Diabetic Peripheral Neuropathy:
Introducing New Interventional Options

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Disclosure

- Consulting Fee (e.g., Advisory Board): Abbott, Avanos, Biotronik, Boston Scientific, Gruenthal, Nalu, Nevro, PainTeq, Saluda, SI Bone, SPR Therapeutics, Vertos
- Contracted Research (Principal Investigators must provide information, even if received by the institution): Avanos, Biotronik, Boston Scientific, Nalu, Nevro, PainTeq, Saluda, SPR Therapeutics
- Stock Shareholder (Individual stocks/Stock options; diversified mutual funds do not need to be disclosed): Nalu, National Spine and Pain Centers
Learning Objectives

- Discuss the pathophysiology of diabetic peripheral neuropathy (DPN)
- Review clinical presentation of DPN
- Define painful diabetic neuropathy (PDN)
- Explore current and new treatment continuum of PDN
- Review body of evidence supporting new PDN treatments
Outline

- Prevalence and impact of diabetes
- Pathophysiology
- Clinical presentation
- Painful diabetic neuropathy (PDN)
- Current and new treatment for PDN
- Review latest clinical evidence
Prevalence of Diabetes in the United States

34.2 million people have diabetes

That’s about 1 in every 10 people

1 in 5 don’t know they have diabetes

Trajectory of Diabetes Prevalence

88 MILLION adults – more than 1 in 3 – have prediabetes

8 IN 10 Adults don’t know they have prediabetes

1 in 3 Americans will have diabetes by 2050
For people of color, this is more like 1 in 2 by 2050.
## Types of Diabetes

<table>
<thead>
<tr>
<th>Type 1 Diabetes (T1D)</th>
<th>Type 2 Diabetes (T2D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune disease</td>
<td>Insulin Resistance</td>
</tr>
<tr>
<td>Destruction of beta cells – leads to limited or no insulin production</td>
<td>Insulin Deficiency</td>
</tr>
<tr>
<td>Genetic link</td>
<td>Stronger genetic component</td>
</tr>
<tr>
<td>Environmental trigger</td>
<td>Increased risk with age, obesity, ethnic background</td>
</tr>
<tr>
<td>Person is often thin at diagnosis</td>
<td></td>
</tr>
<tr>
<td>5-10% of all diabetes</td>
<td>90-95% of all diabetes</td>
</tr>
<tr>
<td>Average age 10-12</td>
<td>After age 30 but becoming more frequent in adolescents</td>
</tr>
</tbody>
</table>

- **Type I Diabetes (T1D):**
  - Autoimmune disease
  - Destruction of beta cells – leads to limited or no insulin production
  - Genetic link
  - Environmental trigger
  - Person is often thin at diagnosis
  - 5-10% of all diabetes
  - Average age 10-12

- **Type 2 Diabetes (T2D):**
  - Insulin Resistance
  - Insulin Deficiency
  - Stronger genetic component
  - Increased risk with age, obesity, ethnic background
  - 90-95% of all diabetes
  - After age 30 but becoming more frequent in adolescents

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 CDC Fact Sheet, 2011
 AACE Diabetes Mellitus Guidelines, Endocrine Practice, 2007;13(Suppl 1).
ADA Criteria for Diagnosis of Diabetes

- 2 abnormal test results from the same sample
  OR
- 1 abnormal from 2 separate samples
- Hyperglycemic with symptoms
  OR
- Hyperglycemic crisis with a random plasma glucose of ≥200 gm/dL

Fasting Plasma Glucose (FPG) ≥126 mg/dL*

OR

2-h Plasma Glucose (PG) ≥200mg/dL during oral glucose tolerance test (OGTT)*

OR

A1C ≥ 6.5%*

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL

*In the absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal test results from the same sample or 2 separate test samples.
Long Term Impact of Uncontrolled Diabetes

- Leading cause of blindness in the developed nations
- Leading cause of non-traumatic lower extremity amputations
- Leading cause of renal failure resulting in dialysis
- PWD: 3 times more likely to have cardiovascular complications
- PWD: 1 in 7 will suffer depression
- Sexual dysfunction (7x Males and 60% Females)
- Gestational diabetes associated with increased perinatal morbidity and mortality
- ~50% of patients will develop peripheral diabetic neuropathy
- PWD spend more than 3 times the average on health care costs
- Diabetes and its complications accounts for 1/3 of the Medicare budget

Complications of Uncontrolled Diabetes

Microvascular Complications
- Eye Retinopathy
- Kidney Nephropathy

Macrovascular Complications
- Brain Cerebrovascular disease (i.e., stroke, transient ischemic attack [TIA])
- Heart Coronary artery disease (CAD), Myocardial infarction (MI)
- Extremities Peripheral arterial disease (PAD)

Challenges with Maintaining Glycemic Control

- Self-monitoring blood glucose
- Dietary/lifestyle modification
- Measurement of blood A1C every 3 months
- Multiple medications for multiple diagnoses (hypertension, hyperlipidemia, cardiovascular disease)
- Insulin requires additional considerations
  - One to four daily subcutaneous injections (or Insulin Pump)
  - Increased self-monitoring of blood glucose or CGM (Continuous Glucose Monitoring)
  - Risk of hypoglycemia (low blood glucose) can lead to life-threatening reactions and/or death
How Successful is Diabetes Management?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled BP (&lt;130/80 mmHg)</td>
<td>51%</td>
</tr>
<tr>
<td>LDL at the goal level (&lt;100 mg/dl)</td>
<td>56%</td>
</tr>
<tr>
<td>A1C at the goal level (&lt;7%)</td>
<td>52%</td>
</tr>
<tr>
<td>What proportion have met all three?</td>
<td>19%</td>
</tr>
</tbody>
</table>
Painful Diabetic Neuropathy (PDN)

- **Diabetic Neuropathy**
  - Nerve damage caused by chronically high blood sugar and diabetes
  - Most common complication of diabetes
  - Develops 5-10 years post onset of diabetes

- **Symptoms**
  - Numbness
  - Loss of sensation
  - Paresthesia
  - May progress into pain

- **Consequences**
  - May not feel heat, cold, or have any sensations in feet, legs, or hands
  - Unaware of cuts or wounds or burns
  - Infections, ulcers, amputations, falls, hospital admissions, QoL or even death
  - May be unable to sleep at night
  - May impact ability to work or complete routine activities

Sources: Trinity Partners Market Research 2017; Mayo Clinic; Nevro Senza-PDN RCT 3-month manuscript
Prevalence and Cost of Painful Diabetic Neuropathy

- Diabetes is a National Epidemic
  - 34.2 million people with diabetes
  - 10.5% of the population
  - Another 88 million people with prediabetes (>1 in 3 adults)
  - Annual cost: $327 billion
    - Direct medical costs = $237 billion
    - Indirect costs = $90 billion

- PDN is common
  - Present in 20% to 26% of those with diabetes

34+ Million Patients with Diabetes
7 Million Patients with PDN

CDC National Diabetes Statistics Report 2020
Davies et al. Diabetes Care 2006
Schmader Clin J Pain 2002
Prevalence of PDN

Diagnosed PWD

26.8 MM PATIENTS

20% with PDN

5.3 MM PATIENTS

45% Refractory to CMM

2.3 MM PATIENTS

Current Treatment Options Demonstrate Mild Efficacy and Low Adherence

PWD = Patients with Diabetes  PDN = Painful Diabetic Neuropathy  CMM = Conventional Medical Management  TAM = Total Addressable Market

Conventional Medical Management of PDN

<table>
<thead>
<tr>
<th>American Academy of Neurology (AAN)</th>
<th>American Diabetes Association (ADA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level A Recommendations</strong></td>
<td><strong>First Line</strong></td>
</tr>
<tr>
<td>Anticonvulsant: Pregabalin</td>
<td>Pregabalin</td>
</tr>
<tr>
<td></td>
<td>Duloxetine</td>
</tr>
<tr>
<td></td>
<td>Gabapentin</td>
</tr>
<tr>
<td><strong>Level B Recommendations</strong></td>
<td><strong>Second Line</strong></td>
</tr>
<tr>
<td>Anticonvulsant: Gabapentin</td>
<td>Tricyclic antidepressant (TCA)</td>
</tr>
<tr>
<td>SNRI: Venlafaxine, Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Opioid: Tramadol, Morphine, Oxycodone</td>
<td></td>
</tr>
</tbody>
</table>

**CMM Effectiveness**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number Needed to Treat (NNT)</th>
<th>Number Needed to Harm (NNH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCAs</td>
<td>3.6</td>
<td>13.4</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>6.3</td>
<td>25.6</td>
</tr>
<tr>
<td>SNRIs</td>
<td>6.4</td>
<td>11.8</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>7.7</td>
<td>13.9</td>
</tr>
</tbody>
</table>

**Target Population:**

45% of PDN patients are refractory to conservative treatments

Painful Diabetic Neuropathy: Existing and New Treatment Options

- Topical anesthetic
- Gabapentin
- Pregabalin
- Duloxetine
- Tricyclic anti-depressant (TCA)
- Opioid
- Pain pump
- Topical 8% capsaicin patch
- 1 kHz high frequency spinal cord stimulation

Unmet Treatment Needs for Painful Diabetic Neuropathy

- Current treatment options often provide insufficient pain relief
- Medications for neuropathic pain can have significant side effects
- Low frequency spinal cord stimulation presents challenges for patients
  - Suboptimal pain relief
  - Need to adjust stimulation based on posture/movement
  - Inability to target feet without uncomfortable stimulation
  - Inability to report changes in due to the confounding presence of paresthesias
Topical 8% Capsaicin Patch

- Capsaicin (1816), chili pepper extract
- Musculoskeletal pain
- Postherpetic neuralgia
- FDA approved 2020 for diabetic peripheral neuropathy
- Binds to TRPV1 receptor
- Na+, Ca++ influx: depolarization
- TRPV1 found on A delta, C nociceptive nerve fibers
- Capsaicin binding leads to loss of mitochondrial function
- Desensitization of sensory afferent axons
- Chemoneurolysis of peripheral nerves
Capsaicin: Mechanism of Action
Transient Receptor Potential Vanilloid-1 Receptor (TRPV1)

- TRPV1 preferentially expressed on sensory nociceptive nerve fibers: C and Aδ
- Activation of TRPV1 by capsaicin results in sensory neuronal depolarization
- Inactivation of voltage-gated Na+ channels and direct pharmacological desensitization
- Ca²⁺ entering through TRPV1 and intracellular stores → activation of calcium-dependent proteases and cytoskeleton breakdown
Multiple mechanisms underlie capsaicin-induced defunctionalization.

- Capsaicin concentration gradient
- Nerve terminal retraction due to mitochondrial dysfunction
- Depth of defunctionalization determined by capsaicin concentration

- Inactivation Na⁺ channels
- Protease activation
- Cytoskeleton breakdown
- Interruption fast axonal transport
- Dysfunctional mitochondria
- Endoplasmic reticulum
- Capsaicin-insensitive nerve terminals
- Inactivation Na⁺ channels
- ↑Ca²⁺

Capsaicin: Mechanism of Action
Mitochondrial Dysfunction & Cellular Defunctionalization

Capsaicin 8% Topical System

Indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.
Topical 8% Capsaicin: STEP Study

Capsaicin 8% Patch in Painful Diabetic Peripheral Neuropathy: A Randomized, Double-Blind, Placebo-Controlled Study

STEP Trial:
Phase III, Randomized, Double-blind Trial (capsaicin 8%)

Key inclusion criteria:
- Aged ≥18 years with a diagnosis of PDPN for at least 1 year
- HbA1c ≤11% at screening and 3–6 months
- Stable doses of pain medication >4 weeks before screening*
- Average NPRS score over the last 24 hours of ≥4 during the screening period

Primary endpoint (weeks 2-8): Percentage change in NPRS as assessed over the previous 24 hours, according to question 5 of the BPI-DN from baseline to mean score over weeks 2 through 8

Secondary endpoints (weeks 2-12):
- NPRS average daily pain score
- Response rates (30% and 50%)
- Change in sleep interference
- Time to treatment response
- PGIC
- EQ-5D

Screening Visit n= 369 → Randomization / capsaicin 8% topical system application → Capsaicin 8% topical system (arm 1) n = 186 → Placebo (arm 2) n = 183 → Week 2 Visit → Week 4 Visit → Week 8 Visit → Week 12 / EoS Visit

(all patients could use opioid rescue medication up to 5 days after; no topical pain medications)
STEP Trial: Results

Ten studies reported the number of patients with a ≥ 30% pain reduction

Nine studies were included, 1 trial was excluded due to shorter treatment duration ≤ 8 weeks
Gate Theory of Pain

- Wall and Melzack, 1965
- Aβ (sensory) and Aδ, C pain fibers compete for passage through physiologic “gate”
- Stimulation of larger Aβ fibers would: closes the gate
Electrical Inhibition of Pain by Stimulation of the Dorsal Columns: Preliminary Clinical Report

C. Norman Shealy, M.D.*

J. Thomas Mortimer, M.S.T.

James B. Reswick, D.S.O.*

Long-term stimulation of the dorsal columns has been proposed recently as a potential method for relief of pain. Acute electrophysiologic and chronic behavioral studies in animals suggested the possibility of this method. Further experimental studies confirmed its potential safety and have thus led to application in patients.

Since submission of the original paper on experimental observations, Wall and Sato* have reported that peripheral nerve stimulation can produce specific focal analgesia and anesthesia. We have confirmed their results in 10 cases in which peripheral nerve stimulation was used. Frequencies of 90 to 100 c.p.s., currents of 0.5 to 1.0 ma., and pulse widths of 0.5 msec. have resulted uniformly in analgesia of the nerve's peripheral area of innervation. With stimulation of the paraspinal nerve, however, no decrease in sensation could be elicited in the lateral part of the foot. This emphasizes the impracticality of peripheral nerve stimulation for relief of diffuse pain.

REPORT OF A CASE

A 70-year-old man was admitted to Lutheran Hospital in early March because of severe diffuse pain in the right lower part of the chest and the upper part of the abdomen. He had previously been determined to have inoperable bronchogenic carcinoma and was suspected of having metastases to the pectoral and liver. He ran a low-grade fever and had considerable nausea and vomiting but was thought to have a life expectancy of 1 to 2 months. He explained in detail to him and his family the experimental nature of dorsal column stimulation. A new anesthesiologist during that time in aiding their acceptance of this treatment. On March 21, 1967, a thoroctic laminectomy (T2-3) was performed and a Vitalumina electrode measuring 3 by 4 mm. was approximated to the dorsal columns at T3 by suturing to the dura. The spinal electrodes was Vitalumina covered with Dow Corning Medical Grade Adhesive and Silastic Special subcutaneous shots were placed beneath...
Traditional SCS Therapy

- Electrical stimulation of dorsal column
- Activation of Aβ sensory fibers
- Generate paresthesia in areas of pain

SCS Contemporary Landmark Studies

- Kemler, et al. NEJM. 2000
- Accurate Trial: pivotal U.S. study DRG stimulation
- Sunburst Trial: pivotal U.S. study for Burst
- SENZA RCT: pivotal U.S. study for HF10
- Accelerate Trial: HF-SCS versus conventional SCS
- Avalon Trial: closed loop SCS study in Australia
- Evoke Trial: pivotal U.S. study for closed loop SCS
- Acute Trial: pivotal U.S. study for DTM
10kHz SCS: Mechanism of Action

- HF-SCS not based on paresthesia coverage of pain
- Most likely different target: dorsal horn
- Rat model suggests direct hyperpolarization of dorsal horn neurons
Peripheral Polyneuropathy: Feasibility Study (SENZA-PPN)

• Major inclusion criteria
  – Diagnosis: Peripheral polyneuropathy (PPN) of upper or lower limb(s)
  – Refractory to conservative therapy > 3 months
  – Mean upper or lower limb VAS intensity ≥5 out of 10 cm

• Major exclusion criteria
  – Mononeuropathy or neuropathies of the trunk
  – Failed prior SCS trials for chronic intractable pain

Galan, V. et al., Pain Management, 2020
SENZA-PPN: 12 Month Results

- **Adverse & Severe Adverse Events**
  - 4 procedure related events
  - All resolved

- **No neurological deficits**

- **12/25 (48%)** subjects had neurological improvement by the end of trial
  - Sensory improvement (N: 11)
  - Motor improvement (N: 1)
  - Reflex improvement (N: 1)
SENZA-PDN Study

- Painful diabetic neuropathy in patients with refractory symptoms
- Failed at least gabapentinoid and one other class of approved medication
- HbA1c < 10%, BMI < 45
- 18 US centers randomized 216 subjects 1:1
- Crossover at 6 months with 24-month follow-up
- Conventional medical management (CMM) vs. 10 kHz SCS + CMM
- 6-month follow-up published in Jama Neurology April 2021
- 12-month data reported at ADA Meeting, 2021
SENZA-PDN: Randomized Multicenter Controlled Trial

Effect of High-frequency (10-kHz) Spinal Cord Stimulation in Patients With Painful Diabetic Neuropathy
A Randomized Clinical Trial

Erika A. Petersen, MD, Thomas G. Staats, MD, James A. Scowcroft, MD, Elizabeth S. Brooks, PhD, Judith L. White, MD, Shawn M. Silk, MD, Karen Amirdelil, MD, Magen N. Guiguis, MD, Jiyou Xu, MD, PhD, Cong Yu, MD, Ali Nouriz, Denis G. Patterson, MD, Kostandinos C. Tsioufas, MD, Michael J. Ciaravino, DO, Vincent Galar, MD, Richard H. Rundisch, MD, Christopher A. Paul, MD, Neel D. Mehta, MD, Hongwei Chai, MD, Darrick Sayed, MD, Shivanand P. Late, MD, PhD, David J. Dilberzadeh, MD, Khadija A. Sethi, MD, Johnathan H. Gerne, MD, Matthew T. Bennett, MD, Nathan J. Harrison, MD, Abi F. Ireland, MD, Paul Chang, MD, Paul W. Wu, MD, Gemmau Gehrli, MD, Charles E. Argoff, MD, Christian E. Naser, MD, Rod S. Taylor, PhD, Joyakumar Subbaraman, PhD, Bradford E. Gilmer, MS, David L. Carraway, MD, PhD, Nagy A. Mehal, MD, PhD

# SENZA-PDN: Patient Demographic

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

*Effect size index (Cohen’s d): ≥ 0.20 = small
≥ 0.50 = medium
≥ 0.80 = large
SENZA-PDN: 6-Month Results

Primary Endpoint met at 6 months

10kHz SCS + CMM Arm Results

- 85% had ≥ 50% Pain Relief
- Average 76% Pain Relief
- 62% reported neurological improvements
  - Numbness
  - Burning
  - Tingling

Petersen, E. et al., JAMA Neurology, 2021

![Proportion of responders](chart.png)

- CMM (n = 93) 5%
- 10 kHz SCS + CMM (n = 87) 85%

p < 0.001
**SENZA-PDN: VAS Over 6 Months**

![Graph showing average pain scores over 6 months](image)

- **Baseline**: CMM (n = 93) - 7.0
  - 10 kHz SCS + CMM (n = 87) - 7.0

- **3 Months**: CMM (n = 93) - 6.7
  - 10 kHz SCS + CMM (n = 87) - 6.5

- **6 Months**: CMM (n = 93) - 6.9
  - 10 kHz SCS + CMM (n = 87) - 1.7

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Petersen, E. et al., JAMA Neurology, 2021
SENZA-PDN: Responders and Remitters

Petersen, E. et al., JAMA Neurology, 2021

5% responders (n = 5/93)
1% remitters
VAS ≤ 3cm: 5%

-2% average pain relief

85% responders (n = 74/87, p < 0.001)
60% remitters (p < 0.001)
VAS ≤ 3cm: 86%

76% average pain relief

Improvement from baseline pain VAS

CMM

10 kHz SCS + CMM

Remission defined as pain VAS ≤ 3.0 cm for 6 consecutive months
SENZA-PDN: QoL and Health Economics

EQ-5D-5L
- Mean 16-point improvement with SCS

Opioid Reduction
- Decreased or eliminated: 23% vs 8%
- Increased: 2% vs 11%

Reduced Hospital & ED Visits
- Over 6 months, 7 fewer visits per 100 patients in the 10 kHz SCS group
SENZA-PDN: Neurological Improvement

Neurological examination:
✓ Lower limb motor strength
✓ Light touch sensation L1-S1
✓ Reflexes: patellar, Achilles, Babinski
✓ 10-point foot assessment
  • pinprick
  • 10-g monofilament

Petersen, E. et al., JAMA Neurology, 2021
SENZA-PDN: Challenging Patient Population

- 2 of 90 permanent implants were explanted due to infection (2.2%)

Reported SCS infection rates:
- 2.45% (Hoelzer et al. 2017)
- 2.5% (PDN RCT, de Vos et al. 2014)
- 3.4% (Kumar et al. 2006)
- 4.5% (Mekhail et al. 2011)
- 4.5% (PDN RCT, Slangen et al. 2014)
- 8.9% (Diabetes cohort, Mekhail et al. 2011)
Summary

• 1 in 10 Americans suffer from chronic pain
• Opioid epidemic: was the #1 health crisis in America
• 34+ Million Americans with diabetes, 1 out of 5 do not know
• 88 Million Americans have pre-diabetes
• 7 Million diabetic patients suffer from PDN
• Conventional medical management of PDN is ineffective
• Recent level 1 evidence for:
  • Capsaicin 8% patch
  • 1kHz spinal cord stimulation
Thank You!