PainWeek®

Evidenced-Based Rationale for Interventional Procedures: Alternative to Medication Management

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Title & Affiliation

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Disclosure

- Consultant/Independent Contractor: Abbott, Biotronik, Boston Scientific, Nalu, Nevro, Saluda, SI-Bone, Vertos
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- Advisory Board: BiotrasStock
- Shareholder: Nalu

Learning Objectives

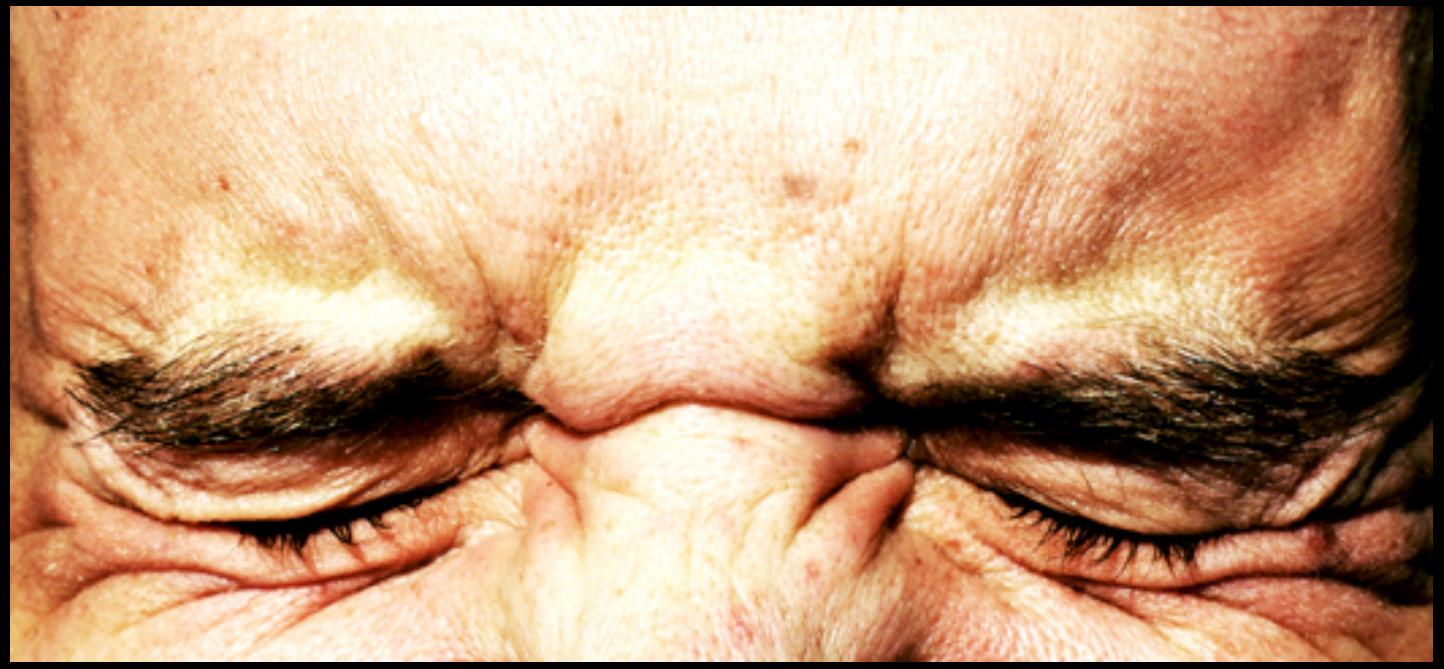
- Review history of analgesia
- Discuss the impact of chronic pain
- Describe the evolution of opioid therapy
- Highlight current and future application of technology in treating chronic pain
- Review supporting evidence

Outline

- Chronic pain
- History of analgesia
- Evolution of pain opioid therapy
- Technologies in treating chronic pain
  - Neuromodulation
  - Peripheral nerve stimulation
  - Vagal nerve stimulation
  - Minimally invasive spinal interventions
- Evidence review in opioid reduction
- Explore the latest clinical trials

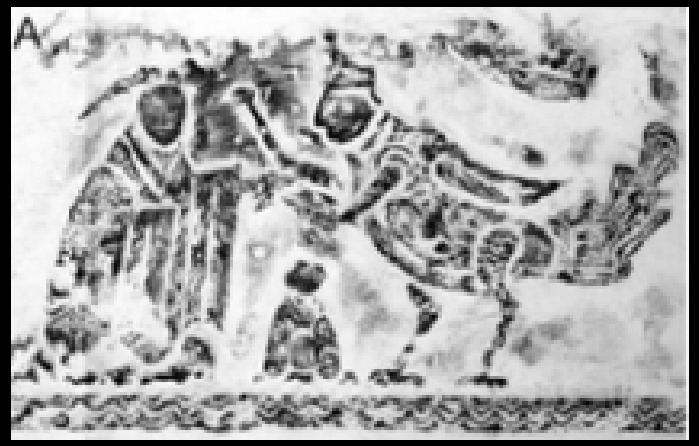
Pain

- “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage...”



Raja, S. el al. IASP Task Force on Taxonomy; Pain, 2020

Ancient Pain Management



Auricular acupuncture depicted during Han dynasty, 200 BC

Cauterizing the external ear to treat migraine, 12th century Persian surgery text

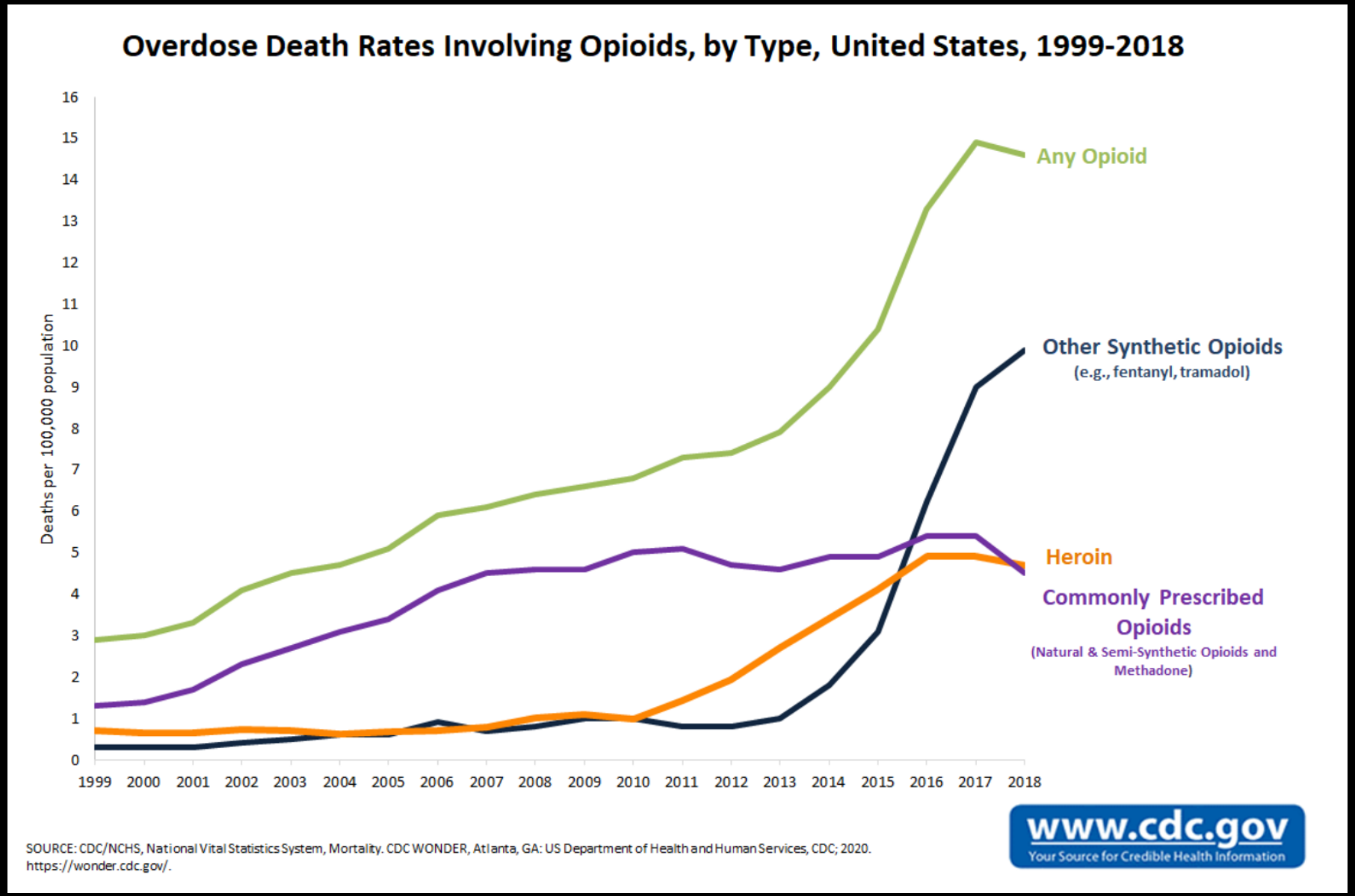
Analgesia

- Sumerians, 3000 B.C. who first cultivated the poppy plant for its opium
- Homer in 300 B.C. Helen of Troy to treat her grief over the absence of Odysseus

Opioid Problem is Not New

- 1849, Mrs. Charlotte Winslow, Bangor, Maine
- 65 mg morphine per ounce
- “sooth any human or animal…effectively quieted restless infants and small children, especially for teething”

https://en.wikipedia.org/wiki/Mrs._Winslow%27s_Soothing_Syrup

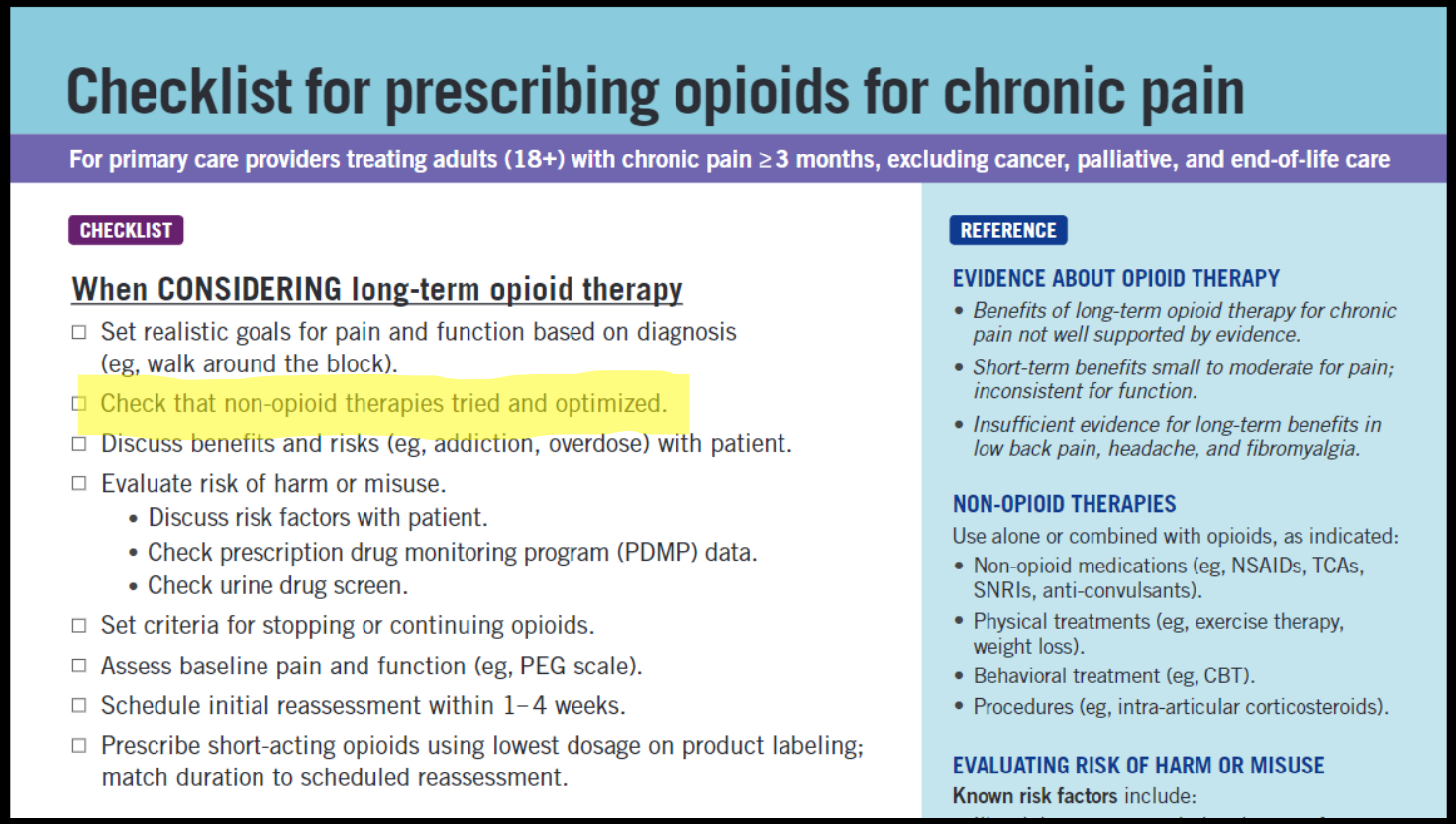


Center for Disease Control (CDC): http://www.cdc.gov

Evolution of Opioid therapy

- Lack of long-term efficacy for treating chronic pain
- Risk for tolerance, dependency, and abuse
- National opioid crisis
- New CDC opioid prescribing guidelines

CDC Guidelines for Chronic Opioids



Checklist for prescribing opioids for chronic pain

For primary care providers treating adults (18+) with chronic pain ≥3 months, excluding cancer, palliative, and end-of-life care

CHECKLIST

When CONSIDERING long-term opioid therapy

- ☐ Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- ☐ Check that non-opioid therapies tried and optimized.
- ☐ Discuss benefits and risks (eg, addiction, overdose) with patient.
- ☐ Evaluate risk of harm or misuse.
  - Discuss risk factors with patient.
  - Check prescription drug monitoring program (PDMP) data.
  - Check urine drug screen.
- ☐ Set criteria for stopping or continuing opioids.
- ☐ Assess baseline pain and function (eg, PEG scale).
- ☐ Schedule initial reassessment within 1–4 weeks.
- ☐ Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

REFERENCE

EVIDENCE ABOUT OPIOID THERAPY

- *Benefits of long-term opioid therapy for chronic pain not well supported by evidence.*
- *Short-term benefits small to moderate for pain; inconsistent for function.*
- *Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.*

NON-OPIOID THERAPIES

Use alone or combined with opioids, as indicated:

- Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (eg, exercise therapy, weight loss).
- Behavioral treatment (eg, CBT).
- Procedures (eg, intra-articular corticosteroids).

EVALUATING RISK OF HARM OR MISUSE

Known risk factors include:

https://stacks.cdc.gov/view/cdc/38025

Chronic Pain in America

- 1 in 5 Americans suffer from chronic pain
- Large economic impact: ~$600 billion/year
- Loss of productivity: ~$300 billion/year
- Opioid epidemic: #1 health crisis in America
- National health survey by NIH 2012
  - 50 million adults experience pain every day
  - Pain→ worse overall health status
  - Female, elderly, non-Hispanics (Asians less likely)

A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients.
http://jama.ama-assn.org/cgi/content/abstract/274/20/1591

Emergence of Electroceuticals

- Bioelectronics
- Therapeutic devices
- External or implanted
- Delivering electricity
- Neuromodulation
- Alter disease states
- Market prediction of $35.5 billion global market by 20252

1. Kristoffer Framm, Nature, 2013
2. https://www.grandviewresearch.com/press-release/global-electroceuticals-bioelectric-medicine-market

Innovations in Neuromodulation

- Adaptive stimulation
- MRI compatibility
- Novel wave forms and targets of stimulation
- *Closed loop technology (not FDA approved)*
- *High frequency spinal cord stimulation*
- *Peripheral nerve stimulation*
- *Vagal nerve stimulation*
- Microdose intrathecal drug delivery

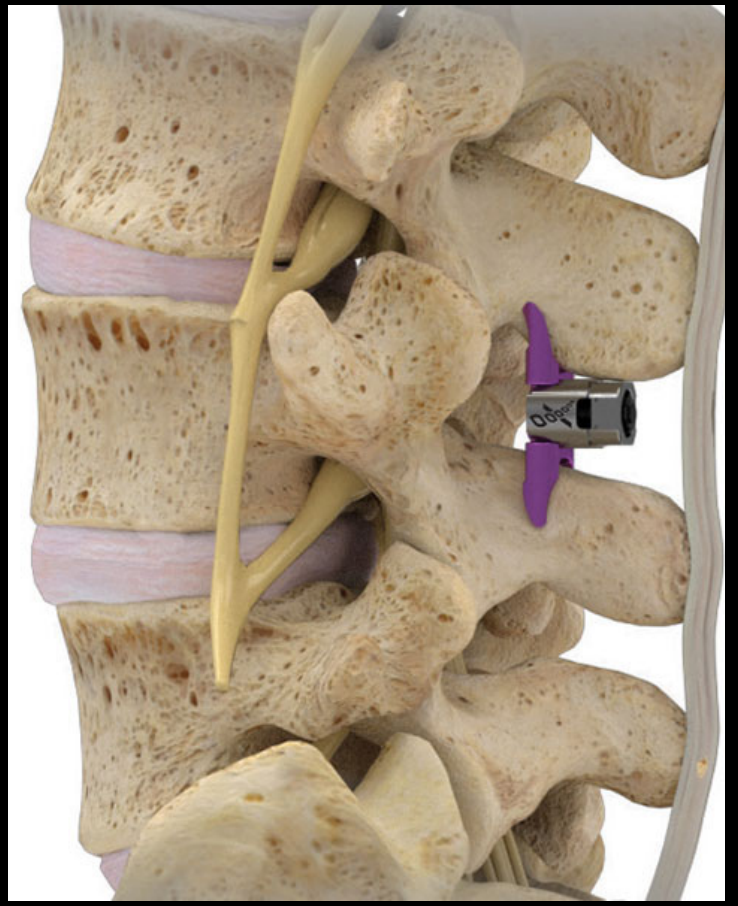
Indications for Neuromodulation Therapy

- SCS: Chronic refractory neuropathic pain of the trunk and limb
- PNS: Focal refractory neuropathic pain

- Examples:
  - FBSS
  - CRPS
  - Peripheral mononeuropathy
  - Post-amputation pain
  - DPN
  - Non-surgical back pain
  - Headache

Emerging Treatment Options in IPM

- *Closed loop stimulation (not FDA approved)*
- *Non-invasive vagal nerve stimulation*
- *Peripheral nerve stimulation*
- *Minimally invasive lumbar decompression*
- *Interspinous decompression*
- *Sacroiliac joint fusion*
- Endoscopic discectomy
- Basovertebral nerve ablation
- Regenerative medicine



#1 Reason for SCS Failure: Loss of Therapeutic Effect

Neuromodulation: Technology at the Neural Interface

Received: March 10, 2017 Revised: April 23, 2017 Accepted: May 20, 2017

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12634

Multicenter Retrospective Study of Neurostimulation With Exit of Therapy by Explant

Jason E. Pope, MD*; Timothy R. Deer, MD†; Steven Falowski, MD‡; David Provenzano, MD§; Michael Hanes, MD¶; Salim M. Hayek, MD, PhD¶;

Neuromodulation: Technology at the Neural Interface

Received: April 19, 2017 Revised: June 2, 2017 Accepted: June 13, 2017

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12642

Therapy-Related Explants After Spinal Cord Stimulation: Results of an International Retrospective Chart Review Study

Jean-Pierre Van Buyten, MD, PhD*; Frank Wille, MD†‡; Iris Smet, MD*;

ORIGINAL ARTICLE

Spinal Cord Stimulator Explantation: Motives for Removal of Surgically Placed Paddle Systems

Derrick A. Dupré, MD; Nestor Tomycz, MD; Donald Whiting, MD;

- 352, explanted, 2011-2016
- 18 centers
- 43.9% (152/346) for lack/loss of efficacy

- 2010-2013
- 955 patients implanted
- 180 were explanted
- 52% (94/180) explanted for inadequate pain relief

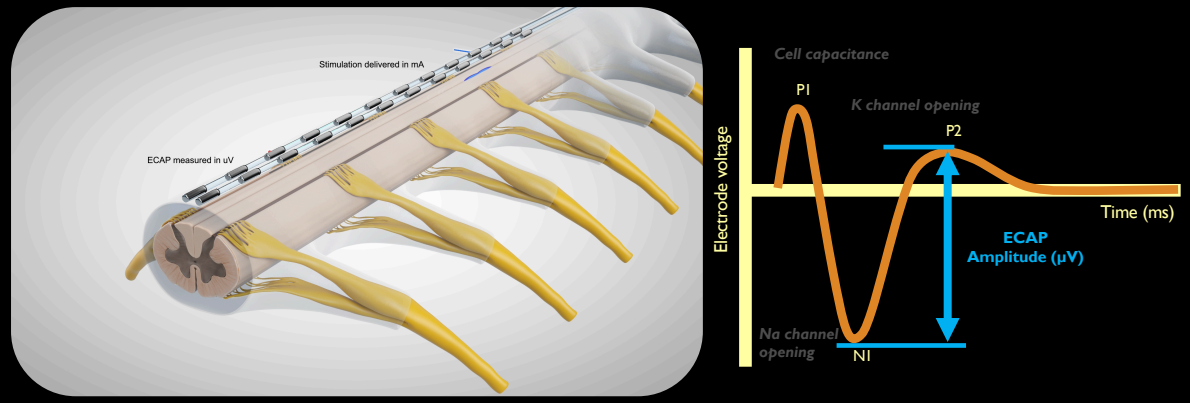
- 595 paddle implants
- 1997-2014
- 165 were explanted
- 73% (121/165) for inadequate pain relief

1. *Pope et al. Neuromodulation. 2017;20(6):543-552.*
2. *Van Buyten et al. Neuromodulation. 2017;20(7):642-649.*
3. *Dupre et al. Pain Pract. 2018;18(4):500-504.*

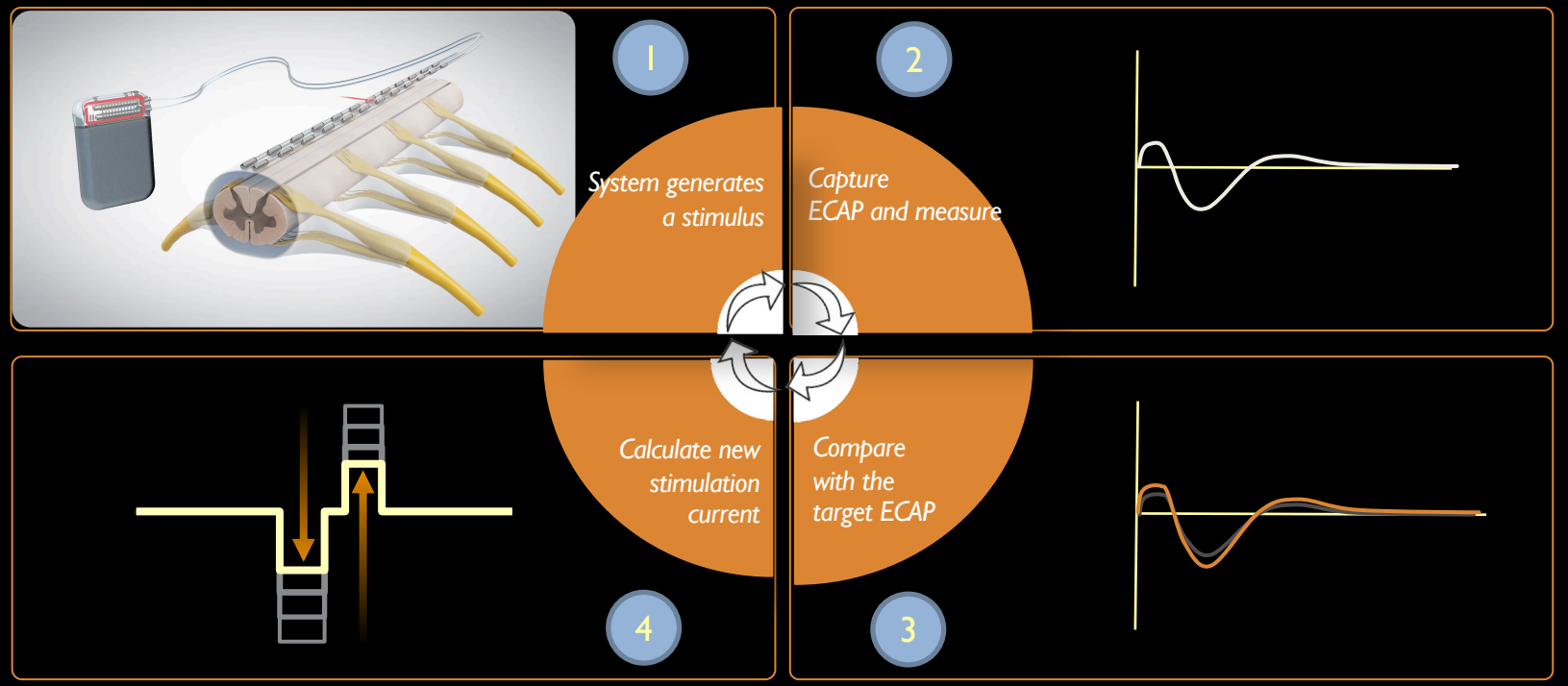
What is an ECAP?

- *Evoked Compound Action Potentials (ECAPs) are the sum of the electrophysiological response from multiple nerve fibers*

- *ECAPs provide insight into the type of fibers stimulated and are a measure of spinal cord (SC) activation*



Closed-Loop Stimulation



Closed-Loop SCS results in millions of stimulation output changes per day

Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial

*Nagy Mekhail, Robert M Levy, Timothy R Deer, Leonardo Kapural, Sean Li, Kasra Amirdelfan, Corey W Hunter, Steven M Rosen, Shrif J Costandi, Steven M Falowski, Abram H Burgher, Jason E Pope, Christopher A Gilmore, Farooq A Qureshi, Peter S Staats, James Scowcroft, Jonathan Carlson, Christopher K Kim, Michael I Yang, Thomas Stauss, Lawrence Poree, on behalf of the Evoke Study Group**

Summary

Background Spinal cord stimulation has been an established treatment for chronic back and leg pain for more than 50 years; however, outcomes are variable and unpredictable, and objective evidence of the mechanism of action is needed. A novel spinal cord stimulation system provides the first in vivo, real-time, continuous objective measure of spinal cord activation in response to therapy via recorded evoked compound action potentials (ECAPs) in patients during daily use. These ECAPs are also used to optimise programming and deliver closed-loop spinal cord stimulation by adjusting the stimulation current to maintain activation within patients' therapeutic window. We aimed to examine pain relief and the extent of spinal cord activation with ECAP-controlled closed-loop versus fixed-output, open-loop spinal cord stimulation for the treatment of chronic back and leg pain.

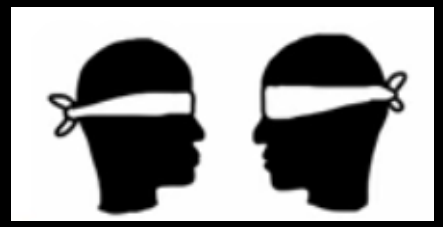
Lancet Neurol 2019

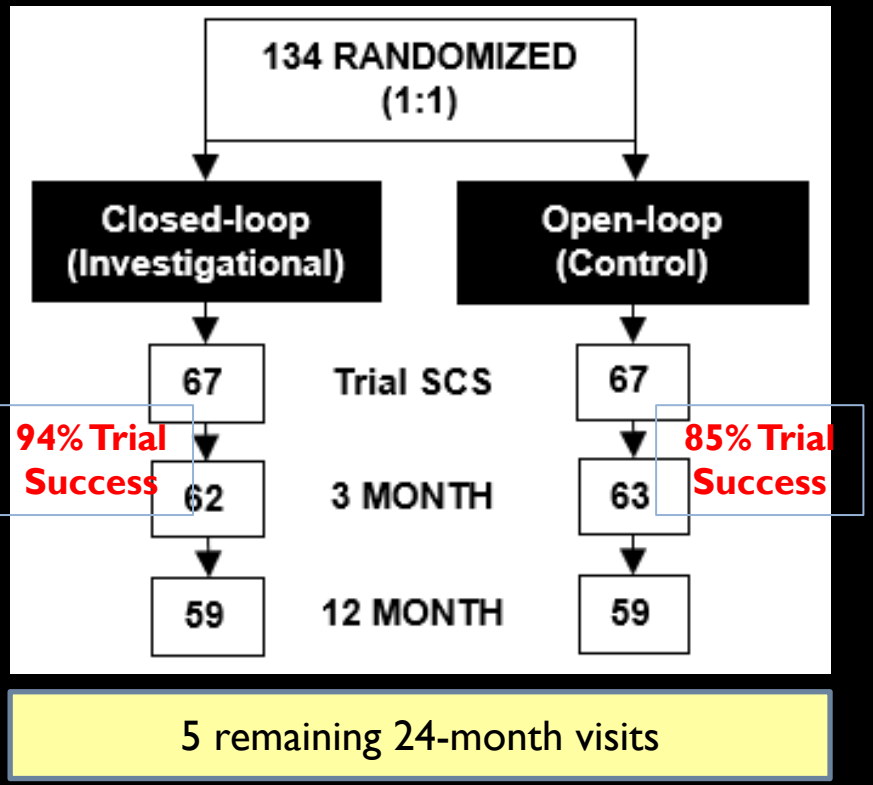
Published Online
December 20, 2019
https://doi.org/10.1016/S1474-4422(19)30414-4

See Online/Comment
https://doi.org/10.1016/S1474-4422(19)30484-3

*Members of the Evoke Study

Evoke Study: Double-Blinded RCT





KEY STUDY POINTS

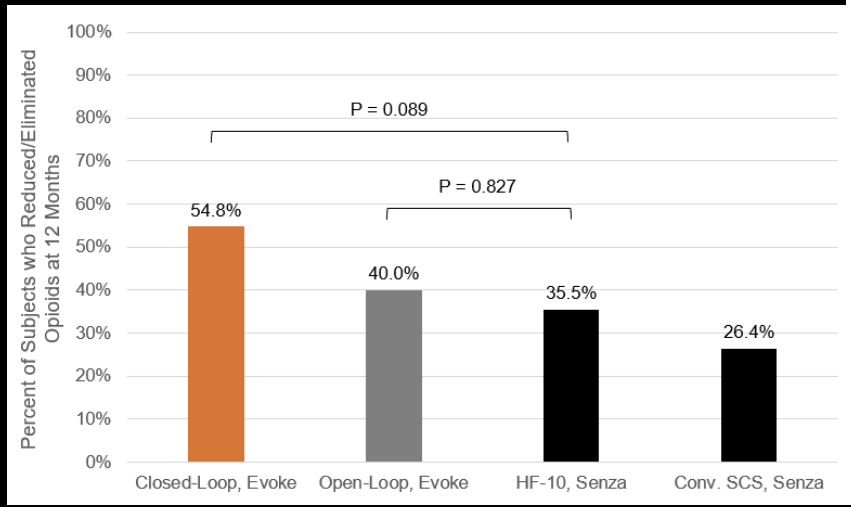
- Multicenter, parallel arm, **double-blinded**
  - 1st double blind approval study in SCS
- Blinding has been **maintained.**
  - Blinding out to **36 months**
- **Overall** back and leg pain reduction (vs. just a region such as back, or foot)
- Difficult patient population in terms of pain chronicity:
  - **>11 years of chronic pain**

89.1%

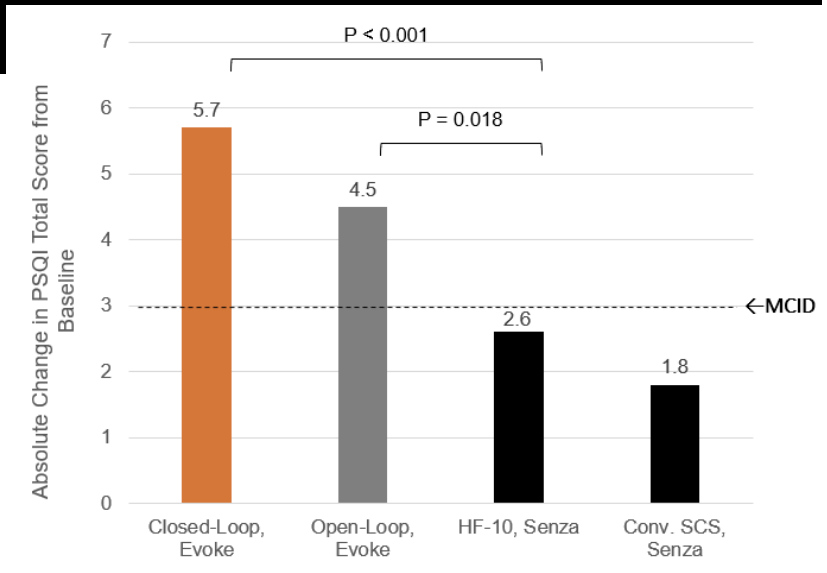
of Evoke Study **closed-loop subjects** were **responders** in overall back and leg pain in the **permanent implant set** (PIS) **at 12 months** and **superior** to open-loop

Beyond the VAS Score: Secondary Outcomes Comparison to Recent Literature at 12 Months

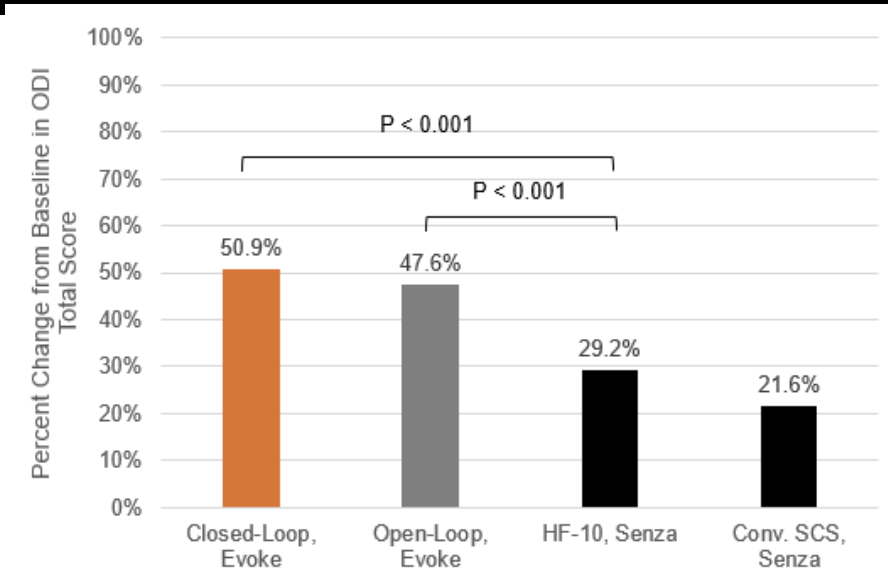
50% more closed-loop patients reduced or eliminated opioids compared Senza



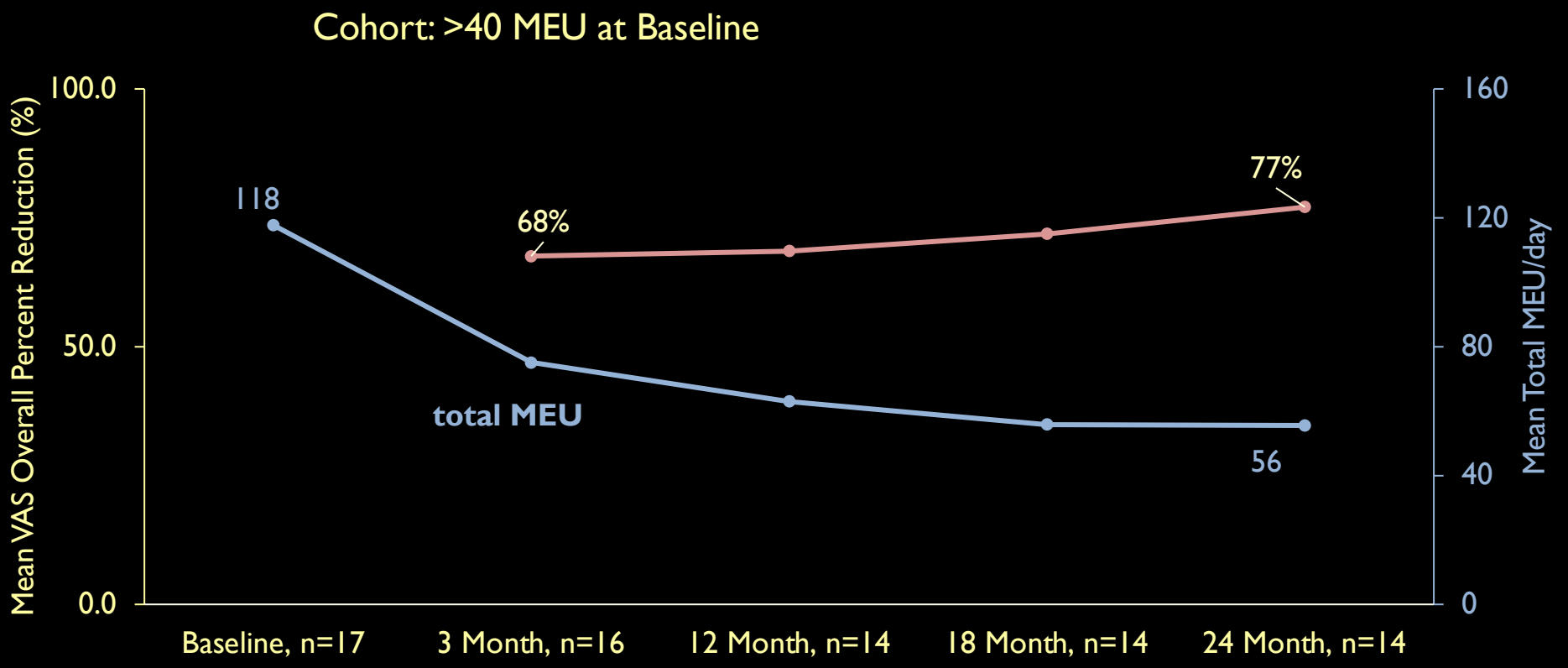
Closed-loop patients sleep 1.3 hours more per day



74% improvement in closed-loop disability compared to Senza

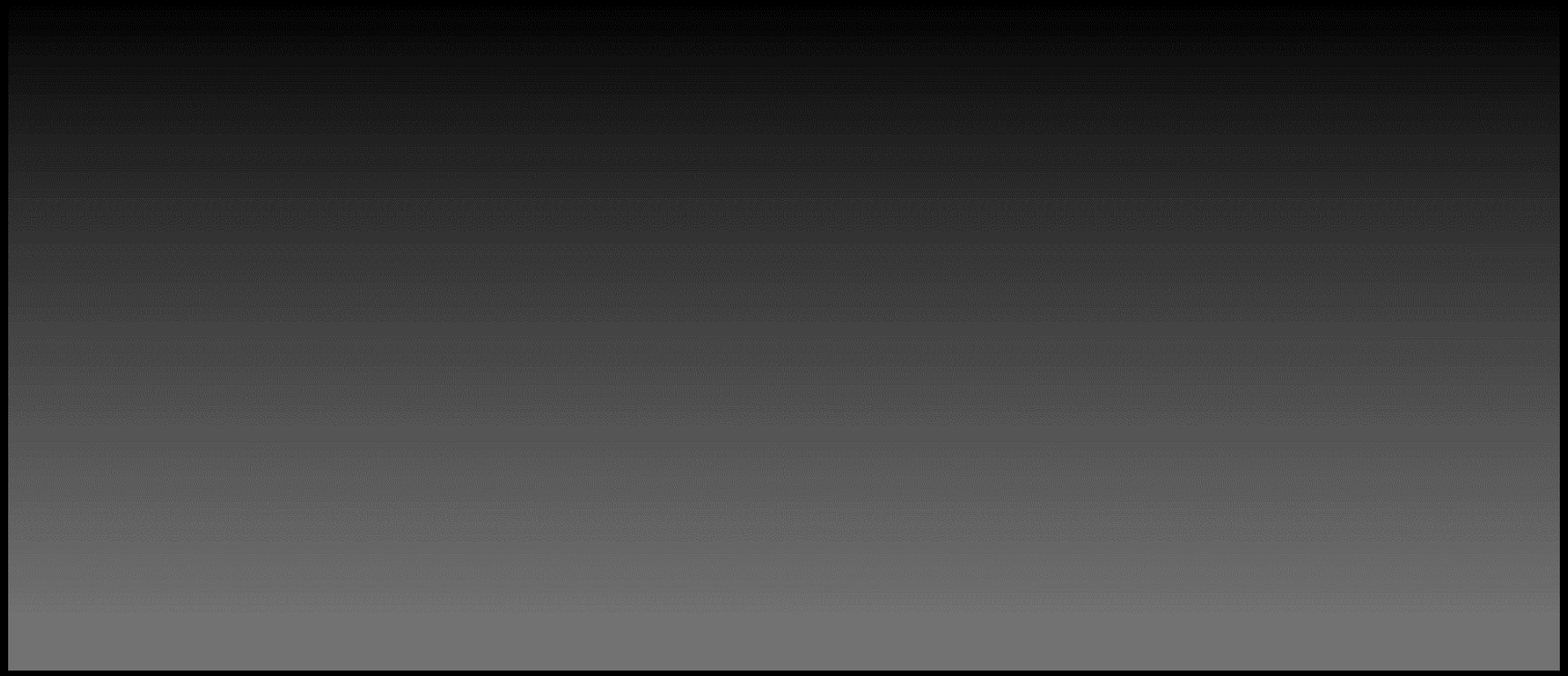


Patients who were on high doses of opioids at baseline reduced their MEUs by half and increased pain relief



Avalon 24-month Study Results, Neurosurgery, 2020

Closed-Loop Stimulation



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Courtesy of Saluda Medical

Challenges and Unmet Needs for PPN/PDN Patients

- Current treatment options often provide insufficient pain relief
- Medications for neuropathic pain can have significant side effects
- Chronic opioid therapy (oral, transdermal, and intrathecal)
- 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 dysesthesias due to confounding presence of paresthesia

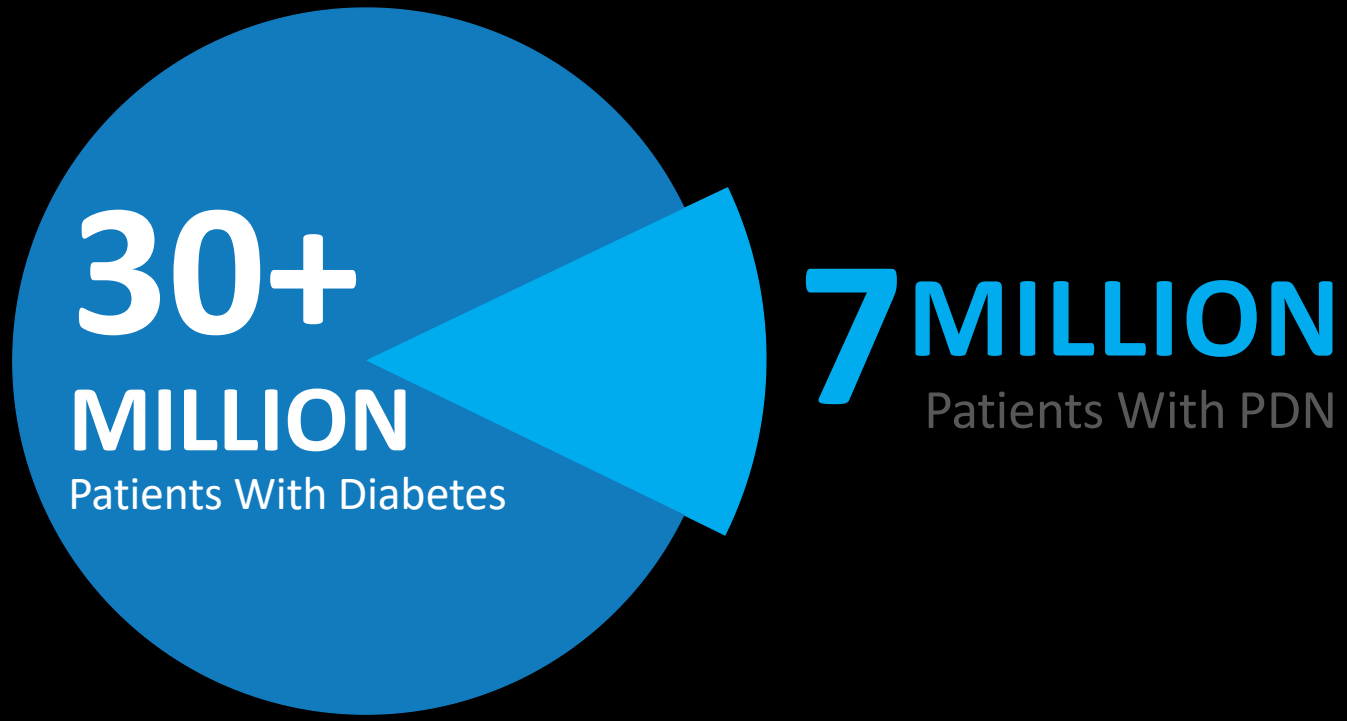
Disease Prevalence and Cost

Diabetes is a National Epidemic

- 30.2 million people with diabetes = 9.3% of the population
- Another 86 million people are pre-diabetic (more than 1 in 3 people)
- Costs: $245 billion
  - Direct medical costs = $176 billion
  - Indirect costs = $69 billion

Painful Diabetic Neuropathy is Common

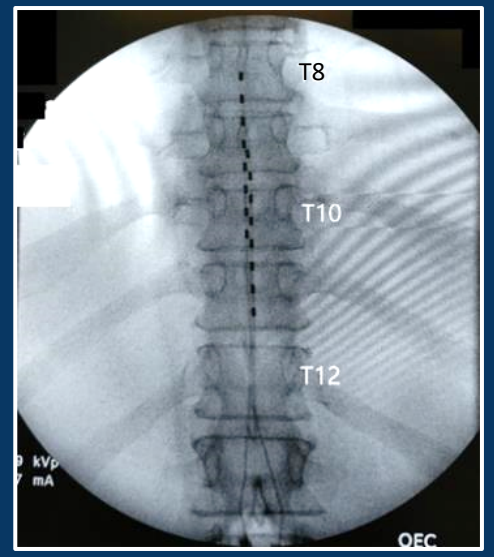
- 20% to 26% of those with diabetes have PDN

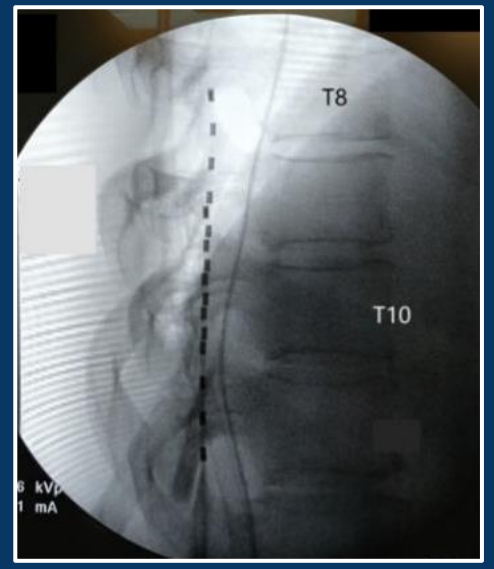


CDC National Diabetes Statistics Report, 2014; Davies M et al. Diabetes Care 2006; Schmader KE. Clin J Pain 2002

SENZA-DPN Study

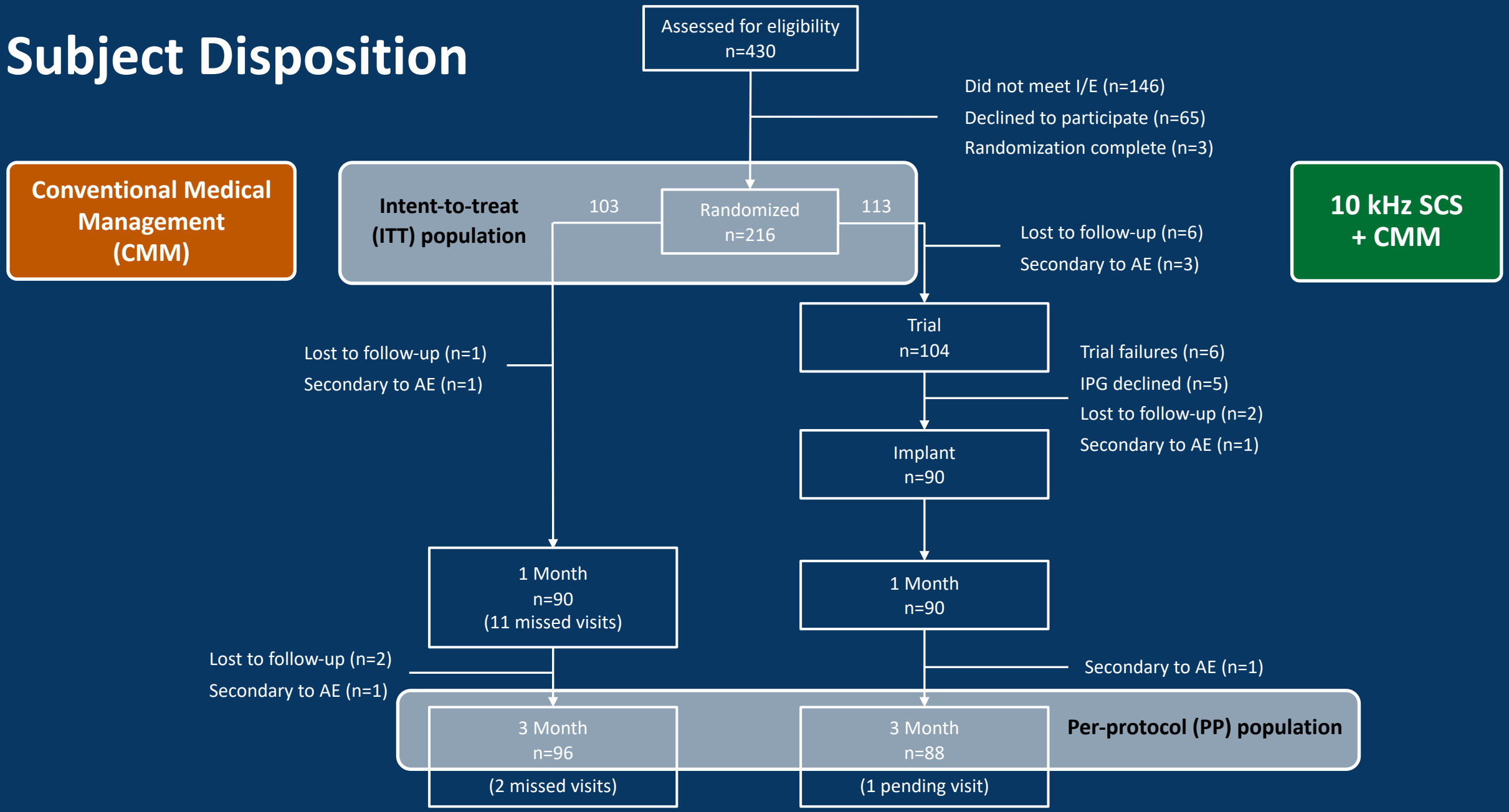
- Painful diabetic neuropathy (PDN) of the lower limbs in patients refractory to conservative treatments
- ≥ 5 of 10 cm on pain VAS, HbA1c < 10%, BMI < 45
- 18 US centers
- Independent Medical Monitors reviewed all subjects
- 216 subjects randomized 1:1 to CMM alone vs. CMM + 10 kHz SCS (Nevro Corp.)
- SCS subjects: At least 50% pain relief during trial stimulation required for implant
- 3-month follow-up assessing
  - Pain
  - Quality of life
  - Neurological function
    - Including diabetic foot exam w/ Semmes-Weinstein 10g monofilament and 40g pinprick tests





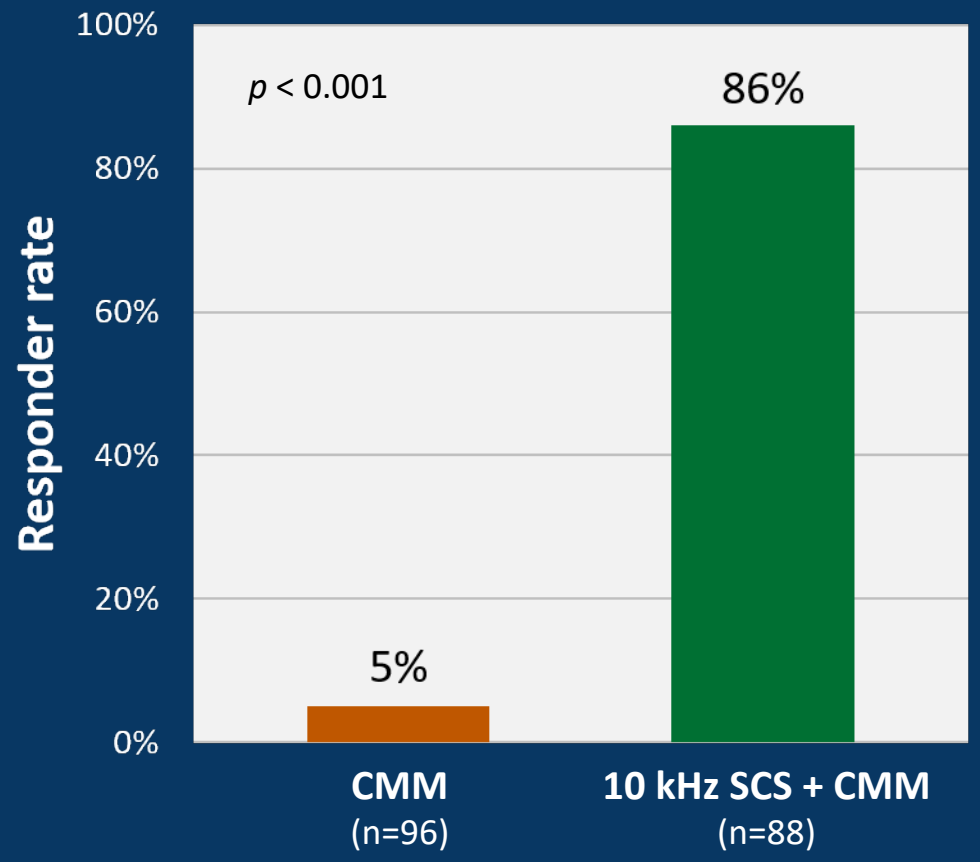
Mekhail et al. *Trials* 2020

Subject Disposition



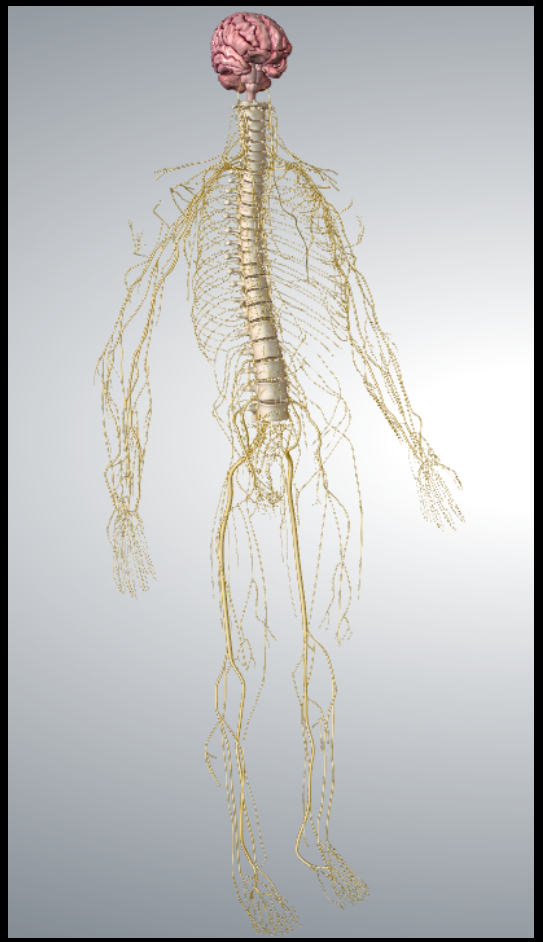
Primary Endpoint Analysis: Per-Protocol Population

- Primary endpoint is a composite of safety & effectiveness at 3 months
  - compare responders (≥ 50% pain relief) without a worsening neurological deficit from baseline
- ITT analysis consistent with PP analysis, significant difference between groups
- Study follow-up will continue for 24 months total with evaluation of health economics and pain medication usage

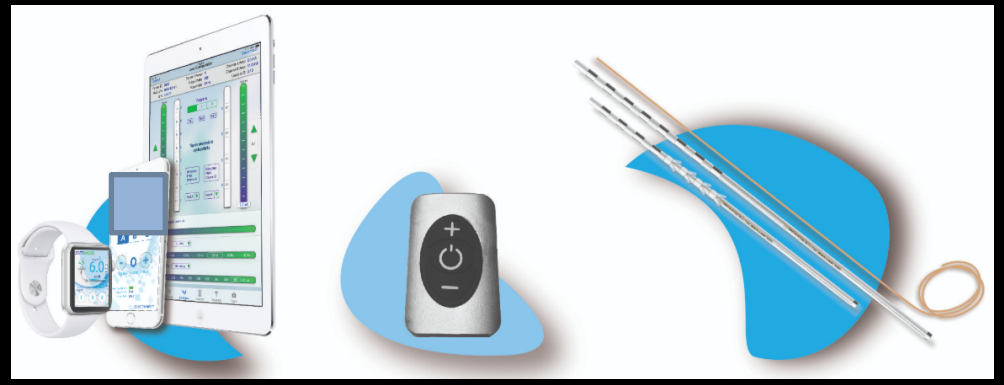


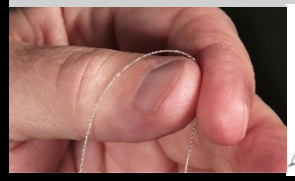
Peripheral Nerve Stimulation

- Form of neuromodulation
- Therapeutic modulation of peripheral nervous system via electricity
- Direct PNS
- Peripheral nerve field stim (PNFS)
- Teaching “old dog” new tricks



PNS: Commercially Available Systems





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PNS: Described Indications

- Post-herpetic neuralgia
- Post-traumatic or surgical neuralgia
- Migraine headache
- Occipital neuralgia
- Complex regional pain syndrome (CRPS)
- Cluster headache
- Post-herniorrhaphy pain
- Coccydynia
- Fibromyalgia?

Neurotherapeutics. 2008;5:100-106

PNS for Chronic Low Back Pain

Reductions in Opioid Consumption with Percutaneous Medial Branch Peripheral Nerve Stimulation for Chronic Low Back Pain

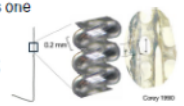
Steven Cohen, MD[1], Christopher Gilmore, MD[2], Leonardo Kapural, MD, PhD[2], Thomas Hopkins MD, MBA[3], Mehul Desai, MD, MPH[4], Michael DePalma, MD[5], Sean Li, MD[6], Abram Burgher, MD[7], Timothy Deer, MD[8], Anthony Plunkett, MD[9], Meredith McGee, PhD[10], Joseph Boggs, PhD[10]

[1] Walter Reed National Military Medical Center, [2] Center for Clinical Research, [3] Duke University, [4] International Spine, Pain and Performance Center, [5] Virginia iSpine Physicians, [6] Premier Pain Centers, [7] Hope Research Institute, [8] The Spine and Nerve Center of The Virginias, [9] Womack Army Medical Center, [10] SPR Therapeutics, Inc.

INTRODUCTION

- Chronic low back pain (LBP) is one of the most prevalent and challenging musculoskeletal conditions[1] and is the leading cause of disability in adults.

MINIMALLY INVASIVE, PERCUTANEOUS PNS:



- Wearable stimulator and percutaneous fine-wire, coiled lead (designed to anchor in tissue with excellent safety profile[2]) could overcome limitations of previous systems

CONVENTIONAL NEUROMODULATION:

- Requires surgery and permanent implant
- Cost may relegate therapy to use later in the treatment continuum

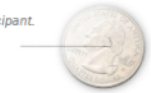
Goal: Evaluate feasibility of 60-day percutaneous PNS to reduce opioid use in patients with chronic LBP.

MATERIALS & METHODS

Ongoing IRB approved study; informed consent was obtained from each participant.

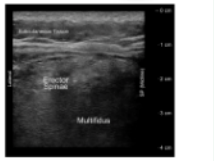
Key Eligibility Criteria:

- Participants with chronic LBP (≥ 3 months); no radicular pain
- Stable medication usage at least 1 month prior to baseline
- No prior lumbar surgery or RFA within prior 6 months
- No anesthetic injections within prior 3 months
- Score of ≤ 20 on Beck Depression Inventory



Lead Placement: Bilateral, percutaneous PNS leads, targeting medial branches of the dorsal ramus in the center of the region of pain

- *Image Guidance:* ultrasound and/or fluoroscopy
- *Confirmation:* Stimulation of medial branch confirmed by selective activation of multifidi



PNS Treatment: Stimulation for 6-12 hrs/day for up to 60 days

- Participants continued normal activities
- Leads removed with gentle traction
- Participants return for long-term follow-up visits

Figure Abbreviations: Dorsal Ramus (DR), Iliocostalis (IL), Lamina (L), Longissimus (LS), Medial Branch (MB), Multifidus (MF), Spinous Process (SP).

RESULTS

Participant Demographics (n = 11):

- Average Age: 60.8 years (40.1 – 82.1)
- Average Baseline Pain Score: 6.3 (BPI-5)
- Average Duration of LBP: 17.0 years
- Spinal Level of Lead Placement: L2 (n=1), L3 (n=1), L4 (n=6), L5 (n=3)

Outcomes:

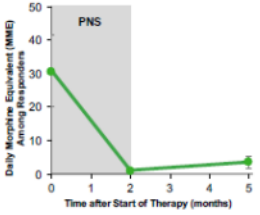
- At End of Treatment (EOT) 64% reported ≥50% reduction in opioid consumption with PNS (n=7/11)
  - *Avg. 29.7 mg morphine equivalent (MME) reduction among responders at EOT*
- At 3 months post EOT, 73% reported ≥50% reduction in opioid (n=8/11)
  - *Avg. 23.1 MME reduction among responders at 3 months post-EOT*
- Majority of participants experienced clinically-significant reductions in average pain intensity, disability, and pain interference.

Safety:

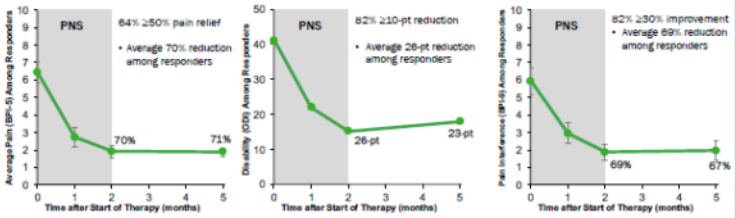
- No serious or unanticipated device-related adverse events

Substantial Reductions in Opioid Analgesic Consumption with PNS:

Participant	Baseline mg Morphine Equivalent (MME)	End of Treatment (EOT)			3-mo Post-EOT		
		MME	MME Reduction from Baseline	% MME Reduction	MME	MME Reduction from Baseline	% MME Reduction
1	80.0	0.0	80.0	100%	0.0	80.0	100%
2	22.1	2.9	19.3	87%	0.0	22.1	100%
3	3.6	0.0	3.6	99%	2.9	0.7	19%
4	13.6	0.0	13.6	100%	6.4	7.1	53%
5	66.4	47.1	19.3	29%	57.8	8.6	13%
6	10.0	9.3	0.7	7%	10.0	0.0	0%
7	3.2	4.3	-1.1	-34%	1.1	2.1	67%
8	1.4	1.4	0.0	0%	0.0	1.4	100%
9	57.9	4.3	53.6	93%	15.0	42.9	74%
10	7.1	0.0	7.1	100%	1.4	5.7	80%
11	31.0	0.5	30.5	98%	5.8	25.2	81%
Average All Participants	26.9	6.3	20.6	62%	9.1	17.8	63%



Clinically Significant[3] Reductions in Average Pain Intensity, Disability, and Pain Interference with PNS:



CONCLUSIONS

- Percutaneous PNS treatment for up to 60 days can significantly reduce usage of opioid analgesic medications in patients with chronic LBP.
- These results support earlier findings that percutaneous PNS delivered for up to 60 days can relieve chronic LBP, which leads to improvement in disability and quality of life, without a permanently implanted device.

REFERENCES & ACKNOWLEDGEMENT

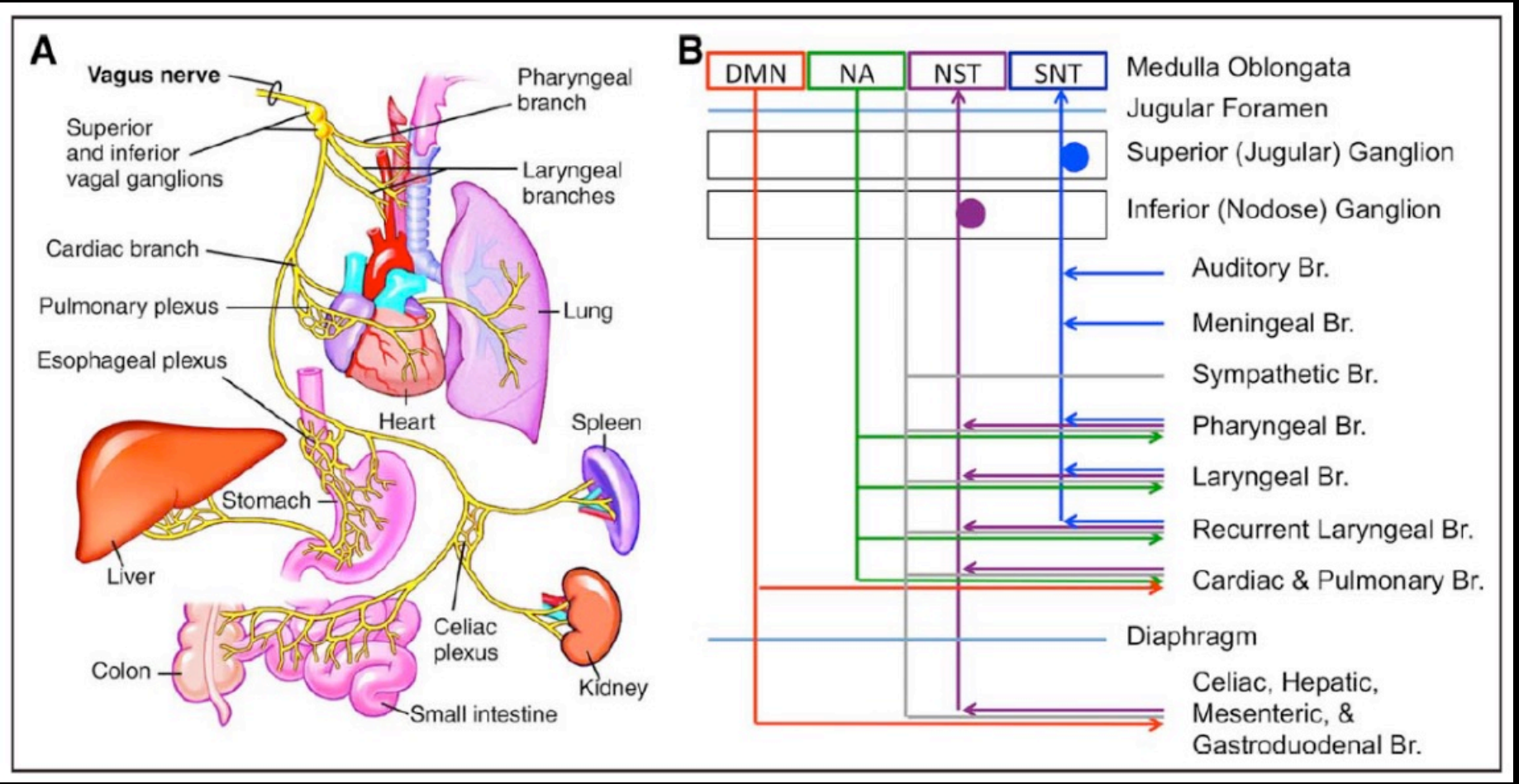
[1] US Burden of Disease Collaborators. The State of US Health, 1990-2010 Burden of Diseases, Injuries, and Risk Factors. *JAMA*. 2013; 310(6):591-606.

[2] Ilfeld et al. "Infection Rates of Electrical Leads Used for Percutaneous Neurostimulation of the Peripheral Nervous System." *Pain Practice* 2016.

[3] Dworkin et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain 2008; 9: 105-121.

Funding: This study was funded by SPR Therapeutics, Inc.

CN X: *the great wandering protector*



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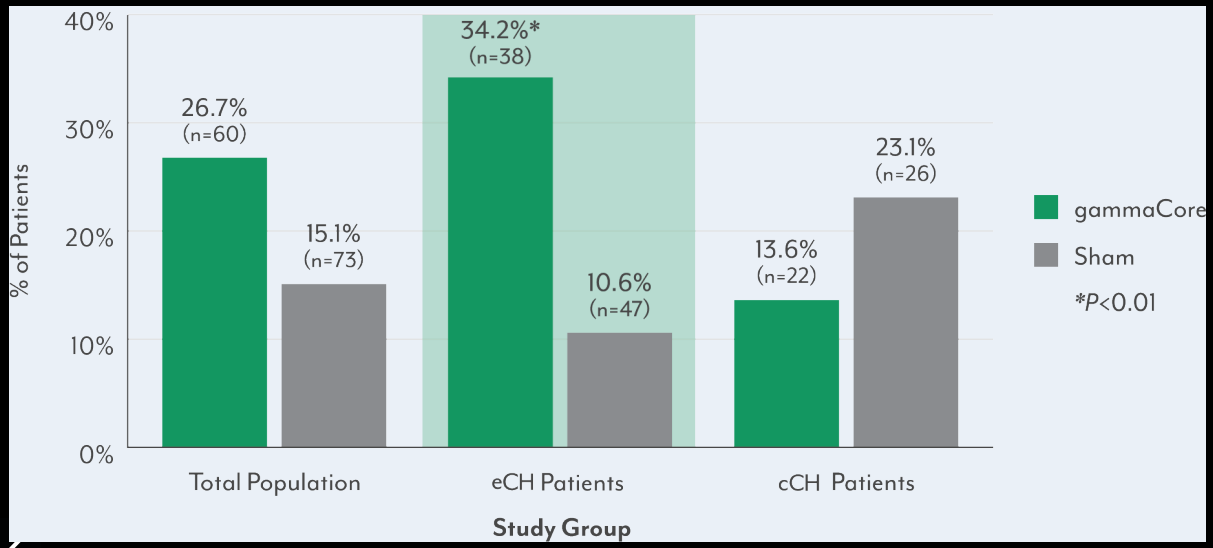
Silberstein et al. Headache, 2015

nVNS for Treating Headache

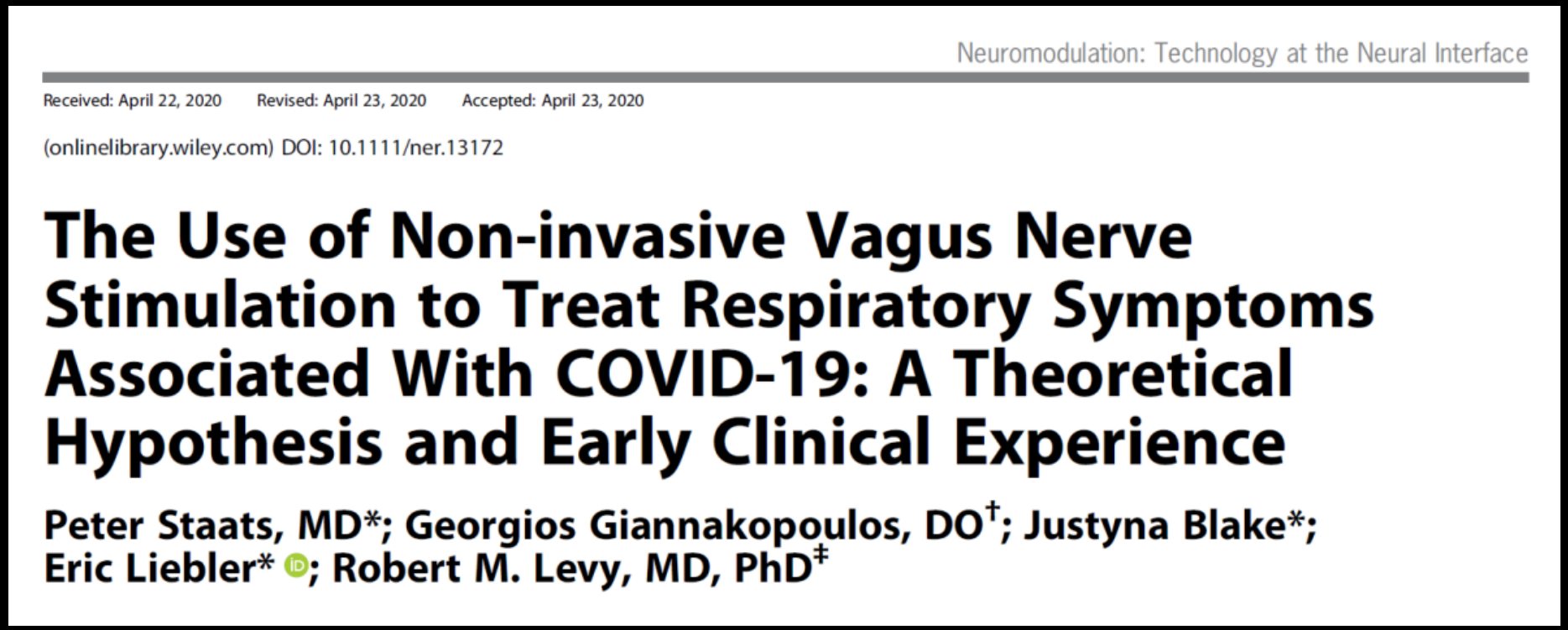
- Migraine HA, 3rd most common disease
- 14.7% prevalence, 2% world affected in the world
- 28 million Americans
- 3:1 female to male ratio
- Cluster HA, 9.8 per 100,000, 1/25 of migraine
- 4:1 male to female ratio
- 2017 FDA approved: episodic cluster HA
- 2018 FDA approved: migraine HA

Vagal Nerve Stimulation

- Non-invasive
- Inhibits cortical spreading depressions
- Suppresses the increase in inflammatory cytokines
- Metered dose device
- FDA approved for cluster and migraine HA



Headache. 2016;56(8):1317-1332.



Neuromodulation: Technology at the Neural Interface

Received: April 22, 2020 Revised: April 23, 2020 Accepted: April 23, 2020

(onlinelibrary.wiley.com) DOI: 10.1111/ner.13172

The Use of Non-invasive Vagus Nerve Stimulation to Treat Respiratory Symptoms Associated With COVID-19: A Theoretical Hypothesis and Early Clinical Experience

Peter Staats, MD*; Georgios Giannakopoulos, DO†; Justyna Blake*; Eric Liebler*; Robert M. Levy, MD, PhD‡

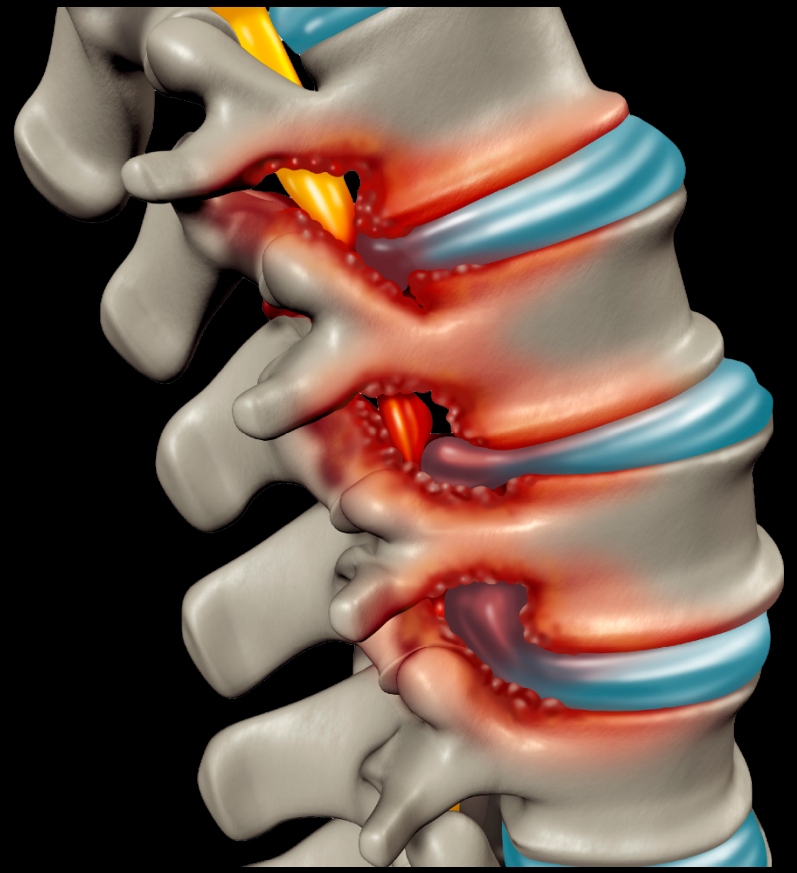
- July 10, 2020
- FDA approved nVNS for emergency use authorization
- COVID-19 related dyspnea and reduced respiratory flow
- Hypothesis: nVNS may suppress the “cytokine storm”

Lumbar Spinal Stenosis (LSS)

- Degenerative condition, 50% with lower back pain
- First described by Sachs and Frankel, 1900
- Clinically description by Henk Verbiest, 1954
- U.S. Social Security Act: LSS as disabling condition

"pseudoclaudication, established by acceptable imaging, manifested by chronic nonradicular pain and weakness, and resulting in inability to ambulate"

- Over $100 billion/year due to reduced productivity

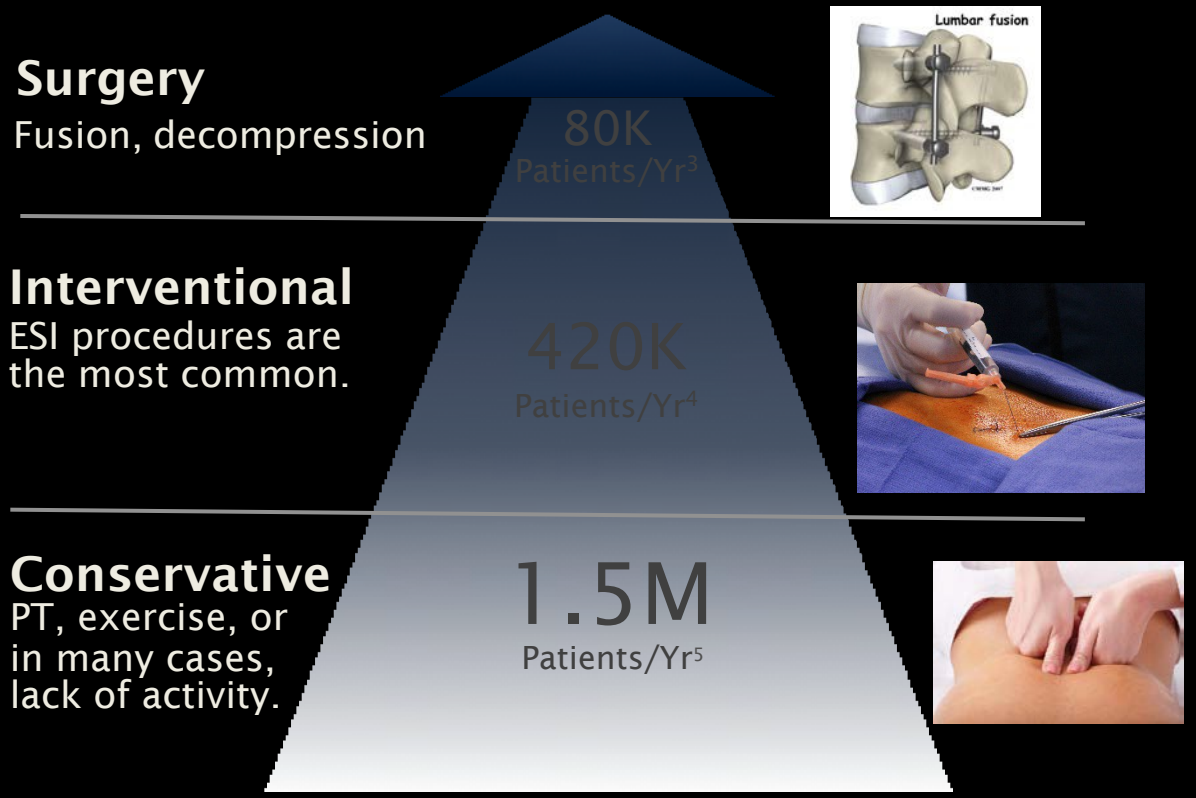


LSS: Prevalence

- Common degenerative spine disorder that affect QOL
- 14 million Americans with symptomatic LSS
- 109,000 diagnosed with LSS per year
- 6% prevalence from 850 myelograms, by De Villiers and Booysen
- Framingham Study, for age 60-69, prevalence up to 47.2%
- Often lead to surgical intervention
- 136 per 100,000 Medicare patients underwent surgery 2002-2007

LSS: Existing Treatment Paradigm

Millions of Patients Seek LSS Treatment Annually



- Many are treated with opioids, physical therapy, serial ESIs or no treatment
- Minimally invasive procedures have expanded interventional pain treatment options

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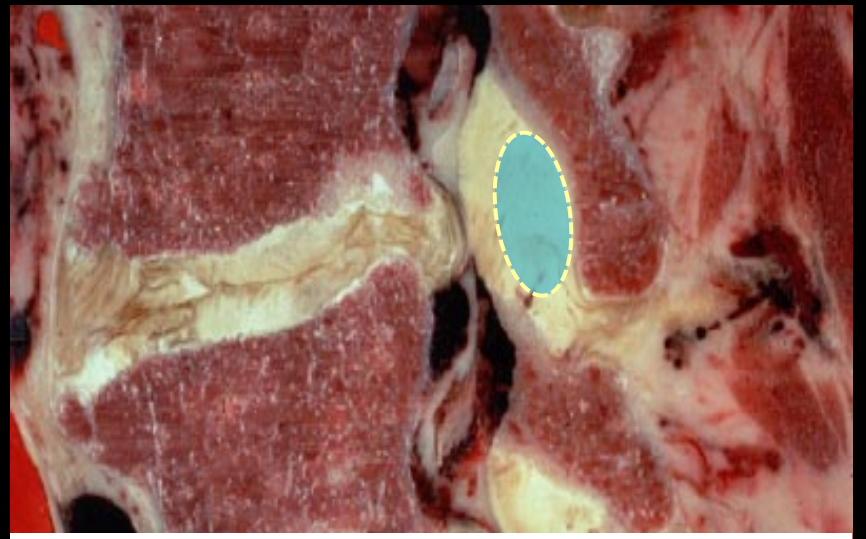
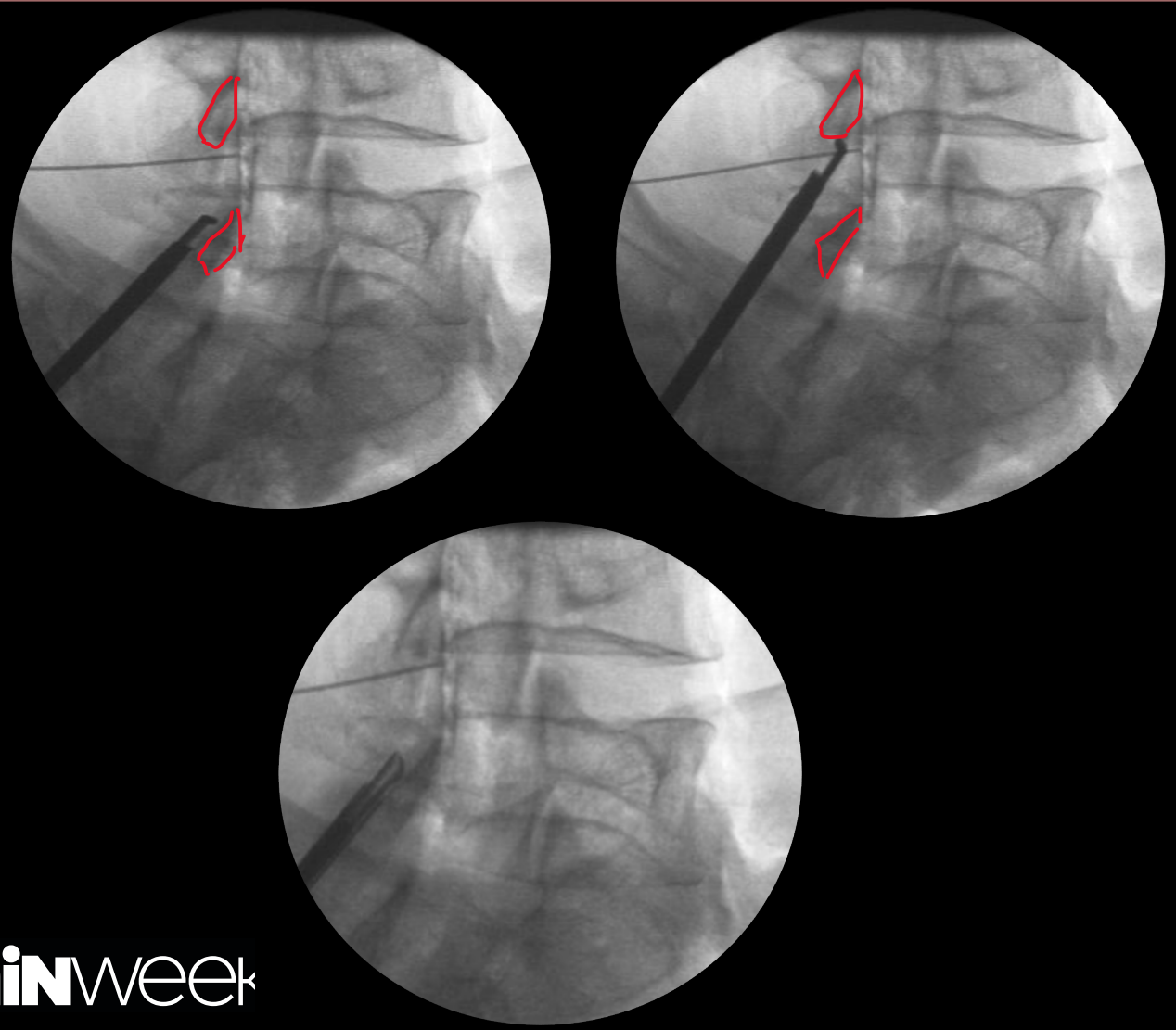
[3]Deyo, Richard A., et al. "Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults." Jama303.13 (2010): 1259-1265 & MTP Report for Vertos Medical 2013.
[4]Laxmaiah, et al. "An updated assessment of utilization of interventional pain management techniques in the Medicare population: 2000–2013." Pain Physician 18.2 (2015): E115-E127 & MTP Report for Vertos Medical 2013.
[5]Estimate based on total LSS Diagnosis HMS and MTP Report for Vertos

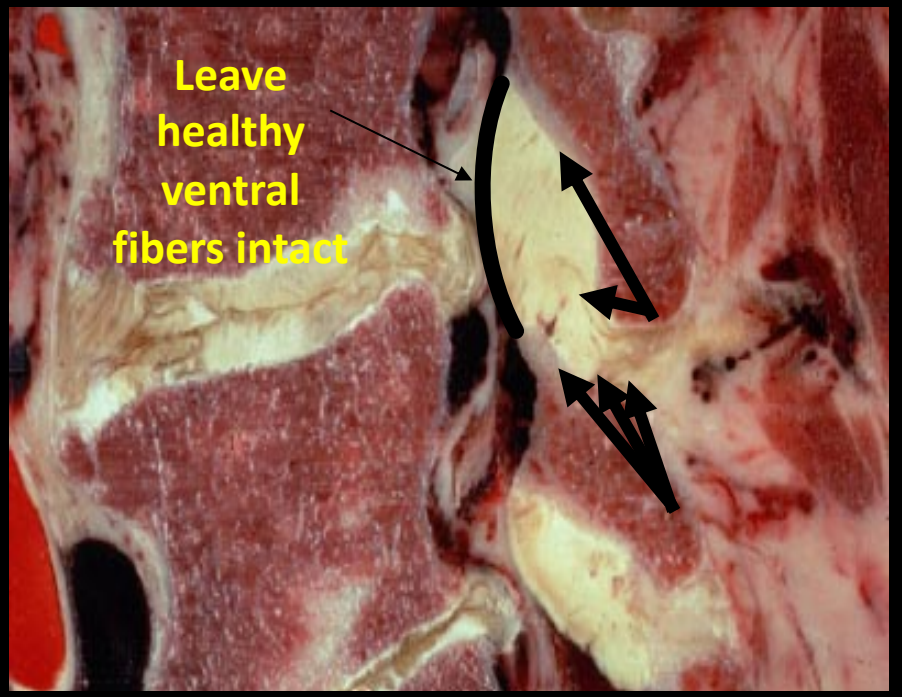
LSS Treatment: Percutaneous Image-Guided Decompression (PILD)

- Debulk the dorsal ligamentum flavum
- Image-guided percutaneous approach
- Key safety factor is the epidurogram
- Ligament greater than 2.5mm
- Outpatient procedure, mild sedation
- 24 month data, MiDAS ENCORE Trial
- Re-Approved by Medicare, 2018



LSS Treatment: PILD Procedure





Decompression of inferior and superior lamina

ENCORE Study 2-year Outcomes

Confirmed Long-term Safety and Efficacy[3]

Study Protocol

- Coverage with evidence development (CED)
- Prospective, multicenter, randomized controlled
- Randomization:
  - *mild* versus ESI
- Study visits:
  - Baseline, 6 month, 1 year, 2 years
- Comparative data through 1 year
  - *mild*-only at 2 years
- Outcome measures:
  - Oswestry Disability Index (ODI)
  - Numeric Pain Rating Scale (NPRS)

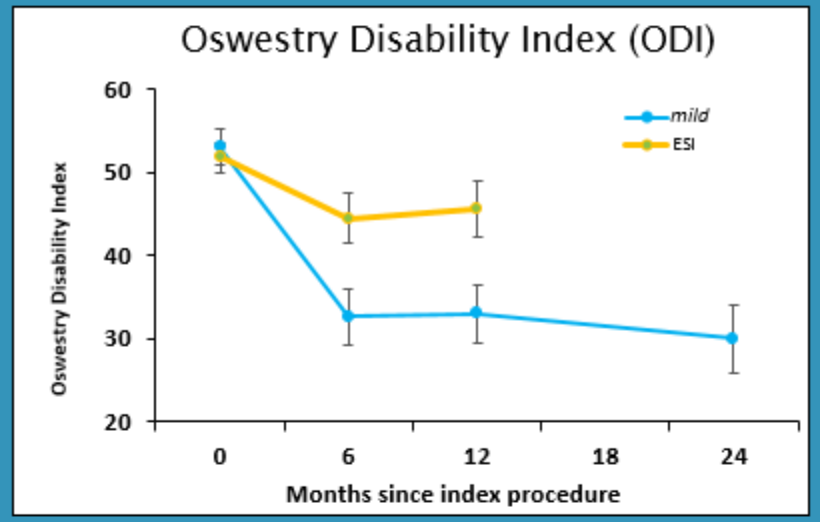
Study Population

- Patients experiencing neurogenic claudication symptoms
- Hypertrophic ligamentum flavum
  - >2.5 mm
- 65 years or older
- ODI >31
- NPRS >5
- No surgery at any treatment level
- Spondylolisthesis
  - < Grade III

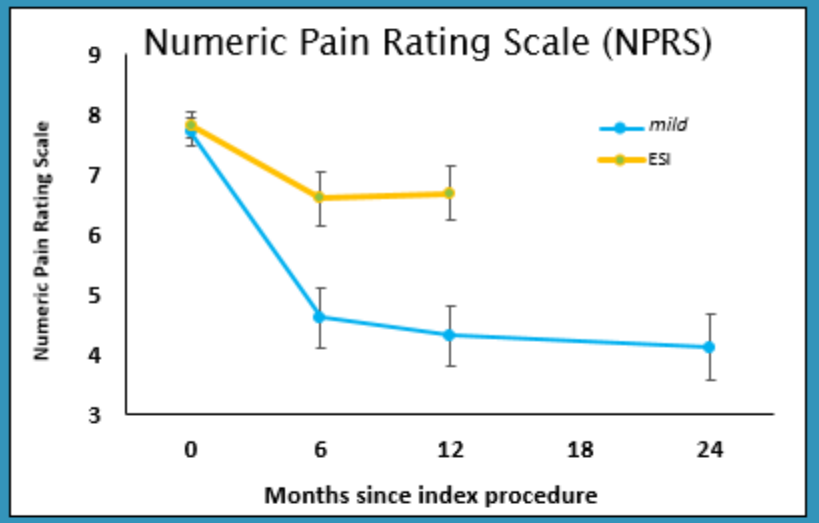
Staats PS, Chafin TB, Golovac S, et al. Long-term safety and efficacy of minimally invasive lumbar decompression procedure for the treatment of lumbar spinal stenosis with neurogenic claudication: 2-year results of MiDAS ENCORE. Reg Anesth Pain Med. 2018;43:789-794.

ENCORE Study 2-year Outcomes

Functional and Pain Improvement Compared to ESIs[3]



- Significant and sustained functional improvement through 2-year follow-up
- Mean ODI improvement of 22.7 points at 2 years
  (10-point improvement is clinically significant.)



- Significant and durable reduction of pain through 2-year follow-up
- Mean NPRS improvement of 3.6 points at 2 years
  (2-point improvement is clinically significant.)

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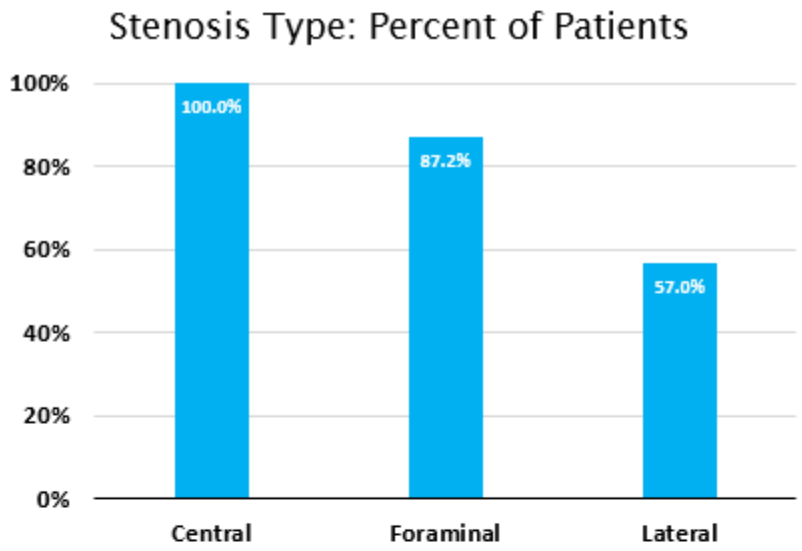
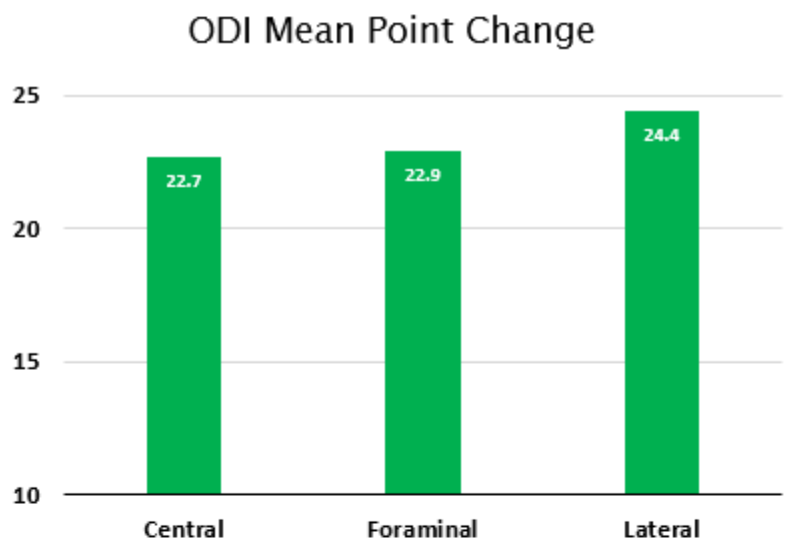
Staats PS, Chafin TB, Golovac S, et al. Long-term safety and efficacy of minimally invasive lumbar decompression procedure for the treatment of lumbar spinal stenosis with neurogenic claudication: 2-year results of MiDAS ENCORE. Reg Anesth Pain Med. 2018;43:789-794.

ENCORE Study 2-year Outcomes

Significant Improvement by Stenosis Type[3]





Majority of patients had multiple types of stenosis

Significant functional improvement regardless of stenosis type

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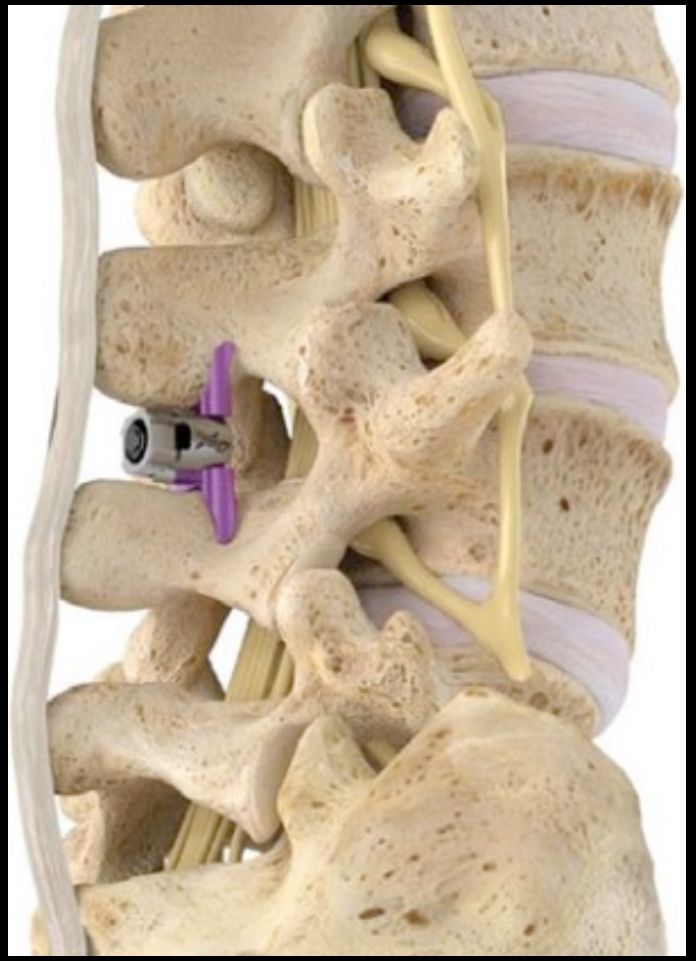
Staats PS, Chafin TB, Golovac S, et al. Long-term safety and efficacy of minimally invasive lumbar decompression procedure for the treatment of lumbar spinal stenosis with neurogenic claudication: 2-year results of MiDAS ENCORE. Reg Anesth Pain Med. 2018;43:789-794.

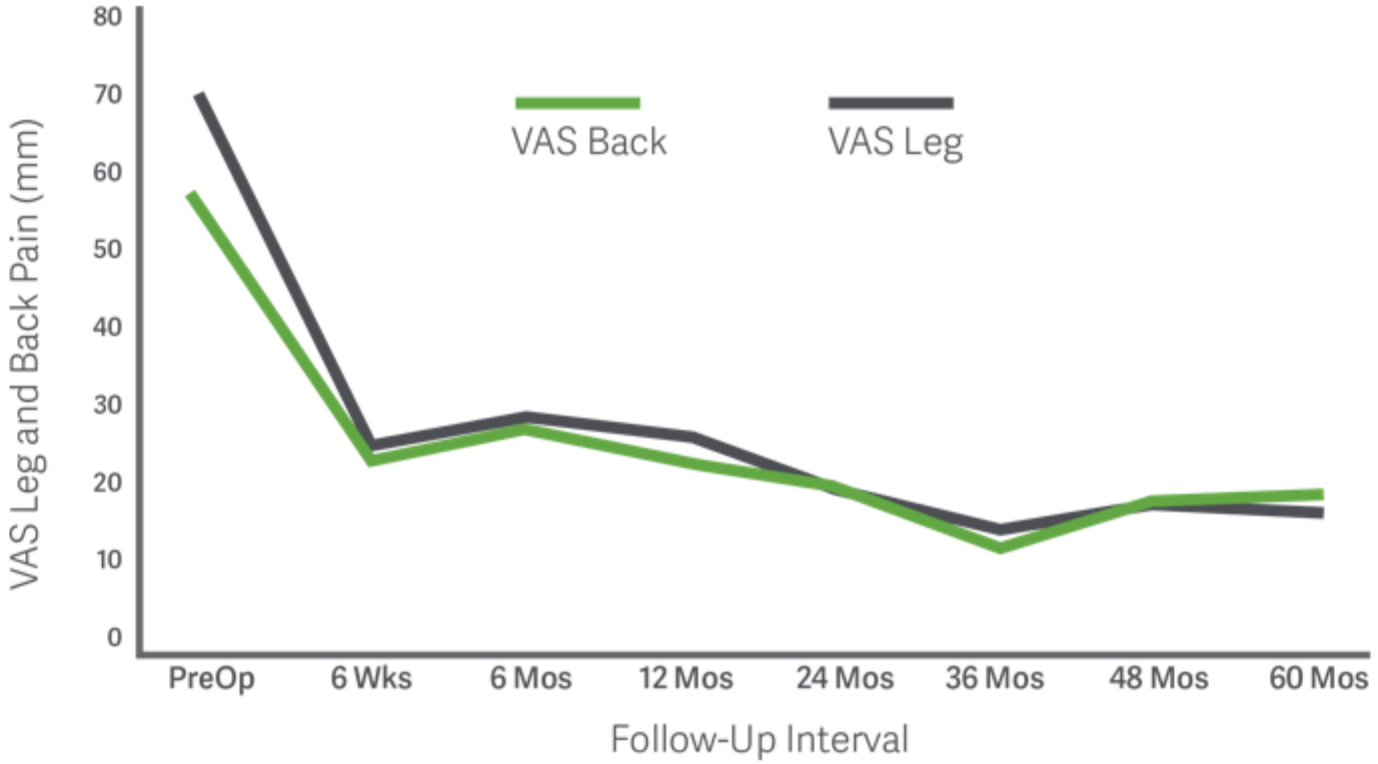
LSS Treatment: Interspinous Process Decompression (IPD)

- Various spacers have been introduced
- 5-year, level 1 evidence
- FDA approved, Medicare coverage
- Back stop preventing compression of the spinal canal and lateral recess during extension



LSS Treatment: IPD 5 Year IDE Study Results

Immediate and Durable Relief of Primary LSS Symptoms



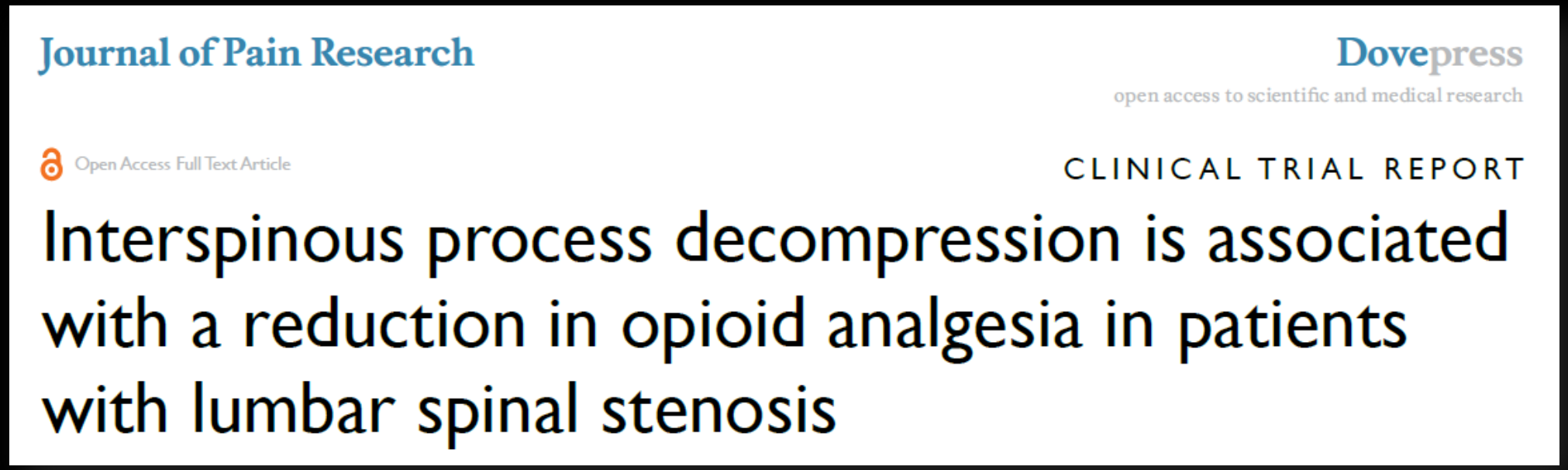
75%
Improvement in Leg Pain from Baseline at 5 Years[1]

Time course of results for leg and back pain severity by VAS[2]

Note: Results reported as mean (95% CI).

[1] Responders.

[2] Nunley, PD, et al. Clinical Interventions in Aging 2017.



- **85%** reduction in the proportion of subjects using opioids at 5 years

- Interspinous process decompression is associated with decrease in the need for opioid medications

Nunely. PD et al. J Pain Research, 2018

Sacroiliac Joint Dysfunction: “The forgotten back pain”

- LBP most common reported pain complaint in adults, 25% Americans
- $200 billion/year in medical expenses, lost wages, and productivity
- 16-30% prevalence among LBP
- Post lumbar fusion: 61% prevalence of SI joint pain

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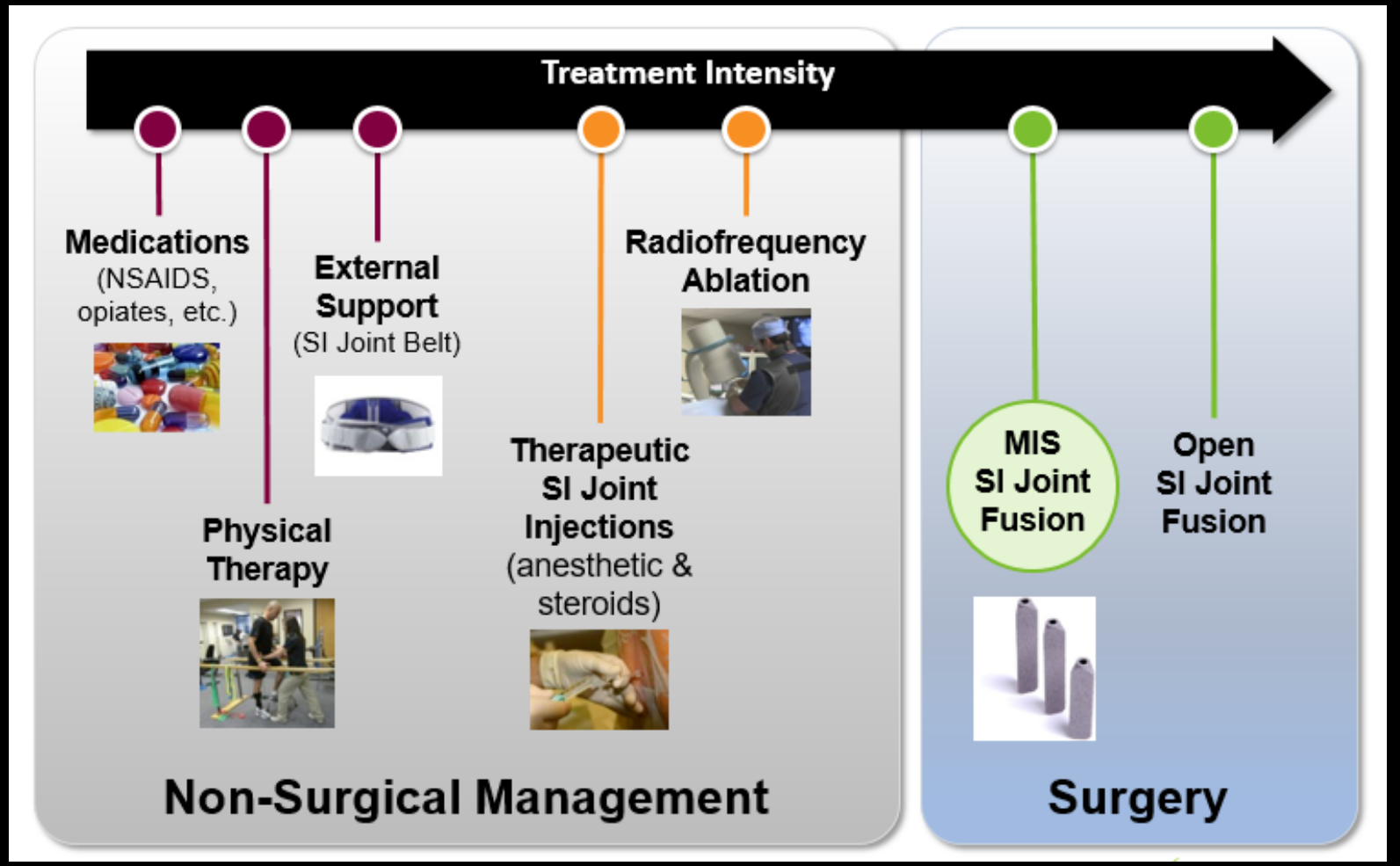
1. Sembrano, J., et al., Current Orthopaedic Practice, 2011

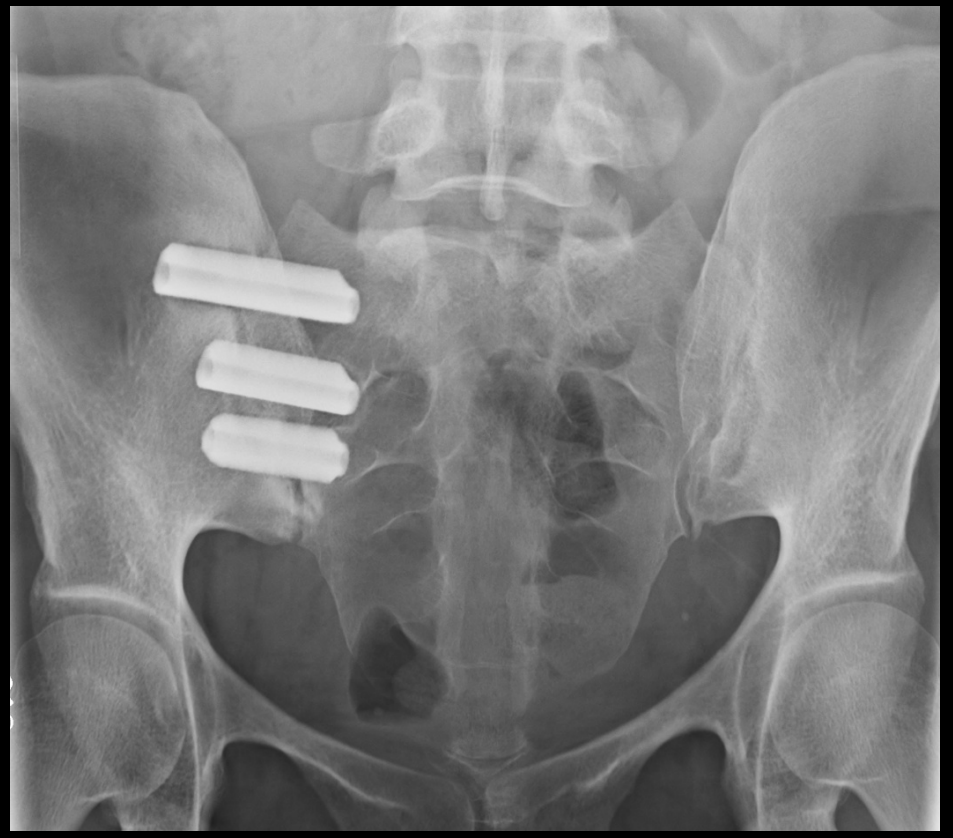
2. Cummings, J., and Capobianco, R., Annals of Surgical Innovation and Research, 2013

SI Joint Treatment Continuum



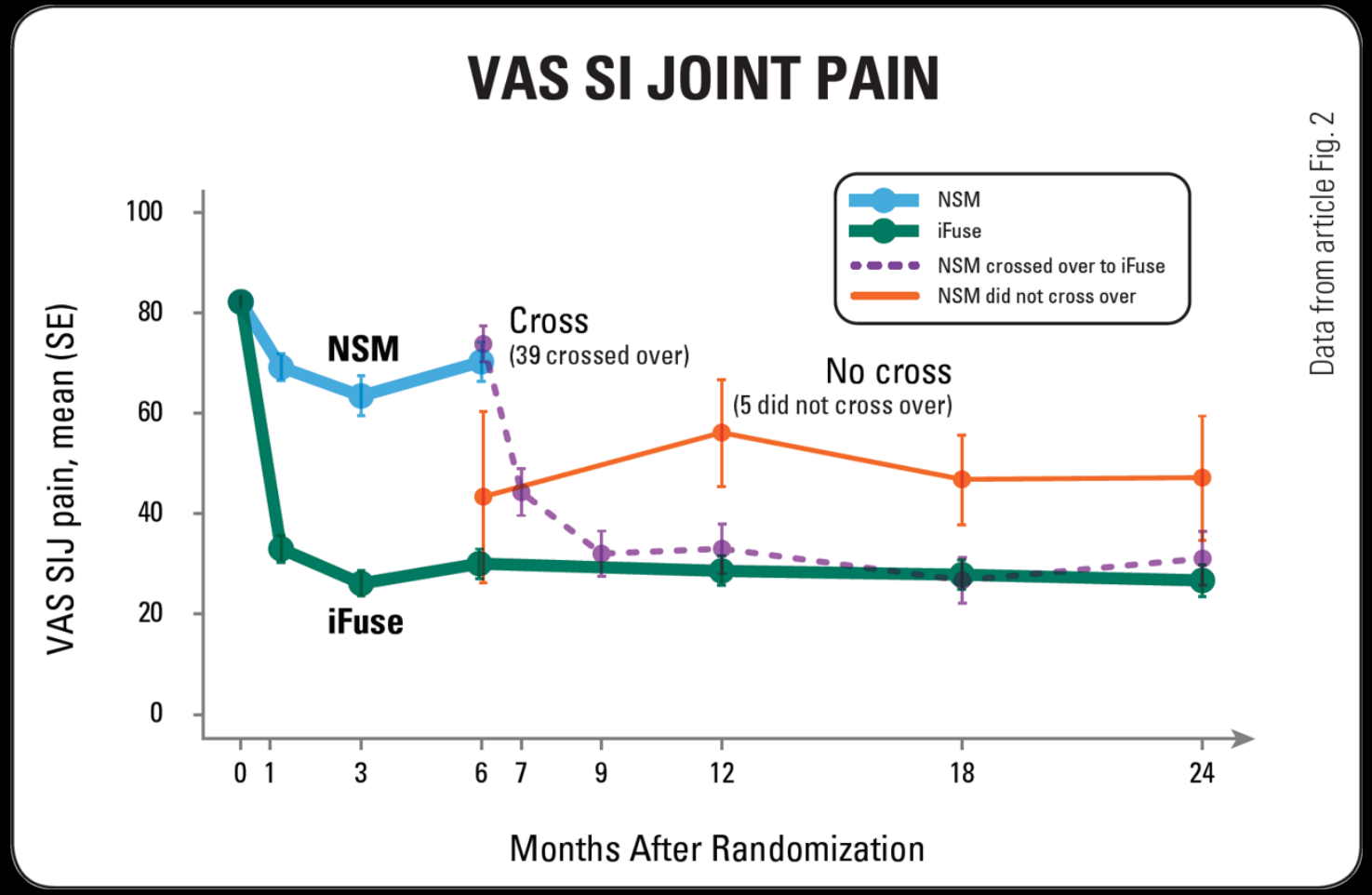
SI Joint Fusion

- Open
  - Invasive
  - Lengthy recovery
  - Rarely performed
- Minimally Invasive
  - Small incision
  - Low blood loss
  - Short procedure (~ 1 hour)
  - No need for bone grafting



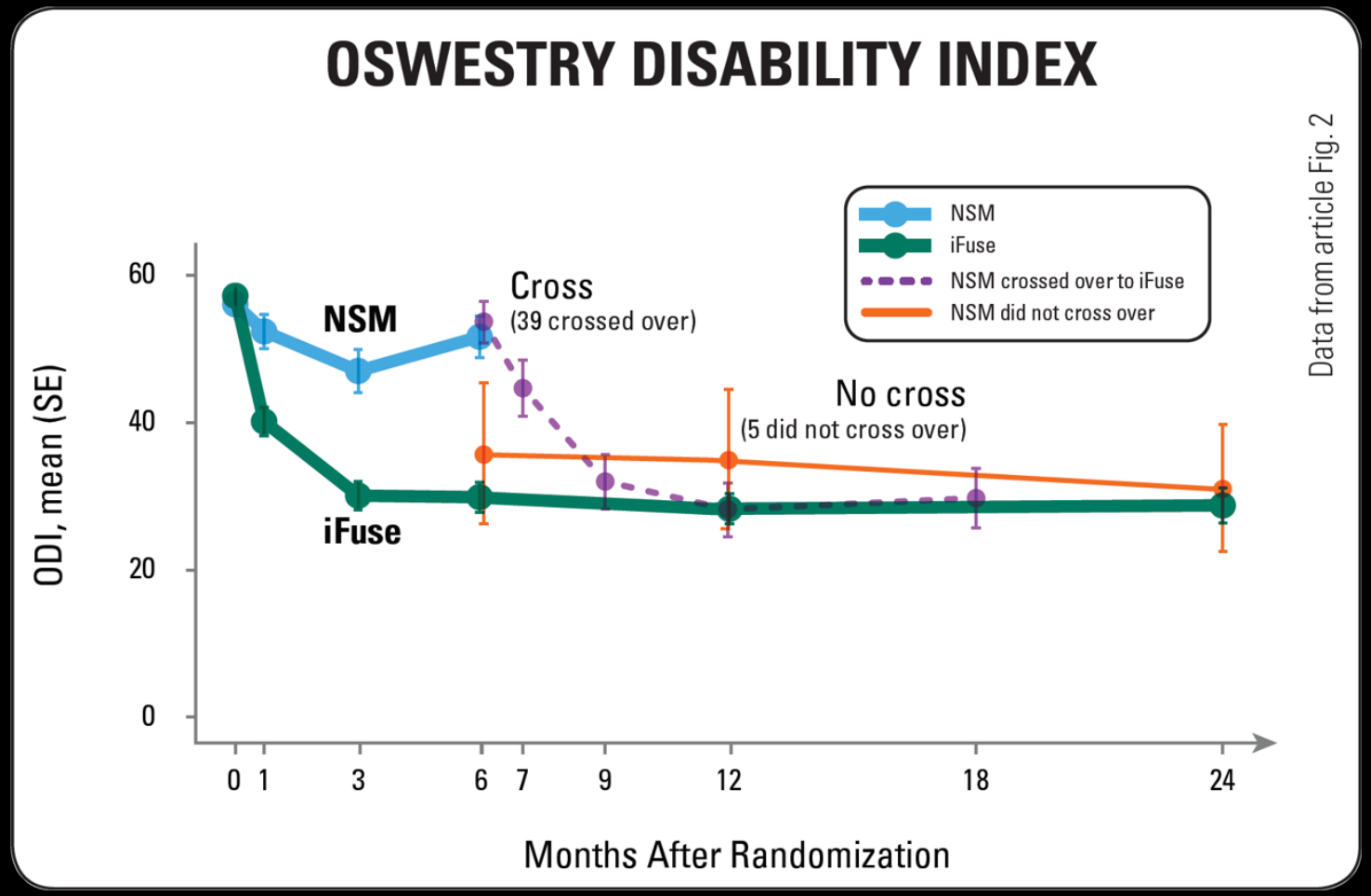
Minimally invasive surgical SI joint fusion

INSITE 2-year results: VAS SI joint pain improves more after SI joint fusion than NSM



Polly – Int J Spine Surg 2016 (INSITE 2yr)

INSITE 2-year results: ODI improves more after SI joint fusion than NSM



Polly – Int J Spine Surg 2016 (INSITE 2yr)

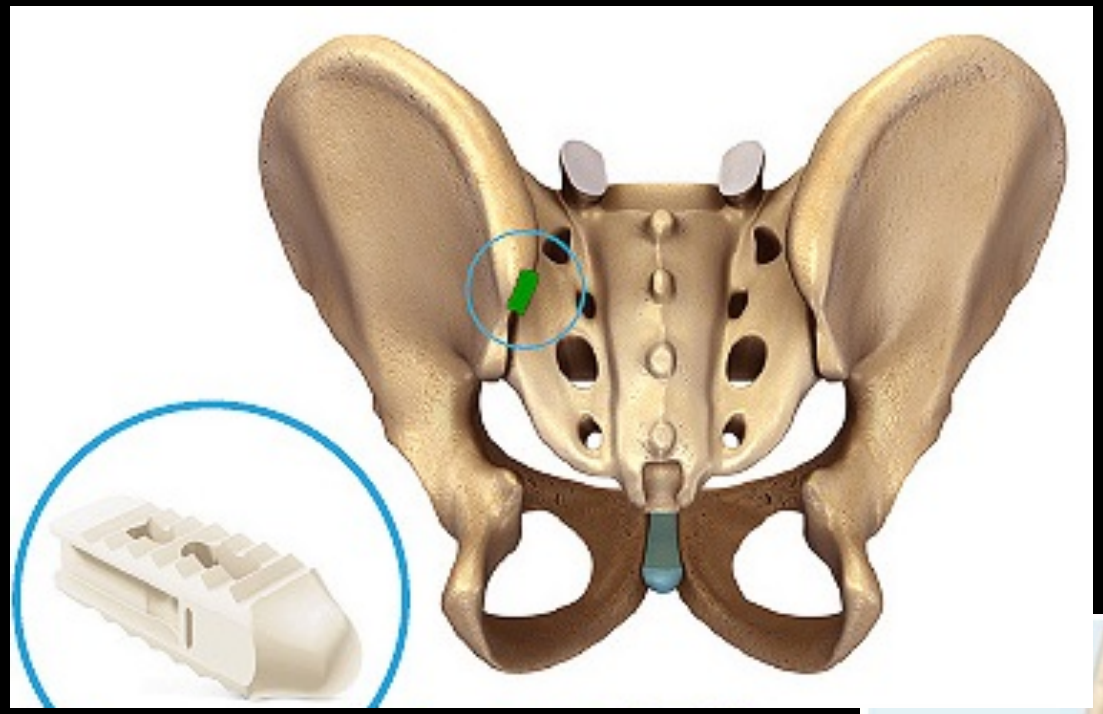
INSITE 2-year Results

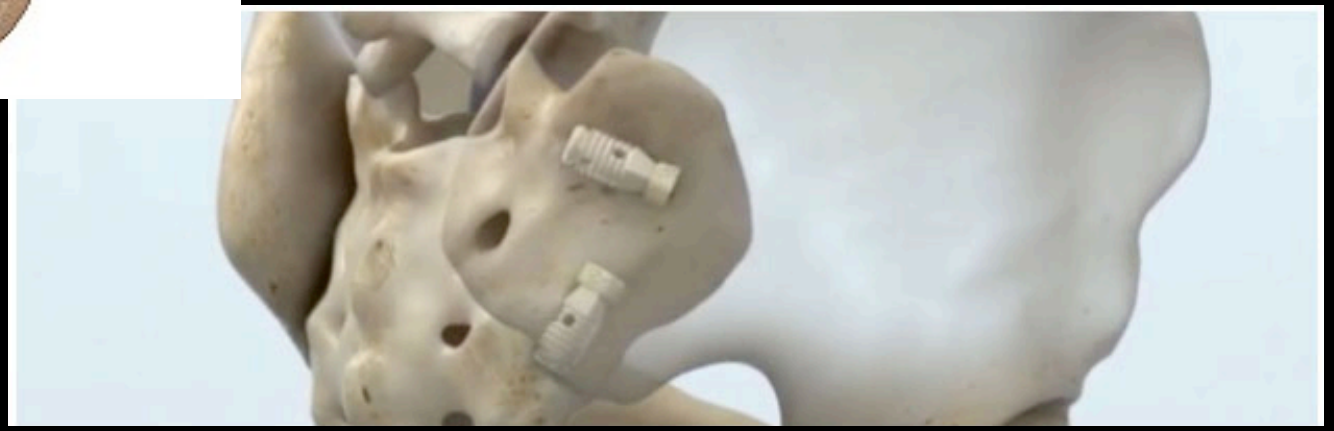
		iFuse % subjects	NSM % subjects
Primary Endpoint *	Success @ 6 mo	82%	26%
Patient Satisfaction	Very or somewhat satisfied	90% (6 mo) 88% (2 yr)	61% (6 mo)
Clinical Improvement (Minimum Clinically Important Difference)	VAS improvement ≥ 20pt	83% (2 yr)	10% (2 yr)
	ODI improvement ≥ 15pt	68% (2 yr)	7.5% (2 yr)
Opioid Use	% change in number of subjects taking opioids	30% ↓ (baseline to 2 yr)	7.5% ↑ (baseline to 6 mo)

* Binary success/failure composite measure. Success if all criteria met: VAS SI joint pain reduction ≥ 20 points, no device-related SAEs, no neurological worsening, and no surgical re-intervention for SI joint pain.

Polly – Int J Spine Surg 2016 (INSITE 2yr)

Minimally Invasive Posterior SI Joint Fusion

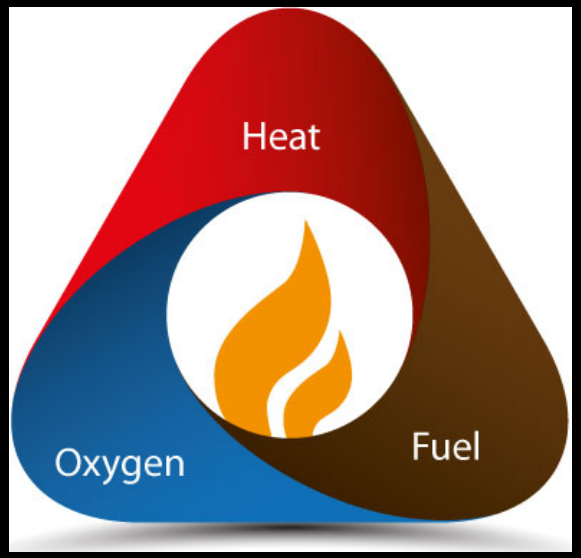




Summary

- Opioid epidemic
- Unmet treatment needs
- Health economics

- Chronic pain
- #1 cause of disability
- Aging population



- IPM alternatives
- Innovation
- Technology
- Level I evidence

Improved Patient Outcomes

Thank You