chinese Health and Nutrition Survey
CI	Confidence interval
CIRCS	Circulatory Risk in the Community Study
CKD	Chronic kidney disease
CrCl	Creatinine clearance
CRIC	Chronic Renal Insufficiency Cohort study
CV	Cardiovascular
CVD	Cardiovascular disease
D	Day
DBP	Diastolic blood pressure
DM	Diabetes mellitus
DONALD	Dortmund Nutritional and Anthropometric Longitudinally Designed Study
DRI	Dietary Reference Intakes
EAR	Estimated Average Requirement
eGFR	Estimated glomerular filtration rate
EPC	Evidence-based Practice Center
ESRD	End Stage Renal Disease
GFR	Glomerular filtration rate
GI	Gastrointestinal
Hg	Mercury
HPFUS	Health Professionals Follow-Up Study
HPT	Hypertension Prevention Trial
HPTRG	Hypertension Prevention Trial Research Group
HR	Hazard ratio
HTN	Hypertension
IHD	Ischemic heart disease
IOM	Institute of Medicine
IQR	Interquartile range
ITT	Intention-to-treat
K	Potassium
KCl	potassium chloride
KQ	Key Question

Acronym/Abbreviation	Definition
LV	Left ventricular
MD	Mean difference
MDRD	Modification of Diet in Renal Disease trial
MI	Myocardial infarction
Mm	Millimeters
Mmol	Millimoles
MMSHT	Minnesota Mount Sinai Hypertension Trial
N/A	Not applicable
Na	Sodium
Na-K	Sodium-Potassium
NGHS	The NHLBI Growth and Health Study
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
N/R	Not reported
NSTEMI	non-ST elevation myocardial infarction
PAPSS	Potassium and Protein Supplementation Study
PICOTSS	Population, intervention/exposure, comparison group, outcome, time, setting, and study design
PREVEND	Prevention of Renal and Vascular End-Stage Disease Study
PTCA	Percutaneous transluminal coronary angioplasty
RCT	Randomized controlled trial
RDA	Recommended Daily Allowance
RoB	Risk of bias
RR	Relative risk
RRID	Renal Risk in Derby study
SBP	Systolic blood pressure
SCr	Serum creatinine
SD	Standard deviation
SHS	Strong Heart Study
SoE	Strength of evidence
SRDR	Systematic Review Data Repository
STEMI	ST-segment elevation myocardial infarction
TCSSSCG	The China Salt Substitute Study Collaborative Group
TAIM	Trial of Antihypertensive Interventions and Management
TEP	Technical expert panel
TIA	Transient ischemic attack
TOHP I	Phase I of the Trials of Hypertension Prevention
TOHP II	Phase II of the Trials of Hypertension Prevention
TONE	US Trial of Nonpharmacologic Interventions on the Elderly
UK	United Kingdom
UL	Tolerable Upper Intake Level
WHI OS	Women's Health Initiative Observational Study
WHO	World Health Organization

Appendix A. Search Methodology

Scoping Search for Existing Systematic Reviews

DATABASE SEARCHED & TIME PERIOD COVERED:
PubMed – 1/1/2003 – present (searched 12 December 2017)

KQ1 and 2

LANGUAGE:
English

ARTICLE TYPE:
Systematic reviews

SEARCH STRATEGY:
(("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR "urinary excretion") OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])
AND
("Blood Pressure"[Mesh] OR "blood pressure" OR hypertens*)
AND
humans[MESH] OR ((inprocess[*sb*] OR publisher[*sb*] OR pubmednotmedline [*sb*] NOT (mice[*ti*] OR mouse[*ti*] OR rats[*ti*] OR dogs[*ti*]))
AND
PUBMED FILTER=Systematic Reviews OR JOURNAL="Cochrane Database of Systematic Reviews"

KQ3 and 4

LANGUAGE:
English

SEARCH STRATEGY:
(("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR "urinary excretion") OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])
AND
"Mortality"[Mesh] OR mortality[*sh*] OR mortality[*tiab*] OR "Cardiovascular Diseases"[Mesh] OR "Kidney Diseases"[Mesh] OR cardiovascular disease*[*tiab*] OR acute coronary syndrome*[*tiab*] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[*tiab*] OR "end stage kidney disease"[*tiab*] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR chronic kidney disease*[*tiab*] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR

kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi OR acute kidney injur*

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

AND

PUBMED FILTER=Systematic Reviews OR JOURNAL="Cochrane Database of Systematic Reviews"

KQ5 and 6

LANGUAGE:

English

"Potassium, Dietary"[Mesh] OR potassium[tiab] OR KLOR-CON[tiab] OR KCL[tiab]

AND

"Blood Pressure"[Mesh] OR "blood pressure" OR hypertens* OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

AND

PUBMED FILTER=Systematic Reviews OR JOURNAL="Cochrane Database of Systematic Reviews"

KQ7 and KQ8

LANGUAGE:

English

"Potassium, Dietary"[Mesh] OR potassium [tiab] OR KLOR-CON[tiab] OR KCL[tiab]

AND

"Mortality"[Mesh] OR mortality[sh] OR mortality[tiab] OR "Cardiovascular Diseases"[Mesh] OR "Kidney Diseases"[Mesh] OR cardiovascular disease*[tiab] OR acute coronary syndrome*[tiab] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[tiab] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR "end stage kidney disease"[tiab] OR chronic kidney disease*[tiab] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR acute kidney injur* OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

AND

PUBMED FILTER=Systematic Reviews OR JOURNAL="Cochrane Database of Systematic Reviews"

Search for Primary Research Studies

KQ1 Effects of interventions to reduce sodium intake on blood pressure

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

((("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR "urinary excretion") OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])

AND

("Blood Pressure"[Mesh] OR "blood pressure" OR hypertens*)

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

AND

(random* OR randomized controlled trial[pt] OR randomized controlled trials OR rct* OR blind* OR double-blind* OR single-blind *))

KQ2 Association between sodium intake and blood pressure

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

((("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR “urinary excretion”) OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])

AND

"Blood Pressure"[Mesh] OR "blood pressure" OR hypertens*

AND

"Prospective Studies"[Mesh] OR "Case-Control Studies"[Mesh:NoExp] OR "prospective cohort" OR "nested case-control" OR “metabolic study” OR experiment*[tiab] OR clinical trial*

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

KQ3 Effects of interventions to reduce sodium intake on cardiovascular disease, kidney disease, and mortality

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

((("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR “urinary excretion”) OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])

AND

"Mortality"[Mesh] OR mortality[sh] OR mortality[tiab] OR "Cardiovascular Diseases"[Mesh] OR "Kidney Diseases"[Mesh] OR cardiovascular disease*[tiab] OR acute coronary syndrome*[tiab] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[tiab] OR "end stage kidney disease"[tiab] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR chronic kidney disease*[tiab] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi OR acute kidney injur*

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti])) AND (random* OR randomized controlled trial[pt] OR randomized controlled trials OR rct* OR blind* OR double-blind* OR single-blind*))

KQ4 Association between sodium intake and cardiovascular disease, coronary heart disease, stroke, kidney disease, or mortality

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

((("Sodium Chloride"[Mesh] OR "Sodium Glutamate"[Mesh] OR "monosodium glutamate"[Title/Abstract] OR salt[Title/Abstract] OR salt[Text Word] OR sodium[Title/Abstract] OR sodium[Text Word]) AND (diet[MeSH Terms] OR diet[Title/Abstract] OR diet[Text Word] OR food[Text Word] OR food[Title/Abstract] OR intake[Title/Abstract] OR intake[Text Word] OR "urinary excretion") OR "Diet, Sodium-Restricted"[Mesh] OR "Sodium, Dietary"[Mesh])

AND

"Cardiovascular Diseases"[Mesh] OR cardiovascular disease*[tiab] OR acute coronary syndrome*[tiab] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[tiab] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR "end stage kidney disease"[tiab] OR "Kidney Diseases"[Mesh] OR chronic kidney disease*[tiab] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR kidney stone* OR acute kidney injur* OR "kidney calculi" OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi OR "Mortality"[Mesh] OR mortality[sh] OR mortality[tiab]

AND

"Prospective Studies"[Mesh]) OR "Case-Control Studies"[Mesh:NoExp] OR "prospective cohort" OR "nested case-control" OR "metabolic study" OR experiment*[tiab] OR clinical trial*

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb]) NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

KQ5 Effect of interventions to increase potassium intake on blood pressure and kidney stone formation

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

"Potassium, Dietary"[Mesh] OR potassium[tiab] OR KLOR-CON[tiab] OR KCL[tiab]

AND

"Blood Pressure"[Mesh] OR "blood pressure" OR hypertens* OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi
AND
humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))
AND
(random* OR randomized controlled trial[pt] OR randomized controlled trials OR rct* OR blind* OR double-blind* OR single-blind *))

KQ6 Association between potassium intake and blood pressure and kidney stone formation

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

"Potassium, Dietary"[Mesh] OR potassium[tiab] OR KLOR-CON[tiab] OR KCL[tiab]
AND
"Blood Pressure"[Mesh] OR "blood pressure" OR hypertens* OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi
AND
"Prospective Studies"[Mesh]) OR "Case-Control Studies"[Mesh:NoExp] OR "prospective cohort" OR "nested case-control" OR "metabolic study" OR experiment*[tiab] OR clinical trial*
AND
humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb]) NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

KQ7 Effects of interventions to increase potassium intake on cardiovascular disease, kidney disease, and mortality

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

"Potassium, Dietary"[Mesh] OR potassium [tiab] OR KLOR-CON[tiab] OR KCL[tiab]
AND
"Mortality"[Mesh] OR mortality[sh] OR mortality[tiab] OR "Cardiovascular Diseases"[Mesh] OR "Kidney Diseases"[Mesh] OR cardiovascular disease*[tiab] OR acute coronary syndrome*[tiab] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[tiab] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR "end stage kidney disease"[tiab] OR chronic kidney disease*[tiab] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR acute kidney injur* OR kidney calculi OR kidney stone* OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi
AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb] NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))
AND
(random* OR randomized controlled trial[pt] OR randomized controlled trials OR rct* OR blind* OR double-blind* OR single-blind*))

KQ8 Association between dietary potassium intake and cardiovascular disease, coronary heart disease, stroke, kidney disease, and mortality

DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2003 – present (searched 12 December 2017)

LANGUAGE:

English

SEARCH STRATEGY:

"Potassium, Dietary"[Mesh] OR potassium[tiab] OR KLOR-CON[tiab] OR KCL[tiab]

AND

"Cardiovascular Diseases"[Mesh] OR cardiovascular disease*[tiab] OR acute coronary syndrome*[tiab] OR "unstable angina" OR myocardial infarct* OR stroke OR strokes OR "heart failure" OR "coronary heart disease" OR renal function* OR kidney disease*[tiab] OR "creatinine clearance" OR "serum creatinine" OR albuminuria OR proteinuria OR "glomerular filtration" OR "end stage kidney disease"[tiab] OR "Kidney Diseases"[Mesh] OR chronic kidney disease*[tiab] OR "albumin-to-creatinine ratio" OR "albumin to creatinine ratio" OR kidney stone* OR acute kidney injur* OR "kidney calculi" OR renal lithiasis OR nephrolith* OR nephrolithiasis OR renal stone OR renal calculi OR "Mortality"[Mesh] OR mortality[sh] OR mortality[tiab]

AND

"Prospective Studies"[Mesh]) OR "Case-Control Studies"[Mesh:NoExp] OR "prospective cohort" OR "nested case-control" OR "metabolic study" OR experiment*[tiab] OR clinical trial*

AND

humans[MESH] OR ((inprocess[sb] OR publisher[sb] OR pubmednotmedline [sb]) NOT (mice[ti] OR mouse[ti] OR rats[ti] OR dogs[ti]))

DIETARY SODIUM & POTASSIUM – SEARCH METHODOLOGIES

EMBASE – REVISION OF 10/19/2016

RUN: 12 December 2017

ALL SEARCHES LIMITED TO THE FOLLOWING EMBASE FILTERS:

English

2011-2016

HUMAN

PUBLICATION TYPES - article OR article in press

SEARCH STRATEGIES

KQ1:

['sodium chloride'/exp OR 'sodium chloride' OR 'glutamate sodium'/exp OR 'glutamate sodium' OR 'monosodium glutamate'/exp OR 'monosodium glutamate' OR 'salt' OR 'salt'/exp OR salt OR 'sodium' OR 'sodium'/exp OR sodium

AND

'diet' OR 'diet'/exp OR diet OR 'food'/exp OR food OR intake OR 'urinary excretion'/exp OR 'urinary excretion'

OR

'sodium restricted' AND ('diet'/exp OR diet) OR 'dietary sodium'/exp OR 'dietary sodium']

AND

'hypertension'/exp OR 'hypertension' OR 'blood pressure'/exp OR 'blood pressure' OR hypertens*

AND

'randomized controlled trial'/exp OR random* OR rct* OR blind* OR 'double blind' OR 'single blind'

KQ2:

['sodium chloride'/exp OR 'sodium chloride' OR 'glutamate sodium'/exp OR 'glutamate sodium' OR 'monosodium glutamate'/exp OR 'monosodium glutamate' OR 'salt' OR 'salt'/exp OR salt OR 'sodium' OR 'sodium'/exp OR sodium

AND

'diet' OR 'diet'/exp OR diet OR 'food'/exp OR food OR intake OR 'urinary excretion'/exp OR 'urinary excretion'

OR

'sodium restricted' AND ('diet'/exp OR diet) OR 'dietary sodium'/exp OR 'dietary sodium']

AND

'hypertension'/exp OR 'hypertension' OR 'blood pressure'/exp OR 'blood pressure' OR hypertens*

AND

'prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials'

KQ3:

['sodium chloride'/exp OR 'sodium chloride' OR 'glutamate sodium'/exp OR 'glutamate sodium' OR 'monosodium glutamate'/exp OR 'monosodium glutamate' OR 'salt' OR 'salt'/exp OR salt OR 'sodium' OR 'sodium'/exp OR sodium

AND

'diet' OR 'diet'/exp OR diet OR 'food'/exp OR food OR intake OR 'urinary excretion'/exp OR 'urinary excretion'

OR

'sodium restricted' AND ('diet'/exp OR diet) OR 'dietary sodium'/exp OR 'dietary sodium']

AND

'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'kidney disease'/exp OR 'kidney disease' OR 'mortality'/exp OR mortality OR 'cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries'

AND

'randomized controlled trial'/exp OR random* OR rct* OR blind* OR 'double blind' OR 'single blind'

KQ4:

['sodium chloride'/exp OR 'sodium chloride' OR 'glutamate sodium'/exp OR 'glutamate sodium' OR 'monosodium glutamate'/exp OR 'monosodium glutamate' OR 'salt' OR 'salt'/exp OR salt OR 'sodium' OR 'sodium'/exp OR sodium

AND

'diet' OR 'diet'/exp OR diet OR 'food'/exp OR food OR intake OR 'urinary excretion'/exp OR 'urinary excretion'

OR

'sodium restricted' AND ('diet'/exp OR diet) OR 'dietary sodium'/exp OR 'dietary sodium']

AND

'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'kidney disease'/exp OR 'kidney disease' OR 'mortality'/exp OR mortality OR 'cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries'

AND

'prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials'

KQ5:

'potassium intake'/exp OR potassium OR 'klor con' OR kcl OR 'potassium chloride'

AND

'hypertension'/exp OR 'hypertension' OR 'blood pressure'/exp OR 'blood pressure' OR hypertens* OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi'

AND

'randomized controlled trial'/exp OR random* OR rct* OR blind* OR 'double blind' OR 'single blind'

KQ6:

'potassium intake'/exp OR potassium OR 'klor con' OR kcl OR 'potassium chloride'

AND

'hypertension'/exp OR 'hypertension' OR 'blood pressure'/exp OR 'blood pressure' OR hypertens* OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi'

AND

'prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials'

=====
KQ7:

'potassium intake'/exp OR potassium OR 'klor con' OR kcl OR 'potassium chloride'

AND

'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'kidney disease'/exp OR 'kidney disease' OR 'mortality'/exp OR mortality OR 'cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries'

AND

'randomized controlled trial'/exp OR random* OR rct* OR blind* OR 'double blind' OR 'single blind'

=====
KQ8:

'potassium intake'/exp OR potassium OR 'klor con' OR kcl OR 'potassium chloride'

AND

'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'kidney disease'/exp OR 'kidney disease' OR 'mortality'/exp OR mortality OR 'cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries'

AND

'prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials'

=====
CINAHL SEARCH STRATEGIES

(RUN ON 12 December 2017)

FILTERS FOR ALL SEARCHES:

Date of Publication: 20110101-20170302

Language: - english

Search modes - Find all search terms

Human

KQ1:

MH "Sodium Chloride, Dietary" OR "Sodium Chloride, Dietary" OR MH "Diet, Sodium-Restricted" OR ("monosodium glutamate" OR salt OR sodium) AND (diet* OR food OR intake OR 'urinary excretion'))

AND

MH "Blood Pressure+" OR MH "Hypertension+" OR TI (blood pressure OR hypertension) OR AB (blood pressure OR hypertension) OR MW (blood pressure OR hypertension)

AND

MH "Randomized Controlled Trials" OR TI (random* OR rct* OR blind* OR 'double blind' OR 'single blind') OR AB (random* OR rct* OR blind* OR 'double blind' OR 'single blind')

=====
KQ2:

MH "Sodium Chloride, Dietary" OR "Sodium Chloride, Dietary" OR MH "Diet, Sodium-Restricted" OR ("monosodium glutamate" OR salt OR sodium) AND (diet* OR food OR intake OR 'urinary excretion'))

AND

MH "Blood Pressure+" OR MH "Hypertension+" OR TI (blood pressure OR hypertension) OR AB (blood pressure OR hypertension) OR MW (blood pressure OR hypertension)

AND

MH "Prospective Studies+" OR MH "Clinical Trials+" OR TI ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR AB ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR MW ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials')

=====
KQ3:

MH "Sodium Chloride, Dietary" OR "Sodium Chloride, Dietary" OR MH "Diet, Sodium-Restricted" OR ("monosodium glutamate" OR salt OR sodium) AND (diet* OR food OR intake OR 'urinary excretion'))

AND

MH "Blood Pressure+" OR MH "Hypertension+" OR TI (blood pressure OR hypertension) OR AB (blood pressure OR hypertension) OR MW (blood pressure OR hypertension)

AND

MH "Cardiovascular Diseases+" OR MH "Kidney Diseases+" OR MH "Mortality+" OR "mortality" OR TI ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions')

OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR AB ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR MW ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') AND MH "Randomized Controlled Trials" OR TI (random* OR rct* OR blind* OR 'double blind' OR 'single blind') OR AB (random* OR rct* OR blind* OR 'double blind' OR 'single blind')

KQ4:

MH "Sodium Chloride, Dietary" OR "Sodium Chloride, Dietary" OR MH "Diet, Sodium-Restricted" OR ("monosodium glutamate" OR salt OR sodium) AND (diet* OR food OR intake OR 'urinary excretion')) AND MH "Blood Pressure+" OR MH "Hypertension+" OR TI (blood pressure OR hypertension) OR AB (blood pressure OR hypertension) OR MW (blood pressure OR hypertension) AND MH "Cardiovascular Diseases+" OR MH "Kidney Diseases+" OR MH "Mortality+" OR "mortality" OR TI ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR AB ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR

'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR MW ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries')

AND

MH "Prospective Studies+" OR MH "Clinical Trials+" OR TI ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR AB ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR MW ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials')

KQ5:

MH "Potassium" OR (MH "Potassium Chloride" OR "potassium" OR 'klor con' OR kcl OR 'potassium chloride'

AND

MH "Hypertension+" OR MH "Blood Pressure+" OR MH "Kidney Calculi" OR TI ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi') OR AB ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi') OR MW ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi')

AND

MH "Randomized Controlled Trials" OR TI (random* OR rct* OR blind* OR 'double blind' OR 'single blind') OR AB (random* OR rct* OR blind* OR 'double blind' OR 'single blind')

KQ6:

MH "Potassium" OR (MH "Potassium Chloride" OR "potassium" OR 'klor con' OR kcl OR 'potassium chloride'

AND

MH "Hypertension+" OR MH "Blood Pressure+" OR MH "Kidney Calculi" OR TI ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi') OR AB ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi') OR MW ('kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi')

AND

MH "Prospective Studies+" OR MH "Clinical Trials+" OR TI ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR AB ('prospective study' OR 'prospective studies'

OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR MW ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials')

=====
KQ7:

MH "Potassium" OR (MH "Potassium Chloride" OR "potassium" OR 'klor con' OR kcl OR 'potassium chloride'

AND

MH "Cardiovascular Diseases+" OR MH "Kidney Diseases+" OR MH "Mortality+" OR "mortality" OR TI ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR AB ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR MW ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries')

AND

MH "Randomized Controlled Trials" OR TI (random* OR rct* OR blind* OR 'double blind' OR 'single blind') OR AB (random* OR rct* OR blind* OR 'double blind' OR 'single blind')

=====
KQ8:

MH "Potassium" OR (MH "Potassium Chloride" OR "potassium" OR 'klor con' OR kcl OR 'potassium chloride'

AND

MH "Cardiovascular Diseases+" OR MH "Kidney Diseases+" OR MH "Mortality+" OR "mortality" OR TI ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR

'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR AB ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries') OR MW ('cardiovascular disease' OR 'cardiovascular diseases' OR 'acute coronary syndrome' OR 'acute coronary syndromes' OR 'unstable angina' OR 'myocardial infarction' OR 'myocardial infarctions' OR stroke OR strokes OR 'heart failure' OR 'coronary heart disease' OR 'renal function' OR 'renal functions' OR 'kidney disease' OR 'kidney diseases' OR 'end stage kidney disease' OR 'creatinine clearance' OR 'serum creatinine' OR albuminuria OR proteinuria OR 'glomerular filtration' OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'albumin-to-creatinine ratio' OR 'albumin to creatinine ratio' OR 'kidney calculi' OR 'kidney stone' OR 'kidney stones' OR 'renal lithiasis' OR nephrolith* OR nephrolithiasis OR 'renal stone' OR 'renal stones' OR 'renal calculi' OR 'acute kidney injury' OR 'acute kidney injuries')

AND
MH "Prospective Studies+" OR MH "Clinical Trials+" OR TI ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR AB ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials') OR MW ('prospective study' OR 'prospective studies' OR cohort* OR 'nested case-control' OR 'nested case control' OR 'natural experiment' OR 'natural experiments' OR 'clinical trial' OR 'clinical trials')

=====

Web of Science Search Methodology

DATABASE SEARCHED & TIME PERIOD COVERED:

Web of Science – 1/1/2003-3/2/2017

LANGUAGE:

English

SEARCH STRATEGY: (NOTE - “TS” STANDS FOR “TOPIC SEARCH”)

KQ1-

TS=("monosodium glutamate" or salt or sodium)

AND

TS=(diet* or food or intake or "urinary excretion")

AND

TS=("blood pressure" or hypertens*)

AND

TS=(random* OR RCT* OR blind* OR double-blind* OR single-blind*)

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

KQ2-

TS= ("monosodium glutamate" or salt or sodium)

AND

TS= (diet* or food or intake or "urinary excretion")

AND

TS= ("blood pressure" or hypertens*)

AND

TS= ("prospective study" OR "prospective studies" OR "case-control" OR "case control" OR cohort* OR "metabolic study" OR "metabolic studies" OR "natural experiment" OR "natural experiments" OR "clinical trial" OR "clinical trials")

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

KQ3-

TS=("monosodium glutamate" or salt or sodium)

AND

TS=(diet* or food or intake or "urinary excretion")

AND

TS=(mortality or "cardiovascular disease" or "cardiovascular diseases" or "acute coronary syndrome" or "acute coronary syndromes" or "unstable angina" or "myocardial infarction" or stroke or strokes or "heart failure" or "coronary heart disease" or "renal function" or "renal functions" or "kidney disease" or "end stage kidney disease" or "creatinine clearance" or "serum creatinine" or albuminuria or proteinuria or "glomerular filtration" or "albumin-to-creatinine ratio" or "albumin to creatinine ratio" or "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" or "acute kidney injury" or "acute kidney injuries")

AND

TS=(random* OR RCT* OR blind* OR double-blind* OR single-blind*)

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

REFINED BY: [excluding] DOCUMENT TYPES: (PROCEEDINGS PAPER)

KQ4-

TS=("monosodium glutamate" or salt or sodium)

AND

TS=(diet* or food or intake or "urinary excretion")

AND

TS=(mortality or "cardiovascular disease" or "cardiovascular diseases" or "acute coronary syndrome" or "acute coronary syndromes" or "unstable angina" or "myocardial infarction" or stroke or strokes or "heart failure" or "coronary heart disease" or "renal function" or "renal functions" or "kidney disease" or "end stage kidney disease" or "creatinine clearance" or "serum creatinine" or albuminuria or proteinuria or "glomerular filtration" or "albumin-to-creatinine ratio" or "albumin to creatinine ratio" or "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" or "acute kidney injury" or "acute kidney injuries")

AND

TS= ("prospective study" OR "prospective studies" OR "case-control" OR "case control" OR cohort* OR "metabolic study" OR "metabolic studies" OR "natural experiment" OR "natural experiments" OR "clinical trial" OR "clinical trials")

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

REFINED BY: [excluding] DOCUMENT TYPES: (PROCEEDINGS PAPER)

KQ5-

TS=(potassium or klor-con or kcl)

AND

TS=("kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" OR "blood pressure" or hypertens*)

AND

TS=(random* OR RCT* OR blind* OR double-blind* OR single-blind*)

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

KQ6-

TS=(potassium or klor-con or kcl)

AND

TS=("kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" OR blood pressure" or hypertens*)

AND

TS=("prospective study" OR "prospective studies" OR "case-control" OR "case control" OR cohort* OR "metabolic study" OR "metabolic studies" OR "natural experiment" OR "natural experiments" OR "clinical trial" OR "clinical trials")

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

KQ7-

TS=(potassium or klor-con or kcl)

AND

TS=(mortality or "cardiovascular disease" or "cardiovascular diseases" or "acute coronary syndrome" or "acute coronary syndromes" or "unstable angina" or "myocardial infarction" or stroke or strokes or "heart failure" or "coronary heart disease" or "renal function" or "renal functions" or "kidney disease" or "end stage kidney disease" or "creatinine clearance" or "serum creatinine" or albuminuria or proteinuria or "glomerular filtration" or "albumin-to-creatinine ratio" or "albumin to creatinine ratio" or "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" or "acute kidney injury" or "acute kidney injuries")

AND

TS=(random* OR RCT* OR blind* OR double-blind* OR single-blind*)

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

KQ8-

TS=(potassium or klor-con or kcl)

AND

TS=(mortality or "cardiovascular disease" or "cardiovascular diseases" or "acute coronary syndrome" or "acute coronary syndromes" or "unstable angina" or "myocardial infarction" or stroke or strokes or "heart failure" or "coronary heart disease" or "renal function" or "renal functions" or "kidney disease" or "end stage kidney disease" or "creatinine clearance" or "serum creatinine" or albuminuria or proteinuria or "glomerular filtration" or "albumin-to-creatinine ratio" or "albumin to creatinine ratio" or "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" or "acute kidney injury" or "acute kidney injuries")

AND

TS= ("prospective study" OR "prospective studies" OR "case-control" OR "case control" OR cohort* OR "metabolic study" OR "metabolic studies" OR "natural experiment" OR "natural experiments" OR "clinical trial" OR "clinical trials")

AND

DOCUMENT TYPES: (Article OR Book OR Book Chapter OR Discussion)

EndNote search Title = rats = 147 Title: Mice = 19 (18) Title = mouse = 7 Title = dogs = 22
Title = pigs = 9 Title = pig = 20 (16) Title = monkey = 1

DATABASE SEARCHED & TIME PERIOD COVERED:

Cochrane CENTRAL – 1/1/2011-10/26/2016

LANGUAGE:

English

SEARCH STRATEGY:

KQ1:

- #1 MeSH descriptor: [Sodium Chloride] explode all trees
- #2 MeSH descriptor: [Sodium Glutamate] explode all trees
- #3 MeSH descriptor: [Diet, Sodium-Restricted] explode all trees
- #4 MeSH descriptor: [Sodium, Dietary] explode all trees
- #5 ("monosodium glutamate" or salt or sodium) and (diet* or food or intake or "urinary excretion"):ti,ab,kw (Word variations have been searched)
- #6 MeSH descriptor: [Diet] explode all trees
- #7 (#1 or #2) and #6
- #8 #7 or #5 or #3 or #4
- #9 MeSH descriptor: [Blood Pressure] explode all trees
- #10 MeSH descriptor: [Hypertension] explode all trees
- #11 9 or #10
- #12 "blood pressure" or hypertens*:ti,ab,kw (Word variations have been searched)
- #13 #11 or #12
- #14 #8 and #13

KQ3:

- #1 mortality or "cardiovascular disease" or "cardiovascular diseases" or "acute coronary syndrome" or "acute coronary syndromes" or "unstable angina" or "myocardial infarction" or stroke or strokes or "heart failure" or "coronary heart disease" or "renal function" or "renal functions" or "kidney disease" or "end stage kidney disease" or "creatinine clearance" or "serum creatinine" or albuminuria or proteinuria or "glomerular filtration" or "albumin-to-creatinine ratio" or "albumin to creatinine ratio" or "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi" or "acute kidney injury" or "acute kidney injuries":ti,ab,kw (Word variations have been searched)
- #2 MeSH descriptor: [Mortality] explode all trees
- #3 MeSH descriptor: [Cardiovascular Diseases] explode all trees
- #4 MeSH descriptor: [Kidney Diseases] explode all trees
- #5 #1 or #2 or #3 or #4
- #6 MeSH descriptor: [Sodium Chloride] explode all trees
- #7 MeSH descriptor: [Sodium Glutamate] explode all trees
- #8 MeSH descriptor: [Diet, Sodium-Restricted] explode all trees
- #9 MeSH descriptor: [Sodium, Dietary] explode all trees
- #10 MeSH descriptor: [Diet] explode all trees

#11 #8 or #9

#12 ("monosodium glutamate" or salt or sodium) and (diet* or food or intake or "urinary excretion"):ti,ab,kw (Word variations have been searched)

#13 #11 or #12

#14 (#6 or #7) and #10

#15 #13 or #14

#16 #5 and #15

KQ5:

#17 MeSH descriptor: [Potassium, Dietary] explode all trees

#18 potassium or klor-con or kcl:ti,ab,kw (Word variations have been searched)

#19 #17 or #18

#20 MeSH descriptor: [Blood Pressure] explode all trees

#21 MeSH descriptor: [Hypertension] explode all trees

#22 "kidney calculi" or "kidney stone" or "kidney stones" or renal lithiasis or nephrolith* or nephrolithiasis or "renal stone" or "renal stones" or "renal calculi":ti,ab,kw (Word variations have been searched)

#23 "blood pressure" or hypertens*:ti,ab,kw (Word variations have been searched)

#24 #20 or #21 or #22 or #23

#25 #19 and #24

KQ7 (NOTE – SEARCH SETS REFER TO KQ3 AND KQ5 SEARCHES)

#26 #19 and #5

Appendix B. List of Excluded Studies

This appendix lists all studies (publications) that were identified in our literature searches that were subsequently excluded during full-text screening.

Population Not of Interest – N = 44

1. Ahmed A, Zannad F, Love TE, et al. A propensity-matched study of the association of low serum potassium levels and mortality in chronic heart failure. *European Heart Journal*. 2007;28(11):1334-43. doi: 10.1093/eurheartj/ehm091.
2. Ahmed MI, Ekundayo OJ, Mujib M, et al. Mild hyperkalemia and outcomes in chronic heart failure: a propensity matched study. *Int J Cardiol*. 2010 Oct 29;144(3):383-8. doi: 10.1016/j.ijcard.2009.04.041. PMID: 19500863.
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5. Andersen AB, Thurnham D, Tomkins A, et al. Effects on mortality of a nutritional intervention for malnourished HIV-infected adults referred for antiretroviral therapy: A randomised controlled trial. *BMC Medicine*. 2015;13(1) PMID: 2015820434 FULL TEXT LINK <http://dx.doi.org/10.1186/s12916-014-0253-8>.
6. Arcand J, Ivanov J, Sasson A, et al. A high-sodium diet is associated with acute decompensated heart failure in ambulatory heart failure patients: a prospective follow-up study. *Am J Clin Nutr*. 2011 Feb;93(2):332-7. doi: 10.3945/ajcn.110.000174. PMID: 21084647.
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12. Ellison DH, Terker AS. Why Your Mother Was Right: How Potassium Intake Reduces Blood Pressure. *Trans Am Clin Climatol Assoc*. 2015;126:46-55. PMID: 26330658.
13. Filteau S, PrayGod G, Kasonka L, et al. Effects on mortality of a nutritional intervention for malnourished HIV-infected adults referred for antiretroviral therapy: a randomised controlled trial. *BMC medicine*. 2015 2015;13:17.
14. Filteau S, PrayGod G, Kasonka L, et al. Effects on mortality of a nutritional intervention for malnourished HIV-infected adults referred for antiretroviral therapy: A randomised controlled trial. *BMC Medicine*. 2015;13(1) PMID: 2015291667 FULL TEXT LINK <http://dx.doi.org/10.1186/s12916-014-0253-8>.
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Intervention Not of Interest – N = 443

1. Adamsson V, Reumark A, Fredriksson IB, et al. Effects of a healthy Nordic diet on cardiovascular risk factors in hypercholesterolaemic subjects: a randomized controlled trial (NORDIET). *J Intern Med*. 2011 Feb;269(2):150-9. doi: 10.1111/j.1365-2796.2010.02290.x. PMID: 20964740.
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Language – N = 4

1. de Almeida Barros CL, Sousa ALL, Chinem BM, et al. Impact of light salt substitution for regular salt on blood pressure of hypertensive patients ORIGINAL (NON-ENGLISH) TITLE Impacto da substituição de sal comum por sal light sobre a pressão arterial de pacientes hipertensos. *Arquivos Brasileiros de Cardiologia*. 2014 2014;104(2):128-35. PMID: 2015893089 MEDLINE PMID 25409877 (<http://www.ncbi.nlm.nih.gov/pubmed/25409877>) FULL TEXT LINK <http://dx.doi.org/10.5935/abc.20140174>.
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Protocol of Interest – N = 7

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Appendix C. Evidence Tables for All Included Studies

Table C1. Evidence table for all trials

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Alli, 1992¹</p> <p>Location: Italy</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 77</p> <p>Intervention 1: % Male: 34.6 Mean Age/Range/Age at Baseline: mean 44.3 (SD 10.2) Race: NR Systolic BP: 150.8 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: mean 51.7 (SD 11) Race: NR Systolic BP: 148.3 Diastolic BP: 97.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.8 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild hypertension not previously known, not taking antihypertensive treatment or medications which interfered with BP; and they were not overweight (BMI < 30). Exclusion: Evidence of cardiovascular complications or secondary hypertension (as per pathological history, physical examination, and lab tests).</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Dietary instructions with the goal of lowering sodium intake Form of Administration: Dietary Modification: low-sodium diet Dose: NR Na/K ratio: 2.7 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: 2.8 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: At 1, 3, 6, 9 and 12 months. Sodium, Method of Validation: Completeness or urine collection was assessed on the basis of 24h creatinine excretion., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 177 mEq Best potassium measure recorded: At 1, 3, 6, 9 and 12 months. Potassium, Method of Validation: Completeness or urine collection was assessed on the basis of 24h creatinine excretion. Potassium Status Intervention 1: 67.2 mEq</p> <p>How was blood pressure measured? BP taken in the supine position after 5 minutes at rest. SBP and DBP recorded at Korotkoff phases I and V. Three BP measurements were recorded at 1-minute intervals and the lowest value was used.</p>	<p>Subgroup: Mild HTN Diastolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 4.00 (95% CI: 1.02 - 6.98) Systolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 3.80 (95% CI: -2.70 - 10.30)</p>
<p>Ambrosioni, 1982²</p> <p>Location: Italy</p> <p>Setting:</p>	<p>Study of: Both adults and children N: 25</p> <p>Participants: % Male: 55 Mean Age/Range/Age at Baseline: 23+/-6</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Low sodium diet to achieve</p>	<p>Sodium measure: Partial urines without validation Best sodium measure recorded: 6 consecutive overnight urines Sodium, Method of Validation: NR Sodium Status Intervention 1: NR</p>	<p>Diastolic BP Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -6.63 - 3.03) Systolic BP</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: NR days</p> <p>Study Years: NR</p>	<p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: young people with elevated BP</p> <p>Exclusion: NR</p>	<p>intake of 3-5g sodium chloride/d</p> <p>Form of Administration: Dietary</p> <p>Modification: Not described</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: 6-10g sodium chloride/d</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p>	<p>Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? automatic device, Dinamap 845; casual readings were recorded after 1 minute and baseline recordings were obtained after 10 minutes. Measurements were performed at 1-minute intervals, seated</p>	<p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -5.00 (95% CI: -10.66 - 0.66)</p>
<p>Applegate, 1992³</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults</p> <p>N: 47</p> <p>Intervention 1:</p> <p>% Male: 43</p> <p>Mean Age/Range/Age at Baseline: mean 65 (SD 3.8)</p> <p>Race: white: 57%</p> <p>Systolic BP: 143</p> <p>Diastolic BP: 86</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 89 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 46</p> <p>Mean Age/Range/Age at Baseline: mean 64 (SD 4.5)</p> <p>Race: white: 65%</p> <p>Systolic BP: 145</p> <p>Diastolic BP: 88</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 81 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Intervention focused on calorie and sodium reduction with increases in moderate levels of physical activity</p> <p>Form of Administration: Dietary</p> <p>Modification: Individual and group sessions</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: Participants asked not to change their usual diet</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 6 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, diet recall</p> <p>Best sodium measure recorded: 0, 2, 3, and 6 months.</p> <p>Sodium Status Intervention 1: 142.5 mmol/d</p> <p>How was blood pressure measured? After a 5-minute rest at each clinic visit, BP was measured in triplicate in the seated position by trained staff using random zero sphygmomanometers.</p>	<p>Subgroup: Mild HTN, modestly overweight</p> <p>Diastolic BP-sitting</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -4.90 (95% CI: NC - NC)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -4.20 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-85, mild diastolic hypertension, modestly overweight (115% of ideal body weight), a Folstein Mini-Mental State score > 22 out of 30, adequate physical health, adequate vision, willingness to participate.</p> <p>Exclusion: MI within the past year, prior diagnosis of angina pectoris or congestive heart failure, stroke within the last year, other serious CVD, or diabetes . Other serious chronic illnesses; a random serum glucose concentration \geq 12.2 mmol/L, a serum creatinine level of > 150 μmol/L, and a serum cholesterol level of more than 6.85 mmol/L; serious physical handicaps; disorders that might affect the implementation of dietary interventions; or use of medications that could impact BP.</p>			
<p>Arroll, 1995⁴</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 87</p> <p>Participants: % Male: 52 Mean Age/Range/Age at Baseline: mean 55 Race: NR Systolic BP: 144.6 Diastolic BP: 89.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Essential hypertension with a SBP > 115 mm Hg or a DBP > 70 mm Hg (on medication); ages 20 - 69 years inclusive; a sedentary lifestyle and under the care of a primary care physician Exclusion: Symptomatic coronary heart disease, immobility that restricted walking; current DBP >105 mm Hg or a SBP greater > 180 mm Hg; regularly performing regular moderate physical activity.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: Education and instruction on reducing salt in diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Exercise + salt restriction Description: NR Form of Administration: Other: Education and instruction on reducing salt in diet + physical activity Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times 3 months apart Sodium Status Intervention 1: median 107 mmol/24h Sodium Status Intervention 2: median 105.5 mmol/24h</p> <p>How was blood pressure measured? BP measured using a Hawksley random zero sphygmomanometers. Three consecutive measurements taken and an average of the last two readings was used.</p>	<p>Subgroup: Treated hypertensive Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.50 (95% CI: -8.24 - -0.76) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -9.04 - 3.44)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		<p>Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		
<p>Australian National Health and Medical Research Council Dietary Salt Study Management Committee, 1989⁹</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 108</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 149.1 Diastolic BP: 91.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 93 Mean Age/Range/Age at Baseline: 58.4 Race: NR Systolic BP: 152.8 Diastolic BP: 95.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: DBP at four run-in visits between 90 and 100 mm Hg, with no single measure above 110 mm Hg or below 85 mm Hg, and gave written informed consent. Exclusion: Being treated for hypertension, a secondary cause of hypertension, hypertension complications, evidence of other cardiovascular disease</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Low sodium Description: NR Form of Administration: Other: placebo Dose: Diet containing less than 80 mmol sodium/day + 8 placebo pills daily Na/K ratio: 1.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Normal Sodium Description: 153 mmol/day Form of Administration: Sodium supplement Dose: Diet containing less than 80 mmol sodium/day + 8 slow-release sodium chloride [10 mmol] pills daily) Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times, every 2 weeks Sodium Status Intervention 1: 90 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 times, every 2 weeks Potassium Status Intervention 1: 71 mmol/day</p> <p>How was blood pressure measured? Seated BP measurements were made after 5 min rest using a sphygmomanometry with oscillometric detection. A large cuff was applied to the left arm and four measurements were taken with intervals of 1 min. The first value was discarded and the mean of the other three measures were used.</p>	<p>Subgroup: Mild HTN Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -4.46 - -1.14) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -5.50 (95% CI: -8.41 - -2.59)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Barcelo, 1993⁶</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 57</p> <p>Participants: % Male: 43.8 Mean Age/Range/Age at Baseline: mean 44 (SD 11) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 0 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Documented active calcium nephrolithiasis concomitant with an isolated hypocitraturic abnormality</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Potassium tablets + advised to increased ingestion of fluids (2 to 3 l. a day) and reduced sodium intake Form of Administration: Oral potassium supplement Dose: 20 mEq. (4 tablets) potassium citrate 3 times a day right after meals. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Placebo + advised to increased ingestion of fluids (2 to 3 l. a day) and reduced sodium intake Form of Administration: Placebo Dose: placebo tablets as potassium citrate groups and at the same dosage and schedule. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Taken at baseline, at 3 months, 6 months, then every 6 months for the remainder of the 3 years Sodium, Method of Validation: Single 24-hour urine analysis with validation Best potassium measure recorded: Taken at baseline, at 3 months, 6 months, then every 6 months for the remainder of the 3 years Potassium Status Intervention 1: 3.36 mmol/day</p>	<p>Subgroup: Nethrolithiasis+hypocitraturia Decrease quality of life Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator RR 0.48 (95% CI: 0.05 - 5.03) Stone formation rate (number per patient year) Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -1.16 - -0.84)</p>
<p>Barros, 2015⁷</p> <p>Location: South America (Argentina, Brazil, Chile, and Colombia)</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p>	<p>Study of: Adults N: 38</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 142.95 Diastolic BP: 86.79 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.38 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: Description: Instructed to consume only the</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Light salt Description: Instructed to consume only the provided salt throughout this study. Instructed to reduce sodium-rich food consumption throughout the study period. Form of Administration: Salt substitute Dose: 28 small plastic bags containing the daily amount of salt. Light salt composition (per gram) was as follows: 130 mg of sodium, 346 mg of potassium and 44 mcg of iodine Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Instructed to consume only the</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times 1 month apart Sodium Status Intervention 1: 127.11 mEq/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 1 month apart Potassium Status Intervention 1: 48.05 mEq/day</p> <p>How was blood pressure measured? Casual BP taken by the same researcher, at least three times and at 1-minute intervals, until the differences between the measurements were lower than 4</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -6.80 (95% CI: -14.11 - 0.51) Systolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -10.08 (95% CI: -22.23 - 2.07) Decreased quality of life Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Study Years: 2012</p>	<p>% Male: 34.3 Mean Age/Range/Age at Baseline: mean 55.5 SD (7.4) Race: NR Systolic BP: 143.44 Diastolic BP: 91.19 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 31 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Hypertensive individuals between ages 20 and 65 years. Patients lived in the metropolitan region of Goiânia, Brazil, on stable doses of antihypertensive drugs for at least 30 days, with uncontrolled hypertension (BP \geq 140 x 90 mmHg) in their last visit. Exclusion: Acute or subacute (up to 3 months before the beginning) and unstable chronic diseases. Those having their meals prepared with a salt different from that provided in the study more than once a week.</p>	<p>provided salt throughout this study. Instructed to reduce sodium-rich food consumption throughout the study period. Form of Administration: Usual diet Dose: 28 small plastic bags containing the daily amount of salt. Regular salt contained (per gram) 390 mg of sodium and 25 mcg of iodine. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>mmHg. The mean of the mean of the last two values was considered, obtained by using a semi-automatic digital device.</p>	
<p>Beard, 1982⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 113</p> <p>Intervention 1: % Male: 60 Mean Age/Range/Age at Baseline: Mean 48.4 Race: white: 100% Systolic BP: 142.3 Diastolic BP: 131.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 79.98 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 53 Mean Age/Range/Age at Baseline: mean 49.6 Race: white: 100% Systolic BP: 138.9 Diastolic BP: 86.2 Magnesium: NR Calcium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: No-added-sodium diet Form of Administration: Dietary Modification: No-added-sodium diet. Shopping guides, small group discussions, recipe exchanges, nutritional counseling Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual salt intake Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, Patients answered a final questionnaire on lifestyle and health; the diet group reported compliance and future intentions. Best sodium measure recorded: 5 times, at baseline, 2, 4, 6, and 11 weeks. Sodium Status Intervention 1: 37.0 mmol/24h Potassium measure: Single 24-hour urine analysis without validation, Patients answered a final questionnaire on lifestyle and health; the diet group reported compliance and future intentions. Best potassium measure recorded: 5 times, at baseline, 2, 4, 6, and 11 weeks. Potassium Status Intervention 1: 79.9 mmol/24h</p> <p>How was blood pressure measured? Casual sitting BP (average of two readings) was measured to the</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.30 (95% CI: -5.04 - 2.44) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -8.63 - 5.03) Average drug consumption (number of pills per day) relative to baseline Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: NC - NC) Failed to stop or reduce medication Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator RR 3.75 (95% CI: 1.94 - 7.27)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Other Minerals: NR Mean BMI: 77.81 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Individuals aged 25-69 years, receiving antihypertensive medication and who had a premedication DBP between 95 and 109 mm Hg and SBP under 200 mm Hg Exclusion: Women who were pregnant or taking an oral contraceptive. Men and women with severe intercurrent illness, serum creatinine >0.20 mmol/l, or history of antihypertensive medication for less than 3 months</p>	<p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>closest 2 mm Hg with the Hawksley random-zero machine, using a 13 cm x 35 cm bag and the 5th-phase DBP. These readings were taken by one of two nurses whose results had shown good agreement and internal consistency in practice sessions.</p>	
<p>Becerra-Tomas, 2015⁹</p> <p>Location: Spain</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: 2013-2014</p>	<p>Study of: Adults N: 24</p> <p>Participants: % Male: 43</p> <p>Mean Age/Range/Age at Baseline: 48</p> <p>Race: NR</p> <p>Systolic BP: 136</p> <p>Diastolic BP: 85</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 27.31</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 18 to 65 ; BMI; SBP ranging 20-159 mm Hg, or DBP between 80 -99 mm Hg; and daily consumption of bread. Exclusion: Severe hypertension; antihypertensive medication, diabetes or another endocrine disease, significant renal or hepatic disease; alcohol, drug, or tobacco abuse; pregnancy or plans to be pregnant, weight loss >5 kg in the previous 3 months; a vegetarian diet or other dietary restrictions related to disease control; previous atherosclerotic disease or target organ damage; use of dietary supplements, mineral or vitamin complexes, or sterols. The presence of any medical conditions that may affect participation in the study.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: (LSB) low-sodium wheat bread enriched in potassium Description: NR Form of Administration: Dietary Modification: NR Dose: Bread with 0.4 g of potassium citrate Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: (LSB+_G) low-sodium wheat bread rich in potassium, GABA, and ACEI peptides Description: NR Form of Administration: Dietary Modification: NR Dose: Bread with low-sodium chloride (1 g/100 g) wheat bread enriched with 0.4 g of potassium citrate and containing 22.8 mg/100 g of GABA Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: (CB) conventional wheat bread Description: NR Form of Administration: Dietary Modification: NR Dose: Bread with 1.4 g/100 g of sodium</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: baseline, before and after each intervention period Sodium, Method of Validation: Intervention compliance determined by recording the bread consumed by each participant, 3 day diet records, Single 24-hour urine analysis with validation Sodium Status Intervention 1: NR Sodium Status Intervention 2: NR Best potassium measure recorded: baseline, before and after each intervention period Potassium, Method of Validation: Intervention compliance determined by recording the bread consumed by each participant, 3 day diet records Potassium Status Intervention 1: NR Potassium Status Intervention 2: NR</p> <p>How was blood pressure measured? Measurements were taken between 8:00 a.m. and 10:00 a.m. SBP and DBP were measured in both arms while patients were using a validated oscillometer. Measurements were taken in triplicate with between 1-minute intervals. The first measurement was thrown out and the average of</p>	<p>Subgroup: Hypertensives Diastolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -1.49 (95% CI: -3.86 - 0.88)</p> <p>Comparison: Intervention 1 vs Intervention 2 MD -1.04 (95% CI: -3.21 - 1.13)</p> <p>Comparison: Intervention 2 vs Comparator MD -0.45 (95% CI: -2.71 - 1.81)</p> <p>Systolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -1.01 (95% CI: -4.39 - 2.37)</p> <p>Comparison: Intervention 1 vs Intervention 2 MD -0.58 (95% CI: -3.76 - 2.60)</p> <p>Comparison: Intervention 2 vs Comparator MD -0.43 (95% CI: -3.96 - 3.10)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		chloride Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 1 month Exposure to Follow Up Time: NR	the other 2 was recorded. The arm with the highest value was used in the study.	
Beckmann, 1995 ¹⁰ Location: Norway Setting: Community Design: Randomized, parallel Number of Sites: Study Years: unclear	Study of: Adults N: 64 Participants: % Male: 100 Mean Age/Range/Age at Baseline: Range: 40-56 Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.7 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Otherwise healthy middle aged men with never-treated hypertension	Intervention Type(s): Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: The goal was a daily intake of sodium chloride of approximately 100 mmol. Form of Administration: Dietary Modification: Subjects instructed on a diet to reduce sodium. For the first 2 weeks they were provided with free food to help with diet compliance Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: BP Control group Description: No dietary advice was given Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 6 months Exposure to Follow Up Time: 12 months	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Taken once for control groups at baseline. Taken at baseline and 12 months for intervention group Sodium Status Intervention 1: 123 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Taken at baseline, weeks 1,2,3 months, 6 months, 12 months Potassium Status Intervention 1: 90 mmol/24 h How was blood pressure measured? BP measurements were taken on the right arm using an oscillometric device. In the study sample, this semiautomatic BP monitor measured SBP and DBP on average 3.5 and 2.0 mm Hg lower than a mercury sphygmomanometer, but without examiner bias. BP recordings were made after 9 and 10 min in the supine position, and also after 9 and 10 min of standing. The mean of the two blood pressure recordings at 9 and 10 min was used for analysis.	Subgroup: HTN MBP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -11.16 - -4.84)
Berry, 2010 ¹¹ Location: UK Setting: Community Design: Randomized Cross-over	Study of: Adults N: 48 Participants: % Male: 52.1 Mean Age/Range/Age at Baseline: Men: mean 45.5 (SD 10.6); Women: mean 44.8 (SD 8.2) Race: Men: White 70%; Women: White 52% Systolic BP: Men: 139.4; Women: 136 Diastolic BP: Men: 88; Women 89.2	Intervention Type(s): Intervention 1: Other: Increased Fruits and Vegetables Description: An extra 20 or 40 mmol Kp/d from fruit and vegetables Form of Administration: Dietary Modification: Extra fruit and vegetable Dose: NR Na/K ratio: 1.9	Sodium Status Intervention 1: 116 mmol/d Sodium Status Intervention 2: 113 mmol/d Potassium measure: Single 24-hour urine analysis without validation, Food diaries without reported validation Best potassium measure recorded: 2	Subgroup: Hypertensives DBP clinical Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD 1.00 (95% CI: -1.20 - 3.20) Comparison: Intervention 1 vs Comparator MD 0.30 (95% CI: -1.90 - 2.50) Comparison: Intervention 2 vs

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
individual Number of Sites: multiple Crossover: Length of washout period: >=35 days Study Years: 2004-2005	Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Men: 27.7; Women: 29.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Seated DBP . 80 and , 100 mmHg on two occasions Exclusion: Clinical history of MI, diabetes mellitus, renal disease, diabetes mellitus, gastrointestinal disease, pancreatitis, cholestatic liver disease or cancer; current use of systemic corticosteroids, androgens, phenytoin, erythromycin, thyroid hormones, lipid lowering, BP-lowering or anticoagulant medication; cigarette smoking; history of substance abuse or alcoholism or alcohol intake exceeding a moderate intake. Pregnancy or having had a baby in the last year; allergy or intolerance to intervention foods; unwillingness to refrain from the use of dietary supplements; weight loss. 3 kg in the last 2 months; BMI< 20 and > 35 kg/m2; and BP and other risk factors that make them eligible for drug treatment of raised BP according to the British Hypertension Society guidelines	Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 40 mmol potassium citrate capsules/d Na/K ratio: 1.5 Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Placebo Description: Participants asked not to change their usual diet Form of Administration: Placebo Dose: NR Na/K ratio: 2.3 Magnesium: NR Calcium: NR Other Minerals: NR Duration: 1.5 months Exposure to Follow Up Time: NR	times, in week 3 of the run-in period and week 5-6 of the treatment period. Potassium Status Intervention 1: 75 mmol/d Potassium Status Intervention 2: 87 mmol/d How was blood pressure measured? Measured over 24 h using an A&D TM-2430 device. BP was measured at 30 min intervals during the day and hourly during the night, and the patients maintained a record of the activities of the recording period.	Comparator MD -0.30 (95% CI: -2.20 - 1.60) SBP clinical Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD 1.90 (95% CI: -1.60 - 5.40) Comparison: Intervention 1 vs Comparator MD 0.70 (95% CI: -2.80 - 4.20) Comparison: Intervention 2 vs Comparator MD -1.50 (95% CI: -4.30 - 1.30)
Braschi, 2008 ¹² Location: UK Setting: Community Design: Randomized, parallel Number of Sites: 1 Study Years: unclear	Study of: Adults N: 114 Intervention 1: % Male: 19.2% Mean Age/Range/Age at Baseline: mean 36.9 (SEM 2.8) Race: Caucasian 76.9%; Middle-Eastern 7.7%; East Asian 7.7%; Afro-Caribbean 7.7% Systolic BP: 114.67 Diastolic BP: 70.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Intervention 2: % Male: 43.3	Intervention Type(s): Intervention 1: Other: KCL supplement Description: NR Form of Administration: Oral potassium supplement Dose: two capsules, 3 times per day with 5 mmol potassium Na/K ratio: 1.55 Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Other: K-cit supplement Description: NR Form of Administration: Oral potassium supplement Dose: two capsules, 3 times per day with 5 mmol potassium Na/K ratio: 1.66 Magnesium: NR Calcium: NR Other Minerals: NR	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times 6 weeks apart Sodium Status Intervention 1: 122.92 mmol/d Sodium Status Intervention 2: 153.48 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 6 weeks apart Potassium Status Intervention 1: 89.58 mmol/d Potassium Status Intervention 2: 98.17 mmol/d How was blood pressure measured? BP was measured around the same time of the day by the same observer using the same instruments throughout the study. Participants were asked to maintain the same	Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 2 vs Comparator MD -4.26 (95% CI: -6.31 - -2.21) Comparison: Intervention 1 vs Comparator MD -4.30 (95% CI: -6.39 - -2.20) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 2 vs Comparator MD -6.69 (95% CI: -8.85 - -4.43) Comparison: Intervention 1 vs Comparator MD -5.24 (95% CI: -7.43 - -3.06)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean Age/Range/Age at Baseline: mean 36.2 (SEM 2.6) Race: Caucasian 86.7%; Middle-Eastern 6.7%; East Asian 6.7%; Systolic BP: 111.88 Diastolic BP: 69.49 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.5 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 41.2 Mean Age/Range/Age at Baseline: mean 33.8 (SEM 2.2) Race: Caucasian 67.6%; Middle Eastern 14.7%; East Asian 14.7%; Afro-Caribbean 2.9% Systolic BP: 107.84 Diastolic BP: 66.33 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.55 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 22 - 65 years, BMI between 19 and 35 kg/m², an alcohol consumption of ≤ 21 units/week (women), ≤ 28 units/week (men), SBP ≤ 160 and DBP ≤ 105 mmHg at screening Exclusion: CVD (including cardiac arrhythmia), diabetes, renal diseases, metabolic acidosis and digestive problems. Those taking anti-hypertensive drugs, cyclosporin, heparin, digoxin, anticholinergics and non-steroidal anti-inflammatory drugs. Patients who, during the study period changed either their usual diet or lifestyle and those undergoing changes in psychological condition (stress, depression, tiredness) were excluded and those with poor compliance.</p>	<p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: placebo Na/K ratio: 1.93 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: NR</p>	<p>habits before each appointment. BP was assessed in the seated position in the left arm after a 10 min rest using a clinically validated semi-automated oscillometric sphygmomanometer. Three readings were taken at 2 min intervals and the values for SBP were then averaged, the reading that had the greatest difference from the mean was discarded together with the corresponding DBP and pulse measurement, and the average of the two remaining readings used for analysis.</p>	
<p>Bulpitt, 1985¹³ Location: UK</p>	<p>Study of: Adults N: 33 Intervention 1:</p>	<p>Intervention Type(s): Intervention 1: Use of potassium supplement to increase potassium levels</p>	<p>Sodium Status Intervention 1: 149 Potassium measure: More than one 24-hour urinary analysis without</p>	<p>Subgroup: Hypertensive on K-losing diuretics Diastolic BP-supine Follow-Up Time: 3 months</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>% Male: 43 Mean Age/Range/Age at Baseline: 56.1 Race: NR Systolic BP: Untreated: 199 Diastolic BP: Untreated: 122 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 47 Mean Age/Range/Age at Baseline: mean 54.2 (SE 1.9) Race: NR Systolic BP: Untreated: 190 Diastolic BP: Untreated: 133 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Hypertensive, using a potassium losing diuretic Exclusion: Using a potassium-sparing diuretic, plasma urea had ever been greater than 9.9 mmol/l or plasma potassium > 5 mmol/l.</p>	<p>Description: NR Form of Administration: Oral potassium supplement Dose: 8 Slow K tablets daily (64 mmol of slow release potassium) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet and drug treatment Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NA</p>	<p>reported quality control measure_1, Food diaries without reported validation Best potassium measure recorded: 2 times, 3 months apart Potassium Status Intervention 1: 95</p> <p>How was blood pressure measured? Measured 2 times, 3 months apart. BP was measured standing and lying by attending physicians and by the research team using the London School of Hygiene (LSH) sphygmomanometer (10) and measuring systolic, diastolic (IVth) and diastolic (Vth) after 3 minutes standing and 5 minutes lying.</p>	<p>Comparison: Intervention 1 vs Comparator MD 4.80 (95% CI: -3.11 - 12.71) Reduced quality of life (indigestion) Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 0.74 (95% CI: 0.05 - 10.79) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD 2.30 (95% CI: -15.16 - 19.76) Significant changes in blood cholesterol Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC) Significant changes in blood glucose Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)</p>
<p>Bulpitt, 1984¹⁴</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p>	<p>Study of: Adults N: 65</p> <p>Intervention 1: % Male: 34.4 Mean Age/Range/Age at Baseline: Mean 54.5 Race: NR Systolic BP: 158 Diastolic BP: 103 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 77.1 Kg % with Hypertension: 100 % with history of CVD: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Dietary advice for a 1 g Na (44 mmol) daily diet. A salt substitute, KCL, was also given. Form of Administration: Dietary Modification: Dietary advice, salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Multiple 48 hour urine analysis; Questionnaire on diet Best sodium measure recorded: 2 times, at baseline and at 3 months Sodium Status Intervention 1: 204 mmol/48-h</p> <p>How was blood pressure measured? Measurements were taken both lying and standing by the attending physician and by the research team using the London School of Hygiene (LSH) sphygmomanometer and measuring</p>	<p>Subgroup: HTN on antihypertensives Decreased quality of life Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD 0.07 (95% CI: NC - NC) Diastolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -2.10 (95% CI: -7.82 - 3.62) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: unclear	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 54.5% Mean Age/Range/Age at Baseline: 54.6 Race: NR Systolic BP: 169 Diastolic BP: 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 80.1 kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: All patients were attending the Hammersmith Hospital Hypertension Clinic agents and had been treated on a long term basis with a variety of agents. The inclusion criterion was unsatisfactory BP control defined as a standing DBP > 95 mm Hg on two successive occasions despite drug treatment</p>	<p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	SBP, DBP to the Korotkoff's 4th and 5th phase after five minutes lying and three minutes standing	<p>MD -6.10 (95% CI: -17.47 - 5.27) Percent of people with major decrease in drug therapy Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 3.01 (95% CI: 0.13 - 72.03)</p>
<p>Calabrese, 1985¹⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Massachusetts Blood Pressure Study, Part 3</p> <p>Number of Sites: multiple</p> <p>Study Years: 1979</p>	<p>Study of: Children N: 102</p> <p>Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 99.6 Diastolic BP: 57.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Males: 34 kg; Females: 29.8 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 99.4 Diastolic BP: 57.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Male: 36.3 kg; Female 33.6 kg</p>	<p>Intervention Type: Arm 1: Other: Low sodium water Description: NR Form of Administration: Dietary Modification: Low sodium water Dose: Low sodium water contained 10 mg/L Na Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Arm 2: Other: Low sodium water with added sodium Description: NR Form of Administration: Dietary Modification: Low sodium water with added sodium Dose: Low sodium water + added sodium such that it contained 110 mg/L Na Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: 2 day food records; Partial or spot urine with validated prediction equation Best sodium measure recorded: Collected at 0,1,2,3 months Sodium, Method of Validation: To measure compliance parents completed a questionnaire at two-week intervals, reporting how their child adhered to the bottled water regimen during that period. Sodium Status Arm 1: Males: 127.2 mEq; Females 128.6 mEq Sodium Status Arm 2: Males 127.6 mEq; Females 135.8 mEq Sodium Status Arm 3: Males 123.2 mEq; Females 109.0 mEq Potassium measure: Partial or spot urine without validated prediction equation, 2 day food records Best potassium measure recorded: Collected at 0,1,2,3 months Potassium, Method of Validation: To measure compliance parents completed a questionnaire at two-</p>	<p>Subgroup: Girls Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Arm 1 vs Arm 4 MD -5.45 (95% CI: -10.53 - -0.37) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Arm 1 vs Arm 4 MD -1.50 (95% CI: -5.61 - 2.61)</p> <p>Subgroup: Boys Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Arm 1 vs Arm 4 MD 1.45 (95% CI: -3.05 - 5.95) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Arm 1 vs Arm 4 MD 0.35 (95% CI: -3.30 - 4.00)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 99.3 Diastolic BP: 57.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Male: 34.3 kg; Female: 32.5 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Children in fourth grade, children's' parents consent</p>	<p>Arm 3: Other: High sodium water Description: NR Form of Administration: Dietary Modification: High sodium water Dose: High sodium water contained 110 mg/ L Na Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>week intervals, reporting how their child adhered to the bottled water regimen during that period. Potassium Status Arm 1: Males 36.8 mEq; Females 32.2 mEq Potassium Status Arm 2: Males 42.4 mEq; Females 36 mEq Potassium Status Arm 3: Males 33.6 mEq; Females 34.9 mEq</p> <p>How was blood pressure measured? Patients sitting casually and BP on the left arm was taken at each station by a nurse using a mercury sphygmomanometer. The pressure was raised approximately 30 mm Hg higher than the point at which the pulse disappeared and then released at a rate of 2 to 3 mm Hg/sec. SBP was taken at the point where two consecutive Korotkoff sounds were audible and DBP at the disappearance of sound.</p>	
<p>Cappuccio, 2006¹⁶</p> <p>Location: Ghana</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of</p>	<p>Study of: Adults N: 1013</p> <p>Intervention 1: % Male: 38 Mean Age/Range/Age at Baseline: mean 54 (SD 11) Race: NR Systolic BP: 129 Diastolic BP: 77 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 21</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Health education programme at the village level Form of Administration: Dietary Modification: Village education program to reduce sodium intake Dose: NR Na/K ratio: 2.2 Magnesium: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times, 3 months apart Sodium Status Intervention 1: 91.8 mm/24 h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 3 times, 3 months apart Potassium Status Intervention 1:</p>	<p>Diastolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD 2.70 (95% CI: 0.73 - 4.67) Systolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: -4.22 - 3.22)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Sites: multiple Study Years: 2001-2002	% with Hypertension: 154 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 38 Mean Age/Range/Age at Baseline: mean 55 (SD 11) Race: NR Systolic BP: 127 Diastolic BP: 76 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 21 % with Hypertension: 28 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR	Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: 1.9 Magnesium: NR Calcium: NR Other Minerals: NR Duration: 6 months Exposure to Follow Up Time: NR	48.2 mm/24 h How was blood pressure measured? BP was measured by a fieldworker	
Chang, 2006 ¹⁷ ; Tsai, 1996 ¹⁸ Location: Taiwan Setting: Veteran retirement home Design: Cluster RCT Parallel Number of Sites: multiple Study Years: 1995-1999	Study of: Adults N: 1981 Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: Kitchen 2: mean 75.6 (SD 7.7); mean 74.8 (SD 7.0) Race: NR Systolic BP: 131.3 Diastolic BP: 71.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 100 Mean Age/Range/Age at Baseline: Kitchen 1: mean 74.8 (SD 7.3); Kitchen 4: 74.7 (SD 6.7); Kitchen 5: 74.6 (SD 6.1) Race: NR Systolic BP: 130.7 Diastolic BP: 71.4 Magnesium: NR Calcium: NR	Intervention Type(s): Intervention 1: Other: Kitchen used potassium salt Description: NR Form of Administration: Salt substitute Dose: potassium-enriched salt was composed of 49% sodium chloride, 49% potassium chloride, and 2% other additives, Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: Kitchen used regular salt Description: NR Form of Administration: Regular Salt Dose: regular salt was composed of 99.6% sodium chloride and 0.4% other additives Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 31 month Exposure to Follow Up Time: NR	Sodium Status Intervention 1: 1.22 sodium-creatinine ratio Potassium measure: Food Diaries discuss, Potassium Status Intervention 1: 0.48 potassium-creatinine Mortality Outcomes-Method of Ascertainment: Death certificate CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Death certificate reports	CHD mortality Follow-Up Time: 31 months Comparison: Intervention 1 vs Comparator RR 1.41 (95% CI: 0.64 - 3.07) CVD mortality (hypertension, ischemic heart disease, cerebrovascular disease, heart failure, diabetes) Follow-Up Time: 31 months Comparison: Intervention 1 vs Comparator RR 1.55 (95% CI: 1.00 - 2.40) Total number of deaths Follow-Up Time: 31 months Comparison: Intervention 1 vs Comparator RR 1.03 (95% CI: 0.88 - 1.20)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Other Minerals: NR Mean BMI: 23 % with Hypertension: 40.4 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Exclusion: High serum creatinine concentrations, sharing kitchens</p>			
<p>Charlton, 2008¹⁹</p> <p>Location: South Africa</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: 2004-2005</p>	<p>Study of: Adults N: 92</p> <p>Intervention 1: % Male: 17.5% Mean Age/Range/Age at Baseline: mean 61.8 (SD 6.6) Race: Black: 100% Systolic BP: 133.9 Diastolic BP: 79.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 32.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 15% Mean Age/Range/Age at Baseline: mean 60.4 (SD 7.4) Race: Black: 100% Systolic BP: 135.4 Diastolic BP: 82.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 35.3 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–75 years, with medication-treated mild-to-moderate hypertension Exclusion: On two or more diuretics; on furosemide for cardiac failure; cerebral infarction or haemorrhage; renal impairment, consuming three or more alcoholic drinks a day; type 1 diabetes mellitus; impaired</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Intervention foods were designed to provide 41% less sodium, 826 % more potassium, 388 % more calcium and 368 % more Magnesium Form of Administration: Dietary Modification: Patients provided food with lower salt, higher potassium content Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Patients were given food without the sodium composition unchanged Form of Administration: Other: Given food with regular sodium content Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 4 weeks apart Sodium, Method of Validation: Completeness of 24 h urine collection was assessed as with sex specific urinary creatinine values., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 154.3 mmol/24h Best potassium measure recorded: 3 times, 4 weeks apart Potassium, Method of Validation: Completeness of 24 h urine collection was assessed as with sex specific urinary creatinine values. Potassium Status Intervention 1: 71.7 mmol/24h</p> <p>How was blood pressure measured? Resting office BP measured following American Heart Association Recommendations using a validated automated method with pre-set inflation (Omron M4-I BP monitor). BP was measured three times on each occasion and the mean of the second and third measurements was used for analyses.</p>	<p>Subgroup: Mild to moderate hypertension 24h Ambulatory DBP Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -2.49 (95% CI: -5.16 - 0.17) 24h Ambulatory SBP Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -4.53 (95% CI: -9.05 - -0.01) Stroke Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.34 (95% CI: 0.01 - 8.14)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	cognitive function; incontinence; and BMI >45kg/m2, severely uncontrolled hypertension.			
<p>China Salt Substitute Study Collaborative, 2007²⁰; Hu, 2009²¹</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 39</p> <p>Study Years: 2004-2005</p>	<p>Study of: Adults N: 608</p> <p>Intervention 1: % Male: 48 Mean Age/Range/Age at Baseline: mean 59 (SD 10) Race: NR Systolic BP: 159 Diastolic BP: 93 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 42 Mean Age/Range/Age at Baseline: mean 61 (SD 9.7) Race: NR Systolic BP: 159 Diastolic BP: 93 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: High risk of future vascular disease based on a physicians diagnosis of any of : coronary, cerebral or peripheral vascular disease, diabetes and aged 55 years or older or a SBP > 160 mmHg. Estimated daily sodium intake > 260 mmol/day.</p> <p>Exclusion: Established clear indication for, or contra-indication to, using the study salt substitute (e.g. potassium-sparing medication or significant renal impairment). Since members might be cooking for families, potential contra-indicators of family members were considered for exclusion. Blood test result considered by the responsible doctor to be possibly abnormal.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake</p> <p>Description: NR</p> <p>Form of Administration: Salt substitute</p> <p>Dose: Salt substitute was 65% sodium chloride, 25% potassium chloride and 10% magnesium sulphate</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Other: Regular salt</p> <p>Description: NR</p> <p>Form of Administration: Regular Salt</p> <p>Dose: normal salt, 100% sodium chloride</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 12 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: Measured at registration, randomization, and 6 and 12-month visits. Concentrations were measured using either the ion selective electrode method or atomic absorption spectrophotometry.</p> <p>Sodium Status Intervention 1: Difference of 8.0 mmol between the salt substitute and regular salt group (p>0.05)</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: Measured at registration, randomization, and 6 and 12-month visits. Concentrations were measured using either the ion selective electrode method or atomic absorption spectrophotometry.</p> <p>Potassium Status Intervention 1: Difference of 7.2 mmol between the salt substitute and regular salt group (p<0.05)</p> <p>How was blood pressure measured? BP was measured using an Omron HEM-770A automatic sphygmomanometer. It was recorded in the right arm with participants seated at rest for at least 5 min beforehand. The average of two measurements made at least two minutes apart was used.</p>	<p>CVD events (non-specified)</p> <p>Follow-Up Time: 12 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>RR 0.63 (95% CI: 0.21 - 1.91)</p> <p>Deaths</p> <p>Follow-Up Time: 12 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>RR 1.01 (95% CI: 0.26 - 4.01)</p> <p>Diastolic BP-sitting</p> <p>Follow-Up Time: 12 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -1.00 (95% CI: -2.80 - -0.80)</p> <p>Hyperkalemia</p> <p>Follow-Up Time: 12 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>RR NC (95% CI: NC - NC)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 12 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -5.40 (95% CI: -8.50 - -2.30)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Cobiac, 1992²²</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 114</p> <p>Intervention 1: % Male: 69.2 Mean Age/Range/Age at Baseline: 67 (SEM +- 1) Race: NR Systolic BP: 132 Diastolic BP: 77 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 64 Mean Age/Range/Age at Baseline: 67 (SEM +- 1) Race: NR Systolic BP: 135 Diastolic BP: 78 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 64 Mean Age/Range/Age at Baseline: 66 (SEM +-1) Race: NR Systolic BP: 133 Diastolic BP: 78 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Low-Sodium Intake - Sunflower Oil Description: 'Low' sodium intake. Subjects are on a low sodium diet. This group is given placebo to keep them at low sodium intake Form of Administration: Placebo Dose: 8 Placebo tablets per day consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Normal-Sodium Intake - Sunflower Oil Description: 'Normal' sodium intake. Subjects are on a low sodium diet. This group is given supplements to raise their sodium to normal levels. Form of Administration: Sodium supplement Dose: 4800 mg/d sodium consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low Sodium Intake - Fish Oil Description: 'Low' sodium intake. Subjects are on a low sodium diet. This group is given placebo to keep them at low sodium intake Form of Administration: Other: placebo Dose: placebo consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal Sodium Intake - Fish Oil Description: 'Normal' sodium intake. Subjects are on a low sodium diet. This group is given supplements to raise their sodium to normal levels. Form of Administration: Sodium supplement Dose: 4800 mg/d sodium consumed Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times 2 weeks apart Sodium, Method of Validation: Regular feedback of the results of urinary sodium analysis, counting unused tablets and capsules. Sodium Status Intervention 1: 79 mmol/day Sodium Status Comparator 1: 152 mmol/day Sodium Status Intervention 2: 70 mmol/day Sodium Status Comparator 2: 145 mmol/day</p> <p>How was blood pressure measured? Every 2 weeks, same time of date with an automated sphygmomanometer (Dinamap model 845XT) after individuals had been sitting quietly for 5 min or more. It was requested that subjects had an empty bladder and to avoid eating and exercise for 2 H prior. SBP, DBP determined through 5 readings at 1 min intervals (first was discarded).</p>	<p>Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator 1 MD 0.80 (95% CI: -1.16 - 2.76)</p> <p>Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator 1 MD -1.70 (95% CI: -5.87 - 2.47)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Comparator 2: NR % Male: 66.7 Mean Age/Range/Age at Baseline: 67 (SEM 1) Race: NR Systolic BP: 130 Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Exclusion: Taking blood pressure medication, history of renal or liver disease, unstable heart, hypercholesterolaemia, DBP>105, BMI>30, smoked 20 or more cigarettes per day, drank 40g of alcohol per day, exercised erratically, institutionalized, had no control over food preparation.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NA</p>		
<p>de Brito-Ashurst, 2013²³</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2008-2009</p>	<p>Study of: NR N: 56</p> <p>Intervention 1: % Male: 56 Mean Age/Range/Age at Baseline: mean 55.7 (SD 15.1) Race: Bangladesh: 100% Systolic BP: 149.3 Diastolic BP: 85 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 17 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 61 Mean Age/Range/Age at Baseline: mean 60.7 (SD 12) Race: Bangladesh: 100% Systolic BP: 156 Diastolic BP: 85 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.1</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Tailored low-salt diet, educational, community sessions Form of Administration: Dietary Modification: Tailored low-salt diet, educational, community sessions Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Low sodium general dietary advice sheet sent by post with the physician's letter Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times 6 months apart Sodium Status Intervention 1: 138 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 6 months apart</p> <p>How was blood pressure measured? BP was taken using TM-2430-13 devices. Daytime measures were taken at 30 min intervals, night-time measures every 60 min. BP collected 2 times 1 time at baseline then at 6 months post intervention</p>	<p>Subgroup: Chronic kidney disease (CKD), eGFR< 60 mL/min, Asian 24h Ambulatory DBP-night time Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.00 (95% CI: -9.00 - -1.00)</p> <p>24h Ambulatory SBP-daytime Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -9.00 (95% CI: -13.00 - -5.00)</p> <p>Deaths Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 14 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: Estimated glomerular filtration rate (eGFR) <60 mL/min and mean SBP >130/80 mm Hg on at least 2 clinic visits or taking antihypertensive medication. Exclusion: Patients on dialysis, those with a BMI <20 or >35 kg/m2, urinary incontinence, or cognitive impairment. Mental problems impairing their ability to participate were excluded</p>			
<p>Dodson, 1989²⁴ Location: US Setting: Community Design: Randomized, parallel Number of Sites: 1 Study Years: unclear</p>	<p>Study of: Adults N: 34</p> <p>Intervention 1: % Male: 71 Mean Age/Range/Age at Baseline: mean 61.9 (SD 7.5) Race: NR Systolic BP: 179 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 65 Mean Age/Range/Age at Baseline: mean 61.1 (SD 6.3) Race: NR Systolic BP: 174 Diastolic BP: 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients with type II diabetes with no past or current history of treatment with insulin. Three</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Moderate sodium restriction Form of Administration: Dietary Modification: Patients advised not to add salt at the table or in cooking and the avoidance of heavily salted foods Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Patients instructed to continue with their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: During run in period then at 1, 2, 3 months Sodium Status Intervention 1: 136.8 mmol/24h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: During run in period then at 1, 2, 3 months Potassium Status Intervention 1: 63.9 mmol/24h</p> <p>How was blood pressure measured? BP was taken in the supine and erect positions (after 5 and two minutes' rest, respectively) with a Hawksley random zero sphygmomanometer. All readings were taken by a separate "blind" observer, DBP was recorded at Korotkoff phase V. When the mid-arm circumference was less than 33 cm A standard width cuff (14 cm) was used ; for larger circumferences a 19 cm cuff was used.</p>	<p>Subgroup: Mild HTN, Diabetes Diastolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -8.48 - 2.88) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -7.10 (95% CI: -19.11 - 4.91)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	consecutive hypertensive BP readings (defined by the SBP > 160 mm Hg or DBP >95 mm Hg) in an established diabetic. Exclusion: Evidence of diabetic or hypertensive nephropathy, pregnancy, and cardiac failure.			
<p>Dubbert, 1995²⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 122</p> <p>Participants: % Male: NR Mean Age/Range/Age at Baseline: mean 62 (SD 8.8) Race: black: 54%</p> <p>Systolic BP: 142.3 Diastolic BP: 85.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: VA enrollees; diagnosis of essential hypertension, a stable DBP such that patients were not expected to need a change in medications for 3 months and urine Na excretion 1> 100 millimoles (mmol)/24 hours Exclusion: Patients requiring immediate dietary intervention for diabetes or other conditions. Patients judged by their primary care provider to be unlikely to benefit from the dietary intervention because of current alcohol abuse, psychosis, or organic brain disease</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Goal is to achieve a 87 mmol/day reduced sodium diet Form of Administration: Dietary Modification: A single session of individualized instruction for 87 mmol/day reduced sodium diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: Goal is to achieve a 87 mmol/day reduced sodium diet Form of Administration: Dietary Modification: A single session of individualized instruction for a 87 mmol/day reduced sodium diet + a means of estimating urine electrolyte excretion at home Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times 3 months apart Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Change of - 55 mmol/24h: blacks, change of -25 mmol/24h whites [estimated - raw data not available] Sodium Status Intervention 2: Change of - 40 mmol/24h: blacks, change of -85 mmol/24h whites [estimated - raw data not available] Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 times 3 months apart</p> <p>How was blood pressure measured? Sitting BP was measured</p>	<p>Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -0.30 (95% CI: NC - NC) Comparison: Intervention 2 vs Comparator MD -0.70 (95% CI: NC - NC) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -0.40 (95% CI: NC - NC) Comparison: Intervention 2 vs Comparator MD -2.40 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Ellison, 1989²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: 2</p> <p>Study Years: NR</p>	<p>Study of: NR N: 309</p> <p>Intervention 1: % Male: 49.2 Mean Age/Range/Age at Baseline: mean 152.2 (SD 0.9) (males); mean 14.9 (SD 0.6) (females) Race: white: 80% (males); white (74%) (females) Systolic BP: 111.9 (males); 105.8 (females) Diastolic BP: 65.8 (males); 66.1 (females) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 141.2 Lb (males); 123.7 Lb (females) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 56.6 Mean Age/Range/Age at Baseline: mean 15.1 (SD 0.9) (Males); mean 14.9 (SD 0.6) (Females) Race: white: 78% (males); white: 75% (females) Systolic BP: 109.3 (males); 101.7 (females) Diastolic BP: 62 (males); 61.7 (females) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 142.7 Lb (males); 124.7 Lb (Females) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Students at participating highschoools taking basic science courses</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: Change of food purchasing at boarding school to help lower salt intake Form of Administration: Dietary Modification: Food purchasing practices were modified and prepared with less salt Dose: NR Na/K ratio: 1.5 (males); 1.5 (females) Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: 1.9 (males); 1.9 (females) Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Composition of salt substitute with intervention/exposure adherence measure, 24-hour diet recall Best sodium measure recorded: 12 times, 1 time per week for the first 6 weeks, during 2 weeks in the winter and 4 weeks during spring Sodium, Method of Validation: Composition of potassium supplement with intervention/exposure adherence measure, 24-hour "diet recall" Sodium Status Intervention 1: 127.2 mEq (males); 83.8 mEq (females) Best potassium measure recorded: 12 times, 1 time per week for the first 6 weeks, during 2 weeks in the winter and 4 weeks during spring Potassium Status Intervention 1: 89.9 mEq (males); 63.5 mEq (females)</p> <p>How was blood pressure measured? At the beginning of each school year, students were instructed on how to use of automatic devices BP measurements. Devices consisted of a Dinamap vital signs monitor (model 845 or 845-A) connected to an Apple II computer. On each occasion, three measurements of SBP and DBP were taken and recorded on a floppy disk. For each set of 3 BP recordings, the average of the second and third was taken</p>	<p>Subgroup: Male Diastolic BP Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD -1.19 (95% CI: -2.6 - .2)</p> <p>Systolic BP Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD -.94 (95% CI: -2.7 - .8)</p> <p>Subgroup: Female Diastolic BP Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD -2.54 (95% CI: -4 - -1.1)</p> <p>Systolic BP Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD -2.55 (95% CI: -4.3 - -.8)</p>
<p>Flack, 2002²⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p>	<p>Study of: Adults N: 112</p> <p>Intervention 1: % Male: 37.5 Mean Age/Range/Age at Baseline: mean 40.3 (SD 8.2) Race: NR Systolic BP: 105.4 Diastolic BP: 69.7 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type: Intervention 1: Placebo Description: NR Form of Administration: Placebo Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation, 3 consecutive pooled overnight 8-hour urine collections; 3 day food diet Best sodium measure recorded: collected 5 times over the study period Sodium Status Intervention 1: mean difference reported, reference group is placebo</p>	<p>24h ambulatory diastolic BP Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.74 (95% CI: -1.72 - 0.24)</p> <p>24h ambulatory systolic BP Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.20 (95% CI: -2.33 - -0.07)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Study Name: Study of Sodium and Potassium (SNaP)</p> <p>Number of Sites: 2</p> <p>Crossover: Length of washout period: 56 days</p> <p>Study Years: unclear</p>	<p>Mean BMI: 29.2</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator: % Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Native born US African-American , normal to high-normal BP. Sodium excretion of 140 mmol in pooled urine collections during screening after 6 weeks of dietary sodium intervention, and 70% adherence to study capsules (as assessed by pill count) during the dietary intervention phase.</p> <p>Exclusion: uncontrolled hypertension at their first eligibility visit, fasting serum glucose ≥ 7.7 mmol/L, taking BP or cardiovascular medication either currently or within the past year, on medications for mental illness , taking more than 4 alcoholic drinks per day , consuming more than 7 restaurant meals per week, actively dieting or trying to lose weight, planning to travel extensively or move from the area, refusal to sign an informed consent form, refusing venipuncture, refusal to take study capsules, refusing to comply with overnight urine collections, otherwise refusing to comply with study protocol, and exhibiting higher than 140 mmol urinary sodium excretion after dietary sodium intervention in the 3 consecutive pooled overnight 8-hour urine collections</p>	<p>sodium intake</p> <p>Description: The aim of the intervention was for patients to comply with a sodium intake of 75-80</p> <p>Form of Administration: NR</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1.5 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured?</p> <p>BP measurement was done using a random zero sphygmomanometer with the bell of the stethoscope.</p> <p>After quietly sitting for 5 minutes with feet flat on the floor and legs uncrossed, the participant's right arm was used to measure two sitting BP readings (with a 30-second interval between readings).</p>	
<p>Franzoni, 2005²⁸</p> <p>Location: Italy</p> <p>Setting:</p>	<p>Study of: Adults</p> <p>N: 104</p> <p>Intervention 1: % Male: 59.6%</p> <p>Mean Age/Range/Age at Baseline: mean 51 (SD 11)</p> <p>Race: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels</p> <p>Description: NR</p> <p>Form of Administration: Oral potassium supplement</p>	<p>Sodium Status Intervention 1: 196.2 mmol/24 h</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: 2 times 1 month apart</p>	<p>Subgroup: Mild to moderate HTN</p> <p>Diastolic BP-24H AMB</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -6.60 (95% CI: -8.16 - -5.04)</p> <p>Systolic BP-24H AMB</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design:</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Systolic BP: 154.4 Diastolic BP: 95 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 24.3 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 65.3% Mean Age/Range/Age at Baseline: mean 53 (SD 12) Race: NR Systolic BP: 153.8 Diastolic BP: 96.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: established or newly diagnosed mild - moderate essential hypertension, Exclusion: Patients with SBP > 200 mmHg and suspected or defined secondary hypertension, coronary artery disease, valvular or primary myocardial heart disease, diabetes, dyslipidemia and arrhythmias</p>	<p>Dose: 30 mmol/day per os of potassium aspartate supplementation Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Instructed to maintain a constant dietary sodium and potassium intake of throughout the study Form of Administration: Usual diet Dose: NR Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Potassium Status Intervention 1: 81.6 mmol/24 h</p> <p>How was blood pressure measured? Office BP and 24-h ambulatory BP were measured at baseline and after the 4 week intervention. Office BP was taken twice in the sitting position by a physician with a mercury sphygmomanometer. A 24-h ambulatory BP monitoring was performed using a SpaceLabs 90207 monitor. Measurements in the non-dominant arm were taken at 30-min intervals during the 24-h period and hourly means were calculated. Day time BP was defined as the mean value from 9:00 AM to 11:00 PM and the night time BP as the mean value from 11:30 PM to 6:00 AM.</p>	<p>Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -8.38 - -3.02)</p>
<p>Geleijnse, 1994²⁹</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p>	<p>Study of: Adults N: 100</p> <p>Intervention 1: % Male: 53 Mean Age/Range/Age at Baseline: mean 65.7 (SD 4.6) Race: NR Systolic BP: 158 Diastolic BP: 89.8 Magnesium: 5.4 mmol/24h Calcium: NR Other Minerals: NR Mean BMI: 27.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: NR Form of Administration: Dietary Modification: Salt substitute for cooking + food made with salt substitute Dose: mineral salt (sodium: potassium: magnesium 8:6:1) to be used for cooking, and food prepared with mineral salt (d bread, cheese, luncheon meats, canned and instant soups, and smoked sausage) Na/K ratio: 1.3 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 4 times 8 weeks apart Sodium Status Intervention 1: 116 mmol/24 h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 4 times 8 weeks apart Potassium Status Intervention 1: 97 mmol/24 h</p> <p>How was blood pressure measured? BP was taken on the right arm by</p>	<p>Subgroup: Mild-moderate HTN Diastolic BP-sitting Follow-Up Time: 24 weeks Comparison: Intervention 1 vs Comparator MD -4.10 (95% CI: -4.57 - -3.63) Follow-Up Time:49 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -4.50 - 2.50) Systolic BP-sitting Follow-Up Time: 24 weeks Comparison: Intervention 1 vs Comparator MD -5.10 (95% CI: -5.84 - -4.36) Follow-Up Time:49 weeks Comparison: Intervention 1 vs</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: 1990-1992	<p>% with history of Kidney stones: NR</p> <p>Comparator: % Male: 49% Mean Age/Range/Age at Baseline: 67.1 (4.5) Race: NR Systolic BP: 157.5 Diastolic BP: 90.8 Magnesium: 5.2 mmol/24h Calcium: NR Other Minerals: NR Mean BMI: 27.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 55-75 with SBP between 140 and 200 mm Hg or DBP between 85 and 110 mm Hg without antihypertensive treatment. Exclusion: History of MI, angina pectoris, diabetes mellitus, or impaired renal function (serum creatinine concentration > 200 µmol/l) or on a salt restricted diet based on medical advice.</p>	<p>Comparator: Other: Regular salt group Description: NR Form of Administration: Regular Salt Dose: regular salt (sodium: potassium: magnesium 8:6:1) to be used for cooking, and food prepared with regular salt (bread, cheese, luncheon meats, canned and instant soups, and smoked sausage) Na/K ratio: 2.1 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>two investigators using an automatic device (Dinamap model 8100) and a 51 cm by 15 cm cuff while the patient was seated. After at least five minutes' rest four measurements were taken, the mean of last three were measurements was used.</p>	<p>Comparator MD 0.80 (95% CI: -4.50 - 6.00)</p>
<p>Gilleran, 1996³⁰ Location: UK Setting: Community Design: Randomized, parallel Number of Sites: 1 Study Years: unclear</p>	<p>Study of: Adults N: 40</p> <p>Intervention 1: % Male: 60% Mean Age/Range/Age at Baseline: 62.5 Race: NR Systolic BP: 163.2 Diastolic BP: 91.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 60% Mean Age/Range/Age at Baseline: mean 59.2 (SD 10.8) Race: NR Systolic BP: 169.6 Diastolic BP: 91.7</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: NR Form of Administration: Salt substitute Dose: salt substitute (Seltin) containing 50% sodium chloride, 40% potassium chloride, 10% magnesium sulphate Na/K ratio: 2.3 Magnesium: 4.2 Urinary excretion (24 h estimation) Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Table salt Description: NR Form of Administration: Regular Salt Dose: Ordinary table salt Na/K ratio: 2.3 Magnesium: 3.7 Calcium: NR Other Minerals: NR</p> <p>Duration: 9 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 0,1,2,3,6,9 months Sodium, Method of Validation: Checks of remaining allotted monthly supplies of Seltin or whole salt, Single 24-hour urine analysis with validation Sodium Status Intervention 1: 166.6 Urinary excretion (24 h estimation) Best potassium measure recorded: 0,1,2,3,6,9 months Potassium, Method of Validation: Checks of remaining allotted monthly supplies of Seltin or whole salt Potassium Status Intervention 1: 77.3 Urinary excretion (24 h estimation)</p> <p>How was blood pressure measured? BP was measured in the supine and erect positions (after 5 min and 2 min rest respectively) with a Hawksley random zero</p>	<p>Subgroup: Hypertensive Type II diabetics Diastolic BP-supine Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator MD 1.70 (95% CI: -5.77 - 9.17) Comparison: Intervention 1 vs Comparator MD -1.70 (95% CI: -9.17 - 5.77) Stroke Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator RR 0.33 (95% CI: 0.01 - 7.72) Comparison: Intervention 1 vs Comparator RR 3.00 (95% CI: 0.13 - 69.52) Systolic BP-supine Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator MD 21.50 (95% CI: 3.62 - 39.38) Comparison: Intervention 1 vs Comparator MD -21.50 (95% CI: -39.38 - -3.62)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 59.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Three consecutive hypertensive BP readings in with established diabetes including patients already taking one antihypertensive medication (provided that the medication had been discontinued for at least 1 month prior to the trial) Exclusion: Treatment with insulin, unstable or poor diabetic control, evidence of diabetic or hypertensive nephropathy (persistent proteinuria on Albustix, or raised serum creatinine concentration: 130 /xmol/l), pregnancy, cardiac failure, or a patient already consuming a low sodium diet</p>		<p>sphygmomanometer. All readings were taken by a blinded observer, DBP was recorded at Korotkoff phase V. A standard width cuff (14 cm) was used with the midarm circumference was less than 33 cm, but for larger circumferences, a 19 cm cuff was used</p>	
<p>Gillum, 1981³¹; Prineas, 1980³²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Minneapolis Children's Blood Pressure Study</p> <p>Number of Sites: multiple</p> <p>Study Years: 1978</p>	<p>Study of: Children N: 80</p> <p>Intervention 1: % Male: 88 (Attendees) Mean Age/Range/Age at Baseline: mean 7.8 (SD 0.7) (Attendees) Race: NR Systolic BP: 110 (Attendees) Diastolic BP: 65 (Attendees) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.4 kg (Attendees) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 92 Mean Age/Range/Age at Baseline: 8 Race: NR Systolic BP: 115 Diastolic BP: 69 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.8 Kg</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Achieve sodium intake of 70 mEq sodium /day Form of Administration: Dietary Modification: Family Education Program Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Composition of salt substitute with intervention/exposure adherence measure Best sodium measure recorded: Controls: At baseline and 1 year follow up, overnight urine was used. Cases: 4 times biweekly, then bimonthly for the rest of the 1 year study period. 24 hour urine collection used Sodium Status Intervention 1: 87 mmol/24h (Attendees)</p> <p>How was blood pressure measured? SBP was measured in the right arm after 5 minutes rest with a random-zero mercury sphygmomanometer. One of four cuff bladder sizes was chosen based on arm circumference. The mean of 2 successive readings of SBP, fourth phase DBP, and fifth phase diastolic DBP were used</p>	<p>Subgroup: Children Diastolic BP-NS Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD 3.90 (95% CI: -5.10 - 12.90) Systolic BP-NS Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD 2.50 (95% CI: -1.19 - 6.19)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Families providing consent, whose children had BP over the 95th percentile for age and sex</p>			
<p>Graham, 2014³³</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: 14-28 days</p> <p>Study Years: 2009-2010</p>	<p>Study of: Adults N: 40</p> <p>Participants: % Male: 80 Mean Age/Range/Age at Baseline: mean 54.8 (S.E.M 1.1) Race: NR Systolic BP: 140.6 Diastolic BP: 86.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 40–70 years; a 10-year cardiovascular disease risk >10% Exclusion: Fasting plasma glucose \geq 7.0 mmol l⁻¹, serum potassium outside of 3.5–5.0 mmol l⁻¹, impaired renal function with estimated glomerular filtration rate <60 ml min⁻¹ per 1.73 m², history of cardiovascular or cerebrovascular disease, a treated BP >140/90 mm Hg, women on oestrogen replacement therapy or oral contraceptives pill and pregnant or lactating women.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 64 mmol potassium chloride Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 4 day food diary Best sodium measure recorded: collected during washout period Sodium Status Intervention 1: 145.6 mmol/24h Potassium measure: Single 24-hour urine analysis without validation, 4 day food diary Best potassium measure recorded: collected during washout period Potassium Status Intervention 1: 103.9 mmol/24h</p> <p>How was blood pressure measured? BP was measured in triplicate after 30 min of supine rest using an Omron M5-I automatic blood pressure monitor. The average of the second and third readings was calculated and used to represent the blood pressure at that visit. The BP taken at the second and forth visits were used in the statistical analysis as end-of-treatment blood pressure.</p>	<p>Subgroup: Hypertensives Diastolic bp Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -2.40 (95% CI: -5.70 - 0.90) Systolic bp Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -5.30 (95% CI: -9.30 - -1.30)</p>
<p>Grimm, 1990³⁴, Grimm, 1988³⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p>	<p>Study of: Adults N: 287</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 57.8 (SD 6.2) Race: NR Systolic BP: 124.7 Diastolic BP: 79.6 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Placebo pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Oral potassium supplement Dose: 96 mmol microcrystalline potassium chloride - 12 capsules, per day Na/K ratio: NR</p>	<p>Potassium measure: Partial or spot urine without validated prediction equation, Food diaries without reported validation Potassium Status Intervention 1: 40 mmol/8h</p>	<p>Subgroup: Hypertensive men Decreased quality of life (diarrhea) Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 0.91 (95% CI: 0.69 - 1.21) Decreased quality of life (stomach pains) Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 0.80 (95% CI: 0.55 - 1.17)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Study Name: Minnesota Mount Sinai Hypertension Trial (MSHT)</p> <p>Number of Sites: multiple</p> <p>Study Years: 1984-1985</p>	<p>Mean BMI: 28.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100</p> <p>Mean Age/Range/Age at Baseline: mean 57.5 (SD 6.5) Race: NR Systolic BP: 126.4 Diastolic BP: 80.7 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 28.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Males, aged 45-68, documentation of long term drug treatment for hypertension in Minneapolis. Currently taking one or two antihypertensive drugs with DBP<95 mm Hg on the first 2 clinic visits, and <90 mm Hg average for both visits. Exclusion: Treatment of hypertension for < 3.5 years, use of cardiovascular drugs, electrocardiographic evidence or clinical evidence of CVD, body weight >15% of the ideal weight, diet incompatible with lowering sodium intake, history of renal disease, documented poor compliance with antihypertensive treatments.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Potassium pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Placebo Dose: 12 placebo capsules per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>		<p>Diastolic BP-NS Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator MD -0.60 (95% CI: NC - NC) Nausea Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 1.16 (95% CI: 0.69 - 1.94) Percent resuming antihypertensives Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator RR 0.98 (95% CI: 0.79 - 1.21) Systolic BP-NS Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator MD -1.90 (95% CI: NC - NC)</p>
<p>Gu, 2001³⁶</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Potassium and</p>	<p>Study of: Adults N: 150</p> <p>Intervention 1: % Male: 37.3</p> <p>Mean Age/Range/Age at Baseline: 56.9 (SD 7.4) Race: NR Systolic BP: 136.9 Diastolic BP: 81.5 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 66.9 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 3 0.5 g potassium chloride pills taken 3 times a day. Or 60 mmol potassium per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo</p>	<p>Sodium Status Intervention 1: 185.7 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 at screening, Once at 6 weeks, then at 12 weeks Potassium, Method of Validation: Pill count Potassium Status Intervention 1: 54.2 mmol/24 h</p> <p>How was blood pressure measured? Trained staff using Hawksley random zero sphygmomanometers.</p>	<p>Subgroup: High normal Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.10 (95% CI: -2.14 - 1.94) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.70 (95% CI: -7.01 - -0.39)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Protein Supplementation Study (PAPSS) Number of Sites: multiple Study Years: unclear	<p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 42.7 Mean Age/Range/Age at Baseline: 55 (SD 7.6) Race: NR Systolic BP: 134 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 45-64. SBP 13-159 mmHg, DBP <95 mmHg OR SBP <160 mmHg AND DBP < 160 mmHg. Able to take potassium supplements in accordance with protocol Exclusion: blood pressure medication in the last 2 months, history of CVD, diabetes at any time, non-skin malignancy in the last 5 years, COPD, psychiatric disease, other life threatening illnesses. serum creatinine >=1.7 mg/dl or K+ >=5.0 mmol/l at screening, alcohol use of >=21 drinks/week or >=40 g/day. Pregnancy, plans to move out of study area, or non-cooperation.</p>	<p>Description: NR Form of Administration: Other: Placebo Dose: 3 placebo pills taken 3 times a day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Taken on the right arm with appropriately sized cuffs after quietly sitting for 5 min. BP recorded three times at each screening, then at follow up visits at 6 and 12 weeks.</p>	
He, 2015 ³⁷ ; He, 2015 ³⁸ Location: China Setting: Community Design: Cluster RCT Parallel Number of Sites: multiple Study Years: 2013	<p>Study of: Both adults and children N: 832</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 120.1 Diastolic BP: 76.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 120.1 Diastolic BP: 76.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Salt education. Aim was to reduce salt intake by a minimum of 20%. Form of Administration: Dietary Modification: Salt education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No salt education Form of Administration: NR Dose: NR Na/K ratio: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, Families put all household salt in a Tupperware container, at the beginning of the trial and it was weighed during follow up. Best sodium measure recorded: 2 times 3.5 months apart Sodium Status Intervention 1: Children: 112.2 mmol/24h; Adults: 178.5 mmol/24h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 times 3.5 months apart Potassium Status Intervention 1: Children: 25.3 mmol/24h; Adults: 38.1 mmol/24h</p>	<p>Subgroup: Children Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -3.44 - 1.44) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -0.60 (95% CI: -2.83 - 1.63)</p> <p>Subgroup: Adults Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: -2.30 - 1.30) Systolic BP-sitting Follow-Up Time: 3.5 months</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% Male: Children: 48. Adults: 48.5 Mean Age/Range/Age at Baseline: Children: mean 10.1 (SD 0.5). Adult: mean 43.8 (SD 12.2) Race: NR Systolic BP: 118.2 Diastolic BP: 75.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Children: 16.9. Adults: 24.9 % with Hypertension: Adults: 13.6 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Primary schools in urban Changzhi Exclusion: Schools in rural areas</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3.5 months Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured? BP Measured using a validated automatic blood pressure monitor (Omron HEM-7301-IT, Amsterdam) with an appropriately sized cuff. After 10 minutes rest in a quiet room, BP was taken 3 times in seated position with the arm at heart level. Average of the last 2 measurement were taken. BP was taken at baseline and at the end of study (3.5 months)</p>	<p>Comparison: Intervention 1 vs Comparator MD -1.60 (95% CI: -3.83 - 0.63)</p>
<p>He, 2010³⁹ Location: UK Setting: Community Design: Randomized Cross-over individual Number of Sites: Crossover: Length of washout period: NR days Study Years: NR</p>	<p>Study of: Adults N: 42</p> <p>Participants: % Male: NR Mean Age/Range/Age at Baseline: 51+/-10 Race: NR Systolic BP: 145+/-11 Diastolic BP: 91+/-7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7+/-4.8 % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Inclusion: ages 18 to 75 years, with sitting systolic BP of 140 to 170 mm Hg or diastolic BP of 90 to 105 mm Hg, with no previous treatment for raised BP Exclusion: impaired renal function with plasma creatinine 150 mol/L, any secondary cause of hypertension, chronic diarrhea, history of ulcer disease, baseline plasma potassium 5.0 mmol/L, previous stroke, ischemic heart disease, heart failure, diabetes mellitus, malignancy, liver disease, pregnancy, breastfeeding, use of oral contraceptives</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Potassium chloride 10 pills/d to achieve 64mmol/d Form of Administration: Oral potassium supplement Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Use of potassium supplement to increase potassium levels Description: Potassium bicarbonate 10 pills/d to achieve 64 mmol Form of Administration: Oral potassium supplement Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Placebo potassium pills, 10/d with usual diet Form of Administration: Placebo Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: two consecutive days Sodium, Method of Validation: creatinine, Composition of potassium supplement with intervention/exposure adherence measure Sodium Status Intervention 1: 134 mmol/d (+/-49) Sodium Status Intervention 2: 129 mmol +/-45 mmol Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 consecutive days Potassium Status Intervention 1: 122 mmol +/-25 Potassium Status Intervention 2: 125 mmol +/-27 mmol</p> <p>How was blood pressure measured? validated automatic digital BP monitor (Omron HEM-705CP) in sitting position after 5 to 10 minute rest and in the same arm throughout the study; three readings at 1- to 2-minute intervals; the mean of last 2 readings was used. Twenty-four-hour ambulatory blood pressure</p>	<p>Subgroup: Hypertensives 24 hr diastolic BP Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 1.00 (95% CI: -1.72 - 4.22) Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -3.58 - 2.06) 24 hr systolic BP Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 0.00 (95% CI: -3.19 - 3.77) Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.89 - 0.41) Left ventricular mass (g) Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -9.00 (95% CI: -23.20 - 7.80) Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -22.58 - 9.25)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Calcium: NR Other Minerals: NR Duration: 4 weeks Exposure to Follow Up Time: 0 months	monitoring was performed using SpaceLabs 90207 devices	
Hofman, 1983 ⁴⁰ Location: Netherlands Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: 1980	Study of: Children N: 476 Intervention 1: % Male: 52 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 87 Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.466 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 51 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 87.7 Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.421 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Infants delivered at home or in an outpatient clinic.	Intervention Type(s): Intervention 1: Other: Low Sodium Description: NR Form of Administration: Dietary Modification: Low sodium formula for infants Dose: Mothers low sodium formula to feed infants. It was similar to that of human milk, and it was three times lower than the normal-sodium milk (6.3 v 19.2 mmole/L). Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: Normal Sodium Description: NR Form of Administration: Usual diet Dose: Mothers given normal-sodium formula to feed infants. It contained an amount of sodium that was regular for Dutch formula milks during the study period Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 6.25 months Exposure to Follow Up Time: NR	Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Casual urine Best sodium measure recorded: weeks 5,13,21 Sodium Status Intervention 1: 11.1 mmoles/L How was blood pressure measured? BP measured in weeks 1, 5, 9, 13, 17, 21, and 25. measurements were taken with a Doppler ultrasound device" connected to a random-zero sphygmomanometer by a trained observer. The average of three readings at each occasion was used in the analyses	Subgroup: Newborn infants Deaths Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator RR 0.94 (95% CI: 0.06 - 14.99) Severe disease (NS) Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator RR 0.63 (95% CI: 0.11 - 3.73) Systolic BP-supine Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.10 - 0.10)
Howe, 1994 ⁴¹ Location: Australia Setting: Community	Study of: Adults N: 28 Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 146	Intervention Type(s): Intervention 1: Other: low sodium with fish oil Description: Sodium intake of 70 mmol/day Form of Administration: Other: placebo Dose: eight placebo tablets per day Na/K ratio: NR Magnesium: NR	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 2 times 1.5 months apart Sodium, Method of Validation: Pill counts, feedback on excretion levels, checking creatinine values., Single 24-hour urine analysis with	Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 2 vs Comparator 2 MD -2.10 (95% CI: -5.70 - 1.50) Systolic BP-sitting Follow-Up Time: 6 weeks

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 143 Diastolic BP: 80 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 145 Diastolic BP: 81 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 55.3 Mean Age/Range/Age at Baseline: mean 55 (SD 1) Race: NR Systolic BP: 145 Diastolic BP: 81 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: normal sodium with fish oil Description: Sodium intake of 150 mmol/day Form of Administration: Sodium supplement Dose: eight slow sodium tablets per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: low sodium with olive oil Description: Sodium intake of 70 mmol/day Form of Administration: Other: placebo Dose: eight placebo tablets per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: normal sodium with olive oil Description: Sodium intake of 150 mmol/day Form of Administration: Sodium supplement Dose: eight slow sodium tablets per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: NR</p>	<p>validation Sodium Status Intervention 1: 78 mmol/24h Sodium Status Comparator 1: 150 mmol/24h Sodium Status Intervention 2: 75 mmol/24h Sodium Status Comparator 2: 150 mmol/24h Best potassium measure recorded: 2 times 1.5 months apart Potassium, Method of Validation: Pill counts, feedback on excretion levels, checking creatinine values.</p> <p>How was blood pressure measured? BP was measured with a Dinamap portable automated sphygmomanometer with a cuff of appropriate size on the right arm. BP values used for analysis were obtained by averaging repeated readings taken at one minute intervals after throwing out an initial reading.</p>	<p>Comparison: Intervention 2 vs Comparator 2 MD -5.00 (95% CI: -10.96 - 0.96)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients with uncomplicated essential hypertension being treated by ACE inhibitor monotherapy Exclusion: History of unstable heart, liver or renal disease or a DBP greater than 105 mmHg. Consuming more than 20 cigarettes or 40 g alcohol per day, exercised erratically, were institutionalized; had no control over the preparation of their food.</p>			
<p>Hwang, 2014⁴²</p> <p>Location: Korea</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 7</p> <p>Study Years: 2012-2013</p>	<p>Study of: Adults N: 256</p> <p>Participants: % Male: 49.8 Mean Age/Range/Age at Baseline: Mean 49.5 (SD 13.3) Race: NR Systolic BP: 130.9 Diastolic BP: 79.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 67.8 kgs % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Aged 19–75, the use of antihypertensive meds or a diagnosis of hypertension. Modification of Diet in Renal Disease study eGFR\geq30 ml/min per 1.73 m², random urine albumin-to-creatinine ratio \geq30 mg/g creatinine more than two times with a \geq1-week interval in the last 6 months. Exclusion: Patients with uncontrolled hypertension (BP.160/110 mmHg), pregnant women, and patients with serum potassium $>$5.5 mEq/L. Malignancy, a diagnosis of CVD (cerebral infarction, hemorrhagic infarction, acute MI or unstable angina, coronary angioplasty, or coronary artery bypass surgery) in the last 6 months, contraindication for angiotensin II receptor blockers (ARBs), and diabetes mellitus, continuous users of steroids or other immunosuppressive agents.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Intensive education Description: Intensive education group. The target amount of daily sodium intake was $>$100 mEq/d, A \geq25% reduction of salt intake was also recommended Form of Administration: Other: Intensive education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Conventional Education Description: Conventional education, a A \geq25% reduction of salt intake was recommended. Form of Administration: Other: Conventional education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 0, 2 and 4 months Sodium, Method of Validation: The adequacy of 24H urine samples with correction was evaluated by calculating the predicted daily creatinine excretion Sodium Status Intervention 1: 122.2 mEq/d</p> <p>How was blood pressure measured? No description</p>	<p>Subgroup: Hypertensive on antihypertensive, All Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.20 (95% CI: -3.69 - 1.29) Hypotension Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -5.00 - 2.20)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Hypertension Prevention Trial Research Group, 1990⁴³; Borhani, 1989⁴⁴; Brown, 1989⁴⁵; Forster, 1990⁴⁶; Jeffery, 1990⁴⁷; Jeffery, 1989⁴⁸; Meinert, 1989⁴⁹; Prud'homme, 1989⁵⁰; Schmid, 1991⁵¹; Shah, 1990⁵²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The hypertension Prevention Trial</p> <p>Number of Sites: 9</p> <p>Study Years: 1981-1984</p>	<p>Study of: Adults N: 587</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 65.3 Mean Age/Range/Age at Baseline: mean 38.6 Race: white 82.2% Systolic BP: 124.3 Diastolic BP: 82.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 2.7 (kg/cm² * 100) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Sodium restriction - Dietary Counseling Description: Urine sodium excretion <= 70 mmol/d Form of Administration: Dietary Modification: Counseling to reduce salt intake in diet Dose: NR Na/K ratio: 2.75 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Other: Usual Diet Dose: None Na/K ratio: BL: 3.33 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Sodium restriction and potassium increase - Dietary Counselling Description: Urine sodium excretion <=70 mmol/d; urine potassium excretion 100 mmol/d Form of Administration: Dietary Modification: Counseling to reduce salt intake in diet and increase K+ intake Dose: NR Na/K ratio: 2.57 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 1: Other: Sodium restriction - Dietary Counseling Description: Urine sodium excretion <= 70 mmol/d Form of Administration: Dietary Modification: Counseling to reduce salt intake in diet Dose: NR Na/K ratio: 2.75 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure, Food diaries with reported validation Best sodium measure recorded: 0, 3, 6, 12, 18, 24, 30, 26 months. Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: 38.6 mmol/8h Sodium Status Comparator 1: 43.4 mmol/8h Sodium Status Intervention 2: 36.3 mmol/8h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 0, 3, 6, 12,18,24,30,26 months.</p> <p>Potassium Status Intervention 1: 14 mmol/8h Potassium Status Comparator 1: 13.0 mmol/8h Potassium Status Intervention 2: 14.1 mmol/8h</p> <p>How was blood pressure measured? BP measured at 0, 3, 6, 12,18,24,30,26 months. Measurements were taken with a random zero sphygmomanometer and standard procedures. All measurements (first and fifth Korotkoff sounds) are the average of two readings on the right arm with the participant seated. The initial measurement was taken approximately 5 minutes after the participant was seated, and the second measurement was taken about 30 seconds after the first.</p>	<p>Subgroup: Low BMI (BL 27) Diastolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator 1 MD 0.20 (95% CI: -1.19 - 1.59) Comparison: Intervention 2 vs Intervention 1 MD -0.90 (95% CI: -2.29 - 0.49) Diastolic blood pressure >=90 mm Hg or systolic blood pressure >=140 mm Hg or treatment for hypertension Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator 1 RR 1.36 (95% CI: 0.99 - 1.88) Comparison: Intervention 2 vs Intervention 1 RR 1.13 (95% CI: 0.78 - 1.64) Systolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator 1 MD 0.10 (95% CI: -1.84 - 2.04) Comparison: Intervention 2 vs Intervention 1 MD -1.30 (95% CI: -3.24 - 0.64)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 25-29, 76<DBP<99 mm Hh at the first baseline visit, 78<DBP<89 at the second baseline visit. Exclusion: Taking antihypertensive medication, evidence of cardiovascular disease, BMI of 0.0035 kg/cm2 or more, had dietary requirements incompatible with the dietary counseling regimens, consumed 21 or more alcoholic beverages a week, or were perceived as unable to comply with the data collection schedule or counseling regimens.</p>	<p>Duration: 36 months Exposure to Follow Up Time: NR</p>		
<p>Hypertension Prevention Collaborative Research Group, 1997⁵³; Hebert, 1995⁵⁴; Cook, 2005⁵⁵; Kumanyika 2005⁵⁶; Cook, 2007⁵⁷; Lasser, 1995⁵⁸; Appel, 1995⁵⁹; Hunt, 1998⁶⁰; Hollis, 1995⁶¹; Cook, 2016⁶²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p>	<p>Study of: Adults N: 2382</p> <p>Intervention 1: % Male: 64.8 Mean Age/Range/Age at Baseline: mean 44.2 (SD 6.1) Race: white 81.1% Systolic BP: 127.7 Diastolic BP: 86.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 68.3 Mean Age/Range/Age at Baseline: mean 43.2 (SD 6.1) Race: white 79.5% Systolic BP: 127.3 Diastolic BP: 85.8 Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 1800 mg (80 mEq) sodium or less per day, Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 7 times, 6 months apart Sodium Status Intervention 1: 135.2 mmol/d Potassium Status Intervention 1: NR</p>	<p>Subgroup: TOHP-2 CVD disease (myocardial infarction, stroke, revascularisation, or death due to cardiovascular causes) Follow-Up Time: 10 years Comparison: Intervention 1 vs Comparator RR 1.13 (95% CI: 0.83 - 1.54) Total mortality Follow-Up Time: Comparison: Intervention 1 vs Comparator RR 1.12 (95% CI: 0.84 - 1.49) Follow-Up Time:10 years Comparison: Intervention 1 vs Comparator RR 1.12 (95% CI: 0.66 - 1.91)</p> <p>Subgroup: Overweight-obese, high-normal BP Cumulative incidence of HTN Follow-Up Time: 48 months Comparison: Intervention 1 vs Comparator RR 1.17 (95% CI: 1.01 - 1.34) Deaths</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Study Name: Trials of Hypertension Prevention (TOHP)</p> <p>Number of Sites: 9</p> <p>Study Years: 1990-1992 (2013 follow-up)</p>	<p>Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: healthy, moderately overweight, 30- to 54-year-old adults (men and women) with a high-normal DBP Exclusion: -Evidence of current hypertension -History of: cardiovascular disease, Diabetes mellitus, malignancy other than nonmelanoma skin cancer during the past 5 y, any other serious life-threatening illness that requires regular medical treatment -Men with BMI < 26.1 or > 37.4; Women with a BMI < 24.4 or > 37.4 kg/m -Current use of prescription medications that affect blood pressure, as well as nonprescription diuretics -Men with Serum creatinine level > 1.7 mg/dL for men or Women with Serum creatinine level > 1.5 mg/dL. Casual serum glucose 200 mg/dL, as determined locally -Current alcohol intake > 21 drinks/wk -For women, current pregnancy or intent to become pregnant during the study -Other: such as planned residence distant from the clinical center or inability to cooperate</p>	<p>Duration: 36 months Exposure to Follow Up Time: NR</p>		<p>Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator RR 0.66 (95% CI: 0.11 - 3.96) Diastolic BP-sitting Follow-Up Time: >=36 months Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: -1.29 - 0.29) Systolic BP-sitting Follow-Up Time: >=36 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -2.03 - 0.03)</p>
<p>Jula, 1992⁶³</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 36</p> <p>Intervention 1: % Male: 42.1 Mean Age/Range/Age at Baseline: mean 44.7 (SD 5.6) Race: NR Systolic BP: 151.9 Diastolic BP: 98.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 47 Mean Age/Range/Age at Baseline: mean 42.5 (SD 3.8) Race: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To reduce daily sodium intake to less than 70 mmol Form of Administration: Dietary Modification: non-pharmacological treatment programme Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 3 months apart Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Intervention 1: 79 mmol 24/h Potassium measure: Food diaries without reported validation Best potassium measure recorded: 3 times, 3 months apart Potassium Status Intervention 1: 88 mmol 24/h</p> <p>How was blood pressure measured? Blood pressure was measured using a mercury sphygmomanometer by a single trained nurse. Subjects were in the supine position, and the average of two measurements taken at approximately 2-min intervals</p>	<p>Subgroup: Mild-mod hypertension Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.16 - -0.24) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -3.30 (95% CI: -10.55 - 3.95)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Systolic BP: 143.9 Diastolic BP: 96.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.7 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild to moderate essential hypertension Exclusion: cardiomyopathy or significant valvular disease, oral contraceptives or any other regular drug treatment. Being treated for hypertension earlier (within the last year).</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>was used to calculate peripheral resistance and end-systolic wall stress. Out-patient clinic BP measurements were done by a single trained technician using a Hawksley random zero sphygmomanometer. Subjects were in the sitting position, always in the morning and in the same quiet room throughout the study. The mean value of two measurements taken with a 2-min interval was calculated.</p>	
<p>Kitaoka, 2013⁹⁴ Location: Japan Setting: Community Design: Number of Sites: 1 Study Years: 2003-2011</p>	<p>Study of: Adults N: 71</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 66.2 (5.4) Race: NR Systolic BP: 150.6 Diastolic BP: 92.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 5.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: mean 64.1 (7.6) Race: NR Systolic BP: 146.9 Diastolic BP: 89.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.8 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 7.7 % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Lecture and a cooking instructions conducted by registered dietitians. Form of Administration: Dietary Modification: lecture and a cooking instructions conducted by registered dietitians. Dose: NR Na/K ratio: mean Na:K ratio = 1.9 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: mean Na:K ratio = 2.9 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Food diaries with reported validation, Partial or spot urine with validated prediction equation Best sodium measure recorded: Two times, at baseline and after 5 months. Kawasaki's formula. Sodium Status Intervention 1: 10.6 g/day Potassium measure: Partial or spot urine with validated prediction equation_1, Food diaries without reported validation Best potassium measure recorded: Two times, at baseline and after 5 months. Kawasaki's formula Potassium Status Intervention 1: 3807 mg/day</p> <p>How was blood pressure measured? BP was measured by trained physicians using a mercury sphygmomanometer. Participants were asked to sit calmly for 5–10 minutes before being measured. These BP values were taken twice and the mean value was calculated for each subject.</p>	<p>Subgroup: Hypertensive Diastolic BP-sitting Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD 2.00 (95% CI: -9.26 - 13.26) Systolic BP-sitting Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD -4.50 (95% CI: -24.66 - 15.66)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	Inclusion: Free-living men, aged 40–75 years, who lived in Kyoto city or neighboring towns. SBP 130 mm Hg and <180 mm Hg or DBP 85 mm Hg and <110 mm Hg.			
<p>Knuist, 1998⁶⁵</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1992-1994</p>	<p>Study of: Adults N: 361</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 27.6 (SD 4.2) Race: NR Systolic BP: NR Diastolic BP: 74.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 70.4 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 27.5 (SD 4.8) Race: NR Systolic BP: NR Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 69.7 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Dutch-speaking nulliparous women, with a DBP pressure < 90 mmHg at their first prenatal visit, taking place before 20 weeks of gestation Exclusion: Women planning to move to another city, conditions associated with an increased risk of pregnancy induced hypertension (for example: diabetes, twins, pre-existing hypertension or renal disease).</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Decrease salt intake, < 50 mmol sodium Form of Administration: Dietary Modification: Low salt diet, Written dietary instructions were given by the midwives Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: Until delivery Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 12 times during pregnancy Sodium, Method of Validation: Creatinine was measured to compare completeness of the 24-hour urine sampling Sodium Status Intervention 1: 84 mmol/24h</p> <p>How was blood pressure measured? BP was measured with the subject in the sitting position, using the same arm with a portable oscillometric sphygmomanometer. Two consecutive readings of at a minimum of four hours apart were required to assign the highest diastolic blood pressure,</p>	<p>Diastolic BP-sitting Follow-Up Time: 35 days Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -2.29 - 2.29)</p>
Kojuri, 2007 ⁶⁶	Study of: Adults N: 80	Intervention Type(s):	Sodium measure: Single 24-hour urinary analysis without reported	Subgroup: Mild to moderate hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: NR</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Intervention 1:</p> <p>% Male: 50</p> <p>Mean Age/Range/Age at Baseline: mean 48.7 (SD 11.1)</p> <p>Race: NR</p> <p>Systolic BP: 147.1</p> <p>Diastolic BP: 136.7</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 69.47 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 50</p> <p>Mean Age/Range/Age at Baseline: mean 46.05 (SD 13.173)</p> <p>Race: NR</p> <p>Systolic BP: 141.2</p> <p>Diastolic BP: 133.3</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 70.85 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: mild to moderate hypertension and not taking any antihypertensive drugs</p>	<p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: NR</p> <p>Form of Administration: Dietary</p> <p>Modification: DASH</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: NR</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1.5 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>quality control measure</p> <p>Best sodium measure recorded: 2 times, 6 weeks apart</p> <p>Sodium Status Intervention 1: 110 meq/dl</p> <p>How was blood pressure measured?</p> <p>24 hour holter monitoring of blood pressure was measured with a Davinsa device from 8 AM to 8 AM next day.</p>	<p>24h Ambulatory DBP-daytime</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -9.20 (95% CI: -11.55 - -6.85)</p> <p>24h Ambulatory DBP-night time</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -7.00 (95% CI: -9.03 - -4.97)</p> <p>24h Ambulatory SBP-daytime</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -17.00 (95% CI: -20.71 - -13.29)</p> <p>24h Ambulatory SBP-night time</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -12.43 (95% CI: -15.44 - -9.42)</p>
<p>Kwakernaak, 2014⁶⁷</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized</p> <p>Cross-over individual</p>	<p>Study of: Adults</p> <p>N: 45</p> <p>Intervention 1:</p> <p>% Male: 84</p> <p>Mean Age/Range/Age at Baseline: 65+/-9</p> <p>Race: 100% white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 32+/-5</p> <p>% with Hypertension: NR</p>	<p>Intervention Type:</p> <p>Intervention 1: Usual Diet</p> <p>Description: Regular sodium diet</p> <p>Form of Administration: Usual diet</p> <p>Dose: 224 mmol/d (+/- 73) sodium; 74 mmol/d potassium</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: once (in the middle and at the end of each intervention period)</p> <p>Sodium, Method of Validation: creatinine clearance, Single 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 224 mmol/d (+/- 73)</p> <p>Best potassium measure recorded: once (in the middle and at the end of each intervention period)</p> <p>Potassium, Method of Validation:</p>	<p>Diastolic BP</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -12.00 (95% CI: -15.20 - -7.80)</p> <p>Systolic BP</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -5.30 (95% CI: -9.10 - -1.50)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: multiple</p> <p>Crossover:</p> <p>Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>% with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Type 2 diabetes, albuminuria (defined as albuminuria >30 mg per day or urinary albumin concentration >20 mg/L or urinary albumin:creatinine ratio >2.5 mg/mmol for men and >3.5 mg/mmol for women) at time of screening and after completion of run-in; age 18 years or older; creatinine clearance of 30 mL/min or higher with a less than 6 mL/min decrease in the previous year</p> <p>Exclusion: systolic blood pressure of 180 mm Hg or higher; diastolic blood pressure of 110 mm Hg or higher; overt nephrotic syndrome at baseline; second primary renal disease in addition to diabetic nephropathy; type 1 diabetes; renovascular hypertension; a cardiovascular or cerebrovascular event within 3 months before inclusion; serum potassium of 6.0 mmol/L or higher; transplantation or immunosuppressive treatment; contraindication for the use of lisinopril or hydrochlorothiazide; pregnancy or lactation; noncompliance with medication; and inability to provide informed consent</p>	<p>dietary advice) to reduce sodium intake</p> <p>Description: To achieve 50mmol sodium intake/d</p> <p>Form of Administration: Dietary</p> <p>Modification: 2 diet counseling sessions</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 4 periods of 6 weeks each</p> <p>Exposure to Follow Up Time: 0 months</p>	<p>NR</p> <p>Potassium Status Intervention 1: 74 mmol/d</p> <p>How was blood pressure measured? measured at 1-min intervals for 15 minutes with a semiautomatic device (Dinamap, GE Medical Systems, Milwaukee, WI, USA) in a semisupine position; used the mean of the second-to-last four readings</p>	
<p>Langford, 1991⁶⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized</p>	<p>Study of: Adults N: 169</p> <p>Intervention 1: % Male: 62.1 Mean Age/Range/Age at Baseline: mean 48.2 Race: white: 66.7 Systolic BP: 141.9 Diastolic BP: 93.4 Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Usual Diet - Chlorthalidone</p> <p>Description: Participants asked not to change their usual diet</p> <p>Form of Administration: Other: usual diet</p> <p>Dose: chlorthalidone 25 mg</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, 3-day food records</p> <p>Best sodium measure recorded: two times 6 months apart</p> <p>Sodium, Method of Validation: Single 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 144.05 mmol/day</p>	<p>Subgroup: Mild HTN</p> <p>Diastolic BP</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 0.05 (95% CI: -2.81 - 2.91)</p> <p>Systolic BP</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Factorial Design individual</p> <p>Study Name: The Trial of Antihypertensive Interventions and Management (TAIM)</p> <p>Number of Sites: 3</p> <p>Study Years: 1985-1987</p>	<p>Calcium: NR Other Minerals: NR Mean BMI: 89.6 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 64.4 Mean Age/Range/Age at Baseline: mean 47.7 Race: white: 69% Systolic BP: 142.8 Diastolic BP: 93.7</p> <p>Intervention 3: % Male: 55.7 Mean Age/Range/Age at Baseline: mean 50.5 Race: white: 70.9% Systolic BP: 144.9 Diastolic BP: 94.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 87.4 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 4: % Male: 55.1 Mean Age/Range/Age at Baseline: mean 48.9 Race: white: 66.3% Systolic BP: 143.1 Diastolic BP: 93.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 86.1 Kg % with Hypertension: 100</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Usual Diet - Atenolol Description: Participants asked not to change their usual diet Form of Administration: Other: usual diet Dose: atenolol 50 mg Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Low Na/high K - Placebo Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: placebo + Low Na/high K diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Other: Low Na/high K - Chlorthalidone Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: Chlorthalidone 25 mg + Low Na/high K diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 5: Other: Low Na/high K - Atenolol Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: Atenolol 50 mg + Low Na/high K diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Usual Diet - Placebo</p>	<p>Sodium Status Intervention 2: 132.44 mmol/day Sodium Status Intervention 3: 95.06 mmol/day Sodium Status Intervention 4: 111.18 mmol/day Sodium Status Intervention 5: 117.41 mmol/day Potassium measure: Food diaries without reported validation Best potassium measure recorded: two times 6 months apart Potassium Status Intervention 1: 67.48 mmol/day Potassium Status Intervention 2: 54.25 mmol/day Potassium Status Intervention 3: 67.83 mmol/day Potassium Status Intervention 4: 72.08 mmol/day Potassium Status Intervention 5: 67.87 mmol/day</p> <p>How was blood pressure measured? BP was taken following American Heart Association guidelines by trained staff with a random zero mercury sphygmomanometer. Blood pressures were measured after the participant had been seated quietly for at least 5 minutes. The mean of two readings of the fifth phase diastolic blood pressure was used in all analyses.</p>	<p>MD 1.68 (95% CI: -3.14 - 6.50) Percent with DBP <90 mmHg Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator RR 0.90 (95% CI: 0.73 - 1.11)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 5: % Male: 65.6 Mean Age/Range/Age at Baseline: mean 51 Race: white: 64.4 Systolic BP: 146.3 Diastolic BP: 94 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 90.2 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 40 Mean Age/Range/Age at Baseline: mean 47.4 Race: white: 67.8% Systolic BP: 144.5 Diastolic BP: 93.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 85.6 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: At preliminary screening, a DBP \leq 100 mm Hg or less for participants currently taking antihypertensive medication or a DBP 90-104 mm Hg for those on no treatment. Patients had to be between 110% and 160% of their ideal weight by recall. Exclusion: History or evidence of MI, stroke or bronchial asthma, a creatinine level \geq 180 μmol/l, diabetes requiring insulin therapy, allergy to thiazides or Beta-blockers, actual or contemplated pregnancy, or likelihood of difficulty in complying with the interventions</p>	<p>Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		
Li, 2016 ⁶⁹ Location:	Study of: Adults N: 2566	Intervention Type(s): Intervention 1: Other: Village level sodium	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: One	Diastolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>China</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2011-2012</p>	<p>Intervention 1:</p> <p>% Male: 50</p> <p>Mean Age/Range/Age at Baseline: mean 55 (SD 14)</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 24</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 50</p> <p>Mean Age/Range/Age at Baseline: mean 55 (SD 14)</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 25</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p>	<p>reduction program</p> <p>Description: Community-based health education, making reduced-sodium, added-potassium salt substitute available at village shops</p> <p>Form of Administration: Dietary</p> <p>Modification: community-based health education + reduced sodium salt</p> <p>Dose: NR</p> <p>Na/K ratio: 5.2</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: Continued their usual practices</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: 6.1</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 18 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>time (end of intervention)</p> <p>Sodium, Method of Validation: Samples rejected if participant reported missing the first morning void, missing more than one void, a collection period less than 22 hours or longer than 26 hours, or spilling more than 10% of the total volume. Urine samples contaminated with feces, where volume was too low or high were excluded. 24-hour creatinine excretion was also used to validate, Single 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 237 mmol/day</p> <p>Best potassium measure recorded: One time (end of intervention)</p> <p>Potassium, Method of Validation: Samples rejected if participant reported missing the first morning void, missing more than one void, a collection period less than 22 hours or longer than 26 hours, or spilling more than 10% of the total volume. Urine samples contaminated with feces, where volume was too low or high were excluded. 24-hour creatinine excretion was also used to validate</p> <p>Potassium Status Intervention 1: 53 mmol/day</p> <p>How was blood pressure measured? BP was measured in duplicate, after participant had rested for 5 min. An automated electronic phygmanometer was used with measurements made at least two minutes apart.</p>	<p>Comparator</p> <p>MD -0.70 (95% CI: -2.20 - 0.80)</p> <p>Percent with hypertension</p> <p>Follow-Up Time: 18 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>RR 1.04 (95% CI: 0.97 - 1.11)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 18 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -1.10 (95% CI: -3.30 - 1.10)</p>
<p>Little, 2004⁷⁰</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design</p>	<p>Study of: Adults</p> <p>N: 296</p> <p>Intervention 1:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 154</p> <p>Diastolic BP: 94</p> <p>Magnesium: NR</p> <p>Calcium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: low sodium salt</p> <p>Description: Pot of low sodium salt (LoSalt; Klinge Foods, East Kilbride) was given to enrollees. They were asked to use it in cooking and on food instead of normal salt.</p> <p>Form of Administration: Salt substitute</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Food diaries with reported validation</p> <p>Best sodium measure recorded: baseline, 4 weeks, and 6 months</p> <p>Sodium, Method of Validation: Single 24-hour urine analysis with validation, Food diaries with reported validation</p> <p>Sodium Status Intervention 1: NR</p> <p>Best potassium measure recorded:</p>	<p>Diastolic BP-sitting</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 1.60 (95% CI: -2.10 - 5.30)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 1.42 (95% CI: -11.20 - 14.00)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>individual</p> <p>Number of Sites: 6</p> <p>Study Years: 1991-2001</p>	<p>Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 56 Mean Age/Range/Age at Baseline: mean 55 (SD 10) Race: NR Systolic BP: 152 Diastolic BP: 92 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: patients over the age of 17 not taking hypertensive drugs with a SBP > 160 mm Hg or DBP > 90 mm Hg on a single reading. Exclusion: Established hypertension, renal impairment, regular nonsteroidal anti-inflammatory drugs; patients who were very ill or who would have trouble changing diet (e.g., severe chronic illness, anorexia, bulimia, pregnancy, breast feeding); and patients with SBP > 200 mm Hg or DBP > 120 mm Hg.</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: NR Description: NR Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: No low sodium salt Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>baseline, 4 weeks, and 6 months Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? At the clinic, BP measured three times after the patient had been seated for five minutes. A Omron HEM-705CP blood pressure monitor was used. Home measurements were taken by patients, who had been trained by the nurse.</p>	
<p>Mascioli, 1991⁷¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of</p>	<p>Study of: Adults N: 48</p> <p>Intervention 1: % Male: 79 Mean Age/Range/Age at Baseline: mean 52 Race: white: 98% Systolic BP: 131 Diastolic BP: 84 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type: Intervention 1: Placebo Description: NR Form of Administration: Placebo Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake Description: NR Form of Administration: Sodium supplement Dose: 96 meq sodium Na/K ratio: NR</p>	<p>Sodium measure: Overnight urine sample Best sodium measure recorded: At weeks 4 and 10. Divided into aliquots and measured with an ion-selective electrode. Sodium, Method of Validation: Pill counts Sodium Status Intervention 1: Group 1: 34.1 meq/8 h; Group 2: 27.7 meq/8 h</p> <p>How was blood pressure measured? BP was measured with patients in a seated position and on the right arm. Two blood pressures were taken at each visit after subjects rested for 5-minutes. This was done</p>	<p>Subgroup: All Diastolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.30 (95% CI: -3.86 - -0.74) Systolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -3.60 (95% CI: -5.33 - -1.87)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>washout period: 14 days</p> <p>Study Years: NR</p>	<p>Comparator:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Ages 30-59 years with seated DBP of 80-89 mm Hg on entry. No treatment/diagnosis of hypertension currently or in the past, SBP < 150 mm Hg, and no serious or life-threatening illnesses.</p>	<p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 4 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>with a random-zero sphygmomanometer (Hawksley) and then the mean was taken averaged.</p>	
<p>Matthesen, 2012⁷²</p> <p>Location: Denmark</p> <p>Setting:</p> <p>Design: Randomized</p> <p>Cross-over individual</p> <p>Number of Sites:</p> <p>Crossover:</p> <p>Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Study of: NR</p> <p>N: 21</p> <p>Participants:</p> <p>% Male: 43</p> <p>Mean Age/Range/Age at Baseline: mean 26 (range: 18-40)</p> <p>Race: 100</p> <p>Systolic BP: 116</p> <p>Diastolic BP: 71</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 23</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Ages 18-40 years; BMI 18.5- 30 kg/m²</p> <p>Exclusion: Arterial hypertension; history of or clinical signs of disease in the heart, lungs, liver, brain or endocrine organs; current medical treatment; malignancies; substance or alcohol abuse; smoking; pregnancy; breast-feeding; no contraceptive treatment for fertile aged women ; clinically significant abnormalities in the blood screening with respect to haemoglobin, white cell count, platelet count, sodium, potassium, creatinine, alanine and aspartate</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels</p> <p>Description: Participants were given a standardized diet</p> <p>Form of Administration: Oral potassium supplement</p> <p>Dose: 50 mmol potassium twice daily</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Placebo</p> <p>Description: Participants were given a standardized diet</p> <p>Form of Administration: Placebo</p> <p>Dose: Placebo</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1 month</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: Sodium Status Intervention 1: 199 mmol/24 h</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice separated by 28 days</p> <p>Potassium Status Intervention 1: 168 mmol/24 h</p> <p>How was blood pressure measured? Ambulatory blood pressure taken using Kiwex TM-2430. In the day, pulse and blood pressure were measured every 15 min. During the night, pulse and blood pressure were measured in 30 min intervals</p>	<p>Subgroup: Normotensive</p> <p>24 h ambulatory- diastolic</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 1.00 (95% CI: -1.80 - 3.80)</p> <p>24 h ambulatory- systolic</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 0.00 (95% CI: -3.42 - 3.42)</p> <p>Aldosterone</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 60.00 (95% CI: -100.65 - 220.65)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	aminotransferase, albumin, cholesterol and glucose. Clinically significant abnormal screening of the urine with respect to albumin and glucose; abnormal electrocardiogram; intercurrent diseases; blood donation less than one month before the trial; unwillingness to participate in the trial; issues with establishing IV access or urine collection.			
<p>Meland, 2009⁷³</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1999-2002</p>	<p>Study of: Adults N: 46</p> <p>Intervention 1: % Male: 74 Mean Age/Range/Age at Baseline: mean 55 Race: NR Systolic BP: 155 Diastolic BP: 92 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 74 Mean Age/Range/Age at Baseline: mean 57 Race: NR Systolic BP: 157 Diastolic BP: 93 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Taking antihypertensive medications, aged 20- 75 years with DBP>90 mmHg and/or SBP>160 mmHg two occasions during a run-in period. Exclusion: Possible drug-induced hypertension, receiving drugs for cardiovascular disease with hypotensive effects, DBP increase to a level of 115 mmHg or SBP 210 mmHg before or during the study.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of salt pills to increase sodium intake Description: Dietary advice outlining a moderate salt reduced diet + salt tablets. Goal was a regular sodium intake diet Form of Administration: Sodium supplement Dose: five capsules of 10 mmol sodium per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Dietary advice outlining a moderate salt reduced diet + placebo. The goal of this arm was a sodium restricted diet Form of Administration: Placebo Dose: five capsules SiO2 per day (placebo) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NA</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: At baseline (inclusion) and the final visit Sodium, Method of Validation: Capsule counts, Single 24-hour urine analysis with validation Sodium Status Intervention 1: Change of -28 mmol/24h (raw numbers not reported) Best potassium measure recorded: At baseline (inclusion) and the final visit Potassium, Method of Validation: Capsule counts Potassium Status Intervention 1: Change of +3 mmol/24h (raw numbers not reported)</p> <p>How was blood pressure measured? BP was measured with a mercury manometer on the right arm in a sitting position after resting for at least two minutes. Three recordings were taken at two-minute intervals, and the average of the last two readings was used for analyses. Appropriate sized cuffs were used and the same cuff was used on each visit. BP readings were done before run-in, at inclusion, and after four and eight weeks.</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -7.00 - -1.00) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -11.00 - 0.00)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Meuleman, 2016⁷⁴</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 4</p> <p>Study Years: 2011-2014</p>	<p>Study of: Adults N: 151</p> <p>Intervention 1: % Male: 79 Mean Age/Range/Age at Baseline: mean 55.6 (SD 11.7) Race: NR Systolic BP: 142 Diastolic BP: 87 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7 % with Hypertension: NR % with history of CVD: 36 % with Type 2 diabetes: 30 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 85 Mean Age/Range/Age at Baseline: mean 54.7 (SD 16) Race: NR Systolic BP: 137 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7 % with Hypertension: NR % with history of CVD: 39 % with Type 2 diabetes: 21 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: moderately decreased kidney function, Dutch speaking, >=18 years old, Being treated by an internist, Protein excretion measurements . 0.2 g/L or 0.3 g/24 h, 2 recent sodium excretion measurements > 120 mmol/24 h, BP >135/85 mm Hg or controlled BP with the use of anti-hypertensive medication, among which at least 1 RAAS blockade. Exclusion: BP >180/100 mm Hg or < 125/75 mm Hg, received a kidney transplant less than 1 y ago, diagnosed with type 1 diabetes, had acute kidney failure, accelerated kidney function decrease (> 6 mL/min/1.73 m2 in previous year). Had a cardiovascular event (ie, MI or cerebrovascular event) < 6 mo ago. diagnoses of malignancy within 5 years (other than basal cell or squamous cell carcinoma of</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Usual care + counselling, education, motivational interviews to reduce sodium in diet Form of Administration: Dietary Modification: counselling, education, motivational interviews to reduce sodium in diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Regular care Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: once a week in the first 6 weeks then every 2 or 3 weeks Sodium Status Intervention 1: 157 mmol/24h</p> <p>How was blood pressure measured? Office BP was measured Microlife WatchBP Home after 5 minutes of rest, the average of 3 measurements was used. Ambulatory BP was measured with validated Spacelabs 90207 and 90217 devices. Monitors were programmed for 24 hours with 15-minute day intervals and 30-minute night intervals.</p>	<p>Subgroup: CKD, hypertensive 24h Ambulatory DBP Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.22 - 0.22) 24h Ambulatory SBP Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -5.33 - 1.33)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	skin), participating in other clinical trial that included medication			
<p>Miller, 2016⁷⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2012-2013</p>	<p>Study of: Adults N: 123</p> <p>Intervention 1: % Male: 34 Mean Age/Range/Age at Baseline: mean 58.8 (SD 8.7) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 34.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 34 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 25 Mean Age/Range/Age at Baseline: mean 58.5 (SD 10.4) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 34.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 21 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Electronic medical record diagnosis of hypertension; age \geq21 years; self-reported African American race; average SBP of 120–140 mmHg or DBP of 80–90 mmHg at the two most recent clinic visits, stable doses of antihypertensive medications for at least 2 months prior to randomization Exclusion: Self-report of a cardiovascular event in last 6 months; a chronic disease that might interfere with trial participation (e.g., CKD defined as an estimated glomerular filtration rate \leq60 mL/minute); unwillingness or inability to adopt a DASH-like diet; consumption of $>$14 alcoholic drinks a week; poorly controlled diabetes (hemoglobin A1c \geq9%); or use of</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Received coach-directed dietary advice and assistance with weekly (\$30/week) online ordering/purchasing of high-potassium foods delivered by a community supermarket to a local library Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Received a printed DASH diet brochure and a debit account with equivalent value to that of the intervention group. Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium, Method of Validation: 24-hour "diet recall" Potassium measure: Spot fasting urine taken. But primary comparisons report pre–post intervention effects using creatinine-normalized measures as an indicator of adherence to the dietary intervention Best potassium measure recorded: Taken 2 times at baseline and 8 weeks Potassium Status Intervention 1: 54 mmol/g creatinine</p> <p>How was blood pressure measured? Measured 5 times: two times during screening visits, once at randomization, then at 3 and 8 weeks follow up. BP taken using an OMRON 907-XL automated BP machine programmed with a 5-minute delay followed by three measurements separated by 30 seconds. Certified trained staff performed and recorded all three measures averaged them at each visit. The average BP of the Screening Visits 1 and 2 established baseline BP, and the average BPs measured at Weeks 3 and 8 were used to determine intervention effects.</p>	<p>Subgroup: African American, HTN Diastolic BP-NS (machine) Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD 1.30 (95% CI: -1.30 - 3.90) Systolic BP-NS (machine) Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD 1.50 (95% CI: -2.57 - 5.57)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>insulin. Individuals using potassium supplements could enroll if they were willing to stop supplements 1 month prior to randomization and refrain throughout the study.</p>			
<p>Miller, 1987⁷⁶ Location: US Setting: Community Design: Number of Sites: multiple Study Years: unclear</p>	<p>Study of: Both adults and children N: 76</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 42 (SD 8.4) Race: white: 100% Systolic BP: 113.2 Diastolic BP: 73.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 76.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8) Race: white: 100% Systolic BP: 100.9 Diastolic BP: 59.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 100.8 Diastolic BP: 60.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 % with Hypertension: NR % with history of CVD: NR</p>	<p>Intervention Type: Intervention 1: Other: Adults - Potassium supplement Description: Participants asked not to change their usual diet Form of Administration: Oral potassium supplement Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men. Na/K ratio: 2.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children Description: K+ supplement to increase potassium intake Form of Administration: Other: liquid potassium supplement Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls. Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Placebo - children Description: NR Form of Administration: Other: Placebo Dose: Placebo Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Sodium, Method of Validation: Measurement of creatinine excretion (if it was ± 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 165 mEq/d Sodium Status Intervention 2: 108.8 mEq/d Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Potassium, Method of Validation: Measurement of creatinine excretion (if it was ± 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete). Potassium Status Intervention 1: 81.6 mEq/d Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	<p>Subgroup: All children Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 0.10 (95% CI: -5.01 - 5.21) Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -0.50 (95% CI: -5.88 - 4.88)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>			
<p>Miller, 1988⁷⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Children N: 298</p> <p>Participants: % Male: 43 Mean Age/Range/Age at Baseline: boys: mean 10.6 (SEM 0.4); girls: mean 9.7 (SEM 0.5) Race: white: 100%</p> <p>Systolic BP: boys 95.3; girls 91 Diastolic BP: boys 54.5; girls 54 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: boys: 38 kg; girls 32.5 kg</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive school-age identical twin pairs recruited from an existing twin panel</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of salt pills to increase sodium intake Description: Low sodium diet + salt pill to achieve normal sodium intake Form of Administration: Sodium supplement Dose: Na chloride supplement Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Maintain an average Na excretion ≤ 60 mmol/d Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Nontwins collected urine samples every other week; twins collected urine samples weekly for a period, over 12 weeks Sodium, Method of Validation: Creatinine excretion in urine samples analyzed to determine if it was representative, Single 24-hour urine analysis with validation Sodium Status Intervention 1: 72.1/mmol/day</p> <p>Best potassium measure recorded: Nontwins collected urine samples every other week; twins collected urine samples weekly for a period, over 12 weeks Potassium, Method of Validation: Creatinine excretion in urine samples analyzed to determine if it was representative Potassium Status Intervention 1: 36.7 mmol/day</p> <p>How was blood pressure measured? Three seated BP measurements were obtained using a Hawksley Random Zero blood pressure device by a research assistant with a certification in blood pressure measurement. The mean of the last two of three blood pressure readings at each visit was used.</p>	<p>Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -0.20 (95% CI: -1.61 - 1.21) Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD 0.30 (95% CI: -0.91 - 1.51)</p>
<p>Morgan, 1987⁷⁸</p> <p>Location: US</p> <p>Setting: Community</p>	<p>Study of: Adults N: 20</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: 'Reduced Sodium diet' Description: NR Form of Administration: Dietary Modification: no further information given</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Week 0,1,4,13,26 Sodium Status Intervention 1: 75 mmol/day</p>	<p>Subgroup: Hypertensive (DBP>100) Diastolic-supine Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -15.07 - -0.93) Systolic-supine</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Systolic BP: 143 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: Mean 60.5 Race: NR Systolic BP: 143 Diastolic BP: 81 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: No clinical evidence of peripheral vascular or cardiac disease, no evidence of left ventricular hypertrophy on electrocardiogram. No detected cause for their hypertension. Well controlled blood pressure</p>	<p>Dose: between 50 and 75 mmol/d consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: NR Dose: between 50 and 75 mmol/d consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured? supine systolic and diastolic blood pressure (mdg) measured at start, before drug stopped, week 1 and month 6.</p>	<p>Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -23.00 (95% CI: -39.86 - -6.14)</p>
<p>Morgan, 1978⁷⁹; Morgan, 1980⁸⁰</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: 1973</p>	<p>Study of: Adults N: 77</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 160 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To reduce sodium intake to 70-100 mmol/day Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Treated with chlorothiazide (500 mg twice d) with the addition of 'Aldomet' if control was inadequate. If control was still not achieved</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 5 times, 6 months apart Sodium Status Intervention 1: 157 mmol/day Sodium Status Intervention 2: 191 mmol/day Sodium Status Intervention 3: 189 mmol/day</p> <p>How was blood pressure measured? BP taken in duplicate with a Bonn amplified sphygmomanometer (by a trained user) after the patients had been in the supine position for ten minutes. The DBP was taken at the 4th phase of the Korotkoff sounds.</p>	<p>Subgroup: HTN males CVD mortality (cerebrovascular accidents, myocardial infarction, congested cardiac failure) Follow-Up Time: 200-2000 days Comparison: Intervention 1 vs Comparator RR 0.83 (95% CI: 0.12 - 5.62) DBP <90 mmHg Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 2.00 (95% CI: 0.77 - 5.20) Diastolic BP-supine Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -11.16 - -2.84) Systolic BP-supine</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 162 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 163 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 165 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: DBP > 90 mm Hg on admission to hospital or at a visit to an outpatient department Exclusion: Malignant disease, severe psychiatric disturbances, severe physical incapacity or a disease</p>	<p>then other drugs were added. Description: NR Form of Administration: Other: chlorothiazide Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Patients treated with propranolol (up to 480 mg/day) and a diuretic, other drugs were considered if control was inadequate Description: NR Form of Administration: Other: propranolol Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>	<p>The BP was again recorded in duplicate after the patient had been standing quietly for five minutes. If the BP differed from previous readings the patient was seen again at the clinic one month later. The procedure was then repeated, and the patient was then included in the study. The mean of the 4 DBPs was taken as the pressure at entry into the study</p>	<p>Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -10.15 - 8.15) Treatment for heart failure Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 1.50 (95% CI: 0.27 - 8.36) Total number of deaths Follow-Up Time: 200-2000 days Comparison: Intervention 1 vs Comparator RR 1.04 (95% CI: 0.30 - 3.58)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	likely to be fatal in the next 2 years. Patients with serum-creatinine levels > 0-18 mmol/l, those with abnormal liver-function tests, and those in cardiac failure or on diuretics			
<p>Morgan, 1981⁸¹</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 24</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: Males: mean 41 (SD 4); Females: mean 36 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 101; Females 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: Males: mean 42 (SD 4); Females: 46 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 123; Females 118 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR Mean Age/Range/Age at Baseline: Males: mean 42 (SD 4); Females: mean 41 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 121; Females: 117 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: DBP low - NA restrict Description: Detailed instructions how to reduce salt intake to 70 mmol a day Form of Administration: Dietary Modification: restricted sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: DBP high - thiazide Description: No diet intervention, patients given were given chlorothiazide (500 mg a day). Form of Administration: Other: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: High DBP Na restrict Description: Detailed instructions how to reduce salt intake to 70 mmol a day Form of Administration: Dietary Modification: Restricted sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: DBP low - control Description: No dietary advice Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: weekly during first stage (up to 1 month), then every 2 weeks during second stage (8 weeks) Sodium Status Intervention 1: Males: 78 mmol/24h; Females: 58 mmol/24h Sodium Status Intervention 2: Males: 181 mmol/24h; Females 138 mmol/24h Sodium Status Intervention 3: Males: 85 mmol/24h; Females: 64 mmol/24h</p> <p>How was blood pressure measured? The same observer measured the patient's BP duplicate at each session with a mercury sphygmomanometer after they had been lying down for 10 minutes and standing for 5 minutes. Korotkoff phase I and IV sounds were used.</p>	<p>Subgroup: Male, DBP<105 mmHg Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -14.92 - 0.92)</p> <p>Subgroup: Female, DBP<105 mmHg Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -10.92 - 4.92)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: Males: mean 38 (SD 3); Females: mean 39 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 99; Females 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 28-50</p>			
<p>Morikawa, 2011⁸²</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 41</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 48.3 (SD 8.7) Race: NR Systolic BP: 149.8 Diastolic BP: 96.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: mean 47.1 (SD 8.5) Race: NR Systolic BP: 149.4 Diastolic BP: 96.3 Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Self-monitoring of daily salt excretion by an electronic salt sensor and personalized advice via sent via cellular phone Description: Group counseling on lifestyle modification from public health nurses and registered dietitians + Intervention Self-monitoring of daily salt excretion by an electronic salt sensor and personalized advice via sent via cellular phone. Aim was to reduce salt intake Form of Administration: Other: Email/Text message alerts Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Group counseling on lifestyle modification from public health nurses and registered dietitians Form of Administration: Usual diet</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation, Food questionnaire without reported validation Best sodium measure recorded: Estimated NaCl₂₄ = 5.76 (NaCl_n - Vn)^{0.53} Taken 2 times, in week 1 and week 4 Sodium Status Intervention 1: Daily salt excretion 10.7 (g) Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? BP was measured two times with a fully automated sphygmomanometer HEM-762; the average of the values was used for the evaluation. BP taken at baseline and after 4 weeks</p>	<p>Subgroup: Hypertensive Diastolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.60 (95% CI: -8.21 - -0.99) Systolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -8.15 - 1.75) NR</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	Calcium: NR Other Minerals: NR Mean BMI: 26.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Employees of a railroad company. Waist circumference < 85 cm. SBP higher than 130 mmHg and/or DBP higher than 85 mmHg. Not currently in treatment for hypertension.	Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 1 month Exposure to Follow Up Time: NR		
Mu, 2009 ⁸³ Location: China Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear	Study of: Both adults and children N: 325 Intervention 1: % Male: 54.5% Mean Age/Range/Age at Baseline: mean 20.3 (SD 3.1) Race: NR Systolic BP: 123.8 Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Intervention 2: % Male: 52.7 Mean Age/Range/Age at Baseline: mean 20.6 (SD 3.1) Race: NR Systolic BP: 121.5 Diastolic BP: 75.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 53 Mean Age/Range/Age at Baseline: mean 21.4 (SD 3.0)	Intervention Type(s): Intervention 1: Other: Potassium-Calcium salt Description: Roughly 10 mmol of potassium and 10 mmol of calcium extra per day through (added to salt) Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Other: Salt restricted group Description: Through health behavior education, the aim was 50–100mmol sodium per person per day at the end of 2 years Form of Administration: Dietary Modification: Health behavior education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 24 months Exposure to Follow Up Time: NR	Sodium measure: partial urine - equation not mentioned, 3 day food consumption questionnaire Best sodium measure recorded: 5 times separated by 6 months Sodium Status Intervention 1: 70 mmol/8h Sodium Status Intervention 2: 45 mmol/8h Potassium measure: Partial or spot urine without validated prediction equation Best potassium measure recorded: 5 times separated by 6 months Potassium Status Intervention 1: 8 mmol/8h Potassium Status Intervention 2: 5 mmol/8h How was blood pressure measured? BP measurements were taken with patients in a sitting position after at least a 5-min rest in quiet a room using a mercury sphygmomanometer with a suitable cuff size. Three measurements were generally performed for calculating the mean values, with 30 seconds between the measurements.	Subgroup: Adolescents Diastolic BP-sitting Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD -5.10 (95% CI: -5.51 - -4.69) Comparison: Intervention 2 vs Comparator MD -3.30 (95% CI: -3.74 - -2.86) Systolic BP-sitting Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD -7.20 (95% CI: -7.61 - -6.79) Comparison: Intervention 2 vs Comparator MD -7.10 (95% CI: -7.62 - -6.58)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: NR Systolic BP: 124.3 Diastolic BP: 77 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: BP _90th percentile by age and sex. No contraindication to the supplementation of potassium and calcium, such as the use of a potassium sparing drugs or significant renal impairment. Exclusion: Abnormal blood tests confirmed by a physician.</p>			
<p>Mulhauser, 1996⁸⁴</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 16</p> <p>Intervention 1: % Male: 62.5 Mean Age/Range/Age at Baseline: mean 35 (SD 11) Race: NR Systolic BP: 134 Diastolic BP: 87 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 87.5 Mean Age/Range/Age at Baseline: mean 37 (SD 9) Race: NR Systolic BP: 139 Diastolic BP: 88 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR</p>	<p>Intervention Type: Intervention 1: Placebo Description: Sodium intake of 90 mmol/day Form of Administration: Placebo Dose: placebo consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake Description: Sodium intake of 190 mmol/day Form of Administration: Sodium supplement Dose: 100 mmol/day sodium supplement consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NA</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, Food diaries with reported validation Best sodium measure recorded: weekly for 12 weeks Sodium, Method of Validation: counting the number of returned pills, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 92 mmol/day Potassium measure: Food diaries without reported validation Best potassium measure recorded: weekly for 12 weeks Potassium Status Intervention 1: 85 mmol/day</p> <p>How was blood pressure measured? BP Measured 12 times, over 12 weeks. Under standardized conditions with a random zero sphygmomanometer (Hawksley, Lancing, UK). For examinations 1-3: Two supine and two sitting blood pressure measurements were taken, the mean all four measurements was used for analysis. For examinations 4 to 12): after the patient had a 10-min rest in the supine position, four supine measurements were taken at</p>	<p>Subgroup: Diabetic with nephropathy Diastolic-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.30 (95% CI: -10.15 - -0.45) Systolic-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.90 (95% CI: -13.95 - 4.15)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: IDDM on intensified insulin therapy, ages 18 -60 years, duration of diabetes more than 5 years, increased proteinuria (> 60 mg/24 h in a minimum of two of three 24-h urine samples). Exclusion: Urinary tract infection, drugs (including oral contraceptives) except insulin, stable retinopathy, pregnancy and effective contraception; untreated 140< SBP < 160 mmHg and/or 85<DBP < 100 mmHg. A history of short-term treatment with antihypertensive drugs in the 4 weeks before start of study</p>		<p>5- min intervals. After another 5 min of rest in the sitting position, four sitting measurements were taken at 5-min intervals. The mean of all eight measurements used in the analysis.</p>	
<p>Naismith, 2003⁸⁵</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 59</p> <p>Intervention 1: % Male: 47 Mean Age/Range/Age at Baseline: mean 44.5 (SD 2.1) Race: European: 83%; Middle-Eastern: 7%; South Asian: 3%; East Asian: 7%</p> <p>Systolic BP: 118 Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26 % with Hypertension: 20 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 65 Mean Age/Range/Age at Baseline: mean 41.7 (SD 2.2) Race: European: 83%; South Asian: 7%; Middle-Eastern: 7%; East Asian 3%</p> <p>Systolic BP: 115 Diastolic BP: 70 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: 28 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Postgraduate and Academic research staff at</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: KCl was given as one slow-release tablet containing 8 mmol KCl Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 6 weeks apart Sodium Status Intervention 1: 166.3 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 6 weeks apart Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? BP taken at the same time of day at each appointment and were performed after the subjects had rested quietly, seated for at least 5 min. Three readings taken at each visit using a semi-automated device employing the oscillometric method. Average of the last two readings were taken and were confirmed by a Hawksley random zero sphygmomanometer</p>	<p>Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -6.47 (95% CI: -8.70 - -4.24) Nausea Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator RR 3.10 (95% CI: 0.13 - 73.14) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -7.60 (95% CI: -10.40 - -4.80)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>King's College London</p> <p>Exclusion: diabetes mellitus, diabetes insipidus, cardiovascular diseases or previous cardiovascular events, any types of renal diseases, metabolic acidosis, current peptic ulcers, dysphagia, general digestive problems, gastric surgery, pregnancy and lactation, taking of anti-hypertensive drugs, and taking drugs known to interfere with K metabolism.</p>			
<p>Nakano, 2016⁸⁶; UMIN-CTR Clinical Trial⁸⁷</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2012-2014</p>	<p>Study of: Adults N: 101</p> <p>Intervention 1: % Male: 31 Mean Age/Range/Age at Baseline: mean 57.5 (SD 13.7) Race: NR Systolic BP: 132 Diastolic BP: 82 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 6 % with Kidney disease: 20 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 45.5% Mean Age/Range/Age at Baseline: mean 60.1 (SD 13.1) Race: NR Systolic BP: 135 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 7 % with Kidney disease: 20 % with history of Kidney stones: NR</p> <p>Inclusion: >20 years old, Stable hypertensive outpatients who are performing antihypertensive and non-antihypertensive treatment. Exclusion: Hemodialysis, Dementia from whom we cannot obtain informed consent, attending doctor</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: The goal was to restrict salt to no more than 6 g of salt per day Form of Administration: Dietary Modification: Nutritionists performed intensive nutritional education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No indication participants asked to change diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Food diaries with reported validation, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, baseline and 3 months Sodium, Method of Validation: Food diaries with reported validation Sodium Status Intervention 1: 6.8 g/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, baseline and 3 months Potassium Status Intervention 1: 1.6 g/24 h</p> <p>How was blood pressure measured? Self-measured home BP was taken in the morning and evenings using a validated upper arm cuff oscillometric device (HEM-5001; Omron, Kyoto, Japan). Ambulatory BP monitoring (ABPM) was performed every 30 minutes using a validated monitor with an upper arm cuff. BP measurements taken at baseline and after 3 months</p>	<p>Subgroup: Hypertensive under pharma or non-pharma treatment Diastolic BP-24H AMB Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -3.23 - 3.23) Systolic BP-24H AMB Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -5.44 - 3.44)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	consider that the patient is not appropriate for the study.			
Nestel, 1993 ⁸⁸ Location: NR Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear	Study of: Adults N: 66 Participants: % Male: 54.5 Mean Age/Range/Age at Baseline: Women: mean 65 (SD 3); Men: mean 66 (SD 5) Race: NR Systolic BP: Women: 120; Men: 129 Diastolic BP: Women: 68; Men: 77 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Women: 24; Men 25 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Normotensive men and women, aged 60-79, free of clinical cardiac, renal, hepatic and endocrine disorders. Not taking any drugs that might affect blood pressure.	Intervention Type(s): Intervention 1: Other: No added salt Description: NR Form of Administration: Other: low salt diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: Added Salt Description: NR Form of Administration: Other: low salt diet + added salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 2.5 months Exposure to Follow Up Time: NR	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 6 times separated by 2 weeks Sodium, Method of Validation: Compliance with urine collection assessed from the within-individual variation in 24-h creatinine excretion between visits, Single 24-hour urine analysis with validation Sodium Status Intervention 1: Women: 77 mmol/day; Men: 106 mmol/day Best potassium measure recorded: 6 times separated by 2 weeks Potassium, Method of Validation: Compliance with urine collection assessed from the within-individual variation in 24-h creatinine excretion between visits Potassium Status Intervention 1: Women: 78 mmol/day; Men: 83 mmol/day How was blood pressure measured? Subjects either had fasted overnight, or had not eating in the 2 hours prior to measurement. After sitting quietly, for 5 min, BP was taken using a Dinamap automated sphygmomanometer fitted with an appropriate arm cuff. After the first reading was discarded, 4 measures were taken and averaged.	Subgroup: Women Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -11.44 - 1.44) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -16.73 - 2.73) Subgroup: Men Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -4.95 - 4.95) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -9.54 - 3.54)
Nowson, 2003 ⁸⁹ Location: Australia Setting: Community Design: Randomized Cross-over individual	Study of: Adults N: 108 Participants: % Male: 41 Mean Age/Range/Age at Baseline: 47 Race: NR Systolic BP: 126.4+/-18.6 Diastolic BP: 79.2+/-11.9 Magnesium: NR Calcium: NR Other Minerals: sodium: 138.7+/-53.9; potassium: 78.6+/-23.7 Mean BMI: 26.1+/-4.2	Intervention Type(s): Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Low sodium/high potassium diet to achieve 50 mmol sodium and 80 mmol potassium Form of Administration: Dietary Modification: Low sodium, high potassium diet and placebo sodium pills Dose: NR Na/K ratio: NR Magnesium: NR	Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase Sodium, Method of Validation: creatinine, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 89.4+/-4.2 mmol/d Best potassium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase Potassium, Method of Validation:	Home measured BP, diastolic Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -1.10 (95% CI: -1.44 - -0.76) Home measured BP, systolic Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.50 (95% CI: -2.95 - -2.05)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: 1</p> <p>Crossover:</p> <p>Length of washout period: NR days</p> <p>Study Years: NR</p>	<p>% with Hypertension: 15</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Twin pairs 30 years or older</p> <p>Exclusion: currently undergoing treatment for cancer or renal disease; requiring insulin treatment for diabetes</p>	<p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Low sodium/high potassium diet to achieve sodium mmol and 80 mmol potassium and sodium supplementation with slow sodium tablets to achieve 130 mmol/d sodium</p> <p>Form of Administration: Dietary</p> <p>Modification: Low sodium, high potassium diet Sodium supplement</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 4 weeks</p> <p>Exposure to Follow Up Time: 0 months</p>	<p>NR</p> <p>Potassium Status Intervention 1: 87.1+/-2.1 mmol/d</p> <p>How was blood pressure measured? mercury sphygmomanometer (model ALPK2; Stethoscope and Sphygmomanometer Specialists, Melbourne, Australia) while seated</p>	
<p>Nowson, 1988⁹⁰, Australian National Health and Medical Research Council Management Committee, 1987⁹¹, Chalmers, 1986⁹²</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: Australian National Health and Medical Research Council dietary</p>	<p>Study of: Adults</p> <p>N: 212</p> <p>Intervention 1:</p> <p>% Male: 81</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Intervention 2:</p> <p>% Male: 83</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 2: Other: High Potassium</p> <p>Description: Increase potassium intake above 100 mmol/day</p> <p>Form of Administration: Dietary</p> <p>Modification: NR</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Other: Low Sodium</p> <p>Description: Reduce sodium intake to 50-70 mmol/day</p> <p>Form of Administration: Dietary</p> <p>Modification: NR</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 3: Other: Low Sodium, High Potassium</p> <p>Description: Reduce sodium intake to 50-70 mmol/day, increase potassium intake above 100 mmol/day</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall</p> <p>Best sodium measure recorded: Every 2 weeks over the 3 month intervention period</p> <p>Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall"</p> <p>Sodium Status Intervention 2: 145 mmol/day</p> <p>Sodium Status Comparator: 86 mmol/day</p> <p>Sodium Status Intervention 3: 73 mmol/day</p> <p>Best potassium measure recorded: Every 2 weeks over the 3 month intervention period</p> <p>Potassium Status Intervention 2: 96 mmol/day Potassium Status Comparator: 70 mmol/day</p> <p>Potassium Status Intervention 3: 87 mmol/day</p> <p>How was blood pressure measured? BP was measured using a Dinamap machine subsequent to subjects being seated for 5 minutes. Three</p>	<p>Subgroup: 90<DBP<100</p> <p>Diastolic BP-sitting</p> <p>Follow-Up Time: 12 weeks</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD -3.10 (95% CI: -4.91 - -1.29)</p> <p>Comparison: Comparator vs Intervention 1</p> <p>MD -4.20 (95% CI: -5.86 - -2.54)</p> <p>Comparison: Intervention 3 vs Comparator</p> <p>MD 1.60 (95% CI: -0.21 - 3.41)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 12 weeks</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD -3.90 (95% CI: -6.81 - -0.99)</p> <p>Comparison: Comparator vs Intervention 1</p> <p>MD -5.10 (95% CI: -7.87 - -2.33)</p> <p>Comparison: Intervention 3 vs Comparator</p> <p>MD 1.00 (95% CI: -1.64 - 3.64)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>salt study in mild hypertension</p> <p>Number of Sites: 3</p> <p>Study Years: 1984-1986</p>	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 89 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 89 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Untreated hypertension, mean 90<=DBP<=100 mmHg Exclusion: Receiving treatment for CVD, hypertension, ischemic disease or any major hypertension complications or of ischemic disease. Grade III or IV hypertensive retinopathy, diabetes, glycosuria, clinical evidence of cardiomegaly or heart failure. Women who were pregnant or on contraceptives. Plasma creatinine>0.12 mmol/L, plasma potassium<3.5 mmol/L or >5.8 mmol/L. Patients receiving prednisone, indomethacin, antihypertensive drugs, or psychotropics.</p>	<p>Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: 70 mmol/day Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>measurements were taken; the first was discarded and the average of last two measures was used.</p>	

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Obel, 1989⁹³</p> <p>Location: Nairobi</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 48</p> <p>Intervention 1: % Male: 47.82%</p> <p>Mean Age/Range/Age at Baseline: 40 (SD 9)</p> <p>Race: NR</p> <p>Systolic BP: Standing: 171; Supine 174</p> <p>Diastolic BP: Standing 103; Supine 100</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator: % Male: 41.67</p> <p>Mean Age/Range/Age at Baseline: 40 (SD 8)</p> <p>Race: NR</p> <p>Systolic BP: Standing: 167; Supine 173</p> <p>Diastolic BP: Standing: 101; Supine 100</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Mild hypertension, age 20-60, 90<DBP<109, SBP >160, serum potassium <4.5 mM, serum creatinine 60-130 uM</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels</p> <p>Description: NR</p> <p>Form of Administration: Oral potassium supplement</p> <p>Dose: 8 tablets of 64 mmol potassium per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Placebo</p> <p>Description: NR</p> <p>Form of Administration: Other: Oral placebo</p> <p>Dose: 8 placebo tablets per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 4 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: 2 times, 16 weeks apart</p> <p>Potassium Status Intervention 1: 102 mmol/24 h</p> <p>How was blood pressure measured? Supine, Standing, patients rested for 30 minutes before readings. Same observer using a Hawksley random zero sphygmomanometer, each record was the mean of two readings. 5 minutes equilibrium period was taken between readings. Measured 5 times, 4 weeks apart.</p>	<p>Subgroup: Black, mild HTN</p> <p>Diastolic BP-supine</p> <p>Follow-Up Time: 16 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -17.00 (95% CI: -19.26 - -14.74)</p> <p>Systolic BP-supine</p> <p>Follow-Up Time: 16 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -39.00 (95% CI: -43.88 - -34.12)</p>
<p>Parker, 1990⁹⁴</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial</p> <p>Design individual</p>	<p>Study of: Adults N: 28</p> <p>Intervention 1: % Male: 100</p> <p>Mean Age/Range/Age at Baseline: mean 49.8 (SD 3.1)</p> <p>Race: NR</p> <p>Systolic BP: 136.1 (supine)</p> <p>Diastolic BP: 83.9 (supine)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 29.3</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Low alcohol - low salt</p> <p>Description: NR</p> <p>Form of Administration: Other: Placebo</p> <p>Dose: low sodium diet (60 mmol/day) + placebo</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator 1: Other: Low alcohol - normal</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Sodium, Method of Validation: detailed food records on the day that urine was collected, weekly tablet counts</p> <p>Sodium Status Intervention 1: 68.6 mmol/day (average of the two low sodium groups)</p> <p>Sodium Status Intervention 2: 68.6 mmol/day (average of the two low sodium groups)</p> <p>Sodium Status Comparator 2: 141.7</p>	<p>Subgroup: Male, HTN on antihypertensives (normal alcohol)</p> <p>Diastolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Comparator 2 vs Intervention 2</p> <p>MD -0.80 (95% CI: -3.84 - 2.24)</p> <p>Systolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Comparator 2 vs Intervention 2</p> <p>MD 0.10 (95% CI: -5.15 - 5.35)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 100 Mean Age/Range/Age at Baseline: mean 51 (SD 3.1) Race: NR Systolic BP: 139.6 (supine) Diastolic BP: 83.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 100 Mean Age/Range/Age at Baseline: mean 52.8 (SD 2) Race: NR Systolic BP: 139.9 (supine) Diastolic BP: 86.6 (supine) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 100 Mean Age/Range/Age at Baseline: mean 54.2 (SD 2.6) Race: NR Systolic BP: 139.9 (supine) Diastolic BP: 86.6 (supine) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR</p>	<p>salt Description: NR Form of Administration: Sodium supplement Dose: low sodium diet (60 mmol/day) + supplementation with 100 mmol enteric-coated sodium chloride (5 10 mmol tablets twice daily) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Normal alcohol - low salt Description: NR Form of Administration: Placebo Dose: low sodium diet (60 mmol/day) + placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal alcohol - normal salt Description: NR Form of Administration: Sodium supplement Dose: low sodium diet (60 mmol/day) + supplementation with 100 mmol enteric-coated sodium chloride (5 10 mmol tablets twice daily) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>mmol/day (average of the normal sodium groups)</p> <p>How was blood pressure measured? average of two sets of five readings measured at 2-minute intervals 1 week apart using with automatic oscillometric device, the Dinamap 845XT</p>	

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with history of Kidney stones: NR</p> <p>Inclusion: Ages 20-70 years, regular treatment with antihypertensive drugs for a minimum of 6 months, alcohol intake of at least 210 ml/wk, no history of renal or hepatic disease or diabetes mellitus, not on current treatment with nonsteroidal anti-inflammatory drugs, and no history of a MI, stroke, or coronary artery bypass surgery within the last 12 months. 125 mm Hg \leq SBP \leq 180 mm Hg, and a DBP of less than 115 mm Hg</p> <p>Exclusion: Underlying renal disease, average 24-hour urinary sodium excretion less than 80 mmol/day (estimated from two urine collections 1 week apart)</p>			
<p>Patki, 1990⁹⁵</p> <p>Location: India</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 37</p> <p>Participants: % Male: 21.6 Mean Age/Range/Age at Baseline: mean 49.9 (SD 7.6) Race: NR Systolic BP: 155 Diastolic BP: 100 Magnesium: 0.88 mmol/l Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: SBP 90-110 mm Hg without any underlying cause Exclusion: renal failure, liver-failure, stroke, ischaemic heart disease, evidence of hyperkalaemia</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: potassium 30 mmol/15 ml Na/K ratio: NR Magnesium: 0.94 mmol/l Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium + magnesium supplement Description: NR Form of Administration: Oral potassium supplement Dose: potassium 30 mmol/15 ml + plus magnesium 10 mmol/15 ml Na/K ratio: NR Magnesium: 0.94 mmol/l Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: placebo Na/K ratio: NR Magnesium: 0.86 mmol/l Calcium: NR Other Minerals: NR</p> <p>Duration: 8 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: at 0 and 8 weeks for each treatment period Sodium Status Intervention 1: 184 mmol/24h Sodium Status Intervention 2: 196 mmol/24h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: at 0 and 8 weeks for each treatment period Potassium Status Intervention 1: 82 mmol/24h Potassium Status Intervention 2: 80 mmol/24h</p> <p>How was blood pressure measured? Phase V DBP was measured with a mercury sphygmomanometer from the left arm, after a five minutes resting in the supine position or two minutes standing.</p>	<p>Subgroup: Hypertensives Diastolic - supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -10.10 (95% CI: -15.60 - -4.60) Comparison: Intervention 1 vs Comparator MD -13.60 (95% CI: -21.00 - -6.20) Systolic - supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -8.90 (95% CI: -13.75 - -4.05) Comparison: Intervention 1 vs Comparator MD -12.10 (95% CI: -18.69 - -5.51)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Pinjuh Markota, 2015⁹⁶</p> <p>Location: Bosnia & Herzegovina</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2012-2013</p>	<p>Study of: NR N: 150</p> <p>Intervention 1: % Male: 47.3 Mean Age/Range/Age at Baseline: mean 59.4 (SD 13) Race: NR Systolic BP: 142.8 Diastolic BP: 84.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: mean 59.3 (SD 12) Race: NR Systolic BP: 143.7 Diastolic BP: 84.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: All consecutive adults who were treated hypertensives</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Individual information leaflets about the negative effects of excessive salt consumption + warning stickers that were mounted on all salt containers Description: NR Form of Administration: Other: Individual information leaflets about the negative effects of excessive salt consumption + warning stickers that were mounted on all salt containers Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Individual information leaflets about the negative effects of excessive salt consumption Description: NR Form of Administration: Other: Individual information leaflets about the negative effects of excessive salt consumption Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times 1 month apart Sodium Status Intervention 1: 176.4 mmol/24h</p> <p>How was blood pressure measured? BP (standard mercury sphygmomanometry) following standard methods. BP taken 3 times 1 month apart</p>	<p>Subgroup: Treated hypertensive Diastolic BP-NS Follow-Up Time: 2 months Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -4.19 - 1.39) Systolic BP-NS Follow-Up Time: 2 months Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -11.26 - -0.14)</p>
<p>Pomeranz, 2002⁹⁷</p> <p>Location: Israel</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p>	<p>Study of: Children N: 58</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 0.76 (SD 0.03) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.2 Kg</p>	<p>Intervention Type: Intervention 1: Other: Control - Breastfeeding Description: Babies fed breastmilk Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium formula Description: NR Form of Administration: Dietary</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, urinary sodium to creatinine ratio Best sodium measure recorded: sodium to creatinine ratio was determined monthly during the initial 2 months Sodium Status Intervention 1: Urinary Na:Cr ratio: 1.1 Sodium Status Intervention 2: Urinary Na:Cr ratio: 1.2</p> <p>How was blood pressure measured?</p>	<p>Subgroup: Newborn infants Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -11.10 (95% CI: -14.43 - -7.77) Systolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -5.30 (95% CI: -9.36 - -1.24)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: unclear	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: mean 0.77 (SD 0.025) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.2 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 0.77 (SD 0.021) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.1 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Jewish infants enrolled in the study hospital's neonatal unit Exclusion: Infants from families with a history of hypertension</p>	<p>Modification: low sodium baby formula Dose: Baby formula with 32 mg/l (8.5 mmol/l) sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: High sodium formula Description: NR Form of Administration: Dietary Modification: high sodium baby formula Dose: Baby formula with 196 mg/l (8.5 mmol/l) sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: 4 months</p>	Non-invasive BP monitoring was performed with a Dinamap 8100 Vital Signs Monitor which measures BP and pulse using the Doppler technique. BP was recorded at the infant's home during sleep after feeding, with an appropriately sized cuff on the right upper extremity.	
Puska, 1983 ⁹⁸ Location: Finland Setting: Community	<p>Study of: Adults N: 114</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Limit salt intake to less than half the level before the study (assumed to</p>	Sodium measure: Single 24-hour urine analysis with validation, Food diaries without reported validation Best sodium measure recorded: 3 times, at run in, after 6 week intervention, then after 4 week washout	Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -0.40 (95% CI: -4.99 - 4.19) Systolic BP-sitting Follow-Up Time: 6 weeks

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1981</p>	<p>Systolic BP: 138.9 Diastolic BP: 89.6 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 76.2 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: Range: 30-50 Race: NR Systolic BP: 137.8 Diastolic BP: 89.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 70.6 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 30 - 50 years old, had no major health problems, not undergoing antihypertensive treatment .</p>	<p>be over 10 g/day).</p> <p>Form of Administration: Dietary Modification: Provided with several low-salt products including salt substitutes, advised to avoid salty foods, counselling with dietitians Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No dietary change Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: 1 month</p>	<p>Sodium, Method of Validation: Comparing urine excretion values and results of the duplicate diet analyses from the previous study, Single 24-hour urine analysis with validation Sodium Status Intervention 1: 77 mmol/24h Potassium measure: Food diaries without reported validation Best potassium measure recorded: 3 times, at run in, after 6 week intervention, then after 4 week washout Potassium, Method of Validation: Comparing urine excretion values and results of the duplicate diet analyses from the previous study Potassium Status Intervention 1: 73mmol/24h</p> <p>How was blood pressure measured? Trained staff measured the BP with an automatic recorder ('Infrasonde SR-2', Sphyngometrics, Inc.). Two blood-pressure measurements were made on the right arm after 5 minutes of quiet sitting. The mean of two measurements was used for analysis. BP Measured 2 times a week for the 3 month duration of the study</p>	<p>Comparison: Intervention 1 vs Comparator MD 1.20 (95% CI: -5.50 - 7.90)</p>
<p>Rahimi, 2007⁹⁹</p> <p>Location: Iran</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2002-2003</p>	<p>Study of: Adults N: 103</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 50.13 (SD 16.54) Race: NR Systolic BP: 133.9 Diastolic BP: 83.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Group C: High calcium diet Description: NR Form of Administration: Dietary Modification: NR Dose: diet with >= 800mg calcium Na/K ratio: NR Magnesium: NR Calcium: 800mg calcium Other Minerals: NR</p> <p>Intervention 2: Other: Group P: High Potassium diet Description: NR Form of Administration: Dietary Modification: NR Dose: Diet with >=4000mg potassium</p>	<p>Sodium Status Intervention 1: difference of urine electrolytes before and after intervention: +581.3 Sodium Status Intervention 2: difference of urine electrolytes before and after intervention: -382.9 Sodium Status Intervention 3: difference of urine electrolytes before and after intervention: +519.25 Potassium measure: Single 24-hour urine analysis without validation, 2-day food record questionnaire Best potassium measure recorded: 1 time (post intervention) Potassium Status Intervention 1: difference of urine electrolytes</p>	<p>Subgroup: Grade one hypertension and high normal Diastolic BP-NS Follow-Up Time: 1 month Comparison: Intervention 3 vs Comparator MD -4.20 (95% CI: -8.44 - 0.04) Comparison: Intervention 1 vs Comparator MD -4.40 (95% CI: -8.01 - -0.79) Comparison: Intervention 2 vs Comparator MD -5.60 (95% CI: -9.29 - -1.91) Systolic BP-NS Follow-Up Time: 1 month Comparison: Intervention 3 vs Comparator MD -11.00 (95% CI: -17.80 - -4.20) Comparison: Intervention 1 vs</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: Mean 46.04 (SD 11.11) Race: NR Systolic BP: 131.6 Diastolic BP: 82.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR Mean Age/Range/Age at Baseline: Mean 47.78 (SD 14) Race: NR Systolic BP: 127.3 Diastolic BP: 83.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 50.71 (SD 15.49) Race: NR Systolic BP: 138 Diastolic BP: 88 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Group CP: High Potassium, high calcium diet Description: NR Form of Administration: Dietary Modification: NR Dose: Diet with >=4000mg potassium + 800mg calcium Na/K ratio: NR Magnesium: NR Calcium: 800mg calcium Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>before and after intervention: +55.32 Potassium Status Intervention 2: difference of urine electrolytes before and after intervention: +935 Potassium Status Intervention 3: difference of urine electrolytes before and after intervention: +907.08</p> <p>How was blood pressure measured? BP measured twice</p>	<p>Comparator MD -4.10 (95% CI: -10.34 - 2.14) Comparison: Intervention 2 vs Comparator MD -6.40 (95% CI: -11.58 - -1.22)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	Inclusion: grade I HTN (140-159/90-99mmHg) or high normal NP (130-139/85-89mmHg)			
<p>Redon-Mas, 1993¹⁰⁰</p> <p>Location: Spain</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 13</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 418</p> <p>Intervention 1: % Male: 47 Mean Age/Range/Age at Baseline: mean 54.5 (SD 11.1) Race: NR Systolic BP: 161.7 Diastolic BP: 100.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 68.8 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 47 Mean Age/Range/Age at Baseline: mean 56.1 (SD 10.2) Race: NR Systolic BP: 165.2 Diastolic BP: 100.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 68.5 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 18-80, BMI<30, mild to moderate essential hypertension. Exclusion: Secondary or severe hypertension, MI or stroke in the last 3 months, unstable angina, heart failure, major arrhythmia or conduction disturbance. Significant renal or hepatic dysfunction, concurrent use of anti-hypertensive drugs or diuretic agents, pregnancy or intended pregnancy, known or suspected contraindication for verapamil, history of poor compliance, drug or alcohol abuse.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Low salt diet Description: Reduce sodium intake Form of Administration: Dietary Modification: reduced sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Regular salt diet Description: Unrestricted sodium intake Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 4 weeks apart Sodium Status Intervention 1: 81.9 mmol/24h</p> <p>How was blood pressure measured? BP measured 3 times at 5 min intervals, after 2 min of sitting, using a conventional mercury sphygomomanometer. Phases I were used for SBP and V for DBP, of the Korotkoff sounds. Mean of 3 readings were used.</p>	<p>Subgroup: Mild-mod hypertension on verapamil Diastolic BP-sitting Follow-Up Time: 28 days Comparison: Intervention 1 vs Comparator MD 1.80 (95% CI: 0.18 - 3.42) Systolic BP-sitting Follow-Up Time: 28 days Comparison: Intervention 1 vs Comparator MD 0.90 (95% CI: -1.86 - 3.66)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Richards, 1984 ¹⁰¹ Location: New Zealand Setting: Community Design: Randomized Cross-over individual Number of Sites: 1 Crossover: Length of washout period: 4 days days Study Years: NR	Study of: Adults N: 12 Participants: % Male: 66 Mean Age/Range/Age at Baseline: 19-52 years Race: NR Systolic BP: 140-180 Diastolic BP: 90-105 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Inclusion: untreated blood-pressure of between 140/90 and 180/105 mm Hg (taking phase V as the diastolic reading) after resting supine for 15 min, on 2 consecutive outpatient visits at least 10 days apart; otherwise well, withdrawn from antihypertensive drugs for 1 month or longer, and normal plasma urea, creatinine, sodium, potassium, calcium, and liver function tests Exclusion: NR	Intervention Type(s): Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To decrease sodium intake to 80 mM Form of Administration: Dietary Modification: instructions to consume low sodium foods Dose: 80 mmol sodium/d consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: NR Description: To increase potassium intake while maintaining usual diet Form of Administration: Oral potassium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: To maintain usual sodium intake, 80mmol sodium diet was supplemented with sodium chloride capsules to achieve 180 mmol/d Form of Administration: Dietary Modification: Low sodium diet Sodium supplement Dose: 180mmol/d sodium consumed; 60 mmol/d potassium consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 3 periods of 4-6 weeks each Exposure to Follow Up Time: 0 months	Sodium, Method of Validation: Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 80 mmol/d Sodium Status Intervention 2: 200 mmol/d Best potassium measure recorded: Multiple 24-hour urine analysis with validation: Twice weekly for 4-6 weeks Potassium, Method of Validation: Creatinine concentration Potassium Status Intervention 1: 60 mmol/d Potassium Status Intervention 2: 180 mmol How was blood pressure measured? Arterial pressures measured twice with an automated version of the London School of Hygiene sphygmomanometer; supine, by one person	Subgroup: Hypertensives Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -1.00 (95% CI: -7.67 - 5.67) Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -8.76 - 5.16) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -1.90 (95% CI: -10.04 - 6.24) Comparison: Intervention 1 vs Comparator MD -5.20 (95% CI: -13.24 - 2.84)
Sacks, 2001 ¹⁰² ; Vollmer, 2001 ¹⁰³ ; Svetkey, 2004 ¹⁰⁴ ; Harsha, 2004 ¹⁰⁵ ; Akita,	Study of: Adults N: 79 Mean Age/Range/Age at Baseline: 49(10) Race: 56% black; 40% NH white; 5% Asian/other Systolic BP: 135(10) Diastolic BP: 86(4)	Intervention Type: Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control High Sodium: To replicate typical diet with high sodium content Form of Administration: Dietary	Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Single 24-hour urine analysis	Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.60 (95% CI: -2.50 - -0.80) Comparison: Intervention 1 vs Comparator

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
2003 ¹⁰⁶ ; Juraschek, 2017 ¹⁰⁷ ; Juraschek, 2017 ¹⁰⁸ Location: US Setting: Community Design: Randomized Cross-over individual Study Name: DASH-Sodium Number of Sites: multiple Crossover: Length of washout period: <5 days Study Years: NR	Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30(5) % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Mean Age/Range/Age at Baseline: 47+/-10 Race: 57% black; 40% NH white; 3% Asian/other Systolic BP: 134+/-10 Diastolic BP: 86+/-5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29+/-5 % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: 22 years old or more, average systolic blood pressure 120 to 159 mm Hg (over 3 visits) and average diastolic blood pressure 80 to 95 mm Hg Exclusion: heart disease, renal insufficiency, poorly controlled hyperlipidemia or diabetes mellitus, diabetes requiring insulin, special dietary requirements, more than 14 alcoholic drinks per week, or use of antihypertensive drugs or other medications that would affect blood pressure or nutrient metabolism	Modification: All foods provided, menu designed to achieve high sodium intake Dose: 150 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Intermediate Sodium: To replicate typical diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve intermediate sodium intake Dose: 100 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Low Sodium: To replicate typical diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 3: NR Description: DASH High Sodium: To impose DASH diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with high sodium intake Dose: 150 mmol sodium/d in DASH diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 4: Prescribed or synthetic diet	without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Sodium, Method of Validation: NR, Chemical analysis of diet with intervention/exposure adherence measure Sodium Status Intervention 1: 141+/-55 mmol/d Sodium Status Intervention 2: 106+/-44 mmol/d Sodium Status Comparator: 64+/-37mmol/d Sodium Status Intervention 3: 144+/-58 mmol/d Sodium Status Intervention 4: 107+/-52 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Potassium, Method of Validation: Adherence checks via food diaries, supervised meals Potassium Status Intervention 1: 40+/-14 mmol/d Potassium Status Intervention 2: 41+/-14 mmol/d Potassium Status Comparator: 42+/-14 mmol/d Potassium Status Intervention 3: 75+/-27 mmol/d Potassium Status Intervention 4: 81+/-31 mmol/d How was blood pressure measured? Random-zero sphygmomanometers, seated, 3 times during screening, weekly during 1st 3 weeks of intervention periods, and 5 times during last 9 days of intervention periods	MD -3.50 (95% CI: -4.30 - -2.60) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -3.00 (95% CI: -4.30 - -1.70) Comparison: Intervention 1 vs Comparator MD -6.70 (95% CI: -8.00 - -5.40)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		<p>(all food provided) with sodium quantified Description: DASH intermediate Sodium: To impose DASH diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with intermediate sodium intake Dose: 100 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH Low Sodium: To achieve DASH diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 periods of 30 days each, including run-in Exposure to Follow Up Time: 0 months</p>		
<p>Santos, 2010¹⁰⁹</p> <p>Location: Portugal</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of</p>	<p>Study of: Adults N: 17</p> <p>Intervention 1: % Male: 47%</p> <p>Mean Age/Range/Age at Baseline: median 29 (range: 24-53) Race: NR Systolic BP: median 115.7 Diastolic BP: median 64.3 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: median 22 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR</p>	<p>Intervention Type: Intervention 1: Other: Low salt water (Vitalis) Description: NR Form of Administration: Dietary Modification: mineral water Dose: mineral water with 3.8 mg/l sodium Na/K ratio: NR Magnesium: 0.7 mg/l Calcium: 0.4 mg/l Other Minerals: NR</p> <p>Comparator: Other: high salt water (Água das Pedras®) Description: NR Form of Administration: Dietary Modification: NR</p>	<p>Sodium Status Intervention 1: 115 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 7 weeks apart Potassium Status Intervention 1: 49.3 mmol/day</p> <p>How was blood pressure measured? BP was taken using a validated automated oscillometric upper arm BP monitor after 5 minutes of rest in the supine position. The blood pressure values used are the average of three recordings.</p>	<p>Diastolic BP Follow-Up Time: 7 weeks Comparison: Intervention 1 vs Comparator MD -0.71 (95% CI: -2.51 - 1.09)</p> <p>Systolic BP Follow-Up Time: 7 weeks Comparison: Intervention 1 vs Comparator MD 0.50 (95% CI: -1.44 - 2.44)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>washout period: 42 days</p> <p>Study Years: unclear</p>	<p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 47%</p> <p>Mean Age/Range/Age at Baseline: median 29 (range: 24-53)</p> <p>Race: NR</p> <p>Systolic BP: median 114</p> <p>Diastolic BP: median 69.7</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: median 22.4</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: SBP/DBP below 140/90 mmHg</p> <p>Exclusion: None of the patients had any chronic disease (heart, liver, kidney, diabetes mellitus), were pregnant or consumed mineral supplements</p>	<p>Dose: mineral water with 622 mg/l sodium</p> <p>Na/K ratio: NR</p> <p>Magnesium: 28 mg/l</p> <p>Calcium: 103 mg/l</p> <p>Other Minerals: NR</p> <p>Duration: 1.75 months</p> <p>Exposure to Follow Up Time: NR</p>		
<p>Saptharishi, 2009¹⁰</p> <p>Location: India</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults</p> <p>N: 58</p> <p>Participants:</p> <p>% Male: 66.7</p> <p>Mean Age/Range/Age at Baseline: mean 22.5 (SD 1.3)</p> <p>Race: NR</p> <p>Systolic BP: 125.5</p> <p>Diastolic BP: 84.6</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 32.4</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Hypertension or pre-hypertension</p> <p>Exclusion: Severe hypertension</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Walking</p> <p>Description: NR</p> <p>Form of Administration: Other: instructed to increase walking</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 2: Other: Salt Reduction</p> <p>Description: The goal was for subjects to reduce their daily salt intake to at least half of their previous intake.</p> <p>Form of Administration: Dietary</p> <p>Modification: NR</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 3: Other: Yoga</p> <p>Description: NR</p> <p>Form of Administration: Other: instructed to do yoga</p>	<p>Sodium measure: The 'questionnaire method'</p> <p>Best sodium measure recorded: No reference or explanation of 'questionnaire method'</p> <p>Sodium Status Intervention 1: NR</p> <p>Sodium Status Intervention 2: NR</p> <p>Sodium Status Intervention 3: NR</p> <p>How was blood pressure measured?</p> <p>Subjects blood pressure was measured using a mercury sphygmomanometer</p>	<p>Subgroup: Pre HTN and HTN</p> <p>Diastolic BP-NS</p> <p>Follow-Up Time: 8 weeks</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -2.50 (95% CI: -5.59 - 0.59)</p> <p>Systolic BP-NS</p> <p>Follow-Up Time: 8 weeks</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -2.90 (95% CI: -7.51 - 1.71)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 2 months Exposure to Follow Up Time: NR		
Sarkkinen, 2011 ¹¹¹ Location: Finland Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear	Study of: Adults N: 50 Participants: % Male: 61 Mean Age/Range/Age at Baseline: mean 54 (SD 11) Race: NR Systolic BP: 138 Diastolic BP: 88 Magnesium: 4.67 mmppl Calcium: NR Other Minerals: NR Mean BMI: 28 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Aged 25-75 years old, with SBP in the range of 130-159 mmHg and/or DBP in the range of 85-99 mmHg, BMI between 23 and 40 kg/m2 and a stable body weight Exclusion: Receiving antihypertensive drugs, non-steroidal antiinflammatory agents, cyclosporine or tacrolimus. Secondary hypertension, diabetes (type 1 or 2), a history of active heart disease or cancer, abnormal electrolytes, proteinuria, abnormal liver, kidney or thyroid function. Currently on a low-salt diet (six or less points in the salt intake test by the Finnish Heart Association, Helsinki). Subjects with alcohol abuse or drug abuse, pregnancy.	Intervention Type(s): Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: The aim was to replace approximately 60% of the regular sources of sodium with Smart Salt products. Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: Daily sodium intake in the Regular Salt arm was designed to stay at the same level as typical for that individual. Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 2 months Exposure to Follow Up Time: NR	Sodium measure: Single 24-hour urine analysis with validation, Food diaries without reported validation Best sodium measure recorded: 2 times, at baseline and at 2 months Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Intervention 1: 100 mmol Potassium measure: Food diaries without reported validation Best potassium measure recorded: 2 times, at baseline and at 2 months Potassium Status Intervention 1: 95 mmol How was blood pressure measured? BP measured using an automatic sphygmomanometer after 10 minutes rest in a sitting position. BP was measured three times with intervals of at least two minutes, between 7:00 am and 12:00 noon. The mean of the last records was used.	Subgroup: High normal Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -4.00 (95% CI: -8.09 - 0.09) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -6.00 (95% CI: -10.70 - -1.30) Decreased quality of life Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.40 (95% CI: 0.17 - 0.95)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Schorr, 1996¹¹²</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 16</p> <p>Intervention 1: % Male: 43.75 Mean Age/Range/Age at Baseline: 64.1 (SD 3.6) Race: NR Systolic BP: Day:136; night 121 Diastolic BP: Day: 83; Night: 68 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: normotensive, elderly, healthy, Exclusion: Hypertension, diabetes, CHF, abnormal renal or liver function</p>	<p>Intervention Type: Intervention 1: Other: Low Sodium Mineral Water Description: NR Form of Administration: Sodium supplement Dose: <.1 mmol/l Sodium consumed Na/K ratio: NR Magnesium: <.1 mmol/l Calcium: <.1 mmol/l Other Minerals: NR</p> <p>Comparator: Other: High sodium chloride mineral water Description: NR Form of Administration: NR Dose: 56.3 mmol/l sodium consumed Na/K ratio: NA Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: High Sodium bicarbonate Mineral Water Description: NR Form of Administration: NR Dose: 26.2 mmol/l sodium consumed Na/K ratio: NA Magnesium: 2.2 mmol/l Calcium: 3.1 mmol/l Other Minerals: NR</p> <p>Duration: 3 periods 4 weeks each Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, baseline, 1 week, 4 weeks Sodium, Method of Validation: 24 h urinary electrolyte excretion Sodium Status Intervention 1: 104.6 mmol/24h Sodium Status Comparator: 175.2 mmol/24h Potassium Status Comparator: NA</p> <p>How was blood pressure measured? Resting blood pressure (Dinamap 1846 SX; Criticon, Tampa, Florida, USA). Also, 24 hour ambulatory BP measurements (90297; SpaceLabs, Redmond, WA, USA). Measured at baseline, week 1, week 4.</p>	<p>Diastolic bp 24 hour ambulatory - daytime Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Intervention 2 MD 0.00 (95% CI: -4.90 - 4.90) Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -4.90 - 4.90) Systolic bp 24 hour ambulatory - daytime Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Intervention 2 MD -1.00 (95% CI: -9.67 - 7.67) Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -9.86 - 7.86)</p>
<p>Sciarrone, 1992¹¹³</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design</p>	<p>Study of: Adults N: 81</p> <p>Intervention 1: % Male: 50 Mean Age/Range/Age at Baseline: mean 51.4 Race: NR Systolic BP: 134.3 Diastolic BP: 83.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2</p>	<p>Intervention Type: Comparator: Other: Normal Sodium - Normal fat/normal fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium supplement Form of Administration: Sodium supplement Dose: 100 mmol NaCl/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Food diaries without reported validation Best sodium measure recorded: Measured 3 times in the screening phase and 5 times over the 8 week intervention Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Comparator: 136.2 mmol/24h Sodium Status Intervention 2: 58.1</p>	<p>Subgroup: HTN Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 3 vs Intervention 1 MD -1.80 (95% CI: -5.40 - 1.80) Comparison: Intervention 2 vs Comparator MD 0.70 (95% CI: -3.17 - 4.57) Systolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 3 vs Intervention 1</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>individual</p> <p>Number of Sites: multiple</p> <p>Study Years: 1987-1988</p>	<p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 68.4 Mean Age/Range/Age at Baseline: mean 53.4 Race: NR Systolic BP: 139 Diastolic BP: 83.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 82.3 Mean Age/Range/Age at Baseline: 54.9 Race: NR Systolic BP: 138.1 Diastolic BP: 82.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.5 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 52.3 Mean Age/Range/Age at Baseline: mean 54.2 Race: NR Systolic BP: 134.6 Diastolic BP: 82.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR</p>	<p>Intervention 2: Other: Low sodium - Normal fat/normal fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium placebo Form of Administration: Dietary Modification: Other: Placebo pill Dose: Placebo (10 lactose tablets per day) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Low Sodium - Low fat/high fibre Description: Diet with an aim of 60 mmol/day sodium intake plus placebo Form of Administration: Dietary Modification: Other: Placebo pill Dose: Placebo (10 lactose tablets per day) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Normal Sodium - Low fat/high fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium supplement Form of Administration: Salt substitute Dietary Modification: NR Dose: 100 mmol NaCl/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>mmol/24h Sodium Status Intervention 3: 53.1 mmol/24h Potassium measure: Food diaries without reported validation Best potassium measure recorded: Measured 3 times in the screening phase and 5 times over the 8 week intervention Potassium Status Comparator: 65.8 mmol/24h Potassium Status Intervention 2: 75.4 mmol/24h Potassium Status Intervention 3: 97.1 mmol/24h</p> <p>How was blood pressure measured? BP measurements taken at the same time of day for a given individual. Taken in a non-fasting state and subjects asked to not smoke, drink coffee or engage in vigorous exercise for 2 hours prior to measurement. A sohygmomanometer cuff appropriate for arm size was applied to the right arm. SBP, DBP were measured using a semi-automatic Dinamap 845XT oscillometric recorder. BP was measured at 2 min intervals for 20 min in the supine position then at 1-min intervals for 5 minutes after standing. Averages of 8 supine and 5 separate standing measures were taken. BP measured once every 2 weeks</p>	<p>MD -8.00 (95% CI: -13.54 - -2.46) Comparison: Intervention 2 vs Comparator MD -4.80 (95% CI: -9.98 - 0.38)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with history of Kidney stones: NR</p> <p>Inclusion: 20-69 years old, <120% ideal body weight, consumed <30 ml ethanol/24h and BP > 1330/80 mmHg (untreated) or 125/85 mmHg (treated)</p> <p>Exclusion: Cardiac failure, diabetes, kidney, liver or heart disease, taking NSAID medications</p>			
<p>Seals, 2001¹¹⁴</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 39</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 65 (SD 10) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 62 (SD 9) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: postmenopausal status (amenorrheic for at least two years and follicle stimulating hormone plasma concentrations .40 IU/l); >50 years of age, during sitting rest: SBP 130 to 159 mm Hg with diastolic BPDDBP<=99 mm Hg. No antihypertensive medications taken in the last two months; and a body mass index (BMI) < 35</p> <p>Exclusion: Other chronic disease, on a low-sodium</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Reduce sodium intake to <100 mmol/day Form of Administration: Dietary Modification: low sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Exercise Description: Exercise arm, no diet changes Form of Administration: Other: Exercise arm Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 3 months apart Sodium Status Intervention 1: 86 mmol/day</p> <p>How was blood pressure measured? BP measured at rest in the upright seated position between 7 and 11 AM after an overnight fast. Recordings were obtained in triplicate in three separate sessions at least one week apart in order to establish the stable readings</p>	<p>Subgroup: Women Diastolic BP-24H AMB Follow-Up Time: 13 weeks Comparison: Intervention 1 vs Comparator MD -2.11 (95% CI: -4.99 - 0.77) Systolic BP-24H AMB Follow-Up Time: 13 weeks Comparison: Intervention 1 vs Comparator MD -7.11 (95% CI: -11.82 - -2.40)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	diet, performed regular exercise during the preceding two years, smoking			
Siani, 1987 ¹¹⁵ Location: Italy Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear	<p>Study of: Adults N: 37</p> <p>Intervention 1: % Male: 61% Mean Age/Range/Age at Baseline: mean 45 (SD 2) Race: NR Systolic BP: 144 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 63.1 Mean Age/Range/Age at Baseline: mean 45 (SD 2) Race: NR Systolic BP: 14 Diastolic BP: 91 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: mild hypertension Exclusion: Possibility that patient has secondary hypertension, or any associated illness or severe complication of the hypertensive disease</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 48 mmol potassium daily Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3.75 months Exposure to Follow Up Time: NR</p>	<p>Sodium, Method of Validation: Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 189 mmol/24 h Best potassium measure recorded: 2 times 15 weeks apart (baseline, end of follow up) Potassium, Method of Validation: Pill counting Potassium Status Intervention 1: 87 mmol/24 h</p> <p>How was blood pressure measured? BP measured 7 times, 1 week apart during baseline, 3 weeks apart during intervention. BP was taken by a single observer, blinded to treatment status, using a Hawksley random zero sphygmomanometer. After quietly resting for 30 minutes in the supine position the SBP (phase V Korotkoff sounds) was measured three times two minutes apart; the same measurements were taken after the patient had been standing upright for two minutes. The average of each measurement in each position for all the patients was used for analysis.</p>	<p>Subgroup: Mild HTN Diastolic BP-supine Follow-Up Time: 15 weeks Comparison: Intervention 1 vs Comparator MD -10.50 (95% CI: -16.32 - -4.68) Systolic BP-supine Follow-Up Time: 15 weeks Comparison: Intervention 1 vs Comparator MD -14.00 (95% CI: -21.78 - -6.22)</p>
Siani, 1991 ¹¹⁶ Location: NR Setting: Community Design: Randomized,	<p>Study of: Adults N: 54</p> <p>Intervention 1: % Male: 57.7 Mean Age/Range/Age at Baseline: mean 48.8 (SD 7.8) Race: NR Systolic BP: 138.2 Diastolic BP: 81.1</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: Dietary advice to selectively increase potassium intake Form of Administration: Oral potassium supplement Dose: NR Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 2 times in run in then monthly over 12 months follow up Sodium, Method of Validation: Assessment of the reliability of urine collection was done by interviewing the patient and by</p>	<p>Subgroup: HTN under control Diastolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 1.10 (95% CI: 0.11 - 2.09) Percent of baseline drug consumption Follow-Up Time: 12 months Comparison: Intervention 1 vs</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
parallel Number of Sites: multiple Study Years: unclear	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 52.3 Mean Age/Range/Age at Baseline: mean 49.3 (SD 9.4) Race: NR Systolic BP: 138.3 Diastolic BP: 80.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: BP under good pharmacologic control, aged 30-65 years and a BP below 160/95 mm Hg at the last two clinic visits. Exclusion: Secondary hypertension, ischemic heart or brain disease, renal failure, any illness requiring adherence to a strict dietary regimen (e.g. diabetes mellitus or obesity). Use of oral contraceptives; poor compliance with their prescribed drug regimen.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>measuring 24-hour creatinine excretion., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 163 mmol/24h Best potassium measure recorded: 2 times in run in then monthly over 12 months follow up Potassium, Method of Validation: Assessment of the reliability of urine collection was done by interviewing the patient and by measuring 24-hour creatinine excretion. Potassium Status Intervention 1: 73 mmol/24h</p> <p>How was blood pressure measured? Blood pressure measured by an operator who was blinded to the patient's assigned treatment. Measurements taken using a Sentron automatic oscillometric recorder. Patients first rested for 10 minutes in the supine position in a quiet and comfortable room. SBP and DBP were measured three times at 2-minute intervals; the average of all measurements was used in the analysis.</p>	<p>Comparator RR 2.50 (95% CI: 1.16 - 5.39) Systolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 3.40 (95% CI: 2.11 - 4.69)</p>
Silman, 1983 ¹¹⁷ Location: UK Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear	<p>Study of: Adults N: 28</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 165.3 Diastolic BP: 158.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: Taught to take a diet with 100 mmol sodium per day Form of Administration: Dietary Modification: Instructed to take a diet that contained 100 mmol sodium per day, as well as general healthy dietary advice Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Advised regarding regular</p>	<p>Sodium measure: First-morning urine specimens and two-day diet records Best sodium measure recorded: Taken 5 times, at 0,1,3,6 and 12 months Sodium Status Intervention 1: 117 mmol/24h Potassium measure: First-morning urine specimens and two-day diet records Best potassium measure recorded: Taken 5 times, at 0,1,3,6 and 12 months Potassium Status Intervention 1: 60.8</p>	<p>Subgroup: HTN Diastolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -6.30 (95% CI: -15.12 - 2.52) Systolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -8.70 (95% CI: -29.16 - 11.76)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 160.5 Diastolic BP: 98.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients who were between 50 and 64 years old from 2 general practices got screened for BP. If DBP was between 95 and 104 mm Hg (fifth diastolic sound, average of two readings at 5 minute intervals) .they were rescreened 12 months later, and if their DBP was in the same range and remained so for a further 1 month, they were included.</p>	<p>healthy eating habits Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured? BP was measured in a standardized manner with a random zero sphygmomanometer by the same observer.</p>	
<p>Sinaiko, 1993¹¹⁸; Gomez-Marin, 1991¹¹⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1986-1987</p>	<p>Study of: Children N: 210</p> <p>Intervention 1: % Male: 50 Mean Age/Range/Age at Baseline: 13.2 Race: NR Systolic BP: 113.6 Diastolic BP: 63.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.5 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 52 Mean Age/Range/Age at Baseline: mean 13.3 (SD 0.1) Race: NR Systolic BP: 114.2 Diastolic BP: 66.6 Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Reduce sodium intake to 70 mmol/day Form of Administration: Dietary Modification: Trained nutritionists instructed patients on how to reduce dietary sodium Dose: NR Na/K ratio: Boys: 2.9 ; Girls: 2.7 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 1 mmol/kg body weight potassium chloride per 24 hours (Max 80 mmol per 24 hours) administered in capsules Na/K ratio: Boys:2.1 mmol/24h; Girls: 2.2</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart Sodium, Method of Validation: Pill counts, Single 24-hour urine analysis with validation Sodium Status Intervention 1: Boys: 162 mmol/24h; Girls: 119 mmol/24h Sodium Status Intervention 2: Boys: 176 mmol/24h; Girls: 173 mmol/24h Best potassium measure recorded: 3 times, 1 year apart Potassium, Method of Validation: Pill counts Potassium Status Intervention 1: Boys: 64 mmol/24h; Girls: 49 mmol/24h Potassium Status Intervention 2: Boys: 100 mmol/24h; Girls: 93 mmol/24h</p> <p>How was blood pressure measured? Measured two times on the right arm and with the student in the</p>	<p>Subgroup: Girls Rate of increase in diastolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.70 (95% CI: -3.09 - -0.31) Comparison: Intervention 2 vs Comparator MD -0.90 (95% CI: -2.29 - 0.49) Rate of increase in systolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.90 (95% CI: -3.01 - -0.79) Comparison: Intervention 2 vs Comparator MD -0.90 (95% CI: -2.01 - 0.21)</p> <p>Subgroup: Boys Rate of increase in diastolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -3.48 - 0.68) Comparison: Intervention 2 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Calcium: NR Other Minerals: NR Mean BMI: 22.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 51 Mean Age/Range/Age at Baseline: mean 13.4 (SD .01) Race: NR Systolic BP: 113.7 Diastolic BP: 65.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Blood pressure at rescreening was > 109 mm Hg for boys and 108 mm Hg for girls Exclusion: SBP>=140/DBP>=90 on average, DBP>100 on any visit, history of renal disease with significant hematuria or proteinuria, or serum creatinine>1.5 mg/dl. Hypokalemia, chronic system illness, compliance issues</p>	<p>mmol/24h Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Participants asked not to change their usual diet Form of Administration: Placebo Dose: placebo capsules same shape and color as the potassium chloride Na/K ratio: Boys: 3; Girls 3.5 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>seated position by trained personnel using a standard clinical sphygmomanometer (following a standardized protocol). Blood pressure was measured every 3 months for 3 years.</p>	<p>MD -1.60 (95% CI: -3.54 - 0.34) Rate of increase in systolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD 0.60 (95% CI: -0.65 - 1.85) Comparison: Intervention 2 vs Comparator MD 0.30 (95% CI: -0.81 - 1.41)</p>
<p>Singer, 1991¹²⁰ Location: UK Setting: Community Design: Randomized Cross-over individual Number of Sites: 1 Crossover: Length of washout period: 0 days</p>	<p>Study of: Adults N: 21</p> <p>Participants: % Male: 62 Mean Age/Range/Age at Baseline: 53.9+/-2.5 Race: 71% white; 29% black Systolic BP: 158+/-5 Diastolic BP: 100+/-2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Sodium restriction diet + slow sodium placebo tablets to achieve low sodium diet Form of Administration: Other: Low sodium diet + placebo salt pills Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake Description: Usual sodium intake achieved</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 2 consecutive 24-hour urine samples Sodium, Method of Validation: creatinine, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 104+/-11 mmol Best potassium measure recorded: 2 consecutive 24-hour urine samples Potassium, Method of Validation: NR Potassium Status Intervention 1: 66+/-3 mmol/d</p> <p>How was blood pressure measured? Supine and standing blood pressure measured every 2 weeks under</p>	<p>Subgroup: Hypertensives Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -4.13 - -1.87) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -9.00 (95% CI: -10.70 - -7.30)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: NR	Inclusion: Essential, uncomplicated hypertension, treated with captopril (50 mg twice daily) and hydrochlorothiazide (25 mg once daily) for at least 1 month before study entry Exclusion: ischemic heart disease; cerebrovascular disease; renal or hepatic impairment; and diabetes mellitus; or receiving any additional treatment	via sodium restriction + slow sodium tablets Form of Administration: Sodium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: NR Exposure to Follow Up Time: NR	identical conditions with semiautomatic ultrasound sphygmomanometers	
Steegers, 1991 ¹²¹ Location: Netherlands Setting: Community Design: Randomized, parallel Number of Sites: 1 Study Years: unclear	Study of: Adults N: 42 Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 27 (Range: 20-34) Race: NR Systolic BP: 122 Diastolic BP: 71 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 69.4 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 27 (Range: 22-35) Race: NR Systolic BP: 125 Diastolic BP: 72 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 65.8 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: nulliparous healthy women with singleton pregnancies	Intervention Type(s): Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Target of 20 mmol sodium daily Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: Continue unrestricted dietary intake Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 5-6 months Exposure to Follow Up Time: NR	Sodium measure: Single 24-hour urine analysis with validation, Food diaries with reported validation Best sodium measure recorded: Measured at 12, 16, 20, 24, 28, 32 and 36 weeks of gestation and then at 1 and 6 weeks postpartum Sodium Status Intervention 1: 58 mmol/24h How was blood pressure measured? BP was measured after patients rested for 5 minutes in a sitting position with an automatic microcomputer assisted instrument (Dinamap).	Diastolic BP-sitting Follow-Up Time: 22 weeks Comparison: Intervention 1 vs Comparator MD 2.00 (95% CI: -3.54 - 7.54) Systolic BP-sitting Follow-Up Time: 22 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -7.93 - 5.93)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sundar, 1985¹²²</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 50</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 164.1 Diastolic BP: 102.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 63.4 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 164.3 Diastolic BP: 102.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 60 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild to moderate essential hypertension Exclusion: Any complications of hypertension, impaired renal function or any other illness</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: Patients given 126 tabs containing 6.47 mEq potassium for 14 days (3 tabs per day) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 5 times 1 weeks apart Sodium Status Intervention 1: 96.6 mEq/L Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 5 times 1 weeks apart Potassium Status Intervention 1: 81.08 mEq/L</p> <p>How was blood pressure measured? Basal supine BP measured on the right arm measured 3 times by the same observer.</p>	<p>Subgroup: Mild-moderate HTN Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -7.40 - 1.00) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -11.30 (95% CI: -22.95 - 0.35)</p>
<p>Suppa, 1988¹²³</p> <p>Location: Italy</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 32</p>	<p>Study of: Adults N: 322</p> <p>Intervention 1: % Male: 64 Mean Age/Range/Age at Baseline: mean 47.1 (SD 9.8) Race: NR Systolic BP: 149.2 Diastolic BP: 93.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: 193.2 Form of Administration: Oral potassium supplement Dose: Twice daily 2-g packets of diet salt (%50 NaCl, 25% KCl, 15% K3C6H5O7) Na/K ratio: NR Magnesium: NR Calcium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times 2 weeks apart Sodium, Method of Validation: 24 hour urinary excretion was considered correct when urinary creatinine was >900 mg/24h in women and >1000 mg/24h in men., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 77.4 Best potassium measure recorded: 3</p>	<p>Subgroup: HTN on antihypertensive Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.02 - 0.02) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.46 - 0.06)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: unclear	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 61 Mean Age/Range/Age at Baseline: mean 47.8 (SD 10.1) Race: NR Systolic BP: 159 Diastolic BP: 93.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: SBP >=95 Exclusion: Contraindications to beta blockers, women of childbearing potential, individuals with secondary hypertension, renal failure, or other major diseases.</p>	<p>Other Minerals: NR</p> <p>Comparator: Other: Regular salt Description: NR Form of Administration: Regular Salt Dose: Twice daily 2-g packets of regular salt (100% NaCl) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>times 2 weeks apart Potassium, Method of Validation: 24 hour urinary excretion was considered correct when urinary creatinine was >900 mg/24h in women and >1000 mg/24h in men.</p> <p>How was blood pressure measured? Measured by standard mercury sphygmomanometer as per WHO guidelines. The first and fifth Korotkoff phases were used for SBP and DBP respectively.</p>	
<p>Svetkey, 1987¹²⁴</p> <p>Location: US</p> <p>Setting:</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 116</p> <p>Intervention 1: % Male: 76 Mean Age/Range/Age at Baseline: mean 51.3 (SD 12.3) Race: white 89% Systolic BP: 147.5 Diastolic BP: 95.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 83.8 (SD 14.4) kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 72 Mean Age/Range/Age at Baseline: mean 50.9 (SD 12.3)</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: NR Dose: 120 mEq/ day potassium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Usual diet, placebo Form of Administration: NR Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium Status Intervention 1: NR Potassium measure: Compliance assessed by pill count Best potassium measure recorded: 0 Potassium, Method of Validation: Compliance assessed by pill count. Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? Measured 2-4 times, weekly during run in, 4 times every 2 weeks during trial. During each visit, three blood pressure measurements were recorded and the average value was considered to be the blood pressure for that day. BP measurements taken at the same time of day and by the same staff. using a random zero sphygmomanometer (Hawksley and Sons, Lancing, Sussex, England) where the subject was seated for 10 minutes before</p>	<p>Subgroup: Mild HTN Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -2.50 (95% CI: -5.39 - 0.39) Lethargy Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 1.04 (95% CI: 0.07 - 16.16) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -6.29 (95% CI: -11.50 - -1.08) Decreased quality of life Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.68 (95% CI: 0.43 - 1.06)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: White 83% Systolic BP: 142.1 Diastolic BP: 147.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 81.7 (SD 11.9) Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ambulatory hypertensive adults Exclusion: history or physical examination revealed any of : a single DBP> 114 mm Hg, prior episode of malignant hypertension or hypertensive encephalopathy, angina, myocardial infarction within the prior 6 months, CHF, arrhythmia, transient ischemic, cerebrovascular accident, attacks, the presence of a terminal illness. Secondary hypertension excluded by physical examination, history, serum electrolyte levels, and measurements of renal function (plasma creatinine concentration, creatinine clearance, and complete urinalysis). Patients who might be at risk from high potassium intake were also excluded: those with renal insufficiency or baseline serum potassium values > 5.0 mEq/L, patients taking digitalis preparations, and those with chronic diarrhea or history of ulcer disease. Pregnant and nursing women.</p>		<p>the readings. DBP was recorded as the fifth Korotkoff sound. Patients were advised not to smoke or eat for 30 minutes before each blood pressure reading.</p>	
<p>Takahashi, 2006¹²⁵</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: 1998-2000</p>	<p>Study of: Adults N: 448</p> <p>Intervention 1: % Male: 31.7 Mean Age/Range/Age at Baseline: mean 56.3 (95% CI 41.2 - 71.4) Race: NR Systolic BP: 127.9 Diastolic BP: 75.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: 23.7 % with history of CVD: NR % with Type 2 diabetes: 3.6 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator:</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Reduce sodium intake to less than 8 and 10 g/day in women and men, respectively Form of Administration: Dietary Modification: Two individual 15-min diet counseling sessions, a group class, and two newsletters Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Not asked to change diet Form of Administration: Usual diet</p>	<p>Sodium measure: Validated dietary questionnaire and 48 hour urine analysis Best sodium measure recorded: Collected two times 1 year apart. Collected two times 1 year apart. For calculating 24 hour urine, samples were analyzed using a flame photometry and creatinine by Jaffe's procedure with an autoanalyzer. The expected intakes were calculated using observed urinary excretion, as reported in a carefully designed balance study. Sodium Status Intervention 1: 199 mmol/day Potassium measure: Validated dietary questionnaire and 48 hour urine analysis Best potassium measure recorded: Collected two times 1 year apart.</p>	<p>Diastolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -0.70 (95% CI: -2.64 - 1.24) Systolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -5.82 - -0.58)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% Male: 33 Mean Age/Range/Age at Baseline: mean 56.4 (95% CI 40.5-72.4) Race: NR Systolic BP: 128 Diastolic BP: 76.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.2 % with Hypertension: 24.1 % with history of CVD: NR % with Type 2 diabetes: 3.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 40–69 years, physician permission to participate for those under medical treatment or dietary control.</p>	<p>Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>For calculating 24 hour urine, samples were analyzed using a flame photometry and creatinine by Jaffe's procedure with an autoanalyzer. The expected intakes were calculated using observed urinary excretion, as reported in a carefully designed balance study. Potassium Status Intervention 1: 59 mmol/day</p> <p>How was blood pressure measured? BP measured by a trained nurse, using sphygmomanometer OKOSE- 300 model based on a common protocol. A single measurement was used.</p>	
<p>The Trials of Hypertension Prevention Collaborative Research Group, 1992¹²⁶; Erratum, 1992¹²⁷; Satterfield, 1991¹²⁸; Whelton, 1992¹²⁹; Whelton, 1997¹³⁰; He, 1999¹³¹; Kumanyika, 1993¹³²; Whelton, 1994¹³³; Cook, 2007⁵⁷; Cook, 1998¹³⁴; Yamamoto, 1995¹³⁵; Cook, 2016⁶²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized,</p>	<p>Study of: Adults N: 744</p> <p>Intervention 1: % Male: 70.9 Mean Age/Range/Age at Baseline: mean 43.4 (SD 6.6) Race: 78 Systolic BP: 124.8 Diastolic BP: 83.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.7 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 69.7 Mean Age/Range/Age at Baseline: mean 43.1 (SD 6.6) Race: 84 Systolic BP: 122.6 Diastolic BP: 81.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 83.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: Life-style interventions, provided by psychologists, nutritionists, or other experienced counselors, mostly group educational sessions, with some individual counseling Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Other: placebo Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Intervention 1: 99.4 mmol/24 h Sodium Status Intervention 2: NR Sodium Status Intervention 3: NR Best potassium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Potassium Status Intervention 1: NR Potassium Status Intervention 2: Change from baseline -2.4 mmol/24 h Potassium Status Intervention 3: Change from baseline 37.4 mmol/24h</p> <p>How was blood pressure measured? Collected at 0, 3, 6, months, 12 and 18 months for lifestyle groups. BP was measured with a Hawksley random-zero sphygmomanometer, after sitting at rest for 5 minutes . The average of three readings (first</p>	<p>Subgroup: TOHP-1 CVD disease (myocardial infarction, stroke, revascularisation, or death due to cardiovascular causes) Follow-Up Time: 15 years Comparison: Intervention 1 vs Comparator RR 1.40 (95% CI: 0.80 - 2.46) Total mortality Follow-Up Time: Comparison: Intervention 1 vs Comparator RR 1.05 (95% CI: 0.68 - 1.60) Follow-Up Time: 15 years Comparison: Intervention 1 vs Comparator RR 1.10 (95% CI: 0.49 - 2.44)</p> <p>Cumulative incidence of HTN Follow-Up Time: 7 years Comparison: Intervention 1 vs Comparator RR 1.47 (95% CI: 2.63 - 0.82) Diastolic BP-sitting Follow-Up Time: 7 years Comparison: Intervention 1 vs Comparator MD 0.45 (95% CI: -2.35 - 0.21) Systolic BP-sitting Follow-Up Time: 7 years Comparison: Intervention 1 vs</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>parallel</p> <p>Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p> <p>Number of Sites: 10</p> <p>Study Years: 1987-1995 (2013 follow-up)</p>	<p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 74.7 Mean Age/Range/Age at Baseline: mean 42.8 (SD 6.5) Race: white 88.8% Systolic BP: 120.7 Diastolic BP: 80.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 81.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 71.7 Mean Age/Range/Age at Baseline: mean 42.6 (SD 6.5) Race: white 76.5% Systolic BP: 125.1 Diastolic BP: 83.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Healthy adults, ages 30-54 with high normal DBP, not taking antihypertensive drugs for the prior 2 months Exclusion: Clinical or lab evidence of cardiovascular or other disabling or life threatening diseases. Conditions that would contraindicate or require any of the interventions. Unwillingness or inability to comply with data collection or intervention procedures.</p>	<p>Dose: potassium chloride, 60 mmol/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: Lifestyle intervention 18 months; Nutritional supplement 6 months Exposure to Follow Up Time: NR</p>	<p>and fifth Korotkoffs sounds) were recorded at each visit.</p>	<p>Comparator MD 0.26 (95% CI: -3.22 - 0.13)</p>
<p>Todd, 2012¹³⁶</p> <p>Location: New Zealand</p> <p>Setting: Community</p>	<p>Study of: Adults N: 23</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR</p>	<p>Intervention Type: Intervention 1: Other: Dietary sodium - low Description: NR Form of Administration: Sodium supplement Dose: Dietary sodium 60 mmol/day Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: 8h urine no mention of equation Best sodium measure recorded: collected at weeks 0 and 4 Sodium, Method of Validation: compliance assessed by dietary diaries, urinary electrolytes and plasma LF</p>	<p>Diastolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD 0.40 (95% CI: -2.10 - 2.90) Comparison: Intervention 1 vs Intervention 2 MD 1.40 (95% CI: -0.50 - 3.30)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Absence of pre-hypertension or hypertension (i.e SBP >130 mmHg and DBP >85 mmHg or current treatment with antihypertensive therapy); ages 20-65 years; non-smokers; BMI <30 (kg/m²); no history of cardiovascular disease, diabetes or renal disease.</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Dietary sodium - medium Description: NR Form of Administration: Sodium supplement Dose: Dietary sodium 150 mmol/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Dietary sodium - medium Description: NR Form of Administration: Sodium supplement Dose: dietary sodium 200–250 mmol/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium Status Intervention 1: Urinary Na : Cr ratio 10.2 Sodium Status Intervention 2: Urinary Na : Cr ratio 18.4</p> <p>How was blood pressure measured? BP measured at the clinic with a calibrated digital blood pressure monitor at screening and at weeks 0, 1, 2 and 4 of each intervention period. The patients were seated for 5 min at rest before a minimum of four blood pressure readings were taken over a 10 min period. The first reading was not used, and the subsequent three readings were averaged.</p>	<p>Comparison: Intervention 2 vs Comparator MD 1.00 (95% CI: 0.30 - 1.70) Systolic bp Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD 0.10 (95% CI: -3.40 - 3.60) Comparison: Intervention 1 vs Intervention 2 MD -0.80 (95% CI: -3.30 - 1.70) Comparison: Intervention 2 vs Comparator MD -1.00 (95% CI: -6.70 - 4.70)</p>
<p>Todd, 2010¹³⁷</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 35</p> <p>Intervention 1: % Male: 38 Mean Age/Range/Age at Baseline: mean 51.8 (SD 7.6) Race: European: 97%; Indian/Asian: 3%</p> <p>Systolic BP: 134 Diastolic BP: 7.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.7 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR</p>	<p>Intervention Type: Intervention 1: Other: No Sodium Tomato Juice Description: NR Form of Administration: Dietary Modification: NR Dose: consumption of 500 mL tomato juice/d with 0 mmol sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: 90 mmol sodium - Tomato Juice Description: NR Form of Administration: Dietary Modification: NR Dose: consumption of 500 mL tomato juice/d with 90 mmol sodium Na/K ratio: NR Magnesium: NR Calcium: NR</p>	<p>Sodium measure: Partial or spot urine without validated prediction equation Best sodium measure recorded: Collected at entry, and at weeks 0 and 4 of intervention Sodium Status Intervention 1: 7.6 sodium:creatinine Sodium Status Comparator: 11.8 sodium:creatinine</p> <p>How was blood pressure measured? BP was measured with a calibrated digital BP monitor during screening and at weeks 0, 1, 2, and 4 of each intervention. Participants sat for 5 min to rest before 4 BP readings were taken over a 10-min period. The first reading was discarded, and the mean of the subsequent 3 readings were used.</p>	<p>Diastolic BP Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Intervention 2 MD -5.60 (95% CI: -8.50 - -2.70) Comparison: Intervention 1 vs Comparator MD -3.30 (95% CI: -5.10 - -1.50) Systolic BP Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Intervention 2 MD -4.40 (95% CI: -7.60 - -1.20) Comparison: Intervention 1 vs Comparator MD -2.40 (95% CI: -4.00 - -0.80)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Prehypertension or hypertension, ages 20-65 years, nonsmoker, BMI<30, no history of cardiovascular disease, diabetes, or renal disease.</p>	<p>Other Minerals: NR</p> <p>Comparator: Other: 140 mmol sodium - Tomato Juice Description: NR Form of Administration: Dietary Modification: NR Dose: consumption of 500 mL tomato juice/d with 140 mmol sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>		
<p>Tuthill, 1985¹³⁸ Location: US Setting: Community Design: Randomized, parallel Study Name: The Massachusetts Blood Pressure Study, Part 4 Number of Sites: 2 Study Years: unclear</p>	<p>Study of: Children N: 65</p> <p>Intervention 1: % Male: 0 Race: NR Mean Age/Range/Age at Baseline: NR Systolic BP: 113 Diastolic BP: 71 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.9 Diastolic BP: 71.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Placebo - Campus 1 Description: NR Form of Administration: Placebo Dose: Placebo tablet twice daily Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Salt pill in evening - Campus 1 Description: NR Form of Administration: Salt substitute Dose: 0.8 gram salt pill in the evening, placebo in morning Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Salt pill in morning - Campus 1 Description: NR Form of Administration: Sodium supplement Dose: 0.8 gram salt pill in the morning, placebo in evening Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Placebo - Campus 2</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 2 times at baseline, then 8 times 1 week apart Sodium, Method of Validation: Study pills were swallowed in the presence of a research staff member, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: +250 mg compared to baseline Sodium Status Intervention 3: +550 mg change from baseline Sodium Status Comparator 1: +650 mg change from baseline Sodium Status Intervention 2: -50 mg change from baseline Sodium Status Intervention 4: +450 mg change from baseline Sodium Status Comparator 2: +800 mg compared to baseline Best potassium measure recorded: 2 times at baseline, then 8 times 1 week apart</p> <p>How was blood pressure measured? BP was measured by two technicians who were blind to each other's readings and also to the girls intervention status</p>	<p>Subgroup: Girls Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Intervention 5 MD -0.79 (95% CI: NC - NC) Comparison: Intervention 2 vs Arm 8 MD -2.70 (95% CI: NC - NC) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Intervention 5 MD 0.76 (95% CI: NC - NC) Comparison: Intervention 2 vs Arm 8 MD -0.64 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Comparator 1: NR % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.4 Diastolic BP: 70.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.1 Diastolic BP: 69.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 4: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 112.4 Diastolic BP: 68.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 0 Mean Age/Range/Age at Baseline: NR</p>	<p>Description: NR Form of Administration: Other: placebo Dose: Placebo tablet twice daily Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Other: Salt pill in evening - Campus 2 Description: NR Form of Administration: NR Dose: 0.8 gram salt pill in the evening, placebo in morning Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Salt pill in morning - Campus 2 Description: NR Form of Administration: Sodium supplement Dose: 0.8 gram salt pill in the morning, placebo in evening Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>		

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: NR Systolic BP: 111.7 Diastolic BP: 69.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Young females in grades 9-12 Exclusion: One or more of the three consulting physicians considered the student at medical risk if exposed to extra dietary salt. A medical condition, or taking medication which might affect their blood pressure.</p>			
<p>Van Buul, 1997¹³⁹</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: 1986-1993</p>	<p>Study of: Adults N: 270</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 28.1 (min 19.8, max 41.3) Race: NR Systolic BP: 120 Diastolic BP: 65 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 28.3 (min 18.1, max 40.5) Race: NR Systolic BP: 121 Diastolic BP: 68 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.5 % with Hypertension: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Diet containing about 20 mmol/day of sodium Form of Administration: Dietary Modification: Trained dietitians gave oral and written dietary instructions as well as guidance throughout pregnancy Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No dietary restrictions Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: 1.5 months</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 11 times over 8.5 months Sodium Status Intervention 1: 75 mmol /24 h</p> <p>How was blood pressure measured? After resting for 5-min, BP was measured in the sitting position using an automatic device (Dinamap 1846 SX, Critikon Inc, Tampa, FL) with an adequately sized cuff. The average of 2 measurements was used for analysis. BP was taken a 9 times over the study period</p>	<p>Diastolic BP-sitting Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.53 - 0.53) Incidence of gestation hypertension Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator RR 0.95 (95% CI: 0.50 - 1.81) Systolic BP-sitting Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -6.54 - 0.54)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Women with healthy nulliparous pregnant woman with singleton pregnancies were considered Exclusion: Preexisting hypertension, diabetes mellitus, cardiovascular disorder, renal diseases.</p>			
<p>Vongpatanasin, 2016¹⁴⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: >=7 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 30</p> <p>Participants: % Male: 47 Mean Age/Range/Age at Baseline: mean 54 (SD 12) Race: black 40% Systolic BP: 125 Diastolic BP: 81 Magnesium: 2.2 mg/dl Calcium: 9.5 mg/dl Other Minerals: NR Mean BMI: 31</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Prehypertension or stage I hypertension. SBP between 120 and 159 mm Hg, and DBP 80 - 99 mm Hg. No history of: diabetes mellitus renal impairment (serum creatinine > 1.4 mg/dl), active cardiac or liver disease, esophageal-gastric ulcer, gastroesophageal reflux disease, chronic diarrhea, chronic nonsteroidal anti-inflammatory drug use, treatment with diuretics, renal tubular acidosis, hypocalcemia, or hypercalcemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Potassium Chloride Description: NR Form of Administration: Oral potassium supplement Dose: 40 meq KCl powder/day Na/K ratio: NR Magnesium: 104 mg/day Calcium: 160 mg/day Other Minerals: NR</p> <p>Intervention 2: Other: Potassium Citrate Description: NR Form of Administration: Oral potassium supplement Dose: 40 meq K3Cit powder/day diluted in water Na/K ratio: NR Magnesium: 100 mg/day Calcium: 148 mg/day Other Minerals: NR</p> <p>Intervention 3: Other: Potassium Magnesium Citrate Description: NR Form of Administration: Oral potassium supplement Dose: KMgCit, 40 meq K, 20 meq Mg, 74 meq citrate powder/day Na/K ratio: NR Magnesium: 121 mg/day Calcium: 158 mg/day Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: Placebo Na/K ratio: NR Magnesium: 97 mg/day Calcium: 181 mg/day</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Collected during the last week of treatment Sodium, Method of Validation: creatinine, Composition of potassium supplement with intervention/exposure adherence measure Sodium Status Intervention 1: 184 meq/day Sodium Status Intervention 2: 190 meq/day Sodium Status Intervention 3: 187 meq/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Collected during the last week of treatment Potassium Status Intervention 1: 58 meq/day Potassium Status Intervention 2: 84 meq/day Potassium Status Intervention 3: 91 meq/day</p> <p>How was blood pressure measured? At each visit, BP was taken by nursing staff with the same validated oscillometric device, after the patient had been in rest quietly for 5 minutes. Four BP measurement during a single visit was repeated 3 times 1 minute apart, and the mean was taken.</p>	<p>Subgroup: Hypertensives and prehypertensives 24 hr diastolic BP Follow-Up Time: 4 weeks Comparison: Intervention 3 vs Comparator MD -1.00 (95% CI: -4.77 - 2.77) Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -5.63 - 1.63) Comparison: Intervention 2 vs Comparator MD -2.00 (95% CI: -5.63 - 1.63) 24 hr systolic BP Follow-Up Time: 4 weeks Comparison: Intervention 3 vs Comparator MD -2.00 (95% CI: -6.34 - 2.34) Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -7.13 - 1.13) Comparison: Intervention 2 vs Comparator MD -2.00 (95% CI: -6.22 - 2.22)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Other Minerals: NR Duration: 4 periods of 4 weeks each Exposure to Follow Up Time: 0 months		
Weir, 2010 ¹⁴¹ Location: US Setting: Community Design: Randomized Cross-over individual Number of Sites: Multiple Crossover: Length of washout period: 0 days Study Years: NR	Study of: Adults N: 132 Intervention 1: % Male: 55 Mean Age/Range/Age at Baseline: 51.5+/-7.4 Race: 86% white; 11% black; 2% Asian; 1% Hispanic Systolic BP: 138.9+/-8.4 Diastolic BP: 87.1+/-7.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.4+/-2.8 % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: 18 to 60 years of age; provision of written informed consent; mean daytime SBP at screening 135 mm Hg and <160 mm Hg, and use of acceptable form of contraception for women of childbearing potential. Exclusion: secondary hypertension, history of myocardial infarction, or heart failure within the preceding 6 months, unstable angina pectoris, second- or third-degree heart block, clinically significant arrhythmias or use of antiarrhythmic drugs (including digoxin), clinically significant valvular heart disease, diabetes mellitus, estimated glomerular filtration rate <60 mL/min per 1.73 m ² , body mass index (BMI) >30	Intervention Type: Intervention 1: Usual Diet Description: To achieve dietary sodium >200 mmol/d sodium Form of Administration: Dietary Modification: low sodium diet, not described Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To achieve sodium status <=100 mmol/d Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 4 weeks Exposure to Follow Up Time: 0 months	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, at baseline and at the end of each treatment period Sodium, Method of Validation: Creatinine Sodium Status Intervention 1: 207.6 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8 Potassium, Method of Validation: NR Potassium Status Intervention 1: NR How was blood pressure measured? calibrated standard mercury sphygmomanometers and the recommended cuff sizes in accordance with the 1988 American Heart Association Committee Report on Blood Pressure Determination; Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8.	Subgroup: Hypertensives Diastolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -6.90 - -4.40) Systolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -9.40 (95% CI: -11.40 - -7.50)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	kg/m2, use of a-blockers or >2 antihypertensive agents, pregnancy or lactation, or history of malignancy within the past 5 years			
<p>Whelton, 1998¹⁴²; Appel, 2001¹⁴³;</p> <p>Espeland, 1999¹⁴⁴;</p> <p>Banson, 1997¹⁴⁵; Appel, 1995¹⁴⁶;</p> <p>Kostis, 1998¹⁴⁷;</p> <p>Whelton, 1997¹⁴⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p> <p>Number of Sites: 4</p> <p>Study Years: 1992-1995</p>	<p>Study of: Adults N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health, independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: Dietary Modification: Nutritionists conducted small group and individual meetings to advise patients on ways to change eating patterns Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: NR Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records</p>	<p>Angina Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.88 (95% CI: 0.85 - 4.17) CVD(Stroke, Transient ischemic attack, MI, Arrythmia, Congestive heart failure, Angina, Other) Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.27 (95% CI: 0.85 - 1.92) Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -3.19 - -0.81) Dizziness Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 0.62 (95% CI: 0.33 - 1.17) MI Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.99 (95% CI: 0.37 - 10.81) Percent free of elevated BP Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.60 (95% CI: 1.29 - 1.98) Stroke Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.99 (95% CI: 0.18 - 21.89) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -5.93 - -2.47)</p>
Whitten, 1980 ¹⁴⁹	Study of: Children N: 27	Intervention Type: Intervention 1: Other: Low salt group	Sodium measure: 72 hour urine analysis	Subgroup: Black male infants Diastolic BP-sitting

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: NR Race: black: 100% Systolic BP: 97 Diastolic BP: 49 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 6.9 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: NR Race: black: 100% Systolic BP: 102 Diastolic BP: 50 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 7 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Infants that had experienced no illnesses other than respiratory infections and were products of full term pregnancies.</p>	<p>Description: Intended sodium intake of 2 mEq Na/100 kcal Form of Administration: Dietary Modification: low salt baby formula Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: High salt Description: Intended sodium intake of 9 mEq Na/100 kcal Form of Administration: Dietary Modification: higher salt baby formula Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 5 months Exposure to Follow Up Time: NR</p>	<p>Best sodium measure recorded: 3 times, 2 months apart Sodium Status Intervention 1: 11.3 mEq 24 h Potassium measure: 72 hour urine analysis Best potassium measure recorded: 3 times, 2 months apart Potassium Status Intervention 1: 13.1 mEq 24 h</p> <p>How was blood pressure measured? BP measurements were done using an Air Shield Blood Pressure Monitor attached to the right arm of infant which automatically inflated the cuff to 180 mmHg every 5 min. Readings were recorded 6 to 12 times during the 3 daily nursing shifts over a 72-hour period or longer. Only measurements made while the infants were asleep and approximately an hour after feeding were used.</p>	<p>Follow-Up Time: 8 years Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -6.16 - 2.16) Diastolic BP-supine Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -4.77 - 2.77) Systolic BP-sitting Follow-Up Time: 8 years Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -5.18 - 3.18) Systolic BP-supine Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -6.16 - 2.16)</p>
<p>Wing, 1998¹⁵⁰</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p>	<p>Study of: Adults N: 17</p> <p>Participants: % Male: 82 Mean Age/Range/Age at Baseline: 61 median Race: NR Systolic BP: 165+/-4 Diastolic BP: 104+/-2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: 0</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Use of low sodium diet and placebo salt pills to reduce sodium intake to <100mM in participants on perindopril Form of Administration: Dietary Modification: Low sodium diet not described Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: NR Sodium, Method of Validation: creatinine Sodium Status Intervention 1: 99 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: NR Potassium, Method of Validation: NR Potassium Status Intervention 1:</p>	<p>Subgroup: Hypertensives 24-h ambulatory diastolic BP Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.11 - 0.11) 24-h ambulatory systolic BP Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -9.22 - -0.78)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Crossover: Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>% with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Inclusion: essential hypertensives; aged 18–80 years; untreated sitting clinic diastolic blood pressure of >95 and <115 mmHg measured by standard mercury sphygmomanometer</p> <p>Exclusion: secondary hypertension of any cause, a past history of malignant hypertension, myocardial infarction or unstable angina in the previous 6 months, a stroke or transient cerebral ischaemic attack in the previous year, any evidence of cardiac failure or haemodynamically significant valvular heart disease, unstable diabetes mellitus (50% of home blood glucose values >12 mmol/L or haemoglobin A1C >8.5%), any significant renal or hepatic disease, any other significant illness likely to interfere with survival (e.g. malignancy), known intolerance to the classes of drug being used in the study or the presence of conditions likely to be exacerbated by the study treatments (e.g. plasma potassium concentration <3.0 mmol/L, gout or plasma uric acid >0.50 mmol/L), were women who were pregnant or lactating or if they had anticipated poor compliance with the study protocol or treatment regimens</p>	<p>Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake Description: Administration of salt tablets to participants on low sodium diet in participants on perindopril to achieve usual sodium intake Form of Administration: Dietary Modification: Low sodium diet not described Sodium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 periods of 4 weeks each Exposure to Follow Up Time: 0 months</p>	<p>NR</p> <p>How was blood pressure measured? semiautomatic sphygmomanometer (Dinamap Vital Signs Monitor 8100, CRITIKON) and an inflatable cuff appropriate for the patient's arm size</p>	
<p>Xie, 1998¹⁵¹</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 169</p> <p>Intervention 1: % Male: 80 Mean Age/Range/Age at Baseline: mean 60 (SD 6) Race: NR Systolic BP: 161.86 Diastolic BP: 96.47 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 62.3 Mean Age/Range/Age at Baseline: mean 55 (SD 6) Race: NR Systolic BP: 168.79 Diastolic BP: 100.41</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: The education included counselling on nonpharmacological treatment (weight reduction, salt moderation, physical exercise, alcohol moderation, and psychological relaxing assisted by biofeedback instrument), medication compliance, monitoring of progress toward target BP, self-measurement of BP, other risk reduction (smoking, lipids), and the keeping of appointments. Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Usual care Description: NR Form of Administration: Usual diet</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times over 3 years Sodium Status Intervention 1: 98.24 mmol/24h</p> <p>How was blood pressure measured? unclear CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Unclear</p>	<p>Subgroup: Chinese Diastolic BP-NS Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 0.50 (95% CI: -1.96 - 2.96) Left ventricular hypertrophy-PWT (cm) Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 0.11 (95% CI: -0.60 - 0.82) Percent under control Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator RR 1.31 (95% CI: 1.04 - 1.65) Systolic BP-NS Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 2.60 (95% CI: -1.99 - 7.19)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: persistently elevated DBP of ≥ 95 mmHg and/or SBP ≥ 160 mmHg</p>	<p>Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>		
<p>Zhao, 2014¹⁵² Location: Tibet Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: 2009</p>	<p>Study of: Adults N: 282</p> <p>Participants: % Male: 41.1 Mean Age/Range/Age at Baseline: 63.1 Race: NR Systolic BP: 176.9 Diastolic BP: 104.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Aged >40, SBP > 140 mmHg Exclusion: Not able to travel, living too far</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: Salt substitute to decrease sodium intake Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Regular salt Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: For 'selected' families, salt that was delivered as part of the study was weighed at baseline then at follow up. Questions were also asked to gauge salt consumption. Daily salt and potassium intake as estimated based on this. Sodium Status Intervention 1: 20 grams/day Potassium measure: For 'selected' families, salt that was delivered as part of the study was weighed at baseline then at follow up. Questions were also asked to gauge salt consumption. Daily salt and potassium intake as estimated based on this. Potassium Status Intervention 1: 7.7 grams/day higher than control group</p> <p>How was blood pressure measured? BP taken with three consecutive blood pressure measurements (with at least one minute's rest between each measurement) from a seated patients' right arm in a quiet room. A previously validated electronic sphygmomanometer was used. BP taken at baseline and after 3 months of follow up.</p>	<p>Subgroup: HTN Deaths Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 2.00 (95% CI: 0.18 - 21.81) Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.64 - -0.36) Percent taking antihypertensives Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 1.34 (95% CI: 0.96 - 1.87) Percent under control Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 2.18 (95% CI: 1.07 - 4.46) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -7.70 (95% CI: -12.78 - -2.62) Decreased quality of life Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 0.50 (95% CI: 0.05 - 5.45)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Zhou, 2016 ¹⁵³ ; Zhou, 2013 ¹⁵⁴	Study of: Both adults and children N: 462 Location: China Setting: Community Design: Cluster RCT Parallel Number of Sites: multiple Study Years: unclear Participants: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Families were at least one member was a hypertension patient; the participant had an estimated daily sodium intake of ≥ 260 mmol per day; Individuals were at least 18 years of age and had no significant renal impairment or other indication for a potassium-sparing medication. Exclusion: Moving	Intervention Type(s): Duration: NR Exposure to Follow Up Time: NR		Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -4.62 (95% CI: -6.62 - -2.62) Percent taking antihypertensives Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator RR 1.68 (95% CI: 1.26 - 2.23) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -5.72 (95% CI: -8.65 - -2.79)
Zhou, 2009 ¹⁵⁵	Study of: Adults N: 248 Location: China Setting: Community Design: Randomized, parallel Number of Sites: 10 Study Years: 2003-2004 Intervention 1: % Male: 43.5 Mean Age/Range/Age at Baseline: mean 67.5 (SD 5.2) Race: NR Systolic BP: 159.7 Diastolic BP: 83.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator 1: NR % Male: 42.2 Mean Age/Range/Age at Baseline: mean 65.7 (SD 6.3) Race: NR Systolic BP: 157.7	Intervention Type(s): Intervention 1: Other: Low sodium salt-Hypertensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator 1: Other: Normal salt - Hypertensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 6 months apart Sodium Status Intervention 1: 162 mmol/24 h Sodium Status Comparator 1: 233 mmol/24 h Sodium Status Intervention 2: 162 mmol/24 h Sodium Status Comparator 2: 231 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 6 months apart Potassium Status Intervention 1: 34.2 mmol/24 h Potassium Status Comparator 1: 27.0 mmol/24 h Potassium Status Intervention 2: 33.1 mmol/24 h	Subgroup: Normotensive Diastolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -4.80 (95% CI: -7.05 - -2.55) Systolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -5.80 (95% CI: -8.66 - -2.94) Subgroup: Hypertensive Diastolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator 1 MD -5.20 (95% CI: -8.09 - -2.31) Systolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator 1 MD -9.80 (95% CI: -13.75 - -5.85)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Diastolic BP: 82.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 49.1 Mean Age/Range/Age at Baseline: mean 68.1 (SD 8.3) Race: NR Systolic BP: 125 Diastolic BP: 74.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.9 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 44.6 Mean Age/Range/Age at Baseline: mean 65.4 (SD 4.5) Race: NR Systolic BP: 123.8 Diastolic BP: 74.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.7 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–80, with normal BP or mild to moderate hypertension. No more than one meal outside the home per week, not currently taking potassium-sparing drugs, willingness to undertake long-term use of ClSalt. Serum potassium <5.5mmol/l and net elevation of serum potassium <1.0mmol/l at the end of the run-in period Exclusion: Heart attack or stroke within the last 6</p>	<p>Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium salt-Normotensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal salt - Normotensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses. Form of Administration: Other: Regular salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Potassium Status Comparator 2: 23.0 mmol/24 h</p> <p>How was blood pressure measured? BP was measured by two experienced physicians. SBP was taken as the point of appearance (phase 1) of Korotkoff sounds and DBP was measured as the point of disappearance (phase 5).</p>	

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	months, current angina pectoris, congestive heart failure, diabetes mellitus, serious mental or physical illness, secondary hypertension, malignancy, use of potassium-sparing diuretics, impairment of renal function.			

Table C2. Evidence table for all observational studies

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Adebamowo, 2015¹⁵⁶; Erratum, 2015¹⁵⁷; Iso, 1999¹⁵⁸; Stampfer, 1985¹⁵⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Nurses Health Study</p>	<p>Study of: Adults N: 180864</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: reported by study cohort and K quartile NHS I q1 mean 58 (SD 7) years q3 mean 60 (SD 7) years q5 mean 62 (SD 7) years NHS II q1 mean 40 (SD 5) years q3 mean 41 (SD 5) years q5 mean 42 (SD 4) years</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: reported by study cohort and K quartiles NHS I q1 26.4 (SD 5.5) q3 26.4 (SD 5.1) q5 26.5 (SD 5.2) NHS II q1 26.0 (SD 6.5) q3 25.6 (SD 5.7) q5 25.6 (SD 5.5)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included female registered nurses between 25 to 55 years old who enrolled in 1976 or 1989</p> <p>Exclusion: Excluded those with prevalent cancer, stroke, or IHD at baseline, and those showed evidence of possible low or high energy intakes, and those failed to provide complete diet info.</p>	<p>Exposure Type: Total potassium intake (dietary + supplemental)</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Total potassium intake (dietary)</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Total potassium intake (supplemental)</p> <p>Exposure Unit: mg/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 30 years of follow-up in NHS I and 22 years of follow-up in NHS II</p> <p>Dose format: median Q1, Dose: 2275 for I; 2381 for II Q1, Dose: 2282 for I; 2386 for II Q1, Dose: NR Q2, Dose: 2623 for I; 2744 for II Q2, Dose: 2633 for I; 2750 for II Q2, Dose: NR Q3, Dose: 2865 for I; 2992 for II Q3, Dose: 2879 for I; 3000 for II Q3, Dose: NR Q4, Dose: 3115 for I; 3248 for II Q4, Dose: 3133 for I; 3257 for II Q4, Dose: NR Q5, Dose: 3500 for I; 3642 for II Q5, Dose: 3526 for I;</p>	<p>Sodium, Method of Validation: Food diaries with reported validation</p> <p>Best potassium measure recorded: Used food frequency questionnaire to collect diet info with specific questions about potassium supplements</p> <p>Potassium, Method of Validation: Cited a validation study testing the correlations between mineral intake assessed by FFQ and by 1-week diet records.</p> <p>Mortality Outcomes-Method of Ascertainment: Death certificate, Postal authorities, National death index, Medical records, Autopsy reports</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Medical files, Followup questionnaire</p>	<p>Total stroke (Self-report and medical record reviews) (mg/day/Outcome): 30 y in the NHS I; 22 y in the NHS II FU</p> <p>Q1 cases: 662, total: 35570, Q1 cases: 666, total: NR, Q1 cases: NR, total: NR, Q2 cases: 679, total: 37364, Q2 cases: 736, total: NR, Q2 cases: NR, total: NR, Q3 cases: 735, total: 35631, Q3 cases: 746, total: NR, Q3 cases: NR, total: NR, Q4 cases: 782, total: NR, Q4 cases: 836, total: 37363, Q4 cases: NR, total: NR, Q5 cases: 850, total: NR, Q5 cases: 868, total: 34936, Q5 cases: NR, total: NR</p> <p>Adjustment: Age, calendar year, total calories (quintiles of kcal), BMI (in kg/m²; .25, 25 to .30, or \$30), parental history of heart disease (aged #60 y), alcohol intake (0, 0 to .5, 5 to .10, 10 to .15, or \$15 g/d), physical activity (.3, 3 to .9, 9 to .18, 18 to .27, or \$27 metabolic equivalent tasks/wk), smoking, postmenopausal hormone therapy, oral contraceptive use (never, past, or current), menopausal status (premenopausal or postmenopausal), aspirin (0 to .2 or \$2 pills/wk), multivitamin, history of hypertension, hypercholesterolemia, diabetes at baseline, and thiazide use (yes or no); for intakes of magnesium and calcium (quintiles of g/d). NHS, Nurses' Health Study.</p> <p>No association between potassium intake and total stroke risk among NHS I and NHS II participants.</p> <p>Total potassium intake was inversely associated with risk of total stroke, but not ischemic or hemorrhagic stroke. Comparing women in the highest to lowest quintiles of total potassium intake, the pooled multivariate RR for total stroke was 0.89 (95% CI: 0.80, 0.99; P-trend = 0.01).</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		3654 for II Q5, Dose: NR		
Alderman, 1997 ¹⁶⁰ ; Alderman, 1995 ¹⁶¹ Location: US Setting: Community Design: Prospective Cohort study	Study of: Adults N: 2937 % Male: 64.7 Mean Age/Range/Age at Baseline: men mean 52 (SD 10) years; women mean 54 (SD 9) years Race: NR Systolic BP: men mean 150; women mean 150 Diastolic BP: men mean 98; women mean 94 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: men mean 27.5; women mean 28.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Need Alderman article to answer this question Exclusion: Need Alderman article to answer this question	Exposure Type: 24-h urinary sodium excretion Exposure Unit: mmol/d Duration(in months): unclear Exposure to Follow Up Time: 3.8 years Dose format: range Q1, Dose: <89 mmol Q2, Dose: 89-126 mmol Q3, Dose: 127-174 mmol Q4, Dose: >=175 mmol	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Single 24-hr urine analysis at beginning of the program Sodium, Method of Validation: Validated by using formula described by Cockcroft and Gault and Robertshaw et al. Only included patients whose estimated urinary creatinine clearance values fall within +/- 35% of the observed values Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports	CVD (Cardiovascular disease, includes myocardial infarction (MI), stroke, coronary revascularization, unstable angina, congestive heart failure. and other CVD deaths. CVD events included MI (code 410) and cerebrovascular disease (codes 430 to 434 and 436 to 43) (mmol/d/Outcome): Average 3.8 years FU Q1 cases: 14.2 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 9.6, total: NR, Q3 cases: 10.5, total: NR, Q4 cases: 7.6, total: NR Adjustment: Unadjusted No statistically significant association was observed. MI (Myocardial Infarction incidence code 410) (mmol/d/Outcome): Average 3.8 years FU Q1 cases: 8.1 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 4.1, total: NR, Q3 cases: 4.5, total: NR, Q4 cases: 2.9, total: NR Adjustment: Unadjusted No statistically significant association was observed. Non-CVD (Includes hospitalizations, emergency room visits, and deaths.) (mmol/d/Outcome): Average 3.8 years FU Q1 cases: 18.8 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 12.7, total: NR, Q3 cases: 11.6, total: NR, Q4 cases: 15.9, total: NR Adjustment: Unadjusted No statistically significant association was observed. Stroke (Stroke Incidence) (mmol/d/Outcome): Average 3.8 years FU Q1 cases: 2.1 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 2.1, total: NR, Q3 cases: 2.2, total: NR, Q4 cases: 1.8, total: NR Adjustment: Unadjusted No statistically significant association was observed.
Alderman, 1998 ¹⁶² Location: US Setting: Community Design: Prospective Cohort study Study Name:	Study of: Adults N: 11346 % Male: 39.5 Mean Age/Range/Age at Baseline: men 52 (SD9) years; women 46 (SD 7) years Race: NR Systolic BP: men 138 women 134 Diastolic BP: men 86 women 82 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight men 76 (SD 6) kg; women 66	Exposure Type: Sodium Exposure Unit: mg Duration: NR Exposure to Follow Up Time: up to 21 years CVD mortality (CVD mortality) Dose format: NR per SD (1313mg),	Sodium measure: 24-hour diet recall Best sodium measure recorded: Single 24h diet recall Sodium, Method of Validation: NR Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths	All-cause mortality (All-cause mortality) (mg/Outcome): NR FU per SD (1313mg) cases: NR, total: 11346 Adjustment: Male, black race, history of CVD, history of hypertension, age (years), BMI (kg/m2), systolic blood pressure (mm Hg), calories (kcal), sodium/calories (mg/kcal), table salt use (always), table salt use (never) No significant association between sodium intake and all-cause mortality. CVD mortality (CVD mortality) (mg/Outcome): NR FU per SD (1313mg) cases: NR, total: 11346 Adjustment: Male, black race, history of CVD, history of hypertension, age (years), BMI (kg/m2), systolic blood pressure (mm Hg), calories (kcal),

Study	Participants	Exposure	Intake Status Ascertainment	Results
NHANES I	(SD 1) kg % with Hypertension: men 18 women 15 % with history of CVD: men 15 women 11 % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: NHANES I participants who underwent medical examination, underwent a 24h recall nutrition investigation Exclusion: Those whose sodium intake data were missing	Dose: NR All-cause mortality (All-cause mortality) Dose format: NR per SD (1313mg), Dose: mean 2515 mg and 1701 mg in men and women	confirmed from death certificates	sodium/calories (mg/kcal), table salt use (always), table salt use (never) No significant association between sodium intake and CVD mortality.
Araki, 2015 ¹⁶³ ; Araki, 2013 ¹⁶⁴ Location: Japan Setting: Community Design: Prospective Cohort study Study Name: Shiga Prospective Observational Follow-up Study	Study of: Adults % Male: 57.8 Mean Age/Range/Age at Baseline: mean 59 (SD 10) years Race: NR Systolic BP: mean 134 (SD 18) Diastolic BP: mean 77 (SD 10) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 23.5 (SD 3.3) % with Hypertension: 46.9 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included patients with type 2 diabetes and with eGFR \geq 60 ml/min per 1.73 m ² Exclusion: Excluded those with a history of CVD and those using any diuretics.	Duration: NR Exposure to Follow Up Time: a median of 11 years	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: completed one 24-hr urine analysis at baseline Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: completed one 24-hr urine analysis at baseline	See subgroup table for results
Ascherio, 1992 ¹⁶⁵ ; Rimm, 1991 ¹⁶⁶ ; Ascherio, 1997 ¹⁶⁷ Location: US Setting: Community Design: Prospective Cohort study	Study of: Adults N: 30681 % Male: 100 Mean Age/Range/Age at Baseline: 40 to 75 yr Race: NR Systolic BP: mean= 125.5 mmHg at age 40-44 and 133.7 mmHg at age 70-75 Diastolic BP: mean= 79.3 mmHg at age 40-44, 80.4 mmHg at age 60-64, and 79.7 at age 70-75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR	Exposure Type: Potassium intake Exposure Unit: g/day Duration(in months): about 4 years Exposure to Follow Up Time: NR Diastolic BP (Self reported), Systolic BP (Self reported) Dose format: continuous All, Dose: NR Q1, Dose: <2.40	Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: 1 time at baseline Potassium, Method of Validation: The reproducibility and validity of the FFQ was previously measured compared with 2 weeks dietary records in a subsample of 127 men. How was blood pressure	Diastolic BP (Self reported) (g/day/Outcome): 4 years FU All cases: NR, total: 18676, Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, age ² , Quetelet's index, alcohol consumption, and intakes of calcium, magnesium, potassium, and fiber No significant association between potassium intake and diastolic blood pressure. Significant inverse association between potassium intake and diastolic blood pressures while the four nutrients were controlled simultaneously. Hypertension (Self reported) (g/day/Outcome): 4 years FU Q1 cases: 79, total: 1466, Q2 cases: 170, total: 3857, Q3 cases: 270, total: 7002, Q4 cases: 322, total: 7520, Q5 cases: 407, total: 10836

Study	Participants	Exposure	Intake Status Ascertainment	Results
Study Name: Health Professionals Follow-up Study	% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: HPFS began in 1986 and follow-up questionnaires were sent in 1987, 1988, and 1990 and included health professionals 40 - 75 years old. Exclusion: Analyses excluded men who did not satisfy the a priori criteria of daily caloric intake between 800 and 4200 kcal and fewer than 70 blanks out of 131 total listed food items in FFQ; and men who reported on the 1986 questionnaire a diagnosis of cancer, MI, angina, stroke, coronary artery surgery, HTN, diabetes, renal failure, high blood cholesterol, or use of digoxin, nitrates, diuretics, beta-blockers, calcium antagonists, or other antihypertensive drugs.	Q2, Dose: 2.40-2.79 Q3, Dose: 2.80-3.19 Q4, Dose: 3.20-3.59 Q5, Dose: >=3.60 Hypertension (Self reported) Dose format: range Q1, Dose: <2.40 Q2, Dose: 2.40-2.79 Q3, Dose: 2.80-3.19 Q4, Dose: 3.20-3.59 Q5, Dose: >=3.60	measured? Self-reported BP and HTN diagnosis at baseline and subsequent biennial questionnaires. A random sample of 100 participants were contacted to obtain confirmation of the HTN diagnosis.	Adjustment: Age, Quetelet's index, alcohol consumption, and intakes of magnesium, potassium, and fiber No significant association between potassium intake and risk for hypertension. Systolic BP (Self reported) (g/day/Outcome): 4 years FU All cases: NR, total: 10911, Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, age^2, Quetelet's index, alcohol consumption, and intakes of calcium, magnesium, potassium, and fiber No significant association between potassium intake and systolic blood pressure. No significant association between potassium intake and systolic blood pressure.
Ascherio, 1998 ¹⁶⁷ ; Ascherio, 1992 ¹⁶⁵ Location: US Setting: Community Design: Prospective Cohort study Study Name: Health Professionals Follow-up Study	Study of: Adults N: 43738 % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 131 Diastolic BP: 82 Magnesium: 277 Calcium: 0.7 Other Minerals: NR Mean BMI: NR % with Hypertension: 18.5 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: HPPS included male health professionals between 40-75 years old, including 1600 podiatrists, 2218 osteopathic physicians, 3745 optometrists, 4185 pharmacists, 10098 veterinary surgeons, and 29 683 dentists. Exclusion: Analysis excluded men who failed to meet a priori criteria of daily caloric intake between 800-4200 kcal and leaving 70/131 food items blank. Excluded men with prior diagnosis of myocardial infarction, angina, coronary artery surgery, stroke, transient ischemic attack, peripheral arterial disease, or diabetes.	Exposure Type: Potassium calculations based on FFQ Exposure Unit: g/d Duration: NR Exposure to Follow Up Time: up to 9 years Dose format: median Q1, Dose: 2.4 Q2, Dose: 3 Q3, Dose: 3.3 Q4, Dose: 3.6 Q5, Dose: 4.3	Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: one food frequency questionnaire Potassium, Method of Validation: Study assessed questionnaire validity in a random sample of 127 men who completed two 1-week diet records. Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Death certificate reports, medical records	Total stroke (Fatal and nonfatal strokes occurring between the return of the baseline questionnaire and January 31, 1994) (g/d/Outcome): 8 years FU Q1 cases: 76, total: NR, person-years: 67605, Q2 cases: 65, total: NR, person-years: 67003, Q3 cases: 62, total: NR, person-years: 65826, Q4 cases: 64, total: NR, person-years: 63708, Q5 cases: 61, total: NR, person-years: 59253 Adjustment: Age (5-year categories), total energy intake (continuous variable), smoking (current, past, and 1-14, 15-24, and 25 cigarettes/d), alcohol consumption (5, 5-9, 10-14, 15-29, 30 g/d), history of hypertension, history of hypercholesterolemia, parental history of myocardial infarction before age 65 years, profession, and quintiles of body mass index and physical activity, fiber intake, magnesium intake Comparing men in the top fifth to those in bottom fifth of potassium intake, the age-adjusted RR of total stroke was 0.59. After adjusting for non-dietary risk factors, this age-adjusted RR was slightly attenuated (RR 0.62); and it was further attenuated by additional adjustment for intakes of magnesium and dietary fiber (RR 0.69).
Bazzano, 2001 ¹⁶⁸	Study of: Adults N: 9805	Exposure Type: Dietary potassium intake	Sodium, Method of Validation: 24-hour "diet recall"	Incident stroke ((ICD-9) code of 430- 434.9, 436, or 437.0 - 437.1 or 1 hospital and/or nursing home stay in which the participant had a discharge diagnosis with 1 of these codes.) (mmol/24h/Outcome):

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Inclusion: NHANES I participants between 25-74 years old at baseline examinations.</p> <p>Exclusion: Excluded those who self-reported history of heart attack, heart failure, or stroke at baseline or had used medication for heart disease 6 months before baseline examinations. Excluded participants who did not complete a 24-hour dietary recall.</p>	<p>Exposure Unit: mmol/24h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 10 years</p> <p>Dose format: range Q1, Dose: <34.6 Q2, Dose: 34.6-49.8 Q2+Q3+Q4 vs Q1, Dose: NR Q3, Dose: 49.8-68.4 Q4, Dose: >68.4</p>	<p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, Death certificate reports</p>	<p>Average 19 years FU</p> <p>Q1 cases: 287, total: 2452, person-years: 39214, Q2+Q3+Q4 vs Q1 cases: NR, total: NR, Q2 cases: 230, total: 2451, person-years: 39945, Q3 cases: 235, total: 2450, person-years: 40978, Q4 cases: 175, total: 2452, person-years: 41834</p> <p>Adjustment: Age, race, sex, energy intake, systolic BP, serum cholesterol, body mass index, history of diabetes, regular alcohol consumption, current cigarette smoking, vitamin supplement use, saturated fat intake, cholesterol intake, sodium intake, calcium intake, dietary fiber, vitamin C intake, and vitamin A intake (n 9244).</p> <p>Among quartiles of potassium intake, stroke hazard was significantly different (likelihood ratio P 0.03); although linear trend across quartiles did not yield statistically significant result (P 0.14).</p> <p>No significant association between potassium intake and risk of stroke.</p>
<p>Bongard, 2016¹⁶⁹</p> <p>Location: France</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MONICA (MONItoring of trends and determinants in Cardiovascular disease) Project</p>	<p>Study of: Adults</p> <p>N: 960</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: mean 55.5 (SD 6.2) years</p> <p>Race: NR</p> <p>Systolic BP: mean 139.5 (SD 19.2)</p> <p>Diastolic BP: mean 86.3 (SD 11.7)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 27.2 (SD 4)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: 62%</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included participants who were randomly selected from nearby French neighborhoods, and who agreed to participate in the study without financial compensation.</p> <p>Exclusion: Excluded those who had incomplete baseline evaluation data.</p>	<p>Exposure Type: Dietary sodium</p> <p>Exposure Unit: mg/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: a median of 14.8 years</p> <p>Dose format: range Q1, Dose: 297-1580 mg/day Q2, Dose: 1580-2061 mg/day Q3, Dose: 2061-2699 mg/day Q4, Dose: 2699-7626 mg/day</p>	<p>Sodium measure: 3-day food record with reported validation</p> <p>Best sodium measure recorded: one 3-day food record at baseline.</p> <p>Sodium, Method of Validation: Participants were followed up by a dietitian to verify the reliability of their food records.</p> <p>Mortality Outcomes-Method of Ascertainment: National database</p>	<p>All-cause mortality (Death from all causes) (mg/day/Outcome):</p> <p>Median 14.8 years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Center, age, payment of income tax, obesity, alcohol consumption (no consumption, moderate intake, high intake or former consumption), smoking habits (never, past or current smoking), physical activity (light, moderate or high), presence of a serious chronic condition and diet quality score.</p> <p>Higher dietary sodium intake associated with greater risk of all-cause mortality.</p>
<p>Buendia, 2015¹⁷⁰; The NHLBI Growth and Health Study, 1992¹⁷¹</p> <p>Location: US</p> <p>Setting:</p>	<p>Study of: Children</p> <p>N: 2185</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: by sodium intake groups g1 mean 10.0 (SD 0.6) g2 mean 10.0 (SD 0.6) g3 mean 10.0 (SD 0.6) g4 mean 10.1 (SD 0.5)</p> <p>Race: NR</p> <p>Systolic BP: by sodium intake groups g1 mean</p>	<p>Exposure Type: Daily potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Daily sodium intake</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Potassium to sodium</p>	<p>Sodium measure: 3-day diet records</p> <p>Best sodium measure recorded: Complete 8 3-day diet records (2 weekdays and 1 weekend day) during examination years 1-5, 7, 8, and 10.</p> <p>Sodium, Method of</p>	<p>Diastolic blood pressure (V-Lok Cuff mercury sphygmomanometer (BaumDesktopModel).) (mg/d/Outcome):</p> <p>10 years FU</p> <p>Category 1 cases: NR, total: 425, Category 1 cases: NR, total: 699, Category 2 cases: NR, total: 644, Category 2 cases: NR, total: 685, Category 3 cases: NR, total: 422, Category 3 cases: NR, total: 905, Category 4 cases: NR, total: 211, Category 4 cases: NR, total: 379</p> <p>Adjustment: Race (for all participant models), height, activity, television/video time, percentage of calories from solid fats and added sugars, and dietary fiber.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Community Design: Prospective Cohort study Study Name: The National Heart, Lung, and Blood Institute's Growth and Health Study (NGHS)	101.4 (SD 9.0) g2 mean 100.4 (SD 9.2) g3 mean 101.8 (SD 9.2) g4 mean 100.9 (SD 8.6) Diastolic BP: by sodium intake groups g1 mean 57.2 (SD 11.5) g2 mean 56.6 (SD 12.3) g3 mean 57.4 (SD 11.8) g4 mean 57.9 (SD 11.7) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: by sodium intake groups g1 mean 19.1 (SD 3.9) g2 mean 18.4 (SD 3.8) g3 mean 18.6 (SD 3.8) g4 mean 18.1 (SD 3.5) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included Black and White girls initially aged 9 to 10 years. Exclusion: Excluded girls with missing data on diet, BP, or potential confounding variables included in the final models.	ratio Exposure Unit: NR Duration: NR Exposure to Follow Up Time: NR Dose format: range Category 1, Dose: <0.6 Category 1, Dose: <1800 Category 1, Dose: <2500 Category 2, Dose: 0.6- <0.7 Category 2, Dose: 1800- <2100 Category 2, Dose: 2500- <3000 Category 3, Dose: 0.7- <0.8 Category 3, Dose: 2100- <2400 Category 3, Dose: 3000- <4000 Category 4, Dose: >= 0.8 Category 4, Dose: >= 2400 Category 4, Dose: >= 4000	Validation: NR Potassium measure: 3-day diet record Best potassium measure recorded: Complete 8 3-day diet records (2 weekdays and 1 weekend day) during examination years 1-5, 7, 8, and 10. Potassium, Method of Validation: NR How was blood pressure measured? Measured annually with a V-Lok Cuff mercury sphygmomanometer (Baum Desktop Model).	No significant association between absolute sodium intake and adolescent diastolic blood pressure. No significant association between potassium to sodium ratio and diastolic blood pressure. Systolic blood pressure (V-Lok Cuff mercury sphygmomanometer (BaumDesktopModel).) (mg/d/Outcome): 10 years FU Category 1 cases: NR, total: 425, Category 1 cases: NR, total: 699, Category 2 cases: NR, total: 644, Category 2 cases: NR, total: 685, Category 3 cases: NR, total: 422, Category 3 cases: NR, total: 905, Category 4 cases: NR, total: 211, Category 4 cases: NR, total: 379 Adjustment: Race (for all participant models), height, activity, television/video time, percentage of calories from solid fats and added sugars, and dietary fiber. Increase in potassium to sodium ratio associated with decrease in systolic blood pressure. No significant association between absolute sodium intake and adolescent systolic blood pressure. Diastolic blood pressure (V-Lok Cuff mercury sphygmomanometer (BaumDesktopModel).) (mg/d/Outcome): 10 years FU Category 1 cases: NR, total: 786, Category 2 cases: NR, total: 573, Category 3 cases: NR, total: 411, Category 4 cases: NR, total: 415 Adjustment: Race (for all participant models), height, activity, television/video time, percentage of calories from solid fats and added sugars, and dietary fiber. Adolescent female being in the highest category of potassium intake was associated with lower diastolic blood pressure. Systolic blood pressure (V-Lok Cuff mercury sphygmomanometer (BaumDesktopModel).) (mg/d/Outcome): 10 years FU Category 1 cases: NR, total: 786, Category 2 cases: NR, total: 573, Category 3 cases: NR, total: 411, Category 4 cases: NR, total: 415 Adjustment: Race (for all participant models), height, activity, television/video time, percentage of calories from solid fats and added sugars, and dietary fiber. Adolescent female being in the highest category of potassium intake was associated with lower systolic blood pressure.
Catena, 2016 ¹⁷² ; Sechi, 2009 ¹⁷³ ; Catena, 2007 ¹⁷⁴ ; Catena, 2006 ¹⁷⁵ ; Catena, 2007 ¹⁷⁶	Study of: Adults N: 65 % Male: 72 Mean Age/Range/Age at Baseline: mean 52 (SD 12) Race: NR Systolic BP: mean 167 (SD 16) Diastolic BP: mean 102 (SD 9) Magnesium: NR	Exposure Type: Urinary sodium excretion Exposure Unit: mmol/d Duration: NR Exposure to Follow Up Time: NR	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, baseline and at the end of follow-up	Change in LVMI (g/m) (Blood pressure measured with Omron M6 device) (mmol/d/Outcome): 12 months FU T1 cases: NR, total: 21, T2 cases: NR, total: 22, T3 cases: NR, total: 22 Adjustment: Patients with or without plasma aldosterone Significant association between changes in LV mass index and urinary sodium excretion (beta=0.334; p=0.012).

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: Italy</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p>	<p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 28.5 (SD 4.2)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Patients with all grades of hypertension living in northeast Italy were included.</p> <p>Exclusion: Patients who had diabetes mellitus, renal insufficiency with 24-h creatinine clearance of less than 30 ml/min per 1.73 m² of body surface area, urinary protein excretion of more than 1.0 g/d; and congestive heart failure were excluded.</p>	<p>Dose format: mean+/-SD</p> <p>T1, Dose: 100+/-25</p> <p>T2, Dose: 137+/-28</p> <p>T3, Dose: 158+/-27</p>	<p>How was blood pressure measured? BP was measured by an automated device (Omron M6; OMRON Healthcare Co, Kyoto, Japan).</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Cardiac ultrasound examination</p>	
<p>Chien, 2008¹⁷⁷</p> <p>Location: Taiwan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chin-Shan Community Cardiovascular Cohort Study (CCCC)</p>	<p>Study of: Adults</p> <p>N: 1520</p> <p>% Male: by sodium excretion quartiles q1 50% q2 47.9% q3 48.7% q4 45.3%</p> <p>Mean Age/Range/Age at Baseline: by sodium excretion quartiles q1 mean 51.5 (SD 12) q2 mean 52.9 (SD 11.9) q3 mean 52.4 (SD 11.4) q4 mean 51.3 (SD 10.6)</p> <p>Race: NR</p> <p>Systolic BP: by sodium excretion quartiles q1 mean 115.1 (SD 11.3) q2 mean 114.5 (SD 11.3) q3 mean 115.5 (SD 10.9) q4 mean 117 (SD 10.8)</p> <p>Diastolic BP: by sodium excretion quartiles q1 mean 72.4 (SD 7.8) q2 mean 72.3 (SD 8.2) q3 mean 72.7 (SD 7.8) q4 mean 74 (SD 7.6)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: by sodium excretion quartiles q1 mean 22.7 (SD 3.1) q2 mean 22.8 (SD 3) q3 mean 23.3 (SD 3) q4 mean 23.6 (SD 3.6)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: by sodium excretion quartiles q1 10.6% q2 9.8% q3 0.3% q4 15.1%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included participants 35 years and older, living in the Chin-Shan township, 30 km north of metropolitan Taipei, Taiwan.</p> <p>Exclusion: Excluded Participants with a baseline diagnosis of hypertension (n = 1096) or incomplete urine collection data at baseline (n = 986).</p>	<p>Exposure Type: Urinary potassium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium to potassium ratio</p> <p>Exposure Unit: mmol/mmol</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>Diastolic blood pressure (BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: single 24hr urine analysis</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: single 24hr urine analysis</p> <p>How was blood pressure measured? Measured twice in the right arm by a mercury sphygmomanometer.</p>	<p>Diastolic blood pressure (BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was used as described previously) (mmol/24h/Outcome): Median 7.93 (IQR 4.07-9.04) years FU</p> <p>All cases: NR, total: 1520</p> <p>Adjustment: Age and sex</p> <p>A positive association between incidence rates of hypertension and increasing quartiles of urinary sodium excretion, except for the first quartile. There was a significant J-shape relationship between urinary sodium excretion and the risk of hypertension.</p> <p>The incidence rates were similar across the quartiles for urinary potassium and sodium as compared with potassium ratio values, and the RRs were not significant.</p> <p>Q1 cases: 160, total: NR, person-years: 2482, Q1 cases: 165, total: NR, person-years: 2432, Q2 cases: 144, total: NR, person-years: 2558, Q2 cases: 163, total: NR, person-years: 2565, Q3 cases: 167, total: NR, person-years: 2581, Q3 cases: 168, total: NR, person-years: 2482, Q4 cases: 178, total: NR, person-years: 2494, Q4 cases: 193, total: NR, person-years: 2432</p> <p>Adjustment: Age groups, sex, BMI groups, smoking (yes/no or abstinence), current alcohol drinking (regular/no), marital status (single, married and living with spouse, or divorced and separated), education level (less than 9 years, at least 9 years), occupation (no work, labor, official or business), and regular exercise habit (yes/no), baseline systolic blood pressure (continuous variable) and diabetes status (yes/no)</p> <p>A positive association between incidence rates of hypertension and increasing quartiles of urinary sodium excretion, except for the first quartile. There was a significant J-shape relationship between urinary sodium excretion and the risk of hypertension.</p> <p>The incidence rates were similar across the quartiles for urinary potassium and sodium as compared with potassium ratio values, and the RRs were not significant.</p> <p>Systolic blood pressure (BP was measured twice in the right arm by a</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>used as described previously), Systolic blood pressure (BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was</p> <p>Dose format: NR All, Dose: NR</p> <p>Hypertension (Incident hypertension cases were ascertained through biennial BP measurements and medication history was obtained from questionnaires, and was defined as sitting systolic BP of at least 140 mmHg, diastolic BP of at least 90 mmHg, or antihypertensive treat)</p> <p>Dose format: NR Q1, Dose: NR Q1, Dose: 63 (<84) Q2, Dose: NR Q2, Dose: 103 (84-122) Q3, Dose: NR Q3, Dose: 147 (122-178) Q4, Dose: NR Q4, Dose: 231 (>=178)</p>		<p>mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was used as described previously) (mmol/24h/Outcome): Median 7.93 (IQR 4.07-9.04) years FU All cases: NR, total: 1520 Adjustment: Age and sex A positive association between incidence rates of hypertension and increasing quartiles of urinary sodium excretion, except for the first quartile. There was a significant J-shape relationship between urinary sodium excretion and the risk of hypertension. The incidence rates were similar across the quartiles for urinary potassium and sodium as compared with potassium ratio values, and the RRs were not significant.</p> <p>Diastolic blood pressure (BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was used as described previously) (mmol/24h/Outcome): Median 7.93 (IQR 4.07-9.04) years FU All cases: NR, total: 1520 Adjustment: Age and sex The incidence rates of hypertension were similar across the quartiles for urinary potassium; the RRs across urinary potassium quartiles were not significant.</p> <p>Hypertension (Incident hypertension cases were ascertained through biennial BP measurements and medication history was obtained from questionnaires, and was defined as sitting systolic BP of at least 140 mmHg, diastolic BP of at least 90 mmHg, or antihypertensive treat) (mmol/24h/Outcome): Median 7.93 (IQR 4.07-9.04) years FU Q1 cases: 151, total: NR, person-years: 2455, Q2 cases: 177, total: NR, person-years: 2498, Q3 cases: 169, total: NR, person-years: 2585, Q4 cases: 172, total: NR, person-years: 2487 Adjustment: Age groups, sex, BMI groups, smoking (yes/no or abstinence), current alcohol drinking (regular/no), marital status (single, married and living with spouse, or divorced and separated), education level (less than 9 years, at least 9 years), occupation (no work, labor, official or business), and regular exercise habit (yes/no), baseline systolic blood pressure (continuous variable) and diabetes status (yes/no) The incidence rates of hypertension were similar across the quartiles for urinary potassium; the RRs across urinary potassium quartiles were not significant.</p> <p>Systolic blood pressure (BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was used as described previously) (mmol/24h/Outcome): Median 7.93 (IQR 4.07-9.04) years FU All cases: NR, total: 1520 Adjustment: Age and sex The incidence rates of hypertension were similar across the quartiles for</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				urinary potassium; the RRs across urinary potassium quartiles were not significant.
Cohen, 2006 ¹⁷⁸ ; US Department of Health and Human Services, 2005 ¹⁷⁹ Location: US Setting: Community Design: Prospective Cohort study Study Name: The NHANES II Mortality study (a followup to NHANES II)	Study of: Adults N: 7154 % Male: 47% Mean Age/Range/Age at Baseline: mean 48 (SE 0.26) Race: White 88% black 9% other 2% Systolic BP: mean 127 (SE 0.60) Diastolic BP: mean 81 (SE 0.52) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 25.7 (SE 0.07) % with Hypertension: BP > 140/90 mmHg 30%; treatment for hypertension 3.9% % with history of CVD: NR % with Type 2 diabetes: 3.1% % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants in NHANES II aged 30 to 73 years at entry were included. Exclusion: People with self-reported history of heart disease or stroke, or who reported a low salt diet for medical reasons, or who died with <= 6 months follow-up, or who reported either the highest or lower 1 % of sodium or calories were excluded.	Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: < residuals adjusted median Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: <2300mg Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg per calorie Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg/d Duration(in months): 164.4 (13.7 years) Exposure to Follow Up Time: NR Cerebrovascular disease (ICD-9 (430-438)), Coronary heart disease (ICD-9 (410-414)) Dose format: NR NR, Dose: NR per 1000mg, Dose: NR CVD (ICD_9 (390-459)) Dose format: range <2300mg, Dose: <2300mg	Sodium measure: 24-hour diet recall Best sodium measure recorded: once, baseline Mortality Outcomes-Method of Ascertainment: Death certificate	All-cause mortality (ICD_9 (390-459)) (mg/Outcome): Mean 13.7 (range 0.5-16.8) years FU <2300mg cases: NR, total: 3443, NR cases: 1343, total: 7154, per 1000mg cases: 1343, total: 7154, >=2300mg cases: NR, total: 3711 Adjustment: Age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education high school, physical activity, body mass index, dietary potassium, history of diabetes, serum cholesterol Inverse associations with all-cause mortality of continuous sodium and sodium/calorie ratio were consistent. Inverse associations with all-cause mortality of continuous sodium and sodium/calorie ratio were consistent. No significant association between sodium intake and all-cause mortality. Compared to those with more than 2300 mg dietary sodium intake, those with less than 2300 mg had significantly higher age-sex adjusted mortality rates for CVD and all causes. CVD (ICD_9 (390-459)) (mg/Outcome): Mean 13.7 (range 0.5-16.8) years FU <2300mg cases: NR, total: 3443, NR cases: 541, total: 7154, Q1 cases: NR, total: NR, per 1000mg cases: 541, total: 7154, >=2300mg cases: NR, total: 3711, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education high school, physical activity, body mass index, dietary potassium, history of diabetes, serum cholesterol Statistically significant inverse association between sodium/ calorie ratio and CVD mortality. Statistically significant inverse association between sodium/ calorie ratio and CVD mortality. When dietary sodium was expressed as a continuous variable (per 1000 mg), there was a statistically significant inverse association between dietary sodium and CVD mortality after adjusting for calories and other covariables. Compared to those with more than 2300 mg dietary sodium intake, those with less than 2300 mg had significantly higher age-sex adjusted mortality rates for CVD and all causes. All-cause, CHD, and stroke mortality had similar HRs across quartiles of sodium intake. Cerebrovascular disease (ICD-9 (430-438)) (mg per calorie/Outcome): Mean 13.7 (range 0.5-16.8) years FU NR cases: 79, total: 7154, per 1000mg cases: 79, total: 7154 Adjustment: Age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education high school, physical activity, body mass index, dietary potassium, history of diabetes, serum cholesterol and calories No significant association between sodium intake and cerebrovascular

Study	Participants	Exposure	Intake Status Ascertainment	Results
		≥2300mg, Dose: ≥2300mg NR, Dose: NR Q1, Dose: NR Q2, Dose: NR Q3, Dose: NR Q4, Dose: NR per 1000mg, Dose: NR All-cause mortality (ICD_9 (390-459)) Dose format: range <2300mg, Dose: <2300mg ≥2300mg, Dose: ≥2300mg NR, Dose: NR per 1000mg, Dose: mean 2719 (SD 23) mg		disease. Coronary heart disease (ICD-9 (410-414)) (mg per calorie/Outcome): Mean 13.7 (range 0.5-16.8) years FU NR cases: 282, total: 7154, per 1000mg cases: 282, total: 7154 Adjustment: Age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education high school, physical activity, body mass index, dietary potassium, history of diabetes, serum cholesterol and calories No significant association between sodium intake and coronary heart disease.
Cook, 2009 ¹⁸⁰ , Satterfield, 1991 ¹²⁸ ; Hebert, 1995 ⁵⁴ ; Cook, 2016 ⁶² ; Cook, 2014 ¹⁸¹ Location: US Setting: Community Design: Prospective Cohort study Study Name: TOHP Follow-up (TOHP I and TOHP II) .	Study of: Adults N: 2306 % Male: 69.4 Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339. Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18 Systolic BP: Men: < 125, 762; ≥ 125, 839; women: <125, 298; ≥ 125, 407 Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318. Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Men: < 25, 238; 25 to <30, 777; ≥ 30 586; Women, <25 138; 25 to <30 279; ≥ 30 288. % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included. Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.	Exposure Type: Potassium Excretion Exposure Unit: linear Exposure Type: Potassium Excretion Exposure Unit: mmol/24 h Exposure Type: Sodium Excretion Exposure Unit: linear Exposure Type: Sodium Excretion Exposure Unit: mmol/24 h Exposure Type: Sodium to Potassium Excretion Ratio Exposure Unit: linear Exposure Type: Sodium to Potassium Excretion Ratio Exposure Unit: mmol/24 h Duration(in months):	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II	1 cases: 45, total: 587, 1 cases: 47, total: 563, NR cases: 166, total: 2084, 2 cases: 39, total: 573, 2 cases: 43, total: 585, 3 cases: 49, total: 589, 3 cases: 56, total: 589, 4 cases: 51, total: 581, 4 cases: 56, total: 554 Adjustment: Age, sex, race/ethnicity, clinic, and treatment assignment, education status, baseline weight, alcohol use, smoking, exercise, and family history of cardiovascular disease, changes in weight, smoking, and exercise After adjustment for baseline and lifestyle variables, there was a significant increasing trend in risk of CVD across quartiles of the sodium to potassium excretion ratio from lowest to highest. After adjustment for baseline and lifestyle variables, there was a nonsignificant trend in risk of CVD across quartiles of urinary sodium excretion from lowest to highest. Among all participants, no association between sodium to potassium excretion ratio and risk of CVD. No statistically significant association between risk of CVD events and sodium to potassium excretion ratio. No statistically significant linear coefficient for risk of CVD events and sodium excretion. Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (mmol/24 h/Outcome): Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II FU 1 cases: 50, total: 543, NR cases: 166, total: 2084, 2 cases: 53, total: 579, 3 cases: 51, total: 589, 4 cases: 39, total: 595 Adjustment: Age, sex, race/ethnicity, clinic, and treatment assignment, education status, baseline weight, alcohol use, smoking, exercise, and family history of cardiovascular disease, changes in weight, smoking, and exercise

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>120 to 180 (10 to 15 years) Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR 1, Dose: NR 2, Dose: NR 3, Dose: NR 4, Dose: NR NR, Dose: NR</p>	<p>Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p>	<p>After adjustment for baseline and lifestyle variables, there was a nonsignificant trend in risk of CVD across quartiles of urinary potassium excretion from lowest to highest. No significant linear coefficient for potassium excretion and CVD events.</p>
<p>Cook, 2014¹⁸¹ Location: US Setting: Community Design: Prospective Cohort study Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p>	<p>Study of: Adults N: 2312 % Male: NR Mean Age/Range/Age at Baseline: by sodium excretion group TOHP I men g1 mean 42.1 g2 mean 42.8 g3 mean 43.3 g4 mean 42.7 TOHP I women g1 mean 44.6 g2 mean 44.7 g3 mean 43.0 g4 mean 42.7 TOHP II men g1 mean 42.7 g2 mean 43.6 g3 mean 43.6 g4 mean 42.5 TOHP II women g1 mean 44.4 g2 mean 43.8 g3 mean 43.1 g4 mean 44.0 Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included TOHP participants who were not in a sodium reduction intervention, had available sodium excretions, and remained alive and CVD free at the end of the trial periods. Exclusion: Excluded those in active sodium intervention, with missing sodium excretion data and those who did not respond to followup questionnaires.</p>	<p>Exposure Type: Urinary sodium excretion Exposure Unit: mg/d Duration(in months): 120 to 180 (10 to 15 years) Exposure to Follow Up Time: NR Dose format: range Q1, Dose: <2300 Q2, Dose: 2300 to <3600 Q3, Dose: 3600 to <4800 Q4, Dose: >=4800</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Sodium, Method of Validation: NR Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke,</p>	<p>Cardiovascular Events (mg/d/Outcome): 10 years for I, 5 years for II FU Q1 cases: 17, total: 236, Q2 cases: 61, total: 893, Q3 cases: 74, total: 768, Q4 cases: 41, total: 415 Adjustment: Age, sex, race/ethnicity, clinic, and treatment assignment; education status, baseline weight, alcohol use, smoking, exercise, potassium excretion, and family history of cardiovascular disease; changes in weight, smoking, and exercise during the trial periods. CI indicates confidence interval; CVD, cardiovascular disease; HR, hazard ratio; and TOHP, Trials of Hypertension Prevention After adjusting for multiple variables, risk of CVD events for those with urinary sodium excretion <2300 mg/d was 32% lower than those with sodium excretion between 3600 to <4800 mg/d (P for trend=0.13).</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
			kidney stones/disease Outcomes-Method of ascertainment: medical records	
Cook, 2016 ⁶² Location: US Setting: Community Design: Prospective Cohort study Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)	Study of: Adults % Male: 68.38 Mean Age/Range/Age at Baseline: mean mean Q1 42.5 Q2 42.7 Q3 42.9 Q4 42.3; women Q1 44.3 Q2 43.9 Q3 43.0 Q4 43.2 Race: % Black men Q1 16.0 Q2 9.7 Q3 10.4 Q4 8.8; women Q1 25.4 28.2 26.9 Q4 26.7 Systolic BP: mean men Q1 124.9 Q2 125.2 Q3 125.7 Q4 126.4; women Q1 126.2 Q2 126.5 Q3 126.8 Q4 126.4 Diastolic BP: mean men Q1 84.3 Q2 84.4 Q3 84.8 Q4 85.0; women Q1 84.2 Q2 84.6 Q3 85.0 Q4 85.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included TOHP participants who were not in a sodium reduction intervention Exclusion: missing sodium excretion or the occurrence of an incident CVD event or death during the period of exposure assessment	Duration: median 25.7 year for TOHP I; median 22.4 years for TOHP II Exposure to Follow Up Time: NR	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Mortality Outcomes-Method of Ascertainment: National death index	See subgroup table for results
Curhan, 2004 ¹⁸² Location: US Setting: Community Design: Prospective Cohort study	Study of: Adults % Male: 0% Mean Age/Range/Age at Baseline: by calcium quintile q1 mean 36.7 q2 mean 36.5 q3 mean 36.2 q4 mean 35.8 q5 mean 35.5 Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR	Exposure Type: 1.2707154E-2 Exposure Unit: dietary potassium Duration: NR Exposure to Follow Up Time: NR Dose format: Q1 mg/d, Dose: NR mg/d, Dose: NR	Potassium measure: semiquantitative food frequency questionnaires Best potassium measure recorded: 2 semiquantitative FFQ in 1991 and 1995 CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: self reported	Kidney stone incident (Kidney) (dietary potassium/Outcome): NR FU mg/d cases: NR, total: NR Adjustment: NR Age (in 5-year categories), body mass index (5 categories), family history of kidney stones, and intake of supplemental calcium (4 categories), dietary calcium, animal protein, potassium, sodium, sucrose, phytate, and fluid (quintile groups for the last 5 variables)

Study	Participants	Exposure	Intake Status Ascertainment	Results
Study Name: The Nurses Health Study II	Mean BMI: by calcium quintile q1 mean 24.6 q2 mean 24.7 q3 mean 24.6 q4 mean 24.6 q5 mean 24.5 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included NHS II participants who provided dietary information in 1991. Exclusion: Excluded those whose kidney stone diagnosis date could not be confirmed and excluded those with asymptomatic stones.	mg/d, Dose: NR mg/d, Dose: NR mg/d, Dose: NR		
Du Shufa, 2014 ¹⁸³ Location: China Setting: Community Design: Prospective Cohort study Study Name: The China Health and Nutrition Survey (CHNS)	Study of: Adults N: (ranged between 6 % Male: 48 Mean Age/Range/Age at Baseline: mean 37.4 (SD 11.0) Race: NR Systolic BP: mean 112.2 (SD 15.6) Diastolic BP: mean 73.5 (SD 10.7) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 21.7 (SD 2.5) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Not data Exclusion: Participants younger than 20 y or older than 60 y at difference follow up time were excluded.	Exposure Type: Potassium intake Exposure Unit: g/day Exposure Type: Sodium intake Exposure Unit: g/d Exposure Type: Sodium potassium ratio Exposure Unit: NR Duration: NR Exposure to Follow Up Time: 18 y (but the percentage of participants who participated previously is different from the follow-up rate) Dose format: range Q1, Dose: <1.2 Q1, Dose: <1.8 Q1, Dose: <3.2 Q2, Dose: 1.2-1.4 Q2, Dose: 1.8-12.5 Q2, Dose: 3.2-4.3 Q3, Dose: 1.5-1.7 Q3, Dose: 2.6-3.4 Q3, Dose: 4.4-5.5 Q4, Dose: 1.8-2.1 Q4, Dose: 3.5-4.8 Q4, Dose: 5.6-7.5 Q5, Dose: >=2.2	Sodium measure: 24-hour diet recall Best sodium measure recorded: 6 times, 1991, 1993, 1997, 2999, 2994, 2996, and 2009 Sodium, Method of Validation: A validation study evaluated the accuracy of estimated sodium and potassium intakes at the individual level in one of the survey provinces (but not with CHNS participants) by measuring urinary sodium and potassium excretions from 24-h urine samples collected for 3 consecutive days and by using p-aminobenzoic acid as a marker of completeness of 24-h urine samples., 24-hour "diet recall" Best potassium measure recorded: 6 times, 1991, 1993, 1997, 2999, 2994, 2996, and 2009 Potassium, Method of Validation: A validation study evaluated the accuracy of estimated sodium and potassium intakes at the individual level in one of the	Hypertension (Standard mercury sphygmomanometers with regular adult cuffs) (g/d/Outcome): 10 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Energy intake, age, sex, education, income, region, BMI, physical activity, smoking status, and alcohol consumption. Flexible parametric models for survival-time data and the macro %EMICM in SAS 9.2 (SAS Institute) were used to compute HRs and the survival curves. Na/K ratio, ratio of sodium to potassium. The region adjustment variable had a significant interaction with the effect of sodium to potassium ratio on the risk of hypertension. Significant dose-response associations between incident hypertension and the third to fifth quintiles. Hypertension (Standard mercury sphygmomanometers with regular adult cuffs) (g/day/Outcome): 10 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Sodium intake, energy intake, age, sex, education, income, region, BMI, physical activity, smoking status, and alcohol consumption. Flexible parametric models for survival-time data and the macro %EMICM in SAS 9.2 (SAS Institute) were used to compute HRs and the survival curves. Na/K ratio, ratio of sodium to potassium. Second to fifth quintiles of potassium intake were associated with lower risk of incident hypertension.

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>Q5, Dose: ≥ 4.9 Q5, Dose: ≥ 7.6</p>	<p>survey provinces (but not with CHNS participants) by measuring urinary sodium and potassium excretions from 24-h urine samples collected for 3 consecutive days and by using p-aminobenzoic acid as a marker of completeness of 24-h urine samples.</p> <p>How was blood pressure measured? Standard mercury sphygmomanometers with regular adult cuffs were used. The cuff was placed on the participant's right arm (the lower edge 25 mm above the elbow) and inflated until the cuff pressure was 30 mm Hg above the level at which the pulse disappeared. DBPs were determined by using the fifth phase of the Korotkoff method. Three measurements were obtained with a 30-s interval between cuff inflations if the first measure was normal. Otherwise, participants were requested to take 10–30 min of rest before a second measurement was taken.</p>	
<p>Dunkler, 2013¹⁸⁴; Kawasaki, 1993¹⁸⁵</p> <p>Location: NR</p> <p>Setting: Clinical research center based</p>	<p>Study of: Adults N: 3726</p> <p>% Male: No renal Event 69.1 Renal Event 66 Died 71.3</p> <p>Mean Age/Range/Age at Baseline: Median (IQR) No Renal event 65 (60-70) Renal Event 66 (61-71) Died 69 (63-74) y</p> <p>Race: NR</p> <p>Systolic BP: Median (IQR) No renal event 142 (130-154) Renal event 145 (133- 156) Died 145</p>	<p>Exposure Type: 24-h Urinary potassium Exposure Unit: g</p> <p>Exposure Type: 24-h Urinary sodium Exposure Unit: g</p> <p>Duration(in months): 66 (5.5 years) Exposure to Follow</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Single 24-hour urine analysis with validation Sodium, Method of Validation: Previous studies have reported that this approach</p>	<p>Incidence or progression of CKD (As at least 1 of the following renal events: new microalbuminuria, new macroalbuminuria, GFR-decline of more than 5% per year, or end-stage renal dis- ease.) (g/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR Adjustment: Age, duration of type 2 diabetes mellitus, albuminuria status, glomerular filtration rate, sex, Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial randomization arms, and urinary-albumin-creatinine ratio (UACR) to progression, which was defined as the difference between the participant-specific cutoff point of developing new microalbuminuria or macroalbuminuria and UACR at baseline on the</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Design: Prospective Cohort study</p> <p>Study Name: Ongoing</p> <p>Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET Sample)</p>	<p>(133-156) mmHg</p> <p>Diastolic BP: Median (IQR) no renal event 82 (75-89) renal event 82 (75-89) died 80 (73-88) mmHg</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Median (IQR) No Renal Event 28.65 (25.71- 31.96) Renal Event 28.70 (25.83- 32.45)</p> <p>Died 28.04 (25.41-31.54) kg/m²</p> <p>% with Hypertension: no renal event 76.4 renal event 81.6 died 78.9</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: 100</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants aged 55 years or older, from the ONTARGET trial, had a history of type 2 diabetes, normoalbuminuria or microalbuminuria at baseline, and UACR and GFR measurements at study entry and end.</p> <p>Exclusion: Not applicable.</p>	<p>Up Time: NR</p> <p>Dose format: Median</p> <p>T1, Dose: 1.7</p> <p>T1, Dose: 3.47</p> <p>T2, Dose: 2.13</p> <p>T2, Dose: 4.89</p> <p>T3, Dose: 2.71</p> <p>T3, Dose: 6.41</p>	<p>provides a valid estimate of sodium intake in healthy control participants and patients taking antihypertensive therapy (ref 15 and 16)., Single 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: Single 24-hour urine analysis with validation</p> <p>Potassium, Method of Validation: Previous studies have reported that this approach provides a valid estimate of sodium intake in healthy control participants and patients taking antihypertensive therapy (ref 15 and 16).</p> <p>Mortality Outcomes-Method of Ascertainment: Unclear</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: New microalbuminuria, new macroalbuminuria, GFR-decline of more than 5% per year, or end-stage renal disease</p>	<p>log scale</p> <p>No association between sodium intake and risk of CKD.</p> <p>Incidence or progression of CKD (As at least 1 of the following renal events: new microalbuminuria, new macroalbuminuria, GFR-decline of more than 5% per year, or end-stage renal disease.) (g/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR</p> <p>Adjustment: Age, duration of type 2 diabetes mellitus, albuminuria status, glomerular filtration rate, sex, Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial randomization arms, and urinary-albumin-creatinine ratio (UACR) to progression, which was defined as the difference between the participant-specific cutoff point of developing new microalbuminuria or macroalbuminuria and UACR at baseline on the log scale</p> <p>Higher potassium was associated with reduced risk of CKD in adjusted single-variable and multivariable models</p>
<p>Dunkler, 2015¹⁸⁶; Teo, 2004¹⁸⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Ongoing</p> <p>Telmisartan Alone and in</p>	<p>Study of: Adults</p> <p>% Male: 66.6%</p> <p>Mean Age/Range/Age at Baseline: median 65 (IQR 60-70)</p> <p>Race: 98.6% Caucasian</p> <p>Systolic BP: median 145 (IQR 133-155)</p> <p>Diastolic BP: median 82 (IQR 76-90)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: median 29.05 (IQR 26.26-32.01)</p> <p>% with Hypertension: 79.2%</p> <p>% with history of CVD: 60.4%</p> <p>% with Type 2 diabetes: 100%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p>	<p>Duration: NR</p> <p>Exposure to Follow Up Time: 0</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: Estimated 24hr urinary sodium excretion from one fasting morning urine sample.</p> <p>Sodium, Method of Validation: NR</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Combination with Ramipril Global Endpoint Trial (ONTARGET Sample)	Inclusion: Included all European participants of The ONTARGET trial; all trial participants aged 55 years or older, and were diagnosed with vascular disease or type 2 diabetes mellitus with end-organ damage. Exclusion: Excluded participants with missing information on the renal outcome or relevant confounders.		recorded: Estimated 24hr urinary potassium excretion from one fasting morning urine sample. Potassium, Method of Validation: NR Mortality Outcomes-Method of Ascertainment: Unclear	
Ekinci, 2011 ¹⁸⁸ Location: Australia Setting: Community Design: Prospective Cohort study	Study of: Adults N: 620 % Male: 56 Mean Age/Range/Age at Baseline: 64 Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 85 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included type 2 diabetes patients originally recruited for a long-term diabetes study. And included patients who reported at least three previous estimations of urinary AER, with at least one AER measure taken in 2000. Exclusion: Excluded participants with type 1 diabetes or diabetes secondary to medication or pancreatitis.	Exposure Type: 24-h urinary sodium Exposure Unit: mmol/24h Duration: NR Exposure to Follow Up Time: not clear CVD mortality (CVD listed as a major contributing cause) Dose format: NR per 100 mmol/day, Dose: NR All-cause mortality (All death) Dose format: NR per 100 mmol/day, Dose: mean 184 mmol/24 h	Sodium measure: Single 24-hour urine analysis with validation, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: patients completed a 24-h urine collection Mortality Outcomes-Method of Ascertainment: Hospital records, Search national death registry	All-cause mortality (All death) (mmol/24h/Outcome): Median 9.9 years FU per 100 mmol/day cases: 175, total: 620 Adjustment: Age, sex, pre-existing CVD, eGFR, atrial fibrillation, log10AER, systolic blood pressure, diabetes duration (decades) No significant association was observed. CVD mortality (CVD listed as a major contributing cause) (mmol/24h/Outcome): per 100 mmol/day cases: 75, total: 620 Adjustment: Age, sex, pre-existing CVD, eGFR, atrial fibrillation, log10AER, systolic blood pressure, diabetes duration (decades) No significant association was observed.
Fan, 2014 ¹⁸⁹ Location: US Setting: Community Design: Prospective Cohort study Study Name: The MDRD (Modification)	Study of: Adults % Male: 60.5 Mean Age/Range/Age at Baseline: mean 51.7 (SD 12.4) years Race: white 85 Systolic BP: mean 131.9 (SD 17.6) Diastolic BP: mean 81.0 (SD 10.1) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 27.1 (SD 4.4) % with Hypertension: NR % with history of CVD: 13.1	Duration: 4 years Exposure to Follow Up Time: NA	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Patients either had three (n=200) or four (n=640) 24-hour urine collections and analysis to calculate 24-h urinary sodium excretion. Mortality Outcomes-	See subgroup table for results

Study	Participants	Exposure	Intake Status Ascertainment	Results
of Diet in Renal Disease) Study	<p>% with Type 2 diabetes: 5.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included CKD patients age between 18 and 70 years. Included men with serum creatinine level of 1.4–7.0 mg/dL and women with serum creatinine level of 1.2–7.0 mg/dL. Exclusion: Excluded those who were pregnant, those with type 1 and 2 diabetes, those with glomerulonephritis caused by autoimmune diseases, those with obstructive uropathy, those with renal artery stenosis, those with proteinuria with protein greater than 10 g/d, those with mean arterial pressure greater than 125 mm Hg, or those with prior kidney transplantation.</p>		Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: renal data system	
Fang, 2000 ¹⁹⁰ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES I	<p>Study of: Adults</p> <p>% Male: 38.2 Mean Age/Range/Age at Baseline: NR Race: 83.5 white Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination. Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	Duration: NR Exposure to Follow Up Time: up to 22 years	Sodium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates	See subgroup table for results
Ferraro, 2016 ¹⁹¹ ; Taylor, 2004 ¹⁹² Location: US Setting:	<p>Study of: Adults</p> <p>% Male: NR Mean Age/Range/Age at Baseline: mean 54.3 (SD 9.8) Race: NR Systolic BP: NR Diastolic BP: NR</p>	Duration: NR Exposure to Follow Up Time: 0	Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: One food frequency questionnaire at baseline and	See subgroup table for results

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Community Design: Prospective Cohort study</p> <p>Study Name: Health Professionals Follow-up Study</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 25.5 (SD 3.4) % with Hypertension: 21% % with history of CVD: NR % with Type 2 diabetes: 3% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included HPFS participants without a history of kidney stones at baseline. Exclusion: Excluded those with a history of malignancy (except for nonmelanoma skin cancer) at baseline and those who developed malignancies during follow-up. Excluded NHS I participants who answered questionnaires before 1992 (the year of the first lifetime kidney stone history inquiry).</p>		<p>additional FFQ every 4 years Potassium, Method of Validation: FFQs were found to be reproducible and valid in the HPFS and the NHS I. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: supplementary questionnaire (self-report)</p>	
<p>Forman, 2012¹⁹³</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Study of: Adults N: 5556</p> <p>% Male: Q1 32.5, Q2 43.5, Q3 48.1, Q4 58.4 Mean Age/Range/Age at Baseline: Median (IQR): Q1 43 (36-52)y, Q2 43 (36-52), Q3 43 (36-51), Q4 44 (37-52) Race: NR Systolic BP: Median (IQR): Q1 116 (108-126), Q2 118 (110-127), Q3 119 (111-128), Q4 121 (112-129) mmHg Diastolic BP: Median (IQR): Q1 69 (64-74), Q2 70 (65-75) Q3 70 (65-75), Q4 71 (66-76)</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Median (IQR): Q1 23.7 (21.7- 26.2), Q2 24.2 (22.2-26.7), Q3 24.9 (22.6-27.3), Q4 25.7 (23.5- 28.4) kg/m² % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants who did not have prevalent hypertension (defined as a systolic pressure \geq 140 mmHG, a diastolic pressure \geq 90 mmHg, or both or the use of antihypertensive medications in concordance with recommendations from the Seventh JointNational Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.) at the time of their initial</p>	<p>Exposure Type: Urine sodium Exposure Unit: NR</p> <p>Duration(in months): 76.8 (6.4 years) Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times, 1st-1997 and 1998; 2 nd-2001 and 2003, 3rd-2003 and 2006</p> <p>How was blood pressure measured? BP was measured on the right arm with an automated device (Dinamap XL model 9300; Johnson & Johnson Medical, Tampa, FL) for 8 to 10 minutes while the participant was supine. The BP for the visit was defined as the mean of the last 2 readings.</p>	<p>Hypertension (Measured on the right arm with an automated device) (NR/Outcome): Median followup 6.4 years FU NR cases: NR, total: NR Adjustment: Baseline level of serum uric acid, age, body mass index, sex, alcohol intake, smoking status, systolic and diastolic blood pressures, estimated glomerular filtration rate, plasma levels of glucose and cholesterol, and urinary levels of potassium, calcium, and creatinine Significant interaction between sodium intake and serum uric acid (SUA) levels. A 1-g-higher sodium intake was associated with higher risk of hypertension among those in the highest tertile of SUA. Significant interaction between sodium intake and urine albumin excretion (UAE). A 1-g-higher sodium intake was associated with greater risk of developing hypertension among participants whose UAE was greater than 15 mg/d.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	examination and had available measurements of urine sodium. Exclusion: People who were taking antihypertensive medications at the first or third examinations and who were with missing data on SUA or UAE.			
Geleijnse, 1990 ¹⁹⁴ Location: Netherlands Setting: suburban town Design: Prospective Cohort study	Study of: Children N: 596 % Male: 46.35 Mean Age/Range/Age at Baseline: mean 13.2 (SD 2.7) Range 5.9-17.0 Race: NR Systolic BP: mean 112.4 (SD 12.9) range 81.0-153.0 Diastolic BP: mean 68.4 (SD 8.7) range 44.0-97.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants aged 5- 19 years were included Exclusion: Children who had established secondary hypertension were excluded.	Exposure Type: 24 hour potassium excretion Exposure Unit: mmol/24 h Exposure Type: 24 hour sodium excretion Exposure Unit: mmol/24 h Exposure Type: Sodium potassium ratio Exposure Unit: NR Duration(in months): 84 (7 years) Exposure to Follow Up Time: immediately Dose format: mean Level in lower third, Dose: 61.5 - 117.7 Level in middle third, Dose: NR Level in upper third, Dose: 147.5 - 251.5	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 6 times, every year Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 6 times, every year How was blood pressure measured? BP measurements were performed with a random zero sphygmomanometer. Cuffs 23 cm by 10 or 14 cm were used depending on the arm circumference. In children aged over 10 generally the largest cuff was used. BP was measured in the left arm after 15 minutes' sitting. DBP was recorded at the fifth Korotkoff phase.	Systolic blood pressure (Random zero sphygmomanometer) (mmol/24 h/Outcome): Level in lower third cases: NR, total: 596, Level in middle third cases: NR, total: 596, Level in upper third cases: NR, total: 596 Adjustment: Sex, initial age, and change in height and body weight. Significant positive association between sodium-potassium ratio and change in systolic blood pressure. No significant association between sodium excretion and change in blood pressure. Systolic blood pressure (Random zero sphygmomanometer) (mmol/24 h/Outcome): Level in lower third cases: NR, total: 596, Level in middle third cases: NR, total: 596, Level in upper third cases: NR, total: 596 Adjustment: Sex, initial age, change in height and body weight, and sodium excretion. Significant inverse association between urinary potassium excretion and systolic blood pressure.
Geleijnse, 2007 ¹⁹⁵ ; Hofman, 1991 ¹⁹⁶ Location: Netherlands Setting: Community	Study of: Adults N: 5531 % Male: 41 Mean Age/Range/Age at Baseline: mean 69.2 (SD 8.7) Race: NR Systolic BP: mean 140 (SD 22) Diastolic BP: mean 74 (SD 11) Magnesium: NR Calcium: NR	Exposure Type: Dietary potassium Exposure Unit: mg/day Exposure Type: Estimated 24-Hour Urinary Potassium Excretion (spot urine) Exposure Unit: mmol/24 h	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: collected 1 overnight urine sample at baseline Sodium, Method of Validation: NR Potassium measure:	All-cause mortality (CVD mortality comprised fatal myocardial infarction, fatal stroke, sudden cardiac death and other forms of fatal CVD (ICD-10 codes I20-I25, I46, I49, I50, I60-I67, I70-I74, and R96).) (mmol/mmol/Outcome): Median 5.5 y FU per 1 unit increase cases: 795, total: control, per standard deviation cases: 795, total: control Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Design: Prospective Cohort study</p> <p>Study Name: The Rotterdam Study</p>	<p>Other Minerals: NR</p> <p>Mean BMI: mean 26.4 (SD 3.8)</p> <p>% with Hypertension: 37</p> <p>% with history of CVD: 17</p> <p>% with Type 2 diabetes: 10</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included all residents aged 55 years and older living in the Ommoord district of Rotterdam. Everyone who live there at a specific point in time and are willing to participate are eligible.</p> <p>Exclusion: Excluded those who did not provide informed consents.</p>	<p>Exposure Type: Urinary sodium</p> <p>Exposure Unit: mmol/24 h</p> <p>Exposure Type: Urinary sodium/potassium ratio</p> <p>Exposure Unit: mmol/mmol</p> <p>Exposure Type: Urinary sodium/potassium ratio</p> <p>Exposure Unit: ratio</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 5 years</p> <p>Dose format: NR per 1 unit increase, Dose: NR for overall per standard deviation, Dose: Random subcohort mean 117 (SD 69) mmol/24h per standard deviation, Dose: Random subcohort mean 3.6 (SD 0.8) g/day per standard deviation, Dose: Random subcohort mean 45 (SD 22) mmol/24h</p>	<p>Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: collected 1 overnight urine sample at baseline</p> <p>Potassium, Method of Validation: NR</p> <p>Mortality Outcomes-Method of Ascertainment: Population registry</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital Discharge Registry, General Practitioner's Records</p>	<p>No significant association between urinary sodium/potassium ratio and mortality.</p> <p>CVD mortality (CVD mortality comprised fatal myocardial infarction, fatal stroke, sudden cardiac death and other forms of fatal CVD (ICD-10 codes I20-I25, I46, I49, I50, I60-I67, I70-I74, and R96).) (ratio/Outcome): Median 5.5 y FU per 1 unit increase cases: 217, total: control, per standard deviation cases: 217, total: control</p> <p>Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion</p> <p>No significant association between urinary sodium/potassium ratio and CVD events.</p> <p>Incidence MI (Myocardial infarction comprised ICD-10 code I21. Both fatal and non- fatal incident events were recorded.) (ratio/Outcome): Median 5.5 y FU per 1 unit increase cases: 206, total: control, per standard deviation cases: 206, total: control</p> <p>Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion</p> <p>No association between sodium potassium ratio and risk of MI.</p> <p>Incidence stroke (Stroke comprised ICD-10 codes I60-I67. Both fatal and non- fatal incident events were recorded.) (ratio/Outcome): Median 5.5 y FU per 1 unit increase cases: 181, total: control, per standard deviation cases: 181, total: control</p> <p>Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion</p> <p>No association between sodium potassium ratio and risk of stroke.</p> <p>All-cause mortality (CVD mortality comprised fatal myocardial infarction, fatal stroke, sudden cardiac death and other forms of fatal CVD (ICD-10 codes I20-I25, I46, I49, I50, I60-I67, I70-I74, and R96).) (mmol/24 h/Outcome): Median 5.5 y FU per standard deviation cases: 795, total: control</p> <p>Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion</p> <p>For dietary potassium, similar results were obtained except for risk of all-cause mortality that was significantly reduced both in the entire cohort (RR = 0.78 (0.65–0.94 per 1-SD) and in subjects initially free of CVD and hypertension (RR = 0.71 (0.51–1.00), model 3).</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>Urinary potassium did neither predict all-cause mortality.</p> <p>CVD mortality (CVD mortality comprised fatal myocardial infarction, fatal stroke, sudden cardiac death and other forms of fatal CVD (ICD-10 codes I20-I25, I46, I49, I50, I60-I67, I70-I74, and R96).) (mmol/24 h/Outcome): Median 5.5 y FU per standard deviation cases: 217, total: control Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion No significant association between potassium intake and risk of CVD mortality. Urinary potassium tended to be positively associated with incident CVD events or mortality, especially in subjects who were initially free of CVD and hypertension. After full adjustment for confounders (model 3), however, none of these associations were statistically significant.</p> <p>Incidence MI (Myocardial infarction comprised ICD-10 code I21. Both fatal and non- fatal incident events were recorded.) (mmol/24 h/Outcome): Median 5.5 y FU per standard deviation cases: 206, total: control Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion After full adjustment for confounders (model 3), however, none of these associations were statistically significant. No significant association between potassium intake and risk of MI.</p> <p>Incidence stroke (Stroke comprised ICD-10 codes I60-I67. Both fatal and non- fatal incident events were recorded.) (mmol/24 h/Outcome): Median 5.5 y FU per standard deviation cases: 181, total: control Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion After full adjustment for confounders (model 3), however, none of these associations were statistically significant. No significant association between potassium intake and risk of stroke.</p>
<p>Green, 2002¹⁹⁷</p> <p>Location: US</p> <p>Setting: Community</p>	<p>Study of: Adults N: 5600</p> <p>% Male: 72.8 Mean Age/Range/Age at Baseline: mean (SD) Race: 15% black Systolic BP: by serum potassium level <=4.0 mEq/L 138; >4.0 mEq/L 135 Diastolic BP: by serum potassium level <=4.0 mEq/L 72; >4.0 mEq/L 70</p>	<p>Exposure Type: Potassium from NCI food frequency questionnaire with reported validation</p>	<p>Method of validation: quality control experiments</p> <p>Outcome method of ascertainment: Interview with participant or proxy at annual visit</p>	

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Design: Prospective Cohort study</p> <p>Study Name: The Cardiovascular Health Study</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: by serum potassium level <=4.0 mEq/L 62%; >4.0 mEq/L 37%</p> <p>% with history of CVD: % with Type 2 diabetes: by serum potassium level <=4.0 mEq/L 62%; >4.0 mEq/L 37%</p> <p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: patients randomly selected from Medicare eligibility lists in 4 U.S. communities: Forsyth County, NC; Sacramento County, CA; Washington County, MD; and Allegheny County, PA. Patients were all 65 years of age or older. An additional 687 minority individuals were recruited from 1992 to 1993.</p> <p>Exclusion: those who did not complete initial enrollment testing, which included a medical history and physical examination.</p>			
<p>Gu, 2001³⁶</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Potassium and Protein Supplementation Study (PAPSS)</p>	<p>Study of: Adults N: 140 N: 150</p> <p>Intervention 1: % Male: 37.3 Mean Age/Range/Age at Baseline: 56.9 (SD 7.4) Race: NR Systolic BP: 136.9 Diastolic BP: 81.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 66.9</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 42.7 Mean Age/Range/Age at Baseline: 55 (SD 7.6) Race: NR Systolic BP: 134 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p> <p>Duration(in months): 3 Exposure to Follow Up Time: NR</p> <p>Dose format: NR all, Dose: NR</p>	<p>Sodium Status Arm 2: 185.7 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 at screening, Once at 6 weeks, then at 12 weeks Potassium, Method of Validation: Pill count Potassium Status Arm 2: 54.2 mmol/24 h</p> <p>How was blood pressure measured? Trained staff using Hawksley random zero sphygmomanometers. Taken on the right arm with appropriately sized cuffs after quietly sitting for 5 min. BP recorded three times at each screening, then at follow up visits at 6 and 12 weeks.</p>	<p>Diastolic blood pressure (Hawksley random zero sphygmomanometers) (mmol/24h/Outcome): 12 weeks FU all cases: NR, total: 140 Adjustment: Gender, baseline SBP, baseline body weight, potassium changes during intervention, sodium changes during intervention No association between urinary sodium excretion during the intervention and DBP.</p> <p>Systolic blood pressure (Hawksley random zero sphygmomanometers) (mmol/24h/Outcome): all cases: NR, total: 140 Adjustment: Gender, baseline DBP, baseline body weight, potassium changes during intervention, sodium changes during intervention Borderline significant association between urinary sodium excretion during the intervention and reduction in SBP.</p> <p>Diastolic blood pressure (Hawksley random zero sphygmomanometers) (mmol/24h/Outcome): 12 weeks FU all cases: NR, total: 140 Adjustment: Gender, baseline SBP, baseline body weight, potassium changes during intervention, sodium changes during intervention No association between urinary excretion of potassium during the intervention and DBP.</p> <p>Systolic blood pressure (Hawksley random zero sphygmomanometers) (mmol/24h/Outcome): all cases: NR, total: 140</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Mean BMI: 27.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 45-64. SBP 13-159 mmHg, DBP<95 mmHg OR SBP<160 mmHg AND DBP < 160 mmHg. Able to take potassium supplements in accordance with protocol Exclusion: blood pressure medication in the last 2 months, history of CVD, diabetes at any time, non-skin malignancy in the last 5 years, COPD, psychiatric disease, other life threatening illnesses. serum creatinine >=1.7 mg/dl or K+>=5.0 mmol/l at screening, alcohol use of >=21 drinks/week or >=40 g/day. Pregnancy, plans to move out of study area, or non-cooperation.</p>			<p>Adjustment: Gender, baseline DBP, baseline body weight, potassium changes during intervention, sodium changes during intervention Significant association between urinary excretion of potassium during the intervention and reduction in SBP.</p>
<p>Hajjar, 2001¹⁹⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: 12267</p> <p>% Male: 48.8% Mean Age/Range/Age at Baseline: ranged 25-74 years Race: White 42 African American 28 Hispanic 26 other 4 Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information. Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>24-hour dietary recall</p>		<p>See Yang, 2011</p>
<p>Haring, 2015¹⁹⁹</p>	<p>Study of: Adults</p>	<p>Duration: 2 years Exposure to Follow</p>	<p>Sodium measure: Food Frequency Questionnaire</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Strong Heart Study</p>	<p>% Male: pre-hypertension/hypertension 46.71%; normal blood pressure 78.04%</p> <p>Mean Age/Range/Age at Baseline: pre-hypertension/hypertension mean 29.29 (SD 6.51) years; normal blood pressure mean 27.4 (SD 6.79) years</p> <p>Race: NR</p> <p>Systolic BP: pre-hypertension/hypertension mean 126 (SD 11); normal blood pressure mean 108 (SD 7)</p> <p>Diastolic BP: pre-hypertension/hypertension mean 82 (SD 9); normal blood pressure mean 69 (SD 7)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: pre-hypertension/hypertension mean 34.58 (SD 8.12); normal blood pressure mean 30.87 (SD 8.27)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: pre-hypertension/hypertension 16.37%; normal blood pressure 5.41%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included study participants between ages 14 to 39.</p> <p>Exclusion: Excluded participants with incomplete data or extreme energy intake. Excluded participants with a history of any cardiovascular disease or stroke, for example, myocardial infarction, angina pectoris, heart failure, coronary bypass surgery, angioplasty, carotid endarterectomy, valve replacement and significant valve disease (aortic or mitral stenosis or more than mild regurgitation).</p>	<p>Up Time: on average 4 years</p>	<p>Best sodium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Sodium, Method of Validation: FFQ administered by interviewer</p> <p>Potassium measure: Food Frequency Questionnaire</p> <p>Best potassium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Potassium, Method of Validation: FFQ administered by interviewer</p> <p>How was blood pressure measured? Blood pressure measured as the average of 2 blood pressure readings at baseline examination.</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Physical examination</p>	
<p>He, 1999²⁰⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults</p> <p>% Male: 38.9</p> <p>Mean Age/Range/Age at Baseline: age reported by sodium quartile and weight status: non overweight q1 mean 46.2 (SD 15.4) years, non overweight q2 mean 48.3 (SD 15.8) years, non overweight q3 mean 49.3 (SD15.9) years, non overweight q4 mean 48.6 (SD 15.8) years; overweight q1 mean 50 (SD 14.9) years, overweight q2 mean 51.1 (SD 15) years, overweight q3 mean 52 (SD15) years, overweight q4 mean 51.3 (SD 14.8) years.</p> <p>Race: White race, % reported by sodium quartile and weight status: non overweight q1 mean 82.3,</p>	<p>Duration: NR</p> <p>Exposure to Follow Up Time: 113,467 person-years; an average of 19 years</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24h dietary recall with 3-dimensional food-portion models</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, Death certificate reports</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>non overweight q2 mean 87.6, non overweight q3 mean 86.3, non overweight q4 mean 90.1; overweight q1 mean 73.5, overweight q2 mean 76.7, overweight q3 mean 77.4, overweight q4 mean 82.4.</p> <p>Systolic BP: Systolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 129.0 (SD 23.2), non overweight q2 mean 129.5 (SD 21.6), non overweight q3 mean 131.4 (SD 22.9), non overweight q4 mean 130.7 (SD 23.2); overweight q1 mean 141.7 (SD 24.1) years, overweight q2 mean 142.4 (SD 24.4), overweight q3 mean 144.8 (SD 25.2), overweight q4 mean 143.5 (SD 24.6).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 80.6 (SD 12.7), non overweight q2 mean 80.2 (SD 11.5), non overweight q3 mean 81.3 (SD 12.1), non overweight q4 mean 80.6 (SD 12.2); overweight q1 mean 89.0 (SD 12.9) years, overweight q2 mean 88.3 (SD 13.0), overweight q3 mean 89.1 (SD 13.4), overweight q4 mean 88.9 (SD 13.2).</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and weight status: non overweight q1 mean 23.1 (SD 2.6), non overweight q2 mean 23.1 (SD 2.7), non overweight q3 mean 23.1 (SD 2.7), non overweight q4 mean 23.2 (SD 2.7); overweight q1 mean 32.0 (SD 4.4) years, overweight q2 mean 31.6 (SD 4.1), overweight q3 mean 32.0 (SD 4.7), overweight q4 mean 31.6 (SD 3.9).</p> <p>% with Hypertension: % with hypertension reported by sodium quartile and weight status: non overweight q1 mean 19.1, non overweight q2 mean 19.1, non overweight q3 mean 21.6, non overweight q4 mean 21.8; overweight q1 mean 42.2, overweight q2 mean 42.8, overweight q3 mean 43.8, overweight q4 mean 42.3.</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: % with type 2 diabetes reported by sodium quartile and weight status: non overweight q1 mean 2.1, non overweight q2 mean 2.6, non overweight q3 mean 2.9, non overweight q4 mean 3.8; overweight q1 mean 4.2, overweight q2 mean 5.4, overweight q3 mean 5.6, overweight q4 mean 5.7.</p> <p>% with Kidney disease: NR % with history of Kidney stones: NR</p>			

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Inclusion: NHANES I participants who were 25-74 years old during survey collection period 1971-1975</p> <p>Exclusion: Exclude those who did not complete 24h dietary recall, who did not report sodium intake information, and those who self-reported history of heart attack, heart failure, or stroke at baseline, or taking medication for heart disease. Also excluded those who were taking a low-salt diet at baseline.</p>			
<p>He, 2002²⁰¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The first National Health and Nutrition Examination Surbey (NHANES I) Epidemiologic Follow-up Study (NHEFS)</p>	<p>Study of: Adults</p> <p>% Male: non overweight 36 overweight 44</p> <p>Mean Age/Range/Age at Baseline: mean (SD) non overweight 48.2 (16.1) overweight mean 52.2 (SD 15.2)</p> <p>Race: African American race non overweight 13% overweight 19%</p> <p>Systolic BP: mean (SD) overweight 129.2(23.4) overweight 141.0 (24.7)</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: nonoverweight 20 overweight 38</p> <p>% with history of CVD: valvular heart disease nonoverweight 5, overweight 5; coronary heart disease nonoverweight 4, overweight 5</p> <p>% with Type 2 diabetes: non overweight 3, overweight 6</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants in NHANES I aged 25 to 74 years were included.</p> <p>Exclusion: People who lacked 240hour dietary recall information, or who lacked sodium intake information, or who had a history of CHF at their baseline examination, or who were consuming a low-salt diet at baseline were excluded.</p>	<p>Duration: NR</p> <p>Exposure to Follow Up Time: 85035 person-years from 1971 through 1992</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: once</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records</p>	<p>See subgroup table for results</p>
<p>He, 2016²⁰²; Yang, 2014²⁰³; Lash, 2009²⁰⁴</p> <p>Location: US</p> <p>Setting: Community</p>	<p>Study of: Adults</p> <p>N: 3757</p> <p>% Male: by sodium excretion group g1 37.8% g2 48.1% g3 64% g4 72.4%</p> <p>Mean Age/Range/Age at Baseline: by sodium excretion group g1 mean 59.7 (SD 10.6) g2 mean 58.4 (SD 10.9) g3 mean 57.6 (SD 10.9) g4 mean 55.2 (SD 10.8)</p>	<p>Exposure Type: 24-h urinary sodium</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 0</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2).</p> <p>Sodium, Method of</p>	<p>All-cause mortality (Death from all causes) (mmol/24h/Outcome): 20,465 person-years FU</p> <p>Q1 cases: 144, total: 940, person-years: 4994, Q2 cases: 145, total: 939, person-years: 5080, Q3 cases: 123, total: 938, person-years: 5195, Q4 cases: 128, total: 940, person-years: 5196</p> <p>Adjustment: Age, sex, race, urinary creatinine excretion, and clinic site. education, waist circumference, lean body mass, body mass index, cigarette smoking, alcohol drinking, physical activity, history of hypercholesterolemia, history of diabetes, history of CVD, use of diuretics,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: by sodium excretion group g1 mean 29.1 (SD 6.9) g2 mean 31.2 (SD 7.2) g3 mean 32.4 (SD 6.8) g4 mean 34.9 (SD 8.1)</p> <p>% with Hypertension: by sodium excretion group g1 83.4% g2 84.5% g3 88.5% g4 87.9%</p> <p>% with history of CVD: by sodium excretion group g1 31.3% g2 35.4% g3 32.3% g4 33%</p> <p>% with Type 2 diabetes: by sodium excretion group g1 40.2% g2 48% g3 47.7% g4 55.2%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included CRIC Study participants with eGFR between 20 and 70 ml/min per 1.73 m² depending on age.</p> <p>Exclusion: Excluded participants who received dialysis, or a kidney transplant and excluded those with GN requiring immunosuppression, with advanced heart failure, cirrhosis, or polycystic kidney disease. Also excluded participants without a 24-hour urine specimen or with incomplete 24-hour urine collection. And excluded those with urinary sodium excretion less than 20 mmol/24 h.</p>	<p>Dose format: range</p> <p>Q1, Dose: <116.8</p> <p>Q2, Dose: 116.8-153.6</p> <p>Q3, Dose: 153.7-194.5</p> <p>Q4, Dose: >=194.6</p>	<p>Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method.,</p> <p>Multiple 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2).</p> <p>Potassium, Method of Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method.</p> <p>Mortality Outcomes-Method of Ascertainment: Death certificate</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit, US Renal Data System</p>	<p>use of renin-angiotensin system blocking agents, and use of other antihypertensive medications. baseline eGFR. plus adjustment for urinary potassium excretion</p> <p>Higher dietary sodium intake associated with a non-significant increased risk of all-cause mortality.</p> <p>After adjusting for SBP, higher dietary sodium intake associated with a non-significant increased risk of all-cause mortality.</p>
<p>Hirvonen, 1999²⁰⁵; The ATBC Cancer Prevention Study Group, 1994²⁰⁶</p> <p>Location: Finland</p> <p>Setting:</p>	<p>Study of: Adults</p> <p>Inclusion: Included male smokers who smoked at least five cigarettes per day at study entry and signed written informed consent.</p> <p>Exclusion: Excluded those with a history of serious disease such as cancer, and those using vitamin E, vitamin A, or p-carotene supplements in excess of</p>	<p>Exposure Type: 1.21847E-2</p> <p>Exposure Unit: Potassium intake</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 5 years</p> <p>Dose format: Q1 g/day, Dose: median</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire</p> <p>Best potassium measure recorded: self-administered diet history questionnaire</p> <p>Potassium, Method of Validation: Dietary assessment method was</p>	<p>Kidney stones (Kidney) (Potassium intake/Outcome): Physician-diagnosed kidney stone for the first time FU</p> <p>g/day cases: NR, total: NR, person-years: 3.8, g/day cases: NR, total: NR, person-years: 4.6, g/day cases: NR, total: NR, person-years: 5.1, g/day cases: NR, total: NR, person-years: 5.7</p> <p>Adjustment: NR</p> <p>Age, supplementation group, vocational training, marital status, and intakes of magnesium, fiber, and alcohol.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: the Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention</p> <p>.</p>	<p>predefined doses; and those receiving treatment with anticoagulant agents.</p>	<p>g/day, Dose: median g/day, Dose: median g/day, Dose: median</p>	<p>validated in a pilot study carried out among 190 men prior to the ATBC Study. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: self reported, followup visit</p>	
<p>Inoue, 2016²⁰⁷</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Study of: Adults</p> <p>% Male: 0 Mean Age/Range/Age at Baseline: mean 34.1 (SD 4.9) Race: NR Systolic BP: mean 102 (SD 10) Diastolic BP: mean 63 (SD 8) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 21.7 (SD 4.7) % with Hypertension: 8.2 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Women with chronic hypertension or multiple pregnancy were included. Exclusion: Women who cannot undergo the first investigation (the first blood and urine sampling, and BP measurement) before the 20th gestational week, and those who had known heart disease or nephropathy were excluded.</p>	<p>Duration: 20 weeks of gestation to 30 weeks of gestation Exposure to Follow Up Time: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, one before the 20th gestational week, and the other after the improvement of hyperemesis gravidarum How was blood pressure measured? HBP was measured twice using an HEM- 7051 (Omron Healthcare, Kyoto, Japan) based on the cuff-oscillometric method. The participants were asked to measure HBP at their upper arm within 1h of waking up, after micturition, before breakfast, while seated, after resting >1 min. HBP was measured for 7 consecutive days including the day of home urine collection before 20 weeks of gestation. In addition, HBP was also measured for 7 consecutive days after 30 weeks of gestation.</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Joosten, 2014²⁰⁸</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Study of: Adults N: 7543</p> <p>% Male: by sodium quartiles q1 48.7 q2 48.7 q3 48.7 q4 48.7</p> <p>Mean Age/Range/Age at Baseline: by sodium quartiles q1 mean 50 (SD 13) q2 mean 49 (SD 13) q3 mean 48 (SD 12) q4 mean 47 (SD 11)</p> <p>Race: NR</p> <p>Systolic BP: by sodium quartiles q1 mean 129 (SD 22) q2 mean 128 (SD 20) q3 mean 128 (SD 20) q4 mean 129 (SD 20)</p> <p>Diastolic BP: by sodium quartiles q1 mean 74 (SD 10) q2 mean 74 (SD 10) q3 mean 74 (SD 10) q4 mean 74 (SD 9)</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: by sodium quartiles q1 mean 25 (SD 3.7) q2 mean 25.5 (SD 3.7) q3 mean 26.1 (SD 4.1) q4 mean 27.5 (SD 4.8)</p> <p>% with Hypertension: by sodium quartiles q1 32.8 q2 30.4 q3 31.4 q4 30.7</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: by sodium quartiles q1 2.2 q2 2.5 q3 2.9 q4 4.7</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included Dutch participants between ages 28 to 75 and those who agreed to participate in questionnaire survey and urine sample collection. Exclusion: Excluded pregnant women and those with type I diabetes.</p>	<p>Exposure Type: Sex-specific quartiles of sodium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: a median of 10.5 years</p> <p>Dose format: range Q1, Dose: male <95 female <122 Q2, Dose: male 95-121 female 122-154 Q3, Dose: male 122-151 female 155-190 Q4, Dose: male >151 female >190 continuous, Dose: per 1-g/d increase</p>	<p>Sodium measure: two 24-hr urine analysis with out reported quality control measure</p> <p>Best sodium measure recorded: During baseline examination, participants collected two 24-hour urines for 2 consecutive days.</p> <p>Mortality Outcomes-Method of Ascertainment: Central Bureau of Statistics</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: national registry of hospital discharge diagnoses</p>	<p>Coronary Heart Disease Events (CHD was defined as myocardial infarction (ICD-code 410), acute and subacute ischemic heart disease (ICD-code 411) and coronary artery bypass grafting or percutaneous transluminal coronary angioplasty.) (mmol/24h/Outcome):</p> <p>Median 10.5 years (Q1-Q3: 9.9-10.8 years; 71491 person years) FU</p> <p>Q1 cases: 123, total: 1885, person-years: 17638, continuous cases: 452, total: 7543, person-years: 71491, Q2 cases: 111, total: 1886, person-years: 17975, Q3 cases: 112, total: 1886, person-years: 17878, Q4 cases: 106, total: 1886, person-years: 18000</p> <p>Adjustment: Age, body mass index, smoking status, sex, alcohol intake, parental history of coronary heart disease, type 2 diabetes, total to high-density lipoprotein cholesterol ratio, and urinary potassium, magnesium, and creatinine excretion</p> <p>In multivariable analysis, there was no significant association between a continuous term of sodium excretion and risk of CHD.</p> <p>In multivariable analysis, there was no significant association between a continuous term of sodium excretion and risk of CHD.</p>
<p>Kagan, 1985²⁰⁹; Kagan, 1974²¹⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Hawaiian Study</p>	<p>Study of: Adults N: 8006</p> <p>% Male: 100</p> <p>Mean Age/Range/Age at Baseline: free of stroke mean 54.3 developed stroke mean 56.9</p> <p>Race: NR</p> <p>Systolic BP: reported by age groups: 45-49 128.6; 50-54 132; 55-59 134.3; 60-64 138.6; 65-69 142.2</p> <p>Diastolic BP: reported by age groups: 45-49 81.8; 50-54 82; 55-59 84.7; 60-64 83; 65-69 83.5</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p>	<p>Exposure Type: Sodium intake</p> <p>Exposure Unit: g</p> <p>Duration(in months): 2-6 years</p> <p>Exposure to Follow Up Time: 10 years</p> <p>Dose format: range Q1, Dose: <=1.78 Q2, Dose: 1.79- Q3, Dose: 2.39- Q4, Dose: 3.01- Q5, Dose: 3.87+</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: 24h dietary recall</p> <p>Sodium, Method of Validation: Data validated by repeating 24-hr recall interviews and 7-day dietary records in a sample of the men examined 2 yr later. Correlation coefficients ranged from 0.4 to 0.6 for most of the nutrients, suggesting good reproducibility.</p>	<p>Total stroke (g/Outcome): 10 years FU</p> <p>Q1 cases: 29.9 (incidence), total: NR, Q2 cases: 31.3 (incidence), total: NR, Q3 cases: 23.9 (incidence), total: NR, Q4 cases: 32.0 (incidence), total: NR, Q5 cases: 28.4 (incidence), total: NR</p> <p>Adjustment: Age</p> <p>No association was found between an index of sodium intake and the incidence of stroke. The determination of sodium intake was based on the 24-hour diet recall method and did not include salt or soy sauce added at the table, so a relation could be obscured by the crudeness of this measure.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included men of Japanese ancestry born between 1900-1010, lived on the island of Oahu. Included those who were successfully identified through Selective Service records from World War II, and also successfully located through searches of telephone, business, and state agency records. In addition, those included also returned a completed questionnaire in early 1965.</p> <p>Exclusion: 1st level analysis excluded 111 men with stroke; 2nd level analysis excluded individuals showing evidence of coroner heart disease or cancer at entry exam, also excluded those who reported atypical diet the day before dietary exam;</p>		<p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Death certificate reports, Physical examination</p>	
<p>Khaw, 1987²¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 859</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: range 50-79 years</p> <p>Race: NR</p> <p>Systolic BP: No stroke associated death (men) mean 141.5 mmHg, stroke-associated death (men) mean 143.2 mmHg; No stroke-associated death (women) mean 136.4 mmHg, stroke-associated death (women) 147.2 mmHg</p> <p>Diastolic BP: No stroke-associated death (men) mean 84.3 mmHg, stroke-associated death (men) mean 83.2; No stroke-associated death (women) mean 81.3 mmHg, stroke-associated death (women) mean 86.3 mmHg</p> <p>Magnesium: No stroke-associated death (men) mean 11.6, stroke-associated death (men) mean 9.9; No stroke-associated death (women) mean 9.1 mmHg, stroke-associated death (women) mean 8.0 mmol</p> <p>Calcium: No stroke-associated death (men) mean 20.2, stroke-associated death (men) mean 16.1; No stroke-associated death (women) mean 15.1 mmHg, stroke-associated death (women) mean 14.9 mmol</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mmol/d</p> <p>Duration(in months): 144 (12 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR per 10 mmol, Dose: mean 64 (range 17-154) mmol/d</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: Once (at baseline)</p> <p>Potassium, Method of Validation: A 24-hour recall of dietary intake was obtained by a certified Lipid Research Clinic dietician. The data were coded for nutrient intake by the Nutrition Coordinating Center, University of Minnesota, with use of their data base.</p> <p>How was blood pressure measured? BP was measured by trained observers who used a standard mercury sphygmomanometer after the subject had been seared at rest for at least five minutes. BP was only measured once at baseline.</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing,</p>	<p>Stroke-associated All-cause mortality (ICDA 430 to 438) (mmol/d/Outcome): 12 y FU per 10 mmol cases: 24, total: 859</p> <p>Adjustment: Calories, protein, fat, fiber, calcium, magnesium, and alcohol, age and sex</p> <p>Dietary potassium remained a significant predictor of stroke-associated mortality, and the relative risk was not changed.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	Inclusion: Men and Women who were 50 to 79 years old and who had no personal history of heart attack, heart failure, or stroke at the base-line examination were included in the study. Exclusion: NR		national death index searches, deaths confirmed from death certificates CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Death certificate reports	
Kieneker, 2014 ²¹² Location: Netherlands Setting: Community Design: Prospective Cohort study Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study	Study of: Adults N: 5511 % Male: 45.3 Mean Age/Range/Age at Baseline: by potassium turtles t1 mean 45.9 (SD 11.6) t2 mean 45.7 (SD 10.8) t3 mean 44.2 (SD 10.1) Race: by potassium turtles t1 white 90.7 t2 white 96.6 t3 white 98.4 Systolic BP: by potassium turtles t1 mean 118 (SD 11) t2 mean 119 (SD 11) t3 mean 119 (SD 11) Diastolic BP: by potassium turtles t1 mean 70 (SD 7) t2 mean 70 (SD 7) t3 mean 70 (SD 7) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: by potassium turtles t1 mean 24.7 (SD 3.8) t2 mean 25.2 (SD 3.8) t3 mean 25.4 (SD 3.9) % with Hypertension: by potassium turtles t1 27.2 t2 29.1 t3 30.8 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included PREVEND cohort participants who completed examinations in 1997 and 1998. Exclusion: Excluded those with hypertension, undergoing dialysis, and those with missing urinary data.	Exposure Type: Na-K excretion ratio Exposure Unit: NR Exposure Type: Urinary Potassium Excretion Exposure Unit: mmol/24 h Duration: NR Exposure to Follow Up Time: up to 10 years Dose format: range T1, Dose: male <68; female <58 T1, Dose: male<1.7; female <1.6 T2, Dose: male 68-86; female 58-74 T2, Dose: male 1.7-2.3; female 1.6-2.2 T2+T3, Dose: Male >=68; female >=58 T3, Dose: male>86; female >74 T3, Dose: male >2.3; female >2.2	Potassium measure: two 24-hr urine analysis without reported validation Best potassium measure recorded: Two 24-hr urine analysis at baseline and second examination, for each analysis participants collected 2 consecutive 24-hr specimens. How was blood pressure measured? Blood pressure was measured as the mean of last 2 readings from each examinations. The study conducted 4 examinations in 1997-1998, 2001-2003, 2003-2006, and 2006-2008.	Hypertension (Systolic BP of ≥ 140 mm Hg, a diastolic BP of ≥ 90 mmHg, or the use of antihypertensive drugs, in concordance with recommendations from the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of H) (NR/Outcome): Median 7.6 years FU T1 cases: 372, total: NR, person-years: 10847, T2 cases: 412, total: NR, person-years: 10751, T3 cases: 388, total: NR, person-years: 10213 Adjustment: Age, sex, body mass index, smoking status, alcohol consumption, parental history of hypertension, and urinary sodium excretion, education and urinary magnesium and calcium excretion, plasma aldosterone Null association between Na-K excretion ratio and risk of hypertension. Hypertension (Systolic BP of ≥ 140 mm Hg, a diastolic BP of ≥ 90 mmHg, or the use of antihypertensive drugs, in concordance with recommendations from the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of H) (mmol/24 h/Outcome): Median 7.6 years FU T1 cases: 401, total: 1836, person-years: 9738, T2 cases: 400, total: 1838, person-years: 10919, T2+T3 cases: 771, total: 3675, person-years: 22071, T3 cases: 371, total: 1837, person-years: 11152 Adjustment: Age, sex, body mass index, smoking status, alcohol consumption, parental history of hypertension, and urinary sodium excretion, education and urinary magnesium and calcium excretion In multivariable analysis, the lowest tertile of potassium intake was associated with an increased risk of hypertension. Found a non-linear inverse association between urinary potassium excretion and risk of hypertension.
Kieneker, 2016 ²¹³ ; Hillege, 2001 ²¹⁴ ; Joosten, 2013 ²¹⁵ Location: Netherlands Setting:	Study of: Adults N: 7795 % Male: Q1: 48.7; Q2: 48.6; Q3 48.7; Q4 48.6; Q5 48.7 Mean Age/Range/Age at Baseline: Q1: mean 50.6 (SD 13.3); Q2 mean 50.3 (SD 12.6); Q3 mean 49.5 (SD 12.2); Q4 mean 48.4 (SD 12.2); Q5 46.7 (11.2) years Race: NR Systolic BP: Q1: mean 130 (SD 22); Q2: mean 129	Exposure Type: 24-h urinary potassium excretion Exposure Unit: mmol/24 h Exposure Type: 24-h urinary sodium excretion Exposure Unit: mmol/24 h	Sodium measure: Discussion., Didn't say anything in the method part but in the results part, the authors conducted analysis between sodium and CVD, IHD, stroke and HF. Potassium measure: More than one 24-hour	All-cause mortality (Linking the number of the death certificate to the primary cause of death as coded by the Dutch Central Bureau of Statistics) (mmol/24 h/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 122, total: NR, person-years: 14966, Q1 cases: 93, total: NR, person-years: 15143, per 1-unit increase cases: 493, total: 7795, person-years: 75725, per 50-mmol/24-h increase cases: 493, total: 7795, person-years: 75725, Q2 cases: 129, total: NR, person-years: 15074, Q2 cases: 91, total: NR, person-years: 15077, Q3 cases: 104, total: NR, person-years: 15142, Q3 cases: 89, total: NR, person-years: 15206, Q4 cases: 118, total: NR, person-years: 15101, Q4 cases: 84, total: NR, person-years: 15195, Q5

Study	Participants	Exposure	Intake Status Ascertainment	Results
Community Design: Prospective Cohort study Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study	(SD 20); Q3: mean 128 (SD 20); Q4: mean 128 (SD 19); Q5: mean 127 (SD 18) mmHg Diastolic BP: Q1: mean 75 (SD 10); Q2: mean 74 (SD 10); Q3: mean 74 (SD 10); Q4: mean 73 (SD 9); Q5: mean 73 (SD 9) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 25.8 (SD 4.3); Q2 mean 25.9 (SD 4.1); Q3 mean 26.0 (SD 4.0); Q4: mean 26.0 (SD 4.2); Q5: mean 26.5 (SD 4.5) kg/ m ² % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants aged 28-75 years with a urinary albumin concentration of ≥10 mg/L and/or a urinary albumin concentration <10 mg/ L were included. Exclusion: People with a history of cardiovascular events, or renal disease requiring dialysis or with missing values of urinary analyses at baseline were excluded.	Exposure Type: Sodium to potassium excretion ratio Exposure Unit: NR Exposure Type: Sodium to potassium excretion ratio Exposure Unit: mmol/mmol Duration(in months): 129.6 (10.5 years) Exposure to Follow Up Time: NR Composite outcome (Cardiovascular disease (including ischemic heart disease and stroke), heart failure, and all-cause mortality) Dose format: median Q1, Dose: 46 Q1, Dose: <1.6 for men and, <1.4 for women Q1, Dose: <115 for men and, <89 for women Q2, Dose: 60 Q2, Dose: 1.6-1.9 for men and 1.4-1.7 for women Q2, Dose: 115-141 for men and 89-110 for women Q3, Dose: 69 Q3, Dose: 142-167 for men and 111-132 for women Q3, Dose: 2.0-2.2 for men and 1.8-2.0 for women Q4, Dose: 81 Q4, Dose: 168-201 for men and 133-160 for women Q4, Dose: 2.3-2.7 for men and 2.1-2.6 for	urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, first: between 1997 and 1998 (baseline); second: between 2001 and 2003. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports	cases: 69, total: NR, person-years: 15284, Q5 cases: 87, total: NR, person-years: 15262 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of all-cause mortality. No statistically significant association was observed. Q1 cases: 204, total: NR, person-years: 14626, Q1 cases: 265, total: NR, person-years: 14278, per 1-unit increase cases: 1099, total: 7795, person-years: 72803, per 50-mmol/24-h increase cases: 1099, total: 7795, person-years: 72803, Q2 cases: 214, total: NR, person-years: 14466, Q2 cases: 246, total: NR, person-years: 14535, Q3 cases: 210, total: NR, person-years: 14619, Q3 cases: 219, total: NR, person-years: 14541, Q4 cases: 190, total: NR, person-years: 14689, Q4 cases: 259, total: NR, person-years: 14419, Q5 cases: 179, total: NR, person-years: 14760, Q5 cases: 212, total: NR, person-years: 14673 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of composit outcome. No statistically significant association was observed. Risk of New-onset heart failure (Criteria described in the Heart Failure Guidelines of the European Society of Cardiology, and an endpoint adjudication committee ascertained the diagnosis of HF as described elsewhere (23)) (NR/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 70, total: NR, person-years: 15040, per 1-unit increase cases: 265, total: 7795, person-years: 75180, Q2 cases: 64, total: NR, person-years: 14953, Q3 cases: 44, total: NR, person-years: 15073, Q4 cases: 42, total: NR, person-years: 15002, Q5 cases: 45, total: NR, person-years: 15112 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of new on-set heart failure. The sodium to potassium excretion ratio was not statistically significantly associated with risk of CVD, IHD, stroke, and HF, with maHRs (95% CIs) per 1-unit increment in the ratio of 0.99 (0.90, 1.09), 1.04 (0.95, 1.15), 0.82 (0.65, 1.03), and 1.05 (0.94, 1.16), respectively

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>women Q5, Dose: 100 Q5, Dose: >2.7 for men and >2.6 for women Q5, Dose: >201 for men and >160 for women per 1-unit increase, Dose: NR for overall per 26-mmol/24-h increase, Dose: Median 70mmol/24h (IQR: 56–84 mmol/24 h) per 50-mmol/24-h increase, Dose: NR</p> <p>All-cause mortality (Linking the number of the death certificate to the primary cause of death as coded by the Dutch Central Bureau of Statistics) Dose format: median Q1, Dose: 46 Q1, Dose: <1.6 for men and, <1.4 for women Q1, Dose: <115 for men and, <89 for women Q2, Dose: 60 Q2, Dose: 1.6-1.9 for men and 1.4-1.7 for women Q2, Dose: 115-141 for men and 89-110 for women Q3, Dose: 69 Q3, Dose: 142–167 for men and 111-132 for women Q3, Dose: 2.0-2.2 for men and 1.8-2.0 for women Q4, Dose: 81 Q4, Dose: 168-201 for men and 133-160 for women Q4, Dose: 2.3-2.7 for</p>		<p>Risk of Cardiovascular disease (The combined incidence of fatal and nonfatal events of IHD, stroke, and vascular interventions such as percutaneous transluminal angioplasty or bypass grafting of aorta and peripheral vessels) (NR/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 165, total: NR, person-years: 14685, per 1-unit increase cases: 641, total: 7795, person-years: 73187, Q2 cases: 146, total: NR, person-years: 14558, Q3 cases: 116, total: NR, person-years: 14670, Q4 cases: 122, total: NR, person-years: 14487, Q5 cases: 92, total: NR, person-years: 14787 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of CVD. The sodium to potassium excretion ratio was not statistically significantly associated with risk of CVD, IHD, stroke, and HF, with maHRs (95% CIs) per 1-unit increment in the ratio of 0.99 (0.90, 1.09), 1.04 (0.95, 1.15), 0.82 (0.65, 1.03), and 1.05 (0.94, 1.16), respectively</p> <p>Risk of Composite cardiovascular (Cardiovascular disease (including ischemic heart disease and stroke), and heart failure) (mmol/24 h/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 186, total: NR, person-years: 14278, per 50-mmol/24-h increase cases: 785, total: 7795, person-years: 72803, Q2 cases: 158, total: NR, person-years: 14535, Q3 cases: 165, total: NR, person-years: 14541, Q4 cases: 140, total: NR, person-years: 14689, Q5 cases: 136, total: NR, person-years: 14760 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No statistically significant association was observed.</p> <p>Risk of Composite cardiovascular outcome (Cardiovascular disease (including ischemic heart disease and stroke), and heart failure) (NR/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 141, total: NR, person-years: 14626, per 1-unit increase cases: 785, total: 7795, person-years: 72803, Q2 cases: 154, total: NR, person-years: 14466, Q3 cases: 147, total: NR, person-years: 14619, Q4 cases: 181, total: NR, person-years: 14419, Q5 cases: 162, total: NR, person-years: 14673 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>men and 2.1-2.6 for women Q5, Dose: 100 Q5, Dose: >2.7 for men and >2.6 for women Q5, Dose: >201 for men and >160 for women per 1-unit increase, Dose: NR for overall per 26-mmol/24-h increase, Dose: Median 70mmol/24h (IQR: 56-84 mmol/24 h) per 50-mmol/24-h increase, Dose: NR for overall</p> <p>Risk of Cardiovascular disease (The combined incidence of fatal and nonfatal events of IHD, stroke, and vascular interventions such as percutaneous transluminal angioplasty or bypass grafting of aorta and peripheral vessels), Risk of IHD (Acute myocardial infarction (code 410), acute and subacute ischemic heart disease (code 411), coronary artery bypass grafting (code 414), or percutaneous transluminal coronary angioplasty (code 36.0)), Risk of stroke (Subarachnoid hemorrhage (code 430), intracerebral hemorrhage (code 431), intracerebral hemorrhage (code 432), or occlusion or stenosis of the precerebral (code 433) or cerebral (code 434) arteries) (NR/Outcome) Dose format: median Q1, Dose: 46 Q1, Dose: <1.6 for men and, <1.4 for women</p>		<p>including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of composite CVD outcomes.</p> <p>Risk of IHD (Acute myocardial infarction (code 410), acute and subacute ischemic heart disease (code 411), coronary artery bypass grafting (code 414), or percutaneous transluminal coronary angioplasty (code 36.0)) (NR/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 117, total: NR, person-years: 14829, per 1-unit increase cases: 465, total: 7795, person-years: 73824, Q2 cases: 103, total: NR, person-years: 14787, Q3 cases: 88, total: NR, person-years: 14649, Q4 cases: 88, total: NR, person-years: 14649, Q5 cases: 69, total: NR, person-years: 14867 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of IHD. The sodium to potassium excretion ratio was not statistically significantly associated with risk of CVD, IHD, stroke, and HF, with maHRs (95% CIs) per 1-unit increment in the ratio of 0.99 (0.90, 1.09), 1.04 (0.95, 1.15), 0.82 (0.65, 1.03), and 1.05 (0.94, 1.16), respectively</p> <p>Risk of stroke (Subarachnoid hemorrhage (code 430), intracerebral hemorrhage (code 431), other intracranial hemorrhage (code 432), or occlusion or stenosis of the precerebral (code 433) or cerebral (code 434) arteries) (NR/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 48, total: NR, person-years: 14990, per 1-unit increase cases: 172, total: 7795, person-years: 75140, Q2 cases: 39, total: NR, person-years: 14965, Q3 cases: 31, total: NR, person-years: 15058, Q4 cases: 32, total: NR, person-years: 14933, Q5 cases: 22, total: NR, person-years: 15194 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No association between sodium to potassium excretion ration and risk of stroke. The sodium to potassium excretion ratio was not statistically significantly associated with risk of CVD, IHD, stroke, and HF, with maHRs (95% CIs) per 1-unit increment in the ratio of 0.99 (0.90, 1.09), 1.04 (0.95, 1.15), 0.82 (0.65, 1.03), and 1.05 (0.94, 1.16), respectively</p> <p>All-cause mortality (Linking the number of the death certificate to the</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>Q2, Dose: 60 Q2, Dose: 1.6-1.9 for men and 1.4-1.7 for women Q3, Dose: 69 Q3, Dose: 2.0-2.2 for men and 1.8-2.0 for women Q4, Dose: 81 Q4, Dose: 2.3-2.7 for men and 2.1-2.6 for women Q5, Dose: 100 Q5, Dose: >2.7 for men and >2.6 for women per 1-unit increase, Dose: NR for overall per 26-mmol/24-h increase, Dose: Median 70mmol/24h (IQR: 56–84 mmol/24 h)</p> <p>Risk of Composite cardiovascular disease (including ischemic heart disease and stroke), and heart failure) Dose format: median Q1, Dose: 46 Q1, Dose: <115 for men and, <89 for women Q2, Dose: 60 Q2, Dose: 115-141 for men and 89-110 for women Q3, Dose: 69 Q3, Dose: 142–167 for men and 111-132 for women Q4, Dose: 81 Q4, Dose: 168-201 for men and 133-160 for women Q5, Dose: 100 Q5, Dose: >201 for men and >160 for women</p>		<p>primary cause of death as coded by the Dutch Central Bureau of Statistics) (mmol/24 h/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 139, total: 1558, person-years: 14991, per 26-mmol/24-h increase cases: 493, total: 7795, person-years: 75725, Q2 cases: 107, total: 1561, person-years: 15209, Q3 cases: 97, total: 1558, person-years: 15150, Q4 cases: 82, total: 1561, person-years: 15209, Q5 cases: 68, total: 1557, person-years: 15165 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No significant association between potassium excretion and all-cause mortality.</p> <p>Composite outcome (Cardiovascular disease (including ischemic heart disease and stroke), heart failure, and all-cause mortality) (mmol/24 h/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 295, total: 1558, person-years: 14220, per 26-mmol/24-h increase cases: 1099, total: 7795, person-years: 72803, Q2 cases: 237, total: 1561, person-years: 14594, Q3 cases: 210, total: 1558, person-years: 14615, Q4 cases: 194, total: 1561, person-years: 14668, Q5 cases: 163, total: 1557, person-years: 14706 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. No significant association between potassium excretion and composite outcome.</p> <p>Risk of Cardiovascular disease (The combined incidence of fatal and nonfatal events of IHD, stroke, and vascular interventions such as percutaneous transluminal angioplasty or bypass grafting of aorta and peripheral vessels) (mmol/24 h/Outcome): Median 10.5y (IQR 9.9 - 10.8y) FU Q1 cases: 165, total: 1558, person-years: 14345, per 26-mmol/24-h increase cases: 641, total: 7795, person-years: 73187, Q2 cases: 146, total: 1561, person-years: 14690, Q3 cases: 116, total: 1558, person-years: 14667, Q4 cases: 122, total: 1561, person-years: 14734, Q5 cases: 92, total: 1557, person-years: 14751 Adjustment: Age, sex, lifestyle and dietary factors, including BMI, smoking status, alcohol consumption, education, and 24-h urinary sodium and magnesium excretion, and additional cardiovascular disease risk factors, including parental history of cardiovascular disease, use of lipid-lowering drugs, presence of type 2 diabetes, total: HDL cholesterol ratio, and urinary creatinine excretion. After adjustment for age and sex, each 1-g/ d increment in urinary</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>per 26-mmol/24-h increase, Dose: Median 70mmol/24h (IQR: 56–84 mmol/24 h)</p> <p>per 50-mmol/24-h increase, Dose: NR</p> <p>Risk of New-onset heart failure (Criteria described in the Heart Failure Guidelines of the European Society of Cardiology, and an endpoint adjudication committee ascertained the diagnosis of HF as described elsewhere (23))</p> <p>Dose format: median Q1, Dose: 46 Q2, Dose: 60 Q3, Dose: 69 Q4, Dose: 81 Q5, Dose: 100</p> <p>per 26-mmol/24-h increase, Dose: Median 70mmol/24h (IQR: 56–84 mmol/24 h)</p> <p>Risk of New-onset heart failure (Criteria described in the Heart Failure Guidelines of the European Society of Cardiology, and an endpoint adjudication committee ascertained the diagnosis of HF as described elsewhere (23)), Risk of Composite cardiovascular outcome (Cardiovascular disease (including ischemic heart disease and stroke), and heart failure)</p> <p>Dose format: range Q1, Dose: <1.6 for</p>		<p>potassium excretion was associated with a 13% lower risk of CVD. However, these associations lost significance after multivariable adjustment for age, sex, BMI, smoking status, alcohol consumption, education, and urinary sodium and magnesium ex</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		men and, <1.4 for women Q2, Dose: 1.6-1.9 for men and 1.4-1.7 for women Q3, Dose: 2.0-2.2 for men and 1.8-2.0 for women Q4, Dose: 2.3-2.7 for men and 2.1-2.6 for women Q5, Dose: >2.7 for men and >2.6 for women per 1-unit increase, Dose: NR for overall		
Kieneker, 2016 ²¹⁶	Study of: Adults N: 5315 Location: Netherlands Setting: Community Design: Prospective Cohort study Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study . Inclusion: Participants aged 28 to 75 were included Exclusion: Pregnant women and subjects with type I diabetes mellitus were excluded. People with CKD at baseline or unknown CKD status, or with renal disease requiring dialysis, or with missing values of urinary analytes, or with no follow-up data available for CKD, or with missing values of body measurements at baseline were also excluded.	Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h Duration: 10.3 year Exposure to Follow Up Time: NR Dose format: range Q1, Dose: M <114 F<90 Q1, Dose: M <60 F<51 Q2, Dose: M 114-140 F 90-110 Q2, Dose: M 60-71 F 51-60 Q3, Dose: M 141-165 F 111-131 Q3, Dose: M 72-82 F 61-69 Q4, Dose: M 166-199 F 132-159 Q4, Dose: M 83-95 F 70-81 Q5, Dose: M >199 F >159	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, (baseline and the second examination) Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, (baseline and the second examination) CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: CKD was defined as a combination of reaching an eGFR of 30 mg/ 24 h de novo, or both	EGFR < 60 ml/min per 173 m ² (mmol/24h/Outcome): Median 10.3 years FU Q1 cases: 83, total: NR, person-years: 9642, Q2 cases: 62, total: NR, person-years: 9940, Q3 cases: 64, total: NR, person-years: 10126, Q4 cases: 47, total: NR, person-years: 10187, Q5 cases: 35, total: NR, person-years: 10464 Adjustment: Age, sex, height, weight, smoking status, alcohol consumption, parental history of CKD, race, diabetes, and urinary potassium, calcium, urea, and creatinine excretion, baseline eGFR and UAE No association between urinary sodium excretion and risk of developing CKD. EGFR < 60 ml/min per 173 m ² (mmol/24h/Outcome): Median 10.3 years FU Q1 cases: 87, total: NR, person-years: 9585, Q2 cases: 73, total: NR, person-years: 9896, Q3 cases: 46, total: NR, person-years: 10099, Q4 cases: 49, total: NR, person-years: 10201, Q5 cases: 36, total: NR, person-years: 10578 Adjustment: Age, sex, height, weight, smoking status, alcohol consumption, parental history of CKD, race, diabetes, and urinary potassium, calcium, urea, and creatinine excretion, baseline eGFR and UAE Significant association between 1 SD (21 mmol/24hr) increase in urinary potassium excretion and a 16% higher risk of developing CKD.

Study	Participants	Exposure	Intake Status Ascertainment	Results
		Q5, Dose: M >95 F >81		
Krupp, 2015 ²¹⁷ ; Shi, 2014 ²¹⁸ ; Kruppe, 2014 ²¹⁹ ; Kroke, 2004 ²²⁰	<p>Study of: Children</p> <p>% Male: 52.4%</p> <p>Mean Age/Range/Age at Baseline: 3 months</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: by gender boys mean 18.9 (SD 2.3) girls mean 18.7 (SD 2.7)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included Germans recruited at 3 months of age and who completed three repeated urinary, dietary and blood pressure measurements in adolescence and one additional blood pressure measurement in young adulthood.</p> <p>Exclusion: Excluded those who were born before 36 weeks gestation and those with missing data.</p>	<p>Duration: NR</p> <p>Exposure to Follow Up Time: an average of 12 years</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 repeated 24-hour urine analysis with validation</p> <p>Sodium, Method of Validation: Minimized errors with creatinine excretion cutoff., Multiple 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: 3 repeated 24-hour urine analysis with validation</p> <p>Potassium, Method of Validation: Minimized errors with creatinine excretion cutoff.</p> <p>How was blood pressure measured? Two blood pressure readings for each BP measurement was assessed by trained nurses with first a random zero sphygmomanometer and with a standard mercury sphygmomanometer. BP values measured with a standard zero sphygmomanometers were multiplied with an internally validated conversion factor (e.g., 1.056 for systolic BP).</p>	See subgroup table for results
Lamelas, 2016 ²²¹	<p>Study of: Adults</p> <p>N: 16549</p> <p>% Male: 40.3</p> <p>Mean Age/Range/Age at Baseline: mean 51.4 (SD 9.6) years</p> <p>Race: NR</p> <p>Systolic BP: mean 132.0 (SD 21.5)</p> <p>Diastolic BP: mean 82.4 (SD 12.5)</p> <p>Magnesium: NR</p>	<p>Exposure Type: 24 h urinary sodium excretion (estimated)</p> <p>Exposure Unit: g/day</p> <p>Duration(in months): 56.4 (4.7 years)</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: once spot urine (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation</p>	<p>All-cause mortality (g/day/Outcome): Median 4.7 y FU</p> <p>G1 cases: 32, total: 1638, G2 cases: 87, total: 3885, G3 cases: 115, total: 4758, G4 cases: 80, total: 3457, G5 cases: 54, total: 1748, G6 cases: 46, total: 1063</p> <p>Adjustment: Age, sex, body mass index, smoking status, diabetes, educational level, alcohol consumption, past CV events, and country</p> <p>Non-significant positive association between sodium excretion of less than 3 g/day and increase in all-cause mortality.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 28.1 (SD 5.5)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: 9.1</p> <p>% with Type 2 diabetes: 7.2</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants aged 35-70 years from urban and rural communities located in 18 countries around the world were included.</p> <p>Exclusion: N/A</p>	<p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-3.99</p> <p>G3, Dose: 4-4.99</p> <p>G4, Dose: 5-5.99</p> <p>G5, Dose: 6-6.99</p> <p>G6, Dose: >7</p>	<p>study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>How was blood pressure measured? The mean of duplicate sitting BP was measured by trained research assistants after at least 3 minutes rest at all centers, following a standardized procedure using an Omron digital BP measuring device (Omron HEM-757) provided for all sites.</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions)</p>	<p>All-cause mortality or major CVD (g/day/Outcome): Median 4.7 y FU</p> <p>G1 cases: 50, total: 1638, G2 cases: 115, total: 3885, G3 cases: 161, total: 4758, G4 cases: 110, total: 3457, G5 cases: 73, total: 1748, G6 cases: 59, total: 1063</p> <p>Adjustment: Age, sex, body mass index, smoking status, diabetes, educational level, alcohol consumption, past CV events, and country</p> <p>There is a possible J-shaped association between sodium excretion and CVD events and mortality. And a non-significant positive association between sodium excretion of less than 3 g/day and increase in primary composite outcome.</p> <p>Major CVD (g/day/Outcome): Median 4.7 y FU</p> <p>G1 cases: 27, total: 1638, G2 cases: 62, total: 3885, G3 cases: 80, total: 4758, G4 cases: 48, total: 3457, G5 cases: 41, total: 1748, G6 cases: 29, total: 1063</p> <p>Adjustment: Age, sex, body mass index, smoking status, diabetes, educational level, alcohol consumption, past CV events, and country</p> <p>Significant positive association between sodium excretion of less than 3 g/day and increase in major CVD disease.</p>
<p>Larsson, 2008²²²</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults</p> <p>N: 26556</p> <p>% Male: 100</p> <p>Mean Age/Range/Age at Baseline: by potassium quintiles q1 mean 57.8 q5 mean 57.3</p> <p>Race: NR</p> <p>Systolic BP: by potassium quintiles q1 mean 143.7 q5 mean 141</p> <p>Diastolic BP: by potassium quintiles q1 mean 88 q5 mean 86.8</p> <p>Magnesium: NR</p> <p>Calcium: NR</p>	<p>Exposure Type: Potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 13.6 years</p> <p>Dose format: Median</p> <p>Q1, Dose: 3912</p> <p>Q2, Dose: 4451</p> <p>Q3, Dose: 4837</p>	<p>Sodium measure: Food frequency questionnaire</p> <p>Sodium, Method of Validation: Use of a published food frequency questionnaire</p> <p>Best potassium measure recorded: completed one 276-item food frequency questionnaire at baseline.</p> <p>Potassium, Method of Validation:</p>	<p>Cerebral infarction (Definition for stroke but reported by subtype: ICD-8 codes 430 through 434 and 436; ICD-9 codes 430, 431, 433, 434, and 436; and ICD-10 codes I60, I61, I63, and I64, excluding ICD-8 codes 431.01 and 431.91 denoting subdural hemorrhage and ICD-9 codes 4330) (mg/d/Outcome):</p> <p>Mean 13.6 years (360187 person-years) FU</p> <p>Q1 cases: 566, total: NR, Q2 cases: 594, total: NR, Q3 cases: 518, total: NR, Q4 cases: 519, total: NR, Q5 cases: 505, total: NR</p> <p>Adjustment: Age, supplementation group, number of cigarettes smoked daily, body mass index, systolic and diastolic blood pressures, serum total cholesterol, serum high-density lipoprotein cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, and intake of alcohol and total energy.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Study Name: The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study</p>	<p>Other Minerals: NR Mean BMI: by potassium quintiles q1 mean 26 q5 mean 26.7 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: by potassium quintiles q1 3.8 q5 9.4 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included Finnish men between ages 50-69, who smoked 5 or more cigarettes per day. Exclusion: Excluded those with a history of cancer or other serious disease, or those received anticoagulant therapy, or used excess doses or vitamin E, vitamin A, or beta carotene supplements.</p>	<p>Q4, Dose: 5237 Q5, Dose: 5859</p>	<p>questionnaire validated in Pietinen P, Hartman AM, Haapa E, et al. Reproducibility and validity of dietary assessment instruments, I: a self-administered food use questionnaire with a portion size picture booklet. Am J Epidemiol. 1988;128(3):655-666. Mortality Outcomes-Method of Ascertainment: National register of causes of death CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital Discharge Registry</p>	<p>Statistically significant inverse association between potassium intake and the risk of cerebral infarction after adjustment for age and supplementation group only; and this association was still significant but attenuated after further adjustment for cardiovascular risk factors.</p> <p>Intracerebral hemorrhage (Definition for stroke but reported by subtype: ICD-8 codes 430 through 434 and 436; ICD-9 codes 430, 431, 433, 434, and 436; and ICD-10 codes I60, I61, I63, and I64, excluding ICD-8 codes 431.01 and 431.91 denoting subdural hemorrhage and ICD-9 codes 4330) (mg/d/Outcome): Mean 13.6 years (360187 person-years) FU Q1 cases: 85, total: NR, Q2 cases: 79, total: NR, Q3 cases: 74, total: NR, Q4 cases: 78, total: NR, Q5 cases: 67, total: NR Adjustment: Age, supplementation group, number of cigarettes smoked daily, body mass index, systolic and diastolic blood pressures, serum total cholesterol, serum high-density lipoprotein cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, and intake of alcohol and total energy. No significant association between potassium intake and risk of stroke (intracerebral hemorrhage).</p> <p>Subarachnoid hemorrhage (Definition for stroke but reported by subtype: ICD-8 codes 430 through 434 and 436; ICD-9 codes 430, 431, 433, 434, and 436; and ICD-10 codes I60, I61, I63, and I64, excluding ICD-8 codes 431.01 and 431.91 denoting subdural hemorrhage and ICD-9 codes 4330) (mg/d/Outcome): Mean 13.6 years (360187 person-years) FU Q1 cases: 37, total: NR, Q2 cases: 36, total: NR, Q3 cases: 35, total: NR, Q4 cases: 39, total: NR, Q5 cases: 49, total: NR Adjustment: Age, supplementation group, number of cigarettes smoked daily, body mass index, systolic and diastolic blood pressures, serum total cholesterol, serum high-density lipoprotein cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, and intake of alcohol and total energy. No significant association between potassium intake and risk of stroke (subarachnoid hemorrhage).</p>
<p>Larsson, 2011²²³</p> <p>Location: Sweden</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Swedish</p>	<p>Study of: Adults N: 34670</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: by potassium quintiles q1 mean 61.6 q5 mean 60.7</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: by potassium quintiles q1 mean 24.8 q5 mean 25.3 % with Hypertension: by potassium quintiles q1</p>	<p>Exposure Type: Potassium intake Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: a mean of 10.4 years</p> <p>Dose format: Median Q1, Dose: 2419 Q2, Dose: 2767 Q3, Dose: 3021 Q4, Dose: 3296 Q5, Dose: 3744</p>	<p>Potassium measure: food frequency questionnaire with reported validation Best potassium measure recorded: One 96-item food frequency questionnaire completed in 1997 Potassium, Method of Validation: The food frequency questionnaire has been validated in Messerer M, Johansson SE, Wolk A. The validity of</p>	<p>Total stroke (Strokes were classified as cerebral infarction (code I63), intracerebral hemorrhage (code I61), subarachnoid hemorrhage (code I60), and unspecified stroke (code I64).) (mg/d/Outcome): Mean 10.4 years FU Q1 cases: 373, total: NR, person-years: 70668, Q2 cases: 340, total: NR, person-years: 71751, Q3 cases: 348, total: NR, person-years: 72067, Q4 cases: 311, total: NR, person-years: 72312, Q5 cases: 308, total: NR, person-years: 72215 Adjustment: Age, smoking status, pack-years of smoking, educational level, body mass index, total physical activity level, history of diabetes, history of hypertension, aspirin use, family history of myocardial infarction, and intakes of total energy, alcohol, protein, cholesterol, total fiber, and folate No overall association between dietary intakes of potassium, and risk of total stroke or cerebral infarction after adjustment for other risk factors</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Mammography Cohort	<p>18.6% q5 20.4% % with history of CVD: NR % with Type 2 diabetes: by potassium quintiles q1 2.2% q5 4.5% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included women born between 1914-1948 and living in central Sweden. Included those who completed both diet questionnaires at baseline and in 1997. Exclusion: Excluded women with incorrect national identification number, with a history of stroke, coronary heart disease, or cancer, or with extreme energy intake.</p>		questionnaire-based micronutrient intake estimates is increased by including dietary supplement use in Swedish men. J Nutr. 2004;134(7):1800-1805. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital Discharge Registry	
Leonberg-Yoo, 2016 ²²⁴ , Klahr, 1994 ²²⁵ Location: US Setting: Community Design: Prospective Cohort study Study Name: The MDRD (Modification of Diet in Renal Disease) Study	<p>Study of: Adults</p> <p>% Male: 60.1 Mean Age/Range/Age at Baseline: mean 51.8 (SD 12.4) years Race: white 85.1 black 8 other 6.9 Systolic BP: mean 131.9 (SD 17.6) Diastolic BP: mean 81 (SD 10.1) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 27.1 (SD 4.5) % with Hypertension: NR % with history of CVD: 13.3 % with Type 2 diabetes: 5.2 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included patients with CKD (serum creatinine levels in men, 1.4-7 mg/dL; in women, 1.2- 7 mg/dL) and between ages 18-70. Exclusion: Excluded those who were pregnant, those with type 1 or 2 diabetes, those with urine protein excretion >10 g/d, or had previous kidney transplantation.</p>	Duration: NR Exposure to Follow Up Time: NR	Potassium measure: multiple 24-hr urine analysis without reported validation Best potassium measure recorded: One 24-hr urine analysis at baseline and additional 24-hr urine collections completed every month. Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: renal data system	See subgroup table for results
Lijie Shi, 2014 ²¹⁸ ; Kruppe, 2014 ²¹⁹ ; Kroke, 2004 ²²⁰ ; Krupp, 2015 ²¹⁷ Location: Germany	<p>Study of: Children</p> <p>% Male: 51 Mean Age/Range/Age at Baseline: boys median 6 (IQR 4.0-8.0) girls median 6.0 (IQR 4.0- 7.0) Race: NR Systolic BP: boys median 97.1 (IQR 90.8 -1.04) girls median 97.0 (IQR 90.0- 102) Diastolic BP: boys median 57.0 (IQR 50.0 - 65.0) girls median 55.0 (IQR 49.6 -64.1)</p>	Duration: NR Exposure to Follow Up Time: no data (approximately 10 years)	Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 yearly repeated 24-hour urine analysis How was blood pressure measured? SBP and DBP had been measured	See subgroup table for results

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: boys median 15.7 (IQR 15.0 - 16.8) girls median 15.3 (IQR 14.7 -16.4) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Children aged 4 -18 year old were included. Exclusion: Children who had taken BP-influencing drugs, regularly or on the day of BP measurements, or whose SBP or DBP data were implausible were excluded.</p>		<p>according to standard procedures with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAllyn) thereafter. Appropriate cuff sizes were used according to arm circumferences. BP was measured in the right arm of the subjects after 5 min of rest. Two consecutive BP measurements were recorded on each measurement occasion, and the arithmetic mean of both readings was used in the analysis.</p>	
<p>Mente, 2016²²⁶; Ontarget Investigators, 2008²²⁷; Telmisartan Randomised Assessment Study in ACEiswcdI, 2008²²⁸</p> <p>Location: Turkey: China: India</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology</p>	<p>Study of: Adults N: 133118</p> <p>Inclusion: Included PURE participants who reported baseline blood pressure measurements and submitted their morning fasting urine samples.</p>	<p>Exposure Type: 24-h urinary excretion of sodium Exposure Unit: Estimated Sodium Excretion (Kawasaki equation) Duration: NR Exposure to Follow Up Time: NR</p> <p>Dose format: range group 1, Dose: <3 g/day group 2, Dose: 3-3.99 g/day group 3, Dose: 4-4.99 g/day group 4, Dose: 5-5.99 g/day group 5, Dose: 6-6.99 g/day group 6, Dose: >=7 g/day</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: morning fasting urine sample collected at baseline Sodium, Method of Validation: validated the method with a study of 1083 participants</p>	<p>All-cause mortality (Death) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 812, total: 14533, group 2 cases: 1177, total: 27463, group 3 cases: 1377, total: 34208, group 4 cases: 1102, total: 27670, group 5 cases: 644, total: 15893, group 6 cases: 573, total: 13331 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p> <p>All-cause mortality or CVD event (Death or major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 1323, total: 14533, group 2 cases: 1996, total: 27463, group 3 cases: 2487, total: 34208, group 4 cases: 1965, total: 27670, group 5 cases: 1148, total: 15893, group 6 cases: 937, total: 13331 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication)</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
(PURE) study				<p>There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality.</p> <p>Major CVD events (Major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 1001, total: 14533, group 2 cases: 1472, total: 27463, group 3 cases: 1852, total: 34208, group 4 cases: 1461, total: 27670, group 5 cases: 857, total: 15893, group 6 cases: 725, total: 13331 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetic medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p>
<p>Mills, 2016²²⁹, He, 2016²⁰², Yang, 2014²⁰³, Lash, 2009²⁰⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 3757</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4; 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: mg/24 h</p> <p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Exposure Type: Calibrated 24-Hour Urinary Potassium Excretion quartile; a Calibrated to mean urinary creatinine exc Exposure Unit: mg/24 h</p> <p>Exposure Type: Calibrated 24-Hour Urinary Sodium Excretion Calibrated to mean urinary creatinine excretion of</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>NR cases: NR, total: 1946, NR cases: NR, total: 3528, Q1 cases: 174, total: 939, person-years: 5804, Q1 cases: 198, total: 940, person-years: 5484, Q2 cases: 159, total: 940, person-years: 5972, Q2 cases: 180, total: 939, person-years: 5659, Q3 cases: 198, total: 939, person-years: 5739, Q3 cases: 218, total: 939, person-years: 5676, Q4 cases: 208, total: 939, person-years: 5707, Q4 cases: 273, total: 939, person-years: 5012 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among all participants, greater sodium excretion was associated with an increased risk of composite CVD. Those in the highest quartile of urinary sodium excretion had an increased risk for composite CVD (Sensitivity analysis without calibrating exposure). Those in the highest quartile of urinary sodium excretion had an increased risk for composite CVD. Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for caloric intake). Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for systolic blood pressure).</p> <p>NR cases: NR, total: 1949, NR cases: NR, total: 3533, Q1 cases: 125, total: 939, person-years: 5938, Q1 cases: 147, total: 940, person-years: 5659, Q2 cases: 117, total: 940, person-years: 6216, Q2 cases: 124, total: 939, person-years: 5855, Q3 cases: 127, total: 939, person-years: 5998, Q3 cases: 153, total: 939, person-years: 5954, Q4 cases: 151, total: 939, person-years: 5920, Q4 cases: 206, total: 939, person-years: 5235 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>1,569 Exposure Unit: 1,000 mg difference</p> <p>Exposure Type: Quartile of 24-Hour Urinary Sodium Excretion not calibrated Exposure Unit: mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for overall NR, Dose: mean 3701 (SD 1443) mg Q1, Dose: <1608 mg/24h Q1, Dose: <2686 mg/24h Q1, Dose: <2894 mg/24h Q2, Dose: 1608-2107 mg/24h Q2, Dose: 2687-3532 mg/24h Q2, Dose: 2894-3649 mg/24h Q3, Dose: 2108-2750 mg/24h Q3, Dose: 3533-4473 mg/24h Q3, Dose: 3650-4547 mg/24h Q4, Dose: >=2751 mg/24h Q4, Dose: >=4474 mg/24h Q4, Dose: >=4548 mg/24h</p>		<p>physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among all participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Those in the highest quartile of urinary sodium excretion had an increased risk for CHF (Sensitivity analysis without calibrating exposure).</p> <p>Those in the highest quartile of urinary sodium excretion had an increased risk for CHF.</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for caloric intake).</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for systolic blood pressure).</p> <p>NR cases: NR, total: 1951, NR cases: NR, total: 3540, Q1 cases: 69, total: 939, person-years: 6195, Q1 cases: 76, total: 940, person-years: 5949, Q2 cases: 54, total: 940, person-years: 6336, Q2 cases: 70, total: 939, person-years: 6015, Q3 cases: 77, total: 939, person-years: 6109, Q3 cases: 83, total: 939, person-years: 6175, Q4 cases: 82, total: 939, person-years: 6202, Q4 cases: 99, total: 939, person-years: 5569</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among all participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>No significant association between the highest quartile of urinary sodium excretion and risk for MI.</p> <p>Those in the highest quartile of urinary sodium excretion had an increased risk for MI (Sensitivity analysis without calibrating exposure).</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for caloric intake).</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for systolic blood pressure).</p> <p>NR cases: NR, total: 1950, NR cases: NR, total: 3542, Q1 cases: 28, total: 939, person-years: 6293, Q1 cases: 36, total: 940, person-years: 6045, Q2 cases: 28, total: 940, person-years: 6479, Q2 cases: 39, total: 939, person-years: 6202, Q3 cases: 39, total: 939, person-years: 6262, Q3 cases: 39, total: 939, person-years: 6337, Q4 cases: 34, total: 939, person-years: 6320, Q4 cases: 53, total: 939, person-years: 5719</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among all participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Those in the highest quartile of urinary sodium excretion had an increased risk for stroke (Sensitivity analysis without calibrating exposure).</p> <p>Those in the highest quartile of urinary sodium excretion had an increased risk for stroke.</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for caloric intake).</p> <p>Greater amount of urinary sodium excretion was associated with increased risk of composite CVD, CHF, MI, and stroke (Sensitivity analysis Basic Model plus adjustment for systolic blood pressure).</p> <p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (mg/24 h/Outcome): Median 6.8 years FU Q1 cases: 185, total: 940, person-years: 5833, Q2 cases: 203, total: 939, person-years: 5628, Q3 cases: 177, total: 938, person-years: 5654, Q4 cases: 239, total: 940, person-years: 5410 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Sensitivity analysis with potassium as exposure</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (mg/24 h/Outcome): Median 6.8 years FU Q1 cases: 134, total: 940, person-years: 6025, Q2 cases: 141, total: 939, person-years: 5844, Q3 cases: 131, total: 938, person-years: 5879, Q4 cases: 169, total: 940, person-years: 5640 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Sensitivity analysis with potassium as exposure</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (mg/24 h/Outcome): Median 6.8 years FU Q1 cases: 66, total: 940, person-years: 6279, Q2 cases: 77, total: 939, person-years: 6067, Q3 cases: 72, total: 938, person-years: 6072, Q4 cases: 90, total: 940, person-years: 5857</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Sensitivity analysis with potassium as exposure</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (mg/24 h/Outcome): Median 6.8 years FU Q1 cases: 38, total: 940, person-years: 6354, Q2 cases: 39, total: 939, person-years: 6233, Q3 cases: 30, total: 938, person-years: 6218, Q4 cases: 41, total: 940, person-years: 6024</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Sensitivity analysis with potassium as exposure</p>
<p>Nerbass, 2015²³⁰; McIntyre, 2011²³¹</p> <p>Location: NR</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Renal Risk in Derby (RRID)</p>	<p>Study of: Adults N: 1607</p> <p>% Male: 39.4 Mean Age/Range/Age at Baseline: mean 72.6 (SD 9.0) Race: Caucasian 97.6% Systolic BP: mean 134 (SD 18) Diastolic BP: mean 73 (SD 11) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 29.1 (SD 15.5) % with Hypertension: 88 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged 18 years or over, who met the Kidney Disease Outcomes Quality Initiative criteria for CKD stage 3, and could attend their general practitioner (GP) surgery for assessments were included. Exclusion: People with previously a solid organ transplant or people who were terminally ill were excluded.</p>	<p>Exposure Type: Sodium intake Exposure Unit: mmol/d</p> <p>Duration(in months): 12 Exposure to Follow Up Time: NR</p> <p>Dose format: Na mean (SD) Decreased, Dose: 111 (10) Increased, Dose: 92 (6) Unchanged, Dose: 114 (36)</p>	<p>Sodium measure: a medical and dietary questionnaire Best sodium measure recorded: twice, 1-year</p> <p>How was blood pressure measured? BP was measured after a minimum of 5 min rest in the sitting position, using a validated oscillometric device, which was recommended by the British Hypertension Society (Digital Blood Pressure Monitor Model UA-767; A&D Instruments Ltd). BP was calculated as the mean of three readings from the same device that differed by <10 %. The MAP was calculated as 1/3 the average systolic BP (SBP) plus 2/3 the average diastolic BP (DBP).</p>	<p>Diastolic blood pressure (Validated oscillometric device) (mmol/d/Outcome): 1 year FU Unchanged cases: NR, total: 1416, Decreased cases: NR, total: 105, Increased cases: NR, total: 86 Adjustment: NR Those who decreased in sodium intake also experienced decreases in diastolic blood pressure.</p> <p>Systolic blood pressure (Validated oscillometric device) (mmol/d/Outcome): 1 year FU Unchanged cases: NR, total: 1416, Decreased cases: NR, total: 105, Increased cases: NR, total: 86 Adjustment: NR Those who decreased in sodium intake also experienced decreases in systolic blood pressure.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011²³²; Ontarget Investigators, 2008²²⁷; Telmisartan Randomised Assessment Study in ACEiswDI, 2008²²⁸; Kawasaki, 1993¹⁸⁵</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults</p> <p>% Male: 70.6</p> <p>Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR</p> <p>Systolic BP: mean 141. 72 (SD 17.29) mmHg</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 28.10 (SD 4.55)</p> <p>% with Hypertension: 69.9</p> <p>% with history of CVD: strok 21.2% MI 48.4%</p> <p>% with Type 2 diabetes: 37.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants aged >=55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included.</p> <p>Exclusion: NA</p>	<p>Duration(in months): 56</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: once, before the run-in period of the trial</p> <p>Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: once, before the run-in period of the trial</p> <p>Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit.</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
			ascertainment: Hospital records	
<p>O'Donnell, 2014²³³</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>Q1, Dose: <1.50</p> <p>Q1, Dose: <3.00</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q2, Dose: 3.00-3.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q3, Dose: 4.00-5.99</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q4, Dose: 6.00-6.99</p> <p>Q5, Dose: >3.00</p> <p>Q5, Dose: >=7.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions,</p>	<p>All-cause mortality (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: 293, total: 10810, Q2 cases: 417, total: 21131, Q3 cases: 826, total: 46663, Q4 cases: 216, total: 12324, Q5 cases: 224, total: 11017</p> <p>Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available).</p> <p>There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality.</p> <p>After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: 462, total: 10810, Q2 cases: 622, total: 21131, Q3 cases: 1437, total: 46663, Q4 cases: 391, total: 12324, Q5 cases: 365, total: 11017</p> <p>Adjustment: Analysis including dietary factors and blood pressure (Analysis including dietary 1.19 (1.05–1.36) 1.01 (0.93–1.10) 1.00 1.03 (0.92–1.15) 1.08 (0.96–1.22) factors and blood pressure)</p> <p>Compared to those with an estimated sodium excretion of 4.00 to 5.99 g per day, a higher estimated sodium excretion (≥ 7.00 g per day) was associated with an increased risk of the composite outcome and increased risks of death and major cardiovascular events.</p> <p>Compared to those with an estimated sodium excretion of 4.00 to 5.99 g per day, a higher estimated sodium excretion (≥ 7.00 g per day) was associated with an increased risk of the composite outcome and increased risks of death and major cardiovascular events.</p> <p>Cardiovascular All-cause mortality (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: 109, total: 10810, Q2 cases: 136, total: 21131, Q3 cases: 258, total: 46663, Q4 cases: 66, total: 12324, Q5 cases: 81, total: 11017</p> <p>Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available).</p> <p>There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality.</p> <p>After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
			<p>Contact family members, Captured best available information from reliable sources CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>Heart Failure (g/day/Outcome): Mean 3.7 y FU Q1 cases: 38, total: 10810, Q2 cases: 57, total: 21131, Q3 cases: 117, total: 46663, Q4 cases: 22, total: 12324, Q5 cases: 27, total: 11017 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality. After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>Major Cardiovascular Events (g/day/Outcome): Mean 3.7 y FU Q1 cases: 278, total: 10810, Q2 cases: 381, total: 21131, Q3 cases: 869, total: 46663, Q4 cases: 241, total: 12324, Q5 cases: 222, total: 11017 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality. After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>Myocardial Infarction (g/day/Outcome): Mean 3.7 y FU Q1 cases: 111, total: 10810, Q2 cases: 185, total: 21131, Q3 cases: 370, total: 46663, Q4 cases: 105, total: 12324, Q5 cases: 86, total: 11017 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>Stroke (All) (g/day/Outcome): Mean 3.7 y FU Q1 cases: 126, total: 10810, Q2 cases: 139, total: 21131, Q3 cases: 388, total: 46663, Q4 cases: 114, total: 12324, Q5 cases: 105, total: 11017 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). There is a U-shaped association between 24-hour urinary sodium excretion (estimated by Kawasaki equation) and total mortality. After adjusting for blood pressure, the association between having an estimated sodium excretion ≥ 7.00 g per day and the primary composite outcome, major cardiovascular events, and stroke was attenuated and became no longer significant.</p> <p>All-cause mortality (g/day/Outcome): Mean 3.7 y FU Q1 cases: 437, total: 14262, Q2 cases: 641, total: 31466, Q3 cases: 537, total: 30956, Q4 cases: 261, total: 17171, Q5 cases: 99, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). As compared with an estimated potassium excretion of less than 1.50 g per day, a higher estimated excretion of potassium was associated with a reduction in the risks of death and cardiovascular events on multivariable analysis (Fig. 2 and Table 3); this association was largely related to a reduction in the risk of death (Table S3 in the Supplementary Appendix). No significant association between potassium intake and risk of all-cause mortality.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU Q1 cases: 573, total: 14262, Q2 cases: 1.5, total: 31466, Q3 cases: 942, total: 30956, Q4 cases: 522, total: 17171, Q5 cases: 227, total: 8032 Adjustment: Analysis including dietary factors and blood pressure (Analysis including dietary 1.19 (1.05–1.36) 1.01 (0.93–1.10) 1.00 1.03 (0.92–1.15) 1.08 (0.96–1.22) factors and blood pressure) No significant association between potassium intake and risk of death and major CVD events. Compared to those with an estimated potassium excretion < 1.50 g per day,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>higher potassium excretion was associated with a reduced risk of the composite outcome.</p> <p>Cardiovascular All-cause mortality (g/day/Outcome): Mean 3.7 y FU Q1 cases: 146, total: 14262, Q2 cases: 214, total: 31466, Q3 cases: 181, total: 30956, Q4 cases: 73, total: 17171, Q5 cases: 335, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). No significant association between potassium intake and risk of CVD death.</p> <p>Heart Failure (g/day/Outcome): Mean 3.7 y FU Q1 cases: 33, total: 14262, Q2 cases: 71, total: 31466, Q3 cases: 81, total: 30956, Q4 cases: 57, total: 17171, Q5 cases: 19, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). No significant association between potassium intake and risk of heart failure.</p> <p>Major Cardiovascular Events (g/day/Outcome): Mean 3.7 y FU Q1 cases: 282, total: 14262, Q2 cases: 623, total: 31466, Q3 cases: 586, total: 30956, Q4 cases: 334, total: 17171, Q5 cases: 163, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available). No significant association between potassium intake and major CVD events. No significant association between potassium intake and risk of major CVD events.</p> <p>Myocardial Infarction (g/day/Outcome): Mean 3.7 y FU Q1 cases: 110, total: 14262, Q2 cases: 278, total: 31466, Q3 cases: 238, total: 30956, Q4 cases: 152, total: 17171, Q5 cases: 77, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available).</p> <p>No significant association between potassium intake and risk of MI.</p> <p>Stroke (All) (g/day/Outcome): Mean 3.7 y FU Q1 cases: 133, total: 14262, Q2 cases: 267, total: 31466, Q3 cases: 272, total: 30956, Q4 cases: 131, total: 17171, Q5 cases: 69, total: 8032 Adjustment: The primary model included age, sex, educational level, ancestry (Asian vs. non-Asian), alcohol intake, body-mass index, and status with respect to diabetes mellitus, a history of cardiovascular events, and current smoking. Additional sensitivity analyses with physical activity (measured in metabolic equivalents per week) included in the model did not materially alter estimates of association (in the cohort with physical-activity data available).</p> <p>No significant association between potassium intake and risk of stroke.</p>
Ohta, 2013 ²³⁴	<p>Study of: Adults</p> <p>Location: Japan % Male: 39.85 Mean Age/Range/Age at Baseline: mean (SD) 59.7 (8.6)</p> <p>Setting: Community Race: NR Systolic BP: mean (SD) 143 (12) Diastolic BP: mean (SD) 85 (8)</p> <p>Design: Prospective Cohort study Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: People with hypertension who visited the National Kyushu Medical Center, and underwent more than five successful 24 h home urine collections during the follow-up period were included. Exclusion: NR</p>	<p>Duration: NR Exposure to Follow Up Time: 126 (10.5 y)</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: more than five, first between 1998 and 2000, last between 2008 and 2010 CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: CKD was considered to be present if the patient had either a decreased estimated GFR (eGFR) (<60 ml min⁻¹ per 1.73m²) or persistent proteinuria</p>	<p>See subgroup table for results</p>
Okayama, 2016 ²³⁵ ; Lida, 2003 ²³⁶	<p>Study of: Adults N: 8283</p> <p>Location: Japan % Male: Q1 44.2; Q2 44.55; Q3 44.45; Q4 44.66; Q5 44.56 Mean Age/Range/Age at Baseline: mean (SD) Q1: 49.9 (12.2); Q2 48.6 (12.0); Q3 48.3 (12.1) Q4 48.1 (12.2); Q5 49.1 (12.08) year</p>	<p>Exposure Type: Quintiles of dietary sodium-to-potassium ratio Exposure Unit: mol/mol Duration(in months):</p>	<p>Sodium measure: the National Nutrition Survey (NNS), in which a 3-day weighing dietary records Best sodium measure recorded: once Potassium measure: the</p>	<p>All-cause mortality (mol/mol/Outcome): 24 years (176926 person-years) FU Q1 cases: 381, total: 1581, person-years: 33581, Q5 vs. Q1, Q2 cases: 365, total: 1652, person-years: 35983, Q3 cases: 368, total: 1685, person-years: 35949, Q4 cases: 388, total: 1684, person-years: 36122, Q5 cases: 436, total: 1681, person-years: 35291 Adjustment: Age Significantly higher relative risk was observed for deaths from all stroke,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Community Design: Prospective Cohort study Study Name: NIPPON DATA80, National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged	Race: NR Systolic BP: mean (SD) Q1 132.9 (19.5) Q2 132.7 (19.5) Q3 131.9 (19.4) Q4 132.7 (18.7) Q5 134.8 (20.2) Diastolic BP: mean (SD) Q1 80.2 (11.6) Q2 80.2 (12.0) Q3 79.8 (11.5) Q4 80.2 (11.5) Q5 80.7 (11.7) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean SD Q1 22.6 (3.2) Q2 22.6 (3.1) Q3 22.6 (3.0) Q4 22.6 (3.0) Q5 23.8 (33.8) % with Hypertension: Q1 40.4 Q2 37.9 Q3 39.2 Q4 40.0 Q5 43.0 % with history of CVD: NR % with Type 2 diabetes: Q1 11.3 Q2 10.7 Q3 9.4 Q4 9.3 Q5 11.8 % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants aged 30 years and over were included. Exclusion: People with a history of myocardial infarction or stroke; or aged 80 years or older; or who reported use of antihypertensive medication were excluded.	288 (24 years) Exposure to Follow Up Time: NR CVD mortality (ICD-9 (390-459); ICD-10 (100-199)), Stroke mortality (ICD-9 (430-438); ICD-10 (160-169)) Dose format: mean (SD) Q1, Dose: 1.25 (0.17) Q2, Dose: 1.59 (0.09) Q3, Dose: 1.84 (0.09) Q4, Dose: 2.13 (0.11) Q5, Dose: 2.72 (0.47) All-cause mortality Dose format: mean (SD) Q1, Dose: 1.25 (0.17) Q2, Dose: 1.59 (0.09) Q3, Dose: 1.84 (0.09) Q4, Dose: 2.13 (0.11) Q5, Dose: 2.72 (0.47) Q5 vs. Q1, Dose: 2.72 (0.47) vs. 1.25(0.17)	National Nutrition Survey (NNS), in which a 3-day weighing dietary records Best potassium measure recorded: once Mortality Outcomes-Method of Ascertainment: Death certificate	CVD and all causes in the highest quintile in total participants for both regression models. HR estimate quadratic non-linear multivariate analysis; p values obtained by quadratic non-linear regression tended to be lower than those for linear regression. CVD mortality (ICD-9 (390-459); ICD-10 (100-199)) (mol/mol/Outcome): 24 years (176926 person-years) FU Q1 cases: 110, total: 1581, person-years: 33581, Q5 cases: 142, total: 1681, person-years: 35291, Q2 cases: 114, total: 1652, person-years: 35983, Q3 cases: 100, total: 1685, person-years: 35949, Q4 cases: 113, total: 1684, person-years: 36122 Adjustment: Age Significantly higher relative risk was observed for deaths from all stroke, CVD and all causes in the highest quintile in total participants for both regression models. HR estimate quadratic non-linear multivariate analysis; p values obtained by quadratic non-linear regression tended to be lower than those for linear regression. Stroke mortality (ICD-9 (430-438); ICD-10 (160-169)) (mol/mol/Outcome): 24 years (176926 person-years) FU Q1 cases: 45, total: 1581, person-years: 33581, Q5 cases: 74, total: 1681, person-years: 35291, Q2 cases: 46, total: 1652, person-years: 35983, Q3 cases: 55, total: 1685, person-years: 35949, Q4 cases: 53, total: 1684, person-years: 36122 Adjustment: Age Significantly higher relative risk was observed for deaths from all stroke, CVD and all causes in the highest quintile in total participants for both regression models. HR estimate quadratic non-linear multivariate analysis; p values obtained by quadratic non-linear regression tended to be lower than those for linear regression.
Pfister, 2014 ²³⁷ Location: UK Setting: Community Design: Prospective Cohort study Study Name: The EPIC-Norfolk study	Study of: Adults N: 19857 % Male: 45.4 Mean Age/Range/Age at Baseline: mean 58.0 (SD 9.2) years Race: NR Systolic BP: reported by quintiles of sodium excretion q1 135 (17) q2 135 (17) q3 136 (17) q4 138 (17) q5 141 (19) Diastolic BP: reported by quintiles of sodium excretion q1 83.1 (10.9) q2 83.1 (10.9) q3 83.9 (10.6) q4 85.2 (10.6) q5 86.8 (11.5) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: reported by quintiles of sodium excretion q1 25.9 (SD 3.1) q2 26.1 (SD 3) q3 26.4	Exposure Type: Urinary sodium excretion Exposure Unit: mmol/day Duration: NR Exposure to Follow Up Time: 3.5 years Dose format: range Q1, Dose: <=127 Q2, Dose: 128 to <=148 Q3, Dose: 149 to <=167 Q4, Dose: 168 to	Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hr urine analysis at baseline and second health check. Sodium, Method of Validation: Obtained spot urine samples in a random sample of 1551 women. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate	Incident heart failure (Heart failure death was defined as ICD-10 I50 anywhere on the death certificate. Incident heart failure was defined as heart failure death or hospital discharge code ICD-10 I50, which proved to be specific in a recent validation study) (mmol/day/Outcome): Mean 12.9 y FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, body mass index, known diabetes, cholesterol, social class, educational level, smoking, physical activity, alcohol consumption, and sex where appropriate No statistically significant association was observed. When further adjusting the analysis for systolic blood pressure and baseline blood pressure medication, the HR for the highest quintile of estimated urinary sodium excretion was strongly attenuated whereas the HR for the lowest quintile was materially unchanged (Tables 2 and 4).

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>(SD 3.2) q4 26.7 (SD 3.2) q5 27.1 (SD 3.5)</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included Norfolk residents between 39-79 years old. Exclusion: Excluded participants with a history of heart attack, stroke, or any cancer. Also excluded those using medical heart failure treatment and those failed to provide data on estimated 24 h urinary sodium excretion.</p>	<p><=190 Q5, Dose: >=191</p>	<p>reports, National Death Index</p>	
<p>Seth, 2014²³⁸, Anderson, 2003²³⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Women's Health Initiative Observational Study (WHI-OS)</p>	<p>Study of: Adults N: 90137</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: mean 63.6 (SD 7.4) years</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included 93676 postmenopausal women aged 50 to 79 years. Exclusion: Excluded women with history of stroke, with missing information on history of stroke, and those with no information on dietary potassium at baseline. Excluded women with <465 calories intake or with >3931 calories intake, whose potassium intake ranged 0.07--1790 mg or ranged 1507 -- 31129 mg.</p>	<p>Exposure Type: Dietary Potassium Intake Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: average 11 years</p> <p>Dose format: range Q1, Dose: <1925.5 Q2, Dose: >=1925.5-2519.4 Q3, Dose: >=2519.4-3193.6 Q4, Dose: >=3193.6</p>	<p>Potassium measure: Food Frequency Questionnaires Best potassium measure recorded: Two food frequency questionnaires (FFQ) at study enrollment and year 3 follow-up Potassium, Method of Validation: Used a sub sample to evaluate FFQ measurement properties Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate, Autopsy reports CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Medical files, self reported</p>	<p>All-cause mortality (mg/d/Outcome): Average 11 years FU Q1 cases: 3096, total: 22534, Q2 cases: 2921, total: 22534, Q3 cases: 2685, total: 22535, Q4 cases: 2894, total: 22534 Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and body mass index There was a statistically significant linear trend for mortality (P=0.0002), The HR in the fully adjusted model comparing highest quartile (Q4) with the lowest quartile (Q1) of potassium intake was 0.90 (95% CI, 0.85–0.95) for all-cause mortality. There was a statistically significant linear trend for mortality (P=0.0002), The HR in the fully adjusted model comparing highest quartile (Q4) with the lowest quartile (Q1) of potassium intake was 0.90 (95% CI, 0.85–0.95) for all-cause mortality.</p> <p>Stroke (All) (Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes.) (mg/d/Outcome): Average 11 years FU Q1 cases: 793, total: 22534, Q2 cases: 769, total: 22534, Q3 cases: 719, total: 22535, Q4 cases: 765, total: 22534 Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and body mass index A statistically significant lower risk in all quartiles of potassium intake compared with lowest quartile, for all stroke, and ischemic stroke; The HR in the fully adjusted model comparing highest quartile (Q4) with the lowest quartile (Q1) of potassium intake was 0.88 (95% CI, 0.79–0.98) for all stroke.</p>
<p>Singer, 2015²⁴⁰</p> <p>Location: US</p>	<p>Study of: Adults N: 3505</p> <p>% Male: 64</p> <p>Mean Age/Range/Age at Baseline: mean 52 (SD</p>	<p>Exposure Type: Urinary sodium quartiles Exposure Unit: mmol/24 h</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure</p>	<p>Diastolic blood pressure level (Only MI, ischemic or hypertensive heart disease, and heart failure) (mmol/24 h/Outcome): 6.5 (4.4) years FU Q1 cases: NR, total: 890, Q2 cases: NR, total: 876, Q3 cases: NR, total: 865, Q4 cases: NR, total: 874</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: a union-sponsored, worksite hypertension program</p> <p>Design: Prospective Cohort study</p>	<p>10)</p> <p>Race: Q1 black 30.2% white 31.7% Hispanic 33.7% other 4.4%; Q2 black 30.5% white 33.7% Hispanic 34.8% other 2.1%; Q4 black 30.5% white 31.7% Hispanic 35.7% other 2.1%; Q4 black 28.6% white 29.3% Hispanic 38.3% other 3.8%</p> <p>Systolic BP: mean (SD) Q1 146.4 (18.5) Q2 145.3 (17.7) Q3 145.2 (16.5) Q4 145.8 (16.3)</p> <p>Diastolic BP: mean (SD) Q1 93.6 (10.0) Q2 93.9 (9.7) Q3 94.1 (9.4) Q5 (95.1 (9.6)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean (SD) Q1 27.4 (4.1) Q2 27.8 (4.1) Q3 28.9 (4.5) Q4 30.0 (4.9)</p> <p>% with Hypertension: drug use Q1 37.0% Q2 39.9% Q3 40.2% Q4 35.2%</p> <p>% with history of CVD: MI Q1 1.1% Q2 0.5% Q3 1.0% Q4 1.5%; Stroke Q1 0.9% Q2 0.6% Q3 0.9% Q4 0.7%</p> <p>% with Type 2 diabetes: Q1 4%; Q2 6.3% Q3 5.6% Q4 6.0%</p> <p>% with Kidney disease: Q1 1.5%; Q2 1.4%; Q3 1.2%; Q4 2.2%</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants with an SBP \geq 140 mm Hg (\geq 160mm Hg before Joint National Committee 5), DBP \geq 90 mmHg (\geq 95 Hg before Joint National Committee 5), or being on antihypertensive medication at the time of screening were included.</p> <p>Exclusion: not report</p>	<p>Duration: NR</p> <p>Exposure to Follow Up Time: in-program 6.5 years, follow-up from initial intake to death or last known alive 18.6 years</p> <p>Dose format: mean (SD)</p> <p>Q1, Dose: 55 (20)</p> <p>Q2, Dose: 102 (17)</p> <p>Q3, Dose: 143 (20)</p> <p>Q4, Dose: 221 (56)</p>	<p>recorded: once at baseline</p> <p>How was blood pressure measured? not reported</p> <p>Mortality Outcomes-Method of Ascertainment: National Death Index Plus and the Social Security Administration Death Master File</p>	<p>Adjustment: NR</p> <p>During study period, mean BP decreased in all sodium quartiles. No significant difference in diastolic blood pressure between different quintiles of urinary sodium excretion.</p> <p>Systolic blood pressure (Only MI, ischemic or hypertensive heart disease, and heart failure) (mmol/24 h/Outcome): 6.5 (4.4) years FU</p> <p>Q1 cases: NR, total: 890, Q2 cases: NR, total: 876, Q3 cases: NR, total: 865, Q4 cases: NR, total: 874</p> <p>Adjustment: NR</p> <p>During study period, mean BP decreased in all sodium quartiles. Those in the lowest quintile of urinary sodium excretion had highest systolic blood pressure.</p>
<p>Sluijs, 2014²⁴¹; Beulens, 2010²⁴²</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: EPIC-NL study</p>	<p>Study of: N: 36094</p> <p>% Male: 25%</p> <p>Mean Age/Range/Age at Baseline: mean 49 (SD 12)</p> <p>Race: NR</p> <p>Systolic BP: mean 126 (SD 19) mmHg</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p>	<p>Exposure Type: Potassium, dietary</p> <p>Intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR</p> <p>Per 1 g/d for dietary potassium, Dose: mean 3672 (SD 903) mg/d</p> <p>Q1, Dose: \leq3059</p> <p>Q2, Dose: 3060-3587</p> <p>Q3, Dose: 3588-4186</p> <p>Q4, Dose: \geq4187</p>	<p>Sodium measure: food frequency questionnaire</p> <p>Potassium measure: food frequency questionnaire</p> <p>Best potassium measure recorded: Filled out one food frequency questionnaire.</p> <p>Potassium, Method of Validation: Calculated relative validity for each food item.</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>Stroke Risk (ICD-9 Clinical Modification codes 430 to 434 and 436) (mg/d/Outcome): 12 years FU</p> <p>Per 1 g/d for dietary potassium cases: 631, total: 36094, Q1 cases: 197, total: NR, person-years: 108467, Q2 cases: 147, total: NR, person-years: 109297, Q3 cases: 161, total: NR, person-years: 109117, Q4 cases: 126, total: NR, person-years: 109387</p> <p>Adjustment: Age, sex, body mass index, education, physical activity, smoking status, total energy, calcium</p> <p>Potassium intakes were not associated with stroke</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Inclusion: Included Dutch participants who signed consents to the EPIC study. Exclusion: NR</p>			
<p>Smyth, 2016²⁴³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: U.S. National Institutes of Health–American Association of Retired Persons Diet and Health Study</p>	<p>Study of: Adults N: 370423</p> <p>% Male: 59.1 Mean Age/Range/Age at Baseline: mean 62.2 (SD 5.4) years Race: White 92.7% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 43.5% % with history of CVD: NR % with Type 2 diabetes: 9.2% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included 567,169 US adults, between ages 50 to 71 years old, and who have completed both a baseline and a follow-up questionnaire. Exclusion: Excluded those with duplicate questionnaires and incomplete records, excluded those who moved away, who had dialysis at baseline, and who had extreme high an slow total energy intakes</p>	<p>Exposure Type: Daily potassium intake Exposure Unit: g/d</p> <p>Duration: NR Exposure to Follow Up Time: a mean of 14.3-year follow-up</p> <p>Dose format: range Q1, Dose: <2.3 Q2, Dose: 2.3-2.9 Q3, Dose: 2.9-3.5 Q4, Dose: 3.5-4.3 Q5, Dose: >4.3</p>	<p>Sodium measure: FoodFrequency questionnaire Best sodium measure recorded: Participants completed 1 validated food frequency questionnaire at baseline Sodium, Method of Validation: FFQ validated in Thompson FE, Kipnis V, Midthune D, et al. Performance of a food- frequency questionnaire in the US NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study. Public Health Nutr. 2008;11:183-195.</p> <p>Potassium measure: Food Frequency Questionnaire Best potassium measure recorded: Participants completed 1 validated food frequency questionnaire at baseline Potassium, Method of Validation: FFQ validated in Thompson FE, Kipnis V, Midthune D, et al. Performance of a food- frequency questionnaire in the US NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study. Public Health Nutr. 2008;11:183-195.</p> <p>Mortality Outcomes-Method of Ascertainment: National</p>	<p>Renal death (ICD 9th(codes 585 and 586) and 10th (codes N180, N183, N185,N188, N189, N19), censored 31st December 2011) (g/d/Outcome): Median 14.3 +/-3.6 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, gender, body mass index, smoking, education, ethnicity, physical activity, diabetes, heart disease, and stroke, and sodium intake. Significant association between being in the highest quintile of potassium intake and a decreased risk of renal death.</p> <p>Self-reported dialysis (Answering a question on followup-questionnaire) (g/d/Outcome): Mean 14.3 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, gender, body mass index, smoking, education, ethnicity, physical activity, diabetes, heart disease, and stroke, and sodium intake. Significant association between higher potassium intake and increased risk of dialysis.</p>

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			Death Index Plus and the Social Security Administration Death Master File CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Followup questionnaire	
<p>Stolarz-Skrzypek, 2011²⁴⁴;</p> <p>Aleksandrova, 2011²⁴⁵;</p> <p>Staessen, 2001²⁴⁶; Li, 2007²⁴⁷</p> <p>Location: Belgium</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Flemish Study on Environment, Genes, and Health Outcomes (FLEMENGHO)</p>	<p>Study of: Adults N: 3681</p> <p>% Male: outcome: 47.3; Hypertension 45.9; BP 47.6</p> <p>Mean Age/Range/Age at Baseline: mean (SD) outcome: 40.9 (16.3) Hypertension: 38.6 (14.6); BP: 38.3 (14.2) y</p> <p>Race: NR</p> <p>Systolic BP: mean (SD) outcome 124.7 (10.6); Hypertension 118.7 (10.4); BP 120.9 (12.8)</p> <p>Diastolic BP: mean (SD) outcome 76.3 (10.6); Hypertension 73.3 (8.0); BP 74.6 (8.9)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean (SD) outcome 25.2 (4.6); Hypertension 24.5 (4.0); BP 24.6 (4.0)</p> <p>% with Hypertension: outcome 25.8</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: outcome 4.1; hypertension 1.9; BP 1.9</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants aged 20 years or older were included.</p> <p>Exclusion: People whose baseline 24-hour urine collection was wither missing or unreliable, and people who had a history of CVD, or took antihypertensive drug treatment at baseline or at follow-up, or had developed CVD at follow-up, and people who during follow-up died, seriously ill or moved out of the study areas were excluded.</p>	<p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline</p> <p>Exposure Unit: mmol/d</p> <p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium-to- Potassium Ratio at Baseline</p> <p>Exposure Unit: NR</p> <p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium-to- Potassium Ratio at Baseline</p> <p>Exposure Unit: mmol</p> <p>Duration(in months): 94.8 (= median 7.9 years) for outcomes cohort; 73.2 (=median 6.1 years) for BP; 78 (= median 6.5 years) for hypertension</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: Mean (SD ,range)</p> <p>High, Dose: women 290.5 (56.2, 222-400); 231.7 (50.9, 178-400)</p> <p>High, Dose: women 4.15 (0.86, 3.2-6.0); men 4.37 (0.84, 3.4-6.0)</p> <p>Low, Dose: women 1.64 (0.36, 0.8-2.1);</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: once, at baseline</p> <p>How was blood pressure measured? Each participant's blood pressure at baseline and follow-up was measured by experienced observers by auscultation of the Korotkoff sounds. After the participants had rested for 5 minutes in the sitting position, they obtained 5 consecutive blood pressure readings (phase V diastolic pressure) to the nearest 2 mm Hg, using mercury sphygmomano meters. The 5 blood pressure readings obtained at baseline or at follow-up were averaged for analysis. Digit preference was checked at 6-month intervals.</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital</p>	<p>Hypertension (ICD code without details) (mmol/d/Outcome): Median (IQR) 7.93 (6.35-17.30) years FU</p> <p>Low cases: 118, total: 1220, Low cases: 41, total: 1241, High cases: 15, total: 1208, High cases: 37, total: 1221, Medium cases: 28, total: 1232, Medium cases: 64, total: 1250</p> <p>Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group.</p> <p>Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.</p> <p>Baseline sodium excretion was not associated with total mortality.</p> <p>Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.</p> <p>Baseline sodium excretion was not associated with total mortality.</p> <p>All cardiovascular Fatal and nonfatal events (ICD code without details) (mmol/d/Outcome): Median (IQR) 7.93 (6.35-17.30) years FU</p> <p>Low cases: 100, total: 1220, Low cases: 93, total: 1241, High cases: 50, total: 1208, High cases: 53, total: 1221, Medium cases: 79, total: 1250, Medium cases: 89, total: 1232</p> <p>Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group.</p> <p>Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.</p> <p>Baseline sodium excretion was not associated with total mortality.</p> <p>Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.</p> <p>Baseline sodium excretion was not associated with total mortality.</p> <p>All-cause mortality (ICD code without details) (mmol/d/Outcome): Median (IQR) 7.93 (6.35-17.30) years FU</p> <p>Low cases: 118, total: 1220, Low cases: 94, total: 1241, High cases: 37, total: 1221, High cases: 47, total: 1208, Medium cases: 64, total: 1250, Medium cases: 78, total: 1232</p> <p>Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>men 1.75 (0.41, 0.8-2.3) Low, Dose: women 95.1 (22.0, 50-126); men 120.1 (28.4, 50-158) Medium, Dose: women 150.2 (15.0, 127-177); men 188.8 (17.6, 159-221) Medium, Dose: women 2.59 (0.27, 2.2-3.1); men 2.80 (0.28, 2.4-3.3)</p>	<p>records, Death certificate reports</p>	<p>Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality.</p> <p>Low cases: 41, total: 1241, Low cases: 50, total: 1220, High cases: 10, total: 1221, High cases: 15, total: 1208, Medium cases: 24, total: 1250, Medium cases: 28, total: 1232 Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality.</p> <p>Low cases: 42, total: 1241, Low cases: 45, total: 1220, High cases: 19, total: 1221, High cases: 23, total: 1208, Medium cases: 33, total: 1232, Medium cases: 34, total: 1250 Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality.</p> <p>Stroke Fatal and nonfatal events (ICD code without details) (mmol/d/Outcome): Median (IQR) 7.93 (6.35-17.30) years FU Low cases: 13, total: 1220, Low cases: 15, total: 1241, High cases: 6, total: 1208, High cases: 7, total: 1221, Medium cases: 12, total: 1232, Medium cases: 13, total: 1250 Adjustment: Note: Comparing the risk in each tertile with the overall risk in the whole study population using multiple Cox regression and deviation from mean coding. This allows computation of Cis for the HR in each tertile without definition of an arbitrary reference group. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings. Baseline sodium excretion was not associated with total mortality.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
The Trials of Hypertension Prevention Collaborative Research Group, 1992 ¹²⁶ ; Erratum, 1992 ¹²⁷ ; Satterfield, 1991 ¹²⁸ ; Whelton, 1992 ¹²⁹ ; Whelton, 1997 ¹³⁰ ; He, 1999 ¹³¹ ; Kumanyika, 1993 ¹³² ; Whelton, 1994 ¹³³ ; Cook, 2007 ⁵⁷ ; Cook, 1998 ¹³⁴ ; Yamamoto, 1995 ¹³⁵ ; Cook, 2016 ⁶²	Study of: Adults N: 328 N: 744 Intervention 1: % Male: 70.9 Mean Age/Range/Age at Baseline: mean 43.4 (SD 6.6) Race: 78 Systolic BP: 124.8 Diastolic BP: 83.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.7 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Intervention 2: % Male: 69.7 Mean Age/Range/Age at Baseline: mean 43.1 (SD 6.6) Race: 84 Systolic BP: 122.6 Diastolic BP: 81.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 83.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Intervention 3: % Male: 74.7 Mean Age/Range/Age at Baseline: mean 42.8 (SD 6.5) Race: white 88.8% Systolic BP: 120.7 Diastolic BP: 80.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 81.6 % with Hypertension: NR % with history of CVD: NR	Exposure Type: Sodium to potassium ratio Exposure Unit: mmol/mmol Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h Duration(in months): Lifestyle intervention 18 months; Nutritional supplement 6 months Exposure to Follow Up Time: NR Diastolic blood pressure (Random-zerosphygmomanometers (Hawksley)), Systolic blood pressure (Random-zerosphygmomanometers (Hawksley)) Dose format: range Q1, Dose: < 20.0 Q1, Dose: <= -1.64 Q2, Dose: -1.64 to -1.04 Q2, Dose: 20.0 to 38.2 Q3, Dose: -1.04 to -0.38 Q3, Dose: 38.2 to 59.7 Q4, Dose: > 59.7 Q4, Dose: >= -0.38 Diastolic blood pressure (Random-zero sphygmomanometer), Systolic blood pressure (Random-	Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Arm 2: 99.4 mmol/24 h Sodium Status Arm 3: NR Sodium Status Arm 4: NR Best potassium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Potassium Status Arm 2: NR Potassium Status Arm 3: Change from baseline -2.4 mmol/24 h Potassium Status Arm 4: Change from baseline 37.4 mmol/24h How was blood pressure measured? Collected at 0, 3, 6, months, 12 and 18 months for lifestyle groups. BP was measured with a Hawksley random-zero sphygmomanometer, after sitting at rest for 5 minutes . The average of three readings (first and fifth Korotkoffs sounds) were recorded at each visit.	Diastolic blood pressure (Random-zero sphygmomanometer) (mmol/24h/Outcome): Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, sex, race, baseline blood pressure (BP), and baseline sodium excretion No significant association between reduced sodium excretion and DBP (P=.09 for DBP) Diastolic blood pressure (Random-zerosphygmomanometers (Hawksley)) (mmol/mmol/Outcome): 6 months FU Q1 cases: NR, total: 53, Q2 cases: NR, total: 57, Q3 cases: NR, total: 73, Q4 cases: NR, total: 145 Adjustment: Age, race, sex, baseline blood pressure (diastolic or systolic), 24-hour urinary potassium and sodium excretion, and postrandomization z, changes in body weight and 24-hour urinary sodium excretion. Compared to those in the lowest quartile, being in the highest quartile of sodium to potassium ratio change was associated with a 2.00-mm Hg larger reduction in DBP. There is a p coefficient of 0.494 (P = 0.001) of change in DBP for each unit change in 24hr urinary potassium excretion Systolic blood pressure (Random-zero sphygmomanometer) (mmol/24h/Outcome): 18 months FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: Age, sex, race, baseline blood pressure (BP), and baseline sodium excretion Significant association between reduced sodium excretion and reduction in SBP (P=0.0s for SBP). Systolic blood pressure (Random-zerosphygmomanometers (Hawksley)) (mmol/mmol/Outcome): 6 months FU Q1 cases: NR, total: 53, Q2 cases: NR, total: 57, Q3 cases: NR, total: 73, Q4 cases: NR, total: 145 Adjustment: Age, race, sex, baseline blood pressure (diastolic or systolic), 24-hour urinary potassium and sodium excretion, and postrandomization z, changes in body weight and 24-hour urinary sodium excretion. No significant association between sodium to potassium ratio and SBP. Diastolic blood pressure (Random-zerosphygmomanometers (Hawksley)) (mmol/24h/Outcome): 6 months FU Q1 cases: NR, total: 177, Q2 cases: NR, total: 62, Q3 cases: NR, total: 47, Q4 cases: NR, total: 42 Adjustment: Age, race, sex, baseline blood pressure (diastolic or systolic), 24-hour urinary potassium and sodium excretion, and postrandomization z, changes in body weight and 24-hour urinary sodium excretion. Compared to those in the lowest quartile, being in the highest quartile

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 71.7 Mean Age/Range/Age at Baseline: mean 42.6 (SD 6.5) Race: white 76.5% Systolic BP: 125.1 Diastolic BP: 83.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Healthy adults, ages 30-54 with high normal DBP, not taking antihypertensive drugs for the prior 2 months Exclusion: Clinical or lab evidence of cardiovascular or other disabling or life threatening diseases. Conditions that would contraindicate or require any of the interventions. Unwillingness or inability to comply with data collection or intervention procedures.</p>	<p>zero sphygmomanometer) Dose format: range Q1, Dose: <65 mmol/24h Q2, Dose: 65-98 mmol/24h Q3, Dose: 99-130 mmol/24h Q4, Dose: 131-178 mmol/24h Q5, Dose: >178 mmol/24h</p>		<p>urinary potassium excretion change was associated with a 1.49-mm Hg larger reduction in DBP. There is a p coefficient of -0.015 (P = 0.021) of change in DBP for each unit change in 24hr urinary potassium excretion</p> <p>Systolic blood pressure (Random-zerosphygmomanometers (Hawksley)) (mmol/24h/Outcome): 6 months FU Q1 cases: NR, total: 177, Q2 cases: NR, total: 62, Q3 cases: NR, total: 47, Q4 cases: NR, total: 42 Adjustment: Age, race, sex, baseline blood pressure (diastolic or systolic), 24-hour urinary potassium and sodium excretion, and postrandomization z, changes in body weight and 24-hour urinary sodium excretion. No significant association between urinary potassium excretion and SBP.</p>
<p>Thomas, 2011²⁴⁸</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Finnish Diabetic Nephropathy Study</p>	<p>Study of: Adults</p> <p>% Male: %male reported by Na quartiles q1 32.6 q2 49.2 q3 71.5 Mean Age/Range/Age at Baseline: age reported by Na quartile q1 mean 38 (SD 13) years q2 mean 39 (SD 12) years q3 mean 39 (SD 12) years Race: NR Systolic BP: reported by Na quartiles q1 132 (SD 18) q2 133 (SD 18) q3 135 (SD 18) Diastolic BP: reported by Na quartiles q1 78 (SD 9) q2 79 (SD 9) q3 81 (SD 10) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: BMI reported by Na quartiles q1 24.7 (SD 3.4) q2 25 (SD 3.5) q3 26.1 (SD 3.5) % with Hypertension: reported by Na quartiles q1 44.5 q2 50.2 q3 53.6 % with history of CVD: NR % with Type 2 diabetes: NR</p>	<p>Duration: NR Exposure to Follow Up Time: median follow-up 10 years</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24-h urine collection at baseline completed with an ion-selective electrode</p> <p>How was blood pressure measured? In the sitting position after a 10-min rest, blood pressure was measured twice at baseline, and the analysis used the average of these two measurements. Mortality Outcomes-</p>	<p>See subgroup table for results</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: All participants with type I diabetes enrolled between January 1998 and December 2002 in the FinnDiane prospective study without ESRD at baseline. Exclusion: Not specified</p>		<p>Method of Ascertainment: Death certificate, Search national death registry CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: National database, Medical files</p>	
<p>Tunstall-Pedoe, 1997²⁴⁹; Tunstall-Pedoe, 1999²⁵⁰; Smith, 1987²⁵¹</p> <p>Location: Scotland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Scottish Heart Health Study</p>	<p>Study of: Adults</p> <p>% Male: 49.5 Mean Age/Range/Age at Baseline: ranged 40-59 years Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 1.5% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included randomly selected patients from general practitioners' offices in 23 local government districts. Participants aged between 40-59. Exclusion: Excluded those who failed to complete the study questionnaire, clinic appointment, or both.</p>	<p>Duration(in months): 3 years Exposure to Follow Up Time: 6 years</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: one 24 hour urine collection Sodium, Method of Validation: Urine was analyzed for electrolytes and creatinine. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports</p>	See subgroup table for results
<p>Tuomilehto, 2001²⁵²</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 2420</p> <p>% Male: 48.2 Mean Age/Range/Age at Baseline: age reported by sodium quartile and gender: men q1 mean 45.4 (SD 11.6) years, men q2 mean 45.3 (SD 11.0) years, men q3 mean 46.2 (SD 10.4) years, men q4 mean 45.4 (SD 10.6) years; women q1 mean 45.7 (SD 11.6) years, women q2 mean 45.4 (SD 11.8) years, women q3 mean 44.8 (SD 11.1) years, women q4 mean 45.6 (SD 11.3) years. Race: NR Systolic BP: Systolic blood pressure reported by sodium quartile and gender: men q1 mean 144 (SD 22), men q2 mean 145 (SD 19), men q3 mean 148 (SD 20), men q4 mean 147 (SD 19); women q1</p>	<p>Exposure Type: 24 h urinary sodium excretion Exposure Unit: mmol</p> <p>Duration: NR Exposure to Follow Up Time: up to 14 years</p> <p>Dose format: NR per 100 mmol increase, Dose: mean 216 mmol (SD 83) and 162 mmol (62) in men and in women, respectively</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p> <p>How was blood pressure measured? Blood pressure was measured once using a standard sphygmomanometer with a 13 cm wide and 42 cm long cuff bladder. CVD, CHD, stroke,</p>	<p>All-cause mortality (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 180, total: 2436 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among all participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Cardiovascular death (Death, ICD 390-448) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 87, total: 2436 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>mean 141 (SD 22) years, women q2 mean 140 (SD 22), women q3 mean 141 (SD 22), women q4 mean 142 (SD 22).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and gender: men q1 mean 86 (SD 11), men q2 mean 86 (SD 12), men q3 mean 89 (SD 13), men q4 mean 90 (SD 13); women q1 mean 83 (SD 12) years, women q2 mean 83 (SD 12), women q3 mean 83 (SD 12), women q4 mean 85 (SD 12).</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and gender: men q1 mean 25.5 (SD 2.4), men q2 mean 26.4 (SD 3.3), men q3 mean 26.9 (SD 3.3), men q4 mean 28.1 (SD 4.2); women q1 mean 24.6 (SD 4.2) years, women q2 mean 25.1 (SD 4.02), women q3 mean 26.3 (SD 4.6), women q4 mean 27.8 (SD 5.4).</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Finnish men and women between 25-64 years old. Analysis of this study included both the 1982 and 1987 cohorts. Exclusion: Excluded those with incomplete collection of urine, and those with incomplete data of risk factors. Also excluded those who had a non-fatal acute coronary event or cerebrovascular event before baseline survey.</p>		<p>kidney stones/disease Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>smoking Among all participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Coronary heart disease death (Death, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 61, total: 2436 Adjustment: Age, study year, smoking, serum total and HDL cholesterol, systolic blood pressure, BMI, and sex Among all participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Coronary heart disease incident (Event, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 128, total: 2402 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among all participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Stroke incident (Event, ICD 430-438) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 84, total: 2420 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among all participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>
<p>Umesawa, 2016²⁵³</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Circulatory</p>	<p>Study of: Adults N: 889</p> <p>% Male: Q1 33; Q2 33; Q3 33; Q4 33 Mean Age/Range/Age at Baseline: Q1: mean 57.7 (range 40-75); Q2: 56.9 (range 40-75); Q3 58.3 (range 40-75); Q4: 56.3 (range 40-75) years Race: NR Systolic BP: Q1 mean 118.4 (SE 0.8); Q2 mean 117.8 (SE 0.8); Q3 118.7 (SE 0.8); Q4 mean 118.2 (SE 0.8) Diastolic BP: Q1 mean 72.7 (SE 0.5); Q2 mean 72.4 (SE 0.5); Q3 mean 74.0 (SE 0.5); Q4 mean 73.0 (SE 0.5) Magnesium: NR Calcium: NR</p>	<p>Exposure Type: Sodium concentration quartiles in spot urine Exposure Unit: mmol/l</p> <p>Duration(in months): 69.6 (5.8 years) Exposure to Follow Up Time: NR</p> <p>Diastolic blood pressure level (Standard mercury sphygmomanometers), Systolic blood</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, at baseline Sodium, Method of Validation: Quality control was undergone three times per day by using normal and abnormal reagent (Consela "Nissui", Nissui pharmaceutical Co., Tokyo, Japan).</p>	<p>Diastolic blood pressure level (Standard mercury sphygmomanometers) (mmol/l/Outcome): Mean 5.8 years FU All cases: NR, total: 889 Adjustment: Age (years), sex, body mass index (kg/m²), drinking status (never, ex-drinkers, current drinkers of ethanol at 1 to 22 g/day and ≥23 g/day), current smoking (yes or no) and baseline eGFR value (ml/min/1.73 m²) Nonsignificant null association between sodium/ potassium ratio and blood pressure changes. For all categories, no significant changes were observed for diastolic blood pressure.</p> <p>Diastolic blood pressure level (mmHg) (Standard mercury sphygmomanometers) (mmol/l/Outcome): Mean 5.8 years FU</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Risk in the Community Study (CIRCS)	<p>Other Minerals: NR Mean BMI: Q1 mean 22.4 (SE 0.2); Q2 mean 22.6 (SE 0.2); Q3 mean 22.9 (SD 0.2); Q4 mean 23.2 (SE 0.2) kg/m² % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: Q1 8; Q2 5; Q3 3; Q4 5 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged 40 to 75 years who were normotensive or hypertensive (systolic blood pressure of ≥ 140 mm Hg and /or diastolic blood pressure of ≥ 90 mmHg and/or under antihypertensive medication) were included. Exclusion: people who refused to take urinalysis or refused to take blood samples, who had high serum creatinine concentrations (≥ 1.4 mg/dl for men and ≥ 1.2 mg/dl for women) or had a history of renal disease, or extremely high sodium to creatinine ratio in spot urine (≥ 15), or non-validated height due to scoliosis, who initiated antihypertensive medication at follow-up surveys or who measured their blood pressure only one at follow-up surveys were excluded.</p>	<p>pressure level (Standard mercury sphygmomanometers) Dose format: continuous All, Dose: 1-SD increment (54 mol/L)</p> <p>Diastolic blood pressure level (mmHg) (Standard mercury sphygmomanometers), Systolic blood pressure level (mmHg) (Standard mercury sphygmomanometers) Dose format: continuous All, Dose: 1-SD increment (54 mol/L) Q1, Dose: 66 (19-94) Q2, Dose: 107 (82-137) Q3, Dose: 145 (119-176) Q4, Dose: 193 (163-307)</p>	<p>How was blood pressure measured? Arterial systolic blood pressure and the fifth-phase of Korotkoff sounds diastolic blood pressure were measured by well-trained observers using standard mercury sphygmomanometers on the right arm at base line survey. All participants had their blood pressure levels measured twice. Participants had their blood pressure levels measured by automated sphygmomanometers (TM-2655P; A&D Company Ltd. Tokyo, Japan) on the right arm twice in the follow-up survey.</p>	<p>All cases: NR, total: 889, Q1 cases: NR, total: 220, Q2 cases: NR, total: 225, Q3 cases: NR, total: 220, Q4 cases: NR, total: 224 Adjustment: Age (years), sex, body mass index (kg/m²), drinking status (never, ex-drinkers, current drinkers of ethanol at 1 to 22 g/day and ≥ 23 g/day), current smoking (yes or no) and baseline eGFR value (ml/min/1.73 m²) For all categories, no significant changes were observed for diastolic blood pressure. For all categories, no significant changes were observed for diastolic blood pressure.</p> <p>Systolic blood pressure level (Standard mercury sphygmomanometers) (mmol/l/Outcome): Mean 5.8 years FU All cases: NR, total: 889 Adjustment: Age (years), sex, body mass index (kg/m²), drinking status (never, ex-drinkers, current drinkers of ethanol at 1 to 22 g/day and ≥ 23 g/day), current smoking (yes or no) and baseline eGFR value (ml/min/1.73 m²) Nonsignificant null association between sodium/ potassium ratio and blood pressure changes.</p> <p>Systolic blood pressure level (mmHg) (Standard mercury sphygmomanometers) (mmol/l/Outcome): Mean 5.8 years FU All cases: NR, total: 889, Q1 cases: NR, total: 220, Q2 cases: NR, total: 225, Q3 cases: NR, total: 220, Q4 cases: NR, total: 224 Adjustment: Age (years), sex, body mass index (kg/m²), drinking status (never, ex-drinkers, current drinkers of ethanol at 1 to 22 g/day and ≥ 23 g/day), current smoking (yes or no) and baseline eGFR value (ml/min/1.73 m²) A 1-SD increase in sodium concentrations is associated with a +0.9 mmHg (P = 0.060) increase in systolic blood pressure. Being in the highest quartile of sodium concentrations was associated with an increase in systolic blood pressure. Being in the highest quartile of sodium concentrations was associated with an increase in systolic blood pressure.</p>
Vitolo, 2013 ²⁵⁴	<p>Study of: Children N: 331</p> <p>Location: Brazil</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>% Male: 56.8% Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR</p>	<p>Exposure Type: Sodium intake Exposure Unit: mg/day</p> <p>Duration: NR Exposure to Follow Up Time: On average 4 years</p> <p>Dose format: categorical All, Dose: >1200 mg/day</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: Two multiple-pass 24-h dietary recalls for each child 2-4 years old. Sodium, Method of Validation: Dietary recalls administered by trained fieldworkers</p> <p>How was blood pressure measured? Two readings</p>	<p>Systolic blood pressure (A calibrated aneroid sphygmomanometer) (mg/day/Outcome): 3-4 years FU All cases: NR, total: 331 Adjustment: Exclusive breastfeeding ≥ 4 months, child overweight, WHtR>0.5, change in BMIz >0.67 Consuming more than 1200 mg/day sodium significantly associated with high systolic blood pressure in children 3-4 years old.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included mother-child pairs from low-income population. Included mothers who gave birth at full-term and infants with a normal birth-weight.</p> <p>Exclusion: Excluded HIV-positive mothers, and those with type I or gestational diabetes. Also excluded infants born with congenital malformations.</p>		<p>for each blood pressure measurement was assessed using a calibrated aneroid sphygmomanometer.</p>	
<p>Whelton, 1998¹⁴²; Appel, 2001¹⁴³; Espeland, 1999¹⁴⁴; Banson, 1997¹⁴⁵; Appel, 1995¹⁴⁶; Kostis, 1998¹⁴⁷; Whelton, 1997¹⁴⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p>	<p>Study of: Adults N: 975 N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR</p> <p>Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24%</p> <p>Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health,</p>	<p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>All, Dose: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Sodium Status Arm 2: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke,</p>	<p>Elevated blood pressure (Primary end point defined as an average SBP >= 150 mm Hg, an average DBP >= 90 mm Hg, the resumption of BP medication, or a CVD event during followup (mean, 27.8 months)) (mmol/24h/Outcome): Mean 27.6 months FU All cases: NR, total: NR Adjustment: NR Across follow-up, assignment to an active intervention (including sodium reduction intervention) was associated with a significantly lower incidence rate of elevated blood pressure.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.		kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records	
Witteaman, 1989 ²⁵⁵ Location: US Setting: Community Design: Prospective Cohort study Study Name: The Nurses Health Study	Study of: Adults N: 58218 Inclusion: Included those who returned the NHS dietary questionnaire (1980). Exclusion: Excluded participants who left 10 or more blanks in the dietary questionnaire, and those who reported very high or low total food scores. Also excluded those who self-reported these diagnoses: high blood pressure, myocardial infarction, angina pectoris, diabetes mellitus, and all cancers, but did not exclude non melanoma skin cancer. Also excluded those on antihypertensive medication, keeping a special diet, or had been pregnant for 6 or more months since 1978.	Exposure Type: Potassium intake Exposure Unit: mg/day Duration: NR Exposure to Follow Up Time: 4 years Dose format: range Category 1, Dose: <2000 Category 2, Dose: 2000-2399 Category 3, Dose: 2400-2799 Category 4, Dose: 2800-3199 Category 5, Dose: >=3200	Potassium measure: food frequency questionnaire Best potassium measure recorded: once in 1980 Potassium, Method of Validation: Authors cited other papers that reported on the reproducibility and validity of FFQ used, references 17-19. How was blood pressure measured? Blood pressure status was self-reported via biennial questionnaires. The validity of this method was assessed using a random sample of 100 nurses.	Hypertension (Self reported) (mg/day/Outcome): 4 years FU Category 1 cases: 395, total: 6190, Category 2 cases: 704, total: 12672, Category 3 cases: 945, total: 16466, Category 4 cases: 705, total: 12624, Category 5 cases: 526, total: 10266 Adjustment: Age, quetelet's index, alcohol consumption, and intakes of calcium, magnesium, potassium and fiber Increase in potassium intake was associated with a slight increase in self-reported hypertension.
Yang, 2011 ²⁵⁶ , Cohen, 2008 ²⁵⁷ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES III	Study of: Adults N: 12267 % Male: 48.1% Mean Age/Range/Age at Baseline: ranged 25-74 years Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included non pregnant adults ages 20 and	Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg Exposure Type: Usual Potassium Intakes Exposure Unit: mg/d Exposure Type: Usual Sodium Intakes Exposure Unit: mg/d Duration: NR Exposure to Follow Up Time: NR CVD mortality (ICD-10 codes I00-I78), IHD All-cause	Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24-hour dietary recall Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall" Best potassium measure recorded: single 24-hour dietary recall Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall Mortality Outcomes-	All-cause mortality (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 2270, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. All-cause mortality (ICD-10 codes I00-I78) (mg/mg/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per unit change cases: 2270, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>older, those who completed a physical examination, and who had mortality follow-up information. Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>mortality (ICD-10 codes I20-I25) Dose format: median Q1, Dose: 0.98 Q1, Dose: 1793 Q1, Dose: 2176 Q2, Dose: 1.17 Q2, Dose: 2476 Q2, Dose: 3040 Q3, Dose: 1.33 Q3, Dose: 3108 Q3, Dose: 3864 Q4, Dose: 1.57 Q4, Dose: 4069 Q4, Dose: 5135 per 1000 mg/d, Dose: NR per unit change, Dose: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.98 Q1, Dose: 1793 Q2, Dose: 1.17 Q2, Dose: 2476 Q3, Dose: 1.33 Q3, Dose: 3108 Q4, Dose: 1.57 Q4, Dose: 4069 per 1000 mg/d, Dose: median 2780 (IQR 2164-3502, range 609-8839) mg per unit change, Dose: median 1.25 (IQR 1.08-1.43, range 0.46-2.98)</p> <p>All-cause mortality Dose format: median Q1, Dose: 2176 Q2, Dose: 3040 Q3, Dose: 3864 Q4, Dose: 5135 per 1000 mg/d, Dose: median 3434 (IQR 2641-4384, range 839-8555) mg</p>	<p>Method of Ascertainment: National death index</p>	<p>total calorie intake The risk of all-cause mortality increased linearly with increasing sodium-potassium ratio, comparing the highest quartile with the lowest quartile.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 825, total: 12267, person-years: 170110, per unit change cases: 825, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Higher sodium potassium ratio is associated with increased risk for CVD mortality. In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>IHD All-cause mortality (ICD-10 codes I20-I25) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 433, total: 12267, person-years: 170110, per unit change cases: 433, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Higher sodium potassium ratio is associated with increased risk for IHD mortality. In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 2270, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher potassium intake was associated with lower mortality risk.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 825, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>No significant association between potassium intake and risk of CVD mortality.</p> <p>Potassium intake was significantly inversely associated with risk of CVD or IHD death, CVD mortality, and IHD mortality comparing the highest quartile with the lowest quartile of potassium intake.</p> <p>IHD All-cause mortality (ICD-10 codes I20-I25) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 433, total: 12267, person-years: 170110, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>No significant association between potassium intake and risk of IHD mortality.</p> <p>Potassium intake was significantly inversely associated with the incidence of CVD or IHD death: the adjusted HR, 0.39 (95% CI, 0.19-0.80), for CVD mortality and HR, 0.26 (95% CI, 0.10-0.71), for IHD mortality comparing the highest quartile with the lowest quartile of potassium intake.</p>

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Appendix D. Subgroup Tables for All Included Studies

Table D1. Subgroup table for trials for children

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Gillum, 1981{#6729}; Prineas, 1980{#12301}</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Minneapolis Children's Blood Pressure Study</p> <p>Number of Sites: multiple</p> <p>Study Years: 1978</p>	<p>Study of: Children N: 80</p> <p>Intervention 1: % Male: 88 (Attendees) Mean Age/Range/Age at Baseline: mean 7.8 (SD 0.7) (Attendees) Race: NR Systolic BP: 110 (Attendees) Diastolic BP: 65 (Attendees) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.4 kg (Attendees)</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 92 Mean Age/Range/Age at Baseline: 8 Race: NR Systolic BP: 115 Diastolic BP: 69 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.8 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Families providing consent, whose children had BP over the 95th percentile for age and sex</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Achieve sodium intake of 70 mEq sodium /day Form of Administration: Dietary Modification: Family Education Program Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Composition of salt substitute with intervention/exposure adherence measure Best sodium measure recorded: Controls: At baseline and 1 year follow up, overnight urine was used. Cases: 4 times biweekly, then bimonthly for the rest of the 1 year study period. 24 hour urine collection used Sodium Status Intervention 1: 87 mmol/24h (Attendees)</p> <p>How was blood pressure measured? SBP was measured in the right arm after 5 minutes rest with a random-zero mercury sphygmomanometer. One of four cuff bladder sizes was chosen based on arm circumference. The mean of 2 successive readings of SBP, fourth phase DBP, and fifth phase diastolic DBP were used</p>	<p>Subgroup: Children Diastolic BP-NS Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD 3.90 (95% CI: -5.10 - 12.90) Systolic BP-NS Follow-Up Time: 1 year Comparison: Intervention 1 vs Comparator MD 2.50 (95% CI: -1.19 - 6.19)</p>

<p>He, 2015{#1954}; He, 2015{#1955}</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2013</p>	<p>Study of: Both adults and children N: 832</p> <p>Intervention 1: % Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 120.1 Diastolic BP: 76.5 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: Children: 48. Adults: 48.5 Mean Age/Range/Age at Baseline: Children: mean 10.1 (SD 0.5). Adult: mean 43.8 (SD 12.2) Race: NR Systolic BP: 118.2 Diastolic BP: 75.5 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Children: 16.9. Adults: 24.9 % with Hypertension: Adults: 13.6 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Primary schools in urban Changzhi Exclusion: Schools in rural areas</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Salt education. Aim was to reduce salt intake by a minimum of 20%.</p> <p>Form of Administration: Dietary Modification: Salt education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No salt education Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3.5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, Families put all household salt in a Tupperware container, at the beginning of the trial and it was weighed during follow up. Best sodium measure recorded: 2 times 3.5 months apart Sodium Status Intervention 1: Children: 112.2 mmol/24h; Adults: 178.5 mmol/24h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 times 3.5 months apart Potassium Status Intervention 1: Children: 25.3 mmol/24h; Adults: 38.1 mmol/24h</p> <p>How was blood pressure measured? BP Measured using a validated automatic blood pressure monitor (Omron HEM-7301-IT, Amsterdam) with an appropriately sized cuff. After 10 minutes rest in a quiet room, BP was taken 3 times in seated position with the arm at heart level. Average of the last 2 measurement were taken. BP was taken at baseline and at the end of study (3.5 months)</p>	<p>Subgroup: Children Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -3.44 - 1.44) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -0.60 (95% CI: -2.83 - 1.63)</p>
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<p>Hofman, 1983 {#6967}</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1980</p>	<p>Study of: Children N: 476</p> <p>Intervention 1: % Male: 52 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 87 Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.466 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 51 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 87.7 Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.421 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Infants delivered at home or in an outpatient clinic.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Low Sodium Description: NR Form of Administration: Dietary Modification: Low sodium formula for infants Dose: Mothers low sodium formula to feed infants. It was similar to that of human milk, and it was three times lower than the normal-sodium milk (6.3 v 19.2 mmole/L). Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Normal Sodium Description: NR Form of Administration: Usual diet Dose: Mothers given normal-sodium formula to feed infants. It contained an amount of sodium that was regular for Dutch formula milks during the study period Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6.25 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Casual urine Best sodium measure recorded: weeks 5,13,21 Sodium Status Intervention 1: 11.1 mmoles/L</p> <p>How was blood pressure measured? BP measured in weeks 1, 5, 9, 13, 17, 21, and 25. measurements were taken with a Doppler ultrasound device" connected to a random-zero sphygmomanometer by a trained observer. The average of three readings at each occasion was used in the analyses</p>	<p>Subgroup: Newborn infants Deaths Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator RR 0.94 (95% CI: 0.06 - 14.99) Severe disease (NS) Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator RR 0.63 (95% CI: 0.11 - 3.73) Systolic BP-supine Follow-Up Time: 25 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.10 - 0.10)</p>
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<p>Miller, 1987{#2237}</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 76</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 42 (SD 8.4) Race: white: 100% Systolic BP: 113.2 Diastolic BP: 73.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 76.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8) Race: white: 100% Systolic BP: 100.9 Diastolic BP: 59.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 100.8 Diastolic BP: 60.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>	<p>Intervention Type: Intervention 1: Other: Adults - Potassium supplement Description: Participants asked not to change their usual diet Form of Administration: Oral potassium supplement Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men. Na/K ratio: 2.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children Description: K+ supplement to increase potassium intake Form of Administration: Other: liquid potassium supplement Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls. Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Placebo - children Description: NR Form of Administration: Other: Placebo Dose: Placebo Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Sodium, Method of Validation: Measurement of creatinine excretion (if it was \pm 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 165 mEq/d Sodium Status Intervention 2: 108.8 mEq/d Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Potassium, Method of Validation: Measurement of creatinine excretion (if it was \pm 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete). Potassium Status Intervention 1: 81.6 mEq/d Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	<p>Subgroup: All children Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 0.10 (95% CI: -5.01 - 5.21) Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -0.50 (95% CI: -5.88 - 4.88)</p>
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Miller, 1988{#6725}	<p>Study of: Children N: 298</p> <p>Participants: % Male: 43</p> <p>Mean Age/Range/Age at Baseline: boys: mean 10.6 (SEM 0.4); girls: mean 9.7 (SEM 0.5)</p> <p>Race: white: 100%</p> <p>Systolic BP: boys 95.3; girls 91 Diastolic BP: boys 54.5; girls 54</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: boys: 38 kg; girls 32.5 kg % with Hypertension: NR</p> <p>% with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive school-age identical twin pairs recruited from an existing twin panel</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of salt pills to increase sodium intake Description: Low sodium diet + salt pill to achieve normal sodium intake Form of Administration: Sodium supplement Dose: Na chloride supplement Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Maintain an average Na excretion \leq60 mmol/d Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Nontwins collected urine samples every other week; twins collected urine samples weekly for a period, over 12 weeks Sodium, Method of Validation: Creatinine excretion in urine samples analyzed to determine if it was representative, Single 24-hour urine analysis with validation Sodium Status Intervention 1: 72.1/mmol/day Best potassium measure recorded: Nontwins collected urine samples every other week; twins collected urine samples weekly for a period, over 12 weeks Potassium, Method of Validation: Creatinine excretion in urine samples analyzed to determine if it was representative Potassium Status Intervention 1: 36.7 mmol/day</p> <p>How was blood pressure measured? Three seated BP measurements were obtained using a Hawksley Random Zero blood pressure device by a research assistant with a certification in blood pressure measurement. The mean of the last two of three blood pressure readings at each visit was used.</p>	<p>Subgroup: Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -0.20 (95% CI: -1.61 - 1.21) Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD 0.30 (95% CI: -0.91 - 1.51)</p>
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<p>Mu, 2009{#9095}</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 325</p> <p>Intervention 1: % Male: 54.5% Mean Age/Range/Age at Baseline: mean 20.3 (SD 3.1) Race: NR Systolic BP: 123.8 Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 52.7 Mean Age/Range/Age at Baseline: mean 20.6 (SD 3.1) Race: NR Systolic BP: 121.5 Diastolic BP: 75.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 53 Mean Age/Range/Age at Baseline: mean 21.4 (SD 3.0) Race: NR Systolic BP: 124.3 Diastolic BP: 77 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: BP _90th percentile by age and sex. No contraindication to the supplementation of potassium and calcium, such as the use of a potassium sparing drugs or significant renal impairment. Exclusion: Abnormal blood tests confirmed by a physician.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Potassium-Calcium salt Description: Roughly 10 mmol of potassium and 10 mmol of calcium extra per day through (added to salt Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Salt restricted group Description: Through health behavior education, the aim was 50–100mmol sodium per person per day at the end of 2 years Form of Administration: Dietary Modification: Health behavior education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: partial urine - equation not mentioned, 3 day food consumption questionnaire Best sodium measure recorded: 5 times separated by 6 months Sodium Status Intervention 1: 70 mmol/8h Sodium Status Intervention 2: 45 mmol/8h Potassium measure: Partial or spot urine without validated prediction equation Best potassium measure recorded: 5 times separated by 6 months Potassium Status Intervention 1: 8 mmol/8h Potassium Status Intervention 2: 5 mmol/8h</p> <p>How was blood pressure measured? BP measurements were taken with patients in a sitting position after at least a 5-min rest in quiet a room using a mercury sphygmomanometer with a suitable cuff size. Three measurements were generally performed for calculating the mean values, with 30 seconds between the measurements.</p>	<p>Subgroup: Adolescents Diastolic BP-sitting Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD -5.10 (95% CI: -5.51 - -4.69) Comparison: Intervention 2 vs Comparator MD -3.30 (95% CI: -3.74 - -2.86) Systolic BP-sitting Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD -7.20 (95% CI: -7.61 - -6.79) Comparison: Intervention 2 vs Comparator MD -7.10 (95% CI: -7.62 - -6.58)</p>
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<p>Pomeranz, 2002{#7007}</p> <p>Location: Israel</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Children N: 58</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 0.76 (SD 0.03) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.2 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: mean 0.77 (SD 0.025) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.2 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 0.77 (SD 0.021) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 3.1 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Jewish infants enrolled in the study hospital's neonatal unit Exclusion: Infants from families with a history of hypertension</p>	<p>Intervention Type: Intervention 1: Other: Control - Breastfeeding Description: Babies fed breastmilk Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium formula Description: NR Form of Administration: Dietary Modification: low sodium baby formula Dose: Baby formula with 32 mg/l (8.5 mmol/l) sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: High sodium formula Description: NR Form of Administration: Dietary Modification: high sodium baby formula Dose: Baby formula with 196 mg/l (8.5 mmol/l) sodium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: 4 months</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, urinary sodium to creatinine ratio Best sodium measure recorded: sodium to creatinine ratio was determined monthly during the initial 2 months Sodium Status Intervention 1: Urinary Na:Cr ratio: 1.1 Sodium Status Intervention 2: Urinary Na:Cr ratio: 1.2</p> <p>How was blood pressure measured? Non-invasive BP monitoring was performed with a Dinamap 8100 Vital Signs Monitor which measures BP and pulse using the Doppler technique. BP was recorded at the infant's home during sleep after feeding, with an appropriately sized cuff on the right upper extremity.</p>	<p>Subgroup: Newborn infants Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -11.10 (95% CI: -14.43 - -7.77) Systolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -5.30 (95% CI: -9.36 - -1.24)</p>
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Table D2. Subgroup table for trials for DRI age group (>70)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sacks, 2001¹⁰ Vollmer, 2001¹¹; Svetkey, 2004¹²; Harsha, 2004¹³; Akita, 2003¹⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Study Name: DASH-Sodium</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: <5 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 79</p> <p>Mean Age/Range/Age at Baseline: 49(10) Race: 56% black; 40% NH white; 5% Asian/other Systolic BP: 135(10) Diastolic BP: 86(4) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30(5) % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0</p> <p>Mean Age/Range/Age at Baseline: 47+/-10 Race: 57% black; 40% NH white; 3% Asian/other Systolic BP: 134+/-10 Diastolic BP: 86+/-5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29+/-5 % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 22 years old or more, average systolic blood pressure 120 to 159 mm Hg (over 3 visits) and average diastolic blood pressure 80 to 95 mm Hg Exclusion: heart disease, renal insufficiency, poorly controlled hyperlipidemia or diabetes mellitus, diabetes</p>	<p>Intervention Type: Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control High Sodium: To replicate typical diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve high sodium intake Dose: 150 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Intermediate Sodium: To replicate typical diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve intermediate sodium intake Dose: 100 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Low Sodium: To replicate typical diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: NR Description: DASH High Sodium: To impose DASH diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with high sodium intake Dose: 150 mmol sodium/d in DASH diet Na/K ratio: NR</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Sodium, Method of Validation: NR, Chemical analysis of diet with intervention/exposure adherence measure Sodium Status Intervention 1: 141+/-55 mmol/d Sodium Status Intervention 2: 106+/-44 mmol/d Sodium Status Comparator: 64+/-37mmol/d Sodium Status Intervention 3: 144+/-58 mmol/d Sodium Status Intervention 4: 107+/-52 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Potassium, Method of Validation: Adherence checks via food diaries, supervised meals Potassium Status Intervention 1: 40+/-14 mmol/d Potassium Status Intervention 2: 41+/-14 mmol/d Potassium Status Comparator: 42+/-14 mmol/d Potassium Status Intervention 3: 75+/-27 mmol/d Potassium Status Intervention 4: 81+/-31 mmol/d</p> <p>How was blood pressure measured? Random-zero sphygmomanometers, seated, 3 times during screening, weekly during 1st 3 weeks of intervention periods, and 5 times during last 9 days of intervention periods</p>	<p>Subgroup: <= 45 Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.10 (95% CI: -2.10 - 0.00) Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -4.00 - -1.70) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.40 (95% CI: -2.90 - 0.20) Comparison: Intervention 1 vs Comparator MD -5.30 (95% CI: -7.00 - -3.50)</p> <p>Subgroup: > 45 Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -2.20 (95% CI: -3.10 - -1.20) Comparison: Intervention 1 vs Comparator MD -3.80 (95% CI: -4.80 - -2.90) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -4.50 (95% CI: -6.00 - -3.00) Comparison: Intervention 1 vs Comparator MD -7.50 (95% CI: -8.90 - -6.10)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>requiring insulin, special dietary requirements, more than 14 alcoholic drinks per week, or use of antihypertensive drugs or other medications that would affect blood pressure or nutrient metabolism</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH intermediate Sodium: To impose DASH diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with intermediate sodium intake Dose: 100 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH Low Sodium: To achieve DASH diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 periods of 30 days each, including run-in Exposure to Follow Up Time: 0 months</p>		
<p>Zhou, 2016¹⁵; Zhou, 2013¹⁶</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 462</p> <p>Participants: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p>	<p>Intervention Type(s): Duration: NR Exposure to Follow Up Time: NR</p>		<p>Subgroup: Age >70 Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: NC - NC) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD 0.03 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Inclusion: Families were at least one member was a hypertension patient; the participant had an estimated daily sodium intake of ≥ 260 mmol per day; Individuals were at least 18 years of age and had no significant renal impairment or other indication for a potassium-sparing medication.</p> <p>Exclusion: Moving</p>			

Table D3. Subgroup table for trials for gender

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Nestel, 1993¹⁷</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 66</p> <p>Participants: % Male: 54.5 Mean Age/Range/Age at Baseline: Women: mean 65 (SD 3); Men: mean 66 (SD 5)</p> <p>Race: NR</p> <p>Systolic BP: Women: 120; Men: 129 Diastolic BP: Women: 68; Men: 77 Magnesium: NR</p> <p>Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Women: 24; Men 25</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive men and women, aged 60-79, free of clinical cardiac, renal, hepatic and endocrine disorders. Not taking any drugs that might affect blood pressure.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: No added salt Description: NR Form of Administration: Other: low salt diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Added Salt Description: NR Form of Administration: Other: low salt diet + added salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2.5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 6 times separated by 2 weeks Sodium, Method of Validation: Compliance with urine collection assessed from the within-individual variation in 24-h creatinine excretion between visits, Single 24-hour urine analysis with validation Sodium Status Intervention 1: Women: 77 mmol/day; Men: 106 mmol/day Best potassium measure recorded: 6 times separated by 2 weeks Potassium, Method of Validation: Compliance with urine collection assessed from the within-individual variation in 24-h creatinine excretion between visits Potassium Status Intervention 1: Women: 78 mmol/day; Men: 83 mmol/day</p> <p>How was blood pressure measured? Subjects either had fasted overnight, or had not eating in the 2 hours prior to measurement. After sitting quietly, for 5 min, BP was taken using a Dinamoa automated sphygmomanometer fitted with an appropriate arm cuff. After the first reading was discarded, 4 measures were taken and averaged.</p>	<p>Subgroup: Women Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -11.44 - 1.44) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -16.73 - 2.73)</p> <p>Subgroup: Men Diastolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -4.95 - 4.95) Systolic BP-sitting Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -9.54 - 3.54)</p>
<p>Nowson, 2003¹⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: NR days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 108</p> <p>Participants: % Male: 41 Mean Age/Range/Age at Baseline: 47</p> <p>Race: NR</p> <p>Systolic BP: 126.4+/-18.6 Diastolic BP: 79.2+/-11.9 Magnesium: NR Calcium: NR Other Minerals: sodium: 138.7+/-53.9; potassium: 78.6+/-23.7 Mean BMI: 26.1+/-4.2</p> <p>% with Hypertension: 15 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Twin pairs 30 years or older Exclusion: currently undergoing treatment for cancer or renal disease; requiring insulin treatment for diabetes</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Low sodium/high potassium diet to achieve 50 mmol sodium and 80 mmol potassium Form of Administration: Dietary Modification: Low sodium, high potassium diet and placebo sodium pills Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Low sodium/high potassium diet to achieve sodium mmol and 80 mmol potassium and sodium supplementation with slow sodium tablets to achieve 130 mmol/d sodium Form of Administration: Dietary Modification: Low sodium, high potassium</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase Sodium, Method of Validation: creatinine, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 89.4+/-4.2 mmol/d Best potassium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase Potassium, Method of Validation: NR Potassium Status Intervention 1: 87.1+/-2.1 mmol/d</p> <p>How was blood pressure measured? mercury sphygmomanometer (model ALPK2; Stethoscope and Sphygmomanometer Specialists, Melbourne, Australia) while seated</p>	<p>Subgroup: Women Home measured BP, diastolic Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.10 (95% CI: -7.98 - 3.78) Home measured BP, systolic Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.40 (95% CI: -8.28 - 3.48)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		diet Sodium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 4 weeks Exposure to Follow Up Time: 0 months		
Sacks, 2001 ¹⁰ Vollmer, 2001 ¹¹ ; Svetkey, 2004 ¹² ; Harsha, 2004 ¹³ ; Akita, 2003 ¹⁴ Location: US Setting: Community Design: Randomized Cross-over individual Study Name: DASH-Sodium Number of Sites: multiple Crossover: Length of washout period: <5 days Study Years: NR	Study of: Adults N: 79 Mean Age/Range/Age at Baseline: 49(10) Race: 56% black; 40% NH white; 5% Asian/other Systolic BP: 135(10) Diastolic BP: 86(4) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30(5) % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Mean Age/Range/Age at Baseline: 47+/-10 Race: 57% black; 40% NH white; 3% Asian/other Systolic BP: 134+/-10 Diastolic BP: 86+/-5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29+/-5 % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR	Intervention Type: Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control High Sodium: To replicate typical diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve high sodium intake Dose: 150 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Intermediate Sodium: To replicate typical diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve intermediate sodium intake Dose: 100 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Low Sodium: To replicate typical diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 3: NR Description: DASH High Sodium: To impose DASH diet with high sodium content	Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Sodium, Method of Validation: NR, Chemical analysis of diet with intervention/exposure adherence measure Sodium Status Intervention 1: 141+/-55 mmol/d Sodium Status Intervention 2: 106+/-44 mmol/d Sodium Status Comparator: 64+/-37mmol/d Sodium Status Intervention 3: 144+/-58 mmol/d Sodium Status Intervention 4: 107+/-52 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Potassium, Method of Validation: Adherence checks via food diaries, supervised meals Potassium Status Intervention 1: 40+/-14 mmol/d Potassium Status Intervention 2: 41+/-14 mmol/d Potassium Status Comparator: 42+/-14 mmol/d Potassium Status Intervention 3: 75+/-27 mmol/d Potassium Status Intervention 4: 81+/-31 mmol/d How was blood pressure measured? Random-zero sphygmomanometers, seated, 3 times during screening, weekly during 1st 3 weeks of intervention periods, and 5 times during last 9 days of intervention periods	Subgroup: Male Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.60 (95% CI: -2.70 - -0.50) Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -4.30 - -2.20) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.70 (95% CI: -3.40 - 0.00) Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -7.30 - -4.10) Subgroup: Female Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.70 (95% CI: -2.60 - -0.80) Comparison: Intervention 1 vs Comparator MD -3.70 (95% CI: -4.70 - -2.70) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -4.00 (95% CI: -5.40 - -2.50) Comparison: Intervention 1 vs Comparator MD -7.50 (95% CI: -9.00 - -6.00)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Inclusion: 22 years old or more, average systolic blood pressure 120 to 159 mm Hg (over 3 visits) and average diastolic blood pressure 80 to 95 mm Hg Exclusion: heart disease, renal insufficiency, poorly controlled hyperlipidemia or diabetes mellitus, diabetes requiring insulin, special dietary requirements, more than 14 alcoholic drinks per week, or use of antihypertensive drugs or other medications that would affect blood pressure or nutrient metabolism</p>	<p>Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with high sodium intake Dose: 150 mmol sodium/d in DASH diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH intermediate Sodium: To impose DASH diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with intermediate sodium intake Dose: 100 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH Low Sodium: To achieve DASH diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 periods of 30 days each, including run-in Exposure to Follow Up Time: 0 months</p>		
<p>Seals, 2001¹⁹ Location: NR Setting: Community Design: Randomized, parallel Number of</p>	<p>Study of: Adults N: 39 Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 65 (SD 10) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s): Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Reduce sodium intake to <100 mmol/day Form of Administration: Dietary Modification: low sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 3 months apart Sodium Status Intervention 1: 86 mmol/day How was blood pressure measured? BP measured at rest in the upright seated position between 7 and 11 AM after an overnight fast. Recordings were obtained in triplicate in three</p>	<p>Subgroup: Women Diastolic BP-24H AMB Follow-Up Time: 13 weeks Comparison: Intervention 1 vs Comparator MD -2.11 (95% CI: -4.99 - 0.77) Systolic BP-24H AMB Follow-Up Time: 13 weeks Comparison: Intervention 1 vs Comparator MD -7.11 (95% CI: -11.82 - -2.40)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sites: multiple</p> <p>Study Years: unclear</p>	<p>Mean BMI: 28.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 62 (SD 9) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: postmenopausal status (amenorrheic for at least two years and follicle stimulating hormone plasma concentrations .40 IU/l); >50 years of age, during sitting rest: SBP 130 to 159 mm Hg with diastolic BPDBP<=99 mm Hg. No antihypertensive medications taken in the last two months; and a body mass index (BMI) < 35 Exclusion: Other chronic disease, on a low-sodium diet, performed regular exercise during the preceding two years, smoking</p>	<p>Comparator: Other: Exercise Description: Exercise arm, no diet changes Form of Administration: Other: Exercise arm Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>separate sessions at least one week apart in order to establish the stable readings</p>	
<p>The Trials of Hypertension Prevention Collaborative Research Group, 1992²⁰; Erratum, 1992²¹; Satterfield, 1991²²; Whelton, 1992²³; Whelton, 1997²⁴; He, 1999²⁵; Kumanyika, 1993²⁶; Whelton, 1994²⁷; Cook, 2007²⁸; Cook, 1998²⁹; Yamamoto, 1995³⁰; Cook,</p>	<p>Study of: Adults N: 744</p> <p>Intervention 1: % Male: 70.9 Mean Age/Range/Age at Baseline: mean 43.4 (SD 6.6) Race: 78 Systolic BP: 124.8 Diastolic BP: 83.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.7 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 69.7 Mean Age/Range/Age at Baseline: mean 43.1 (SD 6.6) Race: 84</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: Life-style interventions, provided by psychologists, nutritionists, or other experienced counselors, mostly group educational sessions, with some individual counseling Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Other: placebo Dose: Placebo Na/K ratio: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Intervention 1: 99.4 mmol/24 h Sodium Status Intervention 2: NR Sodium Status Intervention 3: NR Best potassium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Potassium Status Intervention 1: NR Potassium Status Intervention 2: Change from baseline - 2.4 mmol/24 h Potassium Status Intervention 3: Change from baseline 37.4 mmol/24h</p> <p>How was blood pressure measured? Collected at 0, 3, 6, months, 12 and 18 months for lifestyle groups. BP was measured with a Hawksley random-zero sphygmomanometer, after sitting at rest for 5 minutes . The average</p>	<p>Subgroup: Women Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -1.63 (95% CI: -3.52 - 0.27) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -0.68 (95% CI: -3.20 - 1.84)</p> <p>Subgroup: Men Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -0.54 (95% CI: -1.56 - 0.48) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD 0.07 (95% CI: -1.18 - 1.33)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>2016³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p> <p>Number of Sites: 10</p> <p>Study Years: 1987-1995</p>	<p>Systolic BP: 122.6 Diastolic BP: 81.1</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: weight, kg mean 83.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 74.7 Mean Age/Range/Age at Baseline: mean 42.8 (SD 6.5) Race: white 88.8% Systolic BP: 120.7 Diastolic BP: 80.8 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: weight, kg mean 81.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 71.7 Mean Age/Range/Age at Baseline: mean 42.6 (SD 6.5) Race: white 76.5% Systolic BP: 125.1 Diastolic BP: 83.9 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: weight, kg mean 82.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Healthy adults, ages 30-54 with high normal DBP, not taking antihypertensive drugs for the prior 2 months Exclusion: Clinical or lab evidence of cardiovascular or other disabling or life threatening diseases. Conditions that would contraindicate or require any of the interventions. Unwillingness or inability to comply with data collection or intervention procedures.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: NR Dose: potassium chloride, 60 mmol/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: Lifestyle intervention 18 months; Nutritional supplement 6 months Exposure to Follow Up Time: NR</p>	<p>of three readings (first and fifth Korotkoffs sounds) were recorded at each visit.</p>	
<p>Zhou, 2016¹⁵; Zhou, 2013¹⁶</p> <p>Location:</p>	<p>Study of: Both adults and children N: 462</p> <p>Participants:</p>	<p>Intervention Type(s): Duration: NR Exposure to Follow Up Time: NR</p>		<p>Subgroup: Male Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
China Setting: Community Design: Cluster RCT Parallel Number of Sites: multiple Study Years: unclear	% Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Families were at least one member was a hypertension patient; the participant had an estimated daily sodium intake of ≥ 260 mmol per day; Individuals were at least 18 years of age and had no significant renal impairment or other indication for a potassium-sparing medication. Exclusion: Moving			MD -1.93 (95% CI: -2.03 - -1.83) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -6.48 (95% CI: -11.74 - -1.22) Subgroup: Female Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -3.83 (95% CI: -3.92 - -3.74) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -3.94 (95% CI: -6.85 - -1.03)

Table D4. Subgroup table for trials for gender, race/ethnicity, children <18

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Whitten, 1980³² Location: US Setting: Community Design: Number of Sites: multiple Study Years: unclear</p>	<p>Study of: Children N: 27 Intervention 1: % Male: 100 Race: black: 100% Systolic BP: 97 Diastolic BP: 49 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 6.9 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 100 Mean Age/Range/Age at Baseline: NR Race: black: 100% Systolic BP: 102 Diastolic BP: 50 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 7 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Infants that had experienced no illnesses other than respiratory infections and were products of full term pregnancies.</p>	<p>Intervention Type: Intervention 1: Other: Low salt group Description: Intended sodium intake of 2 mEq Na/100 kcal Form of Administration: Dietary Modification: low salt baby formula Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: High salt Description: Intended sodium intake of 9 mEq Na/100 kcal Form of Administration: Dietary Modification: higher salt baby formula Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: 72 hour urine analysis Best sodium measure recorded: 3 times, 2 months apart Sodium Status Intervention 1: 11.3 mEq 24 h Potassium measure: 72 hour urine analysis Best potassium measure recorded: 3 times, 2 months apart Potassium Status Intervention 1: 13.1 mEq 24 h How was blood pressure measured? BP measurements were done using an Air Shield Blood Pressure Monitor attached to the right arm of infant which automatically inflated the cuff to 180 mmHg every 5 min. Readings were recorded 6 to 12 times during the 3 daily nursing shifts over a 72-hour period or longer. Only measurements made while the infants were asleep and approximately an hour after feeding were used.</p>	<p>Subgroup: Black male infants Diastolic BP-sitting Follow-Up Time: 8 years Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -6.16 - 2.16) Diastolic BP-supine Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -4.77 - 2.77) Systolic BP-sitting Follow-Up Time: 8 years Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -5.18 - 3.18) Systolic BP-supine Follow-Up Time: 5 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -6.16 - 2.16)</p>

Table D5. Subgroup table for trials for gender, children <18

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sinaiko, 1993³³; Gomez-Marín, 1991³⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1986-1987</p>	<p>Study of: Children N: 210</p> <p>Intervention 1: % Male: 50 Mean Age/Range/Age at Baseline: 13.2 Race: NR Systolic BP: 113.6 Diastolic BP: 63.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.5 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 52 Mean Age/Range/Age at Baseline: mean 13.3 (SD 0.1) Race: NR Systolic BP: 114.2 Diastolic BP: 66.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 51 Mean Age/Range/Age at Baseline: mean 13.4 (SD .01) Race: NR Systolic BP: 113.7 Diastolic BP: 65.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 22.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Blood pressure at rescreening was > 109 mm Hg for boys and 108 mm Hg for girls</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Reduce sodium intake to 70 mmol/day Form of Administration: Dietary Modification: Trained nutritionists instructed patients on how to reduce dietary sodium Dose: NR Na/K ratio: Boys: 2.9 ; Girls: 2.7 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 1 mmol/kg body weight potassium chloride per 24 hours (Max 80 mmol per 24 hours) administered in capsules Na/K ratio: Boys:2.1 mmol/24h; Girls: 2.2 mmol/24h Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Participants asked not to change their usual diet Form of Administration: Placebo Dose: placebo capsules same shape and color as the potassium chloride Na/K ratio: Boys: 3; Girls 3.5 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart Sodium, Method of Validation: Pill counts, Single 24-hour urine analysis with validation Sodium Status Intervention 1: Boys: 162 mmol/24h; Girls: 119 mmol/24h Sodium Status Intervention 2: Boys: 176 mmol/24h; Girls: 173 mmol/24h Best potassium measure recorded: 3 times, 1 year apart Potassium, Method of Validation: Pill counts Potassium Status Intervention 1: Boys: 64 mmol/24h; Girls: 49 mmol/24h Potassium Status Intervention 2: Boys: 100 mmol/24h; Girls: 93 mmol/24h</p> <p>How was blood pressure measured? Measured two times on the right arm and with the student in the seated position by trained personnel using a standard clinical sphygmomanometer (following a standardized protocol). Blood pressure was measured every 3 months for 3 years.</p>	<p>Subgroup: Girls Rate of increase in diastolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.70 (95% CI: -3.09 - -0.31) Comparison: Intervention 2 vs Comparator MD -0.90 (95% CI: -2.29 - 0.49) Rate of increase in systolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.90 (95% CI: -3.01 - -0.79) Comparison: Intervention 2 vs Comparator MD -0.90 (95% CI: -2.01 - 0.21)</p> <p>Subgroup: Boys Rate of increase in diastolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -3.48 - 0.68) Comparison: Intervention 2 vs Comparator MD -1.60 (95% CI: -3.54 - 0.34) Rate of increase in systolic BP-sitting Follow-Up Time: 3 years Comparison: Intervention 1 vs Comparator MD 0.60 (95% CI: -0.65 - 1.85) Comparison: Intervention 2 vs Comparator MD 0.30 (95% CI: -0.81 - 1.41)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	Exclusion: SBP \geq 140/DBP \geq 90 on average, DBP $>$ 100 on any visit, history of renal disease with significant hematuria or proteinuria, or serum creatinine $>$ 1.5 mg/dl. Hypokalemia, chronic system illness, compliance issues			

Table D6. Subgroup table for trials for gender, children <18, DRI age group (14-18)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Tuthill, 1985³⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Massachusetts Blood Pressure Study, Part 4</p> <p>Number of Sites: 2</p> <p>Study Years: unclear</p>	<p>Study of: Children N: 191</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113 Diastolic BP: 71 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.9 Diastolic BP: 71.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.4 Diastolic BP: 70.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 0; Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 113.1</p>	<p>Intervention Type(s): Intervention 1: Other: Placebo - Campus 1 Description: NR Form of Administration: Placebo Dose: Placebo tablet twice daily Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Salt pill in evening - Campus 1 Description: NR Form of Administration: Salt substitute Dose: 0.8 gram salt pill in the evening, placebo in morning Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Salt pill in morning - Campus 1 Description: NR Form of Administration: Sodium supplement Dose: 0.8 gram salt pill in the morning, placebo in evening Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Placebo - Campus 2 Description: NR Form of Administration: Other: placebo Dose: Placebo tablet twice daily Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Other: Salt pill in evening - Campus 2 Description: NR Form of Administration: NR Dose: 0.8 gram salt pill in the evening, placebo in morning Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Salt pill in morning - Campus 2 Description: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 2 times at baseline, then 8 times 1 week apart Sodium, Method of Validation: Study pills were swallowed in the presence of a research staff member, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: +250 mg compared to baseline Sodium Status Intervention 3: +550 mg change from baseline Sodium Status Comparator 1: +650 mg change from baseline Sodium Status Intervention 2: -50 mg change from baseline Sodium Status Intervention 4: +450 mg change from baseline Sodium Status Comparator 2: +800 mg compared to baseline Best potassium measure recorded: 2 times at baseline, then 8 times 1 week apart</p> <p>How was blood pressure measured? BP was measured by two technicians who were blind to each other's readings and also to the girls intervention status</p>	<p>Subgroup: Girls Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Comparator 1 vs Intervention 1 MD -1.60 (95% CI: NC - NC) Comparison: Comparator 1 vs Intervention 3 MD -1.60 (95% CI: NC - NC) Comparison: Comparator 2 vs Intervention 2 MD -2.80 (95% CI: NC - NC) Comparison: Comparator 2 vs Intervention 4 MD -0.20 (95% CI: NC - NC) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Comparator 1 vs Intervention 1 MD -0.10 (95% CI: NC - NC) Comparison: Comparator 1 vs Intervention 3 MD -1.70 (95% CI: NC - NC) Comparison: Comparator 2 vs Intervention 2 MD -1.20 (95% CI: NC - NC) Comparison: Comparator 2 vs Intervention 4 MD -1.10 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Diastolic BP: 69.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 4: % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 112.4 Diastolic BP: 68.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 0 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 111.7 Diastolic BP: 69.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Young females in grades 9-12 Exclusion: One or more of the three consulting physicians considered the student at medical risk if exposed to extra dietary salt. A medical condition, or taking medication which might affect their blood pressure.</p>	<p>Form of Administration: Sodium supplement Dose: 0.8 gram salt pill in the morning, placebo in evening Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>		

Table D7. Subgroup table for trials for gender, children <18, DRI age group (9-13)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Calabrese, 1985 ³⁶	Study of: Children N: 153	Intervention Type(s): Comparator: Other: Low sodium water	Sodium measure: 2 day food records; Partial or spot urine with validated	Subgroup: Girls Diastolic BP-sitting

<p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Massachusetts Blood Pressure Study, Part 3</p> <p>Number of Sites: multiple</p> <p>Study Years: 1979</p>	<p>Intervention 1:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 99.4</p> <p>Diastolic BP: 57.3</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Male: 36.3 kg; Female 33.6 kg</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Intervention 2:</p> <p>% Male: NR; Mean Age/Range/Age at Baseline: NR; Race: NR</p> <p>Systolic BP: 99.3</p> <p>Diastolic BP: 57.7</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Male: 34.3 kg; Female: 32.5 kg</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 51; Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 99.6</p> <p>Diastolic BP: 57.1</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Males: 34 kg; Females: 29.8 kg</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Children in fourth grade, children's' parents consent</p>	<p>with added sodium</p> <p>Description: NR</p> <p>Form of Administration: Dietary</p> <p>Modification: Low sodium water with added sodium</p> <p>Dose: Low sodium water + added sodium such that it contained 110 mg/L Na</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 2: Other: High sodium water</p> <p>Description: NR</p> <p>Form of Administration: Dietary</p> <p>Modification: High sodium water</p> <p>Dose: High sodium water contained 110 mg/ L Na</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Other: Low sodium water</p> <p>Description: NR</p> <p>Form of Administration: Dietary</p> <p>Modification: Low sodium water</p> <p>Dose: Low sodium water contained 10 mg/L Na</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 3 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>prediction equation</p> <p>Best sodium measure recorded: Collected at 0,1,2,3 months</p> <p>Sodium, Method of Validation: To measure compliance parents completed a questionnaire at two-week intervals, reporting how their child adhered to the bottled water regimen during that period.</p> <p>Sodium Status Comparator: Males 127.6 mEq; Females 135.8 mEq</p> <p>Sodium Status Intervention 2: Males 123.2 mEq; Females 109.0 mEq</p> <p>Potassium measure: Partial or spot urine without validated prediction equation, 2 day food records</p> <p>Best potassium measure recorded: Collected at 0,1,2,3 months</p> <p>Potassium, Method of Validation: To measure compliance parents completed a questionnaire at two-week intervals, reporting how their child adhered to the bottled water regimen during that period.</p> <p>Potassium Status Comparator: Males 42.4 mEq; Females 36 mEq</p> <p>Potassium Status Intervention 2: Males 33.6 mEq; Females 34.9 mEq</p> <p>How was blood pressure measured?</p> <p>Patients sitting casually and BP on the left arm was taken at each station by a nurse using a mercury sphygmomanometer. The pressure was raised approximately 30 mm Hg higher than the point at which the pulse disappeared and then released at a rate of 2 to 3 mm Hg/ sec. SBP was taken at the point where two consecutive Korotkoff sounds were audible and DBP at the disappearance of sound.</p>	<p>Follow-Up Time: 3 months</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD -6.30 (95% CI: -11.90 - -0.70)</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -1.70 (95% CI: -7.09 - 3.69)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 3 months</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD -1.90 (95% CI: -6.24 - 2.44)</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -0.80 (95% CI: -5.70 - 4.10)</p> <p>Subgroup: Boys</p> <p>Diastolic BP-sitting</p> <p>Follow-Up Time: 3 months</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD 2.30 (95% CI: -3.13 - 7.73)</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD 1.70 (95% CI: -4.06 - 7.46)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 3 months</p> <p>Comparison: Intervention 2 vs Intervention 1</p> <p>MD 0.30 (95% CI: -3.82 - 4.42)</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -0.10 (95% CI: -3.80 - 3.60)</p>
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Table D8. Subgroup table for trials for gender, children <19

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Miller, 1987⁶</p> <p>Location: US</p> <p>Setting:</p>	<p>Study of: Both adults and children</p> <p>N: 76</p> <p>Intervention 1:</p> <p>% Male: NR</p>	<p>Intervention Type:</p> <p>Intervention 1: Other: Adults - Potassium supplement</p> <p>Description: Participants asked not to change their usual diet</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour</p>	<p>Subgroup: Boys</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -1.20 (95% CI: -12.05 - 9.65)</p>

<p>Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Mean Age/Range/Age at Baseline: mean 42 (SD 8.4) Race: white: 100% Systolic BP: 113.2 Diastolic BP: 73.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 76.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR; Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8) Race: white: 100%; Systolic BP: 100.9 Diastolic BP: 59.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 100.8; Diastolic BP: 60.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>	<p>Form of Administration: Oral potassium supplement Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men. Na/K ratio: 2.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children Description: K+ supplement to increase potassium intake Form of Administration: Other: liquid potassium supplement Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls. Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Placebo - children Description: NR Form of Administration: Other: Placebo Dose: Placebo Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>urine samples every two weeks, twins collected the samples every week. Sodium, Method of Validation: Measurement of creatinine excretion (if it was ± 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 165 mEq/d Sodium Status Intervention 2: 108.8 mEq/d Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Potassium, Method of Validation: Measurement of creatinine excretion (if it was ± 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete). Potassium Status Intervention 1: 81.6 mEq/d Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	
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Table D9. Subgroup table for trials for gender, children <21

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Miller, 1987 ⁶	Study of: Both adults and children N: 76	Intervention Type: Intervention 1: Other: Adults - Potassium	Sodium measure: Single 24-hour urine analysis with validation	Subgroup: Boys Diastolic BP-sitting

<p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Intervention 1:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: mean 42 (SD 8.4)</p> <p>Race: white: 100%</p> <p>Systolic BP: 113.2</p> <p>Diastolic BP: 73.1</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 76.1 kg</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Intervention 2:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8)</p> <p>Race: white: 100%</p> <p>Systolic BP: 100.9</p> <p>Diastolic BP: 59.4</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 37.1 kg</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 100.8</p> <p>Diastolic BP: 60.0</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 37.1</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>	<p>supplement</p> <p>Description: Participants asked not to change their usual diet</p> <p>Form of Administration: Oral potassium supplement</p> <p>Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men.</p> <p>Na/K ratio: 2.2</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children</p> <p>Description: K+ supplement to increase potassium intake</p> <p>Form of Administration: Other: liquid potassium supplement</p> <p>Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls.</p> <p>Na/K ratio: 2.4</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Other: Placebo - children</p> <p>Description: NR</p> <p>Form of Administration: Other: Placebo</p> <p>Dose: Placebo</p> <p>Na/K ratio: 3.2</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1 month</p> <p>Exposure to Follow Up Time: NR</p>	<p>Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week.</p> <p>Sodium, Method of Validation: Measurement of creatinine excretion (if it was $\pm 20\%$ of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 165 mEq/d</p> <p>Sodium Status Intervention 2: 108.8 mEq/d</p> <p>Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week.</p> <p>Potassium, Method of Validation: Measurement of creatinine excretion (if it was $\pm 20\%$ of the mean creatinine content of all complete baseline collections for that individual, it was considered complete).</p> <p>Potassium Status Intervention 1: 81.6 mEq/d</p> <p>Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	<p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 2 vs Comparator</p> <p>MD -0.90 (95% CI: -10.13 - 8.33)</p>
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Table D10. Subgroup table for trials for gender, children <23

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Miller, 1987⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 76</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 42 (SD 8.4) Race: white: 100% Systolic BP: 113.2 Diastolic BP: 73.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 76.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR; Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8) Race: white: 100%; Systolic BP: 100.9 Diastolic BP: 59.4; Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 100.8 Diastolic BP: 60.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>	<p>Intervention Type: Intervention 1: Other: Adults - Potassium supplement Description: Participants asked not to change their usual diet Form of Administration: Oral potassium supplement Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men. Na/K ratio: 2.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children Description: K+ supplement to increase potassium intake Form of Administration: Other: liquid potassium supplement Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls. Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Placebo - children Description: NR Form of Administration: Other: Placebo Dose: Placebo Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Sodium, Method of Validation: Measurement of creatinine excretion (if it was \pm 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 165 mEq/d Sodium Status Intervention 2: 108.8 mEq/d Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Potassium, Method of Validation: Measurement of creatinine excretion (if it was \pm 20% of the mean creatinine content of all complete baseline collections for that individual, it was considered complete). Potassium Status Intervention 1: 81.6 mEq/d Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	<p>Subgroup: Girls Systolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -0.10 (95% CI: -5.87 - 5.67)</p>

Table D11. Subgroup table for trials for gender, children <25

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Miller, 1987⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Both adults and children N: 76</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 42 (SD 8.4) Race: white: 100% Systolic BP: 113.2 Diastolic BP: 73.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 76.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: mean 11.6 (SD 3.8) Race: white: 100% Systolic BP: 100.9 Diastolic BP: 59.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR; Mean Age/Range/Age at Baseline: NR Race: NR; Systolic BP: 100.8 Diastolic BP: 60.0 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 37.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Normotensive, school-aged, identical twins and their parents who were already in the twin panel in the Department of Medical Genetics, Indian University School of Medicine</p>	<p>Intervention Type: Intervention 1: Other: Adults - Potassium supplement Description: Participants asked not to change their usual diet Form of Administration: Oral potassium supplement Dose: Average supplementation was 53.7 mEq/day for women, 66 mEq/day for men. Na/K ratio: 2.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Potassium supplementation - children Description: K+ supplement to increase potassium intake Form of Administration: Other: liquid potassium supplement Dose: Average supplementation was 45 mEq/day for boys, 36.2 mEq/day for girls. Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Placebo - children Description: NR Form of Administration: Other: Placebo Dose: Placebo Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Sodium, Method of Validation: Measurement of creatinine excretion (if it was $\pm 20\%$ of the mean creatinine content of all complete baseline collections for that individual, it was considered complete)., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 165 mEq/d Sodium Status Intervention 2: 108.8 mEq/d Best potassium measure recorded: Five times during over a month during a baseline period. Then parents collected 24-hour urine samples every two weeks, twins collected the samples every week. Potassium, Method of Validation: Measurement of creatinine excretion (if it was $\pm 20\%$ of the mean creatinine content of all complete baseline collections for that individual, it was considered complete). Potassium Status Intervention 1: 81.6 mEq/d Potassium Status Intervention 2: 48.6 mEq/d</p> <p>How was blood pressure measured? Three BP measurements were taken with a Hawksley random zero blood pressure device while the subjects were in a seated position. The research assistant was certified in blood pressure measurement. The mean of the last two of three blood pressure measurements was used for analysis.</p>	<p>Subgroup: Girls Diastolic BP-sitting Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 0.60 (95% CI: -5.54 - 6.74)</p>

Table D12. Subgroup table for trials for gender, hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Grimm, 1990³⁷; Grimm, 1988³⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: Minnesota Mount Sinai Hypertension Trial (MSHT)</p> <p>Number of Sites: multiple</p> <p>Study Years: 1984-1985</p>	<p>Study of: Adults N: 287</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 57.8 (SD 6.2) Race: NR Systolic BP: 124.7 Diastolic BP: 79.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: mean 57.5 (SD 6.5) Race: NR Systolic BP: 126.4 Diastolic BP: 80.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Males, aged 45-68, documentation of long term drug treatment for hypertension in Minneapolis. Currently taking one or two antihypertensive drugs with DBP<95 mm Hg on the first 2 clinic visits, and <90 mm Hg average for both visits. Exclusion: Treatment of hypertension for < 3.5 years, use of cardiovascular drugs, electrocardiographic evidence or clinical evidence of CVD, body weight >15% of the ideal weight, diet incompatible with lowering sodium intake, history of renal disease, documented poor compliance with antihypertensive treatments.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Placebo pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Oral potassium supplement Dose: 96 mmol microcrystalline potassium chloride - 12 capsules, per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Potassium pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Placebo Dose: 12 placebo capsules per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>	<p>Potassium measure: Partial or spot urine without validated prediction equation, Food diaries without reported validation Potassium Status Intervention 1: 40 mmol/8h</p>	<p>Subgroup: HTN on antihypertensives, male Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD 0.60 (95% CI: -0.95 - 2.15) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.20 (95% CI: -2.94 - 2.54)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Morgan, 1978³⁹; Morgan, 1980⁴⁰</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: 1973</p>	<p>Study of: Adults N: 77</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 160 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 162 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 163 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 165</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To reduce sodium intake to 70-100 mmol/day Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Treated with chlorothiazide (500 mg twice d) with the addition of 'Aldomet' if control was inadequate. If control was still not achieved then other drugs were added. Description: NR Form of Administration: Other: chlorothiazide Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Patients treated with propranolol (up to 480 mg/day) and a diuretic, other drugs were considered if control was inadequate Description: NR Form of Administration: Other: propranolol Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 5 times, 6 months apart Sodium Status Intervention 1: 157 mmol/day Sodium Status Intervention 2: 191 mmol/day Sodium Status Intervention 3: 189 mmol/day</p> <p>How was blood pressure measured? BP taken in duplicate with a Bonn amplified sphygmomanometer (by a trained user) after the patients had been in the supine position for ten minutes. The DBP was taken at the 4th phase of the Korotkoff sounds. The BP was again recorded in duplicate after the patient had been standing quietly for five minutes. If the BP differed from previous readings the patient was seen again at the clinic one month later. The procedure was then repeated, and the patient was then included in the study. The mean of the 4 DBPs was taken as the pressure at entry into the study</p>	<p>Subgroup: HTN males CVD mortality (cerebrovascular accidents, myocardial infarction, congested cardiac failure) Follow-Up Time: 200-2000 days Comparison: Intervention 1 vs Comparator RR 0.83 (95% CI: 0.12 - 5.62) DBP <90 mmHg Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 2.00 (95% CI: 0.77 - 5.20) Diastolic BP-supine Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -11.16 - -2.84) Systolic BP-supine Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -10.15 - 8.15) Treatment for heart failure Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 1.50 (95% CI: 0.27 - 8.36) Deaths Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 0.33 (95% CI: 0.01 - 7.88) Total number of deaths Follow-Up Time: 200-2000 days Comparison: Intervention 1 vs Comparator RR 1.04 (95% CI: 0.30 - 3.58)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: DBP > 90 mm Hg on admission to hospital or at a visit to an outpatient department Exclusion: Malignant disease, severe psychiatric disturbances, severe physical incapacity or a disease likely to be fatal in the next 2 years. Patients with serum-creatinine levels > 0.18 mmol/l, those with abnormal liver-function tests, and those in cardiac failure or on diuretics</p>			
<p>Morgan, 1981⁴¹</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 24</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: Males: mean 41 (SD 4); Females: mean 36 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 101; Females 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: Males: mean 42 (SD 4); Females: 46 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 123; Females 118 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: DBP low - NA restrict Description: Detailed instructions how to reduce salt intake to 70 mmol a day Form of Administration: Dietary Modification: restricted sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: DBP high - thiazide Description: No diet intervention, patients given were given chlorothiazide (500 mg a day). Form of Administration: Other: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: High DBP Na restrict Description: Detailed instructions how to reduce salt intake to 70 mmol a day Form of Administration: Dietary Modification: Restricted sodium Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: DBP low - control</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: weekly during first stage (up to 1 month), then every 2 weeks during second stage (8 weeks) Sodium Status Intervention 1: Males: 78 mmol/24h; Females: 58 mmol/24h Sodium Status Intervention 2: Males: 181 mmol/24h; Females 138 mmol/24h Sodium Status Intervention 3: Males: 85 mmol/24h; Females: 64 mmol/24h</p> <p>How was blood pressure measured? The same observer measured the patient's BP duplicate at each session with a mercury sphygmomanometer after they had been lying down for 10 minutes and standing for 5 minutes. Korotkoff phase I and IV sounds were used.</p>	<p>Subgroup: Male, DBP<105 mmHg Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -14.92 - 0.92)</p> <p>Subgroup: Female, DBP<105 mmHg Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -10.92 - 4.92)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean Age/Range/Age at Baseline: Males: mean 42 (SD 4); Females: mean 41 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 121; Females: 117 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: Males: mean 38 (SD 3); Females: mean 39 (SD 4) Race: NR Systolic BP: NR Diastolic BP: Males: 99; Females 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 28-50</p>	<p>Description: No dietary advice Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>		
<p>Parker, 1990⁴²</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 28</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 49.8 (SD 3.1) Race: NR Systolic BP: 136.1 (supine) Diastolic BP: 83.9 (supine) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.3 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 100 Mean Age/Range/Age at Baseline: mean 51 (SD 3.1) Race: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Low alcohol - low salt Description: NR Form of Administration: Other: Placebo Dose: low sodium diet (60 mmol/day) + placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Low alcohol - normal salt Description: NR Form of Administration: Sodium supplement Dose: low sodium diet (60 mmol/day) + supplementation with 100 mmol enteric-coated sodium chloride (5 10 mmol tablets twice daily) Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Sodium, Method of Validation: detailed food records on the day that urine was collected, weekly tablet counts Sodium Status Intervention 1: 68.6 mmol/day (average of the two low sodium groups) Sodium Status Intervention 2: 68.6 mmol/day (average of the two low sodium groups) Sodium Status Comparator 2: 141.7 mmol/day (average of the normal sodium groups)</p> <p>How was blood pressure measured? average of two sets of five readings measured at 2-minute intervals 1 week apart using with automatic oscillometric device, the Dinamap 845XT</p>	<p>Subgroup: Male, HTN on antihypertensives (normal alcohol) Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Comparator 2 vs Intervention 2 MD -0.80 (95% CI: -3.84 - 2.24) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Comparator 2 vs Intervention 2 MD 0.10 (95% CI: -5.15 - 5.35)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Systolic BP: 139.6 (supine) Diastolic BP: 83.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 100 Mean Age/Range/Age at Baseline: mean 52.8 (SD 2) Race: NR Systolic BP: 139.9 (supine) Diastolic BP: 86.6 (supine) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 100 Mean Age/Range/Age at Baseline: mean 54.2 (SD 2.6) Race: NR Systolic BP: 139.9 (supine) Diastolic BP: 86.6 (supine) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 20-70 years, regular treatment with antihypertensive drugs for a minimum of 6 months, alcohol intake of at least 210 ml/wk, no history of renal or hepatic disease or diabetes mellitus, not on current treatment with nonsteroidal anti-inflammatory drugs, and no history of a MI, stroke, or coronary artery bypass surgery within the last 12 months. 125 mm Hg \leq SBP \leq 180 mm Hg, and a DBP of less than 115 mm Hg Exclusion: Underlying renal disease, average 24-hour urinary sodium excretion less than 80 mmol/day (estimated from two urine collections 1 week apart)</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Normal alcohol - low salt Description: NR Form of Administration: Placebo Dose: low sodium diet (60 mmol/day) + placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal alcohol - normal salt Description: NR Form of Administration: Sodium supplement Dose: low sodium diet (60 mmol/day) + supplementation with 100 mmol enteric-coated sodium chloride (5 10 mmol tablets twice daily) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>		

Table D13. Subgroup table for trials for hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Alli, 1992⁴³</p> <p>Location: Italy</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 77</p> <p>Intervention 1: % Male: 34.6 Mean Age/Range/Age at Baseline: mean 44.3 (SD 10.2) Race: NR Systolic BP: 150.8 Diastolic BP: 97 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: mean 51.7 (SD 11) Race: NR Systolic BP: 148.3 Diastolic BP: 97.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.8 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild hypertension not previously known, not taking antihypertensive treatment or medications which interfered with BP; and they were not overweight (BMI < 30). Exclusion: Evidence of cardiovascular complications or secondary hypertension (as per pathological history, physical examination, and lab tests).</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Dietary instructions with the goal of lowering sodium intake Form of Administration: Dietary Modification: low-sodium diet Dose: NR Na/K ratio: 2.7 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: 2.8 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: At 1, 3, 6, 9 and 12 months. Sodium, Method of Validation: Completeness or urine collection was assessed on the basis of 24h creatinine excretion., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 177 mEq Best potassium measure recorded: At 1, 3, 6, 9 and 12 months. Potassium, Method of Validation: Completeness or urine collection was assessed on the basis of 24h creatinine excretion. Potassium Status Intervention 1: 67.2 mEq</p> <p>How was blood pressure measured? BP taken in the supine position after 5 minutes at rest. SBP and DBP recorded at Korotkoff phases I and V. Three BP measurements were recorded at 1-minute intervals and the lowest value was used.</p>	<p>Subgroup: Mild HTN Diastolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 4.00 (95% CI: 1.02 - 6.98) Systolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 3.80 (95% CI: -2.70 - 10.30)</p>
<p>Applegate, 1992⁴⁴</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of</p>	<p>Study of: Adults N: 47</p> <p>Intervention 1: % Male: 43 Mean Age/Range/Age at Baseline: mean 65 (SD 3.8) Race: white: 57% Systolic BP: 143 Diastolic BP: 86 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 89 Kg</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Intervention focused on calorie and sodium reduction with increases in moderate levels of physical activity Form of Administration: Dietary Modification: Individual and group sessions Dose: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, diet recall Best sodium measure recorded: 0, 2, 3, and 6 months. Sodium Status Intervention 1: 142.5 mmol/d</p> <p>How was blood pressure measured? After a 5-minute rest at each clinic visit, BP was measured in triplicate in the seated position by trained staff using random zero sphygmomanometers.</p>	<p>Subgroup: Mild HTN, modestly overweight Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.90 (95% CI: NC - NC) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sites: multiple</p> <p>Study Years: unclear</p>	<p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 46 Mean Age/Range/Age at Baseline: mean 64 (SD 4.5) Race: white: 65% Systolic BP: 145 Diastolic BP: 88 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 81 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-85, mild diastolic hypertension, modestly overweight (115% of ideal body weight), a Folstein Mini-Mental State score > 22 out of 30, adequate physical health, adequate vision, willingness to participate. Exclusion: MI within the past year, prior diagnosis of angina pectoris or congestive heart failure, stroke within the last year, other serious CVD, or diabetes . Other serious chronic illnesses; a random serum glucose concentration \geq 12.2 mmol/L, a serum creatinine level of > 150 umol/L, and a serum cholesterol level of more than 6.85 mmol/L; serious physical handicaps; disorders that might affect the implementation of dietary interventions; or use of medications that could impact BP.</p>	<p>Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		
<p>Arroll, 1995⁴⁵</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 87</p> <p>Participants: % Male: 52 Mean Age/Range/Age at Baseline: mean 55 Race: NR Systolic BP: 144.6 Diastolic BP: 89.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Essential hypertension with a SBP > 115 mm Hg or a DBP > 70 mm Hg (on medication); ages 20 - 69 years inclusive; a sedentary lifestyle and under the care of a primary care physician Exclusion: Symptomatic coronary heart disease, immobility that restricted</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: Education and instruction on reducing salt in diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Exercise + salt restriction Description: NR Form of Administration: Other: Education and instruction on reducing salt in diet + physical activity Dose: NR Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times 3 months apart Sodium Status Intervention 1: median 107 mmol/24h Sodium Status Intervention 2: median 105.5 mmol/24h</p> <p>How was blood pressure measured? BP measured using a Hawksley random zero sphygmomanometers. Three consecutive measurements taken and an average of the last two readings was used.</p>	<p>Subgroup: Treated hypertensive Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.50 (95% CI: -8.24 - -0.76) Systolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -9.04 - 3.44)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	walking; current DBP >105 mm Hg or a SBP greater > 180 mm Hg; regularly performing regular moderate physical activity.	Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 6 months Exposure to Follow Up Time: NR		
Australian National Health and Medical Research Council Dietary Salt Study Management Committee, 1989 ⁴⁶ Location: Australia Setting: Community Design: Randomized, parallel Number of Sites: 2 Study Years: unclear	Study of: Adults N: 108 Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 149.1 Diastolic BP: 91.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 93 Mean Age/Range/Age at Baseline: 58.4 Race: NR Systolic BP: 152.8 Diastolic BP: 95.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: DBP at four run-in visits between 90 and 100 mm Hg, with no single measure above 110 mm Hg or below 85 mm Hg, and gave written informed consent. Exclusion: Being treated for hypertension, a secondary cause of	Intervention Type(s): Intervention 1: Other: Low sodium Description: NR Form of Administration: Other: placebo Dose: Diet containing less than 80 mmol sodium/day + 8 placebo pills daily Na/K ratio: 1.4 Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Other: Normal Sodium Description: 153 mmol/day Form of Administration: Sodium supplement Dose: Diet containing less than 80 mmol sodium/day + 8 slow-release sodium chloride [10 mmol] pills daily) Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR Duration: 2 months Exposure to Follow Up Time: NR	Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times, every 2 weeks Sodium Status Intervention 1: 90 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 times, every 2 weeks Potassium Status Intervention 1: 71 mmol/day How was blood pressure measured? Seated BP measurements were made after 5 min rest using a sphygmomanometry with oscillometric detection. A large cuff was applied to the left arm and four measurements were taken with intervals of 1 min. The first value was discarded and the mean of the other three measures were used.	Subgroup: Mild HTN Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -4.46 - -1.14) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -5.50 (95% CI: -8.41 - -2.59)

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	hypertension, hypertension complications, evidence of other cardiovascular disease			
<p>Barros, 2015⁴⁷</p> <p>Location: South America (Argentina, Brazil, Chile, and Colombia)</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2012</p>	<p>Study of: Adults N: 38</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 142.95 Diastolic BP: 86.79 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.38 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 34.3 Mean Age/Range/Age at Baseline: mean 55.5 SD (7.4) Race: NR Systolic BP: 143.44 Diastolic BP: 91.19 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 31 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Hypertensive individuals between ages 20 and 65 years. Patients lived in the metropolitan region of Goiânia, Brazil, on stable doses of antihypertensive drugs for at least 30 days, with uncontrolled hypertension (BP \geq 140 x 90 mmHg) in their last visit. Exclusion: Acute or subacute (up to 3 months before the beginning) and unstable chronic diseases. Those having their meals prepared with a salt different from that provided in the study more than once a week.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Light salt Description: Instructed to consume only the provided salt throughout this study. Instructed to reduce sodium-rich food consumption throughout the study period. Form of Administration: Salt substitute Dose: 28 small plastic bags containing the daily amount of salt. Light salt composition (per gram) was as follows: 130 mg of sodium, 346 mg of potassium and 44 mcg of iodine Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Instructed to consume only the provided salt throughout this study. Instructed to reduce sodium-rich food consumption throughout the study period. Form of Administration: Usual diet Dose: 28 small plastic bags containing the daily amount of salt. Regular salt contained (per gram) 390 mg of sodium and 25 mcg of iodine. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times 1 month apart Sodium Status Intervention 1: 127.11 mEq/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 1 month apart Potassium Status Intervention 1: 48.05 mEq/day</p> <p>How was blood pressure measured? Casual BP taken by the same researcher, at least three times and at 1-minute intervals, until the differences between the measurements were lower than 4 mmHg. The mean of the mean of the last two values was considered, obtained by using a semi-automatic digital device.</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -6.80 (95% CI: -14.11 - 0.51) Systolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -10.08 (95% CI: -22.23 - 2.07) Decreased quality of life Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)</p>
<p>Beard, 1982⁴⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p>	<p>Study of: Adults N: 113</p> <p>Intervention 1: % Male: 60 Mean Age/Range/Age at Baseline: Mean 48.4 Race: white: 100% Systolic BP: 142.3 Diastolic BP: 131.0 Magnesium: NR Calcium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: No-added-sodium diet Form of Administration: Dietary Modification: No-added-sodium diet. Shopping guides, small group discussions, recipe exchanges, nutritional</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, Patients answered a final questionnaire on lifestyle and health; the diet group reported compliance and future intentions. Best sodium measure recorded: 5 times, at baseline, 2, 4, 6, and 11 weeks. Sodium Status Intervention 1: 37.0 mmol/24h Potassium measure: Single 24-hour urine</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.30 (95% CI: -5.04 - 2.44) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -8.63 - 5.03) Average drug consumption (number of pills per day) relative to baseline</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Other Minerals: NR Mean BMI: 79.98 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 53 Mean Age/Range/Age at Baseline: mean 49.6 Race: white: 100% Systolic BP: 138.9 Diastolic BP: 86.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 77.81 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Individuals aged 25-69 years, receiving antihypertensive medication and who had a premedication DBP between 95 and 109 mm Hg and SBP under 200 mm Hg Exclusion: Women who were pregnant or taking an oral contraceptive. Men and women with severe intercurrent illness, serum creatinine >0.20 mmol/l, or history of antihypertensive medication for less than 3 months</p>	<p>counseling Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual salt intake Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>analysis without validation, Patients answered a final questionnaire on lifestyle and health; the diet group reported compliance and future intentions. Best potassium measure recorded: 5 times, at baseline, 2, 4, 6, and 11 weeks. Potassium Status Intervention 1: 79.9 mmol/24h</p> <p>How was blood pressure measured? Casual sitting BP (average of two readings) was measured to the closest 2 mm Hg with the Hawksley random-zero machine, using a 13 cm x 35 cm bag and the 5th-phase DBP. These readings were taken by one of two nurses whose results had shown good agreement and internal consistency in practice sessions.</p>	<p>Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: NC - NC) Failed to stop or reduce medication Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator RR 3.75 (95% CI: 1.94 - 7.27)</p>
<p>Beckmann, 1995⁴⁹</p> <p>Location: Norway</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 64</p> <p>Participants: % Male: 100 Mean Age/Range/Age at Baseline: Range: 40-56 Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.7 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Otherwise healthy middle aged men with never-treated hypertension</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: The goal was a daily intake of sodium chloride of approximately 100 mmol. Form of Administration: Dietary Modification: Subjects instructed on a diet to reduce sodium. For the first 2 weeks they were provided with free food to help with diet compliance Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: BP Control group Description: No dietary advice was given Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Taken once for control groups at baseline. Taken at baseline and 12 months for intervention group Sodium Status Intervention 1: 123 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Taken at baseline, weeks 1,2,3 months, 6 months, 12 months Potassium Status Intervention 1: 90 mmol/24 h</p> <p>How was blood pressure measured? BP measurements were taken on the right arm using an oscillometric device. In the study sample, this semiautomatic BP monitor measured SBP and DBP on average 3.5 and 2.0 mm Hg lower than a mercury sphygmomanometer, but without examiner bias. BP recordings were made after 9 and 10 min in the supine position, and also after</p>	<p>Subgroup: HTN MBP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -11.16 - -4.84)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Calcium: NR Other Minerals: NR Duration: 6 months Exposure to Follow Up Time: 12 months	9 and 10 min of standing. The mean of the two blood pressure recordings at 9 and 10 min was used for analysis.	
Bulpitt, 1985 ⁵⁰ Location: UK Setting: Community Design: Randomized, parallel Number of Sites: 1 Study Years: unclear	Study of: Adults N: 33 Intervention 1: % Male: 43 Mean Age/Range/Age at Baseline: 56.1 Race: NR Systolic BP: Untreated: 199 Diastolic BP: Untreated: 122 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 47 Mean Age/Range/Age at Baseline: mean 54.2 (SE 1.9) Race: NR Systolic BP: Untreated: 190 Diastolic BP: Untreated: 133 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Hypertensive, using a potassium losing diuretic Exclusion: Using a potassium-sparing diuretic, plasma urea had ever been greater than 9.9 mmol/l or plasma potassium > 5 mmol/l.	Intervention Type(s): Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 8 Slow K tablets daily (64 mmol of slow release potassium) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: Participants asked not to change their usual diet and drug treatment Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 3 months Exposure to Follow Up Time: NA	Sodium Status Intervention 1: 149 Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1, Food diaries without reported validation Best potassium measure recorded: 2 times, 3 months apart Potassium Status Intervention 1: 95 How was blood pressure measured? Measured 2 times, 3 months apart. BP was measured standing and lying by attending physicians and by the research team using the London School of Hygiene (LSH) sphygmomanometer (10) and measuring systolic, diastolic (IVth) and diastolic (Vth) after 3 minutes standing and 5 minutes lying.	Subgroup: Hypertensive on K-losing diuretics Diastolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD 4.80 (95% CI: -3.11 - 12.71) Reduced quality of life (indigestion) Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 0.74 (95% CI: 0.05 - 10.79) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD 2.30 (95% CI: -15.16 - 19.76) Significant changes in blood cholesterol Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC) Significant changes in blood glucose Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)
Bulpitt, 1984 ⁵¹ Location: UK Setting: Community Design: Randomized, parallel Number of	Study of: Adults N: 65 Intervention 1: % Male: 34.4 Mean Age/Range/Age at Baseline: Mean 54.5 Race: NR Systolic BP: 158 Diastolic BP: 103 Magnesium: NR Calcium: NR Other Minerals: NR	Intervention Type(s): Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Dietary advice for a 1 g Na (44 mmol) daily diet. A salt substitute, KCL, was also given. Form of Administration: Dietary Modification: Dietary advice, salt substitute	Sodium measure: Multiple 48 hour urine analysis; Questionnaire on diet Best sodium measure recorded: 2 times, at baseline and at 3 months Sodium Status Intervention 1: 204 mmol/48-h How was blood pressure measured? Measurements were taken both lying and standing by the attending physician and by the research team using the London School of Hygiene (LSH) sphygmomanometer and	Subgroup: HTN on antihypertensives Decreased quality of life Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD 0.07 (95% CI: NC - NC) Diastolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -2.10 (95% CI: -7.82 - 3.62) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sites: 1</p> <p>Study Years: unclear</p>	<p>Mean BMI: 77.1 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 54.5% Mean Age/Range/Age at Baseline: 54.6 Race: NR Systolic BP: 169 Diastolic BP: 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 80.1 kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: All patients were attending the Hammersmith Hospital Hypertension Clinic agents and had been treated on a long term basis with a variety of agents. The inclusion criterion was unsatisfactory BP control defined as a standing DBP > 95 mm Hg on two successive occasions despite drug treatment</p>	<p>Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>measuring SBP, DBP to the Korotkoff's 4th and 5th phase after five minutes lying and three minutes standing</p>	<p>MD -6.10 (95% CI: -17.47 - 5.27) Percent of people with major decrease in drug therapy Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 3.01 (95% CI: 0.13 - 72.03)</p>
<p>Charlton, 2008⁵²</p> <p>Location: South Africa</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: 2004-2005</p>	<p>Study of: Adults N: 92</p> <p>Intervention 1: % Male: 17.5% Mean Age/Range/Age at Baseline: mean 61.8 (SD 6.6) Race: Black: 100% Systolic BP: 133.9 Diastolic BP: 79.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 32.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 15% Mean Age/Range/Age at Baseline: mean 60.4 (SD 7.4) Race: Black: 100% Systolic BP: 135.4 Diastolic BP: 82.3 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Intervention foods were designed to provide 41% less sodium, 826 % more potassium, 388 % more calcium and 368 % more Magnesium Form of Administration: Dietary Modification: Patients provided food with lower salt, higher potassium content Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Patients were given food without the sodium composition unchanged Form of Administration: Other: Given food with regular sodium content Dose: NR Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 4 weeks apart Sodium, Method of Validation: Completeness of 24 h urine collection was assessed as with sex specific urinary creatinine values., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 154.3 mmol/24h Best potassium measure recorded: 3 times, 4 weeks apart Potassium, Method of Validation: Completeness of 24 h urine collection was assessed as with sex specific urinary creatinine values. Potassium Status Intervention 1: 71.7 mmol/24h</p> <p>How was blood pressure measured? Resting office BP measured following American Heart Association Recommendations using a validated automated method with pre-set inflation (Omron M4-I BP monitor). BP was measured three times on each occasion and the mean of the second and third measurements was used for analyses.</p>	<p>Subgroup: Mild to moderate hypertension 24h Ambulatory DBP Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -2.49 (95% CI: -5.16 - 0.17) 24h Ambulatory SBP Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -4.53 (95% CI: -9.05 - -0.01) Stroke Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.34 (95% CI: 0.01 - 8.14)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean BMI: 35.3 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–75 years, with medication-treated mild-to-moderate hypertension Exclusion: On two or more diuretics; on furosemide for cardiac failure; cerebral infarction or haemorrhage; renal impairment, consuming three or more alcoholic drinks a day; type 1 diabetes mellitus; impaired cognitive function; incontinence; and BMI >45kg/m2, severely uncontrolled hypertension.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>		
<p>Dubbert, 1995⁵³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 122</p> <p>Participants: % Male: NR Mean Age/Range/Age at Baseline: mean 62 (SD 8.8) Race: black: 54% Systolic BP: 142.3 Diastolic BP: 85.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: VA enrollees; diagnosis of essential hypertension, a stable DBP such that patients were not expected to need a change in medications for 3 months and urine Na excretion 1> 100 millimoles (mmol)/24 hours Exclusion: Patients requiring immediate dietary intervention for diabetes or other conditions. Patients judged by their primary care provider to be unlikely to benefit from the dietary intervention because of current alcohol abuse, psychosis, or organic brain disease</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Goal is to achieve a 87 mmol/day reduced sodium diet Form of Administration: Dietary Modification: A single session of individualized instruction for 87 mmol/day reduced sodium diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: Goal is to achieve a 87 mmol/day reduced sodium diet Form of Administration: Dietary Modification: A single session of individualized instruction for a 87 mmol/day reduced sodium diet + a means of estimating urine electrolyte excretion at home Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times 3 months apart Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Change of -55 mmol/24h: blacks, change of -25 mmol/24h whites [estimated - raw data not available] Sodium Status Intervention 2: Change of -40 mmol/24h: blacks, change of -85 mmol/24h whites [estimated - raw data not available] Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 times 3 months apart</p> <p>How was blood pressure measured? Sitting BP was measured</p>	<p>Subgroup: Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -0.30 (95% CI: NC - NC) Comparison: Intervention 2 vs Comparator MD -0.70 (95% CI: NC - NC) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -0.40 (95% CI: NC - NC) Comparison: Intervention 2 vs Comparator MD -2.40 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Duration: NR Exposure to Follow Up Time: NR		
<p>Franzoni, 2005⁵⁴</p> <p>Location: Italy</p> <p>Setting:</p> <p>Design:</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 104</p> <p>Intervention 1: % Male: 59.6% Mean Age/Range/Age at Baseline: mean 51 (SD 11) Race: NR Systolic BP: 154.4 Diastolic BP: 95 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.3 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 65.3% Mean Age/Range/Age at Baseline: mean 53 (SD 12) Race: NR Systolic BP: 153.8 Diastolic BP: 96.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: established or newly diagnosed mild - moderate essential hypertension, Exclusion: Patients with SBP > 200 mmHg and suspected or defined secondary hypertension, coronary artery disease, valvular or primary myocardial heart disease, diabetes, dyslipidemia and arrhythmias</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 30 mmol/day per os of potassium aspartate supplementation Na/K ratio: 2.4 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Instructed to maintain a constant dietary sodium and potassium intake of throughout the study Form of Administration: Usual diet Dose: NR Na/K ratio: 3.2 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium Status Intervention 1: 196.2 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 1 month apart Potassium Status Intervention 1: 81.6 mmol/24 h</p> <p>How was blood pressure measured? Office BP and 24-h ambulatory BP were measured at baseline and after the 4 week intervention. Office BP was taken twice in the sitting position by a physician with a mercury sphygmomanometer. A 24-h ambulatory BP monitoring was performed using a SpaceLabs 90207 monitor. Measurements in the non-dominant arm were taken at 30-min intervals during the 24-h period and hourly means were calculated. Day time BP was defined as the mean value from 9:00 AM to 11:00 PM and the night time BP as the mean value from 11:30 PM to 6:00 AM.</p>	<p>Subgroup: Mild to moderate HTN Diastolic BP-24H AMB Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -6.60 (95% CI: -8.16 - -5.04) Systolic BP-24H AMB Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -8.38 - -3.02)</p>
<p>Geleijnse, 1994⁵⁵</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p>	<p>Study of: Adults N: 100</p> <p>Intervention 1: % Male: 53 Mean Age/Range/Age at Baseline: mean 65.7 (SD 4.6) Race: NR Systolic BP: 158 Diastolic BP: 89.8 Magnesium: 5.4 mmol/24h Calcium: NR Other Minerals: NR Mean BMI: 27.1</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: NR Form of Administration: Dietary Modification: Salt substitute for cooking + food made with salt substitute Dose: mineral salt (sodium: potassium: magnesium 8:6:1) to be used for cooking, and food prepared with mineral salt (d bread, cheese, luncheon meats, canned and instant soups, and smoked sausage)</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 4 times 8 weeks apart Sodium Status Intervention 1: 116 mmol/24 h Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 4 times 8 weeks apart Potassium Status Intervention 1: 97</p>	<p>Subgroup: Mild-moderate HTN Diastolic BP-sitting Follow-Up Time: 24 weeks Comparison: Intervention 1 vs Comparator MD -4.10 (95% CI: -4.57 - -3.63) Follow-Up Time: 49 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -4.50 - 2.50) Systolic BP-sitting Follow-Up Time: 24 weeks Comparison: Intervention 1 vs Comparator MD -5.10 (95% CI: -5.84 - -4.36) Follow-Up Time: 49 weeks</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites:</p> <p>Study Years: 1990-1992</p>	<p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 49% Mean Age/Range/Age at Baseline: 67.1 (4.5) Race: NR Systolic BP: 157.5 Diastolic BP: 90.8 Magnesium: 5.2 mmol/24h Calcium: NR Other Minerals: NR Mean BMI: 27.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 55-75 with SBP between 140 and 200 mm Hg or DBP between 85 and 110 mm Hg without antihypertensive treatment. Exclusion: History of MI, angina pectoris, diabetes mellitus, or impaired renal function (serum creatinine concentration > 200 μmol/l) or on a salt restricted diet based on medical advice.</p>	<p>Na/K ratio: 1.3 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Regular salt group Description: NR Form of Administration: Regular Salt Dose: regular salt (sodium: potassium: magnesium 8:6:1) to be used for cooking, and food prepared with regular salt (bread, cheese, luncheon meats, canned and instant soups, and smoked sausage) Na/K ratio: 2.1 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>mmol/24 h</p> <p>How was blood pressure measured? BP was taken on the right arm by two investigators using an automatic device (Dinamap model 8100) and a 51 cm by 15 cm cuff while the patient was seated. After at least five minutes' rest four measurements were taken, the mean of last three were measurements was used.</p>	<p>Comparison: Intervention 1 vs Comparator MD 0.80 (95% CI: -4.50 - 6.00)</p>
<p>Gu, 2001⁵⁶</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Potassium and Protein Supplementation Study (PAPSS)</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 150</p> <p>Intervention 1: % Male: 37.3 Mean Age/Range/Age at Baseline: 56.9 (SD 7.4) Race: NR Systolic BP: 136.9 Diastolic BP: 81.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 66.9 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 42.7 Mean Age/Range/Age at Baseline: 55 (SD 7.6) Race: NR Systolic BP: 134 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.3</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 3 0.5 g potassium chloride pills taken 3 times a day. Or 60 mmol potassium per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Other: Placebo Dose: 3 placebo pills taken 3 times a day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium Status Intervention 1: 185.7 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 at screening, Once at 6 weeks, then at 12 weeks Potassium, Method of Validation: Pill count Potassium Status Intervention 1: 54.2 mmol/24 h</p> <p>How was blood pressure measured? Trained staff using Hawksley random zero sphygmomanometers. Taken on the right arm with appropriately sized cuffs after quietly sitting for 5 min. BP recorded three times at each screening, then at follow up visits at 6 and 12 weeks.</p>	<p>Subgroup: High normal Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -0.10 (95% CI: -2.14 - 1.94) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.70 (95% CI: -7.01 - -0.39)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 45-64. SBP 13-159 mmHg, DBP<95 mmHg OR SBP<160 mmHg AND DBP < 160 mmHg. Able to take potassium supplements in accordance with protocol Exclusion: blood pressure medication in the last 2 months, history of CVD, diabetes at any time, non-skin malignancy in the last 5 years, COPD, psychiatric disease, other life threatening illnesses. serum creatinine >=1.7 mg/dl or K+=5.0 mmol/l at screening, alcohol use of >=21 drinks/week or >=40 g/day. Pregnancy, plans to move out of study area, or non-cooperation.</p>			
<p>He, 2010⁵⁷</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites:</p> <p>Crossover:</p> <p>Length of washout period: NR days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 42</p> <p>Participants: % Male: NR Mean Age/Range/Age at Baseline: 51+/-10 Race: NR Systolic BP: 145+/-11 Diastolic BP: 91+/-7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7+/-4.8 % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Inclusion: ages 18 to 75 years, with sitting systolic BP of 140 to 170 mm Hg or diastolic BP of 90 to 105 mm Hg, with no previous treatment for raised BP Exclusion: impaired renal function with plasma creatinine 150_x0001_mol/L, any secondary cause of hypertension, chronic diarrhea, history of ulcer disease, baseline plasma potassium 5.0 mmol/L, previous stroke, ischemic heart disease, heart failure, diabetes mellitus, malignancy, liver disease, pregnancy, breastfeeding, use of oral contraceptives</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Potassium chloride 10 pills/d to achieve 64mmol/d Form of Administration: Oral potassium supplement Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Use of potassium supplement to increase potassium levels Description: Potassium bicarbonate 10 pills/d to achieve 64 mmol Form of Administration: Oral potassium supplement Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Placebo potassium pills, 10/d with usual diet Form of Administration: Placebo Dose: 122 mmol/d +/-38 mmol Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 weeks Exposure to Follow Up Time: 0 months</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: two consecutive days Sodium, Method of Validation: creatinine, Composition of potassium supplement with intervention/exposure adherence measure Sodium Status Intervention 1: 134 mmol/d (+/-49) Sodium Status Intervention 2: 129 mmol +/-45 mmol Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: 2 consecutive days Potassium Status Intervention 1: 122 mmol +/-25 Potassium Status Intervention 2: 125 mmol +/-27 mmol</p> <p>How was blood pressure measured? validated automatic digital BP monitor (Omron HEM-705CP) in sitting position after 5 to 10 minute rest and in the same arm throughout the study; three readings at 1- to 2-minute intervals; the mean of last 2 readings was used. Twenty-four-hour ambulatory blood pressure monitoring was performed using SpaceLabs 90207 devices</p>	<p>Subgroup: Hypertensives 24 hr diastolic BP Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 1.00 (95% CI: -1.72 - 4.22) Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -3.58 - 2.06) 24 hr systolic BP Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD 0.00 (95% CI: -3.19 - 3.77) Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.89 - 0.41) Left ventricular mass (g) Follow-Up Time: 4 weeks Comparison: Intervention 2 vs Comparator MD -9.00 (95% CI: -23.20 - 7.80) Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -22.58 - 9.25)</p>
<p>Howe, 1994⁵⁸</p> <p>Location:</p>	<p>Study of: Adults N: 28</p>	<p>Intervention Type(s): Intervention 1: Other: low sodium with fish oil</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 2 times 1.5</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 6 weeks</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Australia</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Intervention 1:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 146</p> <p>Diastolic BP: 83</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator 1: NR</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 143</p> <p>Diastolic BP: 80</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Intervention 2:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 145</p> <p>Diastolic BP: 81</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator 2: NR</p> <p>% Male: 55.3</p> <p>Mean Age/Range/Age at Baseline: mean 55 (SD 1)</p> <p>Race: NR</p> <p>Systolic BP: 145</p> <p>Diastolic BP: 81</p> <p>Magnesium: NR</p> <p>Calcium: NR</p>	<p>Description: Sodium intake of 70 mmol/day</p> <p>Form of Administration: Other: placebo</p> <p>Dose: eight placebo tablets per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator 1: Other: normal sodium with fish oil</p> <p>Description: Sodium intake of 150 mmol/day</p> <p>Form of Administration: Sodium supplement</p> <p>Dose: eight slow sodium tablets per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Intervention 2: Other: low sodium with olive oil</p> <p>Description: Sodium intake of 70 mmol/day</p> <p>Form of Administration: Other: placebo</p> <p>Dose: eight placebo tablets per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator 2: Other: normal sodium with olive oil</p> <p>Description: Sodium intake of 150 mmol/day</p> <p>Form of Administration: Sodium supplement</p> <p>Dose: eight slow sodium tablets per day</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1.5 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>months apart</p> <p>Sodium, Method of Validation: Pill counts, feedback on excretion levels, checking creatinine values., Single 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 78 mmol/24h</p> <p>Sodium Status Comparator 1: 150 mmol/24h</p> <p>Sodium Status Intervention 2: 75 mmol/24h</p> <p>Sodium Status Comparator 2: 150 mmol/24h</p> <p>Best potassium measure recorded: 2 times</p> <p>1.5 months apart</p> <p>Potassium, Method of Validation: Pill counts, feedback on excretion levels, checking creatinine values.</p> <p>How was blood pressure measured? BP was measured with a Dinamap portable automated sphygmomanometer with a cuff of appropriate size on the right arm. BP values used for analysis were obtained by averaging repeated readings taken at one minute intervals after throwing out an initial reading.</p>	<p>Comparison: Intervention 2 vs Comparator 2</p> <p>MD -2.10 (95% CI: -5.70 - 1.50)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 2 vs Comparator 2</p> <p>MD -5.00 (95% CI: -10.96 - 0.96)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Other Minerals: NR Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients with uncomplicated essential hypertension being treated by ACE inhibitor monotherapy Exclusion: History of unstable heart, liver or renal disease or a DBP greater than 105 mmHg. Consuming more than 20 cigarettes or 40 g alcohol per day, exercised erratically, were institutionalized; had no control over the preparation of their food.</p>			
<p>Hwang, 2014⁵⁹</p> <p>Location: Korea</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 7</p> <p>Study Years: 2012-2013</p>	<p>Study of: Adults N: 256</p> <p>Participants: % Male: 49.8 Mean Age/Range/Age at Baseline: Mean 49.5 (SD 13.3) Race: NR Systolic BP: 130.9 Diastolic BP: 79.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 67.8 kgs % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Aged 19–75, the use of antihypertensive meds or a diagnosis of hypertension. Modification of Diet in Renal Disease study eGFR\geq30 ml/min per 1.73 m², random urine albumin-to-creatinine ratio \geq30 mg/g creatinine more than two times with a \geq1-week interval in the last 6 months. Exclusion: Patients with uncontrolled hypertension (BP.160/110 mmHg), pregnant women, and patients with serum potassium $>$5.5 mEq/L. Malignancy, a diagnosis of CVD (cerebral infarction, hemorrhagic infarction, acute MI or unstable angina, coronary angioplasty, or coronary artery bypass surgery) in the last 6 months, contraindication for angiotensin II receptor blockers (ARBs), and diabetes mellitus, continuous users of steroids or other immunosuppressive agents.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Intensive education Description: Intensive education group. The target amount of daily sodium intake was $>$100 mEq/d, A \geq25% reduction of salt intake was also recommended Form of Administration: Other: Intensive education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Conventional Education Description: Conventional education, a A \geq25% reduction of salt intake was recommended. Form of Administration: Other: Conventional education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 0, 2 and 4 months Sodium, Method of Validation: The adequacy of 24H urine samples with correction was evaluated by calculating the predicted daily creatinine excretion Sodium Status Intervention 1: 122.2 mEq/d</p> <p>How was blood pressure measured? No description</p>	<p>Subgroup: Hypertensive on antihypertensive, All Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.20 (95% CI: -3.69 - 1.29) Hypotension Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -5.00 - 2.20)</p> <p>Subgroup: Hypertensive on antihypertensive, Na reduction $>$25% Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -6.12 - 2.52) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -7.65 - 4.05)</p> <p>Subgroup: Hypertensive on antihypertensive, Na reduction $<$25% Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -0.90 (95% CI: -4.24 - 2.44) Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -5.63 - 3.63)</p>
<p>Jula, 1992⁶⁰</p> <p>Location: NR</p> <p>Setting:</p>	<p>Study of: Adults N: 36</p> <p>Intervention 1: % Male: 42.1</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 3 months apart Sodium, Method of Validation: Single 24-</p>	<p>Subgroup: Mild-mod hypertension Diastolic BP-sitting Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.16 - -0.24)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Mean Age/Range/Age at Baseline: mean 44.7 (SD 5.6)</p> <p>Race: NR</p> <p>Systolic BP: 151.9</p> <p>Diastolic BP: 98.4</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 26.1</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 47</p> <p>Mean Age/Range/Age at Baseline: mean 42.5 (SD 3.8)</p> <p>Race: NR</p> <p>Systolic BP: 143.9</p> <p>Diastolic BP: 96.1</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 25.7</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Mild to moderate essential hypertension</p> <p>Exclusion: cardiomyopathy or significant valvular disease, oral contraceptives or any other regular drug treatment. Being treated for hypertension earlier (within the last year).</p>	<p>sodium intake</p> <p>Description: To reduce daily sodium intake to less than 70 mmol</p> <p>Form of Administration: Dietary</p> <p>Modification: non-pharmacological treatment programme</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: Participants asked not to change their usual diet</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 6 months</p> <p>Exposure to Follow Up Time: NR</p>	<p>hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 79 mmol/24/h</p> <p>Potassium measure: Food diaries without reported validation</p> <p>Best potassium measure recorded: 3 times, 3 months apart</p> <p>Potassium Status Intervention 1: 88 mmol/24/h</p> <p>How was blood pressure measured? Blood pressure was measured using a mercury sphygmomanometer by a single trained nurse. Subjects were in the supine position, and the average of two measurements taken at approximately 2-min intervals was used to calculate peripheral resistance and end-systolic wall stress. Out-patient clinic BP measurements were done by a single trained technician using a Hawksley random zero sphygmomanometer. Subjects were in the sitting position, always in the morning and in the same quiet room throughout the study. The mean value of two measurements taken with a 2-min interval was calculated.</p>	<p>Left ventricular hypertrophy-LVMI(g/m²)</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator MD -13.63 (95% CI: -31.43 - 4.18)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 6 months</p> <p>Comparison: Intervention 1 vs Comparator MD -3.30 (95% CI: -10.55 - 3.95)</p>
<p>Kitaoka, 2013⁶¹</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design:</p> <p>Number of Sites: 1</p> <p>Study Years: 2003-2011</p>	<p>Study of: Adults</p> <p>N: 71</p> <p>Intervention 1:</p> <p>% Male: 100</p> <p>Mean Age/Range/Age at Baseline: mean 66.2 (5.4)</p> <p>Race: NR</p> <p>Systolic BP: 150.6</p> <p>Diastolic BP: 92.8</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 23.6</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: 5.3</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 100</p> <p>Mean Age/Range/Age at Baseline: mean 64.1 (7.6)</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Lecture and a cooking instructions conducted by registered dietitians.</p> <p>Form of Administration: Dietary</p> <p>Modification: lecture and a cooking instructions conducted by registered dietitians.</p> <p>Dose: NR</p> <p>Na/K ratio: mean Na:K ratio = 1.9</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Usual Diet</p> <p>Description: Usual diet</p> <p>Form of Administration: Usual diet</p>	<p>Sodium measure: Food diaries with reported validation, Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: Two times, at baseline and after 5 months. Kawasaki's formula.</p> <p>Sodium Status Intervention 1: 10.6 g/day</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1, Food diaries without reported validation</p> <p>Best potassium measure recorded: Two times, at baseline and after 5 months. Kawasaki's formula</p> <p>Potassium Status Intervention 1: 3807 mg/day</p> <p>How was blood pressure measured? BP was measured by trained physicians using a mercury sphygmomanometer. Participants were asked to sit calmly for 5-10 minutes before being measured. These BP values</p>	<p>Subgroup: Hypertensive</p> <p>Diastolic BP-sitting</p> <p>Follow-Up Time: 5 months</p> <p>Comparison: Intervention 1 vs Comparator MD 2.00 (95% CI: -9.26 - 13.26)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 5 months</p> <p>Comparison: Intervention 1 vs Comparator MD -4.50 (95% CI: -24.66 - 15.66)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: NR Systolic BP: 146.9 Diastolic BP: 89.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.8 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 7.7 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Free-living men, aged 40–75 years, who lived in Kyoto city or neighboring towns. SBP 130 mm Hg and <180 mm Hg or DBP 85 mm Hg and <110 mm Hg.</p>	<p>Dose: NR Na/K ratio: mean Na:K ratio = 2.9 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 5 months Exposure to Follow Up Time: NR</p>	<p>were taken twice and the mean value was calculated for each subject.</p>	
<p>Kojuri, 2007⁶² Location: NR Setting: Community Design: Number of Sites: 1 Study Years: unclear</p>	<p>Study of: Adults N: 80</p> <p>Intervention 1: % Male: 50 Mean Age/Range/Age at Baseline: mean 48.7 (SD 11.1) Race: NR Systolic BP: 147.1 Diastolic BP: 136.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 69.47 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: mean 46.05 (SD 13.173) Race: NR Systolic BP: 141.2 Diastolic BP: 133.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 70.85 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: mild to moderate hypertension and not taking any antihypertensive drugs</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: DASH Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1.5 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 6 weeks apart Sodium Status Intervention 1: 110 meq/dl</p> <p>How was blood pressure measured? 24 hour holter monitoring of blood pressure was measured with a Davinsa device from 8 AM to 8 AM next day.</p>	<p>Subgroup: Mild to moderate hypertension 24h Ambulatory DBP-daytime Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -9.20 (95% CI: -11.55 - -6.85) 24h Ambulatory DBP-night time Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -9.03 - -4.97) 24h Ambulatory SBP-daytime Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -17.00 (95% CI: -20.71 - -13.29) 24h Ambulatory SBP-night time Follow-Up Time: 6 weeks Comparison: Intervention 1 vs Comparator MD -12.43 (95% CI: -15.44 - -9.42)</p>
<p>Langford, 1991⁶³</p>	<p>Study of: Adults N: 169</p>	<p>Intervention Type(s):</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, 3-day food records</p>	<p>Subgroup: Mild HTN Diastolic BP</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: The Trial of Antihypertensive Interventions and Management (TAIM)</p> <p>Number of Sites: 3</p> <p>Study Years: 1985-1987</p>	<p>Intervention 1: % Male: 62.1 Mean Age/Range/Age at Baseline: mean 48.2 Race: white: 66.7 Systolic BP: 141.9 Diastolic BP: 93.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 89.6 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 64.4 Mean Age/Range/Age at Baseline: mean 47.7 Race: white: 69% Systolic BP: 142.8 Diastolic BP: 93.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 88.6 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 55.7 Mean Age/Range/Age at Baseline: mean 50.5 Race: white: 70.9% Systolic BP: 144.9 Diastolic BP: 94.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 87.4 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 4: % Male: 55.1 Mean Age/Range/Age at Baseline: mean 48.9 Race: white: 66.3% Systolic BP: 143.1 Diastolic BP: 93.7 Magnesium: NR</p>	<p>Intervention 1: Other: Usual Diet - Chlorthalidone Description: Participants asked not to change their usual diet Form of Administration: Other: usual diet Dose: chlorthalidone 25 mg Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Usual Diet - Atenolol Description: Participants asked not to change their usual diet Form of Administration: Other: usual diet Dose: atenolol 50 mg Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Low Na/high K - Placebo Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: placebo + Low Na/high K diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Other: Low Na/high K - Chlorthalidone Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: Chlorthalidone 25 mg + Low Na/high K diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 5: Other: Low Na/high K - Atenolol Description: Average sodium target of 87 mmol/day, potassium 103 mmol/day Form of Administration: Dietary Modification: NR Dose: Atenolol 50 mg + Low Na/high K diet Na/K ratio: NR</p>	<p>Best sodium measure recorded: two times 6 months apart Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Intervention 1: 144.05 mmol/day Sodium Status Intervention 2: 132.44 mmol/day Sodium Status Intervention 3: 95.06 mmol/day Sodium Status Intervention 4: 111.18 mmol/day Sodium Status Intervention 5: 117.41 mmol/day Potassium measure: Food diaries without reported validation Best potassium measure recorded: two times 6 months apart Potassium Status Intervention 1: 67.48 mmol/day Potassium Status Intervention 2: 54.25 mmol/day Potassium Status Intervention 3: 67.83 mmol/day Potassium Status Intervention 4: 72.08 mmol/day Potassium Status Intervention 5: 67.87 mmol/day</p> <p>How was blood pressure measured? BP was taken following American Heart Association guidelines by trained staff with a random zero mercury sphygmomanometer. Blood pressures were measured after the participant had been seated quietly for at least 5 minutes. The mean of two readings of the fifth phase diastolic blood pressure was used in all analyses.</p>	<p>Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD 0.05 (95% CI: -2.81 - 2.91) Systolic BP Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD 1.68 (95% CI: -3.14 - 6.50) Percent with DBP <90 mmHg Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator RR 0.90 (95% CI: 0.73 - 1.11)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Calcium: NR Other Minerals: NR Mean BMI: 86.1 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 5: % Male: 65.6 Mean Age/Range/Age at Baseline: mean 51 Race: white: 64.4 Systolic BP: 146.3 Diastolic BP: 94 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 90.2 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 40 Mean Age/Range/Age at Baseline: mean 47.4 Race: white: 67.8% Systolic BP: 144.5 Diastolic BP: 93.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 85.6 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: At preliminary screening, a DBP <= 100 mm Hg or less for participants currently taking antihypertensive medication or a DBP 90-104 mm Hg for those on no treatment. Patients had to be between 110% and 160% of their ideal weight by recall. Exclusion: History or evidence of MI, stroke or bronchial asthma, a creatinine level >= 180 /umol/l, diabetes requiring insulin therapy, allergy to thiazides or Beta-blockers, actual or contemplated pregnancy, or likelihood of difficulty in complying with the interventions</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Usual Diet - Placebo Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		
<p>Meland, 2009⁶⁴ Location: NR Setting: Community</p>	<p>Study of: Adults N: 46 Intervention 1: % Male: 74 Mean Age/Range/Age at Baseline: mean 55 Race: NR</p>	<p>Intervention Type(s): Intervention 1: Use of salt pills to increase sodium intake Description: Dietary advice outlining a moderate salt reduced diet + salt tablets. Goal was a regular sodium intake diet</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: At baseline (inclusion) and the final visit Sodium, Method of Validation: Capsule counts, Single 24-hour urine analysis with validation</p>	<p>Subgroup: HTN on antihypertensives Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -7.00 - -1.00) Systolic BP-sitting Follow-Up Time: 8 weeks</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1999-2002</p>	<p>Systolic BP: 155 Diastolic BP: 92 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 74 Mean Age/Range/Age at Baseline: mean 57 Race: NR Systolic BP: 157 Diastolic BP: 93 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Taking antihypertensive medications, aged 20-_{x0001}75 years with DBP>90 mmHg and/or SBP>160 mmHg two occasions during a run-in period. Exclusion: Possible drug-induced hypertension, receiving drugs for cardiovascular disease with hypotensive effects, DBP increase to a level of _{x0001}115 mmHg or SBP 210 mmHg before or during the study.</p>	<p>Form of Administration: Sodium supplement Dose: five capsules of 10 mmol sodium per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Dietary advice outlining a moderate salt reduced diet + placebo. The goal of this arm was a sodium restricted diet Form of Administration: Placebo Dose: five capsules SiO₂ per day (placebo) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NA</p>	<p>Sodium Status Intervention 1: Change of -28 mmol/24h (raw numbers not reported) Best potassium measure recorded: At baseline (inclusion) and the final visit Potassium, Method of Validation: Capsule counts Potassium Status Intervention 1: Change of +3 mmol/24h (raw numbers not reported)</p> <p>How was blood pressure measured? BP was measured with a mercury manometer on the right arm in a sitting position after resting for at least two minutes. Three recordings were taken at two-minute intervals, and the average of the last two readings was used for analyses. Appropriate sized cuffs were used and the same cuff was used on each visit. BP readings were done before run-in, at inclusion, and after four and eight weeks.</p>	<p>Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -11.00 - 0.00)</p>
<p>Morgan, 1987⁶⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 20</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 143 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: Mean 60.5</p>	<p>Intervention Type(s): Intervention 1: Other: 'Reduced Sodium diet' Description: NR Form of Administration: Dietary Modification: no further information given Dose: between 50 and 75 mmol/d consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: NR Dose: between 50 and 75 mmol/d consumed Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Week 0,1,4,13,26 Sodium Status Intervention 1: 75 mmol/day</p> <p>How was blood pressure measured? supine systolic and diastolic blood pressure (mdg) measured at start, 'before drug stopped, week 1 and month 6.</p>	<p>Subgroup: Hypertensive (DBP>100) Diastolic-supine Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -8.00 (95% CI: -15.07 - -0.93) Systolic-supine Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -23.00 (95% CI: -39.86 - -6.14)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: NR Systolic BP: 143 Diastolic BP: 81 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: No clinical evidence of peripheral vascular or cardiac disease, no evidence of left ventricular hypertrophy on electrocardiogram. No detected cause for their hypertension. Well controlled blood pressure</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		
<p>Morikawa, 2011⁶⁶</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 41</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 48.3 (SD 8.7) Race: NR Systolic BP: 149.8 Diastolic BP: 96.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: mean 47.1 (SD 8.5) Race: NR Systolic BP: 149.4 Diastolic BP: 96.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Employees of a railroad company. Waist circumference < 85 cm. SBP higher than 130 mmHg and/or DBP higher than 85 mmHg. Not currently in treatment for hypertension.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Self-monitoring of daily salt excretion by an electronic salt sensor and personalized advice via sent via cellular phone Description: Group counseling on lifestyle modification from public health nurses and registered dietitians + Intervention Self-monitoring of daily salt excretion by an electronic salt sensor and personalized advice via sent via cellular phone. Aim was to reduce salt intake Form of Administration: Other: Email/Text message alerts Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Group counseling on lifestyle modification from public health nurses and registered dietitians Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation, Food questionnaire without reported validation Best sodium measure recorded: Estimated $NaCl_{24} = 5.76 (NaCl_{In} - V_n)^{0.53}$ Taken 2 times, in week 1 and week 4 Sodium Status Intervention 1: Daily salt excretion 10.7 (g) Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? BP was measured two times with a fully automated sphygmomanometer HEM-762; the average of the values was used for the evaluation. BP taken at baseline and after 4 weeks</p>	<p>Subgroup: Hypertensive Diastolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.60 (95% CI: -8.21 - -0.99) Systolic BP-NS Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -8.15 - 1.75)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Nakano, 2016⁶⁷; UMIN-CTR Clinical Trial⁶⁸</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2012-2014</p>	<p>Study of: Adults N: 101</p> <p>Intervention 1: % Male: 31 Mean Age/Range/Age at Baseline: mean 57.5 (SD 13.7) Race: NR Systolic BP: 132 Diastolic BP: 82 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 6 % with Kidney disease: 20 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 45.5% Mean Age/Range/Age at Baseline: mean 60.1 (SD 13.1) Race: NR Systolic BP: 135 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 7 % with Kidney disease: 20 % with history of Kidney stones: NR</p> <p>Inclusion: >20 years old, Stable hypertensive outpatients who are performing antihypertensive and non-antihypertensive treatment. Exclusion: Hemodialysis, Dementia from whom we cannot obtain informed consent, attending doctor consider that the patient is not appropriate for the study.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: The goal was to restrict salt to no more than 6 g of salt per day Form of Administration: Dietary Modification: Nutritionists performed intensive nutritional education Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: No indication participants asked to change diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Food diaries with reported validation, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, baseline and 3 months Sodium, Method of Validation: Food diaries with reported validation Sodium Status Intervention 1: 6.8 g/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, baseline and 3 months Potassium Status Intervention 1: 1.6 g/24 h</p> <p>How was blood pressure measured? Self-measured home BP was taken in the morning and evenings using a validated upper arm cuff oscillometric device (HEM-5001; Omron, Kyoto, Japan). Ambulatory BP monitoring (ABPM) was performed every 30 minutes using a validated monitor with an upper arm cuff. BP measurements taken at baseline and after 3 months</p>	<p>Subgroup: Hypertensive under pharma or non-pharma treatment Diastolic BP-24H AMB Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -3.23 - 3.23) Systolic BP-24H AMB Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -5.44 - 3.44)</p>
<p>Nowson, 1988⁶⁹; Australian National Health and Medical Research Council Management Committee, 1987⁷⁰; Chalmers, 1986⁷¹</p> <p>Location: Australia</p>	<p>Study of: Adults N: 212</p> <p>Intervention 1: % Male: 81 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: High Potassium Description: Increase potassium intake above 100 mmol/day Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low Sodium Description: Reduce sodium intake to 50-70 mmol/day</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: Every 2 weeks over the 3 month intervention period Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Intervention 1: 145 mmol/day Sodium Status Intervention 2: 86 mmol/day Sodium Status Intervention 3: 73 mmol/day Best potassium measure recorded: Every 2 weeks over the 3 month intervention period Potassium Status Intervention 1: 96 mmol/day Potassium Status Intervention 2:</p>	<p>Subgroup: Mild HTN (DBP 90-100) Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.30 (95% CI: -4.71 - -1.89) Comparison: Intervention 2 vs Comparator MD -4.30 (95% CI: -5.41 - -3.19) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.60 (95% CI: -6.37 - -0.83) Comparison: Intervention 2 vs Comparator MD -4.90 (95% CI: -7.67 - -2.13)</p> <p>Subgroup: 90<DBP<100</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: Australian National Health and Medical Research Council dietary salt study in mild hypertension</p> <p>Number of Sites: 3</p> <p>Study Years: 1984-1986</p>	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 83 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 89 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 89 Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Untreated hypertension, mean 90<=DBP<=100 mmHg Exclusion: Receiving treatment for CVD, hypertension, ischemic disease or any major hypertension complications or of ischemic disease. Grade III or IV hypertensive retinopathy, diabetes, glycosuria, clinical evidence of</p>	<p>Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Low Sodium, High Potassium Description: Reduce sodium intake to 50-70 mmol/day, increase potassium intake above 100 mmol/day Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: 70 mmol/day Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>70 mmol/day Potassium Status Intervention 3: 87 mmol/day</p> <p>How was blood pressure measured? BP was measured using a Dinamap machine subsequent to subjects being seated for 5 minutes. Three measurements were taken; the first was discarded and the average of last two measures was used.</p>	<p>Diastolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.10 (95% CI: -4.91 - -1.29) Comparison: Intervention 2 vs Comparator MD -4.20 (95% CI: -5.86 - -2.54) Comparison: Intervention 3 vs Intervention 2 MD 1.60 (95% CI: -0.21 - 3.41) Systolic BP-sitting Follow-Up Time: 12 weeks Comparison: Intervention 1 vs Comparator MD -3.90 (95% CI: -6.81 - -0.99) Comparison: Intervention 2 vs Comparator MD -5.10 (95% CI: -7.87 - -2.33) Comparison: Intervention 3 vs Intervention 2 MD 1.00 (95% CI: -1.64 - 3.64)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	cardiomegaly or heart failure. Women who were pregnant or on contraceptives. Plasma creatinine>0.12 mmol/L, plasma potassium<3.5 mmol/L or >5.8 mmol/L. Patients receiving prednisone, indomethacin, antihypertensive drugs, or psychotropics.			
<p>Pinjuh Markota, 2015⁷²</p> <p>Location: Bosnia & Herzegovina</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2012-2013</p>	<p>Study of: NR N: 150</p> <p>Intervention 1: % Male: 47.3 Mean Age/Range/Age at Baseline: mean 59.4 (SD 13) Race: NR Systolic BP: 142.8 Diastolic BP: 84.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 50 Mean Age/Range/Age at Baseline: mean 59.3 (SD 12) Race: NR Systolic BP: 143.7 Diastolic BP: 84.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: All consecutive adults who were treated hypertensives</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Individual information leaflets about the negative effects of excessive salt consumption + warning stickers that were mounted on all salt containers Description: NR Form of Administration: Other: Individual information leaflets about the negative effects of excessive salt consumption + warning stickers that were mounted on all salt containers Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Individual information leaflets about the negative effects of excessive salt consumption Description: NR Form of Administration: Other: Individual information leaflets about the negative effects of excessive salt consumption Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times 1 month apart Sodium Status Intervention 1: 176.4 mmol/24h</p> <p>How was blood pressure measured? BP (standard mercury sphygmomanometry) following standard methods. BP taken 3 times 1 month apart</p>	<p>Subgroup: Treated hypertensive Diastolic BP-NS Follow-Up Time: 2 months Comparison: Intervention 1 vs Comparator MD -1.40 (95% CI: -4.19 - 1.39) Systolic BP-NS Follow-Up Time: 2 months Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -11.26 - -0.14)</p>
<p>Rahimi, 2007⁷³</p> <p>Location: Iran</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p>	<p>Study of: Adults N: 103</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: mean 50.13 (SD 16.54) Race: NR Systolic BP: 133.9 Diastolic BP: 83.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Group C: High calcium diet Description: NR Form of Administration: Dietary Modification: NR Dose: diet with \geq 800mg calcium Na/K ratio: NR Magnesium: NR Calcium: 800mg calcium Other Minerals: NR</p> <p>Intervention 2: Other: Group P: High Potassium diet Description: NR</p>	<p>Sodium Status Intervention 1: difference of urine electrolytes before and after intervention: +581.3 Sodium Status Intervention 2: difference of urine electrolytes before and after intervention: -382.9 Sodium Status Intervention 3: difference of urine electrolytes before and after intervention: +519.25 Potassium measure: Single 24-hour urine analysis without validation, 2-day food record questionnaire Best potassium measure recorded: 1 time (post intervention)</p>	<p>Subgroup: Grade one hypertension and high normal Diastolic BP-NS Follow-Up Time: 1 month Comparison: Intervention 3 vs Comparator MD -4.20 (95% CI: -8.44 - 0.04) Comparison: Intervention 1 vs Comparator MD -4.40 (95% CI: -8.01 - -0.79) Comparison: Intervention 2 vs Comparator MD -5.60 (95% CI: -9.29 - -1.91) Systolic BP-NS Follow-Up Time: 1 month Comparison: Intervention 3 vs Comparator MD -11.00 (95% CI: -17.80 - -4.20) Comparison: Intervention 1 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: 2002-2003	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: NR Mean Age/Range/Age at Baseline: Mean 46.04 (SD 11.11) Race: NR Systolic BP: 131.6 Diastolic BP: 82.4 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: NR Mean Age/Range/Age at Baseline: Mean 47.78 (SD 14) Race: NR Systolic BP: 127.3 Diastolic BP: 83.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 50.71 (SD 15.49) Race: NR Systolic BP: 138 Diastolic BP: 88 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: grade I HTN (140-159/90-99mmHg) or high normal NP (130-139/85-89mmHg)</p>	<p>Form of Administration: Dietary Modification: NR Dose: Diet with \geq4000mg potassium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Group CP: High Potassium, high calcium diet Description: NR Form of Administration: Dietary Modification: NR Dose: Diet with \geq4000mg potassium + 800mg calcium Na/K ratio: NR Magnesium: NR Calcium: 800mg calcium Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Potassium Status Intervention 1: difference of urine electrolytes before and after intervention: +55.32 Potassium Status Intervention 2: difference of urine electrolytes before and after intervention: +935 Potassium Status Intervention 3: difference of urine electrolytes before and after intervention: +907.08</p> <p>How was blood pressure measured? BP measured twice</p>	<p>MD -4.10 (95% CI: -10.34 - 2.14) Comparison: Intervention 2 vs Comparator MD -6.40 (95% CI: -11.58 - -1.22)</p>
Redon-Mas, 1993 ⁷⁴	Study of: Both adults and children N: 418	Intervention Type(s):	Sodium measure: Single 24-hour urinary analysis without reported quality control	Subgroup: Mild-mod hypertension on verapamil

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: Spain</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 13</p> <p>Study Years: unclear</p>	<p>Intervention 1:</p> <p>% Male: 47</p> <p>Mean Age/Range/Age at Baseline: mean 54.5 (SD 11.1)</p> <p>Race: NR</p> <p>Systolic BP: 161.7</p> <p>Diastolic BP: 100.4</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 68.8</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: 47</p> <p>Mean Age/Range/Age at Baseline: mean 56.1 (SD 10.2)</p> <p>Race: NR</p> <p>Systolic BP: 165.2</p> <p>Diastolic BP: 100.6</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 68.5 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Ages 18-80, BMI<30, mild to moderate essential hypertension.</p> <p>Exclusion: Secondary or severe hypertension, MI or stroke in the last 3 months, unstable angina, heart failure, major arrhythmia or conduction disturbance. Significant renal or hepatic dysfunction, concurrent use of anti-hypertensive drugs or diuretic agents, pregnancy or intended pregnancy, known or suspected contraindication for verapamil, history of poor compliance, drug or alcohol abuse.</p>	<p>Intervention 1: Other: Low salt diet</p> <p>Description: Reduce sodium intake</p> <p>Form of Administration: Dietary</p> <p>Modification: reduced sodium</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Other: Regular salt diet</p> <p>Description: Unrestricted sodium intake</p> <p>Form of Administration: Usual diet</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1 month</p> <p>Exposure to Follow Up Time: NR</p>	<p>measure</p> <p>Best sodium measure recorded: 2 times, 4 weeks apart</p> <p>Sodium Status Intervention 1: 81.9 mmol/24h</p> <p>How was blood pressure measured? BP measured 3 times at 5 min intervals, after 2 min of sitting, using a conventional mercury sphygomomanometer. Phases I were used for SBP and V for DBP, of the Korotkoff sounds. Mean of 3 readings were used.</p>	<p>Diastolic BP-sitting</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator MD 1.80 (95% CI: 0.18 - 3.42)</p> <p>Systolic BP-sitting</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator MD 0.90 (95% CI: -1.86 - 3.66)</p>
<p>Richards, 1984⁷⁵</p> <p>Location: New Zealand</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p>	<p>Study of: Adults</p> <p>N: 12</p> <p>Participants:</p> <p>% Male: 66</p> <p>Mean Age/Range/Age at Baseline: 19-52 years</p> <p>Race: NR</p> <p>Systolic BP: 140-180</p> <p>Diastolic BP: 90-105</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: 0</p> <p>% with Type 2 diabetes: 0</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: To decrease sodium intake to 80 mM</p> <p>Form of Administration: Dietary</p> <p>Modification: instructions to consume low sodium foods</p> <p>Dose: 80 mmol sodium/d consumed</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p>	<p>Sodium, Method of Validation: Multiple 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 80 mmol/d</p> <p>Sodium Status Intervention 2: 200 mmol/d</p> <p>Best potassium measure recorded: Multiple 24-hour urine analysis with validation: Twice weekly for 4-6 weeks</p> <p>Potassium, Method of Validation: Creatinine concentration</p> <p>Potassium Status Intervention 1: 60 mmol/d</p> <p>Potassium Status Intervention 2: 180 mmol</p> <p>How was blood pressure measured? Arterial pressures measured twice with an automated version of the London School of</p>	<p>Subgroup: Hypertensives</p> <p>Diastolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 2 vs Comparator MD -1.00 (95% CI: -7.67 - 5.67)</p> <p>Comparison: Intervention 1 vs Comparator MD -1.80 (95% CI: -8.76 - 5.16)</p> <p>Systolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 2 vs Comparator MD -1.90 (95% CI: -10.04 - 6.24)</p> <p>Comparison: Intervention 1 vs Comparator MD -5.20 (95% CI: -13.24 - 2.84)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Crossover: Length of washout period: 4 days days Study Years: NR</p>	<p>% with Kidney disease: 0 % with history of Kidney stones: 0 Inclusion: untreated blood-pressure of between 140/90 and 180/105 mm Hg (taking phase V as the diastolic reading) after resting supine for 15 min, on 2 consecutive outpatient visits at least 10 days apart; otherwise well, withdrawn from antihypertensive drugs for 1 month or longer, and normal plasma urea, creatinine, sodium, potassium, calcium, and liver function tests Exclusion: NR</p>	<p>Intervention 2: NR Description: To increase potassium intake while maintaining usual diet Form of Administration: Oral potassium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Comparator: Usual Diet Description: To maintain usual sodium intake, 80mmol sodium diet was supplemented with sodium chloride capsules to achieve 180 mmol/d Form of Administration: Dietary Modification: Low sodium diet Sodium supplement Dose: 180mmol/d sodium consumed; 60 mmol/d potassium consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 3 periods of 4-6 weeks each Exposure to Follow Up Time: 0 months</p>	<p>Hygiene sphygmomanometer; supine, by one person</p>	
<p>Sacks, 2001¹⁰ Vollmer, 2001¹¹; Svetkey, 2004¹²; Harsha, 2004¹³; Akita, 2003¹⁴ Location: US Setting: Community Design: Randomized Cross-over individual Study Name: DASH-Sodium Number of Sites: multiple Crossover: Length of washout period: <5 days</p>	<p>Study of: Adults N: 79 Mean Age/Range/Age at Baseline: 49(10) Race: 56% black; 40% NH white; 5% Asian/other Systolic BP: 135(10) Diastolic BP: 86(4) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30(5) % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0 Mean Age/Range/Age at Baseline: 47+/-10 Race: 57% black; 40% NH white; 3% Asian/other Systolic BP: 134+/-10 Diastolic BP: 86+/-5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29+/-5 % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0</p>	<p>Intervention Type: Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control High Sodium: To replicate typical diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve high sodium intake Dose: 150 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Intervention 2: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Intermediate Sodium: To replicate typical diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve intermediate sodium intake Dose: 100 mmol sodium/d in control diet Na/K ratio: NR</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Sodium, Method of Validation: NR, Chemical analysis of diet with intervention/exposure adherence measure Sodium Status Intervention 1: 141+/-55 mmol/d Sodium Status Intervention 2: 106+/-44 mmol/d Sodium Status Comparator: 64+/-37mmol/d Sodium Status Intervention 3: 144+/-58 mmol/d Sodium Status Intervention 4: 107+/-52 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation;</p>	<p>Subgroup: Hypertensives Percent under control Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 RR 1.31 (95% CI: NC - NC) Comparison: Intervention 1 vs Comparator RR 2.31 (95% CI: NC - NC) Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -2.50 (95% CI: -3.60 - -1.40) Comparison: Intervention 1 vs Comparator MD -4.40 (95% CI: -5.50 - -3.30) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -4.90 (95% CI: -6.60 - -3.30) Comparison: Intervention 1 vs Comparator MD -8.30 (95% CI: -10.00 - -6.60)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Study Years: NR</p>	<p>% with Kidney disease: 0 % with history of Kidney stones: 0</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 22 years old or more, average systolic blood pressure 120 to 159 mm Hg (over 3 visits) and average diastolic blood pressure 80 to 95 mm Hg Exclusion: heart disease, renal insufficiency, poorly controlled hyperlipidemia or diabetes mellitus, diabetes requiring insulin, special dietary requirements, more than 14 alcoholic drinks per week, or use of antihypertensive drugs or other medications that would affect blood pressure or nutrient metabolism</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Low Sodium: To replicate typical diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: NR Description: DASH High Sodium: To impose DASH diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with high sodium intake Dose: 150 mmol sodium/d in DASH diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH intermediate Sodium: To impose DASH diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with intermediate sodium intake Dose: 100 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH Low Sodium: To achieve DASH diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu</p>	<p>Potassium, Method of Validation: Adherence checks via food diaries, supervised meals Potassium Status Intervention 1: 40+/-14 mmol/d Potassium Status Intervention 2: 41+/-14 mmol/d Potassium Status Comparator: 42+/-14 mmol/d Potassium Status Intervention 3: 75+/-27 mmol/d Potassium Status Intervention 4: 81+/-31 mmol/d</p> <p>How was blood pressure measured? Random-zero sphygmomanometers, seated, 3 times during screening, weekly during 1st 3 weeks of intervention periods, and 5 times during last 9 days of intervention periods</p>	

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		<p>designed to follow DASH with low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 periods of 30 days each, including run-in Exposure to Follow Up Time: 0 months</p>		
<p>Saptharishi, 2009⁷⁶</p> <p>Location: India</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 58</p> <p>Participants: % Male: 66.7</p> <p>Mean Age/Range/Age at Baseline: mean 22.5 (SD 1.3)</p> <p>Race: NR</p> <p>Systolic BP: 125.5 Diastolic BP: 84.6</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 32.4 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Hypertension or pre-hypertension Exclusion: Severe hypertension</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Walking Description: NR Form of Administration: Other: instructed to increase walking Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Salt Reduction Description: The goal was for subjects to reduce their daily salt intake to at least half of their previous intake. Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Yoga Description: NR Form of Administration: Other: instructed to do yoga Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: The 'questionnaire method' Best sodium measure recorded: No reference or explanation of 'questionnaire method'</p> <p>Sodium Status Intervention 1: NR Sodium Status Intervention 2: NR Sodium Status Intervention 3: NR</p> <p>How was blood pressure measured? Subjects blood pressure was measured using a mercury sphygmomanometer</p>	<p>Subgroup: Pre HTN and HTN Diastolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -2.50 (95% CI: -5.59 - 0.59)</p> <p>Systolic BP-NS Follow-Up Time: 8 weeks Comparison: Intervention 2 vs Comparator MD -2.90 (95% CI: -7.51 - 1.71)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Sarkkinen, 2011⁷⁷</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 50</p> <p>Participants: % Male: 61 Mean Age/Range/Age at Baseline: mean 54 (SD 11) Race: NR Systolic BP: 138 Diastolic BP: 88 Magnesium: 4.67 mmppl Calcium: NR Other Minerals: NR Mean BMI: 28 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Aged 25-75 years old, with SBP in the range of 130-159 mmHg and/or DBP in the range of 85-99 mmHg, BMI between 23 and 40 kg/m² and a stable body weight Exclusion: Receiving antihypertensive drugs, non-steroidal antiinflammatory agents, cyclosporine or tacrolimus. Secondary hypertension, diabetes (type 1 or 2), a history of active heart disease or cancer, abnormal electrolytes, proteinuria, abnormal liver, kidney or thyroid function. Currently on a low-salt diet (six or less points in the salt intake test by the Finnish Heart Association, Helsinki). Subjects with alcohol abuse or drug abuse, pregnancy.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: The aim was to replace approximately 60% of the regular sources of sodium with Smart Salt products. Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Daily sodium intake in the Regular Salt arm was designed to stay at the same level as typical for that individual. Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Food diaries without reported validation Best sodium measure recorded: 2 times, at baseline and at 2 months Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Intervention 1: 100 mmol Potassium measure: Food diaries without reported validation Best potassium measure recorded: 2 times, at baseline and at 2 months Potassium Status Intervention 1: 95 mmol</p> <p>How was blood pressure measured? BP measured using an automatic sphygmomanometer after 10 minutes rest in a sitting position. BP was measured three times with intervals of at least two minutes, between 7:00 am and 12:00 noon. The mean of the last records was used.</p>	<p>Subgroup: High normal Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -4.00 (95% CI: -8.09 - 0.09) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -6.00 (95% CI: -10.70 - -1.30) Decreased quality of life Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.40 (95% CI: 0.17 - 0.95)</p>
<p>Sciarrone, 1992⁷⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Number of Sites: multiple</p> <p>Study Years: 1987-1988</p>	<p>Study of: Adults N: 81</p> <p>Intervention 1: % Male: 50 Mean Age/Range/Age at Baseline: mean 51.4 Race: NR Systolic BP: 134.3 Diastolic BP: 83.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 68.4 Mean Age/Range/Age at Baseline: mean 53.4 Race: NR Systolic BP: 139 Diastolic BP: 83.5 Magnesium: NR</p>	<p>Intervention Type: Comparator: Other: Normal Sodium - Normal fat/normal fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium supplement Form of Administration: Sodium supplement Dose: 100 mmol NaCl/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium - Normal fat/normal fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium placebo Form of Administration: Dietary Modification: Other: Placebo pill Dose: Placebo (10 lactose tablets per day) Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Food diaries without reported validation Best sodium measure recorded: Measured 3 times in the screening phase and 5 times over the 8 week intervention Sodium, Method of Validation: Single 24-hour urine analysis with validation Sodium Status Comparator: 136.2 mmol/24h Sodium Status Intervention 2: 58.1 mmol/24h Sodium Status Intervention 3: 53.1 mmol/24h Potassium measure: Food diaries without reported validation Best potassium measure recorded: Measured 3 times in the screening phase and 5 times over the 8 week intervention Potassium Status Comparator: 65.8 mmol/24h Potassium Status Intervention 2: 75.4 mmol/24h Potassium Status Intervention 3: 97.1 mmol/24h</p> <p>How was blood pressure measured? BP measurements taken at the same time of day</p>	<p>Subgroup: HTN Diastolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 3 vs Intervention 1 MD -1.80 (95% CI: -5.40 - 1.80) Comparison: Intervention 2 vs Comparator MD 0.70 (95% CI: -3.17 - 4.57) Systolic BP-supine Follow-Up Time: 8 weeks Comparison: Intervention 3 vs Intervention 1 MD -8.00 (95% CI: -13.54 - -2.46) Comparison: Intervention 2 vs Comparator MD -4.80 (95% CI: -9.98 - 0.38)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Calcium: NR Other Minerals: NR Mean BMI: 25.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 82.3 Mean Age/Range/Age at Baseline: 54.9 Race: NR Systolic BP: 138.1 Diastolic BP: 82.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.5 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 52.3 Mean Age/Range/Age at Baseline: mean 54.2 Race: NR Systolic BP: 134.6 Diastolic BP: 82.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 20-69 years old, <120% ideal body weight, consumed <30 ml ethanol/24h and BP > 1330/80 mmHg (untreated) or 125/85 mmHg (treated) Exclusion: Cardiac failure, diabetes, kidney, liver or heart disease, taking NSAID medications</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Other: Low Sodium - Low fat/high fibre Description: Diet with an aim of 60 mmol/day sodium intake plus placebo Form of Administration: Dietary Modification: Other: Placebo pill Dose: Placebo (10 lactose tablets per day) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Normal Sodium - Low fat/high fibre Description: Diet with an aim of 60 mmol/day sodium intake plus sodium supplement Form of Administration: Salt substitute Dietary Modification: NR Dose: 100 mmol NaCl/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>for a given individual. Taken in a non-fasting state and subjects asked to not smoke, drink coffee or engage in vigorous exercise for 2 hours prior to measurement. A sohygmomanometer cuff appropriate for arm size was applied to the right arm. SBP, DBP were measured using a semi-automatic Dinamap 845XT oscillometric recorder. BP was measured at 2 min intervals for 20 min in the supine position then at 1-min intervals for 5 minutes after standing. Averages of 8 supine and 5 separate standing measures were taken. BP measured once every 2 weeks</p>	
<p>Siani, 1987⁷⁹ Location: Italy Setting: Community Design: Randomized, parallel</p>	<p>Study of: Adults N: 37</p> <p>Intervention 1: % Male: 61% Mean Age/Range/Age at Baseline: mean 45 (SD 2) Race: NR Systolic BP: 144 Diastolic BP: 97 Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 48 mmol potassium daily Na/K ratio: NR Magnesium: NR</p>	<p>Sodium, Method of Validation: Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 189 mmol/24 h Best potassium measure recorded: 2 times 15 weeks apart (baseline, end of follow up) Potassium, Method of Validation: Pill counting Potassium Status Intervention 1: 87 mmol/24 h</p>	<p>Subgroup: Mild HTN Diastolic BP-supine Follow-Up Time: 15 weeks Comparison: Intervention 1 vs Comparator MD -10.50 (95% CI: -16.32 - -4.68) Systolic BP-supine Follow-Up Time: 15 weeks Comparison: Intervention 1 vs Comparator MD -14.00 (95% CI: -21.78 - -6.22)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 63.1 Mean Age/Range/Age at Baseline: mean 45 (SD 2) Race: NR Systolic BP: 14 Diastolic BP: 91 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: mild hypertension Exclusion: Possibility that patient has secondary hypertension, or any associated illness or severe complication of the hypertensive disease</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3.75 months Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured? BP measured 7 times, 1 week apart during baseline, 3 weeks apart during intervention. BP was taken by a single observer, blinded to treatment status, using a Hawksley random zero sphygmomanometer. After quietly resting for 30 minutes in the supine position the SBP (phase V Korotkoff sounds) was measured three times two minutes apart; the same measurements were taken after the patient had been standing upright for two minutes. The average of each measurement in each position for all the patients was used for analysis.</p>	
<p>Siani, 1991⁸⁰</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 54</p> <p>Intervention 1: % Male: 57.7 Mean Age/Range/Age at Baseline: mean 48.8 (SD 7.8) Race: NR Systolic BP: 138.2 Diastolic BP: 81.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 52.3 Mean Age/Range/Age at Baseline: mean 49.3 (SD 9.4) Race: NR Systolic BP: 138.3 Diastolic BP: 80.1 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: Dietary advice to selectively increase potassium intake Form of Administration: Oral potassium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 2 times in run in then monthly over 12 months follow up Sodium, Method of Validation: Assessment of the reliability of urine collection was done by interviewing the patient and by measuring 24-hour creatinine excretion., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 163 mmol/24h Best potassium measure recorded: 2 times in run in then monthly over 12 months follow up Potassium, Method of Validation: Assessment of the reliability of urine collection was done by interviewing the patient and by measuring 24-hour creatinine excretion. Potassium Status Intervention 1: 73 mmol/24h</p> <p>How was blood pressure measured? Blood pressure measured by an operator who was blinded to the patient's assigned treatment. Measurements taken using a Sentron</p>	<p>Subgroup: HTN under control Diastolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 1.10 (95% CI: 0.11 - 2.09) Percent of baseline drug consumption Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator RR 2.50 (95% CI: 1.16 - 5.39) Systolic BP-supine Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD 3.40 (95% CI: 2.11 - 4.69)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Mean BMI: 27 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: BP under good pharmacologic control, aged 30-65 years and a BP below 160/95 mm Hg at the last two clinic visits. Exclusion: Secondary hypertension, ischemic heart or brain disease, renal failure, any illness requiring adherence to a strict dietary regimen (e.g. diabetes mellitus or obesity). Use of oral contraceptives; poor compliance with their prescribed drug regimen.</p>		<p>automatic oscillometric recorder. Patients first rested for 10 minutes in the supine position in a quiet and comfortable room. SBP and DBP were measured three times at 2-minute intervals; the average of all measurements was used in the analysis.</p>	
<p>Silman, 1983⁸¹ Location: UK Setting: Community Design: Randomized, parallel Number of Sites: multiple Study Years: unclear</p>	<p>Study of: Adults N: 28</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 165.3 Diastolic BP: 158.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: 160.5 Diastolic BP: 98.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients who were between 50 and 64 years old from 2 general practices got screened for BP. If DBP was between 95 and 104 mm Hg (fifth diastolic sound, average of two readings at 5 minute intervals) .they were rescreened 12 months later, and if their DBP was in the same range and remained so for a further 1 month, they were included.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: Taught to take a diet with 100 mmol sodium per day Form of Administration: Dietary Modification: Instructed to take a diet that contained 100 mmol sodium per day, as well as general healthy dietary advice Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Advised regarding regular healthy eating habits Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: First-morning urine specimens and two-day diet records Best sodium measure recorded: Taken 5 times, at 0,1,3,6 and 12 months Sodium Status Intervention 1: 117 mmol/24h Potassium measure: First-morning urine specimens and two-day diet records Best potassium measure recorded: Taken 5 times, at 0,1,3,6 and 12 months Potassium Status Intervention 1: 60.8</p> <p>How was blood pressure measured? BP was measured in a standardized manner with a random zero sphygmomanometer by the same observer.</p>	<p>Subgroup: HTN Diastolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -6.30 (95% CI: -15.12 - 2.52) Systolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -8.70 (95% CI: -29.16 - 11.76)</p>
<p>Singer, 1991⁸²</p>	<p>Study of: Adults N: 21</p>	<p>Intervention Type(s):</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p>	<p>Subgroup: Hypertensives Diastolic BP-supine</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>Participants:</p> <p>% Male: 62</p> <p>Mean Age/Range/Age at Baseline: 53.9+/-2.5</p> <p>Race: 71% white; 29% black</p> <p>Systolic BP: 158+/-5</p> <p>Diastolic BP: 100+/-2</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: 0</p> <p>% with Type 2 diabetes: 0</p> <p>% with Kidney disease: 0</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Essential, uncomplicated hypertension, treated with captopril (50 mg twice daily) and hydrochlorothiazide (25 mg once daily) for at least 1 month before study entry</p> <p>Exclusion: ischemic heart disease; cerebrovascular disease; renal or hepatic impairment; and diabetes mellitus; or receiving any additional treatment</p>	<p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Sodium restriction diet + slow sodium placebo tablets to achieve low sodium diet</p> <p>Form of Administration: Other: Low sodium diet + placebo salt pills</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake</p> <p>Description: Usual sodium intake achieved via sodium restriction + slow sodium tablets</p> <p>Form of Administration: Sodium supplement</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p>	<p>Best sodium measure recorded: 2 consecutive 24-hour urine samples</p> <p>Sodium, Method of Validation: creatinine, Multiple 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 104+/-11 mmol</p> <p>Best potassium measure recorded: 2 consecutive 24-hour urine samples</p> <p>Potassium, Method of Validation: NR</p> <p>Potassium Status Intervention 1: 66+/-3 mmol/d</p> <p>How was blood pressure measured? Supine and standing blood pressure measured every 2 weeks under identical conditions with semiautomatic ultrasound sphygmomanometers</p>	<p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -4.13 - -1.87)</p> <p>Systolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -9.00 (95% CI: -10.70 - -7.30)</p>
<p>Sundar, 1985⁸³</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults</p> <p>N: 50</p> <p>Intervention 1:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 164.1</p> <p>Diastolic BP: 102.2</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 63.4 Kg</p> <p>% with Hypertension: 100</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Comparator:</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: NR</p> <p>Systolic BP: 164.3</p> <p>Diastolic BP: 102.2</p> <p>Magnesium: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels</p> <p>Description: NR</p> <p>Form of Administration: Oral potassium supplement</p> <p>Dose: Patients given 126 tabs containing 6.47 mEq potassium for 14 days (3 tabs per day)</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Placebo</p> <p>Description: NR</p> <p>Form of Administration: Placebo</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1 month</p> <p>Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: 5 times 1 weeks apart</p> <p>Sodium Status Intervention 1: 96.6 mEq/L</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: 5 times 1 weeks apart</p> <p>Potassium Status Intervention 1: 81.08 mEq/L</p> <p>How was blood pressure measured? Basal supine BP measured on the right arm measured 3 times by the same observer.</p>	<p>Subgroup: Mild-moderate HTN</p> <p>Diastolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -3.20 (95% CI: -7.40 - 1.00)</p> <p>Systolic BP-supine</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -11.30 (95% CI: -22.95 - 0.35)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Calcium: NR Other Minerals: NR Mean BMI: 60 Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild to moderate essential hypertension Exclusion: Any complications of hypertension, impaired renal function or any other illness</p>			
<p>Suppa, 1988⁸⁴ Location: Italy Setting: Community Design: Randomized, parallel Number of Sites: 32 Study Years: unclear</p>	<p>Study of: Adults N: 322</p> <p>Intervention 1: % Male: 64 Mean Age/Range/Age at Baseline: mean 47.1 (SD 9.8) Race: NR Systolic BP: 149.2 Diastolic BP: 93.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 61 Mean Age/Range/Age at Baseline: mean 47.8 (SD 10.1) Race: NR Systolic BP: 159 Diastolic BP: 93.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: SBP \geq95 Exclusion: Contraindications to beta blockers, women of childbearing potential, individuals with secondary hypertension, renal failure, or other major diseases.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: 193.2 Form of Administration: Oral potassium supplement Dose: Twice daily 2-g packets of diet salt (%50 NaCl, 25% KCl, 15% K3C6H5O7) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Regular salt Description: NR Form of Administration: Regular Salt Dose: Twice daily 2-g packets of regular sale (100% NaCl) Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 1 month Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times 2 weeks apart Sodium, Method of Validation: 24 hour urinary excretion was considered correct when urinary creatinine was $>$900 mg/24h in women and $>$1000 mg/24h in men., Single 24-hour urine analysis with validation Sodium Status Intervention 1: 77.4 Best potassium measure recorded: 3 times 2 weeks apart Potassium, Method of Validation: 24 hour urinary excretion was considered correct when urinary creatinine was $>$900 mg/24h in women and $>$1000 mg/24h in men. How was blood pressure measured? Measured by standard mercury sphygmomanometer as per WHO guidelines. The first and fifth Korotkoff phases were used for SBP and DBP respectively.</p>	<p>Subgroup: HTN on antihypertensive Diastolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.02 - 0.02) Systolic BP-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.46 - 0.06)</p>
<p>Svetkey, 1987⁸⁵ Location: US</p>	<p>Study of: Adults N: 116 Intervention 1:</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels</p>	<p>Sodium Status Intervention 1: NR Potassium measure: Compliance assessed by pill count</p>	<p>Subgroup: Mild HTN Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Setting:</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: unclear</p>	<p>% Male: 76 Mean Age/Range/Age at Baseline: mean 51.3 (SD 12.3)</p> <p>Race: white 89% Systolic BP: 147.5 Diastolic BP: 95.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 83.8 (SD 14.4) kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 72 Mean Age/Range/Age at Baseline: mean 50.9 (SD 12.3) Race: White 83% Systolic BP: 142.1 Diastolic BP: 147.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 81.7 (SD 11.9) Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ambulatory hypertensive adults Exclusion: history or physical examination revealed any of : a single DBP> 114 mm Hg, prior episode of malignant hypertension or hypertensive encephalopathy, angina, myocardial infarction within the prior 6 months, CHF, arrhythmia, transient ischemic, cerebrovascular accident, attacks, the presence of a terminal illness. Secondary hypertension excluded by physical examination, history, serum electrolyte levels, and measurements of renal function (plasma creatinine concentration, creatinine clearance, and complete urinalysis). Patients who might be at risk from high potassium intake were also excluded: those with renal insufficiency or baseline serum potassium values > 5.0 mEq/L, patients taking digitalis preparations, and those with chronic diarrhea or history of ulcer disease. Pregnant and nursing women.</p>	<p>Description: NR Form of Administration: NR Dose: 120 mEq/ day potassium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Usual diet, placebo Form of Administration: NR Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Best potassium measure recorded: 0 Potassium, Method of Validation: Compliance assessed by pill count. Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? Measured 2-4 times, weekly during run in, 4 times every 2 weeks during trial. During each visit, three blood pressure measurements were recorded and the average value was considered to be the blood pressure for that day. BP measurements taken at the same time of day and by the same staff. using a random zero sphygmomanometer (Hawksley and Sons, Lancing, Sussex, England) where the subject was seated for 10 minutes before the readings. DBP was recorded as the fifth Korotkoff sound. Patients were advised not to smoke or eat for 30 minutes before each blood pressure reading.</p>	<p>MD -2.50 (95% CI: -5.39 - 0.39) Lethargy Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 1.04 (95% CI: 0.07 - 16.16) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -6.29 (95% CI: -11.50 - -1.08) Decreased quality of life Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator RR 0.68 (95% CI: 0.43 - 1.06)</p>
<p>Takahashi, 2006⁸⁶</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p>	<p>Study of: Adults N: 448</p> <p>Intervention 1: % Male: 31.7 Mean Age/Range/Age at Baseline: mean 56.3 (95% CI 41.2 - 71.4) Race: NR Systolic BP: 127.9 Diastolic BP: 75.9 Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Reduce sodium intake to less than 8 and 10 g/day in women and men, respectively Form of Administration: Dietary Modification: Two individual 15-min diet counseling sessions, a group class,</p>	<p>Sodium measure: Validated dietary questionnaire and 48 hour urine analysis Best sodium measure recorded: Collected two times 1 year apart. Collected two times 1 year apart. For calculating 24 hour urine, samples were analyzed using a flame photometry and creatinine by Jaffe's procedure with an autoanalyzer. The expected intakes were calculated using observed urinary excretion, as reported in a carefully designed balance study. Sodium Status Intervention 1: 199</p>	<p>Subgroup: HTN Diastolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -1.10 (95% CI: -5.02 - 2.82) Systolic BP-NS Follow-Up Time: 12 months Comparison: Intervention 1 vs Comparator MD -7.00 (95% CI: -13.15 - -0.85)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Number of Sites: 2</p> <p>Study Years: 1998-2000</p>	<p>Mean BMI: 23.6 % with Hypertension: 23.7 % with history of CVD: NR % with Type 2 diabetes: 3.6 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 33 Mean Age/Range/Age at Baseline: mean 56.4 (95% CI 40.5-72.4) Race: NR Systolic BP: 128 Diastolic BP: 76.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.2 % with Hypertension: 24.1 % with history of CVD: NR % with Type 2 diabetes: 3.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 40–69 years, physician permission to participate for those under medical treatment or dietary control.</p>	<p>and two newsletters Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Not asked to change diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 12 months Exposure to Follow Up Time: NR</p>	<p>mmol/day Potassium measure: Validated dietary questionnaire and 48 hour urine analysis Best potassium measure recorded: Collected two times 1 year apart. For calculating 24 hour urine, samples were analyzed using a flame photometry and creatinine by Jaffe's procedure with an autoanalyzer. The expected intakes were calculated using observed urinary excretion, as reported in a carefully designed balance study. Potassium Status Intervention 1: 59 mmol/day</p> <p>How was blood pressure measured? BP measured by a trained nurse, using sphygmomanometer OKOSE- 300 model based on a common protocol. A single measurement was used.</p>	
<p>Vongpatanasin, 2016⁸⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: >=7 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 30</p> <p>Participants: % Male: 47 Mean Age/Range/Age at Baseline: mean 54 (SD 12) Race: black 40% Systolic BP: 125 Diastolic BP: 81 Magnesium: 2.2 mg/dl Calcium: 9.5 mg/dl Other Minerals: NR Mean BMI: 31 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Prehypertension or stage I hypertension. SBP between 120 and 159 mm Hg, and DBP 80 - 99 mm Hg. No history of: diabetes mellitus renal impairment (serum creatinine > 1.4 mg/dl), active cardiac or liver disease, esophageal-gastric ulcer, gastroesophageal reflux disease, chronic diarrhea, chronic nonsteroidal anti-inflammatory drug use, treatment with diuretics, renal tubular acidosis, hypocalcemia, or hypercalcemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Other: Potassium Chloride Description: NR Form of Administration: Oral potassium supplement Dose: 40 meq KCl powder/day Na/K ratio: NR Magnesium: 104 mg/day Calcium: 160 mg/day Other Minerals: NR</p> <p>Intervention 2: Other: Potassium Citrate Description: NR Form of Administration: Oral potassium supplement Dose: 40 meq K3Cit powder/day diluted in water Na/K ratio: NR Magnesium: 100 mg/day Calcium: 148 mg/day Other Minerals: NR</p> <p>Intervention 3: Other: Potassium Magnesium Citrate Description: NR Form of Administration: Oral potassium supplement Dose: KMgCit, 40 meq K, 20 meq Mg, 74 meq citrate powder/day Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Collected during the last week of treatment Sodium, Method of Validation: creatinine, Composition of potassium supplement with intervention/exposure adherence measure Sodium Status Intervention 1: 184 meq/day Sodium Status Intervention 2: 190 meq/day Sodium Status Intervention 3: 187 meq/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Collected during the last week of treatment Potassium Status Intervention 1: 58 meq/day Potassium Status Intervention 2: 84 meq/day Potassium Status Intervention 3: 91 meq/day</p> <p>How was blood pressure measured? At each visit, BP was taken by nursing staff with the same validated oscillometric device, after the patient had been in rest quietly for 5 minutes. Four BP measurement during a single visit was repeated 3 times 1 minute apart, and the mean was taken.</p>	<p>Subgroup: Hypertensives and prehypertensives 24 hr diastolic BP Follow-Up Time: 4 weeks Comparison: Intervention 3 vs Comparator MD -1.00 (95% CI: -4.77 - 2.77) Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -5.63 - 1.63) Comparison: Intervention 2 vs Comparator MD -2.00 (95% CI: -5.63 - 1.63) 24 hr systolic BP Follow-Up Time: 4 weeks Comparison: Intervention 3 vs Comparator MD -2.00 (95% CI: -6.34 - 2.34) Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -7.13 - 1.13) Comparison: Intervention 2 vs Comparator MD -2.00 (95% CI: -6.22 - 2.22)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		<p>Magnesium: 121 mg/day Calcium: 158 mg/day Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Placebo Dose: Placebo Na/K ratio: NR Magnesium: 97 mg/day Calcium: 181 mg/day Other Minerals: NR</p> <p>Duration: 4 periods of 4 weeks each Exposure to Follow Up Time: 0 months</p>		
<p>Wing, 1998⁸⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 17</p> <p>Participants: % Male: 82</p> <p>Mean Age/Range/Age at Baseline: 61 median Race: NR Systolic BP: 165+/-4 Diastolic BP: 104+/-2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Inclusion: essential hypertensives; aged 18–80 years; untreated sitting clinic diastolic blood pressure of >95 and <115 mmHg measured by standard mercury sphygmomanometer</p> <p>Exclusion: secondary hypertension of any cause, a past history of malignant hypertension, myocardial infarction or unstable angina in the previous 6 months, a stroke or transient cerebral ischaemic attack in the previous year, any evidence of cardiac failure or haemodynamically significant valvular heart disease, unstable diabetes mellitus (50% of home blood glucose values >12 mmol/L or haemoglobin A1C >8.5%), any significant renal or hepatic disease, any other significant illness likely to interfere with survival (e.g. malignancy), known intolerance to the classes of drug being used in the study or the presence of conditions likely to be exacerbated by the study treatments (e.g. plasma potassium concentration <3.0 mmol/L, gout or plasma uric acid >0.50 mmol/L), were women who were pregnant or lactating or if they had anticipated poor compliance with the study protocol or treatment regimens</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Use of low sodium diet and placebo salt pills to reduce sodium intake to <100mM in participants on perindopril</p> <p>Form of Administration: Dietary Modification: Low sodium diet not described Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Use of salt pills to increase sodium intake</p> <p>Description: Administration of salt tablets to participants on low sodium diet in participants on perindopril to achieve usual sodium intake</p> <p>Form of Administration: Dietary Modification: Low sodium diet not described Sodium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 periods of 4 weeks each Exposure to Follow Up Time: 0 months</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: NR</p> <p>Sodium, Method of Validation: creatinine Sodium Status Intervention 1: 99 mmol/d</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: NR</p> <p>Potassium, Method of Validation: NR</p> <p>Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? semiautomatic sphygmomanometer (Dinamap Vital Signs Monitor 8100, CRITIKON) and an inflatable cuff appropriate for the patient's arm size</p>	<p>Subgroup: Hypertensives</p> <p>24-h ambulatory diastolic BP</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.11 - 0.11)</p> <p>24-h ambulatory systolic BP</p> <p>Follow-Up Time: 6 weeks</p> <p>Comparison: Intervention 1 vs Comparator MD -5.00 (95% CI: -9.22 - -0.78)</p>
<p>Weir, 2010⁸⁹</p> <p>Location: US</p> <p>Setting:</p>	<p>Study of: Adults N: 132</p> <p>Intervention 1: % Male: 55</p>	<p>Intervention Type: Intervention 1: Usual Diet</p> <p>Description: To achieve dietary sodium >200 mmol/d sodium</p> <p>Form of Administration: Dietary</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 times, at baseline and at the end of each treatment period</p>	<p>Subgroup: Hypertensives</p> <p>Death</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator NC (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Community Design: Randomized Cross-over individual</p> <p>Number of Sites: Multiple</p> <p>Crossover: Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>Mean Age/Range/Age at Baseline: 51.5+/-7.4 Race: 86% white; 11% black; 2% Asian; 1% Hispanic</p> <p>Systolic BP: 138.9+/-8.4 Diastolic BP: 87.1+/-7.0</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 27.4+/-2.8 % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 18 to 60 years of age; provision of written informed consent; mean daytime SBP at screening 135 mm Hg and <160 mm Hg, and use of acceptable form of contraception for women of childbearing potential. Exclusion: secondary hypertension, history of myocardial infarction, or heart failure within the preceding 6 months, unstable angina pectoris, second- or third-degree heart block, clinically significant arrhythmias or use of antiarrhythmic drugs (including digoxin), clinically significant valvular heart disease, diabetes mellitus, estimated glomerular filtration rate <60 mL/min per 1.73 m², body mass index (BMI) >30 kg/m², use of a-blockers or >2 antihypertensive agents, pregnancy or lactation, or history of malignancy within the past 5 years</p>	<p>Modification: low sodium diet, not described Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To achieve sodium status <=100 mmol/d Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 weeks Exposure to Follow Up Time: 0 months</p>	<p>Sodium, Method of Validation: Creatinine Sodium Status Intervention 1: 207.6 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8 Potassium, Method of Validation: NR Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? calibrated standard mercury sphygmomanometers and the recommended cuff sizes in accordance with the 1988 American Heart Association Committee Report on Blood Pressure Determination; Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8.</p>	<p>Diastolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.70 (95% CI: -6.90 - -4.40) Discontinued due to dizziness and asthenia Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator NC (95% CI: NC - NC) Systolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -9.40 (95% CI: -11.40 - -7.50)</p>
<p>Whelton, 1998⁹⁰; Appel, 2001⁹¹; Espeland, 1999⁹²; Banson, 1997⁹³; Appel, 1995⁹⁴; Kostis, 1998⁹⁵; Whelton, 1997⁹⁶</p> <p>Location: US</p> <p>Setting: Community</p>	<p>Study of: Adults N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: Dietary Modification: Nutritionists conducted small group and individual meetings to advise patients on ways to change eating patterns Dose: NR Na/K ratio: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p>	<p>Subgroup: Angina Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.88 (95% CI: 0.85 - 4.17) CVD(Stroke, Transient ischemic attack, MI, Arrhythmia, Congestive heart failure, Angina, Other) Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.27 (95% CI: 0.85 - 1.92) Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -3.19 - -0.81)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p> <p>Number of Sites: 4</p> <p>Study Years: 1992-1995</p>	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24%</p> <p>Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health, independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>	<p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: NR Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records</p>	<p>Dizziness Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 0.62 (95% CI: 0.33 - 1.17) MI Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.99 (95% CI: 0.37 - 10.81) Percent free of elevated BP Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.60 (95% CI: 1.29 - 1.98) Stroke Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 1.99 (95% CI: 0.18 - 21.89) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -5.93 - -2.47)</p>
<p>Zhao, 2014⁹⁷</p> <p>Location: Tibet</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 2009</p>	<p>Study of: Adults N: 282</p> <p>Participants: % Male: 41.1 Mean Age/Range/Age at Baseline: 63.1 Race: NR Systolic BP: 176.9 Diastolic BP: 104.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Aged>40, SBP > 140 mmHg Exclusion: Not able to travel, living to far</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium product as salt (sodium) substitute to reduce sodium intake Description: Salt substitute to decrease sodium intake Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Regular salt Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: For 'selected' families, salt that was delivered as part of the study was weighed at baseline then at follow up. Questions were also asked to gauge salt consumption. Daily salt and potassium intake as estimated based on this. Sodium Status Intervention 1: 20 grams/day Potassium measure: For 'selected' families, salt that was delivered as part of the study was weighed at baseline then at follow up. Questions were also asked to gauge salt consumption. Daily salt and potassium intake as estimated based on this. Potassium Status Intervention 1: 7.7 grams/day higher than control group</p> <p>How was blood pressure measured? BP taken with three consecutive blood pressure measurements (with at least one minute's rest between each measurement) from a seated patients' right arm in a quiet room. A previously validated electronic sphygmomanometer was used. BP taken at baseline and after 3 months of follow up.</p>	<p>Subgroup: HTN Deaths Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 2.00 (95% CI: 0.18 - 21.81) Diastolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.64 - -0.36) Percent taking antihypertensives Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 1.34 (95% CI: 0.96 - 1.87) Percent under control Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 2.18 (95% CI: 1.07 - 4.46) Systolic BP-sitting Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -7.70 (95% CI: -12.78 - -2.62) Decreased quality of life Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator RR 0.50 (95% CI: 0.05 - 5.45)</p>
<p>Zhou, 2009⁹⁸</p>	<p>Study of: Adults N: 248</p>	<p>Intervention Type(s): Intervention 1: Other: Low sodium salt-</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control</p>	<p>Subgroup: Hypertensive Diastolic BP-NS</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 10</p> <p>Study Years: 2003-2004</p>	<p>Intervention 1: % Male: 43.5 Mean Age/Range/Age at Baseline: mean 67.5 (SD 5.2) Race: NR Systolic BP: 159.7 Diastolic BP: 83.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 42.2 Mean Age/Range/Age at Baseline: mean 65.7 (SD 6.3) Race: NR Systolic BP: 157.7 Diastolic BP: 82.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 49.1 Mean Age/Range/Age at Baseline: mean 68.1 (SD 8.3) Race: NR Systolic BP: 125 Diastolic BP: 74.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.9 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 44.6 Mean Age/Range/Age at Baseline: mean 65.4 (SD 4.5) Race: NR Systolic BP: 123.8 Diastolic BP: 74.5 Magnesium: NR</p>	<p>Hypertensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Normal salt - Hypertensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium salt - Normotensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal salt - Normotensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses. Form of Administration: Other: Regular salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>measure Best sodium measure recorded: 2 times, 6 months apart Sodium Status Intervention 1: 162 mmol/24 h Sodium Status Comparator 1: 233 mmol/24 h Sodium Status Intervention 2: 162 mmol/24 h Sodium Status Comparator 2: 231 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 6 months apart</p> <p>Potassium Status Intervention 1: 34.2 mmol/24 h Potassium Status Comparator 1: 27.0 mmol/24 h Potassium Status Intervention 2: 33.1 mmol/24 h Potassium Status Comparator 2: 23.0 mmol/24 h</p> <p>How was blood pressure measured? BP was measured by two experienced physicians. SBP was taken as the point of appearance (phase 1) of Korotkoff sounds and DBP was measured as the point of disappearance (phase 5).</p>	<p>Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator 1 MD -5.20 (95% CI: -8.09 - -2.31) Systolic BP-NS</p> <p>Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator 1 MD -9.80 (95% CI: -13.75 - -5.85)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Calcium: NR Other Minerals: NR Mean BMI: 23.7 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–80, with normal BP or mild to moderate hypertension. No more than one meal outside the home per week, not currently taking potassium-sparing drugs, willingness to undertake long-term use of CISalt. Serum potassium <5.5mmol/l and net elevation of serum potassium <1.0mmol/l at the end of the run-in period Exclusion: Heart attack or stroke within the last 6 months, current angina pectoris, congestive heart failure, diabetes mellitus, serious mental or physical illness, secondary hypertension, malignancy, use of potassium-sparing diuretics, impairment of renal function.</p>			

Table D14. Subgroup table for trials for hypertension, diabetes

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Dodson, 1989⁹⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 34</p> <p>Intervention 1: % Male: 71 Mean Age/Range/Age at Baseline: mean 61.9 (SD 7.5) Race: NR Systolic BP: 179 Diastolic BP: 98 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 65 Mean Age/Range/Age at Baseline: mean 61.1 (SD 6.3) Race: NR Systolic BP: 174 Diastolic BP: 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Patients with type II diabetes with no past or current history of treatment with insulin. Three consecutive hypertensive BP readings (defined by the SBP > 160 mm Hg or DBP >95 mm Hg) in an established diabetic. Exclusion: Evidence of diabetic or hypertensive nephropathy, pregnancy, and cardiac failure.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Moderate sodium restriction Form of Administration: Dietary Modification: Patients advised not to add salt at the table or in cooking and the avoidance of heavily salted foods Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Patients instructed to continue with their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: During run in period then at 1, 2, 3 months Sodium Status Intervention 1: 136.8 mmol/24h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: During run in period then at 1, 2, 3 months Potassium Status Intervention 1: 63.9 mmol/24h</p> <p>How was blood pressure measured? BP was taken in the supine and erect positions (after 5 and two minutes' rest, respectively) with a Hawksley random zero sphygmomanometer. All readings were taken by a separate "blind" observer, DBP was recorded at Korotkoff phase V. When the mid-arm circumference was less than 33 cm A standard width cuff (14 cm) was used ; for larger circumferences a 19 cm cuff was used.</p>	<p>Subgroup: Mild HTN, Diabetes Diastolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -8.48 - 2.88) Systolic BP-supine Follow-Up Time: 3 months Comparison: Intervention 1 vs Comparator MD -7.10 (95% CI: -19.11 - 4.91)</p>

Table D15. Subgroup table for trials for hypertension, gender

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Whelton, 1998⁹⁰; Appel, 2001⁹¹; Espeland, 1999⁹²; Banson, 1997⁹³; Appel, 1995⁹⁴; Kostis, 1998⁹⁵; Whelton, 1997⁹⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p> <p>Number of Sites: 4</p> <p>Study Years: 1992-1995</p>	<p>Study of: Adults N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health, independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: Dietary Modification: Nutritionists conducted small group and individual meetings to advise patients on ways to change eating patterns Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: NR Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records</p>	<p>Subgroup: Women Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -1.30 (95% CI: -3.06 - 0.46) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -3.30 (95% CI: -5.97 - -0.63)</p> <p>Subgroup: Men Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -2.60 (95% CI: -4.20 - -1.00) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -5.20 (95% CI: -7.47 - -2.93)</p>

Table D16. Subgroup table for trials for hypertension, race, ethnicity

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Whelton, 1998⁹⁰; Appel, 2001⁹¹; Espeland, 1999⁹²; Banson, 1997⁹³; Appel, 1995⁹⁴; Kostis, 1998⁹⁵; Whelton, 1997⁹⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p> <p>Number of Sites: 4</p> <p>Study Years: 1992-1995</p>	<p>Study of: Adults N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health, independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: Dietary Modification: Nutritionists conducted small group and individual meetings to advise patients on ways to change eating patterns Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: NR Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records</p>	<p>Subgroup: Non-African American Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -1.60 (95% CI: -2.96 - -0.24) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -4.00 (95% CI: -5.99 - -2.01)</p> <p>Subgroup: African American Diastolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.39 - -0.61) Systolic BP-sitting Follow-Up Time: 3.5 months Comparison: Intervention 1 vs Comparator MD 4.90 (95% CI: 1.46 - 8.34)</p>

Table D17. Subgroup table for trials for hypertension, diabetes

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Gilleran, 1996¹⁰⁰</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 40</p> <p>Intervention 1: % Male: 60%</p> <p>Mean Age/Range/Age at Baseline: 62.5</p> <p>Race: NR</p> <p>Systolic BP: 163.2 Diastolic BP: 91.2</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 28.1</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 60%</p> <p>Mean Age/Range/Age at Baseline: mean 59.2 (SD 10.8)</p> <p>Race: NR</p> <p>Systolic BP: 169.6 Diastolic BP: 91.7</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 59.2</p> <p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 100 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Three consecutive hypertensive BP readings in with established diabetes including patients already taking one antihypertensive medication (provided that the medication had been discontinued for at least 1 month prior to the trial)</p> <p>Exclusion: Treatment with insulin, unstable or poor diabetic control, evidence of diabetic or hypertensive nephropathy (persistent proteinuria on Albustix, or raised serum creatinine concentration: 130 /xmol/l), pregnancy, cardiac failure, or a patient already consuming a low sodium diet</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: NR Form of Administration: Salt substitute Dose: salt substitute (Seltin) containing 50% sodium chloride, 40% potassium chloride, 10% magnesium sulphate Na/K ratio: 2.3 Magnesium: 4.2 Urinary excretion (24 h estimation) Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Table salt Description: NR Form of Administration: Regular Salt Dose: Ordinary table salt Na/K ratio: 2.3 Magnesium: 3.7 Calcium: NR Other Minerals: NR</p> <p>Duration: 9 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 0,1,2,3,6,9 months Sodium, Method of Validation: Checks of remaining allotted monthly supplies of Seltin or whole salt, Single 24-hour urine analysis with validation Sodium Status Intervention 1: 166.6 Urinary excretion (24 h estimation) Best potassium measure recorded: 0,1,2,3,6,9 months Potassium, Method of Validation: Checks of remaining allotted monthly supplies of Seltin or whole salt Potassium Status Intervention 1: 77.3 Urinary excretion (24 h estimation)</p> <p>How was blood pressure measured? BP was measured in the supine and erect positions (after 5 min and 2 min rest respectively) with a Hawksley random zero sphygmomanometer. All readings were taken by a blinded observer, DBP was recorded at Korotkoff phase V. A standard width cuff (14 cm) was used with the midarm circumference was less than 33 cm, but for larger circumferences, a 19 cm cuff was used</p>	<p>Subgroup: Hypertensive Type II diabetics Diastolic BP-supine Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator MD 1.70 (95% CI: -5.77 - 9.17) Comparison: Intervention 1 vs Comparator MD -1.70 (95% CI: -9.17 - 5.77)</p> <p>Stroke Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator RR 0.33 (95% CI: 0.01 - 7.72) Comparison: Intervention 1 vs Comparator RR 3.00 (95% CI: 0.13 - 69.52)</p> <p>Systolic BP-supine Follow-Up Time: 9 months Comparison: Intervention 1 vs Comparator MD 21.50 (95% CI: 3.62 - 39.38) Comparison: Intervention 1 vs Comparator MD -21.50 (95% CI: -39.38 - -3.62)</p>

Table D18. Subgroup table for trials for hypertension, gender

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Grimm, 1990³⁷; Grimm, 1988³⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: Minnesota Mount Sinai Hypertension Trial (MSHT)</p> <p>Number of Sites: multiple</p> <p>Study Years: 1984-1985</p>	<p>Study of: Adults N: 287</p> <p>Intervention 1: % Male: 100 Mean Age/Range/Age at Baseline: mean 57.8 (SD 6.2) Race: NR Systolic BP: 124.7 Diastolic BP: 79.6 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.6 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 100 Mean Age/Range/Age at Baseline: mean 57.5 (SD 6.5) Race: NR Systolic BP: 126.4 Diastolic BP: 80.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 28.4 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Males, aged 45-68, documentation of long term drug treatment for hypertension in Minneapolis. Currently taking one or two antihypertensive drugs with DBP<95 mm Hg on the first 2 clinic visits, and <90 mm Hg average for both visits. Exclusion: Treatment of hypertension for < 3.5 years, use of cardiovascular drugs, electrocardiographic evidence or clinical evidence of CVD, body weight >15% of the ideal weight, diet incompatible with lowering sodium intake, history of renal disease, documented poor compliance with antihypertensive treatments.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Placebo pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Oral potassium supplement Dose: 96 mmol microcrystalline potassium chloride - 12 capsules, per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Potassium pills + low sodium diet with a goal of < 80 mmol sodium per day Form of Administration: Placebo Dose: 12 placebo capsules per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 24 months Exposure to Follow Up Time: NR</p>	<p>Potassium measure: Partial or spot urine without validated prediction equation, Food diaries without reported validation Potassium Status Intervention 1: 40 mmol/8h</p>	<p>Subgroup: Hypertensive men Decreased quality of life (diarrhea) Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 0.91 (95% CI: 0.69 - 1.21) Decreased quality of life (stomach pains) Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 0.80 (95% CI: 0.55 - 1.17) Diastolic BP-NS Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator MD -0.60 (95% CI: NC - NC) Nausea Follow-Up Time: 24 months Comparison: Intervention 1 vs Comparator RR 1.16 (95% CI: 0.69 - 1.94) Percent resuming antihypertensives Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator RR 0.98 (95% CI: 0.79 - 1.21) Systolic BP-NS Follow-Up Time: 28 months Comparison: Intervention 1 vs Comparator MD -1.90 (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Weir, 2010⁸⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: Multiple</p> <p>Crossover: Length of washout period: 0 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 132</p> <p>Intervention 1: % Male: 55 Mean Age/Range/Age at Baseline: 51.5+/-7.4 Race: 86% white; 11% black; 2% Asian; 1% Hispanic Systolic BP: 138.9+/-8.4 Diastolic BP: 87.1+/-7.0 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: 27.4+/-2.8 % with Hypertension: 100 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 18 to 60 years of age; provision of written informed consent; mean daytime SBP at screening 135 mm Hg and <160 mm Hg, and use of acceptable form of contraception for women of childbearing potential. Exclusion: secondary hypertension, history of myocardial infarction, or heart failure within the preceding 6 months, unstable angina pectoris, second- or third-degree heart block, clinically significant arrhythmias or use of antiarrhythmic drugs (including digoxin), clinically significant valvular heart disease, diabetes mellitus, estimated glomerular filtration rate <60 mL/min per 1.73 m², body mass index (BMI) >30 kg/m², use of a-blockers or >2 antihypertensive agents, pregnancy or lactation, or history of malignancy within the past 5 years</p>	<p>Intervention Type: Intervention 1: Usual Diet Description: To achieve dietary sodium >200 mmol/d sodium Form of Administration: Dietary Modification: low sodium diet, not described Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: To achieve sodium status <=100 mmol/d Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 weeks Exposure to Follow Up Time: 0 months</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 3 times, at baseline and at the end of each treatment period Sodium, Method of Validation: Creatinine Sodium Status Intervention 1: 207.6 mmol/d Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8 Potassium, Method of Validation: NR Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? calibrated standard mercury sphygmomanometers and the recommended cuff sizes in accordance with the 1988 American Heart Association Committee Report on Blood Pressure Determination; Twenty-four hour ABPM was conducted on all patients at baseline, week 4, and week 8.</p>	<p>Subgroup: Hypertensives, male Systolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -8.80 (95% CI: -11.40 - -6.20)</p> <p>Subgroup: Hypertensives, female Systolic BP, 24 hr mean ambulatory Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -10.20 (95% CI: -13.30 - -7.20)</p>

Table D19. Subgroup table for trials for hypertension, obesity

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Whelton, 1998⁹⁰; Appel, 2001⁹¹; Espeland, 1999⁹²; Banson, 1997⁹³; Appel, 1995⁹⁴; Kostis, 1998⁹⁵; Whelton, 1997⁹⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p> <p>Number of Sites: 4</p> <p>Study Years: 1992-1995</p>	<p>Study of: Adults N: 681</p> <p>Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health, independence in daily living, capacity to alter diet and physical activity in accordance with the intervention Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: Dietary Modification: Nutritionists conducted small group and individual meetings to advise patients on ways to change eating patterns Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: NR Description: 24/h dietary sodium intake <= 80 mmol Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: NR Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: NR Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Intervention 1: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records</p>	<p>Subgroup: Obese Percent free of elevated BP and CVD events and antihypertensive prescription Follow-Up Time: 33 months Comparison: Intervention 1 vs Comparator RR 2.33 (95% CI: 1.53 - 3.55)</p>

Table D20. Subgroup table for trials for hypertension, race/ethnicity

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Xie, 1998¹⁰¹</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Cluster RCT Parallel</p> <p>Number of Sites:</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 169</p> <p>Intervention 1: % Male: 80 Mean Age/Range/Age at Baseline: mean 60 (SD 6) Race: NR Systolic BP: 161.86 Diastolic BP: 96.47 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 62.3 Mean Age/Range/Age at Baseline: mean 55 (SD 6) Race: NR Systolic BP: 168.79 Diastolic BP: 100.41 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: persistently elevated DBP of ≥ 95 mmHg and/or SBP ≥ 160 mmHg</p>	<p>Intervention Type(s):</p> <p>Intervention 1: NR Description: The education included counselling on nonpharmacological treatment (weight reduction, salt moderation, physical exercise, alcohol moderation, and psychological relaxing assisted by biofeedback instrument), medication compliance, monitoring of progress toward target BP, self-measurement of BP, other risk reduction (smoking, lipids), and the keeping of appointments. Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Other: Usual care Description: NR Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 3 times over 3 years Sodium Status Intervention 1: 98.24 mmol/24h</p> <p>How was blood pressure measured? unclear CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Unclear</p>	<p>Subgroup: Chinese Diastolic BP-NS Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 0.50 (95% CI: -1.96 - 2.96) Left ventricular hypertrophy-PWT (cm) Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 0.11 (95% CI: -0.60 - 0.82) Percent under control Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator RR 1.31 (95% CI: 1.04 - 1.65) Systolic BP-NS Follow-Up Time: 2 years Comparison: Intervention 1 vs Comparator MD 2.60 (95% CI: -1.99 - 7.19)</p>

Table D21. Subgroup table for trials for normotension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Zhou, 2009⁹⁸</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 10</p> <p>Study Years: 2003-2004</p>	<p>Study of: Adults N: 248</p> <p>Intervention 1: % Male: 43.5 Mean Age/Range/Age at Baseline: mean 67.5 (SD 5.2) Race: NR Systolic BP: 159.7 Diastolic BP: 83.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 42.2 Mean Age/Range/Age at Baseline: mean 65.7 (SD 6.3) Race: NR Systolic BP: 157.7 Diastolic BP: 82.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 49.1 Mean Age/Range/Age at Baseline: mean 68.1 (SD 8.3) Race: NR Systolic BP: 125 Diastolic BP: 74.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.9 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 44.6 Mean Age/Range/Age at Baseline: mean 65.4 (SD 4.5) Race: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Low sodium salt-Hypertensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Normal salt - Hypertensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium salt-Normotensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal salt - Normotensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses. Form of Administration: Other: Regular salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 6 months apart Sodium Status Intervention 1: 162 mmol/24 h Sodium Status Comparator 1: 233 mmol/24 h Sodium Status Intervention 2: 162 mmol/24 h Sodium Status Comparator 2: 231 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 6 months apart Potassium Status Intervention 1: 34.2 mmol/24 h Potassium Status Comparator 1: 27.0 mmol/24 h Potassium Status Intervention 2: 33.1 mmol/24 h Potassium Status Comparator 2: 23.0 mmol/24 h</p> <p>How was blood pressure measured? BP was measured by two experienced physicians. SBP was taken as the point of appearance (phase 1) of Korotkoff sounds and DBP was measured as the point of disappearance (phase 5).</p>	<p>Subgroup: Normotensive Diastolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -4.80 (95% CI: -7.05 - -2.55) Systolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -5.80 (95% CI: -8.66 - -2.94)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Systolic BP: 123.8 Diastolic BP: 74.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.7 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–80, with normal BP or mild to moderate hypertension. No more than one meal outside the home per week, not currently taking potassium-sparing drugs, willingness to undertake long-term use of ClSalt. Serum potassium <5.5mmol/l and net elevation of serum potassium <1.0mmol/l at the end of the run-in period Exclusion: Heart attack or stroke within the last 6 months, current angina pectoris, congestive heart failure, diabetes mellitus, serious mental or physical illness, secondary hypertension, malignancy, use of potassium-sparing diuretics, impairment of renal function.</p>			
<p>Zhou, 2009⁹⁸</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 10</p> <p>Study Years: 2003-2004</p>	<p>Study of: Adults N: 248</p> <p>Intervention 1: % Male: 43.5 Mean Age/Range/Age at Baseline: mean 67.5 (SD 5.2) Race: NR Systolic BP: 159.7 Diastolic BP: 83.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 1: NR % Male: 42.2 Mean Age/Range/Age at Baseline: mean 65.7 (SD 6.3) Race: NR Systolic BP: 157.7 Diastolic BP: 82.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: 100 % with history of CVD: NR</p>	<p>Intervention Type(s): Intervention 1: Other: Low sodium salt-Hypertensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 1: Other: Normal salt - Hypertensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses Form of Administration: Regular Salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Other: Low sodium salt-Normotensives Description: Total of 3 kg a month of study salt (lower sodium) was given to each participant's family to cover all cooking</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times, 6 months apart Sodium Status Intervention 1: 162 mmol/24 h Sodium Status Comparator 1: 233 mmol/24 h Sodium Status Intervention 2: 162 mmol/24 h Sodium Status Comparator 2: 231 mmol/24 h</p> <p>Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 6 months apart</p> <p>Potassium Status Intervention 1: 34.2 mmol/24 h Potassium Status Comparator 1: 27.0 mmol/24 h Potassium Status Intervention 2: 33.1 mmol/24 h Potassium Status Comparator 2: 23.0 mmol/24 h</p> <p>How was blood pressure measured? BP was measured by two experienced physicians. SBP was taken as the point of appearance (phase 1) of Korotkoff sounds</p>	<p>Subgroup: Normotensive Diastolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -4.80 (95% CI: -7.05 - -2.55)</p> <p>Systolic BP-NS Follow-Up Time: 6 months Comparison: Intervention 2 vs Comparator 2 MD -5.80 (95% CI: -8.66 - -2.94)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 49.1 Mean Age/Range/Age at Baseline: mean 68.1 (SD 8.3) Race: NR Systolic BP: 125 Diastolic BP: 74.3 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.9 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator 2: NR % Male: 44.6 Mean Age/Range/Age at Baseline: mean 65.4 (SD 4.5) Race: NR Systolic BP: 123.8 Diastolic BP: 74.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 23.7 % with Hypertension: 0 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ages 50–80, with normal BP or mild to moderate hypertension. No more than one meal outside the home per week, not currently taking potassium-sparing drugs, willingness to undertake long-term use of ClSalt. Serum potassium <5.5mmol/l and net elevation of serum potassium <1.0mmol/l at the end of the run-in period Exclusion: Heart attack or stroke within the last 6 months, current angina pectoris, congestive heart failure, diabetes mellitus, serious mental or physical illness, secondary hypertension, malignancy, use of potassium-sparing diuretics, impairment of renal function.</p>	<p>and other uses Form of Administration: Salt substitute Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator 2: Other: Normal salt - Normotensives Description: Total of 3 kg a month of normal salt was given to each participant's family to cover all cooking and other uses. Form of Administration: Other: Regular salt Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>and DBP was measured as the point of disappearance (phase 5).</p>	
<p>Matthesen, 2012¹⁰²</p> <p>Location: Denmark</p> <p>Setting:</p>	<p>Study of: NR N: 21</p> <p>Participants: % Male: 43 Mean Age/Range/Age at Baseline: mean 26 (range: 18-40)</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Participants were given a standardized diet Form of Administration: Oral potassium</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice separated by 28 days Sodium Status Intervention 1: 199 mmol/24 h</p>	<p>Subgroup: Normotensive 24 h ambulatory- diastolic Follow-Up Time: 28 days Comparison: Intervention 1 vs Comparator MD 1.00 (95% CI: -1.80 - 3.80) 24 h ambulatory- systolic Follow-Up Time: 28 days</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Design: Randomized Cross-over individual</p> <p>Number of Sites:</p> <p>Crossover: Length of washout period: 14 days</p> <p>Study Years: unclear</p>	<p>Race: 100</p> <p>Systolic BP: 116</p> <p>Diastolic BP: 71</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: 23</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Ages 18-40 years; BMI 18.5- 30 kg/m²</p> <p>Exclusion: Arterial hypertension; history of or clinical signs of disease in the heart, lungs, liver, brain or endocrine organs; current medical treatment; malignancies; substance or alcohol abuse; smoking; pregnancy; breast-feeding; no contraceptive treatment for fertile aged women ; clinically significant abnormalities in the blood screening with respect to haemoglobin, white cell count, platelet count, sodium, potassium, creatinine, alanine and aspartate aminotransferase, albumin, cholesterol and glucose. Clinically significant abnormal screening of the urine with respect to albumin and glucose; abnormal electrocardiogram; intercurrent diseases; blood donation less than one month before the trial; unwillingness to participate in the trial; issues with establishing IV access or urine collection.</p>	<p>supplement</p> <p>Dose: 50 mmol potassium twice daily</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Placebo</p> <p>Description: Participants were given a standardized diet</p> <p>Form of Administration: Placebo</p> <p>Dose: Placebo</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Duration: 1 month</p> <p>Exposure to Follow Up Time: NR</p>	<p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice separated by 28 days</p> <p>Potassium Status Intervention 1: 168 mmol/24 h</p> <p>How was blood pressure measured?</p> <p>Ambulatory blood pressure taken using Kiwex TM-2430. In the day, pulse and blood pressure were measured every 15 min. During the night, pulse and blood pressure were measured in 30 min intervals</p>	<p>Comparison: Intervention 1 vs Comparator</p> <p>MD 0.00 (95% CI: -3.42 - 3.42)</p> <p>Aldosterone</p> <p>Follow-Up Time: 28 days</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD 60.00 (95% CI: -100.65 - 220.65)</p>
<p>Nowson, 2003¹⁸</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Number of Sites: 1</p> <p>Crossover: Length of washout period: NR days</p> <p>Study Years: NR</p>	<p>Study of: Adults</p> <p>N: 108</p> <p>Participants:</p> <p>% Male: 41</p> <p>Mean Age/Range/Age at Baseline: 47</p> <p>Race: NR</p> <p>Systolic BP: 126.4+/-18.6</p> <p>Diastolic BP: 79.2+/-11.9</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: sodium: 138.7+/-53.9; potassium: 78.6+/-23.7</p> <p>Mean BMI: 26.1+/-4.2</p> <p>% with Hypertension: 15</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Twin pairs 30 years or older</p> <p>Exclusion: currently undergoing treatment for cancer or renal disease; requiring insulin treatment for diabetes</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Low sodium/high potassium diet to achieve 50 mmol sodium and 80 mmol potassium</p> <p>Form of Administration: Dietary</p> <p>Modification: Low sodium, high potassium diet and placebo sodium pills</p> <p>Dose: NR</p> <p>Na/K ratio: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Comparator: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake</p> <p>Description: Low sodium/high potassium diet to achieve sodium mmol and 80 mmol potassium and sodium supplementation with slow sodium tablets to achieve 130 mmol/d sodium</p> <p>Form of Administration: Dietary</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase</p> <p>Sodium, Method of Validation: creatinine, Multiple 24-hour urine analysis with validation</p> <p>Sodium Status Intervention 1: 89.4+/-4.2 mmol/d</p> <p>Best potassium measure recorded: 24-hour urine 3 times, 1 week apart during each 4-week phase</p> <p>Potassium, Method of Validation: NR</p> <p>Potassium Status Intervention 1: 87.1+/-2.1 mmol/d</p> <p>How was blood pressure measured?</p> <p>mercury sphygmomanometer (model ALPK2; Stethoscope and Sphygmomanometer Specialists, Melbourne, Australia) while seated</p>	<p>Subgroup: Normotensive</p> <p>Home measured BP, diastolic</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -0.90 (95% CI: -5.78 - 3.98)</p> <p>Home measured BP, systolic</p> <p>Follow-Up Time: 4 weeks</p> <p>Comparison: Intervention 1 vs Comparator</p> <p>MD -2.30 (95% CI: -2.81 - -1.79)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		Modification: Low sodium, high potassium diet Sodium supplement Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 4 weeks Exposure to Follow Up Time: 0 months		

<p>Sacks, 2001¹⁰ Vollmer, 2001¹¹; Svetkey, 2004¹²; Harsha, 2004¹³; Akita, 2003¹⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Cross-over individual</p> <p>Study Name: DASH-Sodium</p> <p>Number of Sites: multiple</p> <p>Crossover: Length of washout period: <5 days</p> <p>Study Years: NR</p>	<p>Study of: Adults N: 79</p> <p>Mean Age/Range/Age at Baseline: 49(10) Race: 56% black; 40% NH white; 5% Asian/other Systolic BP: 135(10) Diastolic BP: 86(4) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 30(5) % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0</p> <p>Mean Age/Range/Age at Baseline: 47+/-10 Race: 57% black; 40% NH white; 3% Asian/other Systolic BP: 134+/-10 Diastolic BP: 86+/-5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29+/-5 % with Hypertension: 41 % with history of CVD: 0 % with Type 2 diabetes: 0 % with Kidney disease: 0 % with history of Kidney stones: 0</p> <p>Comparator: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: 22 years old or more, average systolic blood pressure 120 to 159 mm Hg (over 3 visits) and average diastolic blood pressure 80 to 95 mm Hg Exclusion: heart disease, renal insufficiency, poorly controlled hyperlipidemia or diabetes mellitus, diabetes requiring insulin, special dietary requirements, more than 14 alcoholic drinks per week, or use of antihypertensive drugs or other medications that would affect blood pressure or nutrient metabolism</p>	<p>Intervention Type: Intervention 1: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control High Sodium: To replicate typical diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve high sodium intake Dose: 150 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Intermediate Sodium: To replicate typical diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve intermediate sodium intake Dose: 100 mmol sodium/d in control diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: Control Low Sodium: To replicate typical diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to achieve low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: NR Description: DASH High Sodium: To impose DASH diet with high sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with high sodium intake Dose: 150 mmol sodium/d in DASH diet Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 4: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH intermediate Sodium:</p>	<p>Sodium measure: Chemical analysis of diet with intervention/exposure adherence measure, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Sodium, Method of Validation: NR, Chemical analysis of diet with intervention/exposure adherence measure Sodium Status Intervention 1: 141+/-55 mmol/d Sodium Status Intervention 2: 106+/-44 mmol/d Sodium Status Comparator: 64+/-37mmol/d Sodium Status Intervention 3: 144+/-58 mmol/d Sodium Status Intervention 4: 107+/-52 mmol/d</p> <p>Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Single 24-hour urine analysis without validation measured at least 4 times, 4 weeks apart; chemical analysis of diet; Food diaries completed daily without validation; Potassium, Method of Validation: Adherence checks via food diaries, supervised meals Potassium Status Intervention 1: 40+/-14 mmol/d Potassium Status Intervention 2: 41+/-14 mmol/d Potassium Status Comparator: 42+/-14 mmol/d Potassium Status Intervention 3: 75+/-27 mmol/d Potassium Status Intervention 4: 81+/-31 mmol/d</p> <p>How was blood pressure measured? Random-zero sphygmomanometers, seated, 3 times during screening, weekly during 1st 3 weeks of intervention periods, and 5 times during last 9 days of intervention periods</p>	<p>Subgroup: Normotensive Diastolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.10 (95% CI: -2.00 - -0.10) Comparison: Intervention 1 vs Comparator MD -2.80 (95% CI: -3.80 - -1.90) Systolic BP Follow-Up Time: 30 days Comparison: Intervention 3 vs Intervention 5 MD -1.70 (95% CI: -3.10 - -0.30) Comparison: Intervention 1 vs Comparator MD -5.60 (95% CI: -7.00 - -4.10)</p>
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Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
		<p>To impose DASH diet with intermediate sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with intermediate sodium intake Dose: 100 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Prescribed or synthetic diet (all food provided) with sodium quantified Description: DASH Low Sodium: To achieve DASH diet with low sodium content Form of Administration: Dietary Modification: All foods provided, menu designed to follow DASH with low sodium intake Dose: 50 mmol/d Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 periods of 30 days each, including run-in Exposure to Follow Up Time: 0 months</p>		

Table D22. Subgroup table for trials for pregnancy

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Steegers, 1991¹⁰³</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 42</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 27 (Range: 20-34) Race: NR Systolic BP: 122 Diastolic BP: 71 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 69.4 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 27 (Range: 22-35) Race: NR Systolic BP: 125 Diastolic BP: 72 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 65.8 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: nulliparous healthy women with singleton pregnancies</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Target of 20 mmol sodium daily Form of Administration: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Continue unrestricted dietary intake Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 5-6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation, Food diaries with reported validation Best sodium measure recorded: Measured at 12, 16, 20, 24, 28, 32 and 36 weeks of gestation and then at 1 and 6 weeks postpartum Sodium Status Intervention 1: 58 mmol/24h</p> <p>How was blood pressure measured? BP was measured after patients rested for 5 minutes in a sitting position with an automatic microcomputer assisted instrument (Dinamap).</p>	<p>Subgroup: Diastolic BP-sitting Follow-Up Time: 22 weeks Comparison: Intervention 1 vs Comparator MD 2.00 (95% CI: -3.54 - 7.54) Systolic BP-sitting Follow-Up Time: 22 weeks Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -7.93 - 5.93)</p>
<p>Van Buul, 1997¹⁰⁴</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p>	<p>Study of: Both adults and children N: 270</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 28.1 (min 19.8, max 41.3) Race: NR Systolic BP: 120 Diastolic BP: 65 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Diet containing about 20 mmol/day of sodium Form of Administration: Dietary Modification: Trained dietitians gave oral and written dietary instructions as well as guidance throughout pregnancy Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 11 times over 8.5 months Sodium Status Intervention 1: 75 mmol /24 h</p> <p>How was blood pressure measured? After resting for 5-min, BP was measured in the sitting position using an automatic device (Dinamap 1846 SX, Critikon Inc, Tampa, FL) with an adequately sized cuff. The average of 2 measurements was used for</p>	<p>Subgroup: Diastolic BP-sitting Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.53 - 0.53) Incidence of gestation hypertension Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator RR 0.95 (95% CI: 0.50 - 1.81) Systolic BP-sitting Follow-Up Time: 34 weeks Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -6.54 - 0.54)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
Study Years: 1986-1993	% with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 28.3 (min 18.1, max 40.5) Race: NR Systolic BP: 121 Diastolic BP: 68 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.5 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Women with healthy nulliparous pregnant woman with singleton pregnancies were considered Exclusion: Preexisting hypertension, diabetes mellitus, cardiovascular disorder, renal diseases.	Comparator: Usual Diet Description: No dietary restrictions Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR Duration: 6 months Exposure to Follow Up Time: 1.5 months	analysis. BP was taken a 9 times over the study period	

Table D23. Subgroup table for trials for pregnancy, hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Knuist, 1998¹⁰⁵</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: 1992-1994</p>	<p>Study of: Adults N: 361</p> <p>Intervention 1: % Male: 0 Mean Age/Range/Age at Baseline: mean 27.6 (SD 4.2) Race: NR Systolic BP: NR Diastolic BP: 74.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 70.4 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 0 Mean Age/Range/Age at Baseline: mean 27.5 (SD 4.8) Race: NR Systolic BP: NR Diastolic BP: 75 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 69.7 Kg % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Dutch-speaking nulliparous women, with a DBP pressure < 90 mmHg at their first prenatal visit, taking place before 20 weeks of gestation Exclusion: Women planning to move to another city, conditions associated with an increased risk of pregnancy induced hypertension (for example: diabetes, twins, pre-existing hypertension or renal disease).</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Decrease salt intake, < 50 mmol sodium Form of Administration: Dietary Modification: Low salt diet, Written dietary instructions were given by the midwives Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: Until delivery Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: 12 times during pregnancy Sodium, Method of Validation: Creatinine was measured to compare completeness of the 24-hour urine sampling Sodium Status Intervention 1: 84 mmol/24h</p> <p>How was blood pressure measured? BP was measured with the subject in the sitting position, using the same arm with a portable oscillometric sphygmomanometer. Two consecutive readings of at a minimum of four hours apart were required to assign the highest diastolic blood pressure,</p>	<p>Subgroup: Diastolic BP-sitting Follow-Up Time: 35 days Comparison: Intervention 1 vs Comparator MD 0.00 (95% CI: -2.29 - 2.29)</p>

Table D24. Subgroup table for trials for race/ethnicity, gender

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Hypertension Prevention Collaborative Research Group, 1997¹⁰⁶; Hebert, 1995¹⁰⁷; Cook, 2005¹⁰⁸; Kumanyika, 2005¹⁰⁹; Cook, 2007²⁸; Lasser, 1995¹¹⁰; Appel, 1995¹¹¹; Hunt, 1998¹¹²; Hollis, 1995¹¹³; Cook, 2016³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trials of Hypertension Prevention (TOHP)</p> <p>Number of Sites: 9</p> <p>Study Years: 1990-1992</p>	<p>Study of: Adults N: 2382</p> <p>Intervention 1: % Male: 64.8 Mean Age/Range/Age at Baseline: mean 44.2 (SD 6.1) Race: white 81.1% Systolic BP: 127.7 Diastolic BP: 86.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 68.3 Mean Age/Range/Age at Baseline: mean 43.2 (SD 6.1) Race: white 79.5% Systolic BP: 127.3 Diastolic BP: 85.8 Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Inclusion: healthy, moderately overweight, 30- to 54-year-old adults (men and women) with a high-normal DBP Exclusion: -Evidence of current hypertension -History of: cardiovascular disease, Diabetes mellitus, malignancy other than nonmelanoma skin cancer during the past 5 y, any other serious life-threatening illness that requires regular medical treatment -Men with BMI < 26.1 or > 37.4; Women with a BMI < 24.4 or > 37.4 kg/m -Current use of prescription medications that affect blood pressure, as well as nonprescription diuretics -Men with Serum creatinine level > 1.7 mg/dL for men or Women with Serum creatinine level > 1.5 mg/dL. Casual serum glucose 200 mg/dL, as determined locally -Current alcohol intake > 21 drinks/wk -For women, current pregnancy or intent to become pregnant during the study -Other: such as planned residence distant from the clinical center or inability to cooperate</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: 1800 mg (80 mEq) sodium or less per day, Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 7 times, 6 months apart Sodium Status Intervention 1: 135.2 mmol/d Potassium Status Intervention 1: NR</p>	<p>Subgroup: White women; overweight-obese, high-normal BP Cumulative incidence of HTN Follow-Up Time: 36 -48 months Comparison: Intervention 1 vs Comparator RR 1.05 (95% CI: 0.80 - 1.38) Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -1.50 (95% CI: -3.00 - 0.00) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -1.60 (95% CI: -3.90 - 0.70)</p> <p>Subgroup: White men; overweight-obese, high-normal BP Cumulative incidence of HTN Follow-Up Time: 36 -48 months Comparison: Intervention 1 vs Comparator RR 1.21 (95% CI: 0.99 - 1.47) Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -0.30 (95% CI: -1.30 - 0.70) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -2.23 - 0.23)</p> <p>Subgroup: Black women; overweight-obese, high-normal BP Cumulative incidence of HTN Follow-Up Time: 36 -48 months Comparison: Intervention 1 vs Comparator RR 1.24 (95% CI: 0.89 - 1.73) Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -2.40 (95% CI: -4.26 - -0.54) Systolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -3.00 (95% CI: -5.40 - -0.60)</p> <p>Subgroup: Black men; overweight-obese, high-normal BP Cumulative incidence of HTN Follow-Up Time: 36 -48 months Comparison: Intervention 1 vs Comparator RR 1.09 (95% CI: 0.70 - 1.68) Diastolic BP-sitting Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD 1.30 (95% CI: 0.16 - 2.44) Systolic BP-sitting Follow-Up Time: 36 months</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
				Comparison: Intervention 1 vs Comparator MD 0.50 (95% CI: -0.85 - 1.85)
<p>The Trials of Hypertension Prevention Collaborative Research Group, 1992²⁰; Erratum, 1992²¹; Satterfield, 1991²²; Whelton, 1992²³; Whelton, 1997²⁴; He, 1999²⁵; Kumanyika, 1993²⁶; Whelton, 1994²⁷; Cook, 2007²⁸; Cook, 1998²⁹; Yamamoto, 1995³⁰; Cook, 2016³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p> <p>Number of Sites: 10</p> <p>Study Years: 1987-1995</p>	<p>Study of: Adults N: 744</p> <p>Intervention 1: % Male: 70.9 Mean Age/Range/Age at Baseline: mean 43.4 (SD 6.6) Race: 78 Systolic BP: 124.8 Diastolic BP: 83.7 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.7 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 2: % Male: 69.7 Mean Age/Range/Age at Baseline: mean 43.1 (SD 6.6) Race: 84 Systolic BP: 122.6 Diastolic BP: 81.1 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 83.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Intervention 3: % Male: 74.7 Mean Age/Range/Age at Baseline: mean 42.8 (SD 6.5) Race: white 88.8% Systolic BP: 120.7 Diastolic BP: 80.8 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 81.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 71.7 Mean Age/Range/Age at Baseline: mean 42.6 (SD 6.5)</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: NR Form of Administration: Dietary Modification: Life-style interventions, provided by psychologists, nutritionists, or other experienced counselors, mostly group educational sessions, with some individual counseling Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 2: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Other: placebo Dose: Placebo Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Intervention 3: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: NR Dose: potassium chloride, 60 mmol/day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Participants asked not to change their usual diet Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: Lifestyle intervention 18 months; Nutritional supplement 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Intervention 1: 99.4 mmol/24 h Sodium Status Intervention 2: NR Sodium Status Intervention 3: NR Best potassium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Potassium Status Intervention 1: NR Potassium Status Intervention 2: Change from baseline -2.4 mmol/24 h Potassium Status Intervention 3: Change from baseline 37.4 mmol/24h</p> <p>How was blood pressure measured? Collected at 0, 3, 6, months, 12 and 18 months for lifestyle groups. BP was measured with a Hawksley random-zero sphygmomanometer, after sitting at rest for 5 minutes . The average of three readings (first and fifth Korotkoffs sounds) were recorded at each visit.</p>	<p>Subgroup: White women Diastolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -1.50 (95% CI: -3.50 - 0.50) Systolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.00 - -1.00)</p> <p>Subgroup: White men Diastolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -1.50 (95% CI: -2.40 - -0.20) Systolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -2.50 - 0.50)</p> <p>Subgroup: Black women Diastolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -1.50 (95% CI: -4.00 - 1.00) Systolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -4.20 (95% CI: -8.00 - -1.00)</p> <p>Subgroup: Black men Diastolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -0.50 (95% CI: -3.50 - 2.50) Systolic BP-sitting Follow-Up Time: 18 months Comparison: Intervention 1 vs Comparator MD -3.25 (95% CI: -7.75 - 1.25)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Race: white 76.5% Systolic BP: 125.1 Diastolic BP: 83.9 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight, kg mean 82.8 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Healthy adults, ages 30-54 with high normal DBP, not taking antihypertensive drugs for the prior 2 months Exclusion: Clinical or lab evidence of cardiovascular or other disabling or life threatening diseases. Conditions that would contraindicate or require any of the interventions. Unwillingness or inability to comply with data collection or intervention procedures.</p>			

Table D25. Subgroup table for trials for race/ethnicity, hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Miller, 2016¹⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2012-2013</p>	<p>Study of: Adults N: 123</p> <p>Intervention 1: % Male: 34 Mean Age/Range/Age at Baseline: mean 58.8 (SD 8.7) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 34.9 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 34 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 25 Mean Age/Range/Age at Baseline: mean 58.5 (SD 10.4) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 34.1 % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: 21 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Electronic medical record diagnosis of hypertension; age \geq21 years; self-reported African American race; average SBP of 120–140 mmHg or DBP of 80–90 mmHg at the two most recent clinic visits, stable doses of antihypertensive medications for at least 2 months prior to randomization Exclusion: Self-report of a cardiovascular event in last 6 months; a chronic disease that might interfere with trial participation (e.g., CKD defined as an estimated glomerular filtration rate \leq60 mL/minute); unwillingness or inability to adopt a DASH-like diet; consumption of $>$14 alcoholic drinks a week; poorly controlled diabetes (hemoglobin A1c \geq9%); or use of insulin. Individuals using potassium supplements could enroll if they were willing to stop supplements 1 month prior to randomization and refrain throughout the study.</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Received coach-directed dietary advice and assistance with weekly (\$30/week) online ordering/purchasing of high-potassium foods delivered by a community supermarket to a local library Form of Administration: Dietary Modification: NR Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Received a printed DASH diet brochure and a debit account with equivalent value to that of the intervention group. Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>Sodium, Method of Validation: 24-hour "diet recall" Potassium measure: Spot fasting urine taken. But primary comparisons report pre-post intervention effects using creatinine-normalized measures as an indicator of adherence to the dietary intervention Best potassium measure recorded: Taken 2 time s at baseline and 8 weeks Potassium Status Intervention 1: 54 mmol/g creatinine</p> <p>How was blood pressure measured? Measured 5 times: two times during screening visits, once at randomization, then at 3 and 8 weeks follow up. BP taken using an OMRON 907-XL automated BP machine programmed with a 5-minute delay followed by three measurements separated by 30 seconds. Certified trained staff performed and recorded all three measures averaged them at each visit. The average BP of the Screening Visits 1 and 2 established baseline BP, and the average BPs measured at Weeks 3 and 8 were used to determine intervention effects.</p>	<p>Subgroup: African American, HTN Diastolic BP-NS (machine) Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD 1.30 (95% CI: -1.30 - 3.90) Systolic BP-NS (machine) Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD 1.50 (95% CI: -2.57 - 5.57)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Obel, 1989¹¹⁵</p> <p>Location: Nairobi</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 48</p> <p>Intervention 1: % Male: 47.82% Mean Age/Range/Age at Baseline: 40 (SD 9) Race: NR Systolic BP: Standing: 171; Supine 174 Diastolic BP: Standing 103; Supine 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 41.67 Mean Age/Range/Age at Baseline: 40 (SD 8) Race: NR Systolic BP: Standing: 167; Supine 173 Diastolic BP: Standing: 101; Supine 100 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Mild hypertension, age 20-60, 90<DBP<109, SBP >160, serum potassium <4.5 mM, serum creatinine 60-130 uM</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: Oral potassium supplement Dose: 8 tablets of 64 mmol potassium per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: NR Form of Administration: Other: Oral placebo Dose: 8 placebo tablets per day Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 4 months Exposure to Follow Up Time: NR</p>	<p>Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times, 16 weeks apart Potassium Status Intervention 1: 102 mmol/24 h</p> <p>How was blood pressure measured? Supine, Standing, patients rested for 30 minutes before readings. Same observer using a Hawksley random zero sphygmomanometer, each record was the mean of two readings. 5 minutes equilibrium period was taken between readings. Measured 5 times, 4 weeks apart.</p>	<p>Subgroup: Black, mild HTN Diastolic BP-supine Follow-Up Time: 16 weeks Comparison: Intervention 1 vs Comparator MD -17.00 (95% CI: -19.26 - -14.74) Systolic BP-supine Follow-Up Time: 16 weeks Comparison: Intervention 1 vs Comparator MD -39.00 (95% CI: -43.88 - -34.12)</p>
<p>Svetkey, 1987⁸⁵</p> <p>Location: US</p> <p>Setting:</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 2</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 116</p> <p>Intervention 1: % Male: 76 Mean Age/Range/Age at Baseline: mean 51.3 (SD 12.3) Race: white 89% Systolic BP: 147.5 Diastolic BP: 95.2 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 83.8 (SD 14.4) kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: NR Form of Administration: NR Dose: 120 mEq/ day potassium Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Usual diet, placebo Form of Administration: NR Dose: Placebo Na/K ratio: NR Magnesium: NR</p>	<p>Sodium Status Intervention 1: NR Potassium measure: Compliance assessed by pill count Best potassium measure recorded: 0 Potassium, Method of Validation: Compliance assessed by pill count. Potassium Status Intervention 1: NR</p> <p>How was blood pressure measured? Measured 2-4 times, weekly during run in, 4 times every 2 weeks during trial. During each visit, three blood pressure measurements were recorded and the average value was considered to be the blood pressure for that day. BP measurements taken at the same time of day and by the same staff. using a random</p>	<p>Subgroup: Mild HTN, Blacks Diastolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -13.00 (95% CI: -22.83 - -3.17) Systolic BP-sitting Follow-Up Time: 8 weeks Comparison: Intervention 1 vs Comparator MD -20.00 (95% CI: -41.67 - 1.67)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Comparator: % Male: 72 Mean Age/Range/Age at Baseline: mean 50.9 (SD 12.3) Race: White 83% Systolic BP: 142.1 Diastolic BP: 147.5 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: weight mean 81.7 (SD 11.9) Kg % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Ambulatory hypertensive adults Exclusion: history or physical examination revealed any of : a single DBP> 114 mm Hg, prior episode of malignant hypertension or hypertensive encephalopathy, angina, myocardial infarction within the prior 6 months, CHF, arrhythmia, transient ischemic, cerebrovascular accident, attacks, the presence of a terminal illness. Secondary hypertension excluded by physical examination, history, serum electrolyte levels, and measurements of renal function (plasma creatinine concentration, creatinine clearance, and complete urinalysis). Patients who might be at risk from high potassium intake were also excluded: those with renal insufficiency or baseline serum potassium values > 5.0 mEq/L, patients taking digitalis preparations, and those with chronic diarrhea or history of ulcer disease. Pregnant and nursing women.</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Duration: 2 months Exposure to Follow Up Time: NR</p>	<p>zero sphygmomanometer (Hawksley and Sons, Lancing, Sussex, England) where the subject was seated for 10 minutes before the readings. DBP was recorded as the fifth Korotkoff sound. Patients were advised not to smoke or eat for 30 minutes before each blood pressure reading.</p>	

Table D26. Subgroup table for trials for renal health status

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Barcelo, 1993¹¹⁶</p> <p>Location: NR</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 57</p> <p>Participants: % Male: 43.8 Mean Age/Range/Age at Baseline: mean 44 (SD 11) Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 0 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Documented active calcium nephrolithiasis concomitant with an isolated hypocitraturic abnormality</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of potassium supplement to increase potassium levels Description: Potassium tablets + advised to increased ingestion of fluids (2 to 3 l. a day) and reduced sodium intake Form of Administration: Oral potassium supplement Dose: 20 mEq. (4 tablets) potassium citrate 3 times a day right after meals. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Placebo + advised to increased ingestion of fluids (2 to 3 l. a day) and reduced sodium intake Form of Administration: Placebo Dose: placebo tablets as potassium citrate groups and at the same dosage and schedule. Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 36 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: Taken at baseline, at 3 months, 6 months, then every 6 months for the remainder of the 3 years Sodium, Method of Validation: Single 24-hour urine analysis with validation Best potassium measure recorded: Taken at baseline, at 3 months, 6 months, then every 6 months for the remainder of the 3 years Potassium Status Intervention 1: 3.36 mmol/day</p>	<p>Subgroup: Nethrolithiasis+hypocitraturia Decrease quality of life Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator RR 0.48 (95% CI: 0.05 - 5.03) Stone formation rate (number per patient year) Follow-Up Time: 36 months Comparison: Intervention 1 vs Comparator MD -1.00 (95% CI: -1.16 - -0.84)</p>
<p>de Brito-Ashurst, 2013¹¹⁷</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 1</p> <p>Study Years: 2008-2009</p>	<p>Study of: NR N: 56</p> <p>Intervention 1: % Male: 56 Mean Age/Range/Age at Baseline: mean 55.7 (SD 15.1) Race: Bangladesh: 100% Systolic BP: 149.3 Diastolic BP: 85 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 26.6 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 17 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 61 Mean Age/Range/Age at Baseline: mean 60.7 (SD 12) Race: Bangladesh: 100%</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Tailored low-salt diet, educational, community sessions Form of Administration: Dietary Modification: Tailored low-salt diet, educational, community sessions Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Low sodium general dietary advice sheet sent by post with the physician's letter Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: 2 times 6 months apart Sodium Status Intervention 1: 138 mmol/24 h Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times 6 months apart</p> <p>How was blood pressure measured? BP was taken using TM-2430-13 devices. Daytime measures were taken at 30 min intervals, night-time measures every 60 min. BP collected 2 times 1 time at baseline then at 6 months post intervention</p>	<p>Subgroup: Chronic kidney disease (CKD), eGFR < 60 mL/min, Asian 24h Ambulatory DBP-night time Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -4.00 (95% CI: -9.00 - -1.00) 24h Ambulatory SBP-daytime Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -9.00 (95% CI: -13.00 - -5.00) Deaths Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator RR NC (95% CI: NC - NC)</p>

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
	<p>Systolic BP: 156 Diastolic BP: 85 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 27.1 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 14 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: Estimated glomerular filtration rate (eGFR) <60 mL/min and mean SBP >130/80 mm Hg on at least 2 clinic visits or taking antihypertensive medication.</p> <p>Exclusion: Patients on dialysis, those with a BMI <20 or >35 kg/m², urinary incontinence, or cognitive impairment. Mental problems impairing their ability to participate were excluded</p>	<p>Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>		

Table D27. Subgroup table for trials for renal health status, diabetes, hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Mulhauser, 1996¹¹⁸</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: multiple</p> <p>Study Years: unclear</p>	<p>Study of: Adults N: 16</p> <p>Intervention 1: % Male: 87.5 Mean Age/Range/Age at Baseline: mean 37 (SD 9) Race: NR Systolic BP: 139 Diastolic BP: 88 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 25.2 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 62.5 Mean Age/Range/Age at Baseline: mean 35 (SD 11) Race: NR Systolic BP: 134 Diastolic BP: 87 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 24.9 % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: IDDM on intensified insulin therapy, ages 18 -60 years, duration of diabetes more than 5 years, increased proteinuria (> 60 mg/24 h in a minimum of two of three 24-h urine samples). Exclusion: Urinary tract infection, drugs (including oral contraceptives) except insulin, stable retinopathy, pregnancy and effective contraception; untreated 140< SBP < 160 mmHg and/or 85<DBP < 100 mmHg. A history of short-term treatment with antihypertensive drugs in the 4 weeks before start of study</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Use of salt pills to increase sodium intake Description: Sodium intake of 190 mmol/day Form of Administration: Sodium supplement Dose: 100 mmol/day sodium supplement consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Placebo Description: Sodium intake of 90 mmol/day Form of Administration: Placebo Dose: placebo consumed Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 3 months Exposure to Follow Up Time: NA</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, Food diaries with reported validation Best sodium measure recorded: weekly for 12 weeks Sodium, Method of Validation: counting the number of returned pills, Multiple 24-hour urine analysis with validation Sodium Status Intervention 1: 199 mmol/day Potassium measure: Food diaries without reported validation Best potassium measure recorded: weekly for 12 weeks Potassium Status Intervention 1: 94 mmol/day</p> <p>How was blood pressure measured? BP Measured 12 times, over 12 weeks. Under standardized conditions with a random zero sphygmomanometer (Hawksley, Lancing, UK). For examinations 1-3: Two supine and two sitting blood pressure measurements were taken, the mean all four measurements was used for analysis. For examinations 4 to 12): after the patient had a 10-min rest in the supine position, four supine measurements were taken at 5- min intervals. After another 5 min of rest in the sitting position, four sitting measurements were taken at 5-min intervals. The mean of all eight measurements used in the analysis.</p>	<p>Subgroup: Diabetic with nephropathy Diastolic-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -5.30 (95% CI: -10.15 - -0.45) Systolic-supine Follow-Up Time: 4 weeks Comparison: Intervention 1 vs Comparator MD -4.90 (95% CI: -13.95 - 4.15)</p>

Table D28. Subgroup table for trials for renal health status, hypertension

Study	Participants	Intervention(s)	Intake Status Ascertainment	Findings - Outcomes and Comparison
<p>Meuleman, 2016¹⁹</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Number of Sites: 4</p> <p>Study Years: 2011-2014</p>	<p>Study of: Adults N: 151</p> <p>Intervention 1: % Male: 79; Mean Age/Range/Age at Baseline: mean 55.6 (SD 11.7) Race: NR; Systolic BP: 142 Diastolic BP: 87 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7 % with Hypertension: NR % with history of CVD: 36 % with Type 2 diabetes: 30 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Comparator: % Male: 85 Mean Age/Range/Age at Baseline: mean 54.7 (SD 16) Race: NR Systolic BP: 137 Diastolic BP: 83 Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: 29.7 % with Hypertension: NR % with history of CVD: 39 % with Type 2 diabetes: 21 % with Kidney disease: 100 % with history of Kidney stones: NR</p> <p>Inclusion: moderately decreased kidney function, Dutch speaking, >=18 years old, Being treated by an internist, Protein excretion measurements . 0.2 g/L or 0.3 g/24 h, 2 recent sodium excretion measurements > 120 mmol/24 h, BP >135/85 mm Hg or controlled BP with the use of anti-hypertensive medication, among which at least 1 RAAS blockade. Exclusion: BP >180/100 mm Hg or < 125/75 mm Hg, received a kidney transplant less than 1 y ago, diagnosed with type 1 diabetes, had acute kidney failure, accelerated kidney function decrease (> 6 mL/min/1.73 m2 in previous year). Had a cardiovascular event (ie, MI or cerebrovascular event) < 6 mo ago. diagnoses of malignancy within 5 years (other than basal cell or squamous cell carcinoma of skin), participating in other clinical trial that included medication</p>	<p>Intervention Type(s):</p> <p>Intervention 1: Dietary/lifestyle counseling (single or multiple sessions, including dietary advice) to reduce sodium intake Description: Usual care + counselling, education, motivational interviews to reduce sodium in diet Form of Administration: Dietary Modification: counselling, education, motivational interviews to reduce sodium in diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Comparator: Usual Diet Description: Regular care Form of Administration: Usual diet Dose: NR Na/K ratio: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Duration: 6 months Exposure to Follow Up Time: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: once a week in the first 6 weeks then every 2 or 3 weeks Sodium Status Intervention 1: 157 mmol/24h</p> <p>How was blood pressure measured? Office BP was measured Microlife WatchBP Home after 5 minutes of rest, the average of 3 measurements was used. Ambulatory BP was measured with validated Spacelabs 90207 and 90217 devices. Monitors were programmed for 24 hours with 15-minute day intervals and 30-minute night intervals.</p>	<p>Subgroup: CKD, hypertensive 24h Ambulatory DBP Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -4.22 - 0.22) 24h Ambulatory SBP Follow-Up Time: 6 months Comparison: Intervention 1 vs Comparator MD -2.00 (95% CI: -5.33 - 1.33)</p>

Table D29. Subgroup table for observational studies for age < 60

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 1767</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0</p> <p>Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years</p> <p>Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8%</p> <p>Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg</p> <p>Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m²</p> <p>% with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8</p> <p>% with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7</p> <p>% with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included.</p> <p>Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for age <60</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 times, 1 year apart</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1759</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among age<60 participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1760</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among age<60 participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase–MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed profusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1766</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among age<60 participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1767</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among age<60 participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p>

Table D30. Subgroup table for observational studies for age >= 60

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 1775</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0</p> <p>Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years</p> <p>Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8%</p> <p>Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg</p> <p>Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m²</p> <p>% with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8</p> <p>% with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7</p> <p>% with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included.</p> <p>Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for age >=60</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1769 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among age>=60 participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1773 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among age>=60 participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed profusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1774 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among age>=60 participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1775 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among age>=60 participants, greater sodium excretion was associated with an increased risk of composite CVD.</p>

Table D31. Subgroup table for observational studies for Asian

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among Asian participants.</p>

Table D32. Subgroup table for observational studies for BMD <30

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range G1, Dose: <3 G2, Dose: 3-5.99 G3, Dose: >=6</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p>

Table D33. Subgroup table for observational studies for BMI <30

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those BMI<30.</p>
<p>Cook, 2009¹²⁵; Satterfield, 1991²²; Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p>	<p>Study of: Adults N: 1286</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; >= 125, 839; women: <125, 298; >= 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30. 777; >= 30 586; Women, <25 138; 25 to <30 279; >= 30 288.</p> <p>% with Hypertension: NR</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio</p> <p>Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR</p> <p>NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome): Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II FU</p> <p>NR cases: 100, total: 1286</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise</p> <p>Among BMI<30 participants, no association between sodium to potassium excretion ratio and risk of CVD adjusting for treatment assignment.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Follow-up (TOHP I and TOHP II)	% with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included. Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.		Outcomes-Method of ascertainment: medical records	

Table D34. Subgroup table for observational studies for BMI \geq 30

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2009¹²⁵; Satterfield, 1991²²; Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p> <p>Follow-up (TOHP I and TOHP II)</p>	<p>Study of: Adults N: 798</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; \geq 125, 839; women: <125, 298; \geq 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30, 777; \geq 30 586; Women, <25 138; 25 to <30 279; \geq 30 288.</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included.</p> <p>Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio</p> <p>Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR</p> <p>NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: medical records</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome):</p> <p>Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II FU</p> <p>NR cases: 66, total: 798</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise</p> <p>Among BMI\geq30 participants, there is a significant positive association between sodium to potassium excretion ratio and risk of CVD, adjusting for treatment assignment.</p>

Table D35. Subgroup table for observational studies for BMI ≤30 + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised Assessment Study in ACEiswcdI., 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141.72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: stroke 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged ≥55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 μmol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D36. Subgroup table for observational studies for BMI >30 + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised Assessment Study in ACEiswcdI., 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141.72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: stroke 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged ≥55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D37. Subgroup table for observational studies for BMI \geq 30

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: \geq6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those BMI\geq30.</p>

Table D38. Subgroup table for observational studies for Black

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2009¹²⁵; Satterfield, 1991²²; Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p> <p>Follow-up (TOHP I and TOHP II)</p>	<p>Study of: Adults N: 284</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; >= 125, 839; women: <125, 298; >= 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30, 777; >= 30 586; Women, <25 138; 25 to <30 279; >= 30 288.</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included. Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome): Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II NR cases: 19, total: 284</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise Among Black participants, no association between sodium to potassium excretion ratio and risk of CVD adjusting for treatment assignment.</p>
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 1472</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0</p> <p>Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years</p> <p>Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8%</p> <p>Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg</p> <p>Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m²</p> <p>% with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7;</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for Black</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1460</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1461</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4; 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>			<p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase–MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1468 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among black participants, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1472 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among black participants, greater sodium excretion was associated with an increased risk of composite CVD.</p>

Table D39. Subgroup table for observational studies for Black men

Study	Participants	Exposure	Intake Status Ascertainment	Results
Fang, 2000 ¹³¹ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES I	Study of: Adults N: 595 % Male: 38.2 Mean Age/Range/Age at Baseline: NR Race: 83.5 white Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: NHANES I survey participants aged between 25-74 during baseline examination. Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.	Exposure Type: Dietary potassium intake Exposure Unit: mg/d Duration: NR Exposure to Follow Up Time: up to 22 years Dose format: range T1, Dose: <1260 T2, Dose: 1260-2206 T3, Dose: >2206	Sodium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates	Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome): Average 16.7 years FU T1 cases: 14, total: 198, T2 cases: 11, total: 199, T3 cases: 3, total: 198 Adjustment: Age Men in the lowest tertile of dietary potassium intake, both black and white, had significantly higher stroke mortality than did those with the highest intake. With the highest tertile as reference, the relative risk (RR) for blacks in the lowest tertile (RR, 4.27; 95% CI, 1.88 to 9.19) was more than double than that for whites (RR, 1.66; 95% CI, 1.32 to 2.14).

Table D40. Subgroup table for observational studies for Black women

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fang, 2000¹³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: 1029</p> <p>% Male: 38.2</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: 83.5 white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination.</p> <p>Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	<p>Exposure Type: Dietary potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 22 years</p> <p>Dose format: range</p> <p>T1, Dose: <1017</p> <p>T2, Dose: 1017-1641</p> <p>T3, Dose: >1641</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p>	<p>Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome):</p> <p>Average 16.7 years FU</p> <p>T1 cases: 14, total: 343, T2 cases: 17, total: 343, T3 cases: 16, total: 343</p> <p>Adjustment: Age</p> <p>Among women, regardless of race, there was no significant difference in stroke mortality by tertile of dietary potassium intake.</p>

Table D41. Subgroup table for observational studies for boys

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Krupp, 2015¹³²; Shi, 2014¹³³; Kruppe, 2014¹³⁴; Kroke, 2004¹³⁵</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p>	<p>Study of: Children N: 108</p> <p>% Male: 52.4% Mean Age/Range/Age at Baseline: 3 months Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: by gender boys mean 18.9 (SD 2.3) girls mean 18.7 (SD 2.7)</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included Germans recruited at 3 months of age and who completed three repeated urinary, dietary and blood pressure measurements in adolescence and one additional blood pressure measurement in young adulthood. Exclusion: Excluded those who were born before 36 weeks gestation and those with missing data.</p>	<p>Exposure Type: Daily sodium excretion Exposure Unit: mmol/day</p> <p>Duration: NR Exposure to Follow Up Time: an average of 12 years</p> <p>Dose format: continuous All, Dose: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 repeated 24-hour urine analysis with validation Sodium, Method of Validation: Minimized errors with creatinine excretion cutoff., Multiple 24-hour urine analysis with validation Best potassium measure recorded: 3 repeated 24-hour urine analysis with validation Potassium, Method of Validation: Minimized errors with creatinine excretion cutoff.</p> <p>How was blood pressure measured? Two blood pressure readings for each BP measurement was assessed by trained nurses with first a random zero sphygmomanometer and with a standard mercury sphygmomanometer. BP values measured with a standard zero sphygmomanometers were multiplied with an internally validated conversion factor (e.g., 1.056 for systolic BP).</p>	<p>Systolic blood pressure (Random-zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer thereafter.) (mmol/day/Outcome): 7 years FU All cases: NR, total: 108 Adjustment: Primary model 2: mean pubertal systolic BP SDS and adult age, standardized energy intake, intake of saturated fat (g/day), height SDS, maternal education, maternal BP Higher sodium excretion is significantly associated with higher systolic blood pressure in boys.</p>

Table D42. Subgroup table for observational studies for CKD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 3757</p> <p>% Male: by sodium excretion group g1 37.8% g2 48.1% g3 64% g4 72.4%</p> <p>Mean Age/Range/Age at Baseline: by sodium excretion group g1 mean 59.7 (SD 10.6) g2 mean 58.4 (SD 10.9) g3 mean 57.6 (SD 10.9) g4 mean 55.2 (SD 10.8)</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: by sodium excretion group g1 mean 29.1 (SD 6.9) g2 mean 31.2 (SD 7.2) g3 mean 32.4 (SD 6.8) g4 mean 34.9 (SD 8.1)</p> <p>% with Hypertension: by sodium excretion group g1 83.4% g2 84.5% g3 88.5% g4 87.9%</p> <p>% with history of CVD: by sodium excretion group g1 31.3% g2 35.4% g3 32.3% g4 33%</p> <p>% with Type 2 diabetes: by sodium excretion group g1 40.2% g2 48% g3 47.7% g4 55.2%</p> <p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included CRIC Study participants with eGFR between 20 and 70 ml/min per 1.73 m2 depending on age. Exclusion: Excluded participants who received dialysis, or a kidney transplant and excluded those with GN requiring immunosuppression, with advanced heart failure, cirrhosis, or polycystic kidney disease. Also excluded participants without a 24-hour urine specimen or with incomplete 24-hour urine collection. And excluded those with urinary sodium excretion less than 20 mmol/24 h.</p>	<p>Exposure Type: 24-h urinary potassium Exposure Unit: mmol/24h</p> <p>Duration: NR Exposure to Follow Up Time: 0</p> <p>Dose format: range Q1, Dose: <39.4 Q2, Dose: 39.4-52.1 Q3, Dose: 52.2-67 Q4, Dose: >=67.1</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2). Sodium, Method of Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method., Multiple 24-hour urine analysis with validation Best potassium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2). Potassium, Method of Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method. Mortality Outcomes-Method of Ascertainment: Death certificate CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit, US Renal Data System</p>	<p>All-cause mortality (Death from all causes) (mmol/24h/Outcome): 20,465 person-years FU Q1 cases: 177, total: 939, person-years: 5042, Q2 cases: 150, total: 940, person-years: 5088, Q3 cases: 110, total: 938, person-years: 5139, Q4 cases: 103, total: 940, person-years: 5196</p> <p>Adjustment: Age, sex, race, urinary creatinine excretion, and clinic site. education, waist circumference, lean body mass, body mass index, cigarette smoking, alcohol drinking, physical activity, history of hypercholesterolemia, history of diabetes, history of CVD, use of diuretics, use of renin-angiotensin system blocking agents, and use of other antihypertensive medications. baseline eGFR. plus adjustment for urinary sodium excretion</p> <p>No significant association between urinary potassium excretion and risk of all-cause mortality among CKD patients. No significant association between urinary potassium excretion and risk of all-cause mortality among CKD patients, controlling for SBP.</p>
<p>Leonberg-Yoo, 2016¹³⁶; Klahr, 1994¹³⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MDRD (Modification</p>	<p>Study of: Adults N: 812</p> <p>% Male: 60.1</p> <p>Mean Age/Range/Age at Baseline: mean 51.8 (SD 12.4) years</p> <p>Race: white 85.1 black 8 other 6.9 Systolic BP: mean 131.9 (SD 17.6) Diastolic BP: mean 81 (SD 10.1) Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: mean 27.1 (SD 4.5)</p> <p>% with Hypertension: NR % with history of CVD: 13.3 % with Type 2 diabetes: 5.2</p>	<p>Exposure Type: Baseline urine potassium Exposure Unit: continuous</p> <p>Exposure Type: Baseline urine potassium Exposure Unit: g/d</p> <p>Exposure Type: Time-updated average urine potassium Exposure Unit: continuous</p>	<p>Potassium measure: multiple 24-hr urine analysis without reported validation Best potassium measure recorded: One 24-hr urine analysis at baseline and additional 24-hr urine collections completed every month. Mortality Outcomes-Method of Ascertainment: National death index CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: renal data system</p>	<p>Q1 cases: 83, total: 209, person-years: 3105, Q1 cases: 96, total: 209, person-years: 3393, per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d). cases: 390, total: 812, person-years: 11678, per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d). cases: 430, total: 812, person-years: 12582, Q2 cases: 103, total: 188, person-years: 2690, Q2 cases: 110, total: 188, person-years: 2828, Q3 cases: 120, total: 215, person-years: 2945, Q3 cases: 132, total: 215, person-years: 3160, Q4 cases: 84, total: 200, person-years: 2938, Q4 cases: 92, total: 200, person-years: 3201</p> <p>In fully adjusted models, each 1-SD higher urine potassium excretion was significantly associated with a 17% (95% CI, 0.74-0.94) lower hazard of all-cause mortality</p> <p>In quartile analyses, lower quartiles of urine potassium excretion were associated with higher risk for mortality after multivariable analysis. In fully adjusted models, each 1-SD higher urine potassium excretion was significantly associated with a 17% (95% CI, 0.74-0.94) lower hazard of all-cause mortality</p> <p>Results were similar using time-updated average urine potassium excretion</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
of Diet in Renal Disease) Study	<p>% with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included patients with CKD (serum creatinine levels in men, 1.4-7 mg/dL; in women, 1.2- 7 mg/dL) and between ages 18-70.</p> <p>Exclusion: Excluded those who were pregnant, those with type 1 or 2 diabetes, those with urine protein excretion >10 g/d, or had previous kidney transplantation.</p>	<p>Exposure Type: Time-updated average urine potassium Exposure Unit: g/d</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>Kidney failure (Determined from US Renal Data System data) Dose format: NR Q1, Dose: NR Q1, Dose: 1.41 (0.27) Q2, Dose: NR Q2, Dose: 2.01 (0.14) Q3, Dose: NR Q3, Dose: 2.54 (0.20) Q4, Dose: NR Q4, Dose: 3.60 (0.66) per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d).</p> <p>All-cause mortality Dose format: NR Q1, Dose: NR Q1, Dose: 1.41 (0.27) Q2, Dose: NR Q2, Dose: 2.01 (0.14) Q3, Dose: NR Q3, Dose: 2.54 (0.20) Q4, Dose: NR Q4, Dose: 3.60 (0.66) per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d), Dose: NR per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d), Dose: NR</p>		<p>Q1 cases: 154, total: 209, person-years: 1428, Q1 cases: 169, total: 209, person-years: 1582, per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d). cases: 558, total: 812, person-years: 6203, per 1-SD increase in urine potassium excretion (1 SD = 0.89 g/d). cases: 603, total: 812, person-years: 6647, Q2 cases: 137, total: 188, person-years: 1421, Q2 cases: 143, total: 188, person-years: 1493, Q3 cases: 141, total: 215, person-years: 1635, Q3 cases: 151, total: 215, person-years: 1745, Q4 cases: 126, total: 200, person-years: 1719, Q4 cases: 140, total: 200, person-years: 1827</p> <p>Adjustment: Age, sex, and race, measured glomerular filtration rate, log urine protein per doubling, and cause of kidney disease, history of cardiovascular disease, diabetes, smoking, systolic blood pressure, body mass index, high-density lipoprotein cholesterol level, transferrin level, blood pressure randomization, and diet randomization, diuretics or angiotensin-converting enzyme inhibitor use (dichotomous), urine urea nitrogen excretion, total caloric intake, and urine sodium excretion</p> <p>A nonsignificant change in risk of kidney per 1-SD increase in baseline urine potassium excretion.</p> <p>A nonsignificant change in risk of kidney per 1-SD increase in time-updated average urine potassium excretion.</p> <p>A nonsignificant trend of increased kidney failure events in lower quartiles of baseline urine potassium measurements.</p> <p>No association between events of kidney failure and time-updated average urine potassium measurements.</p>

Table D43. Subgroup table for observational studies for diabetes

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p>	<p>Study of: Adults N: 1684</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for diabetes</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1674 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants with diabetes, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1677 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants with diabetes, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed profusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1682 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants with diabetes, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or deathwithin24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1684 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants with diabetes, greater sodium excretion was associated with an increased risk of compositive CVD.</p>
<p>O'Donnell, 2014¹²⁴</p>	<p>Study of: Adults N: 101945</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation Best sodium measure recorded: collected one</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those with diabetes.</p>

Table D44. Subgroup table for observational studies for female

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Alderman, 1997¹³⁸; Alderman, 1995¹³⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 1037</p> <p>% Male: 64.7</p> <p>Mean Age/Range/Age at Baseline: men mean 52 (SD 10) years; women mean 54 (SD 9) years</p> <p>Race: NR</p> <p>Systolic BP: men mean 150; women mean 150</p> <p>Diastolic BP: men mean 98; women mean 94</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: men mean 27.5; women mean 28.2</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Need Alderman article to answer this question</p> <p>Exclusion: Need Alderman article to answer this question</p>	<p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p> <p>Duration(in months): unclear</p> <p>Exposure to Follow Up Time: 3.8 years</p> <p>Dose format: range</p> <p>Q1, Dose: <89 mmol</p> <p>Q2, Dose: 89-126 mmol</p> <p>Q3, Dose: 127-174 mmol</p> <p>Q4, Dose: >=175 mmol</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: Single 24-hr urine analysis at beginning of the program</p> <p>Sodium, Method of Validation: Validated by using formula described by Cockcroft and Gault and Robertshaw et al. Only included patients whose estimated urinary creatinine clearance values fall within +/-35% of the observed values</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Death certificate reports</p>	<p>CVD (Cardiovascular disease, includes myocardial infarction (MI), stroke, coronary revascularization, unstable angina, congestive heart failure. and other CVD deaths. CVD events included MI (code 410) and cerebrovascular disease (codes 430 to 434 and 436 to 43) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 2.9 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 5.5, total: NR, Q3 cases: 4.3, total: NR, Q4 cases: 7.5, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>MI (Myocardial Infarction incidence code 410) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 1 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 1.8, total: NR, Q3 cases: 2.1, total: NR, Q4 cases: 3.7, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>Non-CVD (Includes hospitalizations, emergency room visits, and deaths.) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 18.5 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 9.1, total: NR, Q3 cases: 13.9, total: NR, Q4 cases: 14.9, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>Stroke (Stroke Incidence) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 1 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 1.8, total: NR, Q3 cases: 1.1, total: NR, Q4 cases: 1.9, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p>
<p>Khaw, 1987¹⁴⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 503</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: range 50-79 years</p> <p>Race: NR</p> <p>Systolic BP: No stroke associated death (men) mean 141.5 mmHg, stroke-associated death (men) mean 143.2 mmHg; No stroke-associated death (women) mean 136.4 mmHg, stroke-associated death (women) 147.2 mmHg</p> <p>Diastolic BP: No stroke-associated death (men) mean 84.3 mmHg, stroke-associated death (men) mean 83.2; No stroke-associated death (women) mean 81.3 mmHg, stroke-associated death (women) mean 86.3 mmHg</p> <p>Magnesium: No stroke-associated death (men) mean 11.6, stroke-associated death (men) mean 9.9; No stroke-associated death (women) mean 9.1 mmHg, stroke-associated death (women) mean 8.0 mmol</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: Dietary Potassium Intake</p> <p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mmol/d</p> <p>Duration(in months): 144 (12 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>DBP (ICDA 430 to 438), SBP (ICDA 430 to 438)</p> <p>Dose format: NR</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: Once (at baseline)</p> <p>Potassium, Method of Validation: A 24-hour recall of dietary intake was obtained by a certified Lipid Research Clinic dietician. The data were coded for nutrient intake by the Nutrition Coordinating Center, University of Minnesota, with use of their data base.</p> <p>How was blood pressure measured? BP was measured by trained observers who used a standard mercury sphygmomanometer after the subject had been seared at rest for at least five minutes. BP was only measured once at baseline.</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p> <p>CVD, CHD, stroke, kidney stones/disease</p>	<p>DBP (ICDA 430 to 438) (Dietary Potassium Intake/Outcome):</p> <p>ICDA 430 to 438 FU</p> <p>mmol/d cases: NR, total: NR, person-years: per unit increase</p> <p>Adjustment: Age</p> <p>After adjusting for age, there is a marginal negative association between potassium intake and DBP in both men and women.</p> <p>SBP (ICDA 430 to 438) (Dietary Potassium Intake/Outcome):</p> <p>ICDA 430 to 438 FU</p> <p>mmol/d cases: NR, total: NR, person-years: per unit increase</p> <p>Adjustment: Age</p> <p>After adjusting for age, there is a marginal negative association between potassium intake and DBP in both men and women.</p> <p>Stroke-associated All-cause mortality (ICDA 430 to 438) (mmol/d/Outcome):</p> <p>12 y FU</p> <p>T1 cases: NR, total: 167, per 10 mmol cases: 15, total: 503, T2+T3 cases: NR, total: 336</p> <p>Adjustment: Age</p> <p>The age-adjusted stroke rates, according to tertile of potassium intake, suggest a dose response (more marked in the women than in the men), with no stroke deaths in the highest tertile.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Calcium: No stroke-associated death (men) mean 20.2, stroke-associated death (men) mean 16.1; No stroke-associated death (women) mean 15.1 mmHg, stroke-associated death (women) mean 14.9 mmol</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Men and Women who were 50 to 79 years old and who had no personal history of heart attack, heart failure, or stroke at the base-line examination were included in the study.</p> <p>Exclusion: NR</p>	<p>mmol/d, Dose: NR</p> <p>Stroke-associated All-cause mortality (ICDA 430 to 438)</p> <p>Dose format: range T1, Dose: <49 T2+T3, Dose: >=49-66, >=67 per 10 mmol</p>	<p>Outcomes-Method of ascertainment: Death certificate reports</p>	<p>Potassium intake was inversely and independently related to stroke. The results were the same when diastolic pressure was used in place of systolic pressure.</p>
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 1592</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0</p> <p>Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years</p> <p>Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8%</p> <p>Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg</p> <p>Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m²</p> <p>% with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8</p> <p>% with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4; 39.7</p> <p>% with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included.</p> <p>Exclusion: People with a history of kidney</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR</p> <p>NR, Dose: NR for Female</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 times, 1 year apart</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome):</p> <p>Median 6.8 years FU</p> <p>NR cases: NR, total: 1582</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among female, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome):</p> <p>Median 6.8 years FU</p> <p>NR cases: NR, total: 1584</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among female, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (per 1000 mg/24 h/Outcome):</p> <p>Median 6.8 years FU</p> <p>NR cases: NR, total: 1589</p> <p>Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR</p> <p>Among female, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.			Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1592 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among female, greater sodium excretion was associated with a non-significant increased risk of composite CVD.
Pfister, 2014 ¹⁴¹ Location: UK Setting: Community Design: Prospective Cohort study Study Name: The EPIC-Norfolk study	Study of: Adults N: 10840 % Male: 45.4 Mean Age/Range/Age at Baseline: mean 58.0 (SD 9.2) years Race: NR Systolic BP: reported by quintiles of sodium excretion q1 135 (17) q2 135 (17) q3 136 (17) q4 138 (17) q5 141 (19) Diastolic BP: reported by quintiles of sodium excretion q1 83.1 (10.9) q2 83.1 (10.9) q3 83.9 (10.6) q4 85.2 (10.6) q5 86.8 (11.5) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: reported by quintiles of sodium excretion q1 25.9 (SD 3.1) q2 26.1 (SD 3) q3 26.4 (SD 3.2) q4 26.7 (SD 3.2) q5 27.1 (SD 3.5) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included Norfolk residents between 39-79 years old. Exclusion: Excluded participants with a history of heart attack, stroke, or any cancer. Also excluded those using medical heart failure treatment and those failed to provide data on estimated 24 h urinary sodium excretion.	Exposure Type: Urinary sodium excretion Exposure Unit: mmol/day Duration: NR Exposure to Follow Up Time: 3.5 years Dose format: mean (SD, range) Q1, Dose: 101 (17, <122) Q2, Dose: 133 (6, 122-144) Q3, Dose: 154 (6, 144-163) Q4, Dose: 175 (7, 163-187) Q5, Dose: 216 (32, >187)	Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hr urine analysis at baseline and second health check. Sodium, Method of Validation: Obtained spot urine samples in a random sample of 1551 women. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports, National Death Index	Incident heart failure (Heart failure death was defined as ICD-10 I50 anywhere on the death certificate. Incident heart failure was defined as heart failure death or hospital discharge code ICD-10 I50, which proved to be specific in a recent validation study) (mmol/day/Outcome): Mean 12.9 y FU Q1 cases: 267, total: 3971, Q2 cases: 212, total: 3971, Q3 cases: 220, total: 3972, Q4 cases: 223, total: 3971, Q5 cases: 288, total: 3972 Adjustment: Age, body mass index, known diabetes, cholesterol, social class, educational level, smoking, physical activity, alcohol consumption, and sex where appropriate There was a suggested U-shaped association between quintiles of estimated urinary sodium excretion and hazard of heart failure in age-adjusted analyses in men and women. When further adjusting the analysis for systolic blood pressure and baseline blood pressure medication, the HR for the highest quintile of estimated urinary sodium excretion was strongly attenuated whereas the HR for the lowest quintile was materially unchanged (Tables 2 and 4).
Tunstall-Pedoe, 1997 ¹⁴² ; Tunstall-Pedoe, 1999 ¹⁴³ ; Smith, 1987 ¹⁴⁴ Location: Scotland	Study of: Adults N: 5875 % Male: 49.5 Mean Age/Range/Age at Baseline: ranged 40-59 years Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR	Exposure Type: Urinary potassium ion excretion Exposure Unit: mmol/day Exposure Type: Urinary sodium ion excretion Exposure Unit: mmol/day	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: one 24 hour urine collection Sodium, Method of Validation: Urine was analyzed for electrolytes and creatinine. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports	All CHD (All coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among female participants, no statistically significant association was observed between urinary sodium excretion and risk of CHD. All-cause mortality (Deaths from all causes) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total:

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Scottish Heart Health Study</p>	<p>Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 1.5% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included randomly selected patients from general practitioners' offices in 23 local government districts. Participants aged between 40-59. Exclusion: Excluded those who failed to complete the study questionnaire, clinic appointment, or both.</p>	<p>Duration(in months): 3 years Exposure to Follow Up Time: 6 years</p> <p>Dose format: range group 1, Dose: 15.3 - 39.7 mmol/day group 1, Dose: 37.8 - 98 mmol/day group 2, Dose: 39.7 - 49.4 mmol/day group 2, Dose: 98 - 123.4 mmol/day group 3, Dose: 123.4 - 149 mmol/day group 3, Dose: 49.4 - 58.5 mmol/day group 4, Dose: 149 - 187.3 mmol/day group 4, Dose: 58.5 - 70.2 mmol/day group 5, Dose: 187.3 - 319.3 mmol/day group 5, Dose: 70.2 - 116.4 mmol/day</p>		<p>NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among female participants, no statistically significant association was observed between urinary sodium excretion and risk of mortality.</p> <p>CHD deaths (Fatal coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among female participants, no statistically significant association was observed between urinary sodium excretion and risk of CHD mortality.</p> <p>All CHD (All coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age No significant association between urinary potassium excretion and CHD incidence among female.</p> <p>All-cause mortality (Deaths from all causes) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Potassium excretion showed a highly significant protective gradient for all deaths in both sexes and significantly protected against all coronary heart disease in men.</p> <p>CHD deaths (Fatal coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age No significant association between urinary potassium excretion and CHD mortality among female.</p>
<p>Tuomilehto, 2001¹⁴⁵</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 1259</p> <p>% Male: 48.2 Mean Age/Range/Age at Baseline: age reported by sodium quartile and gender: men q1 mean 45.4 (SD 11.6) years, men q2 mean 45.3 (SD 11.0) years, men q3 mean 46.2 (SD 10.4) years, men q4 mean 45.4 (SD 10.6) years; women q1 mean 45.7 (SD 11.6) years, women q2 mean 45.4 (SD 11.8) years, women q3 mean 44.8 (SD 11.1) years, women q4 mean 45.6 (SD 11.3) years.</p> <p>Race: NR Systolic BP: Systolic blood pressure reported by sodium quartile and gender: men q1 mean 144 (SD 22), men q2 mean 145 (SD 19), men q3 mean 148 (SD 20), men q4 mean 147 (SD 19); women q1 mean 141 (SD 22) years, women q2 mean 140 (SD 22), women q3 mean 141 (SD 22), women q4 mean 142 (SD 22).</p>	<p>Exposure Type: 24 h urinary sodium excretion Exposure Unit: mmol</p> <p>Duration: NR Exposure to Follow Up Time: up to 14 years</p> <p>Dose format: NR per 100 mmol increase, Dose: mean 162 mmol (SD 62)</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p> <p>How was blood pressure measured? Blood pressure was measured once using a standard sphygmomanometer with a 13 cm wide and 42 cm long cuff bladder. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>All-cause mortality (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 44, total: 1263 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Cardiovascular death (Death, ICD 390-448) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 15, total: 1263 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and gender: men q1 mean 86 (SD 11), men q2 mean 86 (SD 12), men q3 mean 89 (SD 13), men q4 mean 90 (SD 13); women q1 mean 83 (SD 12) years, women q2 mean 83 (SD 12), women q3 mean 83 (SD 12), women q4 mean 85 (SD 12). Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: BMI reported by sodium quartile and gender: men q1 mean 25.5 (SD 2.4), men q2 mean 26.4 (SD 3.3), men q3 mean 26.9 (SD 3.3), men q4 mean 28.1 (SD 4.2); women q1 mean 24.6 (SD 4.2) years, women q2 mean 25.1 (SD 4.02), women q3 mean 26.3 (SD 4.6), women q4 mean 27.8 (SD 5.4). % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Finnish men and women between 25-64 years old. Analysis of this study included both the 1982 and 1987 cohorts. Exclusion: Excluded those with incomplete collection of urine, and those with incomplete data of risk factors. Also excluded those who had a non-fatal acute coronary event or cerebrovascular event before baseline survey.</p>			<p>Coronary heart disease death (Death, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 7, total: 1263 Adjustment: Age, study year, smoking, serum total and HDL cholesterol, systolic blood pressure, and BMI Among female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Coronary heart disease incident (Event, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 30, total: 1257 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Stroke incident (Event, ICD 430-438) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 41, total: 1259 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: 6368</p> <p>% Male: 48.1%</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information. Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet</p>	<p>Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>CVD mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.91 Q1, Dose: 1574 Q1, Dose: 1873 Q2, Dose: 1.07 Q2, Dose: 2126</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24-hour dietary recall Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall" Best potassium measure recorded: single 24-hour dietary recall Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1003, total: 6368, person-years: 89128, per unit change cases: 1003, total: 6368, person-years: 89128, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. Significant association between higher sodium potassium ratio and all-cause mortality among female participants.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 388, total: 6368, person-years: 89128, per unit change cases: 388, total: 6368, person-years: 89128, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. No significant association between sodium potassium ratio and CVD mortality among female participants.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	for hypertension and those with a history of heart attack, stroke, or congestive heart failure.	<p>Q2, Dose: 2549 Q3, Dose: 1.2 Q3, Dose: 2624 Q3, Dose: 3148 Q4, Dose: 1.35 Q4, Dose: 2068 Q4, Dose: 3380 per 1000 mg/d, Dose: NR per unit change, Dose: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.91 Q1, Dose: 1574 Q1, Dose: 1873 Q2, Dose: 1.07 Q2, Dose: 2126 Q2, Dose: 2549 Q3, Dose: 1.2 Q3, Dose: 2624 Q3, Dose: 3148 Q4, Dose: 1.35 Q4, Dose: 2068 Q4, Dose: 3380 per 1000 mg/d, Dose: median 2367 (IQR1177-2932)mg per 1000 mg/d, Dose: median 2838 (IQR 2252-3521)mg per unit change, Dose: median 1.20 (OQR 1.04-1.39)</p>		<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1003, total: 6368, person-years: 89128, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among female participants, no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 388, total: 6368, person-years: 89128, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among female participants, no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D45. Subgroup table for observational studies for female + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised AssessmeNt Study in ACEiswcdI., 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141. 72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: strok 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged >=55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D46. Subgroup table for observational studies for girls

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Krupp, 2015¹³²; Shi, 2014¹³³; Kruppe, 2014¹³⁴; Kroke, 2004¹³⁵</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometri c Longitudinally Designed (DONALD) Study</p>	<p>Study of: Children N: 98</p> <p>% Male: 52.4% Mean Age/Range/Age at Baseline: 3 months Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: by gender boys mean 18.9 (SD 2.3) girls mean 18.7 (SD 2.7)</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included Germans recruited at 3 months of age and who completed three repeated urinary, dietary and blood pressure measurements in adolescence and one additional blood pressure measurement in young adulthood. Exclusion: Excluded those who were born before 36 weeks gestation and those with missing data.</p>	<p>Exposure Type: Daily sodium excretion Exposure Unit: mmol/day</p> <p>Duration: NR Exposure to Follow Up Time: an average of 12 years</p> <p>Dose format: continuous All, Dose: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 repeated 24-hour urine analysis with validation Sodium, Method of Validation: Minimized errors with creatinine excretion cutoff., Multiple 24-hour urine analysis with validation Best potassium measure recorded: 3 repeated 24-hour urine analysis with validation Potassium, Method of Validation: Minimized errors with creatinine excretion cutoff.</p> <p>How was blood pressure measured? Two blood pressure readings for each BP measurement was assessed by trained nurses with first a random zero sphygmomanometer and with a standard mercury sphygmomanometer. BP values measured with a standard zero sphygmomanometers were multiplied with an internally validated conversion factor (e.g., 1.056 for systolic BP).</p>	<p>Systolic blood pressure (Random-zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer thereafter.) (mmol/day/Outcome): 7 years FU All cases: NR, total: 98 Adjustment: Primary model 2: mean pubertal systolic BP SDS and adult age, standardized energy intake, intake of saturated fat (g/day), height SDS, maternal education, maternal BP No significant association between sodium excretion and systolic blood pressure in girls.</p>

Table D47. Subgroup table for observational studies for HPFS

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Ferraro, 2016¹⁴⁸; Taylor, 2004¹⁴⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Health Professionals Follow-up Study</p>	<p>Study of: Adults</p> <p>% Male: NR Mean Age/Range/Age at Baseline: mean 54.3 (SD 9.8)</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 25.5 (SD 3.4) % with Hypertension: 21% % with history of CVD: NR % with Type 2 diabetes: 3% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included HPFS participants without a history of kidney stones at baseline. Exclusion: Excluded those with a history of malignancy (except for nonmelanoma skin cancer) at baseline and those who developed malignancies during follow-up. Excluded NHS I participants who answered questionnaires before 1992 (the year of the first lifetime kidney stone history inquiry).</p>	<p>Exposure Type: 4.5737E-2</p> <p>Exposure Unit: Potassium intake</p> <p>Duration: NR Exposure to Follow Up Time: 0</p> <p>Dose format: Q1 g/day, Dose: median g/day, Dose: median g/day, Dose: median g/day, Dose: median</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: One food frequency questionnaire at baseline and additional FFQ every 4 years Potassium, Method of Validation: FFQs were found to be reproducible and valid in the HPFS and the NHS I. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: supplementary questionnaire (self-report)</p>	<p>Kidney stones (Kidney) (Potassium intake/Outcome): Self reported, accompanied by pain and/or hematuria FU g/day cases: NR, total: NR, person-years: 2601, g/day cases: NR, total: NR, person-years: 3016, g/day cases: NR, total: NR, person-years: 3327, g/day cases: NR, total: NR, person-years: 3667, g/day cases: NR, total: NR, person-years: 4224 Adjustment: Age, body mass index, history of diabetes, history of hypertension, use of thiazides, supplemental calcium, and intakes of fluid, calcium, sodium, fructose, oxalate, phytate, alcohol, and all other types of protein. Second to fifth quintiles of potassium intake were inversely associated with incidence of kidney stones compared to first quintile.</p>

Table D48. Subgroup table for observational studies for hypertensive

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Singer, 2015¹⁵⁰</p> <p>Location: US</p> <p>Setting: a union-sponsored, worksite hypertension program</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 3505</p> <p>% Male: 64 Mean Age/Range/Age at Baseline: mean 52 (SD 10)</p> <p>Race: Q1 black 30.2% white 31.7% Hispanic 33.7% other 4.4%; Q2 black 30.5% white 33.7% Hispanic 34.8% other 2.1%; Q4 black 30.5% white 31.7% Hispanic 35.7% other 2.1%; Q4 black 28.6% white 29.3% Hispanic 38.3% other 3.8%</p> <p>Systolic BP: mean (SD) Q1 146.4 (18.5) Q2 145.3 (17.7) Q3 145.2 (16.5) Q4 145.8 (16.3)</p> <p>Diastolic BP: mean (SD) Q1 93.6 (10.0) Q2 93.9 (9.7) Q3 94.1 (9.4) Q5 (95.1 (9.6)</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: mean (SD) Q1 27.4 (4.1) Q2 27.8 (4.1) Q3 28.9 (4.5) Q4 30.0 (4.9)</p> <p>% with Hypertension: drug use Q1 37.0% Q2 39.9% Q3 40.2% Q4 35.2%</p> <p>% with history of CVD: MI Q1 1.1% Q2 0.5% Q3 1.0% Q4 1.5%; Stroke Q1 0.9% Q2 0.6% Q3 0.9% Q4 0.7%</p> <p>% with Type 2 diabetes: Q1 4%; Q2 6.3% Q3 5.6% Q4 6.0%</p> <p>% with Kidney disease: Q1 1.5%; Q2 1.4%; Q3 1.2%; Q4 2.2%</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants with an SBP >= 140 mm Hg (>= 160mm Hg before Joint National Committee 5), DBP >= 90 mmHg (>= 95 Hg before Joint National Committee 5), or being on antihypertensive medication at the time of screening were included. Exclusion: not report</p>	<p>Exposure Type: Urine sodium Exposure Unit: mmol/24 h</p> <p>Duration: NR Exposure to Follow Up Time: in-program 6.5 years, follow-up from initial intake to death or last known alive 18.6 years</p> <p>All cardiovascular mortality (Coronary artery disease, including MI, ischemic heart disease, heart failure, and hypertensive heart disease: ICD-9: 402.9, 410-414.9, 427.5, 429.2, 429.5, 429.2; ICD-10: I10-11.9, I13-I13.2, I20-I25.9, I46-I46.9; stroke: ICD-9: 434-434.9, 436-438.9, 436-438.9; ICD-10: I61-I64.9; o), Limited cardiovascular mortality (Only MI, ischemic or hypertensive heart disease, and heart failure)</p> <p>Dose format: mean (SD) Q1, Dose: 55 (20) Q2, Dose: 102 (17) Q3, Dose: 143 (20) Q4, Dose: 221 (56)</p> <p>All-cause mortality Dose format: mean (SD) Q2, Dose: 102 (17) Q3, Dose: 143 (20) Q4, Dose: 221 (56)</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: once at baseline</p> <p>How was blood pressure measured? not reported</p> <p>Mortality Outcomes-Method of Ascertainment: National Death Index Plus and the Social Security Administration Death Master File</p>	<p>All cardiovascular mortality (Coronary artery disease, including MI, ischemic heart disease, heart failure, and hypertensive heart disease: ICD-9: 402.9, 410-414.9, 427.5, 429.2; ICD-10: I10-11.9, I13-I13.2, I20-I25.9, I46-I46.9; stroke: ICD-9: 434-434.9, 436-438.9; ICD-10: I61-I64.9; o) (mmol/24 h/Outcome): Mean 18.6 years FU Q1 cases: 128, total: 890, Q2 cases: 97, total: 876, Q3 cases: 96, total: 865, Q4 cases: 78, total: 874 Adjustment: Age, sex, race, BMI, SBP, eGFR, urine potassium, hematocrit, plasma renin activity, HxDm, Hx smoking, history of baseline left ventricular hypertrophy No significant association between urinary sodium excretion and cardiovascular death was observed</p> <p>All-cause mortality (/Outcome): Q2 cases: 276, total: 876, Q3 cases: 234, total: 865, Q4 cases: 216, total: 874</p> <p>Limited cardiovascular mortality (Only MI, ischemic or hypertensive heart disease, and heart failure) (mmol/24 h/Outcome): Mean 18.6 years FU Q1 cases: NR, total: 890, Q2 cases: NR, total: 876, Q3 cases: NR, total: 865, Q4 cases: NR, total: 874 Adjustment: Age, sex, race, BMI, SBP, urine creatinine, plasma renin activity, HxDm, Hx smoking, history of baseline left ventricular hypertrophy No significant association between urinary sodium excretion and limited cardiovascular mortality.</p>
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p>	<p>Study of: Adults N: NR</p> <p>% Male: 48.1% Mean Age/Range/Age at Baseline: ranged 25-74 years</p>	<p>Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg Exposure Type: Usual</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24-hour dietary recall Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1155, total: NR, person-years: 35640, per unit change cases: 1155, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information. Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Potassium Intakes Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.9 Q1, Dose: 1790 Q1, Dose: 2018 Q2, Dose: 1.06 Q2, Dose: 2483 Q2, Dose: 2875 Q3, Dose: 1.18 Q3, Dose: 3123 Q3, Dose: 3705 Q4, Dose: 1.33 Q4, Dose: 4095 Q4, Dose: 4974 per 1000 mg/d, Dose: NR for HYPERTENSIVE per unit change, Dose: NR for HYPERTENSIVE</p> <p>CVD mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.9 Q1, Dose: 1790 Q1, Dose: 2018 Q2, Dose: 1.06 Q2, Dose: 2483 Q2, Dose: 2875 Q3, Dose: 1.18 Q3, Dose: 3123 Q3, Dose: 3705 Q4, Dose: 1.33 Q4, Dose: 4095 Q4, Dose: 4974 per 1000 mg/d, Dose: NR per unit change, Dose: NR</p>	<p>Best potassium measure recorded: single 24-hour dietary recall Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. Significant association between higher sodium potassium ratio and all-cause mortality among those with hypertension.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 490, total: NR, person-years: 35640, per unit change cases: 490, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. Significant association between higher sodium potassium ratio and CVD mortality among those with hypertension.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1155, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 490, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D49. Subgroup table for observational studies for high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
O'Donnell, 2011 ¹²⁷ ; Ontarget Investigators, 2008 ¹²⁸ ; Telmisartan Randomised Assessment Study in ACEiswCDL, 2008 ¹²⁹ ; Kawasaki, 1993 ¹³⁰	Study of: Adults N: 28880 % Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22) Race: NR Systolic BP: mean 141.72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: stroke 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Participants aged ≥55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA	Exposure Type: Estimated 24-Hour Urinary Potassium Excretion (Kawasaki equation) Exposure Unit: g/d Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d Duration(in months): 56 Exposure to Follow Up Time: NR Composite outcome (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8 All-cause mortality (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF), CHF (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF), CV death (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF), MI (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF), Stroke (Composite outcome includes CV mortality, MI, stroke, and	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records	All-cause mortality (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: 123, total: 818, G2 cases: 359, total: 2654, G3 cases: 683, total: 5699, G4 cases: 1537, total: 14156, G5 cases: 404, total: 3380, G6 cases: 183, total: 1326, G7 cases: 141, total: 847 Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary potassium Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis. CHF (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: 52, total: 818, G2 cases: 137, total: 2654, G3 cases: 242, total: 5699, G4 cases: 532, total: 14156, G5 cases: 137, total: 3380, G6 cases: 58, total: 1326, G7 cases: 55, total: 847 Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary potassium Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis. CV death (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: 87, total: 818, G2 cases: 227, total: 2654, G3 cases: 403, total: 5699, G4 cases: 886, total: 14156, G5 cases: 230, total: 3380, G6 cases: 129, total: 1326, G7 cases: 95, total: 847 Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary potassium Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
		<p>hospitalization for CHF)</p> <p>Dose format: range</p> <p>G1, Dose: <2</p> <p>G2, Dose: 2-2.99</p> <p>G3, Dose: 3-3.99</p> <p>G4, Dose: 4-5.99</p> <p>G5, Dose: 6-6.99</p> <p>G6, Dose: 42924</p> <p>G7, Dose: >8</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p> <p>Primary outcome (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF)</p> <p>Dose format: range</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>		<p>death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p> <p>Composite outcome (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome):</p> <p>Median 56 months (IQR 53-60) FU</p> <p>G1 cases: 165, total: 818, G2 cases: 482, total: 2654, G3 cases: 918, total: 5699, G4 cases: 2148, total: 14156, G5 cases: 568, total: 3380, G6 cases: 244, total: 1326, G7 cases: 204, total: 847</p> <p>Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic b blood pressure from baseline to last follow-up, and urinary potassium</p> <p>Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p> <p>MI (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome):</p> <p>Median 56 months (IQR 53-60) FU</p> <p>G1 cases: 42, total: 818, G2 cases: 123, total: 2654, G3 cases: 277, total: 5699, G4 cases: 655, total: 14156, G5 cases: 189, total: 3380, G6 cases: 68, total: 1326, G7 cases: 58, total: 847</p> <p>Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic b blood pressure from baseline to last follow-up, and urinary potassium</p> <p>Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p> <p>Stroke (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome):</p> <p>Median 56 months (IQR 53-60) FU</p> <p>G1 cases: 40, total: 818, G2 cases: 130, total: 2654, G3 cases: 250, total: 5699, G4 cases: 601, total: 14156, G5 cases: 141, total: 3380, G6 cases: 64, total: 1326, G7 cases: 56, total: 847</p> <p>Adjustment: Age, sex, race/ethnicity (white vs nonwhite), prior history of stroke or myocardial infarction, creatinine, body mass index, comorbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL, and high-density lipoprotein), treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy), fruit and vegetable consumption, level of exercise, baseline blood pressure</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>and change in systolic blood pressure from baseline to last follow-up, and urinary potassium</p> <p>Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p> <p>All-cause mortality (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 263, total: 2194, Q2 cases: 1209, total: 9711, Q3 cases: 1203, total: 9877, Q4 cases: 535, total: 4850, Q5 cases: 221, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telmisartan or both) and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy, fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary sodium No significant association between potassium intake and risk of all-cause mortality.</p> <p>CHF (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 97, total: 2194, Q2 cases: 431, total: 9711, Q3 cases: 401, total: 9877, Q4 cases: 187, total: 4850, Q5 cases: 97, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telmisartan or both) and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy, fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary sodium There was no significant association between potassium excretion and CV mortality, MI, and hospitalization for CHF</p> <p>CV death (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 173, total: 2194, Q2 cases: 725, total: 9711, Q3 cases: 695, total: 9877, Q4 cases: 320, total: 4850, Q5 cases: 145, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telmisartan or both) and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy, fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary sodium There was no significant association between potassium excretion and CV mortality, MI, and hospitalization for CHF</p> <p>MI (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 86, total: 2194, Q2 cases: 495, total: 9711, Q3 cases: 483, total: 9877, Q4</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				<p>cases: 241, total: 4850, Q5 cases: 107, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telmisartan or both) and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy, fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary sodium There was no significant association between potassium excretion and CV mortality, MI, and hospitalization for CHF</p> <p>Primary outcome (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 375, total: 2194, Q2 cases: 1633, total: 9711, Q3 cases: 1617, total: 9877, Q4 cases: 750, total: 4850, Q5 cases: 355, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telmisartan or both) and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antithrombotic therapy, fruit and vegetable consumption, level of exercise, baseline blood pressure and change in systolic blood pressure from baseline to last follow-up, and urinary sodium No significant association between potassium intake and risk of composite outcome.</p> <p>Stroke (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU Q1 cases: 135, total: 2194, Q2 cases: 454, total: 9711, Q3 cases: 425, total: 9877, Q4 cases: 189, total: 4850, Q5 cases: 79, total: 2249 Adjustment: Age, sex, ethnicity (white versus non-white), prior history of stroke or myocardial infarction, creatinine, BMI, co-morbid vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, LDL and HDL), treatment allocation (ramipril, telm</p>

Table D50. Subgroup table for observational studies for history of hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Larsson, 2011¹⁵¹</p> <p>Location: Sweden</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Swedish Mammography Cohort</p>	<p>Study of: Adults N: ND3</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: by potassium quintiles q1 mean 61.6 q5 mean 60.7</p> <p>Race: NR</p> <p>Systolic BP: NR Diastolic BP: NR</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: by potassium quintiles q1 mean 24.8 q5 mean 25.3</p> <p>% with Hypertension: by potassium quintiles q1 18.6% q5 20.4%</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: by potassium quintiles q1 2.2% q5 4.5%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included women born between 1914-1948 and living in central Sweden. Included those who completed both diet questionnaires at baseline and in 1997.</p> <p>Exclusion: Excluded women with incorrect national identification number, with a history of stroke, coronary heart disease, or cancer, or with extreme energy intake.</p>	<p>Exposure Type: Potassium intake Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: a mean of 10.4 years</p> <p>Dose format: Median Q1, Dose: 2419 Q2, Dose: 2767 Q3, Dose: 3021 Q4, Dose: 3296 Q5, Dose: 3744</p>	<p>Potassium measure: food frequency questionnaire with reported validation Best potassium measure recorded: One 96-item food frequency questionnaire completed in 1997</p> <p>Potassium, Method of Validation: The food frequency questionnaire has been validated in Messerer M, Johansson SE, Wolk A. The validity of questionnaire-based micronutrient intake estimates is increased by including dietary supplement use in Swedish men. J Nutr. 2004;134(7):1800-1805.</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital Discharge Registry</p>	<p>Total stroke (Strokes were classified as cerebral infarction (code I63), intracerebral hemorrhage (code I61), subarachnoid hemorrhage (code I60), and unspecified stroke (code I64).) (mg/d/Outcome): Mean 10.4 years FU Q1 cases: 134, total: NR, Q2 cases: 115, total: NR, Q3 cases: 125, total: NR, Q4 cases: 113, total: NR, Q5 cases: 96, total: NR</p> <p>Adjustment: Age, smoking status, pack-years of smoking, educational level, body mass index, total physical activity level, history of diabetes, history of hypertension, aspirin use, family history of myocardial infarction, and intakes of total energy, alcohol, protein, cholesterol, total fiber, and folate</p> <p>Potassium intake was statistically significantly inversely associated with risk of total stroke and cerebral infarction among women with a history of hypertension.</p>

Table D51. Subgroup table for observational studies for hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Joosten, 2014¹⁵²</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Study of: Adults N: 2363</p> <p>% Male: by sodium quartiles q1 48.7 q2 48.7 q3 48.7 q4 48.7</p> <p>Mean Age/Range/Age at Baseline: by sodium quartiles q1 mean 50 (SD 13) q2 mean 49 (SD 13) q3 mean 48 (SD 12) q4 mean 47 (SD 11)</p> <p>Race: NR</p> <p>Systolic BP: by sodium quartiles q1 mean 129 (SD 22) q2 mean 128 (SD 20) q3 mean 128 (SD 20) q4 mean 129 (SD 20)</p> <p>Diastolic BP: by sodium quartiles q1 mean 74 (SD 10) q2 mean 74 (SD 10) q3 mean 74 (SD 10) q4 mean 74 (SD 9)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: by sodium quartiles q1 mean 25 (SD 3.7) q2 mean 25.5 (SD 3.7) q3 mean 26.1 (SD 4.1) q4 mean 27.5 (SD 4.8)</p> <p>% with Hypertension: by sodium quartiles q1 32.8 q2 30.4 q3 31.4 q4 30.7</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: by sodium quartiles q1 2.2 q2 2.5 q3 2.9 q4 4.7</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included Dutch participants between ages 28 to 75 and those who agreed to participate in questionnaire survey and urine sample collection.</p> <p>Exclusion: Excluded pregnant women and those with type I diabetes.</p>	<p>Exposure Type: Sex-specific quartiles of sodium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: a median of 10.5 years</p> <p>Dose format: range</p> <p>Q1, Dose: male <95 female <122</p> <p>Q2, Dose: male 95-121 female 122-154</p> <p>Q3, Dose: male 122-151 female 155-190</p> <p>Q4, Dose: male >151 female >190</p> <p>continuous, Dose: per 1-g/d increase</p>	<p>Sodium measure: two 24-hr urine analysis with out reported quality control measure</p> <p>Best sodium measure recorded: During baseline examination, participants collected two 24-hour urines for 2 consecutive days.</p> <p>Mortality Outcomes-Method of Ascertainment: Central Bureau of Statistics</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: national registry of hospital discharge diagnoses</p>	<p>Coronary Heart Disease Events (CHD was defined as myocardial infarction (ICD-code 410), acute and subacute ischemic heart disease (ICD-code 411) and coronary artery bypass grafting or percutaneous transluminal coronary angioplasty.) (mmol/24h/Outcome):</p> <p>Median 10.5 years (Q1-Q3: 9.9-10.8 years; 71491 person years) FU</p> <p>Q1 cases: 76, total: NR, person-years: 5524, continuous cases: 290, total: NR, person-years: 21669, Q2 cases: 70, total: NR, person-years: 5336, Q3 cases: 74, total: NR, person-years: 5472, Q4 cases: 70, total: NR, person-years: 5337</p> <p>Adjustment: Age, body mass index, smoking status, sex, alcohol intake, parental history of coronary heart disease, type 2 diabetes, total to high-density lipoprotein cholesterol ratio, and urinary potassium, magnesium, and creatinine excretion</p> <p>For each 1-g/d increase, the associations between sodium excretion and risk of CHD were significant only among subjects with hypertension.</p> <p>No statistically significant association was observed.</p>
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome):</p> <p>Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome):</p> <p>Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Rural Epidemiology (PURE) study	representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70. Exclusion: Excluded those who refused to participate.	G3, Dose: >=6 Q1, Dose: <1.50 Q2, Dose: 1.50-1.99 Q3, Dose: 2.00-2.49 Q4, Dose: 2.50-3.00 Q5, Dose: >3.00	intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76). Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources	No significant association between potassium intake and risk of death and major CVD events among those with hypertension.
Ohta, 2013 ¹⁵³ Location: Japan Setting: Community Design: Prospective Cohort study	Study of: Adults N: 133 % Male: 39.85 Mean Age/Range/Age at Baseline: mean (SD) 59.7 (8.6) Race: NR Systolic BP: mean (SD) 143 (12) Diastolic BP: mean (SD) 85 (8) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: People with hypertension who visited the National Kyushu Medical Center, and underwent more than five successful 24 h home urine collections during the follow-up period were included. Exclusion: NR	Exposure Type: Urinary sodium excretion Exposure Unit: g/day Duration: NR Exposure to Follow Up Time: 126 (10.5 y) Change in eGFR (Calculated using the Modification of Diet in Renal Disease formula) Dose format: NR continuous, Dose: per 1 g/day EGFR (Calculated using the Modification of Diet in Renal Disease formula) Dose format: range high urinary salt excretion, Dose: >8g/day low urinary salt excretion, Dose: <8g/day	Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: more than five, first between 1998 and 2000, last between 2008 and 2010 CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: CKD was considered to be present if the patient had either a decreased estimated GFR (eGFR) (<60 ml min ⁻¹ per 1.73m ²) or persistent proteinuria	Change in eGFR (Calculated using the Modification of Diet in Renal Disease formula) (g/day/Outcome): Average 10.5 years FU continuous cases: NR, total: 133 Adjustment: Change in serum uric acid, body weight at the first visit, eGFR at the first visit Significant negative association between average sodium excretion and change in eGFR EGFR (Calculated using the Modification of Diet in Renal Disease formula) (g/day/Outcome): Average 10.5 years FU high urinary salt excretion cases: NR, total: 85, low urinary salt excretion cases: NR, total: 48 Adjustment: NR Significant association between those with an average salt excretion <8g/day and slower decline in renal function.
Seth, 2014 ¹⁵⁴ ; Anderson, 2003 ¹⁵⁵ Location: US Setting: Community Design: Prospective	Study of: Adults N: 90137 % Male: 0 Mean Age/Range/Age at Baseline: mean 63.6 (SD 7.4) years Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR	Exposure Type: Dietary Potassium Intake Exposure Unit: mg/d Duration: NR Exposure to Follow Up Time: average 11 years Dose format: range	Potassium measure: Food Frequency Questionnaires Best potassium measure recorded: Two food frequency questionnaires (FFQ) at study enrollment and year 3 follow-up Potassium, Method of Validation: Used a sub sample to evaluate FFQ measurement properties Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate, Autopsy reports	All-cause mortality (Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes.) (mg/d/Outcome): Average 11 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol and body mass index Among women with hypertension, higher potassium intake was associated with lower all-cause mortality, but there was no association with any stroke outcome.

Study	Participants	Exposure	Intake Status Ascertainment	Results
Cohort study Study Name: The Women's Health Initiative Observational Study (WHI- OS)	Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included 93676 postmenopausal women aged 50 to 79 years. Exclusion: Excluded women with history of stroke, with missing information on history of stroke, and those with no information on dietary potassium at baseline. Excluded women with <465 calories intake or with >3931 calories intake, whose potassium intake ranged 0.07--1790 mg or ranged 1507 -- 31129 mg.	Q1, Dose: <1925.5 Q2, Dose: >=1925.5-2519.4 Q3, Dose: >=2519.4-3193.6 Q4, Dose: >=3193.6	CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Medical files, self reported	Stroke (All) (Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes.) (mg/d/Outcome): Average 11 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol and body mass index Among women with hypertension, higher potassium intake was associated with lower all-cause mortality, but there was no association with any stroke outcome.
Whelton, 1998 ⁹⁰ ; Appel, 2001 ⁹¹ ; Espeland, 1999 ⁹² ; Banson, 1997 ⁹³ ; Appel, 1995 ⁹⁴ ; Kostis, 1998 ⁹⁵ ; Whelton, 1997 ⁹⁶ Location: US Setting: Community Design: Randomized Factorial Design individual Study Name: Trial of nonpharmacological interventions in the elderly (TONE)	Study of: Adults N: 681 for all endpo N: 681 Intervention 1: % Male: NR Mean Age/Range/Age at Baseline: NR Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Comparator: % Male: NR Mean Age/Range/Age at Baseline: mean 66.5 (SD 4.6) Race: African American: 24% Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: 100 % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Ages 60-80, SBP<145, DBP <85 while on anti-hypertensive medication, stable health,	Exposure Type: Urinary sodium excretion Exposure Unit: mmol/d Duration: NR Exposure to Follow Up Time: NR Dose format: mean change in urinary sodium excretion Q1, Dose: plus 41 Q2, Dose: plus 3 Q3, Dose: minus 22 Q4, Dose: minus 51 Q5, Dose: minus 93	Sodium measure: Single 24-hour urinary analysis without reported quality control measure, 24-hour diet recall Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up Sodium, Method of Validation: 24-hour "diet recall" Sodium Status Arm 2: Net reduction of -39.8 mmol/day Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up How was blood pressure measured? BP measured while patients were in the seated position using Hawksley random-zero sphygmomanometers. SBP defined as the pressure at which the first Kortkoff sound was heard, DBP when the 5th sound could no longer be heard. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, medical records	Incidence of primary study endpoint, defined as: a (Primary end point defined as an average SBP >= 150 mm Hg, an average DBP >= 90 mm Hg, the resumption of BP medication, or a CVD event during followup (mean, 27.8 months)) (mmol/d/Outcome): Mean 27.8 months FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR Adjustment: NR No association between baseline dietary sodium intake or excretion and the risk of a primary study endpoint. The risk of a primary study endpoint increased with increased reduction in urinary sodium excretion.

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>independence in daily living, capacity to alter diet and physical activity in accordance with the intervention</p> <p>Exclusion: History of a stroke or heart attack within the last 6 months, current angina pectoris, CHF, insulin dependent diabetes, serious physical or mental illness, unexplained weight loss of more than 4.5 kg during the past year, BMI <21 (both sexes), BMI>33 (men), BMI>37(women), hyperglycemia, anemia.</p>			

Table D52. Subgroup table for observational studies for hypertensive

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Singer, 2015¹⁵⁰</p> <p>Location: US</p> <p>Setting: a union-sponsored, worksite hypertension program</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 3505</p> <p>% Male: 64 Mean Age/Range/Age at Baseline: mean 52 (SD 10)</p> <p>Race: Q1 black 30.2% white 31.7% Hispanic 33.7% other 4.4%; Q2 black 30.5% white 33.7% Hispanic 34.8% other 2.1%; Q4 black 30.5% white 31.7% Hispanic 35.7% other 2.1%; Q4 black 28.6% white 29.3% Hispanic 38.3% other 3.8%</p> <p>Systolic BP: mean (SD) Q1 146.4 (18.5) Q2 145.3 (17.7) Q3 145.2 (16.5) Q4 145.8 (16.3)</p> <p>Diastolic BP: mean (SD) Q1 93.6 (10.0) Q2 93.9 (9.7) Q3 94.1 (9.4) Q5 (95.1 (9.6)</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: mean (SD) Q1 27.4 (4.1) Q2 27.8 (4.1) Q3 28.9 (4.5) Q4 30.0 (4.9)</p> <p>% with Hypertension: drug use Q1 37.0% Q2 39.9% Q3 40.2% Q4 35.2%</p> <p>% with history of CVD: MI Q1 1.1% Q2 0.5% Q3 1.0% Q4 1.5%; Stroke Q1 0.9% Q2 0.6% Q3 0.9% Q4 0.7%</p> <p>% with Type 2 diabetes: Q1 4%; Q2 6.3% Q3 5.6% Q4 6.0%</p> <p>% with Kidney disease: Q1 1.5%; Q2 1.4%; Q3 1.2%; Q4 2.2%</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants with an SBP \geq 140 mm Hg (\geq 160mm Hg before Joint National Committee 5), DBP \geq 90 mmHg (\geq 95 Hg before Joint National Committee 5), or being on antihypertensive medication at the time of screening were included. Exclusion: not report</p>	<p>Exposure Type: Urine sodium Exposure Unit: mmol/24 h</p> <p>Duration: NR Exposure to Follow Up Time: in-program 6.5 years, follow-up from initial intake to death or last known alive 18.6 years</p> <p>All cardiovascular mortality (Coronary artery disease, including MI, ischemic heart disease, heart failure, and hypertensive heart disease: ICD-9: 402.9, 410–414.9, 427.5, 429.2, ICD-10: I10–I11.9, I13–I13.2, I20–I25.9, I46–I46.9; stroke: ICD-9: 434–434.9, 436–438.9, ICD-10: I61–I64.9; o), Limited cardiovascular mortality (Only MI, ischemic or hypertensive heart disease, and heart failure)</p> <p>Dose format: mean (SD) Q1, Dose: 55 (20) Q2, Dose: 102 (17) Q3, Dose: 143 (20) Q4, Dose: 221 (56)</p> <p>All-cause mortality Dose format: mean (SD) Q2, Dose: 102 (17) Q3, Dose: 143 (20) Q4, Dose: 221 (56)</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: once at baseline</p> <p>How was blood pressure measured? not reported</p> <p>Mortality Outcomes-Method of Ascertainment: National Death Index Plus and the Social Security Administration Death Master File</p>	<p>All cardiovascular mortality (Coronary artery disease, including MI, ischemic heart disease, heart failure, and hypertensive heart disease: ICD-9: 402.9, 410–414.9, 427.5, 429.2; ICD-10: I10–I11.9, I13–I13.2, I20–I25.9, I46–I46.9; stroke: ICD-9: 434–434.9, 436–438.9; ICD-10: I61–I64.9; o) (mmol/24 h/Outcome): Mean 18.6 years FU Q1 cases: 128, total: 890, Q2 cases: 97, total: 876, Q3 cases: 96, total: 865, Q4 cases: 78, total: 874 Adjustment: Age, sex, race, BMI, SBP, eGFR, urine potassium, hematocrit, plasma renin activity, HxDM, Hx smoking, history of baseline left ventricular hypertrophy No significant association between urinary sodium excretion and cardiovascular death was observed</p> <p>All-cause mortality (/Outcome): Q2 cases: 276, total: 876, Q3 cases: 234, total: 865, Q4 cases: 216, total: 874</p> <p>Limited cardiovascular mortality (Only MI, ischemic or hypertensive heart disease, and heart failure) (mmol/24 h/Outcome): Mean 18.6 years FU Q1 cases: NR, total: 890, Q2 cases: NR, total: 876, Q3 cases: NR, total: 865, Q4 cases: NR, total: 874 Adjustment: Age, sex, race, BMI, SBP, urine creatinine, plasma renin activity, HxDM, Hx smoking, history of baseline left ventricular hypertrophy No significant association between urinary sodium excretion and limited cardiovascular mortality.</p>

<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: NR</p> <p>% Male: 48.1%</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information.</p> <p>Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.9</p> <p>Q1, Dose: 1790</p> <p>Q1, Dose: 2018</p> <p>Q2, Dose: 1.06</p> <p>Q2, Dose: 2483</p> <p>Q2, Dose: 2875</p> <p>Q3, Dose: 1.18</p> <p>Q3, Dose: 3123</p> <p>Q3, Dose: 3705</p> <p>Q4, Dose: 1.33</p> <p>Q4, Dose: 4095</p> <p>Q4, Dose: 4974</p> <p>per 1000 mg/d, Dose: NR for HYPERTENSIVE</p> <p>per unit change, Dose: NR for HYPERTENSIVE</p> <p>CVD mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.9</p> <p>Q1, Dose: 1790</p> <p>Q1, Dose: 2018</p> <p>Q2, Dose: 1.06</p> <p>Q2, Dose: 2483</p> <p>Q2, Dose: 2875</p> <p>Q3, Dose: 1.18</p> <p>Q3, Dose: 3123</p> <p>Q3, Dose: 3705</p> <p>Q4, Dose: 1.33</p> <p>Q4, Dose: 4095</p> <p>Q4, Dose: 4974</p> <p>per 1000 mg/d, Dose: NR</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24-hour dietary recall</p> <p>Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall</p> <p>Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome):</p> <p>Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 1155, total: NR, person-years: 35640, per unit change cases: 1155, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and all-cause mortality among those with hypertension.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome):</p> <p>Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 490, total: NR, person-years: 35640, per unit change cases: 490, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and CVD mortality among those with hypertension.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome):</p> <p>Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 1155, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome):</p> <p>Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 490, total: NR, person-years: 35640, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>
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Study	Participants	Exposure	Intake Status Ascertainment	Results
		per unit change, Dose: NR		

Table D53. Subgroup table for observational studies for hypertensive female

Study	Participants	Exposure	Intake Status Ascertainment	Results
Fang, 2000 ¹³¹ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES I	Study of: Adults N: NR % Male: 38.2 Mean Age/Range/Age at Baseline: NR Race: 83.5 white Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: NHANES I survey participants aged between 25-74 during baseline examination. Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.	Exposure Type: Dietary potassium intake Exposure Unit: mg/d Duration: NR Exposure to Follow Up Time: up to 22 years Dose format: range T1, Dose: <1260 T2, Dose: 1260-2206 T3, Dose: >2206	Sodium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates	Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome): Average 16.7 years FU T1 cases: 36, total: NR, T2 cases: 30, total: NR, T3 cases: 27, total: NR Adjustment: Age, race No significant association between potassium intake and risk of stroke mortality among female participants with hypertension.

Table D54. Subgroup table for observational studies for hypertensive male

Study	Participants	Exposure	Intake Status Ascertainment	Results
Fang, 2000 ¹³¹ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES I	Study of: Adults N: NR % Male: 38.2 Mean Age/Range/Age at Baseline: NR Race: 83.5 white Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: NHANES I survey participants aged between 25-74 during baseline examination. Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.	Exposure Type: Dietary potassium intake Exposure Unit: mg/d Duration: NR Exposure to Follow Up Time: up to 22 years Dose format: range T1, Dose: <2003 T2, Dose: 2003-2879 T3, Dose: >2879	Sodium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates	Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome): Average 16.7 years FU T1 cases: 19, total: NR, T2 cases: 17, total: NR, T3 cases: 9, total: NR Adjustment: Age, race There was a significant association between increased risk of stroke death and low dietary potassium intake among men with hypertension.

Table D55. Subgroup table for observational studies for initially free of CVD and HTN

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Geleijnse, 2007¹⁵⁶; Hofman, 1991¹⁵⁷</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Rotterdam Study</p>	<p>Study of: Adults N: 783</p> <p>% Male: 41</p> <p>Mean Age/Range/Age at Baseline: mean 69.2 (SD 8.7)</p> <p>Race: NR</p> <p>Systolic BP: mean 140 (SD 22)</p> <p>Diastolic BP: mean 74 (SD 11)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 26.4 (SD 3.8)</p> <p>% with Hypertension: 37</p> <p>% with history of CVD: 17</p> <p>% with Type 2 diabetes: 10</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included all residents aged 55 years and older living in the Ommoord district of Rotterdam. Everyone who live there at a specific point in time and are willing to participate are eligible.</p> <p>Exclusion: Excluded those who did not provide informed consents.</p>	<p>Exposure Type: Dietary potassium</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Estimated 24-Hour Urinary Potassium Excretion (spot urine)</p> <p>Exposure Unit: mmol/24 h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 5 years</p> <p>Dose format: NR per standard deviation,</p> <p>Dose: Random subcohort mean 3.6 (SD 0.8) g/day per standard deviation,</p> <p>Dose: Random subcohort mean 45 (SD 22) mmol/24h</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: collected 1 overnight urine sample at baseline</p> <p>Sodium, Method of Validation: NR</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: collected 1 overnight urine sample at baseline</p> <p>Potassium, Method of Validation: NR</p> <p>Mortality Outcomes-Method of Ascertainment: Population registry</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital Discharge Registry, General Practitioner's Records</p>	<p>All-cause mortality (CVD mortality comprised fatal myocardial infarction, fatal stroke, sudden cardiac death and other forms of fatal CVD (ICD-10 codes I20-I25, I46, I49, I50, I60-I67, I70-I74, and R96).) (mmol/24 h/Outcome):</p> <p>Median 5.5 y FU</p> <p>per standard deviation cases: NR, total: 5531</p> <p>Adjustment: Age, sex and (for urinary potassium) 24-h urinary creatinine excretion, body mass index, smoking status, diabetes, use of diuretics and highest completed education, daily intake of total energy, alcohol, calcium, saturated fat and 24-h urinary sodium excretion</p> <p>For dietary potassium, similar results were obtained except for risk of all-cause mortality that was significantly reduced both in the entire cohort (RR = 0.78 (0.65–0.94 per 1-SD) and in subjects initially free of CVD and hypertension (RR = 0.71 (0.51–1.00), model 3).</p>

Table D56. Subgroup table for observational studies for male

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Alderman, 1997¹³⁸; Alderman, 1995¹³⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 1900</p> <p>% Male: 64.7</p> <p>Mean Age/Range/Age at Baseline: men mean 52 (SD 10) years; women mean 54 (SD 9) years</p> <p>Race: NR</p> <p>Systolic BP: men mean 150; women mean 150</p> <p>Diastolic BP: men mean 98; women mean 94</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: men mean 27.5; women mean 28.2</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Need Alderman article to answer this question</p> <p>Exclusion: Need Alderman article to answer this question</p>	<p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p> <p>Duration(in months): unclear</p> <p>Exposure to Follow Up Time: 3.8 years</p> <p>Dose format: range</p> <p>Q1, Dose: <89 mmol</p> <p>Q2, Dose: 89-126 mmol</p> <p>Q3, Dose: 127-174 mmol</p> <p>Q4, Dose: >=175 mmol</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: Single 24-hr urine analysis at beginning of the program</p> <p>Sodium, Method of Validation: Validated by using formula described by Cockcroft and Gault and Robertshaw et al. Only included patients whose estimated urinary creatinine clearance values fall within +/-35% of the observed values</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Death certificate reports</p>	<p>CVD (Cardiovascular disease, includes myocardial infarction (MI), stroke, coronary revascularization, unstable angina, congestive heart failure. and other CVD deaths. CVD events included MI (code 410) and cerebrovascular disease (codes 430 to 434 and 436 to 43) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 20.5 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 12.1, total: NR, Q3 cases: 13.8, total: NR, Q4 cases: 7.7, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>MI (Myocardial Infarction incidence code 410) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 12.2 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 5.5, total: NR, Q3 cases: 5.7, total: NR, Q4 cases: 2.4, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>Non-CVD (Includes hospitalizations, emergency room visits, and deaths.) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 18.9 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 14.8, total: NR, Q3 cases: 10.3, total: NR, Q4 cases: 16.5, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p> <p>Stroke (Stroke Incidence) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>Q1 cases: 2.8 (unadjusted case specific incidence rates per 1000 person-years), total: NR, Q2 cases: 2.2, total: NR, Q3 cases: 2.9, total: NR, Q4 cases: 1.8, total: NR</p> <p>Adjustment: Unadjusted</p> <p>No statistically significant association was observed.</p>
<p>Khaw, 1987¹⁴⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 356</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: range 50-79 years</p> <p>Race: NR</p> <p>Systolic BP: No stroke associated death (men) mean 141.5 mmHg, stroke-associated death (men) mean 143.2 mmHg; No stroke-associated death (women) mean 136.4 mmHg, stroke-associated death (women) 147.2 mmHg</p> <p>Diastolic BP: No stroke-associated death (men) mean 84.3 mmHg, stroke-associated death (men) mean 83.2; No stroke-associated death (women) mean 81.3 mmHg, stroke-associated death (women) mean 86.3 mmHg</p> <p>Magnesium: No stroke-associated death (men) mean 11.6, stroke-associated death (men) mean 9.9; No stroke-associated death (women) mean 9.1 mmHg, stroke-associated death (women) mean 8.0</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: Dietary Potassium Intake</p> <p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mmol/d</p> <p>Duration(in months): 144 (12 years)</p> <p>Exposure to Follow Up Time: NR</p> <p>DBP (ICDA 430 to 438), SBP (ICDA 430 to 438)</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: Once (at baseline)</p> <p>Potassium, Method of Validation: A 24-hour recall of dietary intake was obtained by a certified Lipid Research Clinic dietician. The data were coded for nutrient intake by the Nutrition Coordinating Center, University of Minnesota, with use of their data base.</p> <p>How was blood pressure measured? BP was measured by trained observers who used a standard mercury sphygmomanometer after the subject had been seared at rest for at least five minutes. BP was only measured once at baseline.</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p> <p>CVD, CHD, stroke, kidney stones/disease</p>	<p>DBP (ICDA 430 to 438) (Dietary Potassium Intake/Outcome):</p> <p>ICDA 430 to 438 FU</p> <p>mmol/d cases: NR, total: NR, person-years: per unit increase</p> <p>Adjustment: Age</p> <p>After adjusting for age, there is a marginal negative association between potassium intake and DBP in both men and women.</p> <p>SBP (ICDA 430 to 438) (Dietary Potassium Intake/Outcome):</p> <p>ICDA 430 to 438 FU</p> <p>mmol/d cases: NR, total: NR, person-years: per unit increase</p> <p>Adjustment: Age</p> <p>After adjusting for age, there is a marginal negative association between potassium intake and SBP in both men and women.</p> <p>Stroke-associated All-cause mortality (ICDA 430 to 438) (mmol/d/Outcome):</p> <p>12 y FU</p> <p>T1 cases: NR, total: 118, per 10 mmol cases: 9, total: 356, T2+T3 cases: NR, total: 238</p> <p>Adjustment: Age</p> <p>The age-adjusted stroke rates, according to tertile of potassium intake, suggest a dose response (more marked in the women than in the men), with no stroke deaths in the</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>mmol Calcium: No stroke-associated death (men) mean 20.2, stroke-associated death (men) mean 16.1; No stroke-associated death (women) mean 15.1 mmHg, stroke-associated death (women) mean 14.9 mmol Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Men and Women who were 50 to 79 years old and who had no personal history of heart attack, heart failure, or stroke at the base-line examination were included in the study. Exclusion: NR</p>	<p>Dose format: NR mmol/d, Dose: NR</p> <p>Stroke-associated All-cause mortality (ICDA 430 to 438) Dose format: range T1, Dose: <59 T2+T3, Dose: >=59-76, >=76 per 10 mmol</p>	<p>Outcomes-Method of ascertainment: Death certificate reports</p>	<p>highest tertile. Potassium intake was inversely and independently related to stroke. The results were the same when diastolic pressure was used in place of systolic pressure.</p>
<p>Mills, 2016¹²⁰, He, 2016¹²¹, Yang, 2014¹²², Lash, 2009¹²³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Study of: Adults N: 1950</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4; 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR</p> <p>Dose format: NR NR, Dose: NR for male</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1946 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among male, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1949 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among male, greater sodium excretion was associated with an increased risk of composite CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1951 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among male, greater sodium excretion was associated with an increased risk of composite CVD.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.			Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1950 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among male, greater sodium excretion was associated with an increased risk of composite CVD.
Pfister, 2014 ¹⁴¹ Location: UK Setting: Community Design: Prospective Cohort study Study Name: The EPIC-Norfolk study	Study of: Adults N: 9017 % Male: 45.4 Mean Age/Range/Age at Baseline: mean 58.0 (SD 9.2) years Race: NR Systolic BP: reported by quintiles of sodium excretion q1 135 (17) q2 135 (17) q3 136 (17) q4 138 (17) q5 141 (19) Diastolic BP: reported by quintiles of sodium excretion q1 83.1 (10.9) q2 83.1 (10.9) q3 83.9 (10.6) q4 85.2 (10.6) q5 86.8 (11.5) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: reported by quintiles of sodium excretion q1 25.9 (SD 3.1) q2 26.1 (SD 3) q3 26.4 (SD 3.2) q4 26.7 (SD 3.2) q5 27.1 (SD 3.5) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included Norfolk residents between 39-79 years old. Exclusion: Excluded participants with a history of heart attack, stroke, or any cancer. Also excluded those using medical heart failure treatment and those failed to provide data on estimated 24 h urinary sodium excretion.	Exposure Type: Urinary sodium excretion Exposure Unit: mmol/day Duration: NR Exposure to Follow Up Time: 3.5 years Dose format: mean (SD, range) Q1, Dose: 115 (17, <134) Q2, Dose: 145 (6, 134-154) Q3, Dose: 163 (5, 154-172) Q4, Dose: 182 (6, 172-193) Q5, Dose: 218 (31, >193)	Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 24-hr urine analysis at baseline and second health check. Sodium, Method of Validation: Obtained spot urine samples in a random sample of 1551 women. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports, National Death Index	Incident heart failure (Heart failure death was defined as ICD-10 I50 anywhere on the death certificate. Incident heart failure was defined as heart failure death or hospital discharge code ICD-10 I50, which proved to be specific in a recent validation study) (mmol/day/Outcome): Mean 12.9 y FU Q1 cases: 167, total: 1803, Q2 cases: 131, total: 1803, Q3 cases: 127, total: 1804, Q4 cases: 127, total: 1803, Q5 cases: 150, total: 1804 Adjustment: Age, body mass index, known diabetes, cholesterol, social class, educational level, smoking, physical activity, alcohol consumption, and sex where appropriate There was a suggested U-shaped association between quintiles of estimated urinary sodium excretion and hazard of heart failure in age-adjusted analyses in men and women. When further adjusting the analysis for systolic blood pressure and baseline blood pressure medication, the HR for the highest quintile of estimated urinary sodium excretion was strongly attenuated whereas the HR for the lowest quintile was materially unchanged (Tables 2 and 4).
Tunstall-Pedoe, 1997 ¹⁴² ; Tunstall-Pedoe, 1999 ¹⁴³ ; Smith, 1987 ¹⁴⁴ Location: Scotland	Study of: Adults N: 5754 % Male: 49.5 Mean Age/Range/Age at Baseline: ranged 40-59 years Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR	Exposure Type: Urinary potassium ion excretion Exposure Unit: mmol/day Exposure Type: Urinary sodium ion excretion Exposure Unit:	Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: one 24 hour urine collection Sodium, Method of Validation: Urine was analyzed for electrolytes and creatinine. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Death certificate reports	All CHD (All coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among male participants, no statistically significant association was observed between urinary sodium excretion and risk of CHD. All-cause mortality (Deaths from all causes) (mmol/day/Outcome): Average 7.6 years FU

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Scottish Heart Health Study</p>	<p>Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: 1.5% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included randomly selected patients from general practitioners' offices in 23 local government districts. Participants aged between 40-59. Exclusion: Excluded those who failed to complete the study questionnaire, clinic appointment, or both.</p>	<p>mmol/day</p> <p>Duration(in months): 3 years Exposure to Follow Up Time: 6 years</p> <p>Dose format: range group 1, Dose: 17.6 - 47.2 mmol/day group 1, Dose: 46.8 - 129.6 mmol/day group 2, Dose: 129.6 - 168.4 mmol/day group 2, Dose: 47.2 - 59.5 mmol/day group 3, Dose: 168.4 - 204.1 mmol/day group 3, Dose: 59.5 - 71.3 mmol/day group 4, Dose: 204.1 - 251.3 mmol/day group 4, Dose: 71.3 - 86.3 mmol/day group 5, Dose: 251.3 - 416.7 mmol/day group 5, Dose: 86.3 - 138.1 mmol/day</p>		<p>group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among male participants, no statistically significant association was observed between urinary sodium excretion and risk of mortality.</p> <p>CHD deaths (Fatal coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Among male participants, no statistically significant association was observed between urinary sodium excretion and risk of CHD mortality.</p> <p>All CHD (All coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Potassium excretion showed a highly significant protective gradient for all deaths in both sexes and significantly protected against all coronary heart disease in men.</p> <p>All-cause mortality (Deaths from all causes) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age Potassium excretion showed a highly significant protective gradient for all deaths in both sexes and significantly protected against all coronary heart disease in men.</p> <p>CHD deaths (Fatal coronary heart disease) (mmol/day/Outcome): Average 7.6 years FU group 1 cases: NR, total: NR, group 2 cases: NR, total: NR, group 3 cases: NR, total: NR, group 4 cases: NR, total: NR, group 5 cases: NR, total: NR Adjustment: Age No significant association between urinary potassium excretion and CHD mortality among male.</p>
<p>Tuomilehto, 2001¹⁴⁵</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 1161</p> <p>% Male: 48.2 Mean Age/Range/Age at Baseline: age reported by sodium quartile and gender: men q1 mean 45.4 (SD 11.6) years, men q2 mean 45.3 (SD 11.0) years, men q3 mean 46.2 (SD 10.4) years, men q4 mean 45.4 (SD 10.6) years; women q1 mean 45.7 (SD 11.6) years, women q2 mean 45.4 (SD 11.8) years, women q3 mean 44.8 (SD 11.1) years, women q4 mean 45.6 (SD 11.3) years. Race: NR Systolic BP: Systolic blood pressure reported by sodium quartile and gender: men q1 mean 144 (SD 22), men q2 mean 145 (SD 19), men q3 mean 148 (SD 20), men q4 mean 147 (SD 19); women q1 mean 141 (SD 22) years, women q2 mean 140 (SD 22), women q3 mean 141 (SD 22), women q4 mean</p>	<p>Exposure Type: 24 h urinary sodium excretion Exposure Unit: mmol</p> <p>Duration: NR Exposure to Follow Up Time: up to 14 years</p> <p>Dose format: NR per 100 mmol increase, Dose: mean 216 mmol (SD 83)</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p> <p>How was blood pressure measured? Blood pressure was measured once using a standard sphygmomanometer with a 13 cm wide and 42 cm long cuff bladder. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>All-cause mortality (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 136, total: 1173 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among male participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Cardiovascular death (Death, ICD 390-448) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 72, total: 1173 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among male participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>142 (SD 22). Diastolic BP: Diastolic blood pressure reported by sodium quartile and gender: men q1 mean 86 (SD 11), men q2 mean 86 (SD 12), men q3 mean 89 (SD 13), men q4 mean 90 (SD 13); women q1 mean 83 (SD 12) years, women q2 mean 83 (SD 12), women q3 mean 83 (SD 12), women q4 mean 85 (SD 12). Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: BMI reported by sodium quartile and gender: men q1 mean 25.5 (SD 2.4), men q2 mean 26.4 (SD 3.3), men q3 mean 26.9 (SD 3.3), men q4 mean 28.1 (SD 4.2); women q1 mean 24.6 (SD 4.2) years, women q2 mean 25.1 (SD 4.02), women q3 mean 26.3 (SD 4.6), women q4 mean 27.8 (SD 5.4). % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Finnish men and women between 25-64 years old. Analysis of this study included both the 1982 and 1987 cohorts. Exclusion: Excluded those with incomplete collection of urine, and those with incomplete data of risk factors. Also excluded those who had a non-fatal acute coronary event or cerebrovascular event before baseline survey.</p>			<p>Coronary heart disease death (Death, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 54, total: 1173 Adjustment: Age, study year, smoking, serum total and HDL cholesterol, systolic blood pressure, and BMI Among male participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Coronary heart disease incident (Event, ICD 410-411) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 98, total: 1145 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among male participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Stroke incident (Event, ICD 430-438) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 43, total: 1161 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among male participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: 5899</p> <p>% Male: 48.1%</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Race: NR Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information. Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary</p>	<p>Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>CVD mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 1.01 Q1, Dose: 2276 Q1, Dose: 2908 Q2, Dose: 1.17</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24-hour dietary recall Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall" Best potassium measure recorded: single 24-hour dietary recall Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I20-I25) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1267, total: 5899, person-years: 80982, per unit change cases: 1267, total: 5899, person-years: 80982, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. No association between sodium potassium ratio and all-cause mortality among male participants.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 437, total: 5899, person-years: 80982, per unit change cases: 437, total: 5899, person-years: 80982, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. Significant association between higher sodium potassium ratio and CVD mortality</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.	<p>Q2, Dose: 2973 Q2, Dose: 3785 Q3, Dose: 1.29 Q3, Dose: 3588 Q3, Dose: 4570 Q4, Dose: 1.43 Q4, Dose: 4506 Q4, Dose: 5751 per 1000 mg/d, Dose: NR per unit change, Dose: NR</p> <p>All-cause mortality (ICD-10 codes I20-I25) Dose format: median Q1, Dose: 1.01 Q1, Dose: 2276 Q1, Dose: 2908 Q2, Dose: 1.17 Q2, Dose: 2973 Q2, Dose: 3785 Q3, Dose: 1.29 Q3, Dose: 3588 Q3, Dose: 4570 Q4, Dose: 1.43 Q4, Dose: 4506 Q4, Dose: 5751 per 1000 mg/d, Dose: median 3272 (IQR 2660-3964) mg per 1000 mg/d, Dose: median 4165 (IQR 3390-5043) mg per unit change, Dose: median 1.29 (IQR 1.14-1.46)</p>		<p>among male participants.</p> <p>All-cause mortality (ICD-10 codes I20-I25) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1267, total: 5899, person-years: 80982, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among male participants, no significant association between potassium intake and risk of all-cause mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 437, total: 5899, person-years: 80982, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among male participants, no significant association between potassium intake and risk of all-cause mortality.</p>

Table D57. Subgroup table for observational studies for male + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised Assessment Study in ACEiswcdl, 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141.72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: stroke 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged ≥ 55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D58. Subgroup table for observational studies for men

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2009¹²⁵; Satterfield, 1991²²; Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p> <p>Follow-up (TOHP I and TOHP II)</p>	<p>Study of: Adults N: 1259</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; >= 125, 839; women: <125, 298; >= 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30, 777; >= 30 586; Women, <25 138; 25 to <30 279; >= 30 288.</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included.</p> <p>Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio</p> <p>Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR</p> <p>NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: medical records</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome):</p> <p>Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II</p> <p>NR cases: 141, total: 1459</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise</p> <p>Among male participants, there is a significant positive association between sodium to potassium excretion ratio and risk of CVD adjusting for treatment assignment.</p>
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome):</p> <p>Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome):</p> <p>Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among male participants.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>representativeness. Selected individuals aged between 35-70. Exclusion: Excluded those who refused to participate.</p>	<p>Q4, Dose: 2.50-3.00 Q5, Dose: >3.00</p>	<p>forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	

Table D59. Subgroup table for observational studies for men with hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Alderman, 1997¹³⁸; Alderman, 1995¹³⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 1900</p> <p>% Male: 64.7</p> <p>Mean Age/Range/Age at Baseline: men mean 52 (SD 10) years; women mean 54 (SD 9) years</p> <p>Race: NR</p> <p>Systolic BP: men mean 150; women mean 150</p> <p>Diastolic BP: men mean 98; women mean 94</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: men mean 27.5; women mean 28.2</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Need Alderman article to answer this question</p> <p>Exclusion: Need Alderman article to answer this question</p>	<p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p> <p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: per SD=66.6 mmol/d</p> <p>Duration(in months): unclear</p> <p>Exposure to Follow Up Time: 3.8 years</p> <p>MI (Myocardial Infarction incidence code 410)</p> <p>NR, Dose: Median: Men 126 mmol/d; Women 97 mmol/d</p> <p>Q1, Dose: <89 mmol</p> <p>Q2, Dose: 89-126 mmol</p> <p>Q2+Q3</p> <p>Q3, Dose: 127-174 mmol</p> <p>Q4, Dose: >=175 mmol</p> <p>MI (Myocardial Infarction incidence) per SD=26.4 mmol/d, Dose: Median: Men 60 mmol/d; Women 49 mmol/d</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: Single 24-hr urine analysis at beginning of the program</p> <p>Sodium, Method of Validation: Validated by using formula described by Cockcroft and Gault and Robertshaw et al. Only included patients whose estimated urinary creatinine clearance values fall within +/-35% of the observed values</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Hospital records, Death certificate reports</p>	<p>MI (Myocardial Infarction incidence code 410) (per SD=66.6 mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>NR cases: 46, total: 1900, Q1 cases: 22, total: 483, person-years: 1798, Q2 cases: 10, total: 473, person-years: 1818.6, Q2+Q3 cases: 20, total: 942, Q3 cases: 10, total: 469, person-years: 1741.1, Q4 cases: 4, total: 475, person-years: 1697.5</p> <p>Adjustment: Age at entry, cholesterol, urinary sodium, Log10 PRA, pretreatment systolic, left ventricular hypertrophy, smoker, urinary potassium (estimated by Cox proportional hazard regression: best-fitting).</p> <p>No statistically significant association was observed.</p> <p>No statistically significant association was observed.</p> <p>MI (Myocardial Infarction incidence) (mmol/d/Outcome):</p> <p>Average 3.8 years FU</p> <p>per SD=26.4 mmol/d cases: 46, total: 1900</p> <p>Adjustment: Age at entry, cholesterol, urinary sodium, Log10 PRA, pretreatment systolic, left ventricular hypertrophy, smoker, urinary potassium</p> <p>Estimated by Cox proportional hazard regression: best-fitting</p>

Table D60. Subgroup table for observational studies for Mexican American

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p>	<p>Study of: Adults N: 1859</p> <p>% Male: 48.1%</p> <p>Location: US</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Setting: Community</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Design: Prospective Cohort study</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>Study Name: NHANES III</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information.</p> <p>Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.94</p> <p>Q1, Dose: 1815</p> <p>Q1, Dose: 2079</p> <p>Q2, Dose: 1.08</p> <p>Q2, Dose: 2492</p> <p>Q2, Dose: 2917</p> <p>Q3, Dose: 1.2</p> <p>Q3, Dose: 3110</p> <p>Q3, Dose: 3708</p> <p>Q4, Dose: 1.31</p> <p>Q4, Dose: 4042</p> <p>Q4, Dose: 4906</p> <p>per 1000 mg/d, Dose: NR for Mexican American</p> <p>per unit change, Dose: NR for Mexican American</p> <p>CVD mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.94</p> <p>Q1, Dose: 1815</p> <p>Q1, Dose: 2079</p> <p>Q2, Dose: 1.08</p> <p>Q2, Dose: 2492</p> <p>Q2, Dose: 2917</p> <p>Q3, Dose: 1.2</p> <p>Q3, Dose: 3110</p> <p>Q3, Dose: 3708</p> <p>Q4, Dose: 1.31</p> <p>Q4, Dose: 4042</p> <p>Q4, Dose: 4906</p> <p>per 1000 mg/d, Dose: NR</p> <p>per unit change, Dose: NR</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24-hour dietary recall</p> <p>Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall</p> <p>Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 449, total: 1859, person-years: 51611, per unit change cases: 449, total: 1859, person-years: 51611, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and all-cause mortality among Mexican American participants.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 147, total: 1859, person-years: 51611, per unit change cases: 147, total: 1859, person-years: 51611, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and CVD mortality among Mexican American participants.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 449, total: 1859, person-years: 51611, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 147, total: 1859, person-years: 51611, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D61. Subgroup table for observational studies for NHS I

Table D62. Subgroup table for observational studies for NHS II

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Adebamowo, 2015¹⁵⁸; Erratum, 2015¹⁵⁹; Iso, 1999¹⁶⁰; Stampfer, 1985¹⁶¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Nurses Health Study</p>	<p>Study of: Adults N: 94715</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: reported by study cohort and K quartile NHS I q1 mean 58 (SD 7) years q3 mean 60 (SD 7) years q5 mean 62 (SD 7) years NHS II q1 mean 40 (SD 5) years q3 mean 41 (SD 5) years q5 mean 42 (SD 4) years</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: reported by study cohort and K quartiles NHS I q1 26.4 (SD 5.5) q3 26.4 (SD 5.1) q5 26.5 (SD 5.2) NHS II q1 26.0 (SD 6.5) q3 25.6 (SD 5.7) q5 25.6 (SD 5.5)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included female registered nurses between 25 to 55 years old who enrolled in 1976 or 1989</p> <p>Exclusion: Excluded those with prevalent cancer, stroke, or IHD at baseline, and those showed evidence of possible low or high energy intakes, and those failed to provide complete diet info.</p>	<p>Exposure Type: Total potassium intake (dietary + supplemental)</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Total potassium intake (dietary)</p> <p>Exposure Unit: mg/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 30 years of follow-up in NHS I and 22 years of follow-up in NHS II</p> <p>Dose format: median</p> <p>Q1, Dose: 2381</p> <p>Q1, Dose: 2386</p> <p>Q2, Dose: 2744</p> <p>Q2, Dose: 2750</p> <p>Q3, Dose: 2992</p> <p>Q3, Dose: 3000</p> <p>Q4, Dose: 3248</p> <p>Q4, Dose: 3257</p> <p>Q5, Dose: 3642</p> <p>Q5, Dose: 3654</p>	<p>Sodium, Method of Validation: Food diaries with reported validation</p> <p>Best potassium measure recorded: Used food frequency questionnaire to collect diet info with specific questions about potassium supplements</p> <p>Potassium, Method of Validation: Cited a validation study testing the correlations between mineral intake assessed by FFQ and by 1-week diet records.</p> <p>Mortality Outcomes-Method of Ascertainment: Death certificate, Postal authorities, National death index, Medical records, Autopsy reports</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: Medical files, Followup questionnaire</p>	<p>Total stroke (Self-report and medical record reviews) (mg/day/Outcome): 22 y FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR, Q5 cases: NR, total: NR</p> <p>Adjustment: Age, calendar year, total calories (quintiles of kcal), BMI (in kg/m²; .25, 25 to .30, or \$30), parental history of heart disease (aged #60 y), alcohol intake (0, 0 to .5, 5 to .10, 10 to .15, or \$15 g/d), physical activity (.3, 3 to .9, 9 to .18, 18 to .27, or \$27 metabolic equivalent tasks/wk), smoking, postmenopausal hormone therapy, oral contraceptive use (never, past, or current), menopausal status (premenopausal or postmenopausal), aspirin (0 to .2 or \$2 pills/wk), multivitamin, history of hypertension, hypercholesterolemia, diabetes at baseline, and thiazide use (yes or no); for intakes of magnesium and calcium (quintiles of g/d). NHS, Nurses' Health Study.</p> <p>No association between potassium intake and total stroke risk among NHS II participants.</p>
<p>Ferraro, 2016¹⁴⁸; Taylor, 2004¹⁴⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Health Professionals Follow-up Study</p>	<p>Study of: Adults</p> <p>% Male: NR</p> <p>Mean Age/Range/Age at Baseline: mean 54.3 (SD 9.8)</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 25.5 (SD 3.4)</p> <p>% with Hypertension: 21%</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: 3%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included HPFS participants without a history of kidney stones at baseline.</p> <p>Exclusion: Excluded those with a history of malignancy (except for nonmelanoma skin cancer) at baseline and those who developed malignancies during follow-up. Excluded NHS I participants who answered questionnaires before 1992 (the year of the first lifetime kidney stone history inquiry).</p>	<p>Exposure Type: 3.3256000000000001E-2</p> <p>Exposure Unit: Potassium intake</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 0</p> <p>Dose format: Q1</p> <p>g/day, Dose: median</p> <p>g/day, Dose: median</p> <p>g/day, Dose: median</p> <p>g/day, Dose: median</p> <p>g/day, Dose: median</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire</p> <p>Best potassium measure recorded: One food frequency questionnaire at baseline and additional FFQ every 4 years</p> <p>Potassium, Method of Validation: FFQs were found to be reproducible and valid in the HPFS and the NHS I.</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: supplementary questionnaire (self-report)</p>	<p>Kidney stones (Kidney) (Potassium intake/Outcome): Self reported, accompanied by pain and/or hematuria FU</p> <p>g/day cases: NR, total: NR, person-years: 2275, g/day cases: NR, total: NR, person-years: 2649, g/day cases: NR, total: NR, person-years: 2910, g/day cases: NR, total: NR, person-years: 3180, g/day cases: NR, total: NR, person-years: 3612</p> <p>Adjustment: Age, body mass index, history of diabetes, history of hypertension, use of thiazides, supplemental calcium, and intakes of fluid, calcium, sodium, fructose, oxalate, phytate, alcohol, and all other types of protein.</p> <p>Third to fifth quintiles of potassium intake were inversely associated with incidence of kidney stones compared to first quintile.</p>

Table D63. Subgroup table for observational studies for non-hypertensive

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p>	<p>Study of: Adults N: NR</p> <p>% Male: 48.1%</p> <p>Location: US Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Setting: Community Race: NR Systolic BP: NR Diastolic BP: NR</p> <p>Design: Prospective Cohort study Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>Study Name: NHANES III % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information.</p> <p>Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.97 Q1, Dose: 1793 Q1, Dose: 2220 Q2, Dose: 1.13 Q2, Dose: 2474 Q2, Dose: 3078 Q3, Dose: 1.27 Q3, Dose: 3105 Q3, Dose: 3900 Q4, Dose: 1.41 Q4, Dose: 4063 Q4, Dose: 5169 per 1000 mg/d, Dose: NR for NON-HYPERTENSIVE per unit change, Dose: NR for NON-HYPERTENSIVE</p> <p>CVD mortality (ICD-10 codes I00-I78) Dose format: median Q1, Dose: 0.97 Q1, Dose: 1793 Q1, Dose: 2220 Q2, Dose: 1.13 Q2, Dose: 2474 Q2, Dose: 3078 Q3, Dose: 1.27 Q3, Dose: 3105 Q3, Dose: 3900 Q4, Dose: 1.41 Q4, Dose: 4063 Q4, Dose: 5169 per 1000 mg/d, Dose: NR per unit change, Dose: NR</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24-hour dietary recall Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1115, total: NR, person-years: 134469, per unit change cases: 1115, total: NR, person-years: 134469, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. Significant association between higher sodium potassium ratio and all-cause mortality among those without hypertension.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 335, total: NR, person-years: 134469, per unit change cases: 335, total: NR, person-years: 134469, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake In multivariable analysis, higher sodium intake was associated with increased all-cause mortality. No significant association between sodium potassium ratio and CVD mortality among those without hypertension.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 1115, total: NR, person-years: 134469, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU Q1 cases: NR, total: NR, per 1000 mg/d cases: 335, total: NR, person-years: 134469, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D64. Subgroup table for observational studies for no diabetes

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p>	<p>Study of: Adults N: 1858</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR Dose format: NR NR, Dose: NR for no diabetes</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1854 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1856 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1858 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1858 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p>
<p>O'Donnell, 2014¹²⁴</p>	<p>Study of: Adults N: 101945</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those without diabetes.</p>

Table D65. Subgroup table for observational studies for no history of hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Larsson, 2011¹⁵¹</p> <p>Location: Sweden</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Swedish Mammography Cohort</p>	<p>Study of: Adults N: NR</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: by potassium quintiles q1 mean 61.6 q5 mean 60.7</p> <p>Race: NR</p> <p>Systolic BP: NR Diastolic BP: NR</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: by potassium quintiles q1 mean 24.8 q5 mean 25.3</p> <p>% with Hypertension: by potassium quintiles q1 18.6% q5 20.4%</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: by potassium quintiles q1 2.2% q5 4.5%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included women born between 1914-1948 and living in central Sweden. Included those who completed both diet questionnaires at baseline and in 1997.</p> <p>Exclusion: Excluded women with incorrect national identification number, with a history of stroke, coronary heart disease, or cancer, or with extreme energy intake.</p>	<p>Exposure Type: Potassium intake Exposure Unit: mg/d</p> <p>Duration: NR Exposure to Follow Up Time: a mean of 10.4 years</p> <p>Dose format: Median Q1, Dose: 2419 Q2, Dose: 2767 Q3, Dose: 3021 Q4, Dose: 3296 Q5, Dose: 3744</p>	<p>Potassium measure: food frequency questionnaire with reported validation</p> <p>Best potassium measure recorded: One 96-item food frequency questionnaire completed in 1997</p> <p>Potassium, Method of Validation: The food frequency questionnaire has been validated in Messerer M, Johansson SE, Wolk A. The validity of questionnaire-based micronutrient intake estimates is increased by including dietary supplement use in Swedish men. J Nutr. 2004;134(7):1800–1805.</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital Discharge Registry</p>	<p>Total stroke (Strokes were classified as cerebral infarction (code I63), intracerebral hemorrhage (code I61), subarachnoid hemorrhage (code I60), and unspecified stroke (code I64).) (mg/d/Outcome):</p> <p>Mean 10.4 years FU</p> <p>Q1 cases: 239, total: NR, Q2 cases: 225, total: NR, Q3 cases: 223, total: NR, Q4 cases: 198, total: NR, Q5 cases: 212, total: NR</p> <p>Adjustment: Age, smoking status, pack-years of smoking, educational level, body mass index, total physical activity level, history of diabetes, history of hypertension, aspirin use, family history of myocardial infarction, and intakes of total energy, alcohol, protein, cholesterol, total fiber, and folate</p> <p>Potassium intake was not statistically significantly inversely associated with risk of total stroke and cerebral infarction among women with no history of hypertension.</p>

Table D66. Subgroup table for observational studies for no hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation₁</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those without hypertension.</p>
<p>Seth, 2014¹⁵⁴; Anderson, 2003¹⁵⁵</p> <p>Location: US</p> <p>Setting:</p>	<p>Study of: Adults N: 90137</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: mean 63.6 (SD 7.4) years</p> <p>Race: NR</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: average 11 years</p>	<p>Potassium measure: Food Frequency Questionnaires</p> <p>Best potassium measure recorded: Two food frequency questionnaires (FFQ) at study enrollment and year 3 follow-up</p> <p>Potassium, Method of Validation:</p>	<p>All-cause mortality (Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes.) (mg/d/Outcome): Average 11 years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction,</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
Community Design: Prospective Cohort study Study Name: The Women's Health Initiative Observational Study (WHI-OS)	Systolic BP: NR Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR Inclusion: Included 93676 postmenopausal women aged 50 to 79 years. Exclusion: Excluded women with history of stroke, with missing information on history of stroke, and those with no information on dietary potassium at baseline. Excluded women with <465 calories intake or with >3931 calories intake, whose potassium intake ranged 0.07--1790 mg or ranged 1507 -- 31129 mg.	Dose format: range Q1, Dose: <1925.5 Q2, Dose: >=1925.5-2519.4 Q3, Dose: >=2519.4-3193.6 Q4, Dose: >=3193.6	Used a sub sample to evaluate FFQ measurement properties Mortality Outcomes-Method of Ascertainment: Hospital records, Death certificate, Autopsy reports CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Medical files, self reported	hormone use, alcohol intake, aspirin use, high cholesterol and body mass index Among women with nonhypertension, there was a lower risk of all-cause mortality, all stroke, and ischemic stroke across increasing quartiles for potassium. Stroke (All) (Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes.) (mg/d/Outcome): Average 11 years FU Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR Adjustment: Age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol and body mass index Among women with nonhypertension, there was a lower risk of all-cause mortality, all stroke, and ischemic stroke across increasing quartiles for potassium.

Table D67. Subgroup table for observational studies for no diabetes

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p>	<p>Study of: Adults N: 1858</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR Dose format: NR NR, Dose: NR for no diabetes</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1854 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1856 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed perfusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1858 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or death within 24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 1858 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among participants without diabetes, greater sodium excretion was associated with a non-significant increased risk of composite CVD.</p>
<p>O'Donnell, 2014¹²⁴</p>	<p>Study of: Adults N: 101945</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among those without diabetes.</p>

Table D68. Subgroup table for observational studies for non-Asian

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years</p> <p>Race: 48.4 Asian</p> <p>Systolic BP: mean 131.7 (SD 22.30)</p> <p>Diastolic BP: mean 82.24 (SD 15.65)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: 41.5</p> <p>% with history of CVD: 8.3</p> <p>% with Type 2 diabetes: 9.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70.</p> <p>Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range</p> <p>G1, Dose: <3</p> <p>G2, Dose: 3-5.99</p> <p>G3, Dose: >=6</p> <p>Q1, Dose: <1.50</p> <p>Q2, Dose: 1.50-1.99</p> <p>Q3, Dose: 2.00-2.49</p> <p>Q4, Dose: 2.50-3.00</p> <p>Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation₁</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU</p> <p>Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032</p> <p>Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models.</p> <p>No significant association between potassium intake and risk of death and major CVD events among non-Asian participants.</p>

Table D69. Subgroup table for observational studies for non-Hispanic Black

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: 1540</p> <p>% Male: 48.1%</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information.</p> <p>Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 1.13</p> <p>Q1, Dose: 1442</p> <p>Q1, Dose: 2127</p> <p>Q2, Dose: 1.33</p> <p>Q2, Dose: 2022</p> <p>Q2, Dose: 2961</p> <p>Q3, Dose: 1.48</p> <p>Q3, Dose: 2566</p> <p>Q3, Dose: 3760</p> <p>Q4, Dose: 1.63</p> <p>Q4, Dose: 3408</p> <p>Q4, Dose: 5001</p> <p>per 1000 mg/d, Dose: NR for Non-Hispanic Black</p> <p>per unit change, Dose: NR for Non-Hispanic Black</p> <p>CVD mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 1.13</p> <p>Q1, Dose: 1442</p> <p>Q1, Dose: 2127</p> <p>Q2, Dose: 1.33</p> <p>Q2, Dose: 2022</p> <p>Q2, Dose: 2961</p> <p>Q3, Dose: 1.48</p> <p>Q3, Dose: 2566</p> <p>Q3, Dose: 3760</p> <p>Q4, Dose: 1.63</p> <p>Q4, Dose: 3408</p> <p>Q4, Dose: 5001</p> <p>per 1000 mg/d, Dose: NR</p> <p>per unit change, Dose: NR</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24-hour dietary recall</p> <p>Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall</p> <p>Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 527, total: 1540, person-years: 45934, per unit change cases: 527, total: 1540, person-years: 45934, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and all-cause mortality among non-Hispanic black participants.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 163, total: 1540, person-years: 45934, per unit change cases: 163, total: 1540, person-years: 45934, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and CVD mortality among non-Hispanic black participants.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 527, total: 1540, person-years: 45934, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 163, total: 1540, person-years: 45934, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D70. Subgroup table for observational studies for non-Hispanic White

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Yang, 2011¹⁴⁶, Cohen, 2008¹⁴⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Study of: Adults N: 2269</p> <p>% Male: 48.1%</p> <p>Mean Age/Range/Age at Baseline: ranged 25-74 years</p> <p>Race: NR</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included non pregnant adults ages 20 and older, those who completed a physical examination, and who had mortality follow-up information.</p> <p>Exclusion: Excluded survey participants with incomplete data on one or more 24-hour dietary recalls. Excluded those partaking a reduced salt diet for hypertension and those with a history of heart attack, stroke, or congestive heart failure.</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: NR</p> <p>All-cause mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.93</p> <p>Q1, Dose: 1878</p> <p>Q1, Dose: 2190</p> <p>Q2, Dose: 1.09</p> <p>Q2, Dose: 2563</p> <p>Q2, Dose: 3060</p> <p>Q3, Dose: 1.22</p> <p>Q3, Dose: 3196</p> <p>Q3, Dose: 3889</p> <p>Q4, Dose: 1.35</p> <p>Q4, Dose: 4159</p> <p>Q4, Dose: 5166</p> <p>per 1000 mg/d, Dose: NR for Non-Hispanic White</p> <p>per unit change, Dose: NR for Non-Hispanic White</p> <p>CVD mortality (ICD-10 codes I00-I78)</p> <p>Dose format: median</p> <p>Q1, Dose: 0.93</p> <p>Q1, Dose: 1878</p> <p>Q1, Dose: 2190</p> <p>Q2, Dose: 1.09</p> <p>Q2, Dose: 2563</p> <p>Q2, Dose: 3060</p> <p>Q3, Dose: 1.22</p> <p>Q3, Dose: 3196</p> <p>Q3, Dose: 3889</p> <p>Q4, Dose: 1.35</p> <p>Q4, Dose: 4159</p> <p>Q4, Dose: 5166</p> <p>per 1000 mg/d, Dose: NR</p> <p>per unit change, Dose: NR</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24-hour dietary recall</p> <p>Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall</p> <p>Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 1253, total: 2269, person-years: 65408, per unit change cases: 1253, total: 2269, person-years: 65408, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>Significant association between higher sodium potassium ratio and all-cause mortality among non-Hispanic white participants.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 498, total: 2269, person-years: 65408, per unit change cases: 498, total: 2269, person-years: 65408, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>In multivariable analysis, higher sodium intake was associated with increased all-cause mortality.</p> <p>No significant association between sodium potassium ratio and CVD mortality among non-Hispanic white participants.</p> <p>All-cause mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 1253, total: 2269, person-years: 65408, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p> <p>CVD mortality (ICD-10 codes I00-I78) (mg/d/Outcome): Median 14.8 y FU</p> <p>Q1 cases: NR, total: NR, per 1000 mg/d cases: 498, total: 2269, person-years: 65408, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: Sex, race/ethnicity, educational attainment, body mass index, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of cardiovascular disease, and total calorie intake</p> <p>Among subgroups of Hispanic, non-Hispanic, hypertensive, non-hypertensive participants, there is no evidence of significant interactions between potassium intake and risk of mortality.</p>

Table D71. Subgroup table for observational studies for non-White + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised Assessment Study in ACEiswDI, 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141.72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: stroke 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged >=55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D72. Subgroup table for observational studies for non-diabetic CKD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fan, 2014¹⁶²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MDRD (Modification of Diet in Renal Disease) Study</p>	<p>Study of: Adults N: 840</p> <p>% Male: 60.5</p> <p>Mean Age/Range/Age at Baseline: mean 51.7 (SD 12.4) years</p> <p>Race: white 85</p> <p>Systolic BP: mean 131.9 (SD 17.6)</p> <p>Diastolic BP: mean 81.0 (SD 10.1)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 27.1 (SD 4.4)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: 13.1</p> <p>% with Type 2 diabetes: 5.1</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included CKD patients age between 18 and 70 years. Included men with serum creatinine level of 1.4–7.0 mg/dL and women with serum creatinine level of 1.2–7.0 mg/dL.</p> <p>Exclusion: Excluded those who were pregnant, those with type 1 and 2 diabetes, those with glomerulonephritis caused by autoimmune diseases, those with obstructive uropathy, those with renal artery stenosis, those with proteinuria with protein greater than 10 g/d, those with mean arterial pressure greater than 125 mm Hg, or those with prior kidney transplantation.</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: g/d</p> <p>Duration: 4 years</p> <p>Exposure to Follow Up Time: NA</p> <p>Dose format: NR</p> <p>continuous, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: Patients either had three (n=200) or four (n=640) 24-hour urine collections and analysis to calculate 24-h urinary sodium excretion.</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: renal data system</p>	<p>Kidney failure (Defined as initiation of dialysis or transplantation) (g/d/Outcome): Mean 6 years FU</p> <p>continuous cases: 617, total: 840</p> <p>Adjustment: Age, sex, race, cause of kidney disease, measured GFR, log urine protein, BMI, SBP, LDL cholesterol, HDL cholesterol, smoking, diabetes, history of CVD, ACE inhibitor use, diuretics use, MDRD study A or B, and randomization to BP and dietary protein target.</p> <p>No association between urinary sodium excretion and kidney failure.</p> <p>Kidney failure or all-cause mortality (Kidney failure defined as initiation of dialysis or transplantation; or all-cause mortality) (g/d/Outcome): Mean 6 years FU</p> <p>continuous cases: 617, total: 840</p> <p>Adjustment: Age, sex, race, cause of kidney disease, measured GFR, log urine protein, BMI, SBP, LDL cholesterol, HDL cholesterol, smoking, diabetes, history of CVD, ACE inhibitor use, diuretics use, MDRD study A or B, and randomization to BP and dietary protein target.</p> <p>No association between urinary sodium excretion and composite outcome.</p>

Table D73. Subgroup table for observational studies for nonblack

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mills, 2016¹²⁰; He, 2016¹²¹; Yang, 2014¹²²; Lash, 2009¹²³</p>	<p>Study of: Adults N: 2070</p> <p>% Male: Q1 35.0, Q2 49.9, Q3 61.3 Q4 76.0 Mean Age/Range/Age at Baseline: Q1 mean 57.2 (SD 10.9) Q2 mean 57.6 (SD 11.3) Q3 mean 58.2 (SD 10.8) Q4 mean 58.0 (SD 10.6) years Race: Q1: White 38.6% Black 51.4% Other 10.0 %; Q2: White 45.6% Black 44.0% Other 10.3%; Q3 White 50.6% Black 37.4% Other 12.0%; Q4 White 54.3% Black 32.9% Other 12.8% Systolic BP: Q1: mean 125.6 (SD 21.7); Q2 mean 126.3 (SD 20.9); Q3 mean 128.1 (SD 21.7); Q4 mean 132.3 (SD 22.4) mmHg Diastolic BP: Q1: mean 70.7 (SD 12.7); Q2 mean 71.0 (SD 12.8); Q3: mean 71.4 (SD 12.3); Q4: mean 72.7 (SD 13.0) mmHg Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: Q1: mean 31.7 (SD 8.0); Q2 mean 32.1 (SD 7.5); Q3 mean 31.9 (SD 7.3); Q4 mean 31.8 (SD 7.5) kg/m² % with Hypertension: Q1 80.2; Q2 86.5; Q3 86.7; Q4 90.8 % with history of CVD: Q1 27.3; Q2 30.0; Q3 34.9; Q4: 39.7 % with Type 2 diabetes: Q1 37.7; Q2 43.8; Q3 49.3; Q4 60.3 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participant aged 21 to 74 years with mild to moderate CKD designed to identify and examine risk factors for CKD progression and development of CVD in those with CKD, who met age-specific estimated glomerular filtration rate (eGFR) criteria of 20 to 70 mL/min/1.73 m² were included. Exclusion: People with a history of kidney transplant, dialysis for at least 1 month, glomerulonephritis requiring immunosuppression, advanced heart failure, cirrhosis, or polycystic kidney disease were excluded.</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h Duration(in months): 163.2 (6.8 years) Exposure to Follow Up Time: NR Dose format: NR NR, Dose: NR for NON-black</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, followup visit</p>	<p>Composite CVD (Defined as congestive heart failure, stroke, and myocardial infarction) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 2068 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among non-black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Congestive Heart Failure (Congestive heart failure was identified by hospital admission for new or worsening CHF signs and symptoms, in addition to diminished cardiac output) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 2072 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among non-black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Myocardial Infarction (Myocardial infarction was defined by characteristic changes in troponin and creatinekinase-MB levels, symptoms of myocardial ischemia, electrocardiogram changes, or new fixed profusion abnormalities.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 2072 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among non-black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p> <p>Stroke (Stroke was defined as rapid onset of neurologic deficit, headache, or other nonvascular cause and clinically relevant lesion on brain imaging for longer than 24 hours or deathwithin24 hours.) (per 1000 mg/24 h/Outcome): Median 6.8 years FU NR cases: NR, total: 2070 Adjustment: Age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, baseline eGFR Among non-black participants, greater sodium excretion was associated with an increased risk of compositive CVD.</p>

Table D74. Subgroup table for observational studies for nonhypertensive female

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fang, 2000¹³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: NR</p> <p>% Male: 38.2</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: 83.5 white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination.</p> <p>Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	<p>Exposure Type: Dietary potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 22 years</p> <p>Dose format: range</p> <p>T1, Dose: <1017</p> <p>T2, Dose: 1017-1641</p> <p>T3, Dose: >1641</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p>	<p>Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome):</p> <p>Average 16.7 years FU</p> <p>T1 cases: 35, total: NR, T2 cases: 33, total: NR, T3 cases: 22, total: NR</p> <p>Adjustment: Age, race</p> <p>Among nonhypertensive subjects (n 7632), after age/race adjustment, the sex-specific stroke mortality by dietary potassium intake was not significantly different between dietary potassium intake groups among women.</p>

Table D75. Subgroup table for observational studies for nonhypertensive male

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fang, 2000¹³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: NR</p> <p>% Male: 38.2</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: 83.5 white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination.</p> <p>Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	<p>Exposure Type: Dietary potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 22 years</p> <p>Dose format: range</p> <p>T1, Dose: <1508</p> <p>T2, Dose: 1508-2207</p> <p>T3, Dose: >2207</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p>	<p>Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome):</p> <p>Average 16.7 years FU</p> <p>T1 cases: 30, total: NR, T2 cases: 24, total: NR, T3 cases: 22, total: NR</p> <p>Adjustment: Age, race</p> <p>Among nonhypertensive subjects (n 7632), after age/race adjustment, the sex-specific stroke mortality by dietary potassium intake was not significantly different between dietary potassium intake groups among men.</p>

Table D76. Subgroup table for observational studies for nonoverweight

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>He, 1999¹⁶³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: 6797</p> <p>% Male: 38.9</p> <p>Mean Age/Range/Age at Baseline: age reported by sodium quartile and weight status: non overweight q1 mean 46.2 (SD 15.4) years, non overweight q2 mean 48.3 (SD 15.8) years, non overweight q3 mean 49.3 (SD15.9) years, non overweight q4 mean 48.6 (SD 15.8) years; overweight q1 mean 50 (SD 14.9) years, overweight q2 mean 51.1 (SD 15) years, overweight q3 mean 52 (SD15) years, overweight q4 mean 51.3 (SD 14.8) years.</p> <p>Race: White race, % reported by sodium quartile and weight status: non overweight q1 mean 82.3, non overweight q2 mean 87.6, non overweight q3 mean 86.3, non overweight q4 mean 90.1; overweight q1 mean 73.5, overweight q2 mean 76.7, overweight q3 mean 77.4, overweight q4 mean 82.4.</p> <p>Systolic BP: Systolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 129.0 (SD 23.2), non overweight q2 mean 129.5 (SD 21.6), non overweight q3 mean 131.4 (SD 22.9), non overweight q4 mean 130.7 (SD 23.2); overweight q1 mean 141.7 (SD 24.1) years, overweight q2 mean 142.4 (SD 24.4), overweight q3 mean 144.8 (SD 25.2), overweight q4 mean 143.5 (SD 24.6).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 80.6 (SD 12.7), non overweight q2 mean 80.2 (SD 11.5), non overweight q3 mean 81.3 (SD 12.1), non overweight q4 mean 80.6 (SD 12.2); overweight q1 mean 89.0 (SD 12.9) years, overweight q2 mean 88.3 (SD 13.0), overweight q3 mean 89.1 (SD 13.4), overweight q4 mean 88.9 (SD 13.2).</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and weight status: non overweight q1 mean 23.1 (SD 2.6), non overweight q2 mean 23.1 (SD 2.7), non overweight q3 mean 23.1 (SD 2.7), non overweight q4 mean 23.2 (SD 2.7); overweight q1 mean 32.0 (SD 4.4) years, overweight q2 mean 31.6 (SD 4.1), overweight q3 mean 32.0 (SD 4.7), overweight q4 mean 31.6 (SD 3.9).</p> <p>% with Hypertension: % with hypertension reported by sodium quartile and weight status: non overweight q1 mean 19.1, non overweight q2 mean 19.1, non overweight q3 mean 21.6, non overweight q4 mean 21.8; overweight q1 mean 42.2, overweight q2 mean 42.8, overweight q3</p>	<p>Exposure Type: Dietary Sodium intake Exposure Unit: 100 mmol/d</p> <p>Exposure Type: Quartile of Sodium-to-Energy Ratio (100 mmol/7452 KJ) Exposure Unit: 100 mmol/7452 KJ</p> <p>Exposure Type: Sodium-to-Energy Ratio (100 mmol/7452 KJ) Exposure Unit: 100 mmol/7452 KJ</p> <p>Duration: NR Exposure to Follow Up Time: 113,467 person-years; an average of 19 years</p> <p>Dose format: range Q1, Dose: 0.8-62.3 mmol/7452 kJ Q2, Dose: >62.3-84.0 mmol/7452 kJ Q3, Dose: >84-112.3 mmol/7452 kJ Q4, Dose: >112.3-467.9 mmol/7452 kJ per 100-mmol increase, Dose: NR for overall nonoverweight</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24h dietary recall with 3-dimensional food-portion models CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, Death certificate reports</p>	<p>All-cause mortality from all causes (ICD-9 codes 430-434.9, 436, or 437.0-437.1, 410-414, 436, 437.0-437.1, 402-404, or 428) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 363, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 423, total: 1725, person-years: 28853, Q3 cases: 462, total: 1746, person-years: 28666, Q4 cases: 428, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>CHD incidence (ICD-9 codes 410-414) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 215, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 302, total: 1725, person-years: 28853, Q3 cases: 289, total: 1746, person-years: 28666, Q4 cases: 274, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>CHD mortality (ICD-9 codes 410-414) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 70, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 111, total: 1725, person-years: 28853, Q3 cases: 109, total: 1746, person-years: 28666, Q4 cases: 110, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>CVD mortality (ICD-9 codes 410-414, 430-434.9, 436, 437.0-437.1, 402-404, or 428) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 112, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 151, total: 1725, person-years: 28853, Q3 cases: 147, total: 1746, person-years: 28666, Q4 cases: 156, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>Stroke incidence (ICD-9 codes 430-434.9, 436, or 437.0-437.1) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 95, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 116, total: 1725, person-years: 28853, Q3 cases: 110, total:</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>mean 43.8, overweight q4 mean 42.3. % with history of CVD: NR % with Type 2 diabetes: % with type 2 diabetes reported by sodium quartile and weight status: non overweight q1 mean 2.1, non overweight q2 mean 2.6, non overweight q3 mean 2.9, non overweight q4 mean 3.8; overweight q1 mean 4.2, overweight q2 mean 5.4, overweight q3 mean 5.6, overweight q4 mean 5.7. % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: NHANES I participants who were 25-74 years old during survey collection period 1971-1975 Exclusion: Exclude those who did not complete 24h dietary recall, who did not report sodium intake information, and those who self-reported history of heart attack, heart failure, or stroke at baseline, or taking medication for heart disease. Also excluded those who were taking a low-salt diet at baseline.</p>			<p>1746, person-years: 28666, Q4 cases: 109, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>Stroke mortality (ICD-9 codes 430-434.9, 436, or 437.0-437.1) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 31, total: 1658, person-years: 28250, per 100-mmol increase cases: NR, total: 6797, Q2 cases: 28, total: 1725, person-years: 28853, Q3 cases: 27, total: 1746, person-years: 28666, Q4 cases: 37, total: 1668, person-years: 27698 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p>

Table D77. Subgroup table for observational studies for normal weight men

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Tuomilehto, 2001¹⁴⁵</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 659</p> <p>% Male: 48.2</p> <p>Mean Age/Range/Age at Baseline: age reported by sodium quartile and gender: men q1 mean 45.4 (SD 11.6) years, men q2 mean 45.3 (SD 11.0) years, men q3 mean 46.2 (SD 10.4) years, men q4 mean 45.4 (SD 10.6) years; women q1 mean 45.7 (SD 11.6) years, women q2 mean 45.4 (SD 11.8) years, women q3 mean 44.8 (SD 11.1) years, women q4 mean 45.6 (SD 11.3) years.</p> <p>Race: NR</p> <p>Systolic BP: Systolic blood pressure reported by sodium quartile and gender: men q1 mean 144 (SD 22), men q2 mean 145 (SD 19), men q3 mean 148 (SD 20), men q4 mean 147 (SD 19); women q1 mean 141 (SD 22) years, women q2 mean 140 (SD 22), women q3 mean 141 (SD 22), women q4 mean 142 (SD 22).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and gender: men q1 mean 86 (SD 11), men q2 mean 86 (SD 12), men q3 mean 89 (SD 13), men q4 mean 90 (SD 13); women q1 mean 83 (SD 12) years, women q2 mean 83 (SD 12), women q3 mean 83 (SD 12), women q4 mean 85 (SD 12).</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and gender: men q1 mean 25.5 (SD 2.4), men q2 mean 26.4 (SD 3.3), men q3 mean 26.9 (SD 3.3), men q4 mean 28.1 (SD 4.2); women q1 mean 24.6 (SD 4.2) years, women q2 mean 25.1 (SD 4.02), women q3 mean 26.3 (SD 4.6), women q4 mean 27.8 (SD 5.4).</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Finnish men and women between 25-64 years old. Analysis of this study included both the 1982 and 1987 cohorts. Exclusion: Excluded those with incomplete collection of urine, and those with incomplete data of risk factors. Also excluded those who had a non-fatal acute coronary event or cerebrovascular event before baseline survey.</p>	<p>Exposure Type: 24 h urinary sodium excretion Exposure Unit: mmol</p> <p>Duration: NR Exposure to Follow Up Time: up to 14 years</p> <p>Dose format: NR per 100 mmol increase, Dose: NR for Normal weight</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p> <p>How was blood pressure measured? Blood pressure was measured once using a standard sphygmomanometer with a 13 cm wide and 42 cm long cuff bladder. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>All-cause mortality (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 60, total: 659 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among both normal weight and overweight female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Cardiovascular death (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 29, total: 659 Adjustment: Age, study year Among both normal weight and overweight female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>

Table D78. Subgroup table for observational studies for normotensive

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Haring, 2015¹⁶⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Strong Heart Study</p>	<p>Study of: Adults N: NR</p> <p>% Male: pre-hypertension/hypertension 46.71%; normal blood pressure 78.04%</p> <p>Mean Age/Range/Age at Baseline: pre-hypertension/hypertension mean 29.29 (SD 6.51) years; normal blood pressure mean 27.4 (SD 6.79) years</p> <p>Race: NR</p> <p>Systolic BP: pre-hypertension/hypertension mean 126 (SD 11); normal blood pressure mean 108 (SD 7)</p> <p>Diastolic BP: pre-hypertension/hypertension mean 82 (SD 9); normal blood pressure mean 69 (SD 7)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: pre-hypertension/hypertension mean 34.58 (SD 8.12); normal blood pressure mean 30.87 (SD 8.27)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: pre-hypertension/hypertension 16.37%; normal blood pressure 5.41%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included study participants between ages 14 to 39.</p> <p>Exclusion: Excluded participants with incomplete data or extreme energy intake. Excluded participants with a history of any cardiovascular disease or stroke, for example, myocardial infarction, angina pectoris, heart failure, coronary bypass surgery, angioplasty, carotid endarterectomy, valve replacement and significant valve disease (aortic or mitral stenosis or more than mild regurgitation).</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Urinary potassium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: 2 years</p> <p>Exposure to Follow Up Time: on average 4 years</p> <p>Dose format: NR</p> <p>per 1 unit increase, Dose: NR</p> <p>per unit change</p>	<p>Sodium measure: Food Frequency Questionnaire</p> <p>Best sodium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Sodium, Method of Validation: FFQ administered by interviewer</p> <p>Potassium measure: Food Frequency Questionnaire</p> <p>Best potassium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Potassium, Method of Validation: FFQ administered by interviewer</p> <p>How was blood pressure measured? Blood pressure measured as the average of 2 blood pressure readings at baseline examination.</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Physical examination</p>	<p>Change in LVMI (g/m) (mg/mg/Outcome): Mean 4 years FU per unit change</p> <p>In normotensive participants, sodium/potassium ratio was not associated with changes in LV mass index.</p> <p>Change in LVMI (g/m) (mmol/24h/Outcome): Mean 4 years FU per 1 unit increase, total: NR</p> <p>In normotensive participants, potassium intake was not associated with changes in LV mass index.</p>
<p>Joosten, 2014¹⁵²</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name:</p>	<p>Study of: Adults N: 5180</p> <p>% Male: by sodium quartiles q1 48.7 q2 48.7 q3 48.7 q4 48.7</p> <p>Mean Age/Range/Age at Baseline: by sodium quartiles q1 mean 50 (SD 13) q2 mean 49 (SD 13) q3 mean 48 (SD 12) q4 mean 47 (SD 11)</p> <p>Race: NR</p> <p>Systolic BP: by sodium quartiles q1 mean 129 (SD 22) q2 mean 128 (SD 20) q3 mean 128 (SD 20) q4 mean 129 (SD 20)</p> <p>Diastolic BP: by sodium quartiles q1 mean 74 (SD 10) q2 mean 74 (SD 10) q3 mean 74 (SD 10) q4</p>	<p>Exposure Type: Sex-specific quartiles of sodium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: a median of 10.5 years</p> <p>Dose format: range</p> <p>Q1, Dose: male <95 female <122</p> <p>Q2, Dose: male 95-121 female 122-154</p> <p>Q3, Dose: male 122-151 female</p>	<p>Sodium measure: two 24-hr urine analysis with out reported quality control measure</p> <p>Best sodium measure recorded: During baseline examination, participants collected two 24-hour urines for 2 consecutive days.</p> <p>Mortality Outcomes-Method of Ascertainment: Central Bureau of Statistics</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: national registry of hospital discharge diagnoses</p>	<p>Coronary Heart Disease Events (CHD was defined as myocardial infarction (ICD-code 410), acute and subacute ischemic heart disease (ICD-code 411) and coronary artery bypass grafting or percutaneous transluminal coronary angioplasty.)</p> <p>(mmol/24h/Outcome): Median 10.5 years (Q1-Q3: 9.9-10.8 years; 71491 person years) FU</p> <p>Q1 cases: 47, total: NR, person-years: 12114, continuous cases: 162, total: NR, person-years: 49822, Q2 cases: 41, total: NR, person-years: 12638, Q3 cases: 38, total: NR, person-years: 12406, Q4 cases: 36, total: NR, person-years: 12664</p> <p>Adjustment: Age, body mass index, smoking status, sex, alcohol intake, parental history of coronary heart disease, type 2 diabetes, total to high-density lipoprotein cholesterol ratio, and urinary potassium, magnesium, and creatinine excretion</p> <p>No statistically significant association was observed.</p> <p>No statistically significant association was observed.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
The Prevention of Renal and Vascular End-stage Disease (PREVEND) study	<p>mean 74 (SD 9) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: by sodium quartiles q1 mean 25 (SD 3.7) q2 mean 25.5 (SD 3.7) q3 mean 26.1 (SD 4.1) q4 mean 27.5 (SD 4.8) % with Hypertension: by sodium quartiles q1 32.8 q2 30.4 q3 31.4 q4 30.7 % with history of CVD: NR % with Type 2 diabetes: by sodium quartiles q1 2.2 q2 2.5 q3 2.9 q4 4.7 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included Dutch participants between ages 28 to 75 and those who agreed to participate in questionnaire survey and urine sample collection. Exclusion: Excluded pregnant women and those with type I diabetes.</p>	<p>155-190 Q4, Dose: male >151 female >190 continuous, Dose: per 1-g/d increase</p>		

Table D79. Subgroup table for observational studies for overweight

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>He, 1999¹⁶³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: 2688</p> <p>% Male: 38.9</p> <p>Mean Age/Range/Age at Baseline: age reported by sodium quartile and weight status: non overweight q1 mean 46.2 (SD 15.4) years, non overweight q2 mean 48.3 (SD 15.8) years, non overweight q3 mean 49.3 (SD15.9) years, non overweight q4 mean 48.6 (SD 15.8) years; overweight q1 mean 50 (SD 14.9) years, overweight q2 mean 51.1 (SD 15) years, overweight q3 mean 52 (SD15) years, overweight q4 mean 51.3 (SD 14.8) years.</p> <p>Race: White race, % reported by sodium quartile and weight status: non overweight q1 mean 82.3, non overweight q2 mean 87.6, non overweight q3 mean 86.3, non overweight q4 mean 90.1; overweight q1 mean 73.5, overweight q2 mean 76.7, overweight q3 mean 77.4, overweight q4 mean 82.4.</p> <p>Systolic BP: Systolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 129.0 (SD 23.2), non overweight q2 mean 129.5 (SD 21.6), non overweight q3 mean 131.4 (SD 22.9), non overweight q4 mean 130.7 (SD 23.2); overweight q1 mean 141.7 (SD 24.1) years, overweight q2 mean 142.4 (SD 24.4), overweight q3 mean 144.8 (SD 25.2), overweight q4 mean 143.5 (SD 24.6).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and weight status: non overweight q1 mean 80.6 (SD 12.7), non overweight q2 mean 80.2 (SD 11.5), non overweight q3 mean 81.3 (SD 12.1), non overweight q4 mean 80.6 (SD 12.2); overweight q1 mean 89.0 (SD 12.9) years, overweight q2 mean 88.3 (SD 13.0), overweight q3 mean 89.1 (SD 13.4), overweight q4 mean 88.9 (SD 13.2).</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and weight status: non overweight q1 mean 23.1 (SD 2.6), non overweight q2 mean 23.1 (SD 2.7), non overweight q3 mean 23.1 (SD 2.7), non overweight q4 mean 23.2 (SD 2.7); overweight q1 mean 32.0 (SD 4.4) years, overweight q2 mean 31.6 (SD 4.1), overweight q3 mean 32.0 (SD 4.7), overweight q4 mean 31.6 (SD 3.9).</p> <p>% with Hypertension: % with hypertension reported by sodium quartile and weight status: non overweight q1 mean 19.1, non overweight q2 mean 19.1, non overweight q3 mean 21.6, non overweight q4 mean 21.8; overweight q1 mean 42.2, overweight q2 mean 42.8, overweight q3</p>	<p>Exposure Type: Dietary Sodium intake Exposure Unit: 100 mmol/d</p> <p>Exposure Type: Quartile of Sodium-to-Energy Ratio (100 mmol/7452 KJ) Exposure Unit: 100 mmol/7452 KJ</p> <p>Exposure Type: Sodium-to-Energy Ratio (100 mmol/7452 KJ) Exposure Unit: 100 mmol/7452 KJ</p> <p>Duration: NR Exposure to Follow Up Time: 113,467 person-years; an average of 19 years</p> <p>Dose format: range Q1, Dose: 0.8-62.3 mmol/7452 kJ Q2, Dose: >62.3-84.0 mmol/7452 kJ Q3, Dose: >84-112.3 mmol/7452 kJ Q4, Dose: >112.3-467.9 mmol/7452 kJ per 100-mmol increase, Dose: NR for overall overweight</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: single 24h dietary recall with 3-dimensional food-portion models CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, Interview with participant or proxy, Death certificate reports</p>	<p>All-cause mortality from all causes (ICD-9 codes 430-434.9, 436, or 437.0-437.1, 410-414, 436, 437.0-437.1, 402-404, or 428) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 189, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 184, total: 647, person-years: 10644, Q3 cases: 205, total: 625, person-years: 10037, Q4 cases: 232, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Among those who are overweight, significant association between higher quartile of dietary sodium-to-energy ratio and increased risk of total mortality. Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake.</p> <p>CHD incidence (ICD-9 codes 410-414) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 169, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 160, total: 647, person-years: 10644, Q3 cases: 158, total: 625, person-years: 10037, Q4 cases: 160, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake. No significant association observed.</p> <p>CHD mortality (ICD-9 codes 410-414) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 52, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 46, total: 647, person-years: 10644, Q3 cases: 55, total: 625, person-years: 10037, Q4 cases: 61, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Among those who are overweight, significant association between higher quartile of dietary sodium-to-energy ratio and increased risk of CHD mortality. Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake.</p> <p>CVD mortality (ICD-9 codes 410-414, 430-434.9, 436, 437.0-437.1, 402-404, or 428) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 74, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 70, total: 647, person-years: 10644, Q3 cases: 85, total: 625, person-years: 10037, Q4 cases: 100, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Among those who are overweight, significant association between higher quartile of dietary sodium-to-energy ratio and increased risk of CVD mortality. Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake.</p> <p>Stroke incidence (ICD-9 codes 430-434.9, 436, or 437.0-437.1) (100 mmol/7452 KJ/Outcome):</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
	<p>mean 43.8, overweight q4 mean 42.3. % with history of CVD: NR % with Type 2 diabetes: % with type 2 diabetes reported by sodium quartile and weight status: non overweight q1 mean 2.1, non overweight q2 mean 2.6, non overweight q3 mean 2.9, non overweight q4 mean 3.8; overweight q1 mean 4.2, overweight q2 mean 5.4, overweight q3 mean 5.6, overweight q4 mean 5.7. % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: NHANES I participants who were 25-74 years old during survey collection period 1971-1975 Exclusion: Exclude those who did not complete 24h dietary recall, who did not report sodium intake information, and those who self-reported history of heart attack, heart failure, or stroke at baseline, or taking medication for heart disease. Also excluded those who were taking a low-salt diet at baseline.</p>			<p>Average 19 years FU Q1 cases: 45, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 61, total: 647, person-years: 10644, Q3 cases: 75, total: 625, person-years: 10037, Q4 cases: 69, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Among those who are overweight, significant association between higher quartile of dietary sodium-to-energy ratio and increased risk of stroke. Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake.</p> <p>Stroke mortality (ICD-9 codes 430-434.9, 436, or 437.0-437.1) (100 mmol/7452 KJ/Outcome): Average 19 years FU Q1 cases: 15, total: 713, person-years: 11920, per 100-mmol increase cases: NR, total: 2688, Q2 cases: 17, total: 647, person-years: 10644, Q3 cases: 24, total: 625, person-years: 10037, Q4 cases: 31, total: 703, person-years: 11188 Adjustment: Age, sex, race, systolic blood pressure, serum cholesterol level, body mass index, history of diabetes, diuretic use, physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake Among those who are overweight, significant association between higher quartile of dietary sodium-to-energy ratio and increased risk of stroke mortality. Multivariate relative risk of CVD and total mortality associated with a 100-mmol increase in dietary sodium intake.</p>

Table D80. Subgroup table for observational studies for overweight (BMI >=25)

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>He, 2002¹⁶⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The first National Health and Nutrition Examination Surbey (NHANES I) Epidemiologic Follow-up Study (NHEFS)</p>	<p>Study of: Adults N: 5129</p> <p>% Male: non overweight 36 overweight 44</p> <p>Mean Age/Range/Age at Baseline: mean (SD) non overweight 48.2 (16.1) overweight mean 52.2 (SD 15.2)</p> <p>Race: African American race non overweight 13% overweight 19%</p> <p>Systolic BP: mean (SD) overweight 129.2(23.4) overweight 141.0 (24.7)</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: nonoverweight 20 overweight 38</p> <p>% with history of CVD: valvular heart disease nonoverweight 5, overweight 5; coronary heart disease nonoverweight 4, overweight 5</p> <p>% with Type 2 diabetes: non overweight 3, overweight 6</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants in NHANES I aged 25 to 74 years were included.</p> <p>Exclusion: People who lacked 240hour dietary recall information, or who lacked sodium intake information, or who had a history of CHF at their baseline examination, or who were consuming a low-salt diet at baseline were excluded.</p>	<p>Exposure Type: Dietary sodium intake</p> <p>Exposure Unit: mmol/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 85035 person-years from 1971 through 1992</p> <p>Dose format: NR</p> <p>100-mmol increase, Dose: mean 86.8 (SD 58.2) mmol/d</p> <p>Q1, Dose: 33.7 (11.5, 0-50.2)</p> <p>Q2, Dose: 63.9 (7.4, 50.2-76.2)</p> <p>Q3, Dose: 92.8 (10.7, 76.2-113.6)</p> <p>Q4, Dose: 167.6 (59.8, >113.8)</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: once CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>Congestive Heart Failure (ICD-9 code between 428.0 and 428.9) (mmol/d/Outcome):</p> <p>Average 19 years FU</p> <p>100-mmol increase cases: 679, total: 5129, person-years: 85035, Q1 cases: 208, total: 1401, person-years: 21592, Q2 cases: 177, total: 1279, person-years: 20028, Q3 cases: 146, total: 1239, person-years: 19299, Q4 cases: 148, total: 1210, person-years: 19346</p> <p>Adjustment: Baseline age, sex, race, total calorie, less than a high school education, low recreational physical activity, smoking history, alcohol consumption, history of diabetes mellitus and valvular heart disease, systolic blood pressure, total serum cholesterol level, time-dependent history of coronary heart disease and dietary intake of potassium and calcium</p> <p>Dietary sodium intake was significantly associated with risk of CHF among the overweight individuals.</p> <p>There were borderline statistically significant interactions between sodium intake and overweight status on CHF. Dietary sodium intake was significantly associated with an increased risk of CHF incidence in overweight, but not in nonoverweight, persons.</p>

Table D81. Subgroup table for observational studies for overweight and pre-HTN

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2016³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p>	<p>Study of: Adults N: 417 for TOHP I; 9</p> <p>% Male: 68.38</p> <p>Mean Age/Range/Age at Baseline: mean mean Q1 42.5 Q2 42.7 Q3 42.9 Q4 42.3; women Q1 44.3 Q2 43.9 Q3 43.0 Q4 43.2</p> <p>Race: % Black men Q1 16.0 Q2 9.7 Q3 10.4 Q4 8.8; women Q1 25.4 28.2 26.9 Q4 26.7</p> <p>Systolic BP: mean men Q1 124.9 Q2 125.2 Q3 125.7 Q4 126.4; women Q1 126.2 Q2 126.5 Q3 126.8 Q4 126.4</p> <p>Diastolic BP: mean men Q1 84.3 Q2 84.4 Q3 84.8 Q4 85.0; women Q1 84.2 Q2 84.6 Q3 85.0 Q4 85.0</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included TOHP participants who were not in a sodium reduction intervention Exclusion: missing sodium excretion or the occurrence of an incident CVD event or death during the period of exposure assessment</p>	<p>Exposure Type: Sodium/potassium excretion ratio Exposure Unit: mmol/mmol</p> <p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p> <p>Duration: median 25.7 year for TOHP I; median 22.4 years for TOHP II Exposure to Follow Up Time: NR</p> <p>Dose format: range C1, Dose: <2 C1, Dose: <2300 C2, Dose: 2 to <3 C2, Dose: 2300 to <3600 C3, Dose: 3 to <4 C3, Dose: 3600 to <4800 C4, Dose: >= 4 C4, Dose: >=4800 continuous, Dose: per unit per 1 mg/day, Dose: TOHP I: 167 mmol/24 h (3,839 mg/24 h) in men and 128 mmol/24 h (2,948 mg/24 h) in women; TOHP II: 199 mmol/24 h (4,576 mg/24 h) in men and 154 mmol/24 h (3,541 mg/24 h) in women.</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: twice, at 5 (life-style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life-style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II Mortality Outcomes-Method of Ascertainment: National death index</p>	<p>All-cause mortality (Searched the national death index) (mmol/24h/Outcome): Median 25.7years for TOHP I and 22.4 years for TOHP II FU C1 cases: 22 for TOHP I; 1 for TOHP II, total: 246 for, C1 cases: 37 for TOHP I; 7 for TOHP II, total: 364 for, C2 cases: 73 for TOHP I; 32 for TOHP II, total: 775 for, C2 cases: 81 for TOHP I; 32 for TOHP II, total: 812 for, C3 cases: 45 for TOHP I; 27 for TOHP II, total: 458 for, C3 cases: 63 for TOHP I; 30 for TOHP II, total: 566 for, C4 cases: 26 for TOHP I; 17 for TOHP II, total: 210 for, C4 cases: 31 for TOHP I; 20 for TOHP II, total: 257 for, continuous cases: NR, total: NR, per 1 mg/day cases: NR, total: NR Adjustment: Age, sex, race/ethnicity, clinic, and treatment assignment, plus education status, baseline weight, alcohol use, smoking, exercise, and family history of cardiovascular disease Non-significant increasing trend across categories of sodium/potassium ratio and all-cause mortality. Significant positive association between per unit increase in sodium/potassium ratio and all-cause mortality. There was a direct linear association between average sodium intake and mortality.</p>

Table D82. Subgroup table for observational studies for overweight men

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Tuomilehto, 2001¹⁴⁵</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 514</p> <p>% Male: 48.2</p> <p>Mean Age/Range/Age at Baseline: age reported by sodium quartile and gender: men q1 mean 45.4 (SD 11.6) years, men q2 mean 45.3 (SD 11.0) years, men q3 mean 46.2 (SD 10.4) years, men q4 mean 45.4 (SD 10.6) years; women q1 mean 45.7 (SD 11.6) years, women q2 mean 45.4 (SD 11.8) years, women q3 mean 44.8 (SD 11.1) years, women q4 mean 45.6 (SD 11.3) years.</p> <p>Race: NR</p> <p>Systolic BP: Systolic blood pressure reported by sodium quartile and gender: men q1 mean 144 (SD 22), men q2 mean 145 (SD 19), men q3 mean 148 (SD 20), men q4 mean 147 (SD 19); women q1 mean 141 (SD 22) years, women q2 mean 140 (SD 22), women q3 mean 141 (SD 22), women q4 mean 142 (SD 22).</p> <p>Diastolic BP: Diastolic blood pressure reported by sodium quartile and gender: men q1 mean 86 (SD 11), men q2 mean 86 (SD 12), men q3 mean 89 (SD 13), men q4 mean 90 (SD 13); women q1 mean 83 (SD 12) years, women q2 mean 83 (SD 12), women q3 mean 83 (SD 12), women q4 mean 85 (SD 12).</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: BMI reported by sodium quartile and gender: men q1 mean 25.5 (SD 2.4), men q2 mean 26.4 (SD 3.3), men q3 mean 26.9 (SD 3.3), men q4 mean 28.1 (SD 4.2); women q1 mean 24.6 (SD 4.2) years, women q2 mean 25.1 (SD 4.02), women q3 mean 26.3 (SD 4.6), women q4 mean 27.8 (SD 5.4).</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Finnish men and women between 25-64 years old. Analysis of this study included both the 1982 and 1987 cohorts. Exclusion: Excluded those with incomplete collection of urine, and those with incomplete data of risk factors. Also excluded those who had a non-fatal acute coronary event or cerebrovascular event before baseline survey.</p>	<p>Exposure Type: 24 h urinary sodium excretion Exposure Unit: mmol</p> <p>Duration: NR Exposure to Follow Up Time: up to 14 years</p> <p>Dose format: NR per 100 mmol increase, Dose: NR for overweight</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p> <p>How was blood pressure measured? Blood pressure was measured once using a standard sphygmomanometer with a 13 cm wide and 42 cm long cuff bladder. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records, National database</p>	<p>All-cause mortality (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 76, total: 514 Adjustment: Age and study year, and sex when analyses included both sexes combined, and for the following cardiovascular risk factors: serum total cholesterol, serum HDL cholesterol, blood pressure, body mass index, and smoking Among both normal weight and overweight female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p> <p>Cardiovascular death (Death) (mmol/Outcome): Up to 13 years FU per 100 mmol increase cases: 43, total: 514 Adjustment: Age, study year Among both normal weight and overweight female participants, no significant association was observed between urinary sodium excretion and risk of mortality, stroke, CVD mortality, and coronary heart disease and mortality.</p>

Table D83. Subgroup table for observational studies for patients with eGFR \geq 60 ml/min per 1.73

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Araki, 2015¹⁶⁶, Araki, 2013¹⁶⁷</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Shiga Prospective Observational Follow-up Study</p>	<p>Study of: Adults N: 623</p> <p>% Male: 57.8</p> <p>Mean Age/Range/Age at Baseline: mean 59 (SD 10) years</p> <p>Race: NR</p> <p>Systolic BP: mean 134 (SD 18)</p> <p>Diastolic BP: mean 77 (SD 10)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 23.5 (SD 3.3)</p> <p>% with Hypertension: 46.9</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included patients with type 2 diabetes and with eGFR\geq60 ml/min per 1.73 m²</p> <p>Exclusion: Excluded those with a history of CVD and those using any diuretics.</p>	<p>Exposure Type: Urinary Potassium Excretion</p> <p>Exposure Unit: g/d</p> <p>Exposure Type: Urinary Sodium Excretion</p> <p>Exposure Unit: g/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: a median of 11 years</p> <p>50% decline in eGFR (Calculated using the simplified prediction equation proposed by the Japanese Society of Nephrology), Annual decline rate in eGFR (Calculated using the simplified prediction equation proposed by the Japanese Society of Nephrology), CVD events (The occurrence of myocardial infarction, angina pectoris, stroke, peripheral vascular disease (PAD), and death from cardiovascular causes. Myocardial infarction was defined as a clinical presentation characterized by angiographic evidence)</p> <p>Dose format: range</p> <p>Q1, Dose: <1.72</p> <p>Q2, Dose: 1.72-2.32</p> <p>Q3, Dose: 2.33-2.90</p> <p>Q4, Dose: >2.90</p> <p>Primary endpoint (The first occurrence of any of the renal and cardiovascular events, which were as follows: initiation of RRT for chronic renal failure and the occurrence of myocardial infarction, angina pectoris, stroke, peripheral vascular disease (PAD), and death from car)</p> <p>Dose format: range</p> <p>Q1, Dose: <3.81</p> <p>Q2, Dose: 3.81-5.07</p> <p>Q3, Dose: 5.08-6.5</p> <p>Q4, Dose: >6.5</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: completed one 24-hr urine analysis at baseline</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: completed one 24-hr urine analysis at baseline</p>	<p>Primary endpoint (The first occurrence of any of the renal and cardiovascular events, which were as follows: initiation of RRT for chronic renal failure and the occurrence of myocardial infarction, angina pectoris, stroke, peripheral vascular disease (PAD), and death from car) (g/d/Outcome):</p> <p>Median 11 (IQR 8-16) years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: The baseline data, including age, sex, body mass index, hemoglobin A1c, total cholesterol, log triglyceride, log HDL-cholesterol, LDL-cholesterol, systolic BP, renin-angiotensin system inhibitor, hypertension, log urinary albumin excretion rate, eGFR, current smoking, and urinary sodium excretion (or urinary potassium excretion), in the Cox proportional regression analysis.</p> <p>No association between risk of primary endpoint and being in different quartiles of urinary sodium excretion.</p> <p>50% decline in eGFR (Calculated using the simplified prediction equation proposed by the Japanese Society of Nephrology) (g/d/Outcome):</p> <p>Median 11 (IQR 8-16) years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: The baseline data, including age, sex, body mass index, hemoglobin A1c, total cholesterol, log triglyceride, log HDL-cholesterol, LDL-cholesterol, systolic BP, renin-angiotensin system inhibitor, hypertension, log urinary albumin excretion rate, eGFR, current smoking, and urinary sodium excretion, in the Cox proportional regression analysis.</p> <p>A significant association between lower risk of 50% decline in eGFR and being in the highest quartile of urinary potassium excretion.</p> <p>Annual decline rate in eGFR (Calculated using the simplified prediction equation proposed by the Japanese Society of Nephrology) (g/d/Outcome):</p> <p>Median 11 (IQR 8-16) years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: The baseline data, including age, sex, body mass index, hemoglobin A1c, total cholesterol, log triglyceride, log HDL-cholesterol, LDL-cholesterol, systolic BP, renin-angiotensin system inhibitor, hypertension, log urinary albumin excretion rate, eGFR, current smoking, and urinary sodium excretion, in the Cox proportional regression analysis.</p> <p>A significant association between lower risk of annual decline rate in eGFR and being in the highest quartile of urinary potassium excretion versus the two lowest quartiles of urinary potassium excretion.</p> <p>CVD events (The occurrence of myocardial infarction, angina pectoris, stroke, peripheral vascular disease (PAD), and death from cardiovascular causes. Myocardial infarction was defined as a clinical presentation characterized by angiographic evidence of coronary thro) (g/d/Outcome):</p> <p>Median 11 (IQR 8-16) years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: The baseline data, including age, sex, body mass index, hemoglobin A1c, total cholesterol, log triglyceride, log HDL-cholesterol, LDL-cholesterol, systolic BP, renin-angiotensin system inhibitor, hypertension, log urinary albumin excretion rate, eGFR, current smoking, and urinary sodium excretion, in the Cox proportional regression analysis.</p> <p>A significant association between lower risk of CVD events and being in the highest quartile of urinary potassium excretion.</p> <p>Progression to CKD stage 4 (EGFR<30 ml/min per 1.73 m²) (g/d/Outcome):</p> <p>Median 11 (IQR 8-16) years FU</p> <p>Q1 cases: NR, total: NR, Q2 cases: NR, total: NR, Q3 cases: NR, total: NR, Q4 cases: NR, total: NR</p> <p>Adjustment: The baseline data, including age, sex, body mass index, hemoglobin A1c, total cholesterol, log triglyceride, log HDL-cholesterol, LDL-cholesterol, systolic BP, renin-angiotensin system inhibitor, hypertension, log urinary albumin excretion rate, eGFR, current smoking, and urinary sodium excretion, in the Cox proportional regression analysis.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
				A significant association between lower risk of progression to CKD stage 4 and being in the highest quartile of urinary potassium excretion.

Table D84. Subgroup table for observational studies for pre-hypertensive or hypertensive

Study	Participants	Exposure	Intake Status Ascertainment	Results
Haring, 2015 ¹⁶⁴	<p>Study of: Adults N: NR</p> <p>Location: US % Male: pre-hypertension/hypertension 46.71%; normal blood pressure 78.04%</p> <p>Setting: Community Mean Age/Range/Age at Baseline: pre-hypertension/hypertension mean 29.29 (SD 6.51) years; normal blood pressure mean 27.4 (SD 6.79) years</p> <p>Design: Prospective Cohort study Race: NR Systolic BP: pre-hypertension/hypertension mean 126 (SD 11); normal blood pressure mean 108 (SD 7) Diastolic BP: pre-hypertension/hypertension mean 82 (SD 9); normal blood pressure mean 69 (SD 7)</p> <p>Study Name: The Strong Heart Study Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: pre-hypertension/hypertension mean 34.58 (SD 8.12); normal blood pressure mean 30.87 (SD 8.27) % with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: pre-hypertension/hypertension 16.37%; normal blood pressure 5.41% % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Included study participants between ages 14 to 39. Exclusion: Excluded participants with incomplete data or extreme energy intake. Excluded participants with a history of any cardiovascular disease or stroke, for example, myocardial infarction, angina pectoris, heart failure, coronary bypass surgery, angioplasty, carotid endarterectomy, valve replacement and significant valve disease (aortic or mitral stenosis or more than mild regurgitation).</p>	<p>Exposure Type: Sodium-Potassium Ratio Exposure Unit: mg/mg</p> <p>Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h</p> <p>Duration: 2 years Exposure to Follow Up Time: on average 4 years</p> <p>per 1 unit increase, Dose: NR per unit change</p>	<p>Sodium measure: Food Frequency Questionnaire Best sodium measure recorded: One 119-item food frequency questionnaire at baseline Sodium, Method of Validation: FFQ administered by interviewer Potassium measure: Food Frequency Questionnaire Best potassium measure recorded: One 119-item food frequency questionnaire at baseline Potassium, Method of Validation: FFQ administered by interviewer</p> <p>How was blood pressure measured? Blood pressure measured as the average of 2 blood pressure readings at baseline examination. CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Physical examination</p>	<p>Change in LVMI (g/m) (mg/mg/Outcome): per unit change In prehypertensives/hypertensives patients, there is a positive association between sodium/potassium ratio and LVmass index.</p> <p>Change in LVMI (g/m) (mmol/24h/Outcome): per 1 unit increase, total: NR In pre-hypertensive or hypertensive participants, potassium intake was not associated with changes in LV mass index.</p>

Table D85. Subgroup table for observational studies for pre-pubertal group

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Lijie Shi, 2014¹³³; Kruppe, 2014¹³⁴; Kroke, 2004¹³⁵; Krupp, 2015¹³²</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p>	<p>Study of: Children N: NR</p> <p>% Male: 51</p> <p>Mean Age/Range/Age at Baseline: boys median 6 (IQR 4.0-8.0) girls median 6.0 (IQR 4.0- 7.0)</p> <p>Race: NR</p> <p>Systolic BP: boys median 97.1 (IQR 90.8 -1.04) girls median 97.0 (IQR 90.0- 102)</p> <p>Diastolic BP: boys median 57.0 (IQR 50-0 - 65.0) girls median 55.0 (IQR 49.6 -64.1)</p> <p>Magnesium: NR Calcium: NR Other Minerals: NR</p> <p>Mean BMI: boys median 15.7 (IQR 15.0 - 16.8) girls median 15.3 (IQR 14.7 -16.4)</p> <p>% with Hypertension: NR % with history of CVD: NR % with Type 2 diabetes: NR % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Children aged 4 -18 year old were included.</p> <p>Exclusion: Children who had taken BP-influencing drugs, regularly or on the day of BP measurements, or whose SBP or DBP data were implausible were excluded.</p>	<p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/MJ per day</p> <p>Duration: NR Exposure to Follow Up Time: no data (approximately 10 years)</p> <p>Dose format: continuous All, Dose: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 yearly repeated 24-hour urine analysis</p> <p>How was blood pressure measured? SBP and DBP had been measured according to standard procedures with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) thereafter. Appropriate cuff sizes were used according to arm circumferences. BP was measured in the right arm of the subjects after 5 min of rest. Two consecutive BP measurements were recorded on each measurement occasion, and the arithmetic mean of both readings was used in the analysis.</p>	<p>Diastolic blood pressure (BP was measured with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) after 1994.) (mmol/MJ per day/Outcome): All cases: NR, total: NR Adjustment: Age, age2, age3, sex, pubertal group, intra-individual change in Na excretion £ pubertal group and person-specific mean-Na excretion £ pubertal group. TEI, TEI £ pubertal group, BMI-SDS, height-SDS, growth velocity, full breast-feeding status, maternal diastolic BP, FVI, FVI £ pubertal group and Ca intake. In pre-pubertal stage, no between-person effect observed for sodium excretion and DBP. In pre-pubertal stage, no within-person effect observed for sodium excretion and DBP.</p> <p>Systolic blood pressure (BP was measured with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) after 1994.) (mmol/MJ per day/Outcome): 7 years FU All cases: NR, total: NR Adjustment: Age, age2, age3, sex, pubertal group, intra-individual change in Na excretion £ pubertal group and person-specific mean-Na excretion £ pubertal group. total energy intake (TEI), TEI £ pubertal group, BMI-standard deviation scores (SDS), height-SDS, birth weight, full breast-feeding status, maternal systolic BP, fruit and vegetable intake (FVI), and FVI £ pubertal group. In pre-pubertal stage, no between-person effect observed for sodium excretion and SBP. In pre-pubertal stage, no within-person effect observed for sodium excretion and SBP.</p>

Table D86. Subgroup table for observational studies for pregnant

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Inoue, 2016¹⁶⁸</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Study of: Adults N: 184</p> <p>% Male: 0</p> <p>Mean Age/Range/Age at Baseline: mean 34.1 (SD 4.9)</p> <p>Race: NR</p> <p>Systolic BP: mean 102 (SD 10)</p> <p>Diastolic BP: mean 63 (SD 8)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: mean 21.7 (SD 4.7)</p> <p>% with Hypertension: 8.2</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Women with chronic hypertension or multiple pregnancy were included.</p> <p>Exclusion: Women who cannot undergo the first investigation (the first blood and urine sampling, and BP measurement) before the 20th gestational week, and those who had known heart disease or nephropathy were excluded.</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion averaged until the 30th gestational week</p> <p>Exposure Unit: mmol/24h</p> <p>Duration: 20 weeks of gestation to 30 weeks of gestation</p> <p>Exposure to Follow Up Time: NR</p> <p>Dose format: NR</p> <p>All, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, one before the 20th gestational week, and the other after the improvement of hyperemesis gravidarum</p> <p>How was blood pressure measured? HBP was measured twice using an HEM- 7051 (Omron Healthcare, Kyoto, Japan) based on the cuff- oscillometric method. The participants were asked to measure HBP at their upper arm within 1h of waking up, after micturition, before breakfast, while seated, after resting >1 min. HBP was measured for 7 consecutive days including the day of home urine collection before 20 weeks of gestation. In addition, HBP was also measured for 7 consecutive days after 30 weeks of gestation.</p>	<p>Home systolic blood pressure (Home BP was measured twice at each occasion using an HEM- 7051 (Omron Healthcare, Kyoto, Japan) based on the cuff- oscillometric method.) (mmol/24h/Outcome):</p> <p>From before the 20th gestational week to after the 30th gestational week</p> <p>FU</p> <p>All cases: NR, total: 184</p> <p>Adjustment: Multivariables, but ND</p> <p>Estimated urinary salt excretion was not significantly correlated with either HBP before the 20th gestational week or HBP after the 30th gestational week.</p> <p>Pregnancy-induced hypertension (PIH was defined as gestational hypertension (rise in BP to $\geq 140/90$ mmHg); pre-eclampsia (newly developed hypertension $\geq 140/90$ mmHg with proteinuria ≥ 300 mg/day); or superimposed pre-eclampsia after the 20th gestat) (mmol/24h/Outcome):</p> <p>From before the 20th gestational week to after the 30th gestational week</p> <p>FU</p> <p>All cases: 22, total: 184</p> <p>Adjustment: Age, pregnancy >40 years, BMI, parity, multiple pregnancy, family history of hypertension, chronic hypertension, BUN, serum creatinine, eGFR, Serum uric acid, Hematocrit, HBP before the 20th gestational week, clinic BP before the 20th gestational week</p> <p>Neither urinary salt excretion averaged until the 30th gestational week nor change in urinary salt excretion was associated with the development of PIH.</p>

Table D87. Subgroup table for observational studies for pubertal group

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Lijie Shi, 2014¹³³; Kruppe, 2014¹³⁴; Kroke, 2004¹³⁵; Krupp, 2015¹⁶⁹</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p>	<p>Study of: Children N: NR</p> <p>% Male: 51</p> <p>Mean Age/Range/Age at Baseline: boys median 6 (IQR 4.0-8.0) girls median 6.0 (IQR 4.0- 7.0)</p> <p>Race: NR</p> <p>Systolic BP: boys median 97.1 (IQR 90.8 -1.04) girls median 97.0 (IQR 90.0- 102)</p> <p>Diastolic BP: boys median 57.0 (IQR 50-0 - 65.0) girls median 55.0 (IQR 49.6 -64.1)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: boys median 15.7 (IQR 15.0 - 16.8) girls median 15.3 (IQR 14.7 -16.4)</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Children aged 4 -18 year old were included.</p> <p>Exclusion: Children who had taken BP-influencing drugs, regularly or on the day of BP measurements, or whose SBP or DBP data were implausible were excluded.</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/MJ per day</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: no data (approximately 10 years)</p> <p>Dose format: continuous</p> <p>All, Dose: NR</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 yearly repeated 24-hour urine analysis</p> <p>How was blood pressure measured? SBP and DBP had been measured according to standard procedures with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) thereafter.</p> <p>Appropriate cuff sizes were used according to arm circumferences. BP was measured in the right arm of the subjects after 5 min of rest. Two consecutive BP measurements were recorded on each measurement occasion, and the arithmetic mean of both readings was used in the analysis.</p>	<p>Diastolic blood pressure (BP was measured with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) after 1994.) (mmol/MJ per day/Outcome):</p> <p>All cases: NR, total: NR</p> <p>Adjustment: Age, age2, age3, sex, pubertal group, intra-individual change in Na excretion £ pubertal group and person-specific mean-Na excretion £ pubertal group, TEI, TEI £ pubertal group, BMI-SDS, height-SDS, growth velocity, full breast-feeding status, maternal diastolic BP, FVI, FVI £ pubertal group and Ca intake.</p> <p>In pubertal stage, a non-significant association between intra-individual increase in DBP and an intra-individual increase in Na excretion.</p> <p>In pubertal stage, no between-person effect observed for sodium excretion and DBP.</p> <p>Systolic blood pressure (BP was measured with a random zero sphygmomanometer until 1994 and with a standard mercury sphygmomanometer (Mercurio 300, WelchAlllyn) after 1994.) (mmol/MJ per day/Outcome):</p> <p>7 years FU</p> <p>All cases: NR, total: NR</p> <p>Adjustment: Age, age2, age3, sex, pubertal group, intra-individual change in Na excretion £ pubertal group and person-specific mean-Na excretion £ pubertal group, total energy intake (TEI), TEI £ pubertal group, BMI-standard deviation scores (SDS), height-SDS, birth weight, full breast-feeding status, maternal systolic BP, fruit and vegetable intake (FVI), and FVI £ pubertal group.</p> <p>In pubertal stage, a non-significant association between intra-individual increase in SBP and an intra-individual increase in Na excretion.</p> <p>In pubertal stage, no between-person effect observed for sodium excretion and SBP.</p>

Table D88. Subgroup table for observational studies for Type 1 diabetes

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Thomas, 2011¹⁷⁰</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Finnish Diabetic Nephropathy Study</p>	<p>Study of: Adults N: 2807</p> <p>% Male: %male reported by Na quartiles q1 32.6 q2 49.2 q3 71.5</p> <p>Mean Age/Range/Age at Baseline: age reported by Na quartile q1 mean 38 (SD 13) years q2 mean 39 (SD 12) years q3 mean 39 (SD 12) years</p> <p>Race: NR</p> <p>Systolic BP: reported by Na quartiles q1 132 (SD 18) q2 133 (SD 18) q3 135 (SD 18)</p> <p>Diastolic BP: reported by Na quartiles q1 78 (SD 9) q2 79 (SD 9) q3 81 (SD 10)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: BMI reported by Na quartiles q1 24.7 (SD 3.4) q2 25 (SD 3.5) q3 26.1 (SD 3.5)</p> <p>% with Hypertension: reported by Na quartiles q1 44.5 q2 50.2 q3 53.6</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: All participants with type I diabetes enrolled between January 1998 and December 2002 in the FinnDiane prospective study without ESRD at baseline.</p> <p>Exclusion: Not specified</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: median follow-up 10 years</p> <p>continuous, Dose: NR</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: single 24-h urine collection at baseline completed with an ion-selective electrode</p> <p>How was blood pressure measured? In the sitting position after a 10-min rest, blood pressure was measured twice at baseline, and the analysis used the average of these two measurements.</p> <p>Mortality Outcomes-Method of Ascertainment: Death certificate, Search national death registry</p> <p>CVD, CHD, stroke, kidney stones/disease</p> <p>Outcomes-Method of ascertainment: National database, Medical files</p>	<p>All-cause mortality (mmol/d/Outcome):</p> <p>Median 10 years FU</p> <p>continuous cases: 217, total: 2807</p> <p>Adjustment: Microalbuminuria, macroalbuminuria, age, macrovascular disease, high sensitivity CRP, HbA1c, estimated GFR, HDL cholesterol.</p> <p>Significant nonlinear association between urinary sodium excretion and all-cause mortality (P , 0.001). Participants with the highest and lowest daily urinary sodium excretions both had reduced cumulative survival.</p> <p>End- stage renal disease (ESRD) (ESRD was de- fined as the requirement for dialysis or kidney transplantation and identified via a search of the renal registries and center databases and verified from medical files.)</p> <p>(mmol/d/Outcome):</p> <p>Median 10 years FU</p> <p>continuous cases: 126, total: 2807</p> <p>Adjustment: Age, HbA1c, estimated GFR, interaction term between sodium excretion and estimated GFR.</p> <p>Significant association between urinary sodium excretion and ESRD. Those with the lowest sodium excretion had the highest cumulative ESRD incidence.</p>

Table D89. Subgroup table for observational studies for Type 2 DM

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Dunkler, 2015¹⁷¹; Teo, 2004¹⁷²</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Ongoing</p> <p>Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET Sample)</p>	<p>Study of: Adults N: 3088</p> <p>% Male: 66.6%</p> <p>Mean Age/Range/Age at Baseline: median 65 (IQR 60-70)</p> <p>Race: 98.6% Caucasian</p> <p>Systolic BP: median 145 (IQR 133-155)</p> <p>Diastolic BP: median 82 (IQR 76-90)</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: median 29.05 (IQR 26.26-32.01)</p> <p>% with Hypertension: 79.2%</p> <p>% with history of CVD: 60.4%</p> <p>% with Type 2 diabetes: 100%</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Included all European participants of The ONTARGET trial; all trial participants aged 55 years or older, and were diagnosed with vascular disease or type 2 diabetes mellitus with end-organ damage.</p> <p>Exclusion: Excluded participants with missing information on the renal outcome or relevant confounders.</p>	<p>Exposure Type: 24 h urinary potassium</p> <p>Exposure Unit: g</p> <p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/d</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: 0</p> <p>Dose format: Median</p> <p>T1, Dose: 1.76</p> <p>T1, Dose: 3.58</p> <p>T2, Dose: 2.2</p> <p>T2, Dose: 4.98</p> <p>T3, Dose: 2.78</p> <p>T3, Dose: 6.51</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: Estimated 24hr urinary sodium excretion from one fasting morning urine sample.</p> <p>Sodium, Method of Validation: NR</p> <p>Potassium measure: Single 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: Estimated 24hr urinary potassium excretion from one fasting morning urine sample.</p> <p>Potassium, Method of Validation: NR</p> <p>Mortality Outcomes-Method of Ascertainment: Unclear</p>	<p>All-cause mortality (Incidence or progression of CKD was defined as new micro- or macro-albuminuria, a clinically relevant decline in the estimated glomerular filtration rate (GFR) of >5% per year, or end-stage renal disease (ESRD).) (g/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR</p> <p>Adjustment: Age, gender, duration of diabetes, ONTARGET randomization arms, albuminuria status (normo- or micro- albuminuria), GFR and δ-UACR. The multivariable model included the number of servings (per week) of high-carbohydrate foods, vegetables, fruit and fruit juice, as well as animal and plant proteins (g/kg/d), regular consumption of transfat (yes/ no), alcohol (no, moderate or heavy intake), 24-h urinary potassium and sodium (g).</p> <p>Among type II diabetes patients, sodium measurements were not associated with mortality.</p> <p>CKD (Incidence or progression of CKD was defined as new micro- or macro-albuminuria, a clinically relevant decline in the estimated glomerular filtration rate (GFR) of >5% per year, or end-stage renal disease (ESRD).) (g/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR</p> <p>Adjustment: Age, gender, duration of diabetes, ONTARGET randomization arms, albuminuria status (normo- or micro- albuminuria), GFR and δ-UACR. The multivariable model included the number of servings (per week) of high-carbohydrate foods, vegetables, fruit and fruit juice, as well as animal and plant proteins (g/kg/d), regular consumption of transfat (yes/ no), alcohol (no, moderate or heavy intake), 24-h urinary potassium and sodium (g).</p> <p>Among type II diabetes patients, sodium measurements were not associated with CKD.</p> <p>All-cause mortality (Incidence or progression of CKD was defined as new micro- or macro-albuminuria, a clinically relevant decline in the estimated glomerular filtration rate (GFR) of >5% per year, or end-stage renal disease (ESRD).) (g/d/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR</p> <p>Adjustment: Age, gender, duration of diabetes, ONTARGET randomization arms, albuminuria status (normo- or micro- albuminuria), GFR and δ-UACR. The multivariable model included the number of servings (per week) of high-carbohydrate foods, vegetables, fruit and fruit juice, as well as animal and plant proteins (g/kg/d), regular consumption of transfat (yes/ no), alcohol (no, moderate or heavy intake), 24-h urinary potassium and sodium (g).</p> <p>Increased potassium excretion was associated with reduced risk of death.</p> <p>CKD (Incidence or progression of CKD was defined as new micro- or macro-albuminuria, a clinically relevant decline in the estimated glomerular filtration rate (GFR) of >5% per year, or end-stage renal disease (ESRD).) (g/Outcome): 5.5 y FU</p> <p>T1 cases: NR, total: NR, T2 cases: NR, total: NR, T3 cases: NR, total: NR</p> <p>Adjustment: Age, gender, duration of diabetes, ONTARGET randomization arms, albuminuria status (normo- or micro- albuminuria), GFR and δ-UACR. The multivariable model included the number of servings (per week) of high-carbohydrate foods, vegetables, fruit and fruit juice, as well as animal and plant proteins (g/kg/d), regular consumption of transfat (yes/ no), alcohol (no, moderate or heavy intake), 24-h urinary potassium and sodium (g).</p> <p>No significant between potassium excretion and risk of CKD.</p>

Table D90. Subgroup table for observational studies for white

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2009¹²⁵, Satterfield, 1991²², Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p> <p>Follow-up (TOHP I and TOHP II)</p>	<p>Study of: Adults N: 1743</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; >= 125, 839; women: <125, 298; >= 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30, 777; >= 30 586; Women, <25 138; 25 to <30 279; >= 30 288.</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included.</p> <p>Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio</p> <p>Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR</p> <p>NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome):</p> <p>Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II FU</p> <p>NR cases: 141, total: 1743</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise</p> <p>Among White participants, there is a significant positive association between sodium to potassium excretion ratio and risk of CVD, adjusting for treatment assignment.</p>

Table D91. Subgroup table for observational studies for white + high risk for CVD

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2011¹²⁷; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised AssessmeNt Study in ACEiswcdI., 2008¹²⁹; Kawasaki, 1993¹³⁰</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Study of: Adults N: 28880</p> <p>% Male: 70.6 Mean Age/Range/Age at Baseline: mean 66.52 (SD 7.22)</p> <p>Race: NR Systolic BP: mean 141. 72 (SD 17.29) mmHg Diastolic BP: NR Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: mean 28.10 (SD 4.55) % with Hypertension: 69.9 % with history of CVD: strok 21.2% MI 48.4% % with Type 2 diabetes: 37.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Participants aged >=55 years with established CV disease or high-risk diabetes mellitus, who had heart failure, low ejection fraction, significant valvular disease, serum creatinine greater than 3.0 mg/dL (265 mol/l), renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg were included. Exclusion: NA</p>	<p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/d</p> <p>Duration(in months): 56 Exposure to Follow Up Time: NR</p> <p>Dose format: range G1, Dose: <2 G2, Dose: 2-2.99 G3, Dose: 3-3.99 G4, Dose: 4-5.99 G5, Dose: 6-6.99 G6, Dose: 42924 G7, Dose: >8</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: once, before the run-in period of the trial Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation Best potassium measure recorded: once, before the run-in period of the trial Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conduct in subsample at 2- year follow-up and final visit. Mortality Outcomes-Method of Ascertainment: Hospital records CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>CV events (Composite outcome includes CV mortality, MI, stroke, and hospitalization for CHF) (g/d/Outcome): Median 56 months (IQR 53-60) FU G1 cases: NR, total: 818, G2 cases: NR, total: 2654, G3 cases: NR, total: 5699, G4 cases: NR, total: 14156, G5 cases: NR, total: 3380, G6 cases: NR, total: 1326, G7 cases: NR, total: 847 Adjustment: Univariate Compared to those with estimated baseline sodium excretion of 4 to 5.99 g per day, higher baseline sodium excretion was associated with an increased risk of CVD death, MI, stroke, and hospitalization for CHF. Lower sodium excretion was associated with an increased risk of CVD death, and hospitalization for CHF in multivariable analysis.</p>

Table D92. Subgroup table for observational studies for white men

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fang, 2000¹³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: 3169</p> <p>% Male: 38.2</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: 83.5 white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination.</p> <p>Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	<p>Exposure Type: Dietary potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 22 years</p> <p>Dose format: range</p> <p>T1, Dose: <2003</p> <p>T2, Dose: 2003-2879</p> <p>T3, Dose: >2879</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p>	<p>Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome):</p> <p>Average 16.7 years FU</p> <p>T1 cases: 37, total: 1056, T2 cases: 39, total: 1057, T3 cases: 17, total: 1056</p> <p>Adjustment: Age</p> <p>Men in the lowest tertile of dietary potassium intake, both black and white, had significantly higher stroke mortality than did those with the highest intake.</p>

Table D93. Subgroup table for observational studies for white women

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Fang, 2000¹³¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p>	<p>Study of: Adults N: 5073</p> <p>% Male: 38.2</p> <p>Mean Age/Range/Age at Baseline: NR</p> <p>Race: 83.5 white</p> <p>Systolic BP: NR</p> <p>Diastolic BP: NR</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: NR</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: NHANES I survey participants aged between 25-74 during baseline examination.</p> <p>Exclusion: Excluded those with missing potassium intake data. Excluded those with unknown vital status, and excluded those not being either black or white. Excluded the extreme 1% in both tails of the 24 hour dietary potassium intake. Excluded those with a history of myocardial infarction and/or stroke.</p>	<p>Exposure Type: Dietary potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Duration: NR</p> <p>Exposure to Follow Up Time: up to 22 years</p> <p>Dose format: range</p> <p>T1, Dose: <1508</p> <p>T2, Dose: 1508-2207</p> <p>T3, Dose: >2207</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: one 24 hour dietary recall</p> <p>Mortality Outcomes-Method of Ascertainment: Interview, tracing, national death index searches, deaths confirmed from death certificates</p>	<p>Stroke death (Stroke deaths were determined by ICD-9 codes 430 to 438) (mg/d/Outcome):</p> <p>Average 16.7 years FU</p> <p>T1 cases: 50, total: 1691, T2 cases: 49, total: 1690, T3 cases: 37, total: 1692</p> <p>Adjustment: Age</p> <p>Among women, regardless of race, there was no significant difference in stroke mortality by tertile of dietary potassium intake.</p>

Table D94. Subgroup table for observational studies for with hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mente, 2016¹⁷³; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised AssessmeNt Study in ACEiswDI, 2008¹²⁹</p> <p>Location: Turkey: China: India</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 63559</p> <p>Inclusion: Included PURE participants who reported baseline blood pressure measurements and submitted their morning fasting urine samples.</p>	<p>Exposure Type: 24-h urinary excretion of sodium Exposure Unit: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>Dose format: range group 1, Dose: <3 g/day group 2, Dose: 3-3.99 g/day group 3, Dose: 4-4.99 g/day group 4, Dose: 5-5.99 g/day group 5, Dose: 6-6.99 g/day group 6, Dose: >=7 g/day</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: morning fasting urine sample collected at baseline Sodium, Method of Validation: validated the method with a study of 1083 participants</p>	<p>All-cause mortality (Death) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 555, total: 7006, group 2 cases: 774, total: 12297, group 3 cases: 902, total: 15700, group 4 cases: 728, total: 13430, group 5 cases: 478, total: 8066, group 6 cases: 451, total: 7060 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p> <p>All-cause mortality or CVD event (Death or major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 930, total: 7006, group 2 cases: 1328, total: 12297, group 3 cases: 1650, total: 15700, group 4 cases: 1333, total: 13430, group 5 cases: 855, total: 8066, group 6 cases: 739, total: 7060 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p> <p>Major CVD events (Major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 739, total: 7006, group 2 cases: 1020, total: 12297, group 3 cases: 1279, total: 15700, group 4 cases: 1052, total: 13430, group 5 cases: 648, total: 8066, group 6 cases: 594, total: 7060 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p>

Table D95. Subgroup table for observational studies for without hypertension

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Mente, 2016¹⁷³; Ontarget Investigators, 2008¹²⁸; Telmisartan Randomised AssessmeNt Study in ACEiswDI, 2008¹²⁹</p> <p>Location: Turkey: China: India</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 69559</p> <p>Inclusion: Included PURE participants who reported baseline blood pressure measurements and submitted their morning fasting urine samples.</p>	<p>Exposure Type: 24-h urinary excretion of sodium Exposure Unit: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Duration: NR Exposure to Follow Up Time: NR</p> <p>Dose format: range group 1, Dose: <3 g/day group 2, Dose: 3-3.99 g/day group 3, Dose: 4-4.99 g/day group 4, Dose: 5-5.99 g/day group 5, Dose: 6-6.99 g/day group 6, Dose: >=7 g/day</p>	<p>Sodium measure: Single 24-hour urine analysis with validation Best sodium measure recorded: morning fasting urine sample collected at baseline Sodium, Method of Validation: validated the method with a study of 1083 participants</p>	<p>All-cause mortality (Death) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 257, total: 7547, group 2 cases: 403, total: 15166, group 3 cases: 475, total: 18508, group 4 cases: 374, total: 14240, group 5 cases: 166, total: 7827, group 6 cases: 122, total: 6271 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p> <p>All-cause mortality or CVD event (Death or major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 393, total: 7547, group 2 cases: 668, total: 15166, group 3 cases: 837, total: 18508, group 4 cases: 632, total: 14240, group 5 cases: 293, total: 7827, group 6 cases: 198, total: 6271 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p> <p>Major CVD events (Major cardiovascular events included death from cardiovascular causes, myocardial infarction, stroke, and heart failure) (Estimated Sodium Excretion (Kawasaki equation)/Outcome): NR FU group 1 cases: 262, total: 7547, group 2 cases: 452, total: 15166, group 3 cases: 573, total: 18508, group 4 cases: 409, total: 14240, group 5 cases: 209, total: 7827, group 6 cases: 131, total: 6271 Adjustment: Age, sex, ancestry (Asian vs non-Asian), educational level, alcohol intake, body-mass index, current smoking, physical activity, status with respect to diabetes mellitus and a history of cardiovascular events, treatment allocation (ramipril, telmisartan, or both, and treatment with statins, beta-blockers, diuretic therapy, calcium antagonist, and antidiabetes medication) Among those with hypertension, there is a U-shaped association between sodium excretion and risk of cardiovascular events and mortality.</p>

Table D96. Subgroup table for observational studies for women

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>Cook, 2009¹²⁵, Satterfield, 1991²², Hebert, 1995¹⁰⁷; Cook, 2016³¹; Cook, 2014¹²⁶</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP</p> <p>Follow-up (TOHP I and TOHP II)</p>	<p>Study of: Adults N: 625</p> <p>% Male: 69.4</p> <p>Mean Age/Range/Age at Baseline: Men: 30-44y, 915; 45-54y, 686; Women: 30-44y, 366; 45-55y, 339.</p> <p>Race: Men: white 1418; Black, 139; Other, 44; Women: white 504; Black, 183; Other, 18</p> <p>Systolic BP: Men: < 125, 762; >= 125, 839; women: <125, 298; >= 125, 407</p> <p>Diastolic BP: Men: 80-84, 894; 85-89, 707; women: 80-84, 387; 85-89, 318.</p> <p>Magnesium: NR</p> <p>Calcium: NR</p> <p>Other Minerals: NR</p> <p>Mean BMI: Men: < 25, 238; 25 to <30, 777; >= 30 586; Women, <25 138; 25 to <30 279; >= 30 288.</p> <p>% with Hypertension: NR</p> <p>% with history of CVD: NR</p> <p>% with Type 2 diabetes: NR</p> <p>% with Kidney disease: NR</p> <p>% with history of Kidney stones: NR</p> <p>Inclusion: Participants who had not been randomized to an active sodium reduction intervention in TOHP I and II were included.</p> <p>Exclusion: Participants who had CVD events during the trial periods, and who had no valid urinary excretion measures were excluded.</p>	<p>Exposure Type: Sodium to Potassium Excretion Ratio</p> <p>Exposure Unit: linear</p> <p>Duration(in months): 120 to 180 (10 to 15 years)</p> <p>Exposure to Follow Up Time: 10 years after the end of TOHP I and 5 years after the end of TOHP II</p> <p>Dose format: NR</p> <p>NR, Dose: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p>	<p>Cardiovascular Events (Including stroke, myocardial infarction (MI), coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and death from cardiovascular causes) (linear/Outcome):</p> <p>Median, 5; range, 1-7 in TOHP I; median, 4; range, 1-5 in TOHP II FU</p> <p>NR cases: 25, total: 625</p> <p>Adjustment: Clinic,treatment assignment, age, sex, race/ethnicity, education status, family history of cardiovascular disease, baseline weight, alcohol, smoking, exercise, and changes in weight, smoking, and exercise</p> <p>Among female participants, no association between sodium to potassium excretion ratio and risk of CVD adjusting for treatment assignment.</p>

Study	Participants	Exposure	Intake Status Ascertainment	Results
<p>O'Donnell, 2014¹²⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Study of: Adults N: 101945</p> <p>% Male: 42.5 Mean Age/Range/Age at Baseline: mean 51.01 (SD 9.72) years Race: 48.4 Asian Systolic BP: mean 131.7 (SD 22.30) Diastolic BP: mean 82.24 (SD 15.65) Magnesium: NR Calcium: NR Other Minerals: NR Mean BMI: NR</p> <p>% with Hypertension: 41.5 % with history of CVD: 8.3 % with Type 2 diabetes: 9.1 % with Kidney disease: NR % with history of Kidney stones: NR</p> <p>Inclusion: Study selected a number of countries representing different economic levels, and selected urban and rural communities based on predetermined guidelines. Households and individuals were selected to fulfill maximum representativeness. Selected individuals aged between 35-70. Exclusion: Excluded those who refused to participate.</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation) Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation) Exposure Unit: g/day</p> <p>Duration: NR Exposure to Follow Up Time: mean 3.7 years</p> <p>Dose format: range G1, Dose: <3 G2, Dose: 3-5.99 G3, Dose: >=6 Q1, Dose: <1.50 Q2, Dose: 1.50-1.99 Q3, Dose: 2.00-2.49 Q4, Dose: 2.50-3.00 Q5, Dose: >3.00</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula) Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76). Potassium measure: Partial or spot urine with validated prediction equation_1 Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula) Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76). Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Interview with participant or proxy, Standardized case-report forms (adjudicated by trained physicians using standardized definitions), Captured best available information from reliable sources</p>	<p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU G1 cases: NR, total: 10810, G2 cases: NR, total: 67794, G3 cases: NR, total: 23341 Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models. The association between estimated sodium excretion and the composite outcome was strongest among participants with hypertension, with an increased risk at an estimated sodium excretion of 6.00 g or more per day.</p> <p>All-cause mortality and Major Cardiovascular Event (g/day/Outcome): Mean 3.7 y FU Q1 cases: NR, total: 14262, Q2 cases: NR, total: 31466, Q3 cases: NR, total: 30956, Q4 cases: NR, total: 17171, Q5 cases: NR, total: 8032 Adjustment: All analyses adjusted for age, sex, education, ethnicity (Asian versus non-Asian), alcohol intake, diabetes mellitus, body mass index, a history of cardiovascular events and current smoking, using logistic regression with generalized estimating equation models. No significant association between potassium intake and risk of death and major CVD events among female participants.</p>

References for Appendix D

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Appendix E. Quality of Included Studies

Risk of Bias Assessment Methods

Risk of Bias Assessment for RCTs

1. Random sequence generation (selection bias)

For RCTs, is the sequence generation (recruitment) described as being random?

For CCTs, is the allocation described in such a way that it appears to be free of obvious (intentional) bias?

For crossover trials, was the order of receiving treatments randomized adequately?

Low risk: The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).

High risk: The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number. Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorization of participants, for example: allocation by judgement of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; allocation by availability of the intervention.

Unclear risk: Insufficient information about the sequence generation process to permit judgement of 'Low risk' or 'High risk'

2. Allocation concealment

Was the group allocation concealed (such that assignments could not be predicted)

Low risk: Use of a third party and opaque envelopes or their equivalent are low risk. Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.

High risk: Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered);

alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear risk: Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed

Not applicable: Study is a CCT

3. Blinding of participants and personnel

Were participants and key study personnel blinded to their intervention or exposure status?

Low risk: Any one of the following: no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.

High risk: Any one of the following: no blinding of outcome assessment, and the outcome is likely to be influenced by lack of blinding; blinding of participants and key study personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.

Unclear risk: Any one of the following: insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; the study did not address this outcome. Just mentioning “placebo” =”unclear”

4. Blinding of outcome assessment

Low risk: Any one of the following: no blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
apply same criteria as for patients

High risk: Any one of the following: no blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.

Unclear risk: Any one of the following: insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; the study did not address this outcome.
"double blind" and no further info on assessor (e.g., external assessor)

5. Incomplete outcome data (Attrition bias)

For RCTs and CCTs, could high attrition or uneven attrition across study arms have contributed to bias?

For crossover studies, only, was outcome reporting complete for all phases?

Low risk: Similar loss to follow-up across groups OR analyses took loss to follow-up into account (e.g., by intent-to-treat (ITT) analysis, “censoring,” imputing missing data [e.g., by carrying the last observation forward] or qualitatively or quantitatively comparing the characteristics of people who dropped out with those who remained in the analysis)

High risk: Differential loss to follow-up across groups with no attempt to take into account or to assess differences between dropouts and retained participants

Unclear risk: Nothing mentioned about evaluating impacts or taking into account in analysis.

6. Selective reporting of outcome data

For studies that purport to be reporting the prespecified study outcomes, do the outcomes reported match those listed in the Methods section under “Outcomes,” or does the article state that some of the prespecified outcomes will be reported in subsequent articles?

Low risk: Any of the following: the study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).

High risk: Any one of the following: not all of the study’s pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear risk: Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. It is likely that the majority of studies will fall into this category.

Not applicable: Article reports on post-hoc analysis of data from a study initially published elsewhere.

7. Other: Adherence

Did the investigators describe rates of adherence to the intervention or some measure of adherence?

Low risk: Adherence was described as high (e.g., based on biomarkers) or as $\geq 80\%$.

High risk: Adherence was described as low.

Unclear risk: Nothing about adherence mentioned

8. Other: Unequal distribution among groups of potential confounders at baseline

Was distribution of demographics (e.g., age, gender, race/ethnicity), comorbidities, and other potentially critical confounding factors (e.g., blood pressure, use of antihypertensives) similar across study arms at baseline (or if not, does the analysis control for baseline characteristics)?

Yes (Low risk): No significant difference between arms in demographic and important comorbidity characteristics (e.g., blood pressure) according to table and/or described by investigators, or difference(s) taken into account in analysis

No (High risk): Significant difference between arms in age, race, gender, important comorbidity with no attempt to control for the differences

9. Demonstration that outcome of interest was not present at start of study for all participants

For example, analysis of the number of people with stroke includes patients that had a stroke before start of study not after the intervention or had a recurring stroke. Note: Incidence vs recurrence.

This item is a trigger for excluding individual studies from analyses. Please specify for which outcome this is an issue.

Low risk: no problem

High risk: People with an outcome of interest were not excluded (specify the outcome, and exclude study for that analysis)

10. Other: Valid method of exposure assessment

Was exposure to intervention assessed using a valid method?

Low risk: For sodium or sodium to potassium ratio, exposure was assessed with at least one 24-hour urinary analysis with reported quality control measure.

For potassium, exposure was assessed using at least one 24-hour urinary analysis with reported quality control measure, chemical analysis of diet or food diary with intervention/exposure adherence measure, or composition of potassium supplement with intervention/exposure adherence measure.

High risk: For sodium or sodium to potassium ratio or potassium, exposure was assessed with chemical analysis of diet, composition of salt substitute, or food diaries. Exposure was assessed less than 24-hours or through a published food frequency questionnaire.

Moderate risk or unclear: For sodium, 24-hour urinary analysis without reported quality control measure. Chemical analysis of diet without intervention/exposure adherence measure, or composition of potassium supplement without intervention/exposure adherence measure. For potassium, use of food diaries without quality control.

11. Other: Valid method of outcome assessment

Were outcomes assessed using valid methods?

Low risk: definitions of outcomes are provided by investigators, outcomes are not self-reported, and method of ascertainment is described.

High risk: definitions are not provided (e.g., for CVD morbidity); one or more outcomes is described as self-reported

Unclear risk: No description of outcome definitions, no mention of method of ascertainment.

12. Other: Valid statistical assessment (for crossover trials only)

Did the authors report how they did their analysis and did they do the correct analysis for a crossover (a paired analysis of some type)?

Yes, they report how they analyzed the data, and they report a paired analysis of some type

No, they report an analysis but it was not paired

Unclear: they don't report how the analysis was done and the outcomes don't appear to have come from pairing people with themselves.

Risk of Bias Assessment for Observational Studies

1. Representativeness of the exposed cohort

Low risk: Truly representative of the average named cohort in the community.

High risk: Select group (e.g. only doctors)

Moderate risk or unclear: Somewhat representative of average named population or no description of the derivation of the cohort

2. Selection of the nonexposed cohort

Low risk: The recruitment or allocation strategy was similar across exposure groups (drawn from the same community as exposed cohort)

High risk: Drawn from a different source

Unclear risk: No description

3. Ascertainment of sodium and potassium exposure (dietary assessment/urinary assessment)

Low RoB:

Multiple days (more than four on average, preferably non-consecutive) 24-hour urines with reported quality control measures (i.e., instructions given, measure of completeness of collection, e.g., creatinine, urine volume, questionnaire)

Moderate RoB:

Two to four 24-hour urine specimens with reported quality control measures or correction for regression dilution bias with repeated 24-hour urine collection on a sample of participants.

Multiple days of food diaries

Multiple non-consecutive days (more than 4) 24-hour diet recalls or food records or correction for regression dilution bias with repeated (non-consecutive) 24-hour diet recalls for a sample of participants

High RoB:

24-hour urine without any reported quality control measures

A single 24-hour urine collection (high random error)

Timed-urine collection of less than 24 hours

FFQ

Single-day food diaries/records or 24-hour diet recalls

Spot urine with or without use of a prediction equation for estimating 24-hour excretion

Potassium exposure assessment

Low RoB:

Multiple non-consecutive days (more than 4) 24-hour diet recalls or food records

Multiple (more than four, preferably non-consecutive) 24-hour urines with reported quality control measures (i.e., instructions given, measure of completeness of collection, e.g., creatinine, urine volume, questionnaire)

Moderate RoB:

Two to four 24-hour urine specimens or correction for regression dilution bias with repeated 24-hour urine collection on a sample of participants

Two to four non-consecutive 24-hour recalls/food records or correction for regression dilution bias with repeated (non-consecutive) 24-hour diet recalls for a sample of participants.

FFQ validated for potassium intake within a subset of the study population against duplicate diets or multiple 24-hour urine collections

High RoB:

Single 24-hour urine specimen

Use of more than one 24-hour urine specimen without any reported quality control measures

Timed-urine collection of less than 24 hours

FFQ other than that specified above under Moderate RoB

Single-day food records

Single day of 24-hour recall

Spot urine specimen(s) with or without use of an equation for estimating 24-hour excretion

4. Demonstration that outcome of interest was not present at start of study for all participants?

For example, analysis of the number of people with stroke includes patients that had a stroke before start of study not after the intervention or had a recurring stroke. Note: Incidence vs recurrence.

This item is a trigger for excluding individual studies from analyses. Please specify for which outcome this is an issue.

5. Comparability

Comparability of cohorts on the basis of the design or analysis (was distribution of health status, demographics, and other critical confounding factors similar across study groups at baseline or did the analysis control for baseline differences between groups?)

Low risk: Study provides explanation for and controls for the most important factors likely to affect outcomes, including blood pressure for non-BP studies or BMI.

High risk: Study does not control for blood pressure or other important factors (e.g., demographics)

Moderate risk or Unclear: Study does not describe the exact factors controlled for in analysis.

6. Assessment of outcome

Ascertainment of outcome should be appropriate for the type of outcome.

Low risk: The authors describe independent or blind assessment or confirmation of the outcome by reference to secure records (e.g., x-rays, medical records) or use of record linkage (e.g., identification of outcome through ICD codes on database records).

High risk: Outcomes are described as being self-reported.

Moderate risk/Unclear: No description

Table E1. Quality assessment of trials (N=105 studies)

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Alli, 1992 ¹	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Ambrosioni, 1982 ²	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	Yes	*Public	No mention of author COI	N/A	Moderate risk
Applegate, 1992 ³	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Arroll, 1995 ⁴	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Australian National Health and Medical Research Council Dietary Salt Study Manage	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
ment Committ ee, 1989 ⁵																
Barcelo, 1993 ⁶	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	High risk	Low	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Barros, 2015 ⁷	High risk	High risk	Low risk	High risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High
Beard, 1982 ⁸	Unclear risk	Unclear risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	High

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Becerra-Tomas, 2015 ⁹	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	Private corporation with no statement of involvement in study	Yes, it says that one or more of the authors received payment for some services performed for a private funder	Yes	Low risk
Beckmann, 1995 ¹⁰	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Berry, 2010 ¹¹	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														work done for private industry		
Braschi, 2008 ¹²	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	High risk	Low risk/no problem	Low risk	Low risk	N/A	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	Low risk
Bulpitt, 1984 ¹³	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low	Low risk	N/A	Private corporation with no statement of involvement in study	No mention of author COI	No	Unclear
Bulpitt, 1985 ¹⁴	Unclear risk	Unclear risk	High risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	Private corporation with no statement of involvement in study	No mention of author COI	No	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Calabrese, 1985 ¹⁵	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Cappuccio, 2006 ¹⁶	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Chang, 2006 ¹⁷	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	Private corporation with no statement of involvement in study	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	Moderate risk
Charlton, 2008 ¹⁸	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	**Private corporation	None of the authors had any conflict of	Yes	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														interest to declare or none of the authors received payment for work done for private industry		
China Salt Substitute Study Collaborative, 2007 ¹⁹	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Cobiac, 1992 ²⁰	High risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
de Brito-Ashurst, 2013 ²¹	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Low risk
Dodson, 1989 ²²	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Dubbert, 1995 ²³	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk	Unclear risk	High risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Ellison, 1989 ²⁴	Unclear risk	N/A	High risk	High risk	Low risk	Low risk	Low risk	High risk	N.A	High risk	High risk	No	*Public	No mention of	No	High risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														author COI		
Flack, 2002 ²⁵	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	Yes	*Public	No mention of author COI	N/A	Moderate risk
Franzoni, 2005 ²⁶	High risk	High	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Moderate risk
Geleijns e, 1994 ²⁷	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	Private corporation with no statement of involvement in study	No mention of author COI	No	Low risk
Gilleran, 1996 ²⁸	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Gillum, 1981 ²⁹	Unclear risk	Unclear risk	High risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Unclear
Graham, 2014 ³⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	No description of source of funding	None of the authors had any conflict of interest	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														to declare or none of the authors received payment for work done for private industry		
Grimm, 1990 ³¹	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Gu, 2001 ³²	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	No	Low risk
He, 2010 ³³	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	None of the authors had any conflict of interest to declare or none of the authors received	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														payment for work done for private industry		
He, 2015 ³⁴	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	Yes, it says that one or more of the authors received payment for some services performed for a private funder	N/A	Moderate risk
Hofman, 1983 ³⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Howe, 1994 ³⁶	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	Private corporation with no statement of involvement in study	No mention of author COI	No	Moderate risk
Hwang, 2014 ³⁷	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	**Private corporation	None of the authors	No	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														had any conflict of interest to declare or none of the authors received payment for work done for private industry		
Trials of Hypertension Prevention Collaborative Research Group, 1997 ³⁸	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Hypertension Prevention Trial Research Group, 1990 ³⁹	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Jula, 1992 ⁴⁰	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Kitaoka, 2013 ⁴¹	High risk	High risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Knuist, 1998 ⁴²	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Kojuri, 2007 ⁴³ 9850	Unclear risk	Not applicable	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	None of the authors had any conflict of	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														interest to declare or none of the authors received payment for work done for private industry		
Kwakernak, 2014 ⁴⁴	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear/might want to discuss	Low risk	Low risk	Yes	There was no funding for this study	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Low risk
Langford, 1991 ⁴⁵	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
6979														author COI		
Li, 2016 ⁴⁶	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk		*Public	Yes, it says that one or more of the authors received payment for some services performed for a private funder	N/A	Moderate risk
Little, 2004 ⁴⁷	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low risk	Low risk	No	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														private industry		
Mascioli, 1991 ⁴⁸	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk/no problem	High risk	Low risk	Yes	*Public	No mention of author COI	N/A	Moderate risk
Matthesen, 2012 ⁴⁹	Low risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Meland E, 2009 ⁵⁰	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	Moderate	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														or none of the authors received payment for work done for private industry		
Meuleman, 2016 ⁵¹	Low risk	Unclear risk	High risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Miller, 1987 ⁵²	High	High	High risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	Unclear	*Public	No mention of author COI	N/A	High

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Miller, 1988 ⁵³	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Miller, 2016 ⁵⁴	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High
Morgan, 1978 ⁵⁵	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Morgan, 1981 ⁵⁶	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low	Low risk	N/A	*Public	No mention of author COI	N/A	Unclear

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Morgan, 1987 ⁵⁷	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Morikawa, 2011 ⁵⁸	High risk	High risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Mu, 2009 ⁵⁹	Low risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the	N/A	Unclear

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														authors received payment for work done for private industry		
Mulhauser, 1996 ⁶⁰	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Naismith, 2003 ⁶¹	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Nakano, 2016 ⁶²	Low risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	High risk	N/A	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for	N/A	High risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														private industry		
Nestel, 1993 ⁶³	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	Private corporation with no statement of involvement in study	No mention of author COI	No	Low risk
Nowson, 1988 ⁶⁴	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Unclear
Nowson, 2003 ⁶⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	No mention of author COI	N/A	Low risk
Obel, 1989 ⁶⁶ 193	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Parker, 1990 ⁶⁷	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Patki, 1990 ⁶⁸	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	No description of source of funding	No mention of author COI	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Pinjuh Markota, 2015 ⁶⁹	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Pomera n, 2002 ⁷⁰	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Unclear risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Puska, 1983 ⁷¹	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Rahimi, 2007 ⁷²	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Redon-Mas, 1993 ⁷³	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Unclear risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Richard s, 1984 ⁷⁴	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	No mention of author COI	N/A	Moderate risk
Sacks, 2001 ⁷⁵	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	No mention of author COI	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Santos, 2010 ⁷⁶	Unclear risk	Unclear risk	High risk	High risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	Yes	*Public	No mention of author COI	N/A	Moderate risk
Saptharishi, 2009 ⁷⁷	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Sarkkineen, 2011 ⁷⁸	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	Private corporation with no statement of involvement in study	None of the authors had any conflict of interest to declare or none of the	No	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														authors received payment for work done for private industry		
Schorr, 1996 ⁷⁹	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk/no problem	Unclear risk	Low risk	Unclear	No description of source of funding	No mention of author COI	N/A	Moderate risk
Sciarrone, 1992 ⁸⁰	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Seals, 2001 ⁸¹	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Siani, 1987 ⁸²	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Low risk
Siani, 1991 ⁸³	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Silman, 1983 ⁸⁴	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	High risk	Low risk/no problem	Unclear risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Sinaiko, 1993 ⁸⁵	Unclear risk	Unclear risk	Low risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Singer, 1991 ⁸⁶	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low	Low risk	Low risk	Yes	No description of source of funding	No mention of author COI	N/A	Low risk
Steegers, 1991 ⁸⁷	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	High risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Unclear
Sundar, 1985 ⁸⁸	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Moderate risk
Suppa, 1988 ⁸⁹	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Svetkey, 1987 ⁹⁰	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	High risk	Low risk/no problem	High risk	Low risk	N/A	Private corporation with no statement of	No mention of author COI	No	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
													involvement in study			
Takahashi, 2006 ⁹¹	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
The Trials of Hypertension Prevention Collaborative Research Group, 1992 ⁹²	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Todd, 2010 ⁹³	Low risk	Low risk	High risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	Yes	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														done for private industry		
Todd, 2012 ⁹⁴	Low risk	Low risk	Unclear risk	Low risk	Low risk	Unclear risk	High risk	Low risk	Low risk/no problem	High risk	Low risk	Yes	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Tuthill, 1985 ⁹⁵	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Low risk
Van Buul BJA, 1997 ⁹⁶	Unclear risk	Low risk	Unclear risk	Unclear risk	High risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of author COI	N/A	Moderate risk
Vongpatanasin, 2016 ⁹⁷	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Unclear risk	Low risk	Low	Low risk	Low risk	Yes	*Public	None of the authors	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														had any conflict of interest to declare or none of the authors received payment for work done for private industry		
Weir, 2010 ⁹⁸	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Private corporation with no statement of involvement in study	Yes, it says that one or more of the authors received payment for some services performed for a private funder	No	Moderate risk
Whelton, 1998 ⁹⁹	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	*Public	No mention of	N/A	Low risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														author COI		
Whitten, 1980 ¹⁰⁰	High risk	High risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk/no problem	Low risk	Low risk	N/A	No description of source of funding	No mention of author COI	N/A	Moderate risk
Wing, 1998 ¹⁰¹	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Yes	Private corporation with no statement of involvement in study	No mention of author COI	No	Low risk
Xie, 1998 ¹⁰²	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk/no problem	Low risk	High risk	N/A	No description of source of funding	No mention of author COI	N/A	Unclear
Zhao, 2014 ¹⁰³	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
Zhou, 2009 ¹⁰⁴	Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Moderate	Low risk	N/A	No description of source of funding	private industry None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Zhou, 2016 ¹⁰⁵	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk/no problem	High risk	Low risk	N/A	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment	N/A	Moderate risk

Author, Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (Attrition bias)	Selective reporting of outcome data	Adherence	Unequal distribution among groups of potential confounders at	Demonstration that outcome of interest was not present at start of study for all	Valid method of exposure assessment	Valid method of outcome assessment	Valid statistical assessment (for crossover trials)	Funding source (sponsor)	Other: Funding source (author COI)	Funding source (private source)	Overall risk of bias
														t for work done for private industry		

Public=Public = Research was funded by a government entity, university, or private foundation not affiliated with private industry

**Private corporation= Research was funded by a private corporation but does not state that the funder had no involvement in the study

Table E2. Quality assessment of observational studies (N=66 studies)

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Adebamowo, 2015 ¹⁰⁶	High risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Unclear risk	Low risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Alderman, 1997 ¹⁰⁷	Unclear risk	Unclear	Moderate risk	N/A	Low risk	Low risk	Low risk	Low risk	*Public	No mention of author COI	N/A	Moderate risk
Alderman, 1998 ¹⁰⁸	Low risk	Low risk	High risk	N/A	Low risk	Unclear risk	High risk	Low risk	*Public	No mention of author COI	N/A	High risk
Araki, 2015 ¹⁰⁹	Unclear risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	Private corporation with no statement of involvement in study	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	High risk
Ascherio, 1992 ¹¹⁰	High risk	High risk	Moderate risk	N/A	Low risk	High risk	High risk	Low risk	No funding for the study	No mention of author COI	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Ascherio, 1998 ¹¹¹	High risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Unclear risk	Low risk	*Public	No mention of author COI	N/A	Moderate risk
Bazzano, 2001 ¹¹²	Low risk	Low risk	N/A	High risk	Low risk	Low risk	Low risk	Low risk	Private corporation with no statement of involvement in study	No mention of author COI	N/A	High risk
Bongard, 2016 ¹¹³	Unclear risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	Low risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Buendia, 2015 ¹¹⁴	Unclear risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Catena, 2016 ¹¹⁵	High risk	Low risk	High risk	N/A	Unclear risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Chien, 2008 ¹¹⁶	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Cohen, 2006 ¹¹⁷	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Cook, 2009 ¹¹⁸	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had	N/A	Low risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										any conflict of interest to declare or none of the authors received payment for work done for private industry		
Cook, 2014 ¹¹⁹	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	One or more of the authors received payment for some services performed for a private funder	N/A	Low risk
Cook, 2016 ¹²⁰	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Low risk
Curhan, 2004 ¹²¹	High risk	Low risk	N/A	High risk	Low risk	Low risk	High risk	Unclear risk	*Public	No mention of author COI	N/A	High risk
Dunkler, 2013 ¹²²	High risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	**Private corporation	None of the authors had any conflict of interest to	No	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										declare or none of the authors received payment for work done for private industry		
Dunkler, 2015 ¹²³	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	Yes	High risk
Ekinci, 2011 ¹²⁴	High risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Low risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	High risk
Fan, 2014 ¹²⁵	Low risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	Unclear risk	*Public	No mention of author COI	N/A	Moderate risk
Fang, 2000 ¹²⁶	Low risk	Low risk	High risk	N/A	Low risk	Unclear risk	Low risk	Unclear risk	*Public	No mention of author COI	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Ferraro, 2016 ¹²⁷	High risk	Low risk	N/A	High risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	One or more of the authors received payment for some services performed for a private funder	N/A	High risk
Forman, 2012 ¹²⁸	Low risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Geleijnse, 1990 ¹²⁹	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Unclear risk	No description of source of funding	No mention of author COI	N/A	Low risk
Geleijnse, 2007 ¹³⁰	Low risk	Unclear	High risk	High risk	Low risk	Low risk	Low risk	Unclear risk	*Public	No mention of author COI	N/A	High risk
Green, 2002 ¹³¹	Low risk	Low risk	N/A	High risk	Low risk	Low risk	Unclear risk	Low risk	*Public	No mention of author COI	N/A	High risk
Hajjar, 2001 ¹³²	Low risk	Low risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	*Public	No mention of author COI	N/A	High risk
Haring, 2015 ¹³³	High risk	Low risk	N/A	High risk	Unclear risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had any conflict of interest to	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										declare or none of the authors received payment for work done for private industry		
He, 1999 ¹³⁴	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Low risk	*Public	No mention of author COI	N/A	High risk
He, 2002 ¹³⁵	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Low risk	*Public	No mention of author COI	N/A	High risk
He, 2016 ¹³⁶	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Hirvonen, 1999 ¹³⁷	Low risk	Low risk	N/A	High risk	Low risk	Low risk	High risk	Low risk	*Public	No mention of author COI	N/A	High risk
Inoue, 2016 ¹³⁸	Low risk	Low risk	High risk	N/A	Low risk	Unclear risk	Low risk	Unclear risk	No description of source of funding	One or more of the authors received payment for some services performed for a private funder	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Joosten, 2014 ¹³⁹	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	High risk
Kagan, 1985 ¹⁴⁰	Low risk	Low risk	High risk	N/A	Low risk	Unclear risk	Low risk	Unclear risk	No description of source of funding	No mention of author COI	N/A	High risk
Khaw, 1987 ¹⁴¹	Low risk	Low risk	N/A	High risk	Low risk	Unclear risk	Low risk	Low risk	*Public	No mention of author COI	N/A	High risk
Kieneker, 2014 ¹⁴²	Low risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Kieneker, 2016 ¹⁴³	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the	No	Moderate risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										authors received payment for work done for private industry		
Kieneker, 2016 ¹⁴⁴	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Krupp, 2015 ¹⁴⁵	Low risk	Low risk	Moderate risk	Moderate risk	Unclear risk	Low risk	Low risk	Low risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Lamelas, 2016 ¹⁴⁶	Low risk	Low risk	High risk	N/A	Unclear risk	Low risk	Low risk	Unclear risk	Private corporation with no statement of involvement	No mention of author COI	No	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
									ent in study			
Larsson, 2008 ¹⁴⁷	Unclear risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Larsson, 2011 ¹⁴⁸	Unclear risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Leonberg-Yoo, 2016 ¹⁴⁹	Low risk	Low risk	N/A	High risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Mente, 2016 ¹⁵⁰	Low risk	Unclear	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	Private corporation with no statement of involvement in study	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	High risk
Mills, 2016 ¹⁵¹	Unclear risk	Low risk	Moderate risk	N/A	Unclear risk	Low risk	Unclear risk	Low risk	*Public	One or more of the authors received payment for some services performed for a private funder	N/A	Moderate risk
Nerbas, 2015 ¹⁵²	Unclear risk	Low risk	High risk	N/A	Low risk	Unclear risk	Low risk	Low risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	High risk
O'Donnell, 2011 ¹⁵³	Unclear risk	Low risk	High risk	High risk	Low risk	Low risk	Unclear risk	Low risk	**Private corporation	One or more of the authors received payment for some services	No	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										performed for a private funder		
O'Donnell, 2014 ¹⁵⁴	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Unclear risk	Low risk	Private corporation with no statement of involvement in study	One or more of the authors received payment for some services performed for a private funder	No	High risk
Ohta, 2013 ¹⁵⁵	Unclear risk	Low risk	Low risk	N/A	Low risk	Unclear risk	Low risk	Unclear risk	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Low risk
Okayama, 2016 ¹⁵⁶	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Low risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Pfister, 2014 ¹⁵⁷	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Seth, 2014 ¹⁵⁸	Low risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Shi, 2014 ¹⁵⁹	Low risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Shufa, 2014 ¹⁶⁰	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Sodium: Moderate risk Potassium: Low risk
Singer, 2015 ¹⁶¹	High risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Sluijs, 2014 ¹⁶²	Low risk	Low risk	N/A	High risk	Unclear risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Smyth, 2016 ¹⁶³	High risk	Low risk	N/A	Moderate risk	Low risk	Low risk	Unclear risk	Unclear risk	*Public	None of the authors had	N/A	Moderate risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										any conflict of interest to declare or none of the authors received payment for work done for private industry		
Stolarz - Skrzypek, 2011 ¹⁶⁴	Low risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	Low risk	**Private corporation	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	No	Moderate risk
Thomas, 2011 ¹⁶⁵	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk
Tunstall-Pedoe, 1997 ¹⁶⁶	Low risk	Low risk	Moderate risk	N/A	Low risk	High risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
										declare or none of the authors received payment for work done for private industry		
Tuomilehto, 2001 ¹⁶⁷	Low risk	Low risk	High risk	N/A	Low risk	Low risk	Low risk	Unclear risk	No description of source of funding	No mention of author COI	N/A	High risk
Umesawa, 2016 ¹⁶⁸	Unclear risk	Low risk	Moderate risk	N/A	Low risk	Low risk	Low risk	High risk	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk
Vitolo, 2013 ¹⁶⁹	Unclear risk	Low risk	High risk	N/A	Unclear risk	Unclear risk	Low risk	Unclear risk	*Public	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	High risk

Author, year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of sodium exposure	Ascertainment of potassium exposure	Outcome of interest not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Adequacy of follow-up	Funding source (sponsor)	Funding source (author COI)	Funding source (private source)	Overall risk of bias
Witteman, 1989 ¹⁷⁰	Low risk	Low risk	N/A	High risk	Low risk	Low risk	High risk	Low risk	*Public	One or more of the authors received payment for some services performed for a private funder	N/A	High risk
Yang, 2011 ¹⁷¹	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	No description of source of funding	None of the authors had any conflict of interest to declare or none of the authors received payment for work done for private industry	N/A	Moderate risk

*Public= Research was funded by a government entity, university, or private foundation not affiliated with private industry

**Private corporation= Research was funded by a private corporation but funder had no involvement in the study

Table E3. Exposure ROB for observational studies

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Adebamowo, 2015¹⁰⁶; Erratum, 2015¹⁷²; Iso, 1999¹⁷³; Stampfer, 1985¹⁷⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Nurses Health Study</p> <p>.</p>	<p>Exposure Type: Total potassium intake (dietary + supplemental)</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Total potassium intake (dietary)</p> <p>Exposure Unit: mg/day</p> <p>Exposure Type: Total potassium intake (supplemental)</p> <p>Exposure Unit: mg/day</p>	<p>Sodium, Method of Validation: FFQ without reported validation</p> <p>Best potassium measure recorded: Used food frequency questionnaire to collect diet info with specific questions about potassium supplements</p> <p>Potassium, Method of Validation: Cited a validation study testing the correlations between mineral intake assessed by FFQ and by 1-week diet records.</p>	<p>High risk</p> <p>Food diaries no validation</p> <p>Sodium exposure and analyses were excluded. ROB for sodium exposure should be deleted.</p>	<p>Moderate risk</p> <p>FFQ with validation</p>
<p>Alderman, 1997¹⁰⁷; Alderman, 1995¹⁷⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: Single 24-hr urine analysis at beginning of the program</p> <p>Sodium, Method of Validation: Validated by using formula described by Cockcroft and Gault and Robertshaw et al. Only included patients whose estimated urinary creatinine clearance values fall within +/-35% of the observed values (Alderman, 1995¹⁷⁵)</p>	<p>Moderate risk</p> <p>Single 24hr yes validation</p>	
<p>Alderman, 1998¹⁰⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p> <p>.</p>	<p>Exposure Type: Sodium</p> <p>Exposure Unit: mg</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: Single 24h diet recall</p> <p>Sodium, Method of Validation: NR</p>	<p>High risk</p> <p>Single 24hr diet recall no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Araki, 2015¹⁰⁹; Araki, 2013¹⁷⁶</p> <p>Location: Japan</p> <p>Setting: Community Design: Prospective Cohort study Study Name: Shiga Prospective Observational Follow-up Study</p>	<p>Exposure Type: Sodium Exposure Type: Potassium</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: completed one 24-hr urine analysis at baseline Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: completed one 24-hr urine analysis at baseline</p>	<p>High risk Single 24hr no validation</p>	<p>High risk Single 24hr no validation</p>
<p>Ascherio, 1992¹¹⁰; Rimm, 1991¹⁷⁷; Ascherio, 1997¹¹¹</p> <p>Location: US</p> <p>Setting: Community Design: Prospective Cohort study Study Name: Health Professionals Follow-up Study</p>	<p>Exposure Type: Potassium intake Exposure Unit: g/day</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: 1 time at baseline Potassium, Method of Validation: The reproducibility and validity of the FFQ was previously measured compared with 2 weeks dietary records in a subsample of 127 men.</p>	<p>Sodium measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>Moderate risk Single FFQ yes validation</p>
<p>Ascherio, 1998¹¹¹; Ascherio, 1992¹¹⁰</p> <p>Location: US</p> <p>Setting: Community Design: Prospective Cohort study Study Name: Health Professionals Follow-up Study</p>	<p>Exposure Type: Potassium calculations based on FFQ Exposure Unit: g/d</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: one food frequency questionnaire Potassium, Method of Validation: Study assessed questionnaire validity in a random sample of 127 men who completed two 1-week diet records.</p>	<p>Sodium measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>Moderate risk Single FFQ yes validation</p>
<p>Bazzano, 2001¹¹²</p> <p>Location: US</p> <p>Setting: Community Design: Prospective Cohort study Study Name: NHANES I</p>	<p>Exposure Type: Dietary potassium intake Exposure Unit: mmol/24h</p>	<p>Potassium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall</p>		<p>High risk Single 24hr diet recall no validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Bongard, 2016¹¹³</p> <p>Location: France</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MONICA (MONItoring of trends and determinants in Cardiovascular disease) Project</p>	<p>Exposure Type: Dietary sodium</p> <p>Exposure Unit: mg/day</p>	<p>Sodium measure: 3-day food record with reported validation</p> <p>Best sodium measure recorded: 3-day food records at baseline. Sodium, Method of Validation: Participants were followed up by a dietitian to verify the reliability of their food records.</p>	<p>Moderate risk</p> <p>3-day food records yes validation</p>	
<p>Buendia, 2015¹¹⁴; The NHLBI Growth and Health Study, 1992¹⁷⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The National Heart, Lung, and Blood Institute's Growth and Health Study (NGHS)</p>	<p>Exposure Type: Daily potassium intake</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Daily sodium intake</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Potassium to sodium ratio</p> <p>Exposure Unit: NR</p>	<p>Sodium measure: 3-day diet records</p> <p>Best sodium measure recorded: Complete 8 3-day diet records (2 weekdays and 1 weekend day) during examination years 1-5, 7, 8, and 10.</p> <p>Sodium, Method of Validation: NR</p> <p>Potassium measure: 3-day diet record</p> <p>Best potassium measure recorded: Complete 8 3-day diet records (2 weekdays and 1 weekend day) during examination years 1-5, 7, 8, and 10.</p> <p>Potassium, Method of Validation: NR</p>	<p>High risk</p> <p>8 3-day diet record no validation</p>	<p>High risk</p> <p>8 3-day diet record no validation</p>
<p>Catena, 2016¹¹⁵; Sechi, 2009¹⁷⁹; Catena, 2007¹⁸⁰; Catena, 2006¹⁸¹; Catena, 2007¹⁸²</p> <p>Location: Italy</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/d</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, baseline and at the end of follow-up</p>	<p>High risk</p> <p>Two 24hr no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Chien, 2008¹¹⁶</p> <p>Location: Taiwan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chin-Shan Community Cardiovascular Cohort Study (CCCC)</p>	<p>Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium to potassium ratio Exposure Unit: mmol/mmol</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24hr urine analysis</p> <p>Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: single 24hr urine analysis</p>	<p>High risk Single 24hr no validation</p>	<p>High risk Single 24hr no validation</p>
<p>Cohen, 2006¹¹⁷; US Department of Health and Human Services, 2005¹⁸³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The NHANES II Mortality study (a followup to NHANES II)</p>	<p>Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: < residuals adjusted median</p> <p>Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: <2300mg</p> <p>Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg</p> <p>Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg per calorie</p> <p>Exposure Type: Sodium from 24-hour dietary recall Exposure Unit: mg/d</p>	<p>Sodium measure: 24-hour diet recall Best sodium measure recorded: once, baseline</p>	<p>High risk Single 24hr diet recall no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Cook, 2009¹¹⁸; Satterfield, 1991¹⁸⁴; Hebert, 1995¹⁸⁵; Cook, 2016¹²⁰; Cook, 2014¹¹⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP Follow-up (TOHP I and TOHP II)</p>	<p>Exposure Type: Potassium Excretion Exposure Unit: linear</p> <p>Exposure Type: Potassium Excretion Exposure Unit: mmol/24 h</p> <p>Exposure Type: Sodium Excretion Exposure Unit: linear</p> <p>Exposure Type: Sodium Excretion Exposure Unit: mmol/24 h</p> <p>Exposure Type: Sodium to Potassium Excretion Ratio Exposure Unit: linear</p> <p>Exposure Type: Sodium to Potassium Excretion Ratio Exposure Unit: mmol/24 h</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis with reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p> <p>Sodium, Potassium Method of Validation: See below.</p>	<p>Low risk</p> <p>Multiple days with quality control</p>	<p>Low risk</p> <p>Multiple days with quality control</p>
<p>Cook, 2014¹¹⁹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP Follow-up (TOHP I and TOHP II)</p>	<p>Exposure Type: Urinary sodium excretion Exposure Unit: mg/d</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Sodium, Method of Validation: NR</p> <p>Potassium measure: More than one 24-hour urinary analysis with reported quality control measure_1 Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: medical records</p> <p>Sodium, Potassium Method of Validation: See below.</p>	<p>Low risk</p> <p>Multiple days with quality control</p>	<p>Low risk</p> <p>Multiple days with quality control</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Cook, 2016¹²⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: TOHP Follow-up (TOHP I and TOHP II)</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure</p> <p>Best sodium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Potassium measure: More than one 24-hour urinary analysis with reported quality control measure_1</p> <p>Best potassium measure recorded: twice, at 5 (life- style interventions) or 7 (nutritional supplement interventions) scheduled collections in TOHP I and at 3 to 5 scheduled collections during TOHP II</p> <p>Mortality Outcomes-Method of Ascertainment: National death index</p> <p>Sodium, Potassium Method of Validation: In Cook 2014 (PMID 24415713), the authors conducted a sensitivity analysis to explore "whether the relationships could be affected by under-collection, measures of creatinine were computed over the same collections, along with the creatinine-to-weight ratio (Cr/Wt), the sodium-to-creatinine ratio (Na/Cr), the potassium/creatinine ratio (K/Cr), and the sodium/potassium ratio (Na/K)." The take away point is "When excluding those with a CV for Cr/Wt of 30% or greater, or when controlling for Cr/Wt or the CV of Cr/Wt in the model, there was little change in the estimated coefficients, though the effect of sodium became stronger with control for the CV of Cr/Wt."</p>	<p>Low risk</p> <p>Multiple days with quality control</p>	<p>Low risk</p> <p>Multiple days with quality control</p>
<p>Curhan, 2004¹²¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Nurses Health Study II</p>	<p>Exposure Type: Potassium</p> <p>Exposure Unit: dietary potassium</p>	<p>Potassium measure: semiquantitative food frequency questionnaires</p> <p>Best potassium measure recorded: 2 semiquantitative FFQ in 1991 and 1995</p>		<p>High risk</p> <p>Two FFQ no validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Du Shufa, 2014¹⁶⁰</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The China Health and Nutrition Survey (CHNS)</p>	<p>Exposure Type: Potassium intake Exposure Unit: g/day</p> <p>Exposure Type: Sodium intake Exposure Unit: g/d</p> <p>Exposure Type: Sodium potassium ratio Exposure Unit: NR</p>	<p>Sodium measure: weighing methods in combination with 3 consecutive 24-hour diet recall Best sodium measure recorded: 6 times, 1991, 1993, 1997, 2999, 2994, 2996, and 2009 Sodium, Method of Validation: A validation study evaluated the accuracy of estimated sodium and potassium intakes at the individual level in one of the survey provinces (but not with CHNS participants) by measuring urinary sodium and potassium excretions from 24-h urine samples collected for 3 consecutive days and by using p-aminobenzoic acid as a marker of completeness of 24-h urine samples., 24-hour "diet recall" Best potassium measure recorded: 6 times, 1991, 1993, 1997, 2999, 2994, 2996, and 2009 Potassium, Method of Validation: A validation study evaluated the accuracy of estimated sodium and potassium intakes at the individual level in one of the survey provinces (but not with CHNS participants) by measuring urinary sodium and potassium excretions from 24-h urine samples collected for 3 consecutive days and by using p-aminobenzoic acid as a marker of completeness of 24-h urine samples.</p>	<p>Moderate risk 6 24hr diet recall yes validation</p>	<p>Moderate risk 6 24hr diet recall yes validation</p>
<p>Dunkler, 2013¹²²; Kawasaki, 1993¹⁸⁶</p> <p>Location: NR</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET Sample)</p>	<p>Exposure Type: 24-h Urinary potassium Exposure Unit: g</p> <p>Exposure Type: 24-h Urinary sodium Exposure Unit: g</p>	<p>Sodium measure: Spot urine with estimated equation Best sodium measure recorded: Single 24-hour urine analysis with validation Sodium, Method of Validation: Only cited other studies. Previous studies have reported that this approach provides a valid estimate of sodium intake in healthy control participants and patients taking antihypertensive therapy. Best potassium measure recorded: Single 24-hour urine analysis without validation Potassium, Method of Validation: Only cited other studies. Previous studies have reported that this approach provides a valid estimate of sodium intake in healthy control participants and patients taking antihypertensive therapy.</p>	<p>High risk Spot urine with estimated equation</p>	<p>High risk Spot urine with estimated equation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Dunkler, 2015¹²³; Teo, 2004¹⁸⁷</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET Sample)</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p>	<p>Sodium measure: Spot urine with estimated equation Best sodium measure recorded: Estimated 24hr urinary sodium excretion from one fasting morning urine sample. Sodium, Method of Validation: NR</p> <p>Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: Estimated 24hr urinary potassium excretion from one fasting morning urine sample. Potassium, Method of Validation: NR</p> <p>Mortality Outcomes-Method of Ascertainment: Unclear</p>	<p>High risk</p> <p>Spot urine with estimated equation</p>	<p>High risk</p> <p>Spot urine with estimated equation</p>
<p>Ekinci, 2011¹²⁴</p> <p>Location: Australia</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p>	<p>Exposure Type: 24-h urinary sodium</p> <p>Exposure Unit: mmol/24h</p>	<p>Sodium measure: Single 24-hour urine analysis without validation, Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: patients completed a 24-h urine collection</p>	<p>High risk</p> <p>Single 24hr no validation</p>	
<p>Fan, 2014¹²⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MDRD (Modification of Diet in Renal Disease) Study</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: Patients either had three (n=200) or four (n=640) 24-hour urine collections and analysis to calculate 24-h urinary sodium excretion.</p> <p>Sodium, Method of Validation: 24-h urine creatinine was used to assess accuracy of the urine collections</p>	<p>Moderate risk</p> <p>3 to 4 24hr with validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
Fang, 2000 ¹²⁶ Location: US Setting: Community Design: Prospective Cohort study Study Name: NHANES I .	Exposure Type: Sodium	Sodium, Method of Validation: 24-hour "diet recall" Best potassium measure recorded: one 24 hour dietary recall	High risk Single 24hr diet recall no validation	
Ferraro, 2016 ¹²⁷ ; Taylor, 2004 ¹⁸⁸ Location: US Setting: Community Design: Prospective Cohort study Study Name: Health Professionals Follow-up Study .	Exposure Type: Sodium Exposure Type: Potassium	Sodium, Method of Validation: Use of a published food frequency questionnaire Best potassium measure recorded: One food frequency questionnaire at baseline and additional FFQ every 4 years Potassium, Method of Validation: FFQs were found to be reproducible and valid in the HPFS and the NHS I.	Measured with FFQ (confirmed that sodium data in this study was excluded from this report)	High risk More than one FFQ no validation
Forman, 2012 ¹²⁸ Location: Netherlands Setting: Community Design: Prospective Cohort study Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study .	Exposure Type: Urine sodium Exposure Unit: NR	Sodium measure: More than one 24-hour urinary analysis with reported quality control measure Best sodium measure recorded: 3 times , 1st- 1997 and 1998; 2nd- 2001 and 2003, 3rd- 2003 and 2006 Quality control: used the mean value of the two 24-hour collections for each examination	Moderate risk 3 24hr yes validation	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Geleijnse, 1990¹²⁹</p> <p>Location: Netherlands</p> <p>Setting: suburban town</p> <p>Design: Prospective Cohort study</p>	<p>Exposure Type: 24 hour potassium excretion Exposure Unit: mmol/24 h</p> <p>Exposure Type: 24 hour sodium excretion Exposure Unit: mmol/24 h</p> <p>Exposure Type: Sodium potassium ratio Exposure Unit: NR</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure Best sodium measure recorded: 6 times, every year Quality control: detailed instructions given on collection containers</p> <p>Potassium measure: More than one 24-hour urinary analysis with reported quality control measure_1 Best potassium measure recorded: 6 times, every year Quality control: detailed instructions given on collection containers</p>	<p>Low risk 6 24hr yes validation</p>	<p>Low risk 6 24hr yes validation</p>
<p>Geleijnse, 2007¹³⁰; Hofman, 1991¹⁸⁹</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Rotterdam Study</p>	<p>Exposure Type: Dietary potassium Exposure Unit: mg/day</p> <p>Exposure Type: Estimated 24-Hour Urinary Potassium Excretion (spot urine) Exposure Unit: mmol/24 h</p> <p>Exposure Type: Urinary sodium Exposure Unit: mmol/24 h</p> <p>Exposure Type: Urinary sodium/potassium ratio Exposure Unit: mmol/mmol</p> <p>Exposure Type: Urinary sodium/potassium ratio Exposure Unit: ratio</p>	<p>Sodium measure: Partial urine Best sodium measure recorded: collected 1 overnight urine sample at baseline Sodium, Method of Validation: NR Potassium measure: Partial urine Best potassium measure recorded: collected 1 overnight urine sample at baseline Potassium, Method of Validation: NR</p>	<p>High risk Partial urine no validation</p>	<p>High risk Partial urine no validation</p>
<p>Gu, 2001³²</p> <p>Location: China</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Potassium and Protein Supplementation Study (PAPSS)</p>	<p>Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p>	<p>Sodium Status Arm 2: 185.7 mmol/24 h need full text Potassium measure: Single 24-hour urine analysis without validation Best potassium measure recorded: 3 at screening, Once at 6 weeks, then at 12 weeks Potassium, Method of Validation: Pill count Potassium Status Arm 2: 54.2 mmol/24 h</p>	<p>High risk 3 24hr no validation</p>	<p>High risk 3 24hr no validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Haring, 2015¹³³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Strong Heart Study</p> <p>.</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p> <p>Exposure Type: Sodium-potassium Ratio</p>	<p>Sodium measure: Food Frequency Questionnaire</p> <p>Best sodium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Sodium, Method of Validation: FFQ administered by interviewer</p> <p>Potassium measure: Food Frequency Questionnaire</p> <p>Best potassium measure recorded: One 119-item food frequency questionnaire at baseline</p> <p>Potassium, Method of Validation: FFQ administered by interviewer</p>	<p>Measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>High risk</p> <p>Single FFQ no validation</p>
<p>He, 1999¹³⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES I</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24h dietary recall with 3-dimensional food-portion models</p>	<p>High risk</p> <p>Single 24hr diet recall no validation</p>	
<p>He, 2002¹³⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS)</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: once</p>	<p>High risk</p> <p>Single 24hr diet recall no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>He, 2016¹³⁶, Yang, 2014¹⁹⁰; Lash, 2009¹⁹¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p> <p>.</p>	<p>Exposure Type: 24-h urinary sodium</p> <p>Exposure Unit: mmol/24h</p> <p>Exposure Type: Potassium</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2).</p> <p>Sodium, Method of Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method., Multiple 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: 24-hour urine analysis at baseline and twice during follow-up (years 1 and 2).</p> <p>Potassium, Method of Validation: Measured urinary sodium levels with flame emission spectrophotometry, and measured urinary creatinine using the Jaffe method, and measured urine total protein using the turbidimetric reaction method.</p>	<p>Moderate risk</p> <p>3 24hr yes validation</p>	<p>Moderate risk</p> <p>3 24hr yes validation</p>
<p>Hirvonen, 1999¹³⁷; The ATBC Cancer Prevention Study Group, 1994¹⁹²</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: the Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention</p> <p>.</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p> <p>Exposure Type: 1.21847E-2</p> <p>Exposure Unit: Potassium intake</p>	<p>Sodium, Method of Validation: Use of a published food frequency questionnaire</p> <p>Best potassium measure recorded: self-administered diet history questionnaire</p> <p>Potassium, Method of Validation: Dietary assessment method was validated in a pilot study carried out among 190 men prior to the ATBC Study.</p>	<p>Measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>High risk</p> <p>Single diet history questionnaire yes validation</p>
<p>Inoue, 2016¹³⁸</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: More than one 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: twice, one before the 20th gestational week, and the other after the improvement of hyperemesis gravidarum</p>	<p>High risk</p> <p>2 24hr no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Joosten, 2014¹³⁹</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p> <p>.</p>	<p>Exposure Type: Sex-specific quartiles of sodium excretion</p> <p>Exposure Unit: mmol/24h</p>	<p>Sodium measure: two 24-hr urine analysis with out reported quality control measure</p> <p>Best sodium measure recorded: During baseline examination, participants collected two 24-hour urines for 2 consecutive days.</p>	<p>High risk</p> <p>2 24hr no validation</p>	
<p>Kagan, 1985¹⁴⁰; Kagan, 1974¹⁹³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Hawaiian Study</p> <p>.</p>	<p>Exposure Type: Sodium intake</p> <p>Exposure Unit: g</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: 24h dietary recall</p> <p>Sodium, Method of Validation: Data validated by repeating 24-hr recall interviews and 7-day dietary records in a sample of the men examined 2 yr later. Correlation coefficients ranged from 0.4 to 0.6 for most of the nutrients, suggesting good reproducibility.</p>	<p>High risk</p> <p>Single 24hr diet recall yes validation</p>	
<p>Khaw, 1987¹⁴¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mmol/d</p>	<p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Best potassium measure recorded: Once (at baseline)</p> <p>Potassium, Method of Validation: A 24-hour recall of dietary intake was obtained by a certified Lipid Research Clinic dietician. The data were coded for nutrient intake by the Nutrition Coordinating Center, University of Minnesota, with use of their data base.</p>		<p>High risk</p> <p>Single 24hr diet recall yes validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Kieneker, 2014¹⁴²</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Exposure Type: Na-K excretion ratio</p> <p>Exposure Unit: NR</p> <p>Exposure Type: Urinary Potassium Excretion</p> <p>Exposure Unit: mmol/24 h</p>	<p>Potassium measure: two 24-hr urine analysis with reported validation</p> <p>Best potassium measure recorded: Two 24-hr urine analysis at baseline and second examination, for each analysis participants collected 2 consecutive 24-hr specimens.</p>		<p>Moderate risk</p> <p>2 24hr no validation</p>
<p>Kieneker, 2016¹⁴³; Hillege, 2001¹⁹⁴, Joosten, 2013¹⁹⁵</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Exposure Type: 24-h urinary potassium excretion</p> <p>Exposure Unit: mmol/24 h</p> <p>Exposure Type: 24-h urinary sodium excretion</p> <p>Exposure Unit: mmol/24 h</p> <p>Exposure Type: Sodium to potassium excretion ratio</p> <p>Exposure Unit: NR</p> <p>Exposure Type: Sodium to potassium excretion ratio</p> <p>Exposure Unit: mmol/mmol</p>	<p>Sodium measure: Discussion,, Didn't say anything in the method part but in the results part, the authors conducted analysis between sodium and CVD, IHD, stroke and HF. We assume sodium measure is same as potassium measure because they were from the same urinary sample collections.</p> <p>Potassium measure: More than one 24-hour urinary analysis with reported quality control measure_1</p> <p>Best potassium measure recorded: twice, first: between 1997 and 1998 (baseline); second: between 2001 and 2003.</p> <p>Sodium and Potassium, Method of Validation: 24-h urinary creatinine excretion was included in the multivariate regression.</p>	<p>Moderate risk</p> <p>2 24hr with validation</p>	<p>Moderate risk</p> <p>2 24hr with validation</p>
<p>Kieneker, 2016¹⁴⁴</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prevention of Renal and Vascular End-stage Disease (PREVEND) study</p>	<p>Exposure Type: Urinary potassium excretion</p> <p>Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/24h</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure</p> <p>Best sodium measure recorded: twice, (baseline and the second examination)</p> <p>Potassium measure: More than one 24-hour urinary analysis without reported quality control measure_1</p> <p>Best potassium measure recorded: twice, (baseline and the second examination)</p> <p>Sodium and Potassium, Method of Validation: 24-h urinary creatinine excretion was included in the multivariate regression.</p>	<p>Moderate risk</p> <p>2 24hr with validation</p>	<p>Moderate risk</p> <p>2 24hr with validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Krupp, 2015¹⁴⁵; Shi, 2014¹⁵⁹; Kruppe, 2014¹⁹⁶; Kroke, 2004¹⁹⁷</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 repeated 24-hour urine analysis with validation</p> <p>Sodium, Method of Validation: Minimized errors with creatinine excretion cutoff., Multiple 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: 3 repeated 24-hour urine analysis with validation</p> <p>Potassium, Method of Validation: Minimized errors with creatinine excretion cutoff.</p>	<p>Moderate risk</p> <p>3 24hr yes validation</p>	<p>Moderate risk</p> <p>3 24hr yes validation</p>
<p>Lamelas, 2016¹⁴⁶</p> <p>Location: South America (Argentina, Brazil, Chile, and Colombia)</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) South America cohort</p>	<p>Exposure Type: 24 h urinary sodium excretion (estimated)</p> <p>Exposure Unit: g/day</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: once spot urine (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p>	<p>High risk</p> <p>Single spot urine</p>	
<p>Larsson, 2008¹⁴⁷</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study</p>	<p>Exposure Type: Potassium intake</p> <p>Exposure Unit: mg/d</p>	<p>Sodium measure: Food frequency questionnaire</p> <p>Sodium, Method of Validation: Use of a published food frequency questionnaire</p> <p>Best potassium measure recorded: completed one 276-item food frequency questionnaire at baseline.</p> <p>Potassium, Method of Validation: questionnaire validated in Pietinen P, Hartman AM, Haapa E, et al. Reproducibility and validity of dietary assessment instruments, I: a self-administered food use questionnaire with a portion size picture booklet. Am J Epidemiol. 1988;128(3):655-666.</p>	<p>Measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>Moderate risk</p> <p>Single FFQ with validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Larsson, 2011¹⁴⁸</p> <p>Location: Sweden</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Swedish Mammography Cohort</p> <p>.</p>	<p>Exposure Type: Potassium intake</p> <p>Exposure Unit: mg/d</p>	<p>Potassium measure: food frequency questionnaire with reported validation</p> <p>Best potassium measure recorded: One 96-item food frequency questionnaire completed in 1997</p> <p>Potassium, Method of Validation: The food frequency questionnaire has been validated in Messerer M, Johansson SE, Wolk A. The validity of questionnaire-based micronutrient intake estimates is increased by including dietary supplement use in Swedish men. J Nutr. 2004;134(7):1800–1805.</p>		<p>Moderate risk</p> <p>Single FFQ with validation</p>
<p>Leonberg-Yoo, 2016¹⁴⁹; Klahr, 1994¹⁹⁸</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The MDRD (Modification of Diet in Renal Disease) Study</p> <p>.</p>	<p>Exposure Type: Potassium</p>	<p>Potassium measure: multiple 24-hr urine analysis without reported validation</p> <p>Best potassium measure recorded: One 24-hr urine analysis at baseline and additional 24-hr urine collections completed every month.</p>		<p>High risk</p> <p>Single 24hr no validation</p>
<p>Shi, 2014¹⁵⁹; Kruppe, 2014¹⁹⁶; Kroke, 2004¹⁹⁷; Krupp, 2015¹⁴⁵</p> <p>Location: Germany</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: 3 yearly repeated 24-hour urine analysis</p> <p>Quality control: given detailed instructions</p>	<p>Moderate risk</p> <p>3 24hr yes validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Mente, 2016¹⁵⁰; Ontarget Investigators, 2008¹⁹⁹; Telmisartan Randomised Assessment Study in ACEiswcDI, 2008²⁰⁰</p> <p>Location: Turkey: China: India</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Pooled analysis of PURE, EPIDREAM, and ONTARGET/TRANSCEND In</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: once spot urine (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p>	<p>High risk</p> <p>Single spot urine</p>	<p>High risk</p> <p>Single 24hr yes validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Mills, 2016¹⁵¹; He, 2016¹³⁶; Yang, 2014¹⁹⁰; Lash, 2009¹⁹¹</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Chronic Renal Insufficiency Cohort (CRIC) Study</p>	<p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: mg/24 h</p> <p>Exposure Type: 24 h urinary sodium excretion calibrated to mean urinary creatinine excretion of 1569 mg/24 hours in Exposure Unit: per 1000 mg/24 h</p> <p>Exposure Type: Calibrated 24-Hour Urinary Potassium Excretion quartile; a Calibrated to mean urinary creatinine exc Exposure Unit: mg/24 h</p> <p>Exposure Type: Calibrated 24-Hour Urinary Sodium Excretion Calibrated to mean urinary creatinine excretion of 1,569 Exposure Unit: 1,000 mg difference</p> <p>Exposure Type: Quartile of 24-Hour Urinary Sodium Excretion not calibrated Exposure Unit: mg/24 h</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation Best sodium measure recorded: 3 times, 1 year apart</p> <p>Quality control: participants were instructed to recollect if total urine volume was less than 500 mL at the end of 24 hours or the duration of collection was not between 22 and 24 hours.</p>	<p>Moderate risk 3 24hr yes validation</p>	
<p>Nerbass, 2015¹⁵²; McIntyre, 2011²⁰¹</p> <p>Location: NR</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Renal Risk in Derby (RRID)</p>	<p>Exposure Type: Sodium intake Exposure Unit: mmol/d</p>	<p>Sodium measure: a medical and dietary questionnaire Best sodium measure recorded: twice, 1-year</p>	<p>High risk 2 diet questionnaire no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>O'Donnell, 2011¹⁵³; Ontarget Investigators, 2008¹⁹⁹; Telmisartan Randomised Assessment Study in ACEiswcDI, 2008²⁰⁰; Kawasaki, 1993¹⁸⁶</p> <p>Location: 40 countries</p> <p>Setting: Clinical research center based</p> <p>Design: Prospective Cohort study</p> <p>Study Name: Cohorts from ONTARGET and TRANSCEND</p>	<p>Exposure Type: Sodium</p> <p>Exposure Type: Potassium</p>	<p>Sodium measure: Single spot urine with estimated equation</p> <p>Best sodium measure recorded: once, before the run-in period of the trial</p> <p>Sodium, Method of Validation: The Kawasaki formula was used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample and the approach was valid by previous studies in healthy control participants (ref 18) and patients taking antihypertensive therapy (ref 19). Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit., Single 24-hour urine analysis with validation</p> <p>Best potassium measure recorded: once, before the run-in period of the trial</p> <p>Potassium, Method of Validation: The Kawasaki formula was used to estimate 24-hour potassium urinary excretion from a fasting morning urine sample. Additional assessment of validity was conducted in subsample at 2- year follow-up and final visit.</p> <p>Mortality Outcomes-Method of Ascertainment: Hospital records</p> <p>CVD, CHD, stroke, kidney stones/disease Outcomes-Method of ascertainment: Hospital records</p>	<p>High risk</p> <p>Single spot urine with estimated equation</p>	<p>High risk</p> <p>Single spot urine with estimated equation</p>
<p>O'Donnell, 2014¹⁵⁴</p> <p>Location: 17 low-, middle-, and high-income countries</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Prospective Urban and Rural Epidemiology (PURE) study</p>	<p>Exposure Type: Estimated Potassium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p> <p>Exposure Type: Estimated Sodium Excretion (Kawasaki equation)</p> <p>Exposure Unit: g/day</p>	<p>Sodium measure: Partial or spot urine with validated prediction equation</p> <p>Best sodium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Sodium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Potassium measure: Partial or spot urine with validated prediction equation_1</p> <p>Best potassium measure recorded: collected one morning fasting midstream urine sample (Kawasaki formula)</p> <p>Potassium, Method of Validation: A validation study using the Kawasaki formula with actual 24-hour urine collection in 1,083 people from 11 countries showed an intraclass correlation coefficient of 0.71 (95% confidence interval (CI), 0.65 to 0.76).</p> <p>Mortality Outcomes-Method of Ascertainment: Standardized case-report forms (adjudicated by trained physicians using standardized definitions, Contact family members, Captured best available information from reliable sources</p>	<p>High risk</p> <p>Spot urine yes validation</p>	<p>High risk</p> <p>Spot urine yes validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Ohta, 2013¹⁵⁵</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure</p> <p>Best sodium measure recorded: more than five, first between 1998 and 2000, last between 2008 and 2010</p> <p>Quality control: If the 24 h creatinine excretion was within $\pm 30\%$ of the estimated values, the urine collection was considered successful.</p>	<p>Low risk</p> <p>5 24hr yes validation</p>	
<p>Okayama, 2016¹⁵⁶; Lida, 2003²⁰²</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NIPPON DATA80, National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged</p> <p>.</p>	<p>Exposure Type: Quintiles of dietary sodium-to-potassium ratio</p> <p>Exposure Unit: mol/mol</p>	<p>Sodium measure: the National Nutrition Survey (NNS), in which a 3-day weighing dietary records for household.</p> <p>Nutrient intake of each household member was estimated by dividing household intake data of NNS in 1980 proportionally with average intake as categorized by sex and age group calculated for the 1995 NNS.</p> <p>Best sodium measure recorded: once</p> <p>Potassium measure: the National Nutrition Survey (NNS), in which a 3-day weighing dietary records</p> <p>Best potassium measure recorded: once</p>	<p>High risk</p> <p>3-day weighing diet record for a household</p>	<p>High risk</p> <p>3-day diet weighing record for a household</p>
<p>Pfister, 2014¹⁵⁷</p> <p>Location: UK</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The EPIC-Norfolk study</p> <p>.</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/day</p>	<p>Sodium measure: Spot urine with estimated equation (INTERSALT)</p> <p>Best sodium measure recorded: 24-hr urine analysis at baseline and second health check.</p> <p>Sodium, Method of Validation: Obtained measurements of 24 h urinary sodium excretion in a subsample of 163 men and women participating in continuing validation and calibration studies within the EPIC-Norfolk study who had up to six 24 h urine collections over 1 year.</p>	<p>High risk</p> <p>Spot urine with estimated equation (INTERSALT)</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Seth, 2014¹⁵⁸, Anderson, 2003²⁰³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Women's Health Initiative Observational Study (WHI-OS)</p>	<p>Exposure Type: Dietary Potassium Intake</p> <p>Exposure Unit: mg/d</p>	<p>Potassium measure: Food Frequency Questionnaires</p> <p>Best potassium measure recorded: Two food frequency questionnaires (FFQ) at study enrollment and year 3 follow-up</p> <p>Potassium, Method of Validation: Used a sub sample to evaluate FFQ measurement properties</p>		<p>Moderate risk</p> <p>2 FFQ yes validation</p>
<p>Singer, 2015¹⁶¹</p> <p>Location: US</p> <p>Setting: a union- sponsored, worksite hypertension program</p> <p>Design: Prospective Cohort study</p>	<p>Exposure Type: Urinary sodium quartiles</p> <p>Exposure Unit: mmol/24 h</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: once at baseline</p>	<p>High risk</p> <p>Single 24hr no validation</p>	
<p>Sluijs, 2014¹⁶²; Beulens, 2010²⁰⁴</p> <p>Location: Netherlands</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: EPIC-NL study</p>	<p>Exposure Type: Potassium, dietary Intake</p> <p>Exposure Unit: mg/d</p>	<p>Sodium measure: food frequency questionnaire</p> <p>Potassium measure: food frequency questionnaire</p> <p>Best potassium measure recorded: Filled out one food frequency questionnaire.</p> <p>Potassium, Method of Validation: Calculated relative validity for each food item.</p>	<p>Measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>High risk</p> <p>Single FFQ no validation</p>

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Smyth, 2016¹⁶³</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: U.S. National Institutes of Health–American Association of Retired Persons Diet and Health Study</p> <p>.</p>	<p>Exposure Type: Daily potassium intake</p> <p>Exposure Unit: g/d</p>	<p>Sodium measure: FoodFrequency questionnaire Best sodium measure recorded: Participants completed 1 validated food frequency questionnaire at baseline Sodium, Method of Validation: FFQ validated in Thompson FE, Kipnis V, Midthune D, et al. Performance of a food-frequency questionnaire in the US NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study. Public Health Nutr. 2008;11:183-195. Potassium measure: Food Frequency Questionnaire Best potassium measure recorded: Participants completed 1 validated food frequency questionnaire at baseline Potassium, Method of Validation: FFQ validated in Thompson FE, Kipnis V, Midthune D, et al. Performance of a food-frequency questionnaire in the US NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study. Public Health Nutr. 2008;11:183-195.</p>	<p>Measured with FFQ (confirmed that sodium data in this study was excluded from this report)</p>	<p>Moderate risk Single FFQ with validation</p>
<p>Stolarz-Skrzypek, 2011¹⁶⁴; Aleksandrova, 2011²⁰⁵; Staessen, 2001²⁰⁶; Li, 2007²⁰⁷</p> <p>Location: Belgium</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Flemish Study on Environment, Genes, and Health Outcomes (FLEMENGHO)</p> <p>.</p>	<p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline</p> <p>Exposure Unit: mmol/d</p> <p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium-to-Potassium Ratio at Baseline</p> <p>Exposure Unit: NR</p> <p>Exposure Type: Tertiles of the 24-Hour Urinary Sodium-to-Potassium Ratio at Baseline</p> <p>Exposure Unit: mmol</p>	<p>Sodium measure: More than one 24-hour urinary analysis with reported quality control measure Best sodium measure recorded: twice, each time measured about 1 week after BP measurement</p> <p>Sodium, Method of Validation: Excluded inaccurate urine collections that were defined as a volume less than 300 mL per 24 hours, a 24-hour creatinine excretion of less than 4 mmol or higher than 25 mmol in women and less than 6 mmol or more than 30 mmol in men.</p>	<p>Moderate risk 2 24hr no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>The Trials of Hypertension Prevention Collaborative Research Group, 1992²²; Erratum, 1992²⁰⁸; Satterfield, 1991¹⁸⁴; Whelton, 1992²⁰⁹; Whelton, 1997²¹⁰; He, 1999²¹¹; Kumanyika, 1993²¹²; Whelton, 1994²¹³; Cook, 2007²¹⁴; Cook, 1998²¹⁵; Yamamoto, 1995²¹⁶; Cook, 2016¹²⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized, parallel</p> <p>Study Name: The Trials of Hypertension Prevention, phase 1 (TOHP-1)</p>	<p>Exposure Type: Sodium to potassium ratio Exposure Unit: mmol/mmol</p> <p>Exposure Type: Urinary potassium excretion Exposure Unit: mmol/24h</p> <p>Exposure Type: Urinary sodium excretion Exposure Unit: mmol/24h</p>	<p>Sodium measure: Multiple 24-hour urine analysis with validation, 24-hour diet recall Best sodium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups</p> <p>Sodium, Method of Validation: Multiple 24-hour urine analysis with validation, 24-hour "diet recall" Sodium Status Arm 2: 99.4 mmol/24 h Sodium Status Arm 3: NR Sodium Status Arm 4: NR</p> <p>Best potassium measure recorded: 0, 3, 6, months, 12 and 18 months for lifestyle groups Potassium Status Arm 2: NR Potassium Status Arm 3: Change from baseline -2.4 mmol/24 h Potassium Status Arm 4: Change from baseline 37.4 mmol/24h</p>	<p>Low risk 5 24hr yes validation</p>	<p>Low risk 5 24hr yes validation</p>
<p>Thomas, 2011¹⁶⁵</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Finnish Diabetic Nephropathy Study</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure Best sodium measure recorded: single 24-h urine collection at baseline completed with an ion-selective electrode</p>	<p>High risk Single 24hr no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Tunstall-Pedoe, 1997¹⁶⁶; Tunstall-Pedoe, 1999²¹⁷; Smith, 1987²¹⁸</p> <p>Location: Scotland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Scottish Heart Health Study</p> <p>.</p>	<p>Exposure Type: Sodium</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: one 24 hour urine collection Sodium, Method of Validation: Urine was analyzed for electrolytes and creatinine.</p>	<p>Moderate risk</p> <p>Single 24hr yes validation</p>	
<p>Tuomilehto, 2001¹⁶⁷</p> <p>Location: Finland</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: 24 h urinary sodium excretion</p> <p>Exposure Unit: mmol</p>	<p>Sodium measure: Single 24-hour urinary analysis without reported quality control measure</p> <p>Best sodium measure recorded: single 24 hour urinary analysis without reported quality control measure</p>	<p>High risk</p> <p>Single 24hr no validation</p>	
<p>Umesawa, 2016¹⁶⁸</p> <p>Location: Japan</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Circulatory Risk in the Community Study (CIRCS)</p> <p>.</p>	<p>Exposure Type: Sodium concentration quartiles in spot urine</p> <p>Exposure Unit: mmol/l</p>	<p>Sodium measure: Single 24-hour urine analysis with validation</p> <p>Best sodium measure recorded: once, at baseline Sodium, Method of Validation: Quality control was undergone three times per day by using normal and abnormal reagent (Consela “Nissui”, Nissui pharmaceutical Co., Tokyo, Japan).</p>	<p>Moderate risk</p> <p>Single 24hr yes validation</p>	
<p>Vitolo, 2013¹⁶⁹</p> <p>Location: Brazil</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>.</p>	<p>Exposure Type: Sodium intake</p> <p>Exposure Unit: mg/day</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: Two multiple-pass 24-h dietary recalls for each child 2-4 years old.</p> <p>Sodium, Method of Validation: Dietary recalls administered by trained fieldworkers</p>	<p>High risk</p> <p>2 diet recall no validation</p>	

Study	Exposure	Intake Status Ascertainment	Ascertainment of Sodium Exposure	Ascertainment of Potassium Exposure
<p>Whelton, 1998⁹⁹; Appel, 2001²¹⁹; Espeland, 1999²²⁰; Banson, 1997²²¹; Appel, 1995²²²; Kostis, 1998²²³; Whelton, 1997²²⁴</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Randomized Factorial Design individual</p> <p>Study Name: Trial of nonpharmacological interventions in the elderly (TONE)</p>	<p>Exposure Type: Urinary sodium excretion</p> <p>Exposure Unit: mmol/24h</p>	<p>Sodium measure: Multiple 24-hour urinary analysis without reported quality control measure, 24-hour diet recall</p> <p>Best sodium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p> <p>Sodium, Method of Validation: 24-hour "diet recall"</p> <p>Sodium Status Arm 2: Net reduction of -39.8 mmol/day</p> <p>Potassium measure: Multiple 24-hour urine analysis without validation</p> <p>Best potassium measure recorded: 2 times during enrollment, then at 9, and 18 months, and at the final follow up</p>	<p>High risk</p> <p>5 24hr no validation</p>	<p>High risk</p> <p>5 24hr no validation</p>
<p>Witteaman, 1989¹⁷⁰</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: The Nurses Health Study</p>	<p>Exposure Type: Potassium intake</p> <p>Exposure Unit: mg/day</p>	<p>Potassium measure: food frequency questionnaire</p> <p>Best potassium measure recorded: once in 1980</p> <p>Potassium, Method of Validation: Authors cited other papers that reported on the reproducibility and validity of FFQ used, references 17-19.</p>		<p>High risk</p> <p>Single FFQ no validation</p>
<p>Yang, 2011¹⁷¹; Cohen, 2008²²⁵</p> <p>Location: US</p> <p>Setting: Community</p> <p>Design: Prospective Cohort study</p> <p>Study Name: NHANES III</p>	<p>Exposure Type: Sodium-Potassium Ratio</p> <p>Exposure Unit: mg/mg</p> <p>Exposure Type: Usual Potassium Intakes</p> <p>Exposure Unit: mg/d</p> <p>Exposure Type: Usual Sodium Intakes</p> <p>Exposure Unit: mg/d</p>	<p>Sodium measure: 24-hour diet recall</p> <p>Best sodium measure recorded: single 24-hour dietary recall</p> <p>Sodium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall, 24-hour "diet recall"</p> <p>Best potassium measure recorded: single 24-hour dietary recall</p> <p>Potassium, Method of Validation: a subgroup of 8% adults provided a second 24-hour dietary recall</p>	<p>Moderate risk</p> <p>Single 24hr diet recall yes validation</p>	<p>Moderate risk</p> <p>Single 24hr diet recall yes validation</p>

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Appendix F. Strength of Evidence

Table F1. Strength of evidence table

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Sodium										
KQ1 Effect of Sodium Reduction on Blood Pressure Outcomes										
KQ1b Effects of sodium by demographic subgroups (Age [adults vs. children and reproductive status], sex, race/ethnicity)										
Effects of sodium by demographic subgroups	Age (adults vs. children)	SBP	Pooled Estimate Adult: (MD -3.2; 95% CI -4.1 -2.4) 54 comparisons in 47 RCTs ¹⁻⁴⁷	47 RCTs High: 3 Moderate: 20 Low: 20 Unclear: 4	Direct	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence for a beneficial effect of sodium reduction on systolic BP in adults
			Pooled estimate Child: (MD -0.7; CI -1.8, 0.4) 11 comparisons in 8 RCTs ^{23, 48-54}	8 RCTs High: 0 Moderate: 4 Low: 2 Unclear: 2	Direct	Inconsistent	Precise	NA	Low	Low strength of evidence for a lack of beneficial effect of sodium reduction on systolic BP in children
			P=0.002 for difference between adults and children	NA	Indirect	NA	NA	NA	Low	Low strength of evidence for a difference in the effect of sodium reduction on systolic BP in adults vs. children

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Effects of sodium by demographic subgroups	Age	DBP	Pooled Estimate Adult (MD -2.2; -2.9, -1.6) 57 comparisons in 50 RCTs ^{1-47, 55}	48 RCTs High: 3 Moderate: 20 Low: 20 Unclear: 5	Direct	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence for a beneficial effect of sodium reduction on diastolic BP in adults
			Pooled Estimate Child (MD -2.1, CI -4.8, 0.6) 10 comparisons in 7 RCTs ^{23, 48-51, 53, 54}	7 RCTs High: 0 Moderate: 3 Low: 1 Unclear: 3	Direct	Inconsistent	Precise	NA	Low	Low strength of evidence for a lack of beneficial effect of sodium reduction on diastolic BP in children but significant effect for low and moderate RoB studies
			p=0.807 for difference						Low	Low strength of evidence for no difference in the effects of sodium reduction on diastolic BP in children vs. adults

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Effects of sodium by demographic subgroups	Age (adults)	Achievement of BP goal	Sodium reduction increases likelihood of achieving goal (RR 1.7, 95% CI 1.2, 2.4): 6 RCTs ^{1, 2, 13, 18, 25, 38}	6 RCTs High: 1 Moderate: 1 Low: 2 Unclear: 2	Direct	Consistent	Precise	NA	Low	Low SoE in support of a beneficial effect of sodium reduction on achieving a blood pressure goal
Effects of sodium by demographic subgroups	Age (adults)	HTN Incidence	Sodium reduction decreases risk for HTN (RR 0.8, 95% CI 0.7, 1.0): 3 RCTs ^{17, 27, 29}	3 RCTs High: 0 Moderate: 1 Low: 2 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Low	Insufficient evidence to support a conclusion that sodium reduction decreases HTN incidence in adults
	Age (adults vs. children)	HTN Incidence	0 RCTs	NA	NA	NA	NA	NA	Insufficient	Evidence is insufficient to support a conclusion regarding differences in effects of sodium restriction on HTN incidence by age
	Age (adults)	Adverse effects of sodium reduction	Sodium reduction does not affect blood lipid levels 3 RCTs ^{7, 19, 38}	3 RCTs High: 0 Moderate: 0 Low: 3 Unclear: 0	Direct	Consistent	Imprecise	NA	Low	Low strength of evidence for no effect of sodium reduction on blood lipids
	Age (adults)	Adverse effects of sodium reduction	Influence of sodium reduction on dizziness, headache, insulin sensitivity, muscle cramping 5 RCTs ^{7, 13, 18, 19, 38}	5 RCTs High: 0 Moderate: 0 Low: 4 Unclear: 1	Direct	NA	NA	NA	Insufficient	Evidence is insufficient, based on one to two studies per type of adverse event, to assess the effects of sodium reduction
Effects of sodium by demographic subgroups	Sex (men vs. women)	SBP	Pooled Estimate male (MD -2.7; CI -5.1, -0.3) 7 RCTs ^{9, 10, 17, 18, 25, 35, 38} Pooled Estimate female (MD -4.4; CI -6.1, -2.6) 6 RCTs ^{9, 17, 18, 27, 35, 38, 46}	8 RCTs High: 0 Moderate: 3 Low: 5 Unclear: 0	Direct and indirect	Inconsistent	Imprecise	NA	Low	Low strength of evidence for apparent lack of moderating effect of sex on effects of sodium reduction on systolic BP

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Effects of sodium by demographic subgroups	Sex	DBP	Pooled Estimate male (MD -1.4; CI -3.5, 0.6) 7 RCTs ^{9, 10, 17, 18, 25, 38, 55} Pooled Estimate female (MD -1.8; CI -2.4, -1.3) 7 RCTs ^{9, 17, 18, 38, 55}	8 RCTs High: 0 Moderate: 2 Low: 5 Unclear: 1	Direct and indirect	Inconsistent	Imprecise	NA	Low	Low strength of evidence for an apparent lack of moderating effect of sex on effects of sodium reduction on diastolic BP
Effects of sodium by demographic subgroups	Sex	% at goal	0 RCTs	NA	NA	NA	NA	NA	Insufficient	No conclusion
Effects of sodium by demographic subgroups	Sex	HTN Incidence	Pooled Estimate male (RR 0.8; CI 0.5, 1.4) 1 RCT ¹⁷ , Total N = 767 Pooled Estimate female (RR 0.9; CI 0.7, 1.2) 1 RCT ¹⁷ , Total N = 634	1 RCT High: 0 Moderate: 0 Low: 1 Unclear: 0	Indirect	Inconsistent	Precise	NA	Insufficient	Evidence is insufficient to support a conclusion regarding sex differences in effects of sodium restriction on incident HTN
Effects of sodium by demographic subgroups	Race/ethnicity	SBP	Pooled Estimate Black: (MD -3.8; CI -6.2, 1.3) 4 RCTs ^{17, 18, 27, 38} Pooled Estimate Other race: (MD -2.6; CI -4.2, -1.0) 4 RCTs ^{17, 18, 27, 38}	4 RCTs High: 0 Moderate: 0 Low: 4 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Insufficient	Evidence is insufficient to support a conclusion regarding differences in effects of sodium restriction on systolic BP by race/ethnicity
Effects of sodium by demographic subgroups	Race/ethnicity	DBP	Pooled Estimate Black: (MD -1.8; 95% CI -3.6, -0.04) 4 RCTs, ^{17, 18, 27, 38} Pooled Estimate Other race (MD -1.4; 95% CI -2.0, -0.8) 4 RCTs, ^{17, 18, 27, 38}	4 RCTs High: 0 Moderate: 0 Low: 4 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Insufficient	Evidence is insufficient to support a conclusion regarding differences in effects of sodium restriction on diastolic BP by race/ethnicity

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Effects of sodium by demographic subgroups	Race/ethnicity	HTN Incidence	Pooled Estimate Black (RR 0.84; 95% CI 0.4, 2.0), Other race (RR 0.90; 95% CI 0.4,2.0): 1 RCT: ¹⁷	1 RCT High: 0 Moderate: 0 Low: 1 Unclear: 0	Direct	NA	NA	NA	Insufficient	Evidence is insufficient to support a conclusion regarding differences in effects of sodium restriction on incident HTN by race/ethnicity
KQ1c comorbidities (Hypertension, CVD, Diabetes/kidney disease, Obesity)										
Effects of sodium by comorbidities	Hypertension vs. normotension	SBP	Pooled estimate hypertensives: (MD -4.4; 95% CI -5.6, -3.3) 38 comparisons in 36 RCTs ^{1-4, 6-8, 10-19, 22, 24-28, 30, 31, 34-38, 41, 45, 46, 56-58}	36 RCTs High: 3 Moderate: 12 Low: 15 Unclear: 6	Direct and indirect	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence that sodium reduction decreases systolic BP in populations with HTN
	Adults with normal BP	SBP	Pooled estimate: (MD -1.5; 95% CI -2.8, -0.) 14 comparisons in 9 RCTs ^{9, 20, 29, 38, 40, 42-44, 47}	9 RCTs High: 0 Moderate: 6 Low: 3 Unclear: 0	Direct	Inconsistent	Precise	NA	Moderate	Moderate SoE that sodium reduction decreases systolic BP in adults with normal BP
	Hypertension vs. normotension	SBP	P<0.001 for difference	N/A	Indirect	NA	NA	NA	Moderate	Moderate strength of evidence that sodium restriction decreases systolic BP more in populations with HTN than in normotensive populations
Effects of sodium by comorbidities	Adults with Hypertension	DBP	Pooled estimate hypertensives (MD -2.6; 95% CI -3.3, -1.9) 37 RCTs ^{1-4, 6-8, 10-19, 22, 24-28, 30, 31, 34-38, 41, 45, 46, 55-59}	37 RCTs High: 3 Moderate: 12 Low: 16 Unclear: 7	Direct	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence that sodium restriction decreases diastolic BP in populations with HTN

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Adults with normal BP	DBP	Pooled estimate (MD -0.6; CI -1.3, 0.1) 15 comparisons in 9 RCTs ^{9, 17, 20, 23, 29, 38, 40, 42-44, 47, 48, 60, 61}	10 RCTs High: 0 Moderate: 7 Low: 3 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Low	Low strength of evidence for no significant effect of reduced sodium on diastolic BP in normotensive adults
	Hypertension vs. normotension	DBP	P<0.003 for difference	N/A	Indirect	NA	NA	NA	Low	Low strength of evidence for a moderating effect of HTN status on the effect of sodium reduction on diastolic BP
	Diabetes and/or kidney disease	BP	6 RCTs ^{4, 15, 30, 33, 39, 56} No pooling	6 RCTs Low: 5 Moderate: 1	Indirect	NA	NA	NA	Insuffic ient	Insufficient evidence on which to base a conclusion regarding moderating effects of diabetes or kidney disease on effects of sodium reduction on BP
	Overweight or obesity	BP	Two RCTs ^{18, 38} found inconsistent effects on overweight or obese vs. normal weight	2 RCTs Low: 2	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence on which to base a conclusion regarding moderating effects of obesity or overweight on effects of sodium reduction on BP
KQ1a Moderating effect of other minerals on effect of sodium reduction										

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Low Na+K vs low Na	Adults	SBP	MD -0.6 (-2.9, 1.8) 5 RCTs ^{11, 29, 62-64} N=1,029	5 RCTs High: 0 Moderate: 2 Low: 2 Unclear: 1	Direct	Inconsistent	Imprecise	NA	Low	Low strength of evidence for no apparent moderating effect of K supplementation on systolic BP
Low Na+K vs low Na	Adults	DBP	MD -0.1 (-1.9, 1.7) 5 RCTs ^{11, 29, 62-64} N=1,029	5 RCTs High: 0 Moderate: 2 Low: 2 Unclear: 1	Direct	Inconsistent	Imprecise	NA	Low	Low strength of evidence for no apparent moderating effect of K supplementation on effect of sodium reduction on diastolic BP
Low Na+K vs low Na	Adults	% at goal	No moderating effect of potassium supplementation: 2 RCTs ^{62, 63} N=453	2 RCTs High: 0 Moderate: 1 Low: 1 Unclear: 0	Direct	Consistent	NR	NA	Insufficient	Insufficient evidence to draw a conclusion on the moderating effect of K supplementation on the effect of sodium reduction on percent at goal BP
Low Na+K vs low Na	Adults	HTN Incidence	No moderating effect of potassium: 1 RCT ²⁹	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Indirect	NR	NR	NA	Insufficient	No conclusion possible
Low Na+K vs low Na	Adults	AEs	No significant difference between groups: 1 RCT ⁶²	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NR	NR	NA	Insufficient	No conclusion possible
Potassium-rich salt substitutes vs usual diet	Adults	SBP	MD -5.6 (-7.1, -4.1) 13 RCTs ^{21, 33, 64-74} N=4,563	13 RCTs High: 1 Moderate: 6 Low: 4 Unclear: 2	Direct	Consistent	Imprecise	Low	Moderate	Moderate strength of evidence that salt substitute decreases SBP

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Potassium- rich salt substitutes vs usual diet	Adults	DBP	MD -2.9 (-3.9, - 1.8) 13 RCTs ^{21, 33, 64-74} N=4,563	13 RCTs High: 1 Moderate: 6 Low: 4 Unclear: 2	Direct	Consistent	Imprecise	Low	Moderate	Moderate strength of evidence that salt substitute decreases DBP
Potassium- rich salt substitutes vs usual diet	Adults	% at goal	Salt substitute increased proportion under BP control: 1 RCT ⁶⁸ n=282	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NR	Precise	NA	Insufficient	Insufficient evidence regarding effects of salt substitute on % of adults at BP goal
Potassium- rich salt substitutes vs usual diet	Adults	HTN Incidence	Inconsistent effects on need for HTN medication: 2 RCTs ^{67, 68} n=744	2 RCTs High: 0 Moderate: 2 Low: 0 Unclear: 0	Indirect	Consistent	NR	NA	Insufficient	Insufficient evidence regarding effects of salt substitute on HTN incidence in adults
Potassium- rich salt substitutes vs usual diet	Adults	AEs	Inconsistent findings (no hyperkalemia; mild gastrointestinal symptoms in 2 of 3 studies): 3 RCTs ^{65, 66, 68} n=935	3 RCTs High: 0 Moderate: 2 Low: 1 Unclear: 0	Direct	Inconsistent	NR	NA	Low	Low strength of evidence for an effect of salt substitutes on risk for mild gastrointestinal symptoms
KQ2 Associations of sodium with blood pressure										
KQ2a (sex, race, age/reproductive status)										
Associations of sodium with BP by demographics	Sex	SBP and DBP	No consistent associations of change in SBP with sex: 3 cohort studies ^{75, 76, 77} in adults	3 studies High: 2 Moderate: 1 Low: 0 Unclear: 0	Indirect	Inconsistent	NA	NA	Insufficient	Insufficient strength of evidence to draw conclusions regarding effect of sex on the association of decrease in systolic and diastolic BP with decreasing urinary Na excretion

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Associations of sodium with BP by demographics	Race	SBP and DBP	1 cohort study ⁷⁶	1 study High: 1 Moderate:0 Low:0 Unclear: 0	Direct	Inconsistent	NA	NA	Insuffic ient	Insufficient evidence to draw a conclusion regarding a moderating effect of race on the association of sodium status with SBP and DBP in adults
Associations of sodium with BP by demographics	Age: adults	SBP and DBP	5 prospective cohort studies ^{27, 78-81}	5 studies High: 3 Moderate: 1 Low: 1 Unclear: 0	Direct	Inconsistent	NA	NA	Low	A low strength of evidence supports a weak association of sodium exposure with systolic BP but absence of association with diastolic BP in adults based on observational studies
Associations of sodium with BP by demographics	Age: adults	Incident hypertensio n	6 prospective cohort studies ^{18, 77, 80, 82-84}	6 studies High: 2 Moderate: 3 Low: 1 Unclear: 0	Direct	Inconsistent	NA	NA	Low	A low strength of evidence supports a weak association of sodium exposure with incident hypertension in adults
Associations of sodium with BP by demographics	Age: children	SBP and DBP	4 prospective cohort studies in 5 publications ^{75, 76, 85-87}	4 studies High:2 Moderate: 3 Low: 1 Unclear: 0 estimated urinary Na; 1	Direct	Inconsistent	NA	NA	Low	Evidence is insufficient to draw conclusions about the association between sodium exposure and BP in children
KQ2b Comorbidities	HTN, DM, Obesity									

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	HTN	SBP	Inconsistent findings regarding moderating effect of HTN status on associations of Na exposure to SBP and DBP: 3 cohort studies, ^{78, 18, 88}	3 studies High:1 Moderate:0 Low: 2 Unclear: 0	Inconsistent	NA	NA	NA	insufficient	Evidence is insufficient to draw conclusions regarding the moderating effect of hypertension on the association between sodium exposure and BP
	Kidney Disease	SBP	One cohort study of kidney disease patients, but no comparison with healthy persons ⁸¹	1 study High:1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient strength of evidence regarding a moderating effect of kidney disease on the association between sodium status and SBP
		DBP	One cohort study of kidney disease patients, but no comparison with healthy person ⁸¹	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient strength of evidence regarding a moderating effect of kidney disease on the association between sodium status and DBP
	Obesity	SBP	Sodium excretion association with SBP only in non-overweight; 1 cohort study ⁷⁹	1 study High:0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insufficient	Insufficient strength of evidence regarding a moderating effect of overweight on the association between sodium status and SBP
		DBP	No difference between overweight and non-overweight; 1 cohort study ⁷⁹	1 study High: 0 Moderate: 1 Low: 0	Direct	NA	NA	NA	Insufficient	Insufficient strength of evidence regarding a moderating effect of overweight on the association between sodium status and DBP

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ3 Dietary sodium and clinical outcomes										
KQ3b	Effects of sodium by demographic subgroups									
	Age: adults	All-cause mortality	Borderline decrease in risk (RR 0.97, 95% CI 0.94, 1.0) 7 RCTs ^{17, 25, 27, 35, 56, 66, 89}	7 RCTs High: 0 Moderate: 4 Low: 3 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Insufficient	Insufficient evidence that sodium reduction decreases the risk for all-cause mortality
	Age: adults	CVD mortality	No effects found in 2 RCTs reported in 3 publications ^{25, 89, 90}	2 RCTs High: 0 Moderate: 1 Low: 2 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Insufficient	Insufficient evidence to draw a conclusion regarding effect of sodium reduction on risk for CVD mortality
	Age: adults	Stroke	No effects of sodium reduction: 3 RCTs ^{18, 33, 64} (RR 0.7, 95% CI 0.05, 9.9)	3 RCTs High: 0 Moderate: 0 Low: 3 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Low	Low strength of evidence for apparent lack of effect of sodium reduction on the risk for stroke
	Age: adults	MI	No effect of sodium reduction: 2 RCTs ^{18, 27}	2 RCT High: 0 Moderate: 0 Low: 2 Unclear: 0	Direct	NA	Imprecise	NA	Insufficient	Insufficient strength of evidence to draw a conclusion regarding effect of sodium reduction on the risk for MI.
	Age: adults	Number of patients with any CVD event as reported by the study authors	Significant effects of sodium reduction: 7 RCTs ^{17, 18, 25, 27, 65, 66, 89, 91} (RR 0.8, 95% CI 0.7, 0.96, I ² 0%; n=4,328)	7 RCTs High: 0 Moderate: 3 Low: 4 Unclear: 0	Direct	Inconsistent	Precise	NA	Low	Low strength of evidence that sodium reduction decreases the risk for composites of any CVD event

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
		Combined CVD morbidity and mortality	Inconsistent and non-significant effects of sodium reduction (RR 0.8, 95% CI 0.7, 0.98): 8 RCTs ^{64, 33, 66, 17, 18, 25, 27, 89}	8 RCTs High: 0 Moderate: 3 Low: 5 Unclear: 0	Direct	Inconsistent	Imprecise	NA	Low	Low strength of evidence that sodium reduction decreases the risk for combined CVD morbidity and mortality
KQ3b Demographic moderators (Sex, Race/ethnicity, age)	Sex	Number of patients with any CVD event as reported by the study authors	2 RCTs: (males: HR 0.72, 95% CI 0.56, 0.94, p=0.01; females: HR 0.64, 95% CI 0.49, 0.83, p=0.001) ^{18, 27}	2 RCTs High: 0 Moderate: 0 Low: 2 Unclear: 0	Direct	Consistent	Precise	NA	Insufficient	insufficient evidence to draw conclusions about the effects of sex on the effects of sodium reduction on CVD or CHD outcomes
	Race/ethnicity	All-cause mortality or any CVD outcome	2 RCTs ^{18, 27} showed inconsistent effects	2 RCTs High: 0 Moderate: 0 Low: 2 Unclear: 0	Direct	Inconsistent	Precise	NA	Insufficient	insufficient evidence to draw conclusions about the effects of race/ethnicity on the effects of sodium reduction on all-cause mortality or any CVD or CHD outcomes
KQ3c	Hypertension		0 RCTs	NA	NA	NA	NA	NA	Insufficient	Insufficient evidence to draw a conclusion
	Obesity	Number of patients with any CVD event as reported by the study authors	Inconsistent moderating effects of overweight/obesity: 2 RCTs ^{18, 92}	2 studies High: 1 Moderate: 0 Low: 1 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence to draw a conclusion
	Other comorbidities (Diabetes, kidney disease)		0 RCTs	NA	NA	NA	NA	NA	Insufficient	Insufficient evidence to draw a conclusion

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ3a effect of other minerals	Low sodium/high potassium diet	All-cause mortality	1 RCT ²⁹	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence to draw conclusions on whether the effects of sodium reduction on all- cause mortality are affected by higher dietary potassium
KQ3a effect of other minerals	Low sodium/high potassium diet	Other CVD outcomes (gross morbidity)	1 RCT ²⁹	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence to draw conclusions on whether the effects of sodium reduction on CVD outcomes is affected by higher dietary potassium
KQ3a effect of other minerals	Salt substitute	All-cause mortality	No effects of salt substitute: 2 RCTs ^{66, 68} n=653	2 RCTs High: 0 Moderate: 2 Low: 0 Unclear: 0	Direct	Inconsistent	NA	NA	Insuffic ient	Insufficient evidence that salt substitute influences the risk for all-cause mortality
KQ3a effect of other minerals	Salt substitute	Any CVD event	Inconsistent findings across 2 RCTs ^{65, 66}	2 RCTs High: 0 Moderate: 1 Low: 1 Unclear: 0	Direct	Inconsistent	NA	NA	Insuffic ient	Insufficient evidence that salt substitute influences the risk for any CVD event
KQ4										

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	All-cause mortality	14 cohort studies; Sodium intake levels were assessed by 24-hour urinary sodium excretion in 5 studies, ^{90, 93-96} by spot-urine samples in 4 studies, ^{97 98-100} by 24-hour dietary recall in 4 studies, ¹⁰¹⁻¹⁰⁴ , and by 3-day dietary records in 1 study. ¹⁰⁵	14 studies High: 9 Moderate: 4 Low: 1 Unclear: 0	24-hr urinary excretion: null or positive linear relationship Estimated 24-hr urinary excretion: U- or J-shaped relationship Dietary sodium intake: null or positive linear relationship	24-hr urinary excretion: Inconsistent Estimated 24-hr urinary excretion: Consistent Dietary sodium intake: Inconsistent	Precise	NA	Low	Low level evidence that higher sodium intake levels are associated with higher risks of all-cause mortality (insufficient evidence for non-linear associations)
	Generally healthy	CVD mortality	9 cohort studies; Sodium intake levels were assessed by 24-hour urinary sodium excretion in 2 studies, ^{93, 96} by spot-urine samples in 3 studies, ⁹⁸⁻¹⁰⁰ by 24-hour dietary recalls in 4 studies. ¹⁰¹⁻¹⁰⁴	9 studies High: 7 Moderate: 2 Low: 0 Unclear: 0	}	24-hr urinary excretion: Inconsistent Estimated 24-hr urinary excretion: Inconsistent Dietary sodium intake: Inconsistent	Precise	NA	Insufficient	Insufficient evidence for both linear and non-linear associations between sodium intake levels and CVD mortality.

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	CHD mortality	5 cohort studies; Sodium intake levels were assessed by 24- hour urinary sodium excretion in 2 studies, ^{94, 96} and by 24-hour dietary recall in 3 studies. ^{101, 103, 104}	5 studies High: 4 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null or positive linear relationship Dietary sodium intake: null linear relationship	24-hr urinary excretion: Inconsistent Dietary sodium intake: Consistent	Imprecise	NA	Insuffi- cient	Insufficient evidence for associations between sodium intake levels and risks of CHD mortality
	Generally healthy	Stroke	7 cohort studies; Sodium intake levels were assessed by 24- hour urinary sodium excretion in 2 studies, ^{93, 96} by spot-urine samples in 2 studies, ^{98, 100} and by 24-hour dietary recalls in 3 studies. ^{101, 103, 106}	7 studies High: 6 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null linear relationship Estimated 24-hr urinary excretion: null or J- shaped relationship Dietary sodium intake: null linear relationship	24-hr urinary excretion: Consistent Estimated 24- hr urinary excretion: Inconsistent Dietary sodium intake: Consistent	Precise	NA	Low	Insufficient evidence for the association between sodium intake levels and risks for stroke due to the limitations in sodium exposure assessment methods across studies.
	Generally healthy	Myocardial infarction	2 cohort studies; Sodium intake levels were assessed by spot- urine samples in both studies. ^{98, 100}	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Estimated 24-hr urinary excretion: null or J- shaped relationship	Estimated 24- hr urinary excretion: Inconsistent	Imprecise	NA	Insuffi- cient	Insufficient evidence for associations between sodium intake levels and risks of MI

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	Combined CVD morbidity and mortality	7 cohort studies; Sodium intake levels were assessed by 24-hour urinary sodium excretion in 4 studies, ^{92, 93, 95, 107} and by spot-urine samples in 3 studies. ⁹⁷⁻⁹⁹	7 studies High: 6 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null or positive linear relationship Estimated 24-hr urinary excretion: U-shaped relationship	24-hr urinary excretion: Inconsistent Estimated 24-hr urinary excretion: Consistent	Precise	NA	Insufficient	Insufficient evidence for associations between sodium intake levels and risks of combined CVD morbidity and mortality due to the limitations in the sodium exposure assessment methods and heterogeneity in outcome definitions
	Generally healthy	Combined CHD morbidity/mortality	5 cohort studies; Sodium intake levels were assessed by 24-hour urinary sodium excretion in 4 studies, ^{93, 94, 96, 108} and by 24-hour dietary recall in 1 study. ¹⁰¹	5 studies High: 3 Moderate: 2 Low: 0 Unclear: 0	24-hr urinary excretion: inverse, null or positive linear relationship Dietary sodium intake: null linear relationship	24-hr urinary excretion: Inconsistent Dietary sodium intake: NA	Precise	NA	Insufficient	Insufficient evidence for associations between sodium intake levels and risks of combined CHD morbidity and mortality due to the limitations in the sodium exposure assessment methods and heterogeneity in outcome definition
	Generally healthy	Other CVD Outcomes	2 cohort studies; Sodium intake levels were assessed by spot-urine samples in 1 study, ¹⁰⁹ and 24-hour dietary recall in 1 study. ¹¹⁰	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Estimated 24-hr urinary excretion: U-shaped relationship Dietary sodium intake: positive linear relationship	NA	Imprecise	NA	Insufficient	Insufficient evidence for associations between sodium intake levels and risks of heart failure

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	Mean difference between groups in eGFR	1 cohort study; Sodium intake levels were assessed by 24-hour urinary sodium excretion in 1 study. ¹¹¹	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null linear relationship	NA	NA	NA	Insufficient	Insufficient evidence for associations between sodium intake levels and changes in eGFR
	Generally healthy	Number of patients with end stage renal disease	0 cohort study	NA	NA	NA	NA	NA	Insufficient	Insufficient evidence for associations between sodium intake levels and the risk for ESRD
KQ4a Effect of other minerals	Healthy populations	0 RCTs	NA	NA	NA	NA	NA	NA	Insufficient	Insufficient evidence regarding effects of other minerals on associations between sodium and outcomes of interest
KQ4b	Sex, Race/ethnicity, age	0 RCTs	NA	NA	NA	NA	NA	NA	Insufficient	Insufficient evidence regarding effects of sex, race/ethnicity or age on associations between sodium and outcomes of interest
KQ4c	HTN	All-cause mortality	1 cohort study: No association ¹¹²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		CVD morbidity and mortality	Inverse association for men only ¹¹²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		MI morbidity and mortality	Inverse association for men only ¹¹²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
		Stroke	No association ¹¹²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		CHD morbidity	1 cohort study: significant linear association ¹⁰⁸	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		eGFR	1 cohort study: significant association ¹¹³	1 study High: 0 Moderate: 0 Low: 1 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
	CVD	All-cause mortality	1 cohort study: U-shaped association with estimated sodium excretion ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		CVD mortality	1 cohort study: U-shaped association with estimated sodium excretion ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		Stroke	1 cohort study: linear association ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
		Diabetes	4 cohort studies: inconsistent relationships with all-cause mortality ¹¹⁵⁻¹¹⁸	4 studies High: 4 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
			1 cohort study: Inverse association with CVD mortality ¹¹⁵	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
		Obesity	3 cohort studies (overlapping cohorts): association with all-cause mortality ^{92, 96, 101}	3 studies High: 2 Moderate: 0 Low: 1 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
			3 cohort studies (overlapping cohorts): CVD mortality ^{92, 96, 101}	3 studies High: 2 Moderate: 0 Low: 1 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
KQ5 Effects of Potassium Supplementati on SBP, DBP, incident HTN, % at goal, incidence of kidney stones, and AEs										
KQ5b Potassium Effects by demographic subgroups										
Potassium supplements	Age: adults vs. children	SBP: adults	Beneficial effect on SBP (MD -6.4, 95% CI -11.1, -1.8) 18 RCTs ^{11, 27, 36, 88, 119-132}	18 RCTs High: 0 Moderate: 6 Low: 10 Unclear: 2	Direct	Inconsistent	Precise	NA	Moderate	Moderate SoE in support of a beneficial effect of potassium supplementation on Systolic BP in adults
	Age: children	SBP	1 RCT ⁵⁰	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	Precise	NA	Insufficient	Insufficient evidence to draw a conclusion regarding effects of potassium supplementation on systolic BP in children

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Age; adults vs. children	SBP	No significant difference between effect sizes for adults and children (p=0.345)	NA	Indirect	NA	NA	NA	Insuffi- cient	Insufficient evidence to draw a conclusion regarding difference in effect of potassium supplementation on systolic BP in adults vs. children
	Age: adults	DBP	Significant effect of potassium (MD - 3.5, 95% CI -6.1, - 0.9) 18 RCTs ^{11, 27, 36, 88, 119-132}	18 RCTs High: 0 Moderate: 6 Low: 10 Unclear: 2	Direct	Inconsistent	Precise	NA	Moder- ate	Moderate strength of evidence for a beneficial effect of potassium supplementation on diastolic BP in adults
	Age: children	DBP	1 RCT ⁵⁰	1 RCT High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	Consistent	Precise	NA	Insuffi- cient	Insufficient strength of evidence to support a conclusion regarding the effect of potassium on diastolic BP in children
	Age: adults vs. children	DBP	No difference between adults and children (p=0.509)	NA	NA	NA	NA	NA	Insuffi- cient	Insufficient evidence based on only one study in children to draw a conclusion regarding difference in effect of potassium supplementation on diastolic BP in adults vs. children
	Age: Adults	Kidney stones	1 RCT (MD -1.00, CI -1.16, -0.84) ¹³³	1 RCT High: 0 Moderate: 0 Low: 0 Unclear: 1	Direct	NA	NA	NA	Insuffi- cient	Evidence insufficient to draw a conclusion regarding effects of potassium supplementation on risk for kidney stones

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
Potassium from food sources	Age: adults	BP	2 RCTs ^{134, 135}	2 RCTs High: 1 Moderate: 1 Low: 0 Unclear: 0	Direct	Consistent	Imprecise	NA	Insuffic ient	Evidence is insufficient to draw a conclusion about the effects of increasing dietary potassium from foods on BP
	Age: Adults	Adverse effects	6 RCTs ^{120, 121, 127, 129, 131, 133}	High:0 Moderate: 2 Low: 3 Unclear: 1	Direct	NA	NA	NA	Low	Low SoE for an increase in risk for gastrointestinal discomfort from potassium supplements
KQ5b Potassium Effects by demographic subgroups	Sex: adults	SBP, DBP	1 parallel RCT ^{27, 50} No significant differences between sexes in effects of K on BP	2 RCTs High: 0 Moderate: 1 Low: 1 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient to draw a conclusion regarding modifying effect of sex on effect of potassium on SBP
	Race/ethnicity	BP	4 RCTs ^{27, 122, 127, 134} Significant difference in SBP response between Blacks and overall group ¹²⁷ but not between Blacks and Whites; ²⁷ significant effect on SBP in RCT of all Blacks (MD -39.00, CI -43.88, - 34.12); ¹²² but no effect in another ¹³⁴	4 RCTs High: 1 Moderate: 1 Low: 2 Unclear: 0	Indirect	Inconsistent	Imprecise	NA	Insuffic ient	Insufficient evidence to draw a conclusion regarding moderating effect of race/ethnicity on the effect of potassium supplementation on BP

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ5c Potassium (HTN, T2DM, Obesity, Renal Health)										
KQ5c Potassium	Adults with HTN	SBP	Significant effect (MD -7.0, 95% CI - 12.6, -1.3) 17 RCTs of adults with HTN ^{27, 36, 88, 120, 122-124, 126-132, 135}	15 RCTs High: 0 Moderate: 5 Low: 9 Unclear: 1	Direct	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence for a beneficial effect of potassium supplementation on systolic BP adults with HTN
	Adults with normal BP	SBP	No significant effect (MD -4.4, 95% CI - 13.9, 5.0) 3 RCTs ^{119, 121, 136}	3 RCTs High: 0 Moderate: 1 Low: 2 Unclear: 0	Direct	Inconsistent	Precise	NA	Low	Low strength of evidence for a lack of effect of potassium supplementation on systolic BP in normotensive adults
	Adults with HTN vs. adults with normal BP	SBP	No statistically significant difference between hypertensives and normotensives Based on indirect comparison above (p=0.756)	N/A	Indirect	NA	NA	NA	Insufficient	Insufficient evidence to support a conclusion regarding differences in the effect of potassium supplementation on systolic BP in normotensive vs. hypertensive adults
	Adults with HTN	DBP	Significant effect in adults with HTN (MD -3.6, 95% CI - 6.7, -0.4) 15 RCTs ^{27, 36, 88, 120, 122-124, 126-132, 135}	17 RCTs High: 0 Moderate: 5 Low: 9 Unclear: 1	Direct	Inconsistent	Precise	NA	Moderate	Moderate strength of evidence for a beneficial effect of potassium supplementation on diastolic BP in adults with HTN

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Normotensive adults	DBP	No effect (MD -3.4, 95% CI -12.8, 6.1) 3 RCTs ^{119, 121, 136}	3 RCTs High: 0 Moderate: 1 Low: 2 Unclear: 0	Direct	Inconsistent	Precise	NA	Low	Low strength of evidence for no significant effect of potassium supplementation on diastolic BP in normotensive adults
	Hypertensive vs. normotensive adults	DBP	No difference between hypertensives and normotensives based on studies describe above (p=0.757)	NA	Indirect	NA	NA	NA	Insuffic ient	Insufficient evidence on which to base a conclusion regarding differences in effects of potassium supplementation on diastolic BP between hypertensive and normotensive adults
KQ5a Potassium and other minerals										
Potassium plus calcium	Adults	SBP, DBP	1 parallel RCT ¹²³ K alone vs. K+ Ca	1 RCT High: 0 Moderate: 0 Low: 0 Unclear: 1	Indirect	NA	NA	NA	Insuffic ient	Insufficient to draw a conclusion regarding modifying effect of calcium on effect of potassium on BP
Potassium plus magnesium	Adults	SBP, DBP	1 crossover RCT ¹³¹ K alone vs. K+ Mg	1 RCT High: 0 Moderate: 0 Low: 1 Unclear: 0	Indirect	NA	NA	NA	Insuffic ient	Insufficient to draw a conclusion regarding modifying effect of magnesium on effect of potassium on BP
Potassium plus low vs. usual sodium	Adults	BP	1 crossover RCT ¹³⁷ ; significant effect of low sodium vs. usual sodium but only when measured at home	1 RCT High: 0 Moderate: 0 Low: 1 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence to draw conclusion regarding additional effects of reducing sodium on BP effects of high potassium diet

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ6 Potassium										
KQ6a Association of K with BP: moderating effects of age/reproducti ve status, sex, race										
KQ6a	Age: Adults	SBP, DBP	Inconsistent associations with SBP, DBP in adults: 7 cohorts reported in 6 studies ^{27, 76, 80, 88, 138, 139}	6 studies High: 4 Moderate: 0 Low: 2 Unclear:	Direct	NA	NA	NA	Low	A low strength of evidence supports a lack of association between higher potassium exposure status and lower adjusted BP in adults.
	Age: children	SBP, DBP	Association with SBP and DBP in youth: 2 cohort studies ^{76, 85}	2 studies High: 1 Moderate: 0 Low: 1 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence to support a conclusion regarding an association of K intake with BP in children
	Age: Adults	Incident HTN	Inconsistent findings across 5 cohort studies with 2 showing direct association ^{80, 83, 84, 138, 140}	5 studies High: 3 Moderate: 1 Low: 1 Unclear: 0	Direct	Inconsistent	NA	NA	Low	A low strength of evidence supports a lack of association between high potassium exposure status and risk for incident hypertension in adults
	Age: Adults	Risk for kidney stones	K intake associated with decreased risk: 1 single cohort, ¹⁴¹ 3 combined cohort studies ¹⁴²	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Indirect	Inconsistent	NA	NA	Insuffic ient	A low strength of evidence supports an association between higher potassium exposure and lower risk for kidney stones in adults.

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ6a	Sex	SBP, DBP	No difference in association of K with SBP or DBP by sex: 3 cohort studies ^{76, 138, 139}	3 studies High: 3 Moderate: 0 Low: 0 Unclear: 0	Indirect	Inconsistent	NA	NA	Insufficient	Evidence is insufficient, based on lack of direct comparisons, to draw conclusions regarding sex differences in the association between potassium exposure and BP
	Sex	Incident HTN	No difference by sex: 2 cohort studies ^{138, 140}	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Indirect	Inconsistent	NA	NA	Insufficient	Insufficient evidence to support a conclusion regarding the moderating effect of sex on the association of K intake with incident HTN
	Sex: M vs. F	Risk for kidney stones	K intake associated with decreased risk No difference between men and women: 1 single cohort, ¹⁴¹ 3 combined cohort studies ¹⁴²	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Indirect	Inconsistent	NA	NA	Insufficient	Insufficient evidence to support a conclusion regarding the moderating effect of sex on the association of potassium status with risk for kidney stones
KQ6b	HTN	SBP, DBP	1 cohort study of individuals with HTN ⁸⁸ :	1 study High: 0 Moderate: 0 Low: 1 Unclear: 0	Indirect	Consistent	NA	NA	Insufficient	Evidence is insufficient, based on lack of direct comparisons and only one study, to draw conclusions regarding a moderating effect of hypertension on the association between potassium exposure and BP

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Obesity	Incident HTN	No effect of obesity: 1 cohort study ¹³⁸	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Insufficient evidence to support a conclusion regarding the moderating effect of obesity on the association of K intake with incident HTN
KQ7 potassium		CVD/CHD/r enal morbidity/m ortality outcomes								
KQ7b	Sex, race/ethnicity/a ge	No studies	0 studies	NA	NA	NA	NA	NA	Insuffic ient	Evidence is insufficient to draw conclusions regarding potential moderating effects of sex, race/ethnicity, or age on the effects of potassium on outcomes of interest
kQ7c	HTN, CVD, diabetes, obesity	No studies	0 studies	NA	NA	NA	NA	NA	Insuffic ient	Evidence is insufficient to draw conclusions regarding potential moderating effects of HTN, CVD, diabetes, or obesity on the effects of potassium on outcomes of interest
7a Effects of other minerals	All populations	All-cause mortality	1 RCT potassium- enriched salt substitute decreased all- cause mortality risk at 2.5 years ⁸⁹	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Evidence is insufficient to draw conclusions on the effect of potassium supplementation on the risk for all-cause mortality

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
		CVD mortality	1 RCT potassium- enriched salt substitute decreased all- cause mortality risk at 2.5 years ⁸⁹	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Evidence is insufficient to draw conclusions on the effect of potassium supplementation on the risk for CVD mortality
		CHD mortality	1 RCT potassium- enriched salt substitute decreased all- cause mortality risk at 2.5 years ⁸⁹	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	Direct	NA	NA	NA	Insuffic ient	Evidence is insufficient to draw conclusions on the effect of potassium supplementation on the risk for CHD mortality
KQ8 potassium										

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	All-cause mortality	5 cohort studies and 1 case-cohort study; Potassium intake levels were assessed by 24-hour urinary potassium excretion in 2 studies, ^{94, 95} by spot-urine samples in 2 studies, ^{98, 100} by food frequency questionnaire in 2 studies, ^{100, 143} and by 24-hour dietary recalls in 1 study. ^{104, 105}	7 studies High: 3 Moderate: 4 Low: 0 Unclear: 0	24-hr urinary excretion: null or inverse linear relationship Estimated 24-hr urinary excretion: null or inverse linear relationship Dietary sodium intake: inverse linear relationship	24-hr urinary excretion: Inconsistent Estimated 24-hr urinary excretion: Inconsistent Dietary sodium intake: Consistent	Precise	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	CVD mortality	2 cohort studies and 1 case-cohort study; Potassium intake levels were assessed by spot-urine samples in 2 studies, ^{98, 100} by food frequency questionnaire in 1 study, ¹⁰⁰ and by 24-hour dietary recalls in 1 study. ¹⁰⁴	3 studies High: 1 Moderate: 2 Low: 0 Unclear: 0	Estimated 24-hr urinary excretion: null or inverse linear relationship Dietary sodium intake: inverse linear relationship	Estimated 24-hr urinary excretion: Inconsistent Dietary sodium intake: Consistent	Imprecise	NA	Insufficient	Evidence is insufficient to draw conclusions

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	CHD mortality	2 cohort studies; Potassium intake levels were assessed by 24-hour urinary excretion in 1 study, ⁹⁴ and by 24-hour dietary recall in 1 study. ¹⁰⁴	2 studies High: 1 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: inverse linear relationship Dietary sodium intake: inverse linear relationship	24-hr urinary excretion: NA Dietary sodium intake: NA	Imprecise	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	Renal disease mortality	0 studies	NA	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	Stroke	12 cohort studies and 1 case-cohort study; Potassium intake levels were assessed by 24-hour urinary potassium excretion in 1 study, ⁹⁵ by spot-urine samples in 2 studies, ^{98, 100} by food frequency questionnaires in 8 studies, ^{100, 143-149} and by 24-hour dietary recalls in 3 studies. ^{139, 150, 151} Among these, 1 study assessed both urinary and dietary potassium intake levels. ¹⁰⁰	13 studies High: 7 Moderate: 6 Low: 0 Unclear: 0	24-hr urinary excretion: null linear relationship Estimated 24-hr urinary excretion: null linear relationship Dietary sodium intake: null or inverse linear relationship	24-hr urinary excretion: NA Estimated 24-hr urinary excretion: Consistent Dietary sodium intake: Inconsistent	Precise	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	CHD	0 studies	NA	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	MI	1 cohort study and 1 case-cohort study; Potassium intake levels were assessed by spot-urine samples in both studies. ^{98, 100}	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	Estimated 24-hr urinary excretion: null linear relationship	Estimated 24-hr urinary excretion: Consistent	Imprecise	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	Number of patients with any CVD event	0 studies	NA	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions
	Generally healthy	Combined CHD morbidity/mortality	2 cohort studies; Potassium intake levels were assessed by 24-hour urinary potassium excretion in both studies. ^{94, 95}	2 studies High: 1 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null or inverse linear relationship	24-hr urinary excretion: Inconsistent	Imprecise	NA	Insufficient	Evidence is insufficient to draw a conclusion regarding association with combined CHD morbidity and mortality
	Generally healthy	Combined CVD morbidity/mortality	3 cohort studies; Potassium intake levels were assessed by 24-hour urinary potassium excretion in 2 studies, ^{92, 95} and by spot-urine samples in 1 study. ⁹⁸	2 studies High: 1 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: null linear relationship Estimated 24-hr urinary excretion: null linear relationship	24-hr urinary excretion: Consistent Estimated 24-hr urinary excretion: NA	Imprecise	NA	Insufficient	Evidence is insufficient to draw a conclusion regarding association with combined CVD morbidity and mortality
	Generally healthy	Mean difference in eGFR	1 cohort study; Potassium intake levels were assessed by 24-hour urinary potassium excretion. ¹¹¹	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	24-hr urinary excretion: inverse linear relationship	NA	NA	NA	Insufficient	Evidence is insufficient to draw a conclusion regarding association with mean difference in eGFR

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
	Generally healthy	Number of patients with ESRD	1 cohort study; Potassium intake levels were assessed by food frequency questionnaire. ¹⁵²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions regarding association with number of patients with ESRD
KQ8a	Other minerals		0 studies	NA	NA	NA	NA	NA	Insufficient	
KQ8b	Effect of sex	All-cause mortality	2 cohort studies; Potassium intake levels were assessed by 24-hour dietary recalls in 1 study ¹⁰⁴ and by food frequency questionnaire in 1 study. ¹⁴³	2 studies High: 0 Moderate: 2 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions regarding moderating effects of sex, race/ethnicity, or age
		CVD mortality	1 cohort study; Potassium intake levels were assessed by 24-hour dietary recalls. ¹⁵¹	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions regarding moderating effects of sex
		CHD mortality	2 cohort studies; Potassium intake levels were assessed by 24-hour urinary potassium excretion in both studies. ^{94, 139}	2 studies High: 2 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions regarding moderating effects of sex
	Effects of race/ethnicity	Stroke	1 cohort study; Potassium intake levels were assessed by 24-hour dietary recalls. ¹⁵¹	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Evidence is insufficient to draw conclusions regarding moderating effects of sex
	Effect of age		0 studies	NA						

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
KQ8c comorbidities	HTN	All-cause mortality	1 cohort study; Potassium intake levels were assessed by 24- hour dietary recalls in 1 study. ¹⁰⁴	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	Significant inverse linear relationship with baseline dietary K	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	HTN	CVD mortality	1 cohort study; Potassium intake levels were assessed by 24- hour dietary recalls in 1 study. ¹⁰⁴	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	Significant inverse linear relationship with baseline K	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	HTN	Stroke	1 cohort study; Potassium intake levels were assessed by 24- hour dietary recalls. ¹⁵¹	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	HTN	MI	1 cohort study; Potassium intake levels were assessed by 24- hour urinary potassium excretion. ¹¹²	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0	No significant linear association with 24- hour urinary K	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	HTN	Number of patients with any CVD event	0 studies	NA	NA	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	CVD	All-cause mortality	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	No significant linear association	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion
comorbidities	CVD	CVD mortality	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	No significant linear association	NA	NA	NA	Insuffic ient	Insufficient evidence on which to draw a conclusion

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
comorbidities	CVD	CHD	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	NA	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion.
comorbidities	CVD	Stroke	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Significant association with quintiles of estimated sodium excretion	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
comorbidities	CVD	MI	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹¹⁴	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	No significant linear association	NA	NA	NA	Insufficient	Insufficient evidence on which to draw a conclusion
comorbidities	Diabetes	All-cause mortality	1 cohort study; Potassium levels were assessed by food frequency questionnaire. ¹¹⁶	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence on which to draw conclusion
comorbidities	Diabetes	CKD	1 cohort study; Potassium levels were assessed by food frequency questionnaire. ¹¹⁸	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence for association
comorbidities	Diabetes	Renal function outcome	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹⁵³	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0	Indirect	NA	NA	NA	Insufficient	Insufficient evidence for association
comorbidities	CKD	All-cause mortality	2 cohort studies; Potassium levels were assessed by 24-hour urinary potassium excretion in both studies. ^{154, 155}	2 studies High: 1 Moderate: 1 Low: 0 Unclear: 0						

Intervention/ exposure	Population/ subpopulation	Outcome	Pooled ES (# studies, n)	Study Limitations*	Directness #	Consistency	Precision	Reporting Bias	Grade	Conclusion
comorbidities	CKD	Composite CVD	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹⁵⁶	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0						
comorbidities	CKD	MI	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹⁵⁶	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0						
comorbidities	CKD	Stroke	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹⁵⁶	1 study High: 0 Moderate: 1 Low: 0 Unclear: 0						
comorbidities	CKD	Kidney failure	1 cohort study; Potassium levels were assessed by 24-hour urinary potassium excretion. ¹⁵⁵	1 study High: 1 Moderate: 0 Low: 0 Unclear: 0						

BP=blood pressure; CHD=coronary heart disease; CVD=cardiovascular disease; ESRD=end-stage renal disease; GI=gastrointestinal; HTN=hypertension;
K=potassium; Mi=myocardial infarction; NA=not applicable; Na=sodium; SoE=strength of evidence *Includes study design(s), RoB score, and applicability;
#Dose-response relationship for key questions 4 and 8

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Appendix G. List of Systematic Reviews Reference Mined

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Appendix H. Results From the Observational Studies (Key Question 4)

Total Mortality Outcome

Figure H1. Categorical analysis of the association between urinary sodium levels and total mortality outcome in generally healthy populations

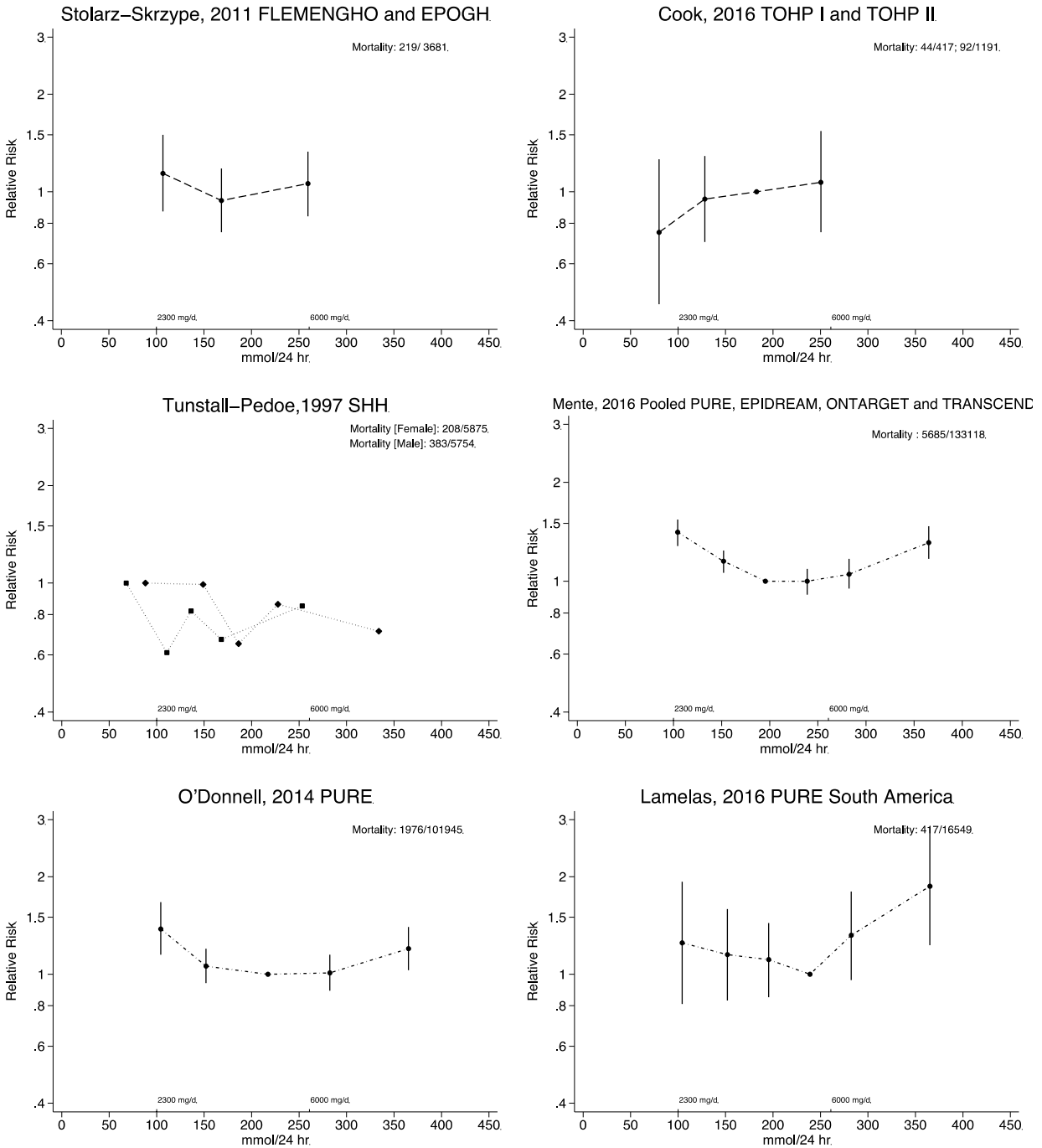


Figure H2. Categorical analysis of the association between dietary sodium levels and total mortality outcome in generally healthy populations

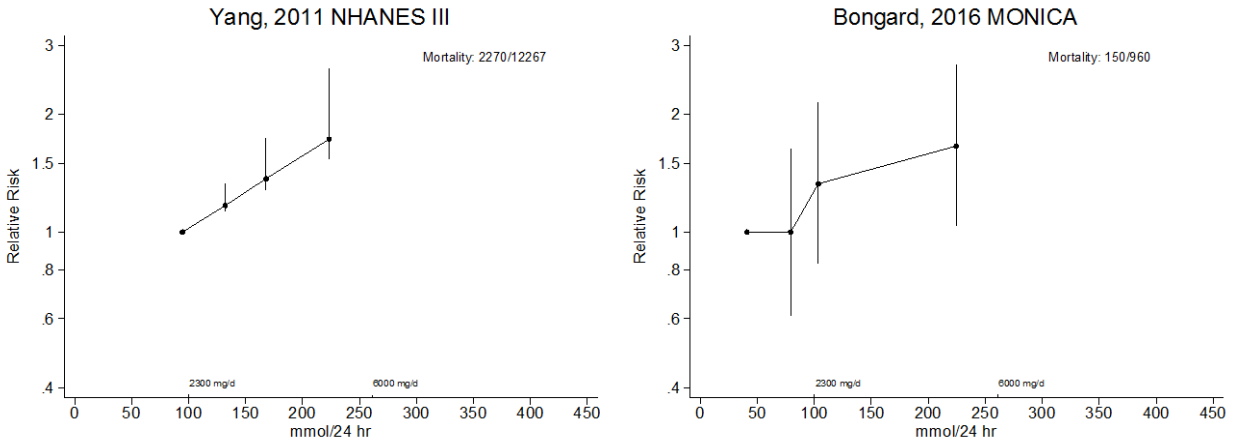
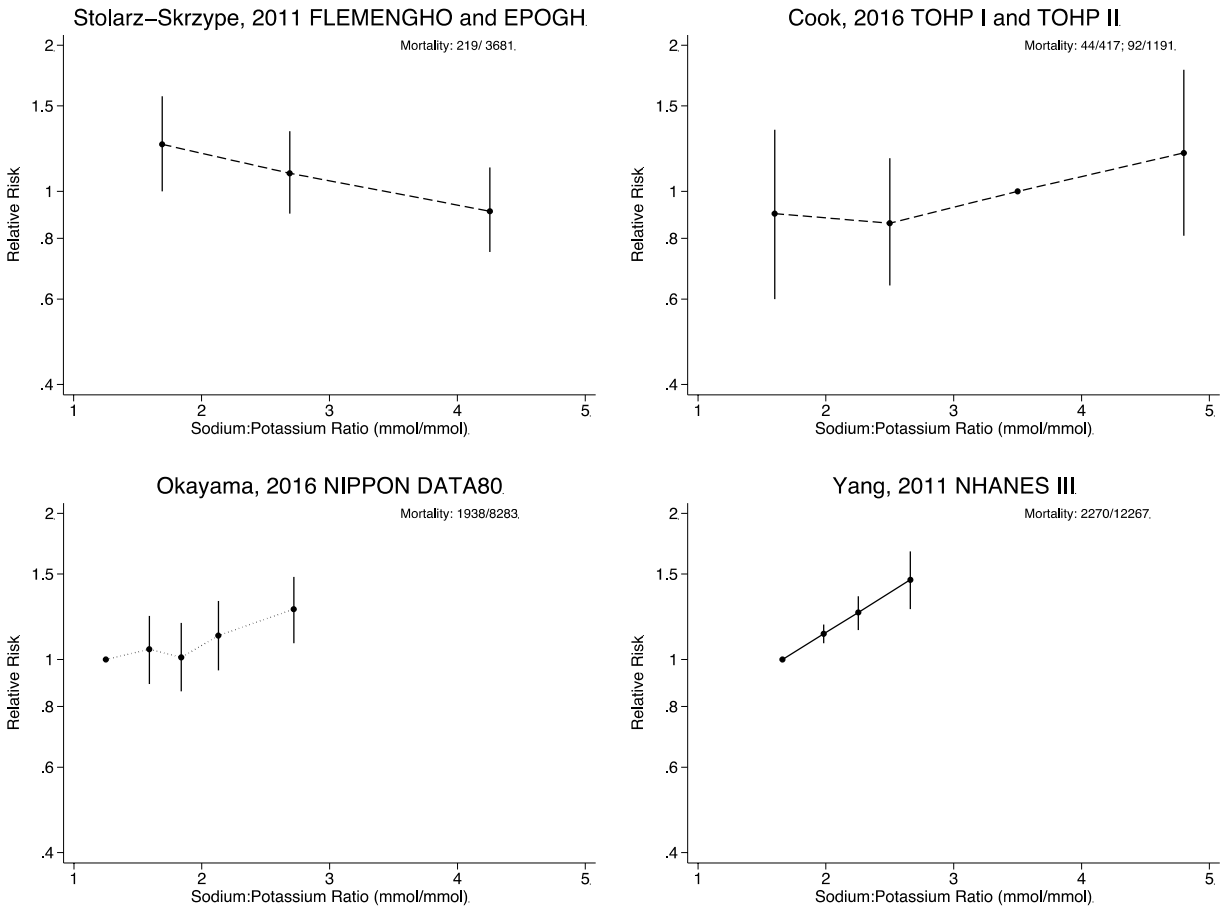


Figure H3. Categorical analysis of the association between levels of sodium to potassium ratio and total mortality outcome in generally healthy populations



CVD Mortality Outcome

Figure H4. Categorical analysis of the association between urinary or dietary sodium levels and CVD mortality outcome in generally healthy populations

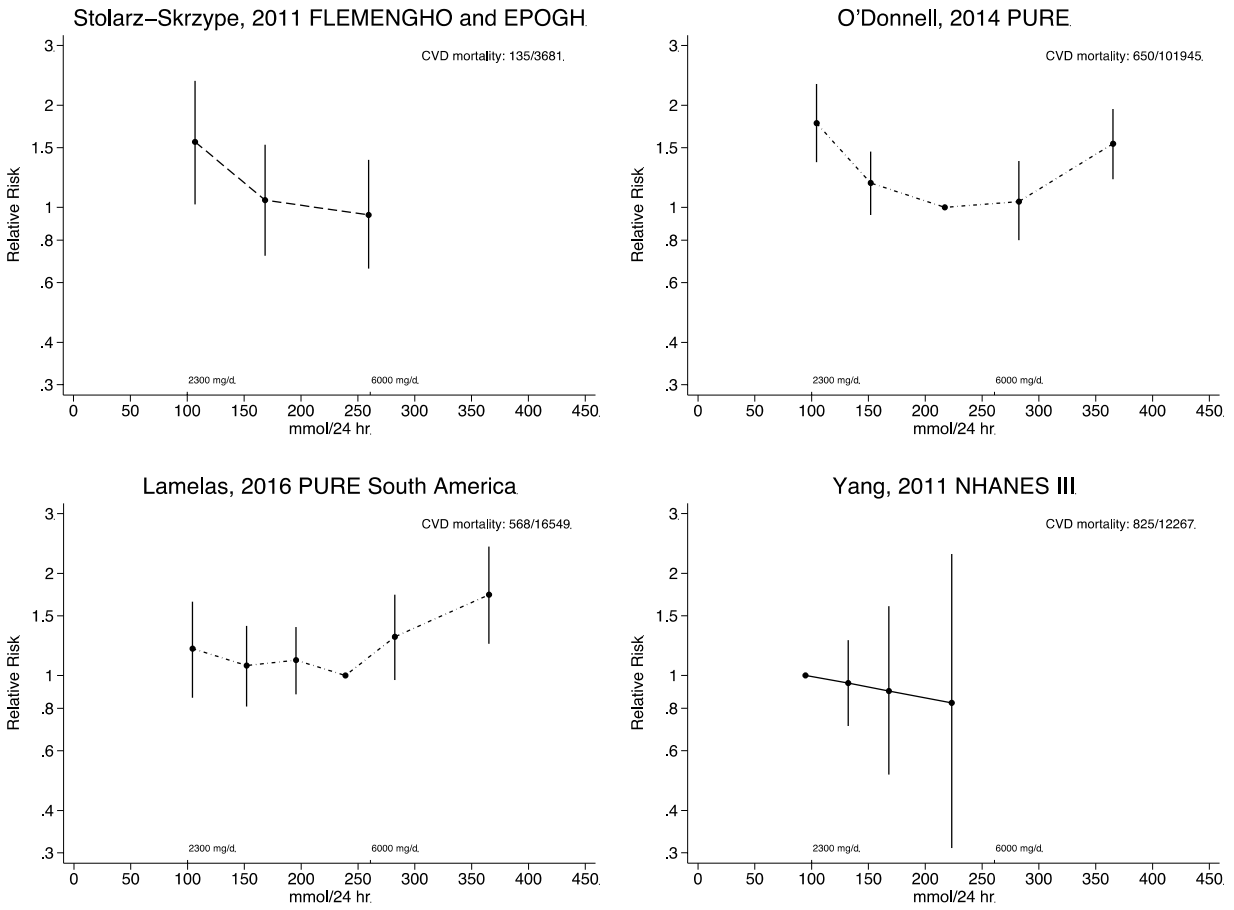
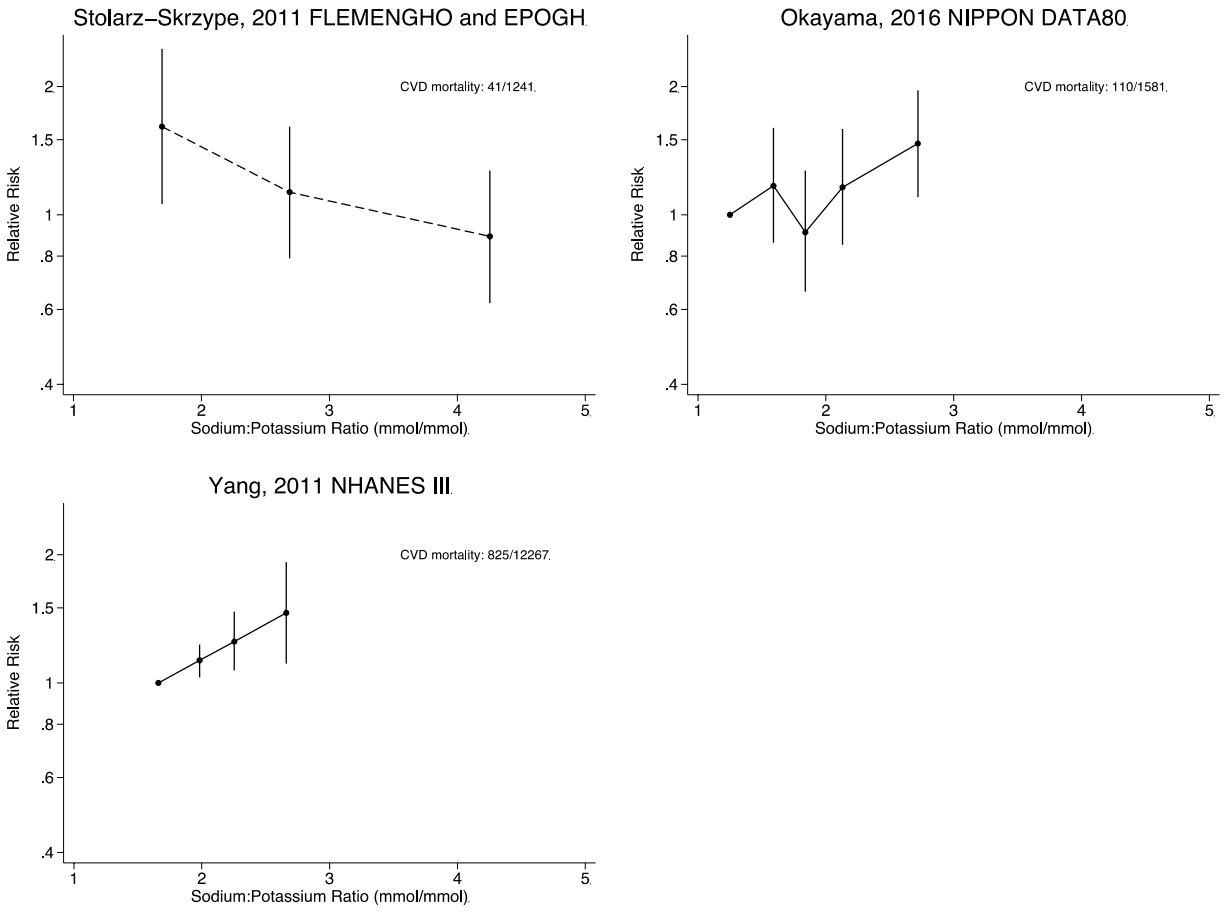
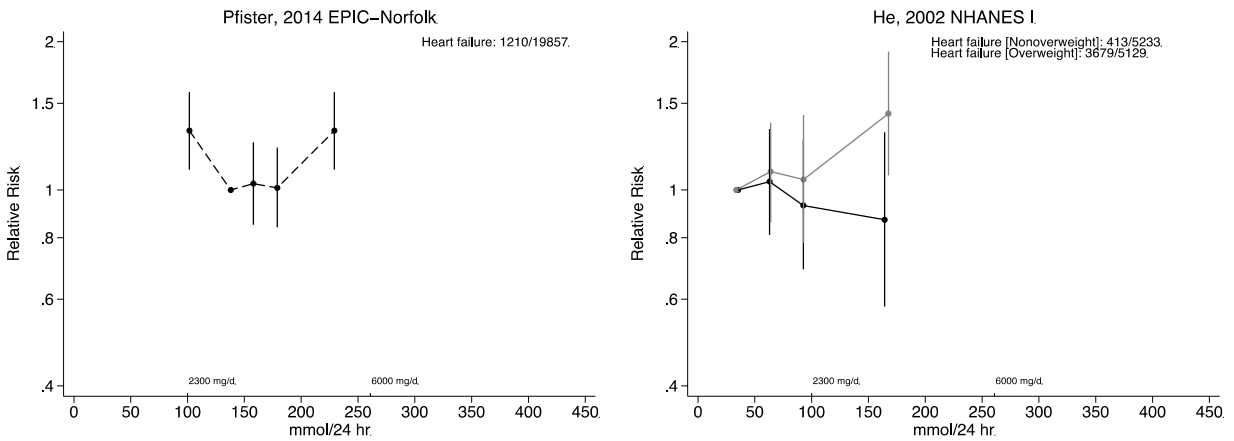


Figure H5. Categorical analysis of the association between sodium levels and CVD mortality outcome in generally healthy populations



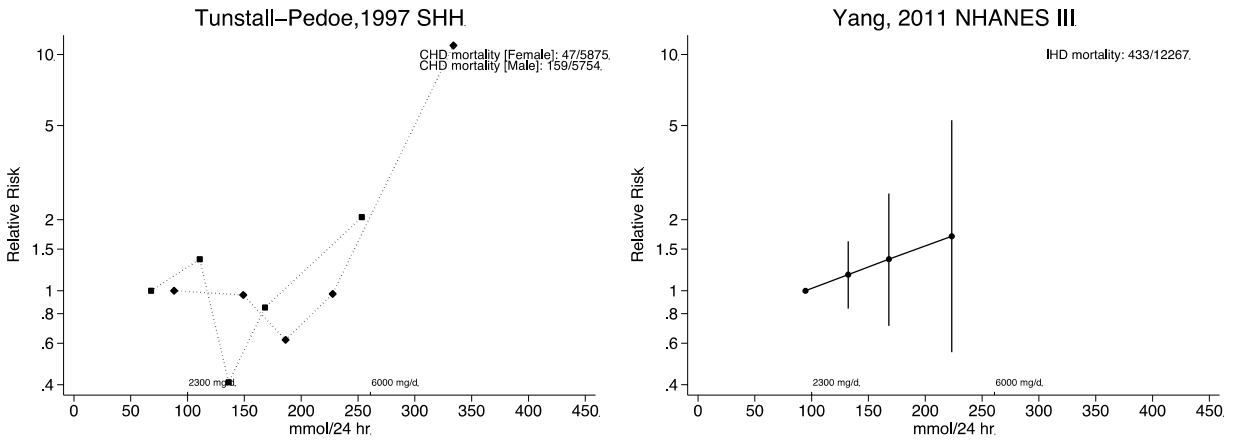
Other CVD Outcomes

Figure H6. Categorical analysis of the association between urinary or dietary sodium levels and heart failure outcome in generally healthy populations



Coronary Heart Disease Mortality

Figure H7. Categorical analysis of the association between urinary or dietary sodium levels and CHD mortality outcome in generally healthy populations



Stroke

Figure H8. Categorical analysis of the association between urinary sodium levels and stroke outcome in generally healthy populations

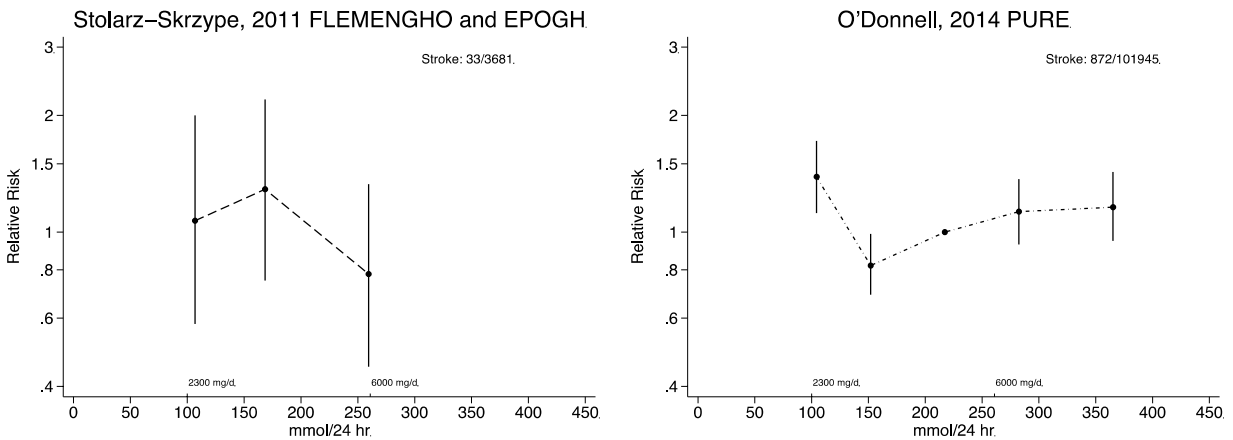
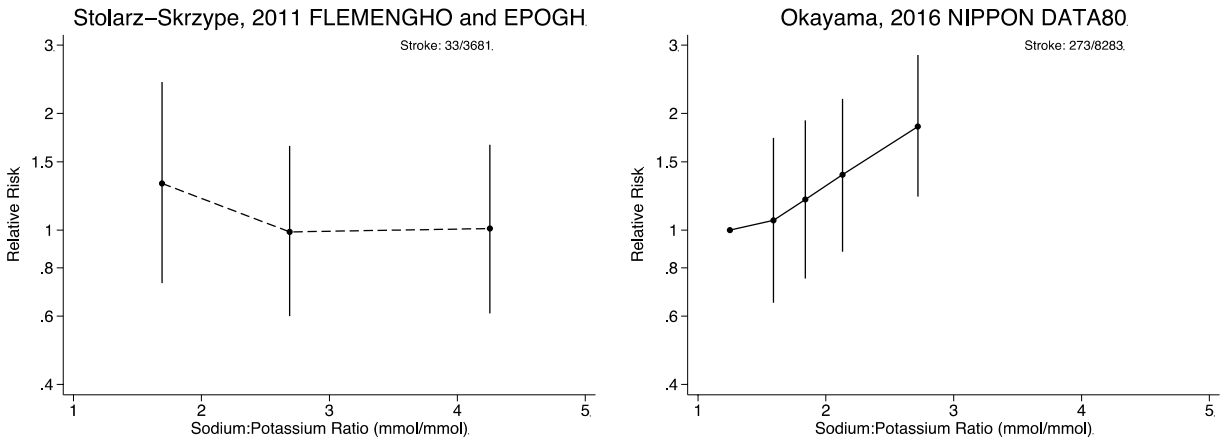
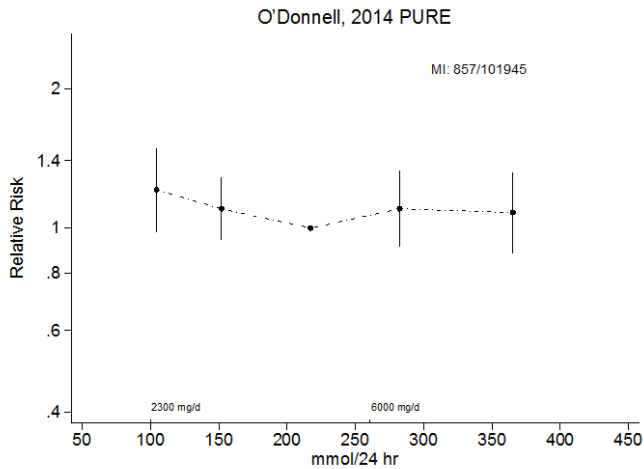


Figure H9. Categorical analysis of the association between levels of sodium to potassium ratio and stroke outcome in generally healthy populations



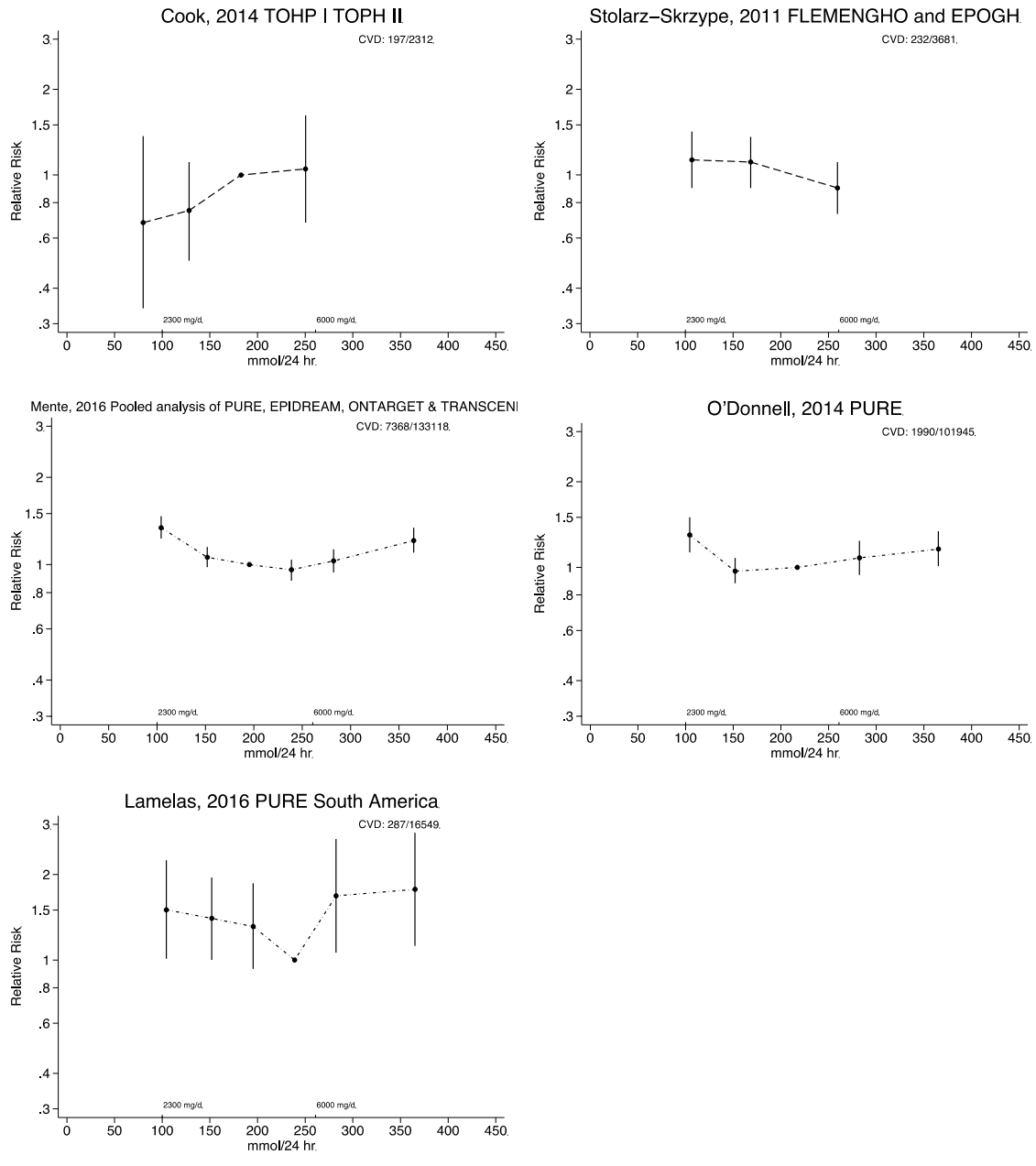
Myocardial Infarction

Figure H10. Categorical analysis of the association between urinary sodium levels and MI outcome in generally healthy populations



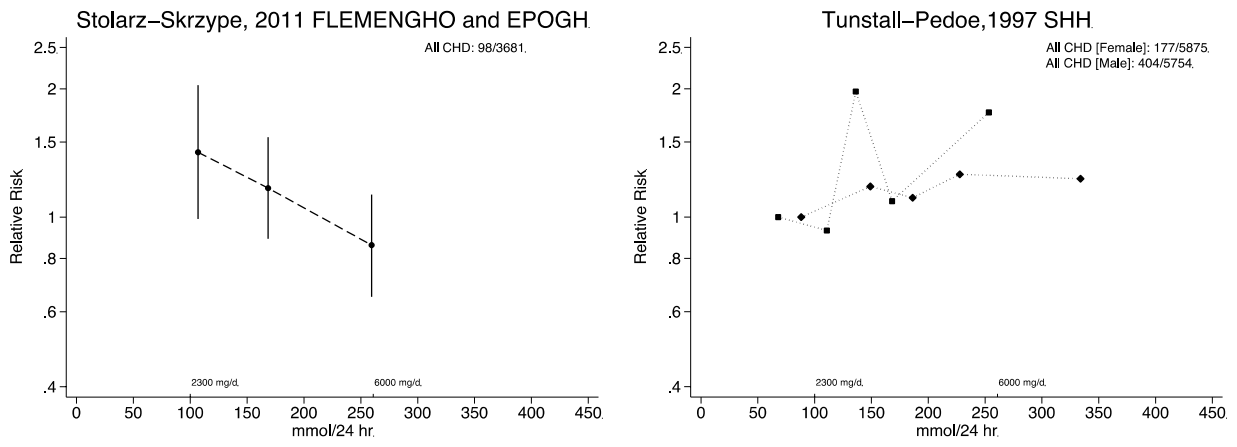
Combined CVD Morbidity and Mortality

Figure H11. Categorical analysis of the association between urinary sodium levels and combined CVD morbidity and mortality outcome in generally healthy populations



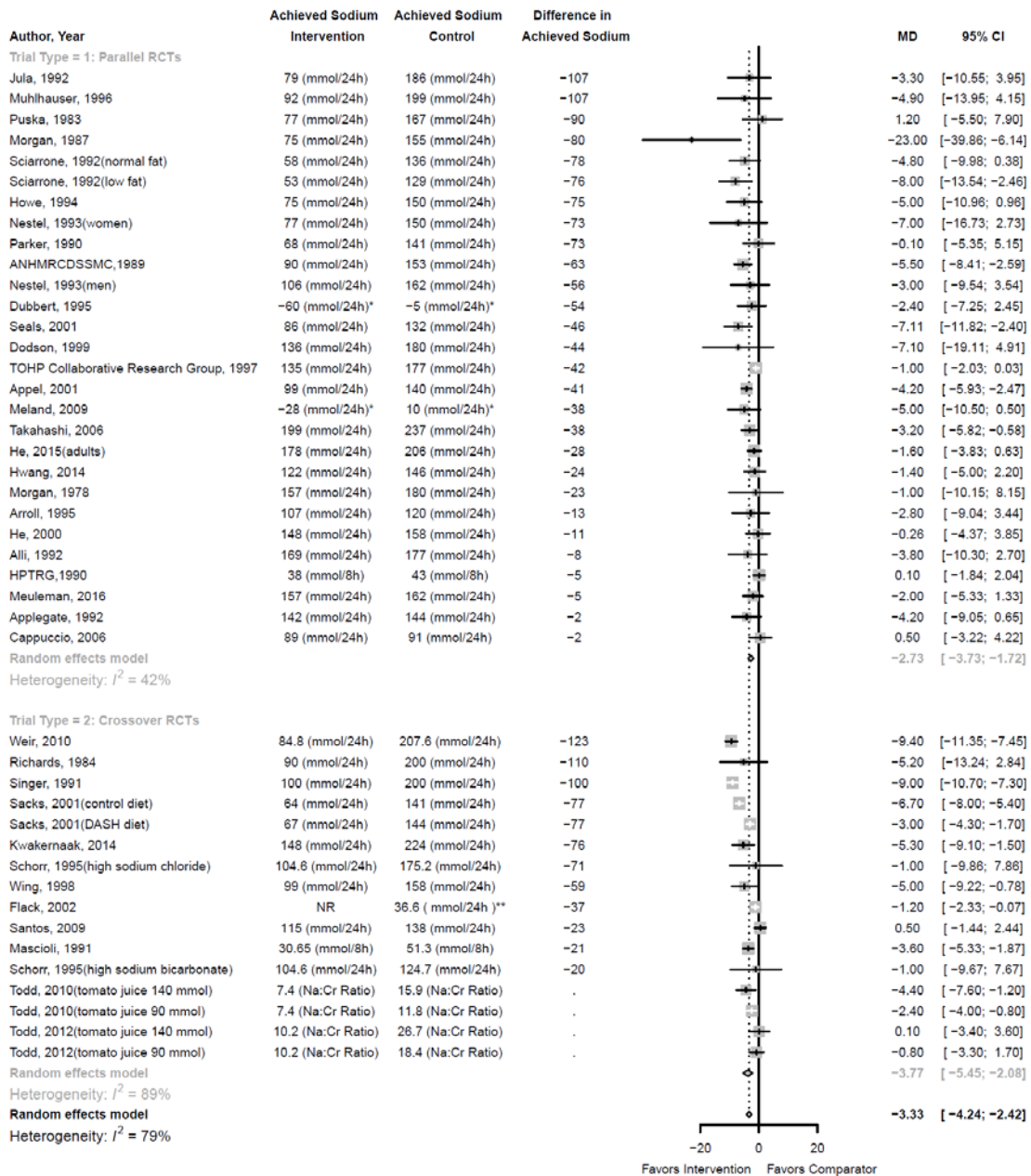
Combined CHD Morbidity and Mortality

Figure H12. Categorical analysis of the association between urinary sodium levels and combined CHD morbidity and mortality outcome in generally healthy populations



Appendix I. Sensitivity Analyses Removing High and Unclear Risk of Bias Studies

Figure I1. KQ1. Sensitivity analysis for systolic blood pressure in adults



* change from baseline

** difference between intervention and control

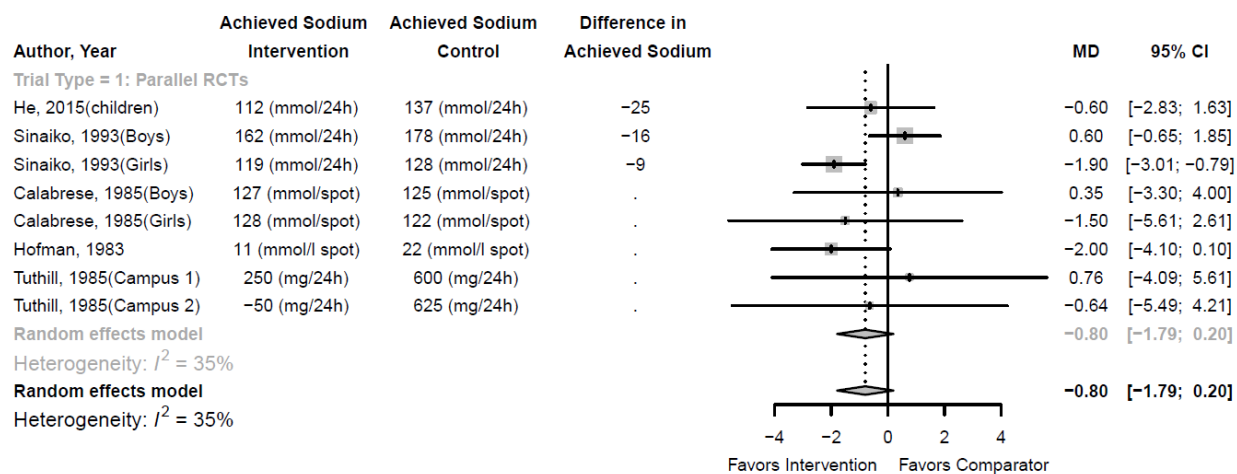
ANHMRCDSMCMC=Australian National Health and Medical Research Council Dietary Salt Study Management Committee

HPTRG=Hypertension Prevention Trial Research Group

Studies dropped from figure I1:

Author, year	Overall ROB
Nakano, 2016	High risk
Morikawa, 2011	High risk
Silman, 1983	Unclear
Beard, 1982	High
Bulpitt, 1984	Unclear
Nowson, 1988	Unclear
Xie, 1998	Unclear

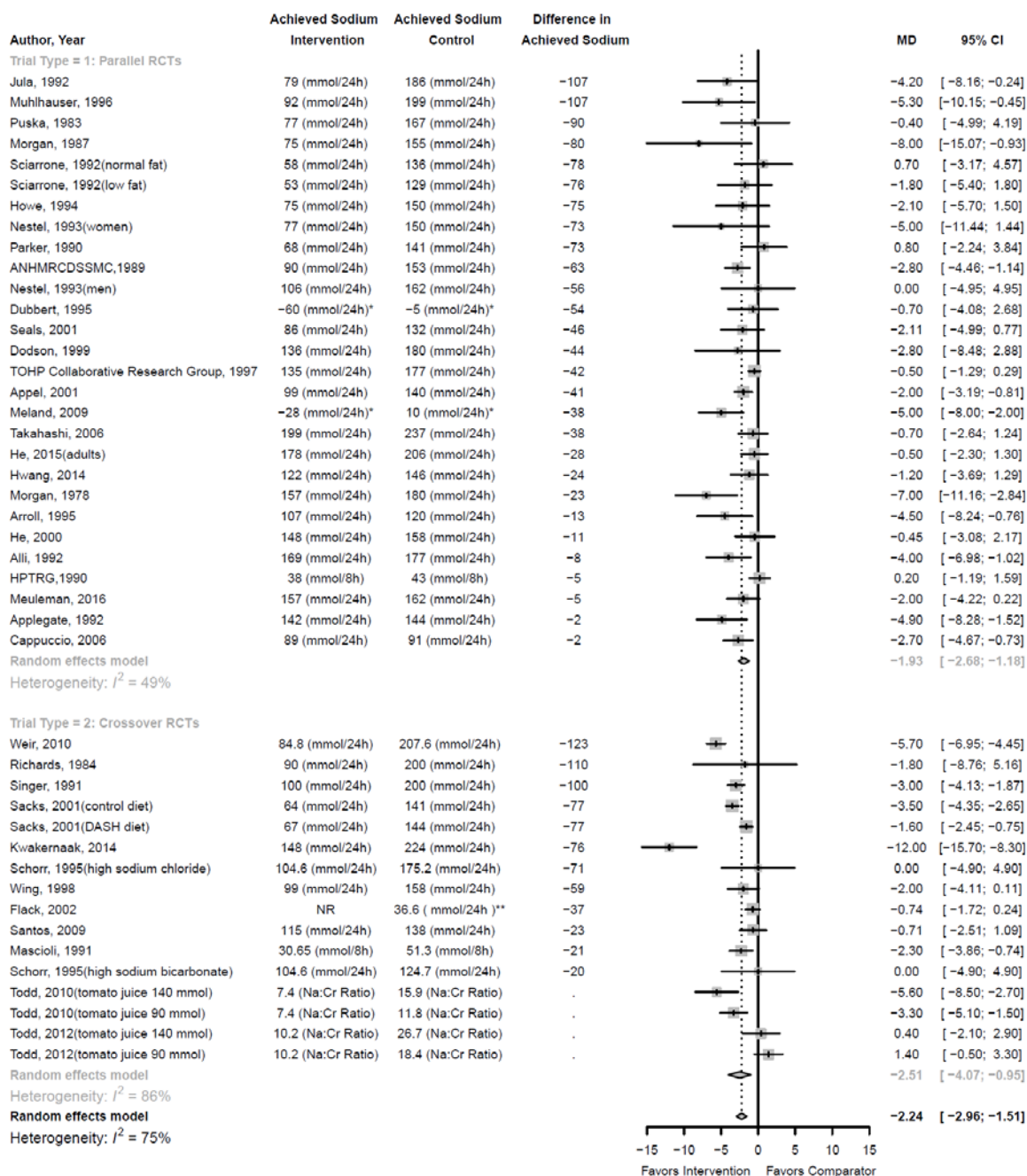
Figure I2. KQ1. Sensitivity analysis for systolic blood pressure in children



Studies dropped from I2:

Author, year	Overall ROB
Miller, 1988	Unclear
Gillum, 1981	Unclear
Pomeranz, 2002	Unclear

Figure I3. KQ1. Sensitivity analysis for diastolic blood pressure in adults



* change from baseline

** difference between intervention and control

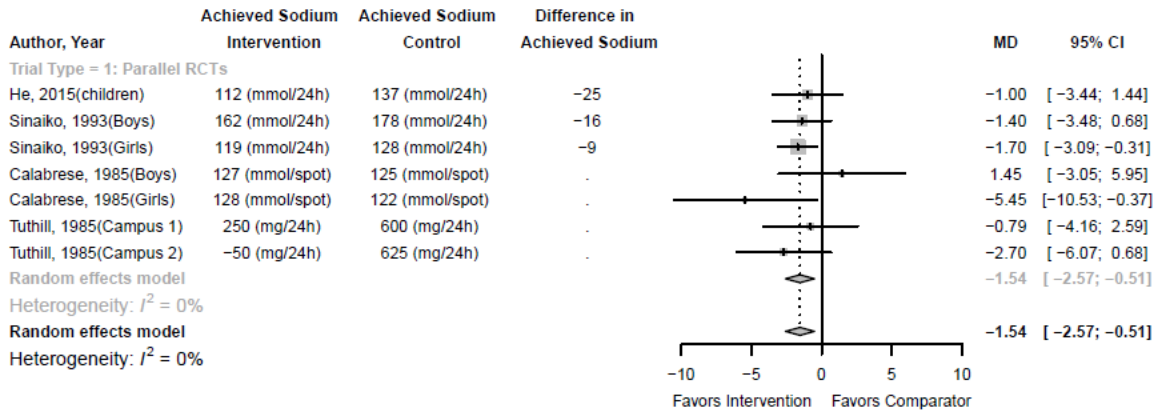
ANHMRCDSMC=Australian National Health and Medical Research Council Dietary Salt Study Management Committee

HPTRG=Hypertension Prevention Trial Research Group

Studies dropped from I3

Author, year	Overall ROB
Nakano, 2016	High risk
Morikawa, 2011	High risk
Silman, 1983	Unclear
Morgan, 1981(female, DBP<105 mmHg)	Unclear
Morgan, 1981(male, DBP<105 mmHg)	Unclear
Beard, 1982	High
Bulpitt, 1984	Unclear
Nowson, 1988	Unclear
Xie, 1998	Unclear

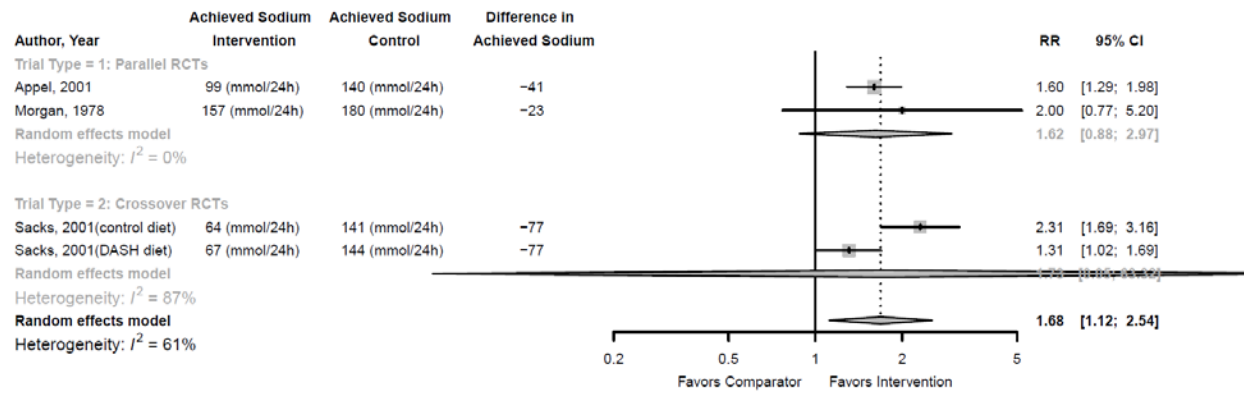
Figure I4. KQ1. Sensitivity analysis for diastolic blood pressure in children



Studies dropped from I4

Author, year	Overall ROB
Miller, 1988	Unclear
Gillum, 1981	Unclear
Pomeranz, 2002	Unclear

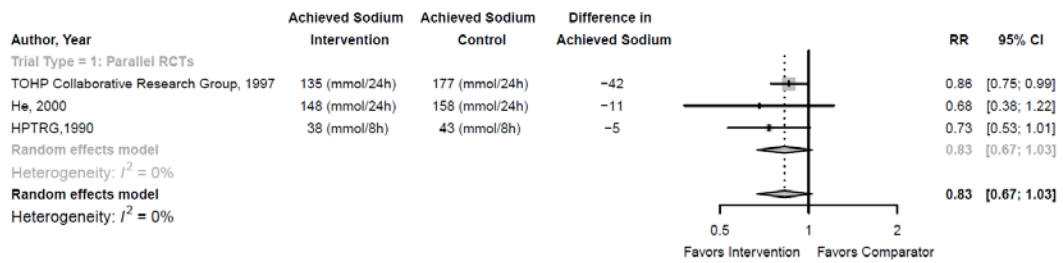
Figure I5. KQ1. Sensitivity analysis for achievement of blood pressure control goal



Studies dropped from figure I5:

author	year	id	Overall risk of bias
323	Beard, 1982	6821	High
327	Bulpitt, 1984	6822	Unclear
466	Xie, 1998	12380	Unclear

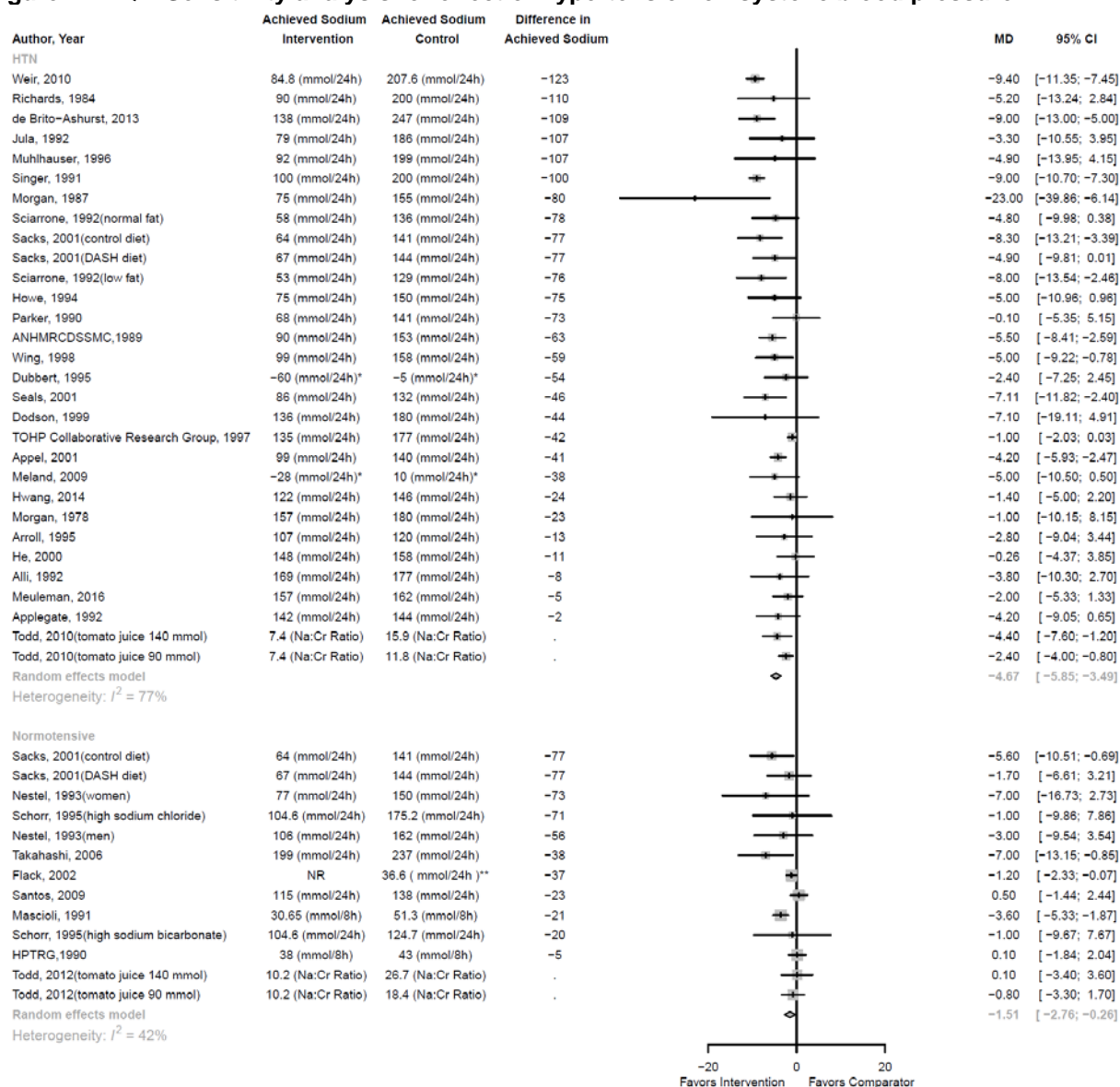
Figure I6. KQ1. Sensitivity analysis for hypertension incident



HPTRG=Hypertension Prevention Trial Research Group

Studies dropped in I6:
None

Figure I7. KQ1. Sensitivity analysis for effect of hypertension on systolic blood pressure

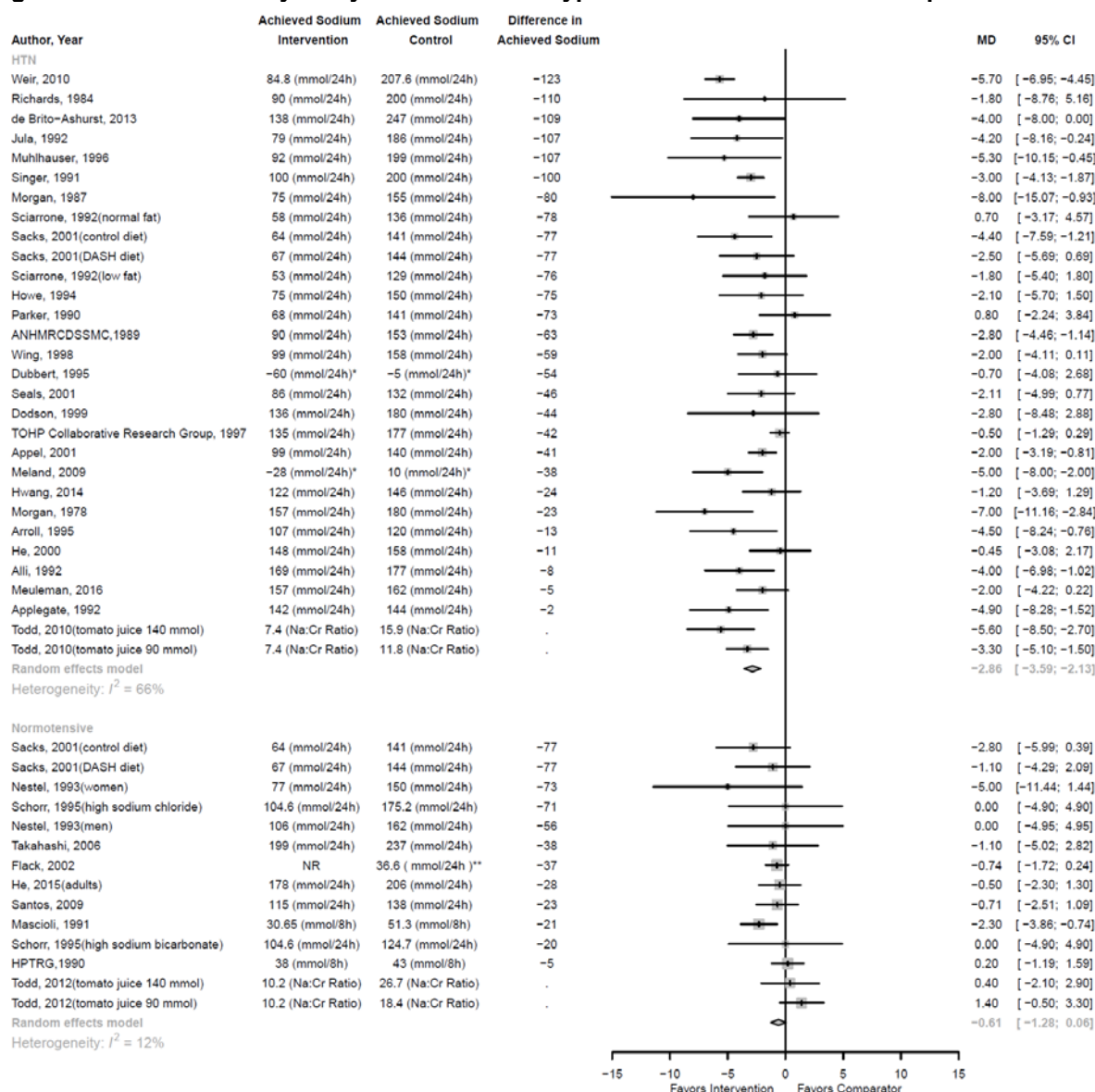


* change from baseline
 ANHMRCDSMCM=Australian National Health and Medical Research Council Dietary Salt Study Management Committee
 HPTRG=Hypertension Prevention Trial Research Group

Studies dropped from figure I7:

Author, year	Overall ROB
Nakano, 2016	High risk
Morikawa, 2011	High risk
Pinjuh Markota, 2015	Unclear
Silman, 1983	Unclear
Beard, 1982	High
Bulpitt, 1984	Unclear
Redon-Mas, 1993	Unclear
Nowson, 1988	Unclear
Xie, 1998 12380	Unclear

Figure I8. KQ1. Sensitivity analysis for effect of hypertension on diastolic blood pressure

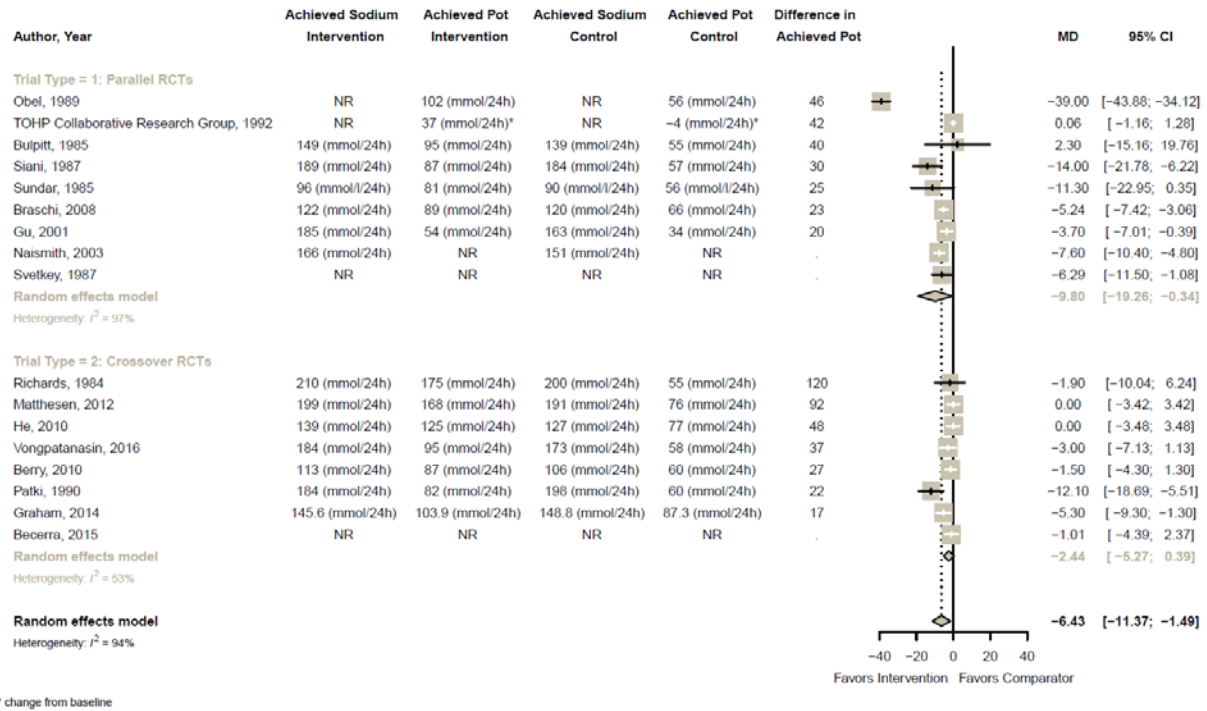


* change from baseline
 ANHMRCDSMCM-Australian National Health and Medical Research Council Dietary Salt Study Management Committee
 HPTRG-Hypertension Prevention Trial Research Group

Studies dropped from figure I8:

Author, year	Overall ROB
Nakano, 2016	High risk
Morikawa, 2011	High risk
Pinjuh Markota, 2015	Unclear
Silman, 1983	Unclear
Morgan, 1981(female, DBP<105 mmHg)	Unclear
Morgan, 1981(male, DBP<105 mmHg)	Unclear
Beard, 1982	High
Bulpitt, 1984	Unclear
Redon-Mas, 1993	Unclear
Nowson, 1988	Unclear
Xie, 1998	Unclear

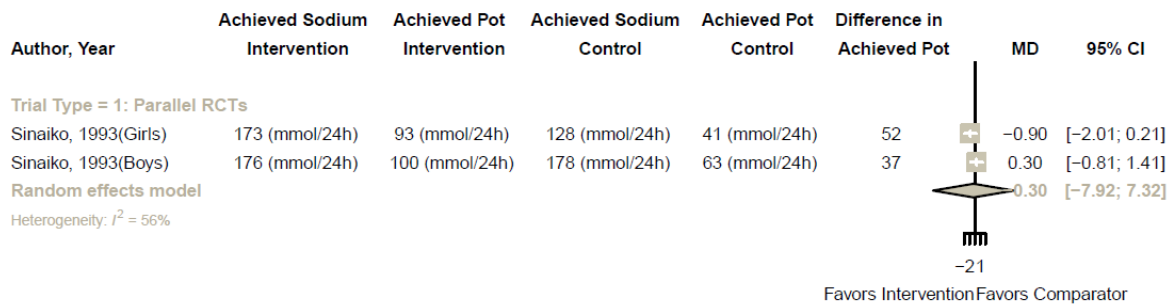
Figure I9. KQ5. Sensitivity analysis for systolic blood pressure in adults



Studies dropped in I9:

Author, year	Overall ROB
Rahimi, 2007	Unclear

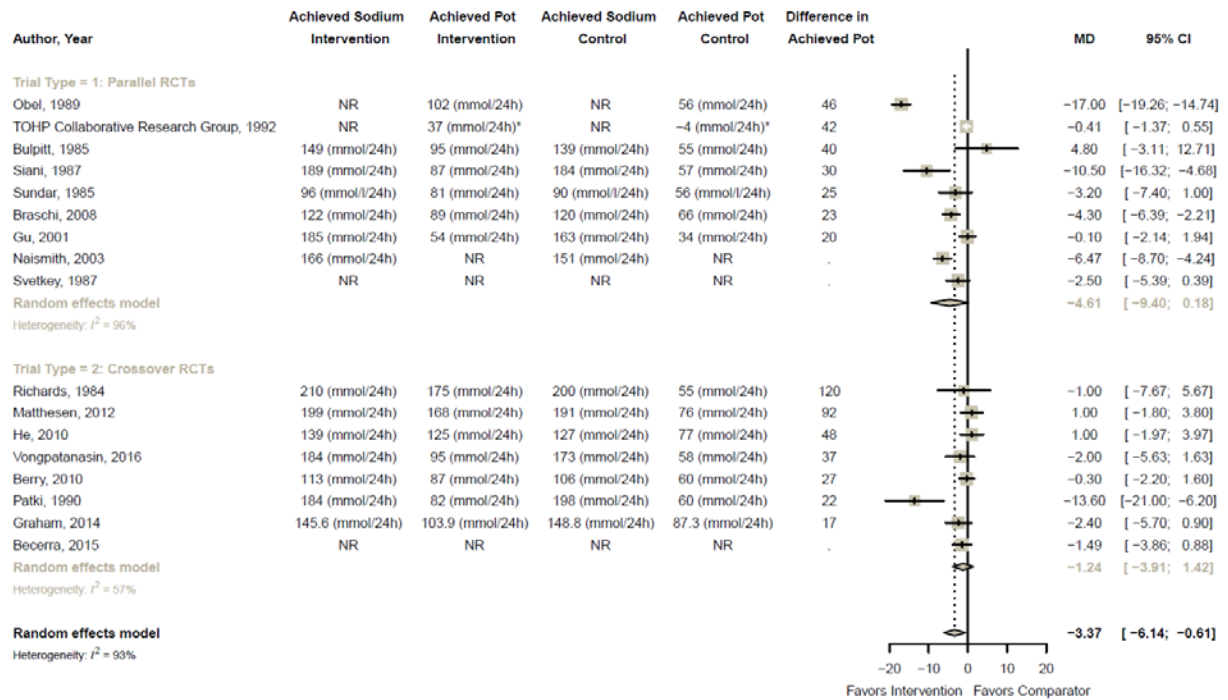
Figure I10. KQ5. Sensitivity analysis for systolic blood pressure in children



Studies dropped in I10:

None

Figure I11. KQ5. Sensitivity analysis for diastolic blood pressure in adults

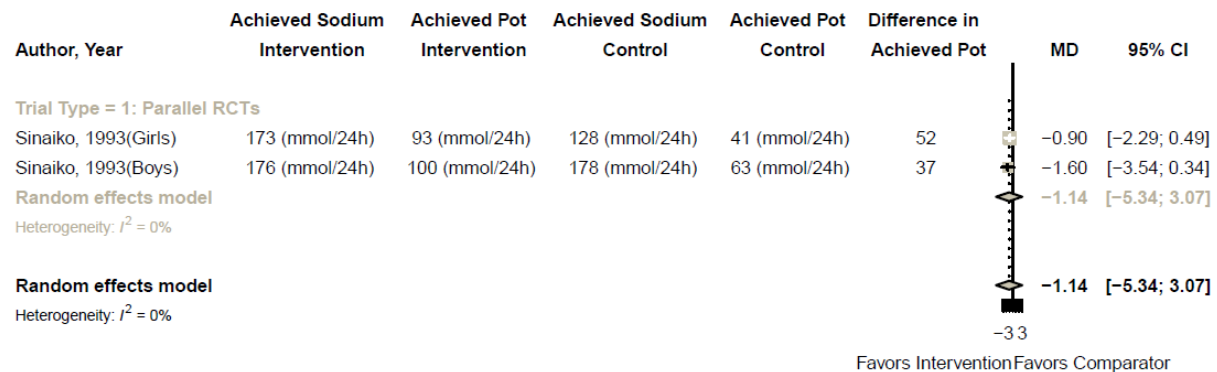


* change from baseline

Studies dropped in I11:

Author, year Overall ROB
Rahimi, 2007 Unclear

Figure I12. KQ5. Sensitivity analysis for diastolic blood pressure in children



Studies dropped in I10:

None