

# Revolutionizing the Treatment of Painful Diabetic Neuropathy (PDN) with High Frequency (10 kHz) Spinal Cord Stimulation



# Introducing

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## **Erika Petersen, MD, FAANS, FACS**

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Control Trial (RCT)  
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# Prevalence of Painful Diabetic Neuropathy (PDN)

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Adults Diagnosed with  
Diabetes in the U.S.

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**28.7** Million

~50% of Adults with  
Diabetes Have Neuropathy

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**14** Million

Painful Diabetic Neuropathy  
(PDN) is **Common**

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**5.7** Million

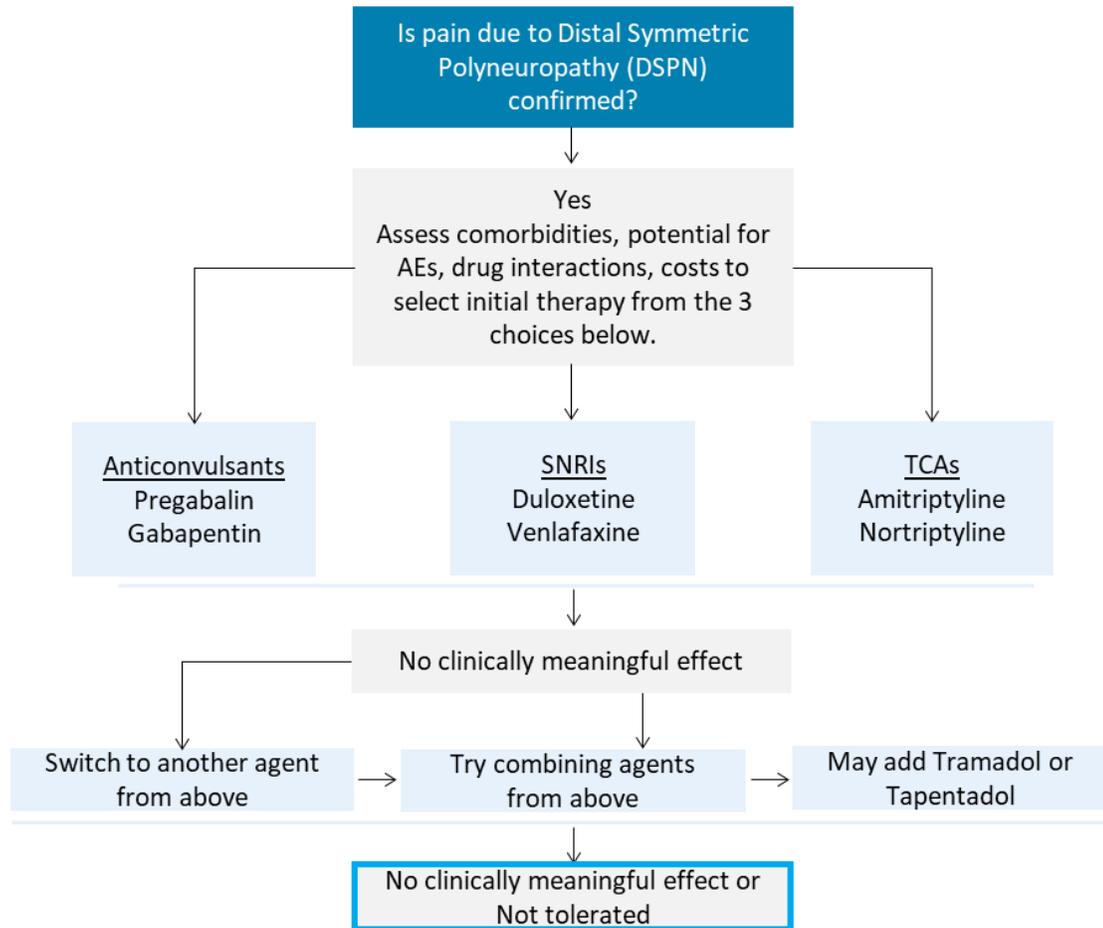
CDC National Diabetes Statistics Report 2022

Mayo Clinic, Diabetic Neuropathy. <https://www.mayoclinic.org/diseases-conditions/diabetic-neuropathy/symptoms-causes/syc-20371580> – accessed Dec 2021

Yang M. et al. Suboptimal Treatment of Diabetic Peripheral Neuropathic Pain in the United States. *Pain Medicine*, Nov 2015.

# Limits to Conventional Treatments

## ADA Position Statement | Diabetic Neuropathy



45% of patients are refractory despite available conventional treatment options



Approved in July 2021,  
Nevro HFX is the most effective  
treatment for refractory  
painful diabetic neuropathy (PDN)<sup>1</sup>

1. Petersen E. et al. Effect of high frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: a randomized clinical trial. JAMA Neurology Apr 2021

# Nevro HFX™ for PDN

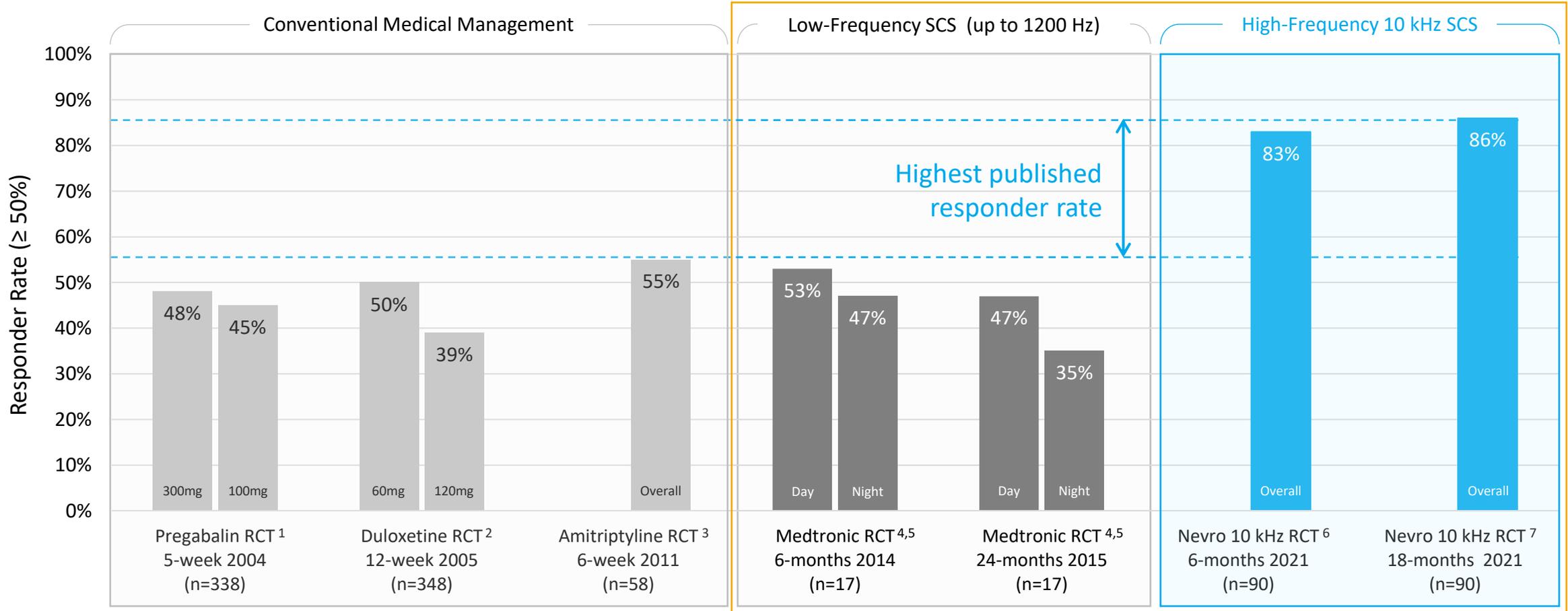
HFX uses spinal cord stimulation (SCS), a safe, well-established treatment that uses an implanted neuromodulation system to deliver mild electrical impulses to the pain-sensing pathways of the dorsal horn, effectively interrupting the pain signals that travel to the brain.

- First and only high-frequency (10 kHz) paresthesia-free SCS therapy with a specific indication to treat PDN
- Nondrug treatment
- Minimally invasive and fully reversible therapy
- Launched in 2015
- 80,000+ patients treated
- Test trial HFX therapy to ensure pain relief before implant



# Clinical Evidence Comparison for Painful Diabetic Neuropathy (PDN)

Responder Rate Comparison  
(≥ 50% pain relief for all who received treatment)



1. Pregabalin RCT reference – Lesser, H, et. al. Pregabalin Relieves Symptoms of Painful Diabetic Neuropathy. Neurology, 2004.
2. Duloxetine RCT reference – Raskin, J, et. al. A Double-blind, Randomized, Multicenter Trial Comparing Duloxetine with Placebo in the Management of Diabetic Peripheral Neuropathic Pain. Pain Med, 2005.
3. Amitriptyline RCT reference - Kaur, H, et. al. A Comparative Evaluation of Amitriptyline and Duloxetine in Painful Diabetic Neuropathy. Diabetes Care, 2011.
4. Slangen R, Schaper N, Faber C, et al. Spinal Cord Stimulation and Pain Relief in Painful Diabetic Peripheral Neuropathy: A Prospective Two-Center Randomized Controlled Trial. Diabetes Care. 2014;37:3016-3024.
5. van Beek, M. et al. Sustained Treatment Effect of Spinal Cord Stimulation in Painful Diabetic Peripheral Neuropathy: 24-Month Follow-up of a Prospective Two-Center Randomized Controlled Trial. Diabetes Care 2015;38:e132-e134
6. Petersen, E, et. al. Durability of high-frequency 10 kHz spinal cord stimulation for patients with painful diabetic neuropathy refractory to conventional treatments. Diabetes Care, November 2021
7. Petersen E. et. al. Durability of 10 kHz spinal cord stimulation for painful diabetic neuropathy: 18-month results. NANS, Jan 2022.

# 24 Month Results for 10 kHz Spinal Cord Stimulation (SCS) in Treating Painful Diabetic Neuropathy (PDN)

Erika Petersen, MD, FAANS, FACS

Professor of Neurosurgery

Director of Functional & Restorative Neurosurgery and Neuromodulation

University of Arkansas for Medical Sciences

Little Rock, AR

# Nevro PDN Randomized Controlled Trial (RCT)

## Methods

- Subjects with lower extremity (LE) PDN refractory to medications (minimum of 2 classes, one of which is gabapentinoids)
- $\geq 5$  of 10 cm on pain VAS, HbA1c  $\leq 10\%$ , BMI  $< 45$
- 18 US centers, 216 randomized subjects 1:1
- Conventional Medical Management (CMM) vs. 10 kHz Therapy (Nevro Corp.) + CMM.
- Option to crossover to alternate treatment arm at 6 months
- (93% of those eligible crossed over from CMM)



6-month<sup>1</sup>  
JAMA Neurology  
Apr 2021

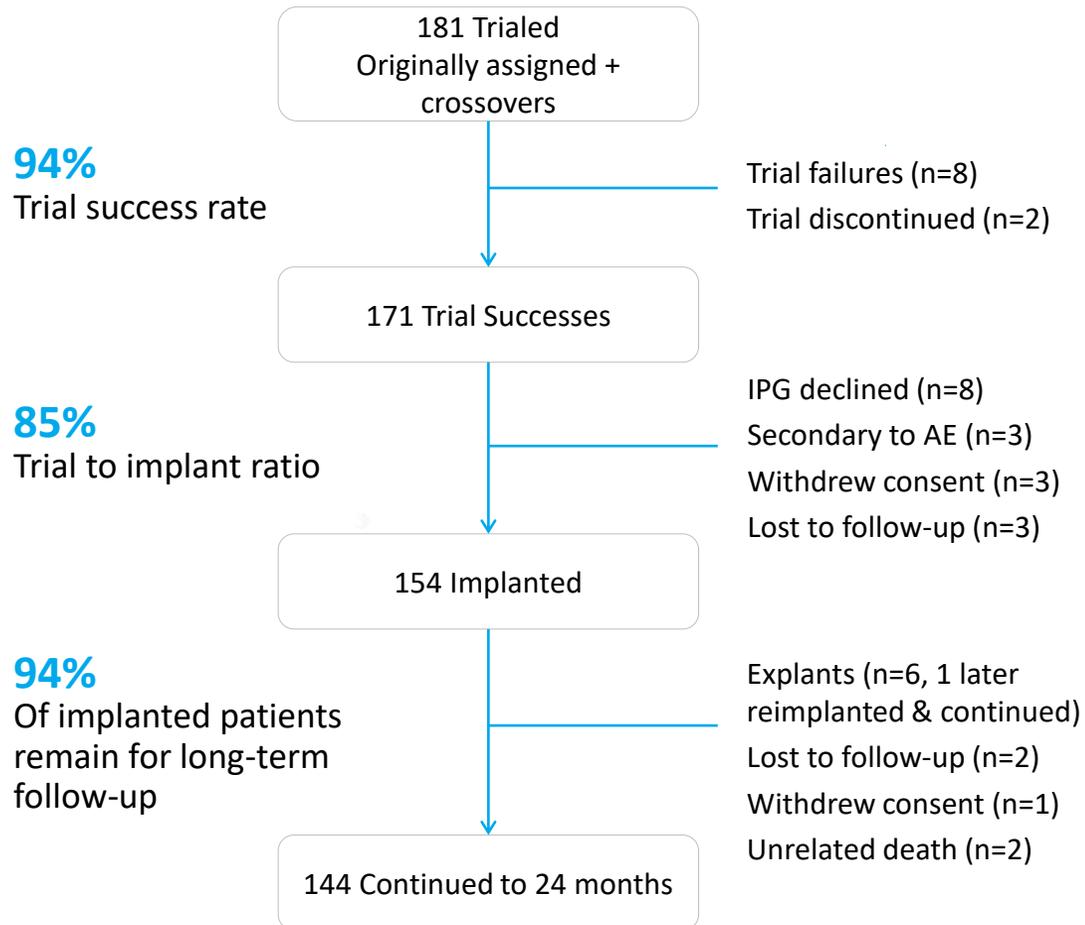


12-month<sup>2</sup>  
Diabetes Care  
Nov 2021

1. Petersen E. et al. Effect of high frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: a randomized clinical trial. *JAMA Neurology* Apr 2021
2. Petersen E. et al. Durability of high-frequency 10 kHz spinal cord stimulation for patients with painful diabetic neuropathy refractory to conventional treatments. *Diabetes Care*, Nov 2021.

# Nevro PDN RCT

## Subject Disposition: 10 kHz SCS



### Safety

No stimulation-related neurological deficits

No explants for loss of efficacy

8 procedure-related infections (5.2%)

3 resolved with antibiotics

5 required explant (3.2%, 1 patient reimplanted)

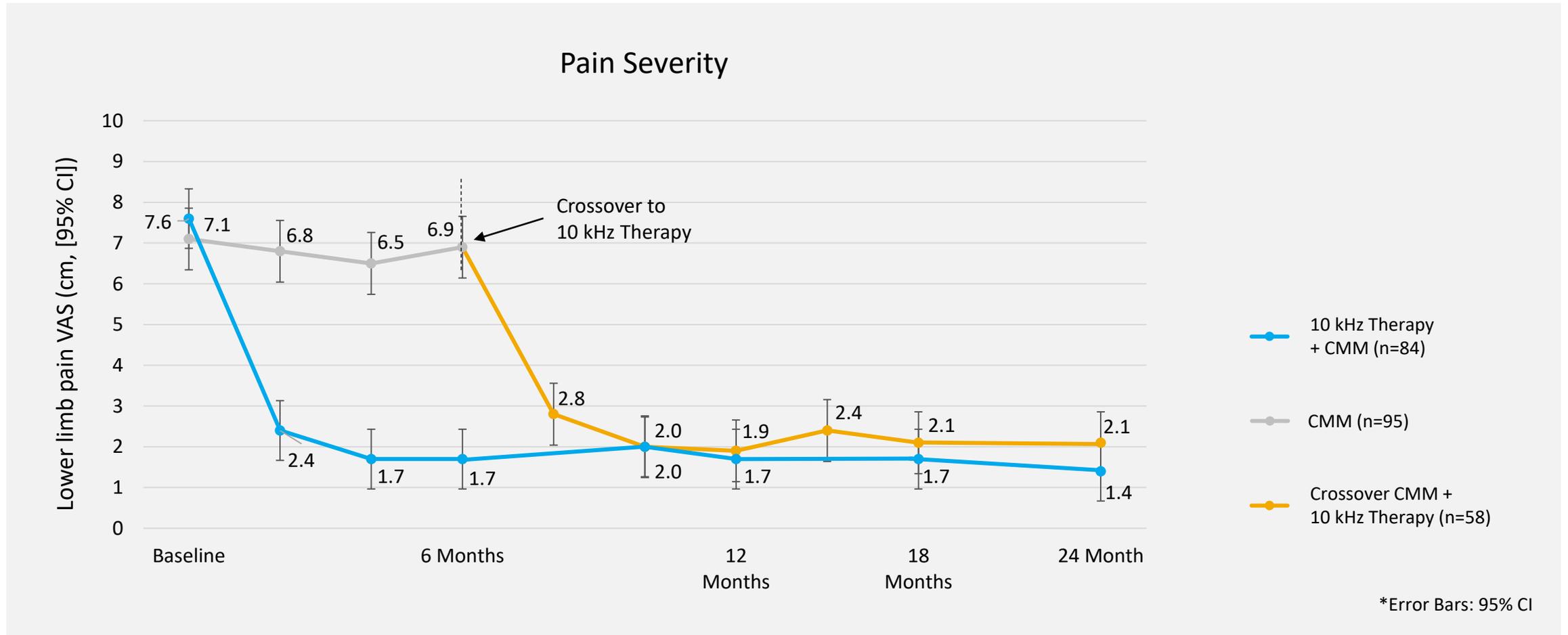
1 explant as a precaution for an unrelated infection

# Nevro PDN RCT | Baseline Characteristics

	CMM n = 103	10 kHz SCS + CMM n = 113	Standardized Difference
Age in years, mean (SD)	60.8 (9.9)	60.7 (11.4)	0.01
Male, n (%)	66 (64%)	70 (62%)	0.04
Race			
White, n (%)	85 (82.5%)	87 (77.0%)	0.14
Black or African American, n (%)	13 (12.6%)	18 (15.9%)	
Native Hawaiian or other Pacific Islander, n (%)	1 (1.0%)	3 (2.7%)	
American Indian or Alaska Native, n (%)	0 (0.0%)	2 (1.8%)	
Asian, n (%)	1 (1.0%)	1 (0.9%)	
Other, n (%)	3 (2.9%)	2 (1.8%)	
Diabetes			
Type 1, n (%)	3 (3%)	8 (7%)	0.19
Type 2, n (%)	100 (97%)	105 (93%)	
Duration in years			
Diabetes, mean (SD)	12.2 (8.5)	12.9 (8.5)	0.09
Peripheral neuropathy, mean (SD)	7.1 (5.1)	7.4 (5.7)	0.06
Lower limb pain VAS in cm, mean (SD)	7.1 (1.6)	7.5 (1.6)	0.22
< 7.5 cm, n (%)	57 (55%)	54 (48%)	0.15
≥ 7.5 cm, n (%)	46 (45%)	59 (52%)	
HbA1c, mean (SD)	7.4% (1.2%)	7.3% (1.1%)	0.11
< 7.0%, n (%)	40 (39%)	46 (41%)	0.04
≥ 7.0%, n (%)	63 (61%)	67 (59%)	
BMI, mean (SD)	33.9 (5.2)	33.6 (5.4)	0.06

Effect size index (Cohen's d):  
 ≥ 0.20 = small  
 ≥ 0.50 = medium  
 ≥ 0.80 = large

# Nevro PDN RCT | Pain Relief over 24-Months



# Nevro PDN RCT

## 24 Month Individual Pain Relief

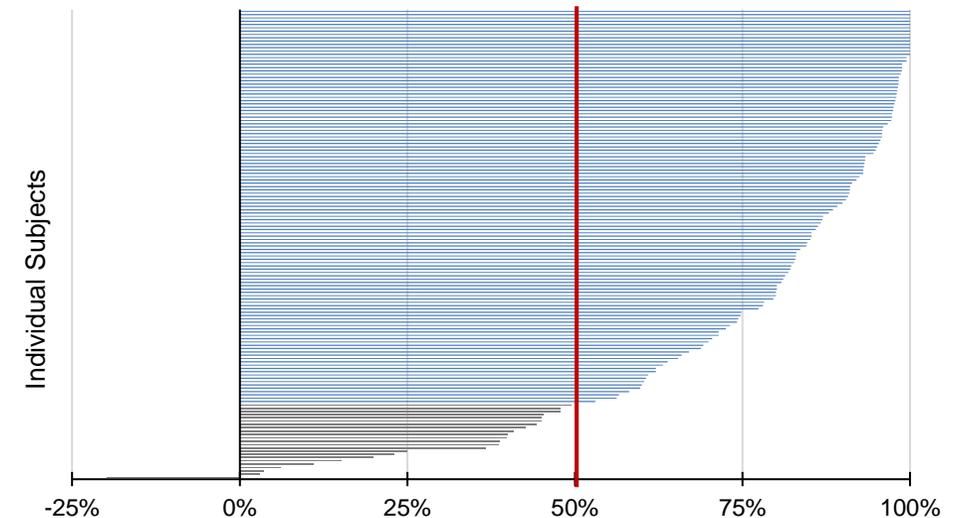
**84%** Responders (119/142)

**77%** Average Pain Relief

**61%\*** Profound Responders (87/142)

**1.3** Number Needed to Treat

Implanted Patients at 24 Months

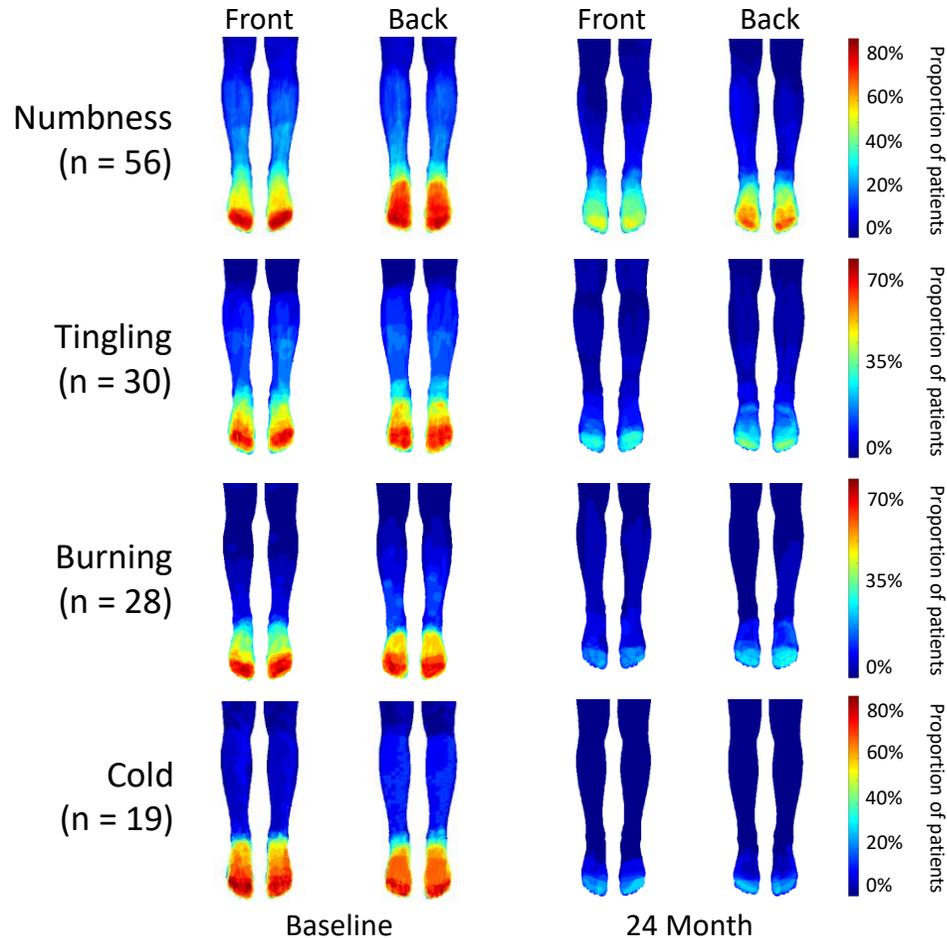


Improvement from baseline pain VAS

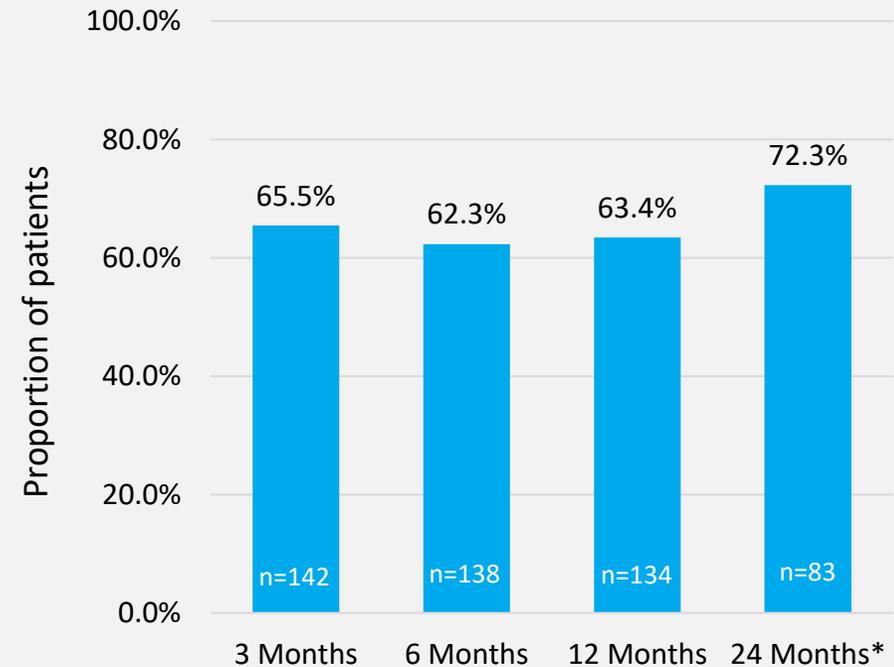
\*Profound responder defined as  $\geq 80\%$  pain relief

# Nevro PDN RCT | Neurological Symptom Improvements with 10 kHz SCS

## Patient-reported reductions in dysesthesias

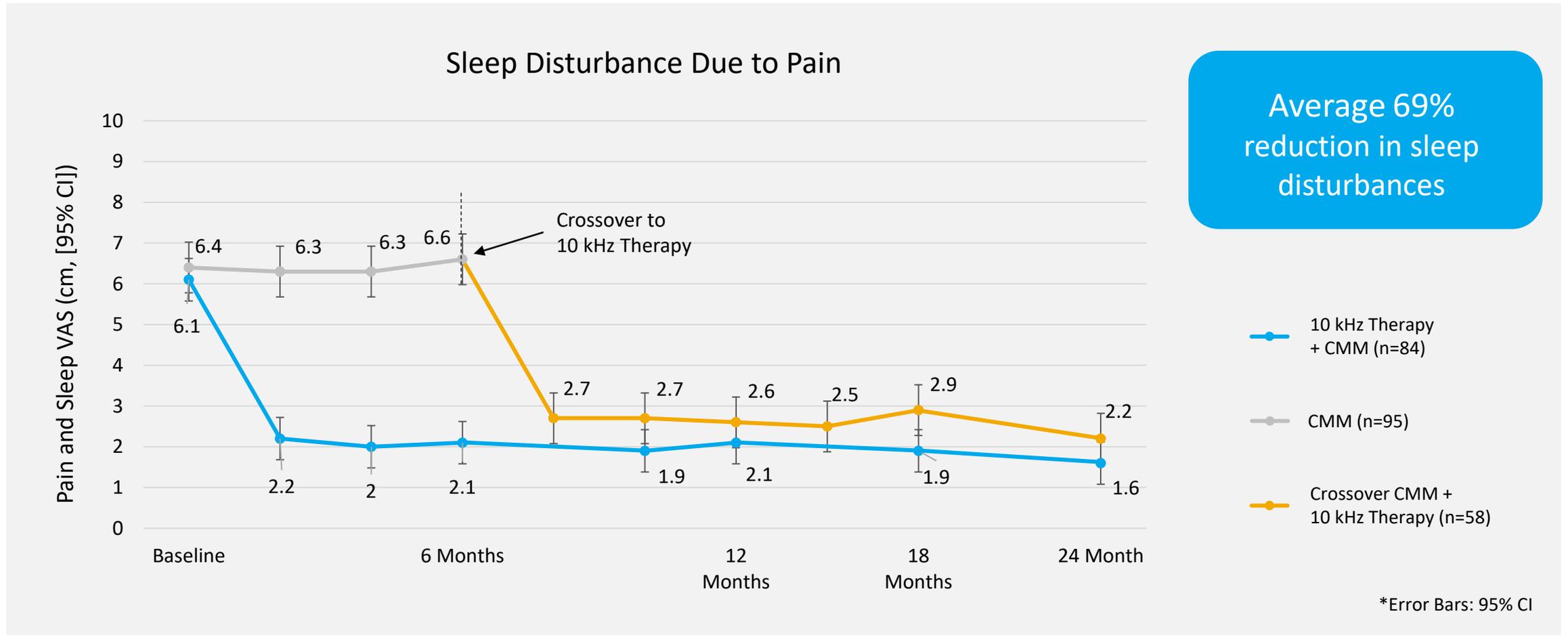


Did the investigator note improvement compared to baseline in motor, sensory, or reflex function, without deterioration in any category?



\*Subjects who have completed 24-month observation

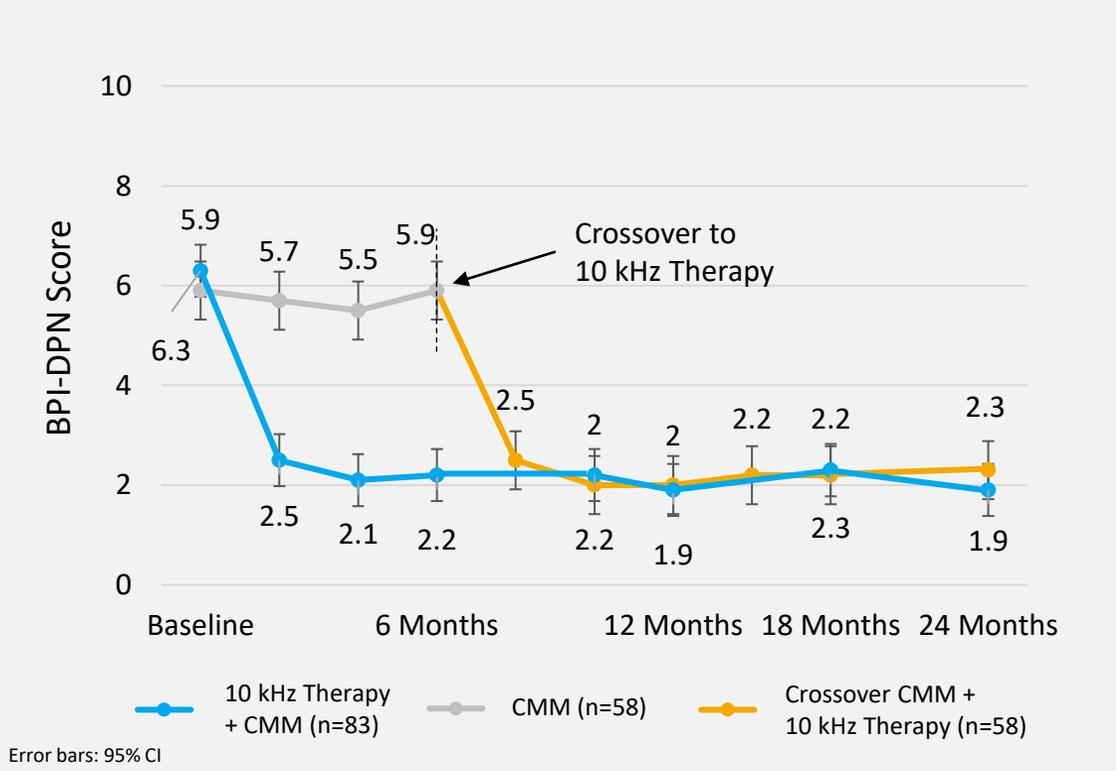
# Nevro PDN RCT | Reduction in Sleep Disturbance



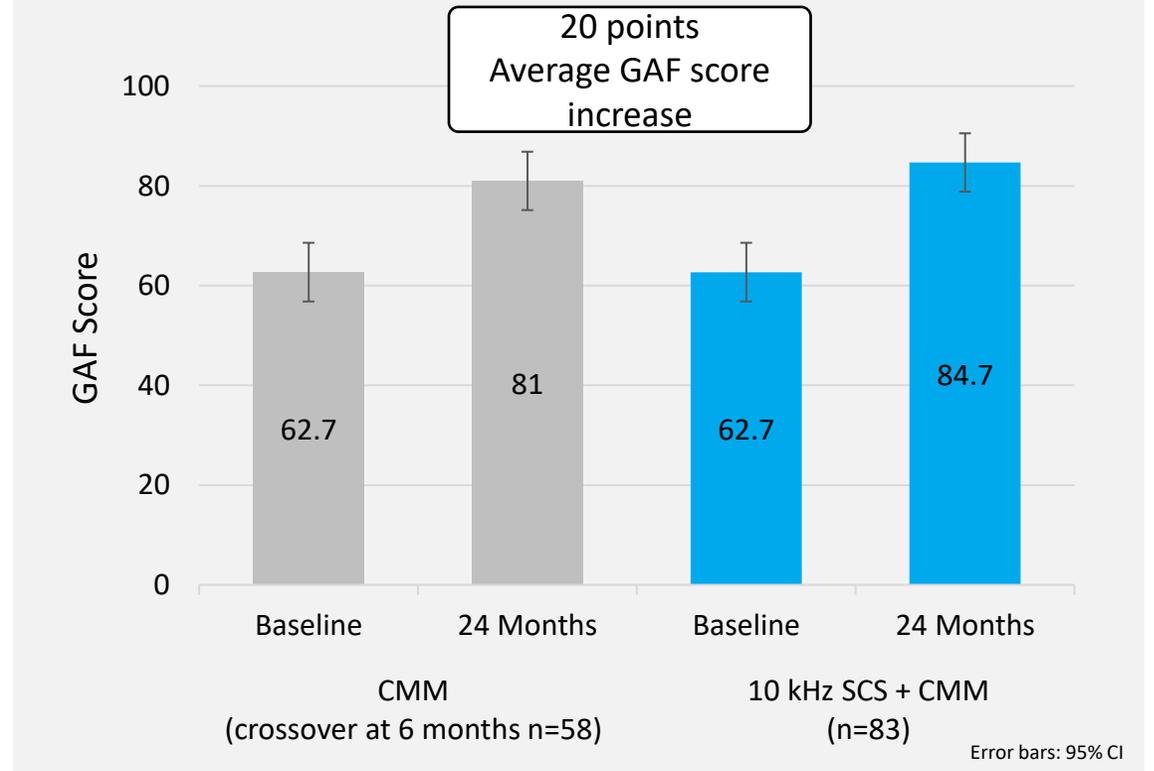
Reported by patients as of 24-month check-in

# Nevro PDN RCT | Quality of Life Improvements

## Pain Interference with Mood and Daily Activities

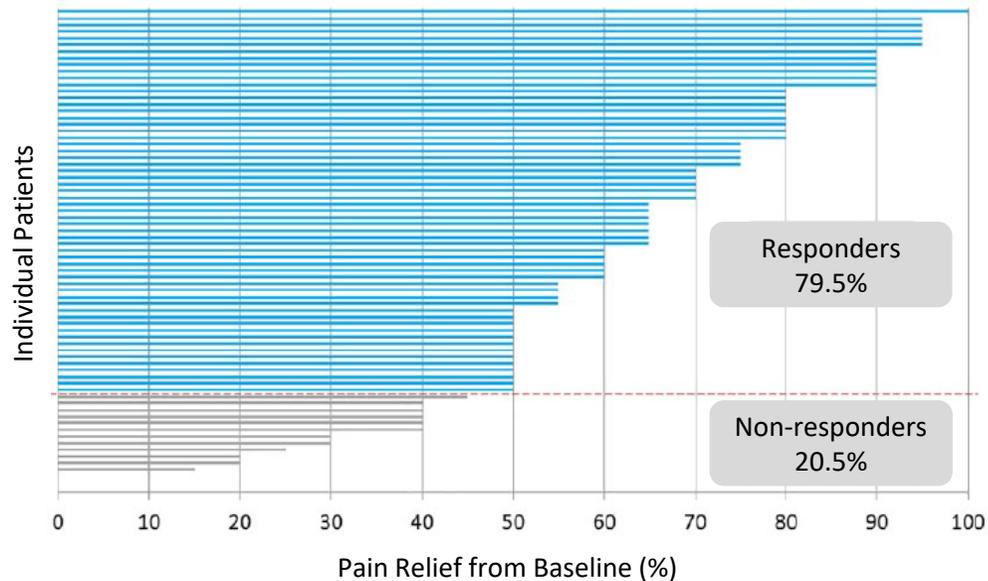


## Global Assessment of Functioning

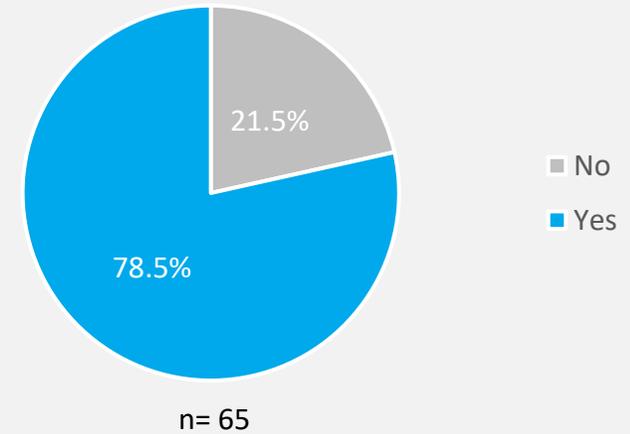


# Real-World Analysis of 10 kHz SCS for Treatment of PDN

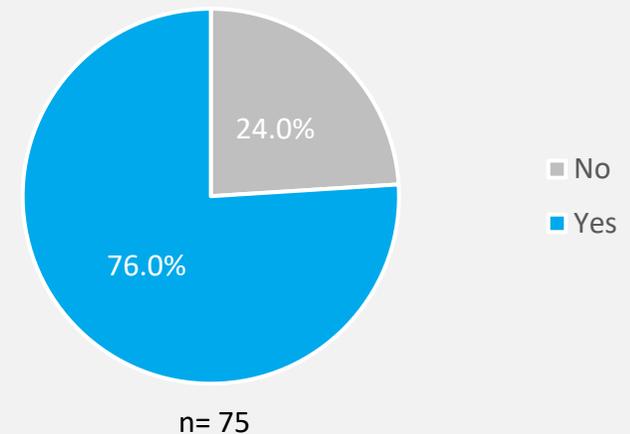
Retrospective, multi-center, real-world review assessed pain relief and functional improvements for patients (n= 89) with diabetic neuropathy who were implanted with a high-frequency 10 kHz SCS.



Improvement in Sleep?



Improvement in Function?



1. Chen J, et al. A Real-World Analysis of High-Frequency 10 kHz Spinal Cord Stimulation for the Treatment of Painful Diabetic Peripheral Neuropathy. *Journal of Diabetes Science and Technology*, Nov 2021.

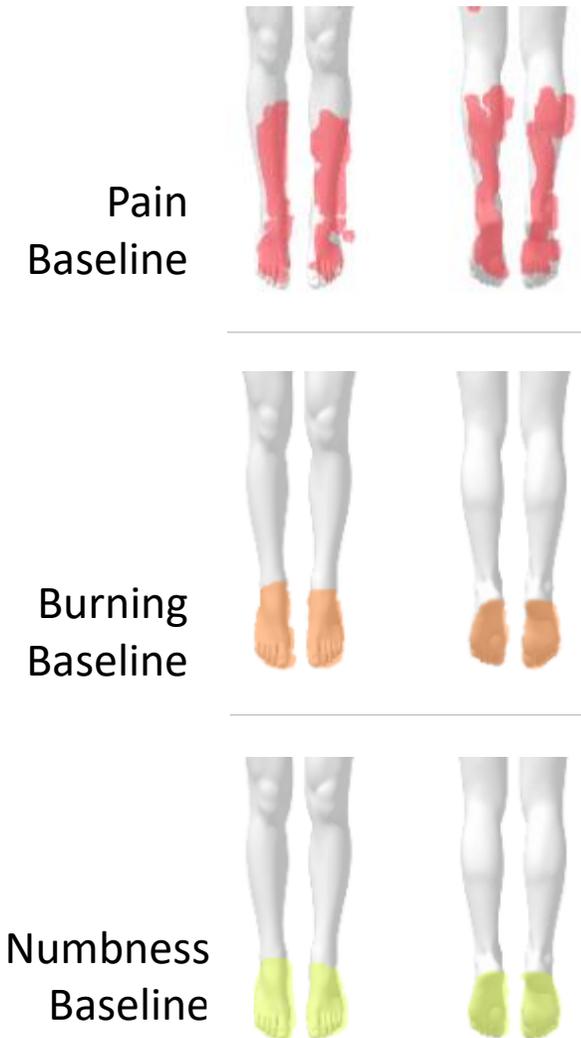
# Patient Case #1 - PDN

## Background

- 64-year-old Caucasian male
- Diagnosed with type 2 DM in 2005, PDN in 2015
- HbA1c = 8.6%, BMI = 32.3 kg/m<sup>2</sup>
- Baseline medications included
  - Gabapentin 800 mg TID
  - Metformin 1,000 mg BID
- Neurologic exam (128 Hz tuning fork, pinprick, & 10-g monofilament)
  - Sensation diminished or absent in both feet

## Pain History

- Bilateral foot pain up to the knees
  - Described intense burning in feet
  - Baseline VAS = 7.95 cm



# Patient Case #1 – Nevro HFX

Implanted October 2018

Pain completely resolved, VAS = 0.0 cm at 24-mo. visit

Burning resolved, Numbness reduced

HbA1c = 6.7% at 24-mo. visit

- Empagliflozin, Semaglutide, & Repaglinide added

Functional improvements

- More active, able to complete household activities

Sleeping improvements

- “The burning feeling was the worst at night, now that’s gone”

Pain  
24 months



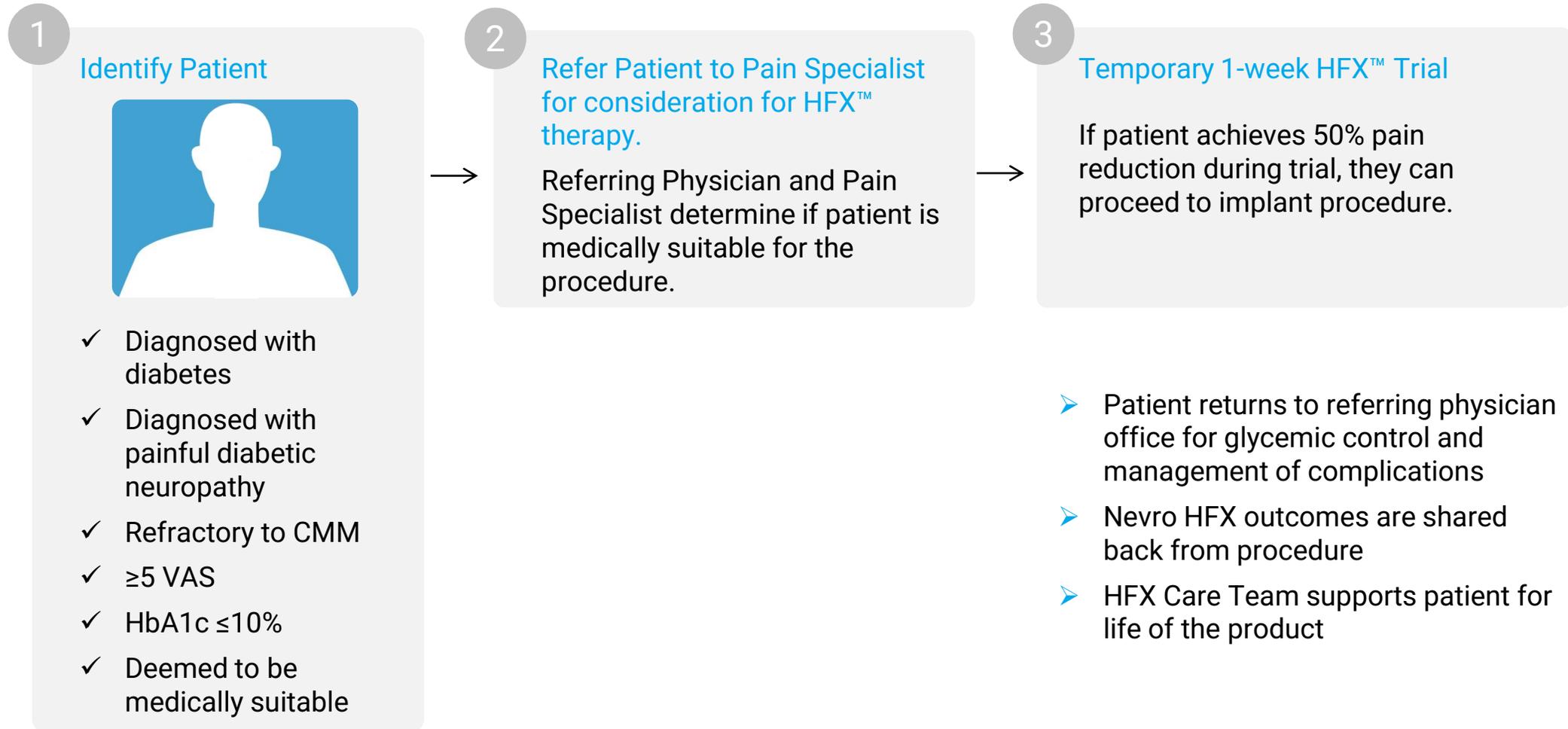
Burning  
24 months



Numbness  
24 months



# What is the Process from Referral to Return?



# Nevro HFX™ is the most effective treatment for refractory Painful Diabetic Neuropathy (PDN)<sup>1</sup>

Poster Presentation Today at 12:00 CT (Hall D-E)

Visit the Nevro booth (#1119) to learn more, speak to real patients and connect with a local Nevro representative.