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Strenuous work in hot environments is associated with negative impacts on biomarkers of kidney function over the workday and over five months. Appropriate access to water, rest and shade during work offers relief from high levels of heat stress and reduces effects on kidney function.

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## Intervention to diminish dehydration and kidney damage among sugarcane workers

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**Objective** The aim of this study was to assess the potential to reduce kidney function damage during the implementation of a water, rest, shade (WRS) and efficiency intervention program among sugarcane workers.

**Methods** A WRS intervention program adapted from the US Occupational Safety and Health Administration (OSHA) coupled with an efficiency program began two months into the 5-month harvest. One of the two groups of workers studied was provided with portable water reservoirs, mobile shaded tents, and scheduled rest periods. Health data (anthropometric and questionnaires), blood, and urine were collected at baseline and at three subsequent times over the course of the harvest. Daily wet bulb globe temperatures (WBGT) were recorded.

**Results** Across a working day there were changes in biomarkers indicating dehydration (urine osmolality) and serum albumin and reduced estimated glomerular filtration rate (eGFR). Cross-shift eGFR decrease was present in both groups; -10.5 mL/min/1.73m<sup>2</sup> [95% confidence interval (95% CI) -11.8– -9.1], but smaller for the intervention group after receiving the program. Decreased eGFR over the 5-month harvest was seen in both groups: in the one receiving the intervention -3.4 mL/min/1.73m<sup>2</sup> (95% CI -5.5– -1.3) and in the other -5.3 (95% CI -7.9– -2.7). The decrease appeared to halt after the introduction of the intervention in the group receiving the program.

**Conclusion** A WRS and efficiency intervention program was successfully introduced for workers in sugarcane fields and appears to reduce the impact of heat stress on acute and over-harvest biomarkers of kidney function. Further research is needed to determine whether biomarker changes predict reduced risk of chronic kidney disease in this type of work.

**Key terms** chronic; chronic kidney disease; CKD; El Salvador; epidemiology; heat; heat exposure; heat stress; Mesoamerican nephropathy.

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An epidemic of chronic kidney disease (CKD) of unknown etiology (CKDu) unrelated to known risk factors such as diabetes and hypertension is dramatically impacting rural communities throughout Central America (1). El Salvador has been identified as one of the hotspots for this epidemic, also called Mesoamerican nephropathy (MeN) (1).

One essential risk factor for MeN is believed to be chronic heat stress and dehydration from strenuous work in hot climates (1–3), conditions characteristic of sugarcane cutting (4–6). A previous report from this study documented that cutters spent almost 80% of their working hours in conditions above 26°C wet bulb globe temperature (WBGT), exceeding permissible heat exposure threshold limits for continuous heavy labor for the majority of their workday (5, 7). We have also reported that sugarcane cutting is repetitive high-intensity work, where workers spend over half of their work day at or above 50% of their maximal heart rate (6).

Several studies suggest a causal association between MeN and chronic heat stress and dehydration (8–13) and experimental data have shown that repeated dehydration can induce CKD in mice (14, 15). Heat exposure, strenuous exercise and dehydration pose a significant challenge to the cardiovascular system, and the transport of oxygen to exercising muscles and vital organs, such as the kidney (16). It has also been shown that muscles under these conditions release myoglobin that can produce acute kidney damage, especially in combination with dehydration (17–19). In addition, systems regulating water and electrolyte balance become overwhelmed, resulting in urine acidification, concentration, and uricosuria (15, 20). Eventually, with repeated subclinical kidney injury, CKD may evolve (21). Although other causal factors have been proposed to have a role in the MeN epidemic [ie, pesticides (22, 23), nephrotoxic medication, alcohol nonsteroidal anti-inflammatory drugs (NSAID) etc] to date none have been shown to be a major cause of MeN (24). The known detrimental effect of heat strain and dehydration on work performance (25, 26) plus the current causal evidence relating MeN, chronic heat stress, and dehydration demands attention.

The intervention program was designed to examine the efficacy and effectiveness of a two-component intervention program in an extreme environment among sugarcane cutters associated with a mill in El Salvador. The first component was a water, rest, shade (WRS) program adapted from the US Occupational Safety and Health Administration (OSHA) guidelines for work in hot environments (7). The second component was an approach to efficiency improvements based on expert advice from Australian consultants familiar with sugarcane cultivation.

Previously we demonstrated the intervention was successful in reducing the immediate impacts of excess heat exposure over a harvest season (5). In this paper,

we assess the intervention's potential to reduce effects on kidney function.

## Methods

For a detailed description of study context, study population, data collection and intervention perspectives see Bodin et al (5).

### Study population

Briefly, the study includes two cane cutting groups working in relatively distinct climates – inland (~450 m altitude, cooler climate) and coastland (sea level, hotter climate) – chosen because other studies have demonstrated higher prevalence of kidney dysfunction in hotter environments at sea level (8, 27, 28). Both groups participated in a previous project (8) and the workers and their leaders were willing to participate again. All the inland group of cutters were invited to participate (N=60). A similar number of workers in the coastland group (N=57) were invited although the total group was much larger (~300). The workers invited to participate were those from two of five subgroups, selected by the subcontractor because each regularly traveled to the fields in a single truck.

All those invited participated at baseline. Despite transient reluctance among coastland workers to participate, we know of no workers who declined participation at the end of the harvest. However, there was a reduction in cohort size for other reasons. In the inland group, 4 people had to be excluded due to questions about identity. A further 6 people never showed up again during the harvest and likely were not cutting cane during the harvest. Of the 57 participants at baseline in the coastland group, 15 never showed up again. We believe they also were not workers.

Finally, to study effects over the course of the harvest, we chose to include only the workers that participated at both baseline and the end of the harvest. Of the 50 inland workers participating more than once, 40 participated both at baseline and the final visit. Of the 42 coastland workers participating more than once, 40 participated both at baseline and the final visit. The 12 workers not seen at end of harvest were all men, slightly younger and compared with the included cutters, had less work experience in cane-cutting (median age: 27 versus 32 years; number of harvests worked: 4 versus 6).

### The intervention

Details of the intervention program are provided in Bodin et al (5). In short, the WRS intervention provided

each cutter with a Camelbak 3-liter water backpack, easy access to a 40 L water thermos of water for refills, a mobile shade tent kept nearby the workers as they progressed through each day's cutting assignment, and formally scheduled 10–15-minute rests, every 1–1.5 hours.

The efficiency program provided each worker with a one-pound-lighter machete that had an angled curved blade and a more ergonomic handle. The field cutting protocol was revised to reduce the width of the individual worker's cutting area decreasing lateral movement and hence increasing efficiency.

These two components were provided to the inland group starting in January 2015, two months into the 5-month harvest season. The original plan was to initiate the same intervention in the coastland group but security concerns along with low participation at the second data collection led to delaying their intervention until the following year.

### Environmental and productivity measurements

Wet bulb globe temperature (WBGT) was measured continuously, using a QUESTemp 34 (3M), during each workday in the cane fields, from November 28, 2014 until the end of the harvest April 17, 2015 (5).

Productivity was assessed using tons cut/individual as recorded daily by the mill exclusively for the inland group.

### Physical exam and questionnaire

At baseline, all participants' weight and height was measured on a combined digital scale with a mechanical height rod (SECA electronic AD 769, Seca, Birmingham, UK) and body mass index (BMI) was calculated. Blood pressure and heart rate were measured once using an automatic blood pressure gauge (Omron Healthcare) after participants had been seated and resting for a minimum of five minutes.

The baseline interview survey (~45 minutes) included questions regarding (i) sociodemographic data; (ii) past and present work history including exposure to occupational and environmental hazards focusing on heat, cane-burning and pesticides; (iii) use of tobacco, alcohol, and recreational drugs; (iv) general health, history of hypertension and diabetes as well as current physical pains; (v) medication used for reported conditions as well as use of other known nephrotoxic drugs; (vi) family history of CKD and (vii) past and present heat stress and dehydration symptoms.

### Blood, serum, and urine measurements

Baseline blood and urine samples were collected one morning two weeks before the start of the harvest sea-

son. Pre- and post-shift blood and urine samples were thereafter collected on three occasions during the harvest: the second week of January right before the start of the intervention, in mid-February (inland only) and during the final week of the harvest in the beginning of April. At the two visits to the inland group in January and February, 35 and 37 of the 40 workers in our study population participated, respectively. At the January visit to the coastal group, only 11 of the 42 workers participated.

Venous blood was drawn, serum was separated by centrifugation in the field, transported on ice to a city laboratory, and then transferred to a cryo-safe tube. This tube was frozen and sent to Sweden for further analyses. To report creatinine results to individuals in a timely manner, a separate tube was sent to a local laboratory for analysis of serum creatinine.

The specific biomarkers of kidney function, dehydration, and muscle tissue breakdown selected for this study's purposes were serum albumin, sodium, chloride, creatine phosphokinase, creatinine, uric acid, and urea nitrogen. Details of handling and analysis of samples are in the supplementary materials ([www.sjweh.fi/index.php?page=data-repository](http://www.sjweh.fi/index.php?page=data-repository)). Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation (29).

Basic urine analysis was done in the field: dipstick (glucose, pH and specific gravity) and osmolality by refractometry.

### Descriptive analysis

Counts and percentages of sociodemographic, health, and work characteristics are provided in table 1A and in further detail in the supplementary materials (table A). Absolute values of the variables in table 1B as well as

**Table 1A.** Sociodemographic, health and work characteristics at baseline for participants who were seen at both baseline and end of harvest and the subset with largest cross-harvest estimated glomerular filtration rate (eGFR) changes. [CKD=chronic kidney disease]

	Inland (N=40)		Coastland (N=40)		eGFR droppers <sup>a</sup> (N=20)		Both groups (N=80)	
	N	%	N	%	N	%	N	%
Sex								
Male	39	98	28	70	15	75	67	84
Female	1	3	12	30	5	25	13	16
Family history of CKD	4	10	6	15	3	15	10	13
Doctor diagnosed								
Elevated blood sugar	2	5	0		0		2	3
Kidney stones	1	3	0		1	5	1	1
High blood pressure	4	10	0		1	5	4	5

<sup>a</sup> Quartile with largest negative eGFR changes during the harvest (inland 8; coastland 13).

**Table 1B.** Sociodemographic, health and work characteristics at baseline for participants who were seen at both baseline and end of harvest and for the subset with largest cross-harvest estimated glomerular filtration rate (eGFR) changes. [BMI=body mass index; BP=blood pressure; IQR=inter-quartile range]

	Inland		Coastland		eGFR droppers <sup>a</sup>		Both groups	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (years)								
Male	32	14	33	10	37	7	32	13
Female <sup>b</sup>			33	14	31	16	31	15
Education (years)	7	5	3	5	4	6	6	7
Number of harvests worked	4	8	7	5	5	6	6	7
BMI (kg/m <sup>2</sup> )	24	5	24	5	26	5	24	5
BP (mmHg)								
Systolic	128	14	121	16	122	16	123	16
Diastolic	74	15	71	11	72	11	72	14
eGFR (mL/min/1.73 m <sup>2</sup> )								
Baseline	119	17	108	30	104	35	114	24
Final visit	116	19	100	37	88	40	108	30

<sup>a</sup> Quartile with largest negative eGFR changes during the harvest (inland 8; coastland 13).

<sup>b</sup> Only one female participant in the Inland group – data not presented for privacy.

all biomarkers measured were non-normally distributed (except for BMI). Thus, median values and inter-quartile ranges are presented. Cross-shift and cross-harvest differences were normally distributed. Therefore, we estimated mean relative change in eGFR over the course of the day and over the harvest. We used paired t-tests when analyzing differences within groups and unpaired t-test when comparing the two groups.

Acute *cross-shift* change in serum creatinine was assessed according to clinical criteria for acute kidney injury (AKI): an increase of 26 µmol/L within 48 hours or an increase of 1.5 to 1.9 times the reference value (30). These changes were examined on available test days: three days for the inland group (January 7, February 18 and April 8) and two days for the coastland group (January 9 and April 10). *Cross-harvest* kidney function responses were assessed using baseline measures of eGFR compared end-of-harvest pre-shift eGFR and stratified according to eGFR values for CKD stages (30).

### Statistical modelling

We used multivariate linear regression models to assess the impact of the intervention for both cross-shift and cross-harvest analyses. To take the potential intra-subject correlation into account in the cross-shift analysis, we used generalized estimating equations (GEE) with an exchangeable working correlation matrix. P-values <0.05 were considered statistically significant. All statistical analyses were performed in Stata version 13 (StataCorp, College Station, TX, USA).

The *cross-shift* analysis was performed only on the

inland group. The coastland group did not have adequate participation or production data. The dependent variable in the analysis was the relative change in eGFR between pre- and post-shift (percentage of am value). The independent variables were: age, hypertension, pre-shift eGFR value, production (in tons), same day maximum WBGT and a dummy variable indicating pre- or post-intervention. Other known CKD risk factors were not included (only two had elevated blood sugar and NSAID information was not considered sufficiently reliable to use as a model variable). Additional sensitivity analysis included WBGT values for one and for two days prior to the sampling day.

In the *cross-harvest* analysis, the dependent variable was the relative change in eGFR (in percentage of baseline value). The independent variables were: time (months) since intervention, age at baseline, and an interaction between time since intervention and a post-intervention indicator. Without production data for the coastland group, comparisons between the groups were adjusted in regression models only for age, with additional sensitivity analysis for sex and accumulated hours working above WBGT of 30°C or 32°C. Hypertension was not included due to model instability with additional variables. In addition, those with the largest eGFR cross-harvest changes (“eGFR droppers”) did not have a different distribution of measured hypertension (tables 1A and 1B).

### Ethics statement

The National Ethics Committee for Clinical Research (Comité Nacional de Ética de Investigación de Salud) of El Salvador approved this study (OHRP IRB No. 0005660, FWA No. 00010986).

## Results

### Study population characteristics

Participants were primarily males, with a higher proportion in the inland group compared with the coastland group (98% versus 71%). Mean age was 33 and 35 years, respectively (range 18–63). Risk factors for CKD (report of physician diagnosed hypertension and elevated blood sugar) were uncommon. NSAID use, measured systolic pressure >140 mmHg, and reports of relatives with CKD were more common. However, participants in the quartile with largest negative eGFR changes (“eGFR droppers”) did not have a higher proportion of these variables (tables 1A and 1B).

Sixty percent in both groups reported less-than-good general health and a quarter of men were current smok-

ers. Alcohol consumption was more common among males and self-reported use of recreational drugs was negligible. Most of the participants had a work history in subsistence farming and some had also worked in heat-exposed jobs such as construction and cotton-picking. Only one had worked in the mining industry.

Self-reported use of agrochemicals (pesticides and fertilizers) was commonly reported at baseline as most were engaged in other types of agriculture off-season. Little use of these agents was reported during the harvest months. There was widespread use of painkillers, especially NSAID.

The inland group worked 8–10 hours, including a lunch break, while the coastland group only worked 4–5 hours, finishing before lunch. Production data, available from the mill for the inland group, showed daily average production at 5.1 tons/worker which increased by ~40% to 7.3 tons/worker after the intervention. As a result of the scheduled breaks for the intervention, the inland group rested 25% of their workday. Nonetheless, both groups worked a significant number of hours more than recommended by the OSHA guidelines for heat exposure (5).

### Cross-shift change in eGFR

Cross-shift changes in biomarkers were as expected in both groups (supplementary tables B-1 and B-2). The mean decrease of eGFR over the course of a working day was -10.5 mL/min/1.73m<sup>2</sup> (95% CI -11.8– -9.1).

In January, 3 of 34 inland workers met the AKI criteria, none met it in February, and 4 of 40 met it in April. The values for WBGT<sub>max</sub>, workday length and tons cut/individual were greater for the two of three days when workers met AKI criteria (both days WBGT<sub>max</sub> = 32.3°C·workday length = 9.75 hours, tons cut/individual = 5.8) versus the one day with no AKI (WBGT<sub>max</sub> = 30.5°C·workday length = 8 hours, tons cut/individual = 3.5).

Among coastland workers in January, 1 of 11 met AKI criteria, and 3 of 40 met it in April (January WBGT<sub>max</sub> = 28.7°C·workday length = 5.25; April WBGT<sub>max</sub> = 31.6°C, workday length = 4.25 hours). Production data were not available for the coastland group. None of the 11 workers who presented with AKI did so more than once.

In the inland group, biomarker cross-shift changes were somewhat smaller after the introduction of the intervention (supplementary table B1). In the multivariate estimation of relative cross-shift changes (table 2), we found the intervention led to a positive effect of the intervention leading to a smaller cross-shift decrease in eGFR and smaller increase in uric acid as compared to before the intervention. Models including sex, weight or BMI, and individual production relative to other workers did not affect relative cross-shift changes in biomarkers from those shown in table 2.

In the inland group, the multivariate models showed that higher individual production was associated with a larger cross-shift decrease in eGFR and increase in serum creatine phosphokinase (S-CPK), suggesting a relationship between higher effort and kidney effects as well as muscle tissue breakdown (table 2). Environmental heat exposure was associated with a larger increase in serum albumin, despite small differences in WBGT on the three study days.

### Cross-harvest change in eGFR

Most of the workforce in both groups had eGFR values within normal limits. The median eGFR was lower at baseline in the coastland group: 108 mL/min/1.73m<sup>2</sup> compared to 119 in the inland group (table 1B and supplementary table A). The mean change in pre-shift eGFR between baseline and the end of harvest was, compared with the coastland group, smaller for the inland group that received the intervention (table 3). Examining CKD stages, the Coastland group exceeded the Inland group

**Table 2.** Multivariate generalized estimating equation (GEE) models of biomarker cross-shift change<sup>a</sup> by selected independent variables (inland group only). **Bold values** indicate P<0.05. N=40 workers providing a total of 112 am and pm values [95% CI=95% confidence interval; eGFR=eGFR=estimated glomerular filtration rate; S-CPK=serum creatine phosphokinase; U-Osm=urine osmolality; WBGT=wet bulb globe temperatures]

	eGFR		S-CPK		U-Osm		S-Albumin		S-Uric acid	
	Δ <sup>b</sup>	95% CI	Δ	95% CI	Δ	95% CI	Δ	95% CI	Δ	95% CI
Age (per year increase)	<b>-0.2</b>	<b>-0.4–0.0</b>	0.1	-0.3–0.5	0.3	-0.7–1.3	-0.1	-0.1–0.0	<b>0.2</b>	<b>0.1–0.4</b>
Hypertension (systolic ambulatory blood pressure >140 mmHg - Yes/No)	0.0	-0.1–0.0	0.0	-0.1–0.1	<b>-0.2</b>	<b>-0.4–0.0</b>	0.0	0.0–0.0	0.0	0.0–0.0
Morning (am) value on sample day	0.0	-0.1–0.1	<b>-4.6</b>	<b>-7.7– -1.5</b>	<b>-0.4</b>	<b>-0.4– -0.3</b>	<b>-0.6</b>	<b>-1.0– -0.3</b>	<b>0.0</b>	<b>-0.1–0.0</b>
Post-intervention <sup>a</sup> (compared to pre-intervention – Yes/No)	<b>6.1</b>	<b>1.6–10.6</b>	0.8	-13.5–15.0	7.0	-20.5–34.6	-2.0	-4.8–0.9	<b>-7.3</b>	<b>-12.5– -2.1</b>
WBGT max on the given day (per degree C)	-1.0	-2.9–0.9	0.6	-5.4–6.7	-0.1	-6.5–6.3	<b>1.5</b>	<b>0.2–2.7</b>	0.1	-2.1–2.3
Individual production in tons	<b>-0.9</b>	<b>-1.3– -0.4</b>	<b>2.5</b>	<b>1.1–4.0</b>	3.2	-0.2–6.6	-0.2	-0.5–0.1	0.0	-0.5–0.5

<sup>a</sup> After January 20, 2015.

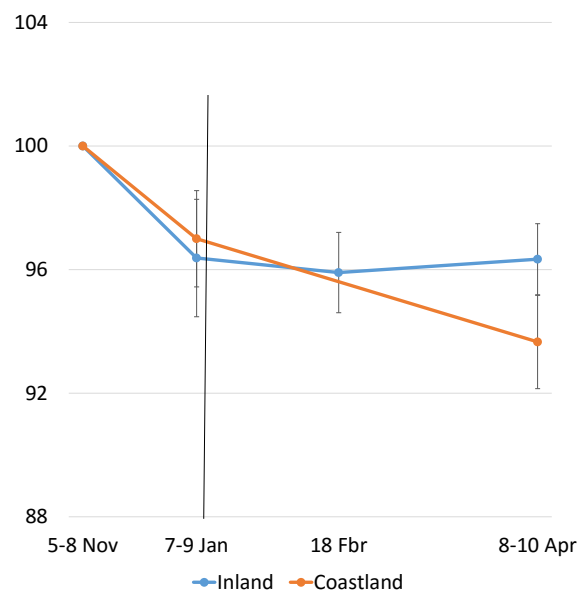
<sup>b</sup> Cross-shift change in percentage points calculated as [(pm value – am value)/am value]×100.

as well: more workers with eGFR <60 in the Coastland group at baseline (5 versus 2), as well as at the end of the harvest (7 versus 2) (table 3). The same individuals who had eGFR <60 at baseline remained below that level over the harvest with two more in the coastland group dropping <60 by the end of the harvest (overall, 5% in the inland and 18% in the coastland group). Although numbers were small, the decrease in eGFR over the harvest was larger among those whose baseline values began at <90 versus ≥90: inland 15.5 mL/min/1.73m<sup>2</sup> [standard deviation (SD) 9.5] versus 2.1 (SD 4.6); coastland 6.6 (SD 7.3) versus 4.7 (SD 8.5).

There was a trend towards a larger relative decrease in eGFR over the full harvest in the coastland group as shown, unadjusted, in figure 1. The inland group began on a similar slope as the coastland group, but, after the intervention, the slope flattened. There were no interme-

**Table 3.** Mean cross-harvest changes by group and stratified by clinical cut-off points for chronic kidney disease stages. [eGFR=estimated glomerular filtration rate; 95% CI=95% confidence interval.] (32)

	N	Δ eGFR		eGFR (mL/min/1.73m <sup>2</sup> )			
		Mean	95% CI	<30	30–<60	60–<90	≥90
Inland baseline	40	-3.4	-5.5–-1.3	0	2	2	36
Inland April	40			0	2	2	36
Coastland baseline	40	-5.3	-7.9–-2.7	1	4	8	27
Coastland April	40			2	5	8	25



**Figure 1.** Mean eGFR as percentage of baseline value over the course of the harvest (Nov–April) in both groups (curves based on eGFR values only). (Vertical line marks the start of the intervention in the inland group. Error bars = SEM). Note: there were only 11 workers sampled in the coastland group in January.

diate measurements for the coastland group. When all data for inland and coastland participants were included in the GEE model, the mean monthly decline in eGFR was 1.3 percentage points (95% CI 0.8–1.8). After the start of the intervention the inland group's eGFR downward trend leveled at -0.15 percentage points/month (95% CI -1.05–0.75).

Unpaired t-tests comparing group differences in eGFR (ie, changes from baseline to end of harvest) showed a smaller decrease in the inland group compared with the coastland group that was close to significant; 2.8 percentage points (95% CI -1.1–6.5). In the GEE model, allowing adjustment for age, the end-of-harvest eGFR was 3.4 percentage points (95% CI 0.1–6.7) lower in the inland compared to the coastland group. Models including accumulated hours working above WBGT of 30°C or 32°C did not change this end-of-harvest eGFR estimate.

The magnitude of the individual eGFR change from baseline to the end of harvest were evaluated for all coastland and inland participants. A change (decrease or increase in eGFR) of <10% was treated as within normal variation. Applying this criterion, a larger effect was demonstrated among the coastland participants with 28% showing an eGFR decrease of ≥10% as compared to 15% of inland participants (supplementary material figure A).

There was no clear correlation between cross-harvest and cross-shift changes in eGFR. Only at the end of harvest a significant correlation was found between mean cross-shift and cross-harvest eGFR, but adjusted R-square was very low (0.067).

## Discussion

Biomarkers of dehydration, kidney function, and muscle tissue breakdown were examined to evaluate a WRS intervention and efficiency training among sugarcane cutters. Across a work day there were significant changes in biomarkers indicating some dehydration and acute loss of kidney function as well as muscle tissue breakdown.

Previous studies among sugarcane cutters in Brazil, El Salvador and Nicaragua have also observed similar changes in hydration and kidney function biomarkers that have been attributed to heat stress (8, 11, 13). Some of the workers in this study met the criteria for AKI over the course of a working day as reported among Brazilian cane cutters (11). In this study, these negative changes were related to the individual's production, a finding not previously reported. A cross-shift decrease in eGFR was present but although this decrease was attenuated after the intervention was introduced. This indicates

that the intervention had an apparent positive effect on AKI. Cross-shift increases in S-CPK were within normal ranges indicating that S-CPK increases were caused by muscle breakdown from strenuous labor rather than severe acute rhabdomyolysis. In Brazil, cane cutters had a higher increase in S-CPK during a workday (11). This study also showed a significant change in eGFR over the course of the harvest. Two previous studies in Nicaragua also observed sugarcane workers over a harvest. They found higher S-creatinine and lower eGFR at the end of the observation period (10, 13). In the above-mentioned Brazilian study, no increase in S-creatinine was observed over the harvest, but these cutters had worked an average of only three harvests and the population was very small (11). In the present study, decreasing eGFR appeared to halt after the introduction of the intervention (See figure 1). The long-term impact of the intervention should be treated with caution. Nevertheless, both cross-shift and cross-harvest findings suggest that the intervention could have positive effects on kidney function.

Evidence of a production-related reduction in kidney function calls attention to the potential importance that piecework payment could have on mediating work-related kidney function changes, as suggested elsewhere (11, 31–33). In the present study, the intervention group increased production more than other comparable groups. This increased production may have counteracted, to some extent, the positive effects of the WRS part of the intervention. The impact of payment schemes and production efficiencies should be examined in future interventions recognizing that maintaining productivity is important if OSH improvements are to be accepted.

### Limitations

There are several inherent limitations for drawing firm conclusions from this study. Sample size was kept manageable small to test feasibility and assess the magnitude of changes in biomarkers over the harvest. The original study design provided for comparisons pre- and post-intervention, and comparisons between two groups in different environments. Participation and security issues led to postponing the intervention for the coastland group (5). Consequently, we were unable to examine the impact of the different WBGT loads in the two groups, controlling for intervention. Instead WBGT load could only be considered as a confounder. The relatively small sample size prevented a robust examination of confounders in multivariate analyses. Most confounders, however were distributed similarly in the two groups and were not differently distributed in “eGFR droppers”. We did not have data on individual working time so we had to assign the same daily duration to all individuals in the group working that day. Consequently, we had to consider individual production data as a proxy both

for workload and heat exposure. Although this problem was greatest in the cross-shift analysis, we suspect it to be a limitation in the longitudinal analysis as well. Our efforts were successful in reliably collecting, labeling, storing and transporting biological samples leading to all but one of several thousand samples being analyzed in an accredited laboratory while permitting report of urine dipstick and serum creatinine results to workers in a timely fashion.

### Concluding remarks

This WRS and efficiency intervention among sugarcane cutters is a promising approach to reduce heat stress and subsequently preventing dehydration and kidney damage. The intervention was associated with less adverse impacts on kidney function both across a day and across an entire harvest. It is still premature to conclude that the intervention prevents kidney disease; more observations and rigorous evaluation over a longer timeframe are needed before determining that such a program prevents CKDu. Regardless, the provision of water and shaded rest is a basic necessity.

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### Competing interests

The authors declare no competing interests.

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