24-Month Outcomes of the Evoke Study

Double-Blind Randomized Controlled Trial of Evoke Closed-Loop vs. Open-Loop SCS to Treat Chronic Back and Leg Pain

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- Independent Medical Monitor for:
  - Accurate Trial: Abbott
  - HF-10 for PDN: Nevro
  - EVOKE Trial: Saluda
  - MOTION Trial: Vertos
  - RESTORE Trial: Mainstay Medical
  - Via Disc-NP Trial: Vivex Therapeutics

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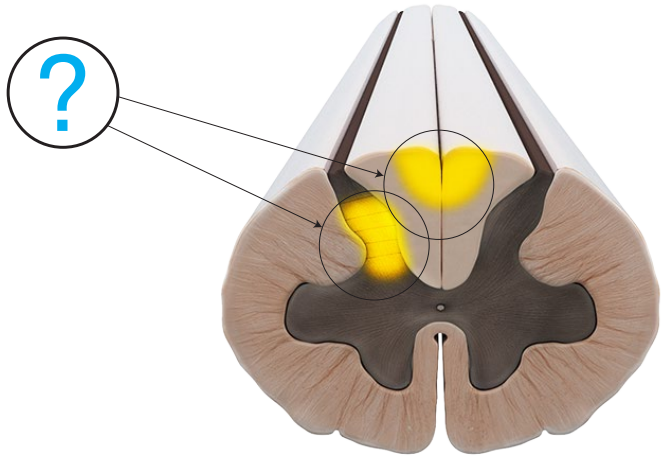
Objectives.

- Current State of Neuromodulation
- What is Closed Loop SCS?
- 24-Month Evoke Study Design and Outcomes

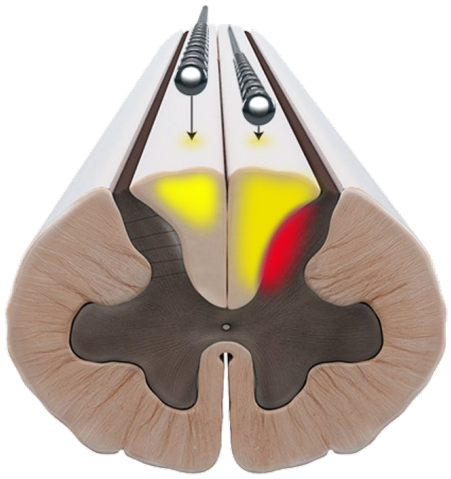
Current State of SCS Technologies
Unknown & Inconsistent Neural Activation

Unknown
Neural Activation



Regardless of Neural Target
- Dorsal Column
- Dorsal Horn
- Dorsal Root Ganglion

Inconsistent
Neural Activation



Regardless of Waveform
- Traditional Paresthesia
- Low-Rate, Sub-perception
- 10 kHz, Burst, Multiplexed
- Low-energy (LE) dosing or cycling

Inconsistent activation leads to frequent therapy adjustments that ***titrate from failure***

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Issues with the Current SCS…

- We have no idea what is the appropriate dose of stimulation?
- We have no clear idea of what is (are) the target(s) for stimulation and are we able to reach the specific target(s)?
- If yes, how does the spinal cord target respond to the stimulation?
- We do not have the ability to record the target fibers response??
- IT IS TRIAL AND ERROR WITHOUT ANY CONFIRMATION OF RESPONSE?

Current State of SCS

Opportunity to Reduce Explants and Therapy Burden

Lack of Durability

~11-22%

of devices are explanted

due to loss of efficacy at **2** years[1-5]

Significant Burden

3-4

visits

for re-programming per patient per year[6]

Medication Utilization

<35%

of patients

reduce opioid use[7]

1. Nevro Senza SCS System SSED P130022
2. Pope et al. Multicenter Retrospective Study of Neurostimulation With Exit of Therapy by Explant. *euromodulation.* 2017;20(6):543-552.
3. Van Buyten et al. Therapy-Related Explants After Spinal Cord Stimulation: Results of an International Retrospective Chart Review Study. *Neuromodulation.* 2017;20(7):642-649.
4. Al-Kaisy et al. Explant rates of electrical neuromodulation devices in 1177 patients in a single center over an 11-year period. Reg Anesth Pain Med. 2020 Nov;45(11):883-890.
5. Wang et al. Explantation Rates of High Frequency Spinal Cord Stimulation in Two Outpatient Clinics. *Neuromodulation.* https://doi.org/10.1111/ner.13280.
6. *eINS presentation, Abbott Remote Programming.*
7. *Neuromodulation 2020 Jan;23(1):126-132. doi: 10.1111/ner.13054.*

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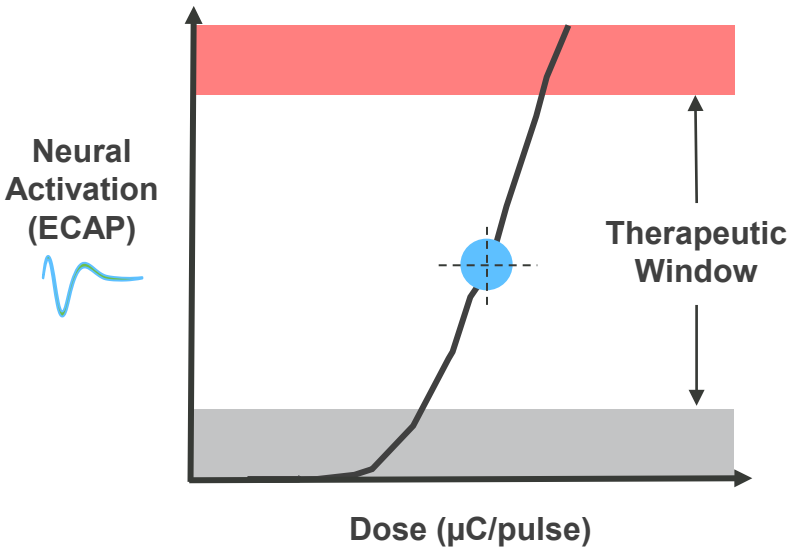
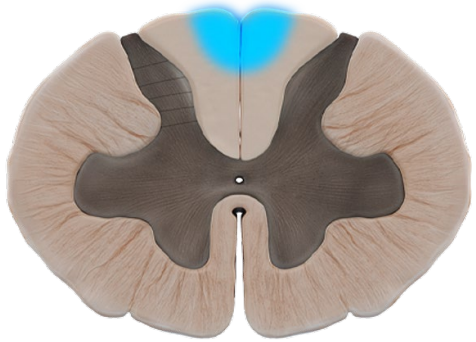
EVOKE Removes Programming Guesswork
Objective, Prescribed Level of Neural Activation

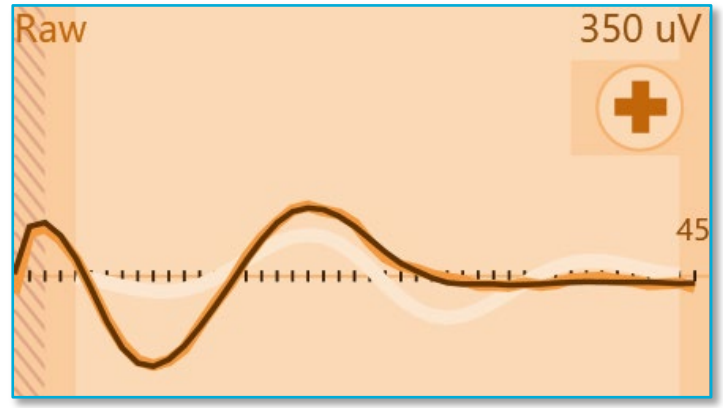
PRESCRIBED NEURAL ACTIVATION



VOLUME OF NERVE ACTIVATION



ECAP SHOWN ON PROGRAMMER CONFIRMS ACTIVATION



For the first time, patients are programmed with an **objective measure of activation**

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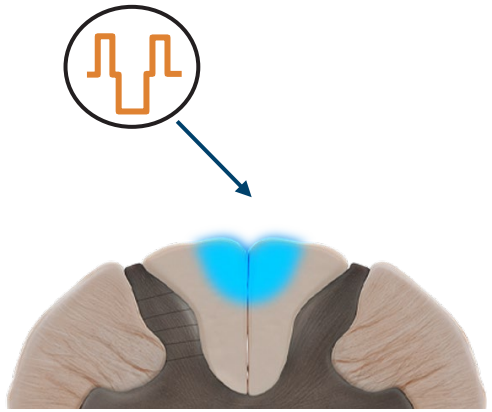
How does EVOKE Closed-Loop Stimulation Work?

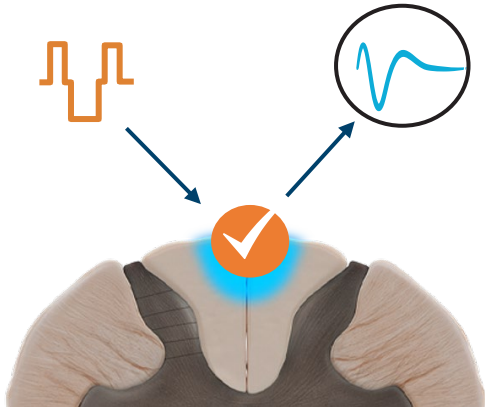
Consistent Neural Activation Is Maintained Through Instantaneous and Precise Adjustments

Stimulate



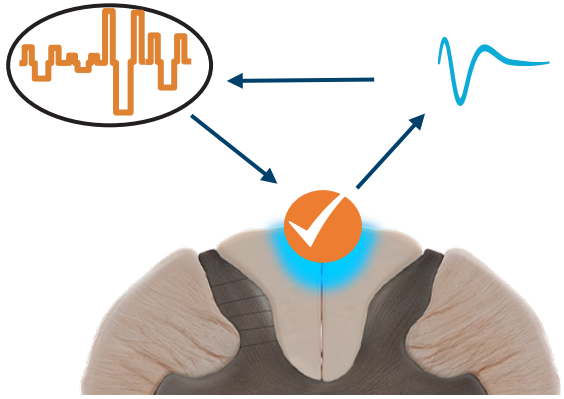
1 Generate stimulation

Sense



2 Sense ECAP signal and compare to prescribed level of neural activation

Adjust



3 Auto-adjust current on each stimulation pulse to tightly control the level of neural activation

100+ Precise Adjustments Per Second

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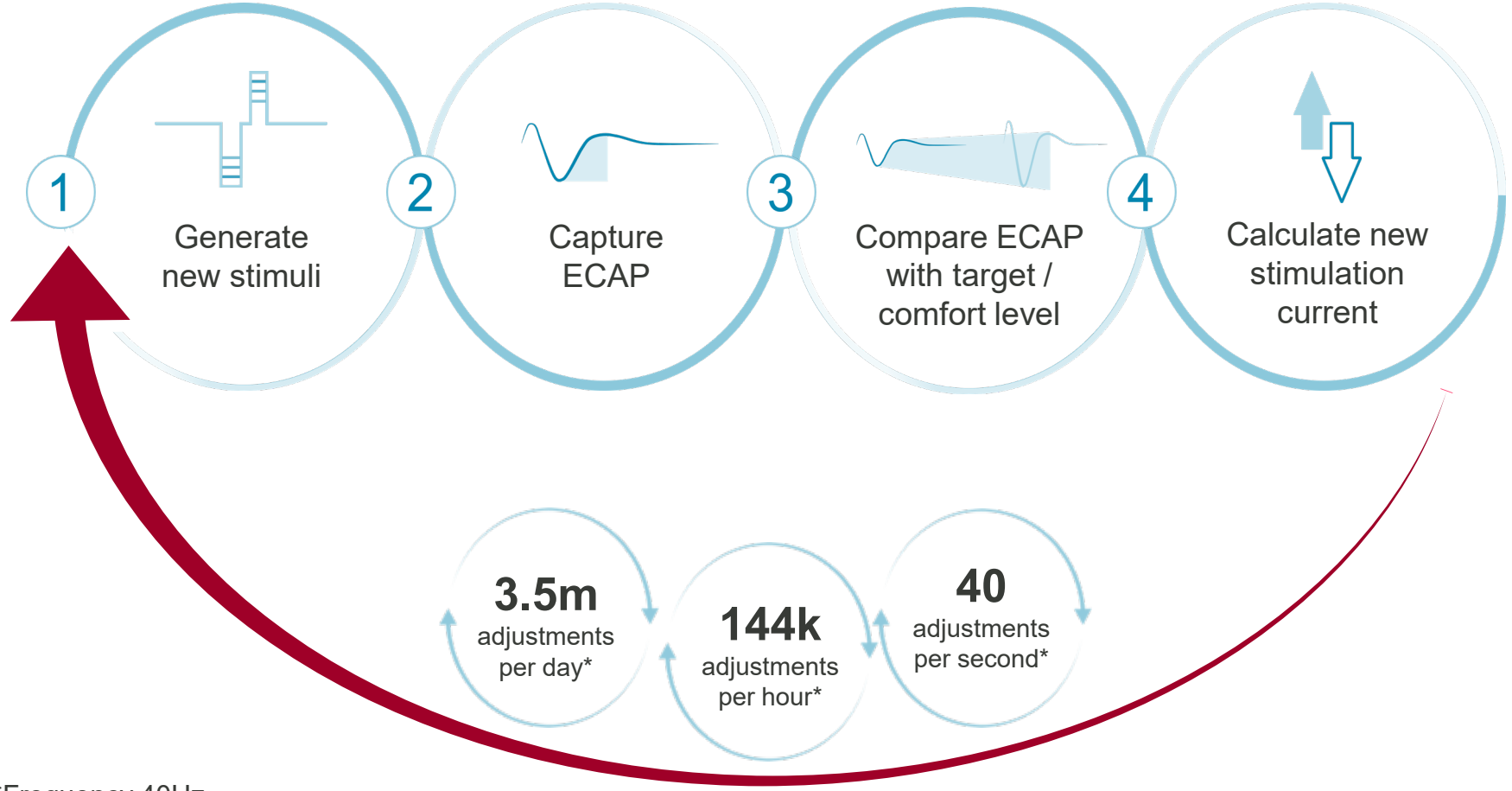
Stimulation adjustments are made at the same rate as frequency.

How Closed-Loop SCS Works



*Frequency 40Hz

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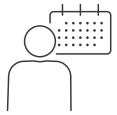
EVOKE Study:

The Only Double-Blind Pivotal RCT

- **Multicenter, parallel arm**
- **Longest-term RCT data in SCS** (collecting out to 36m)
- **134 randomized patients across 13 U.S. sites**
  - ECAP confirmation in both arms
- **Challenging patient population** studied

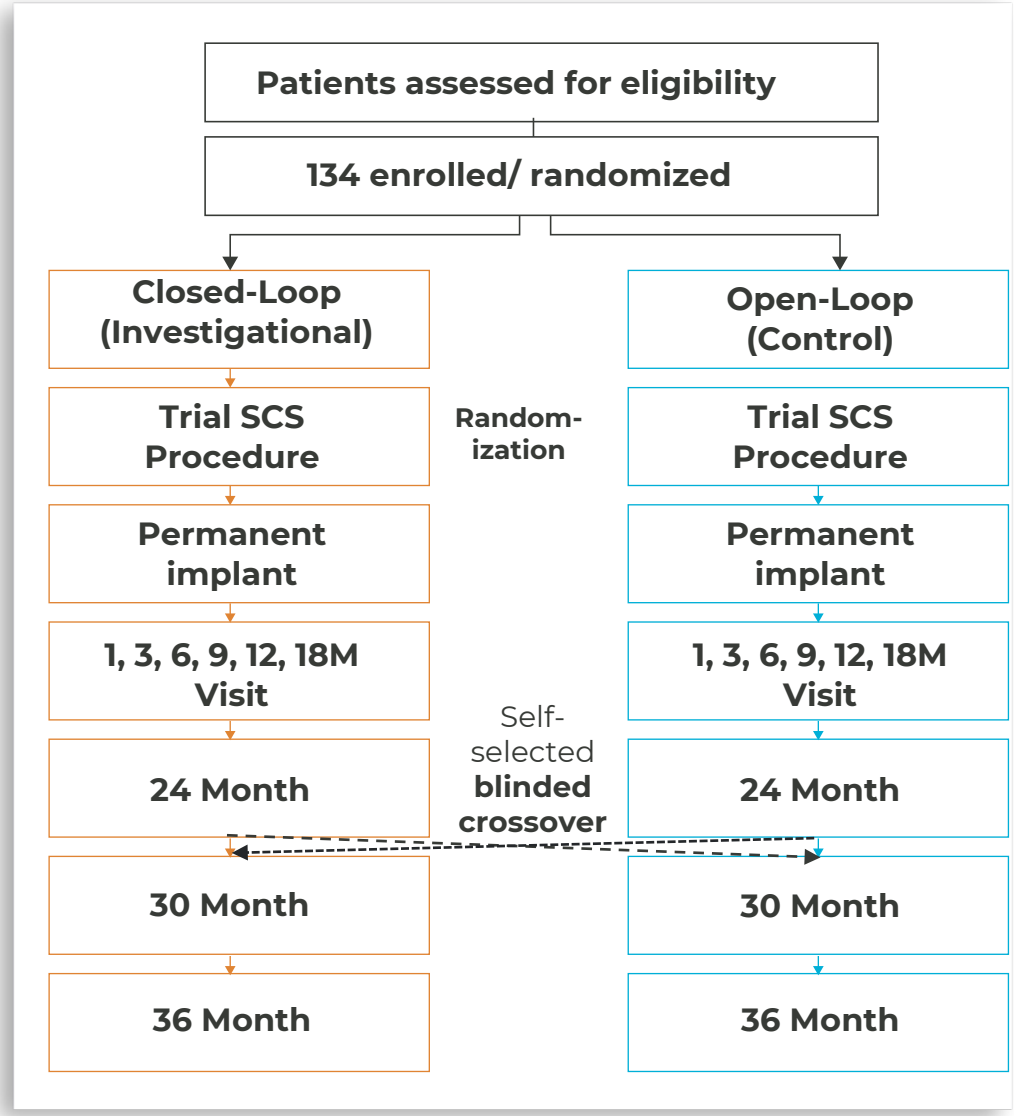
Overall pain
(not just in leg or just back)

Baseline VAS >80MM
(average)



>11 years
of chronic pain

Severely disabled or crippled
requirement (ODI)



AE Rate consistent with literature.

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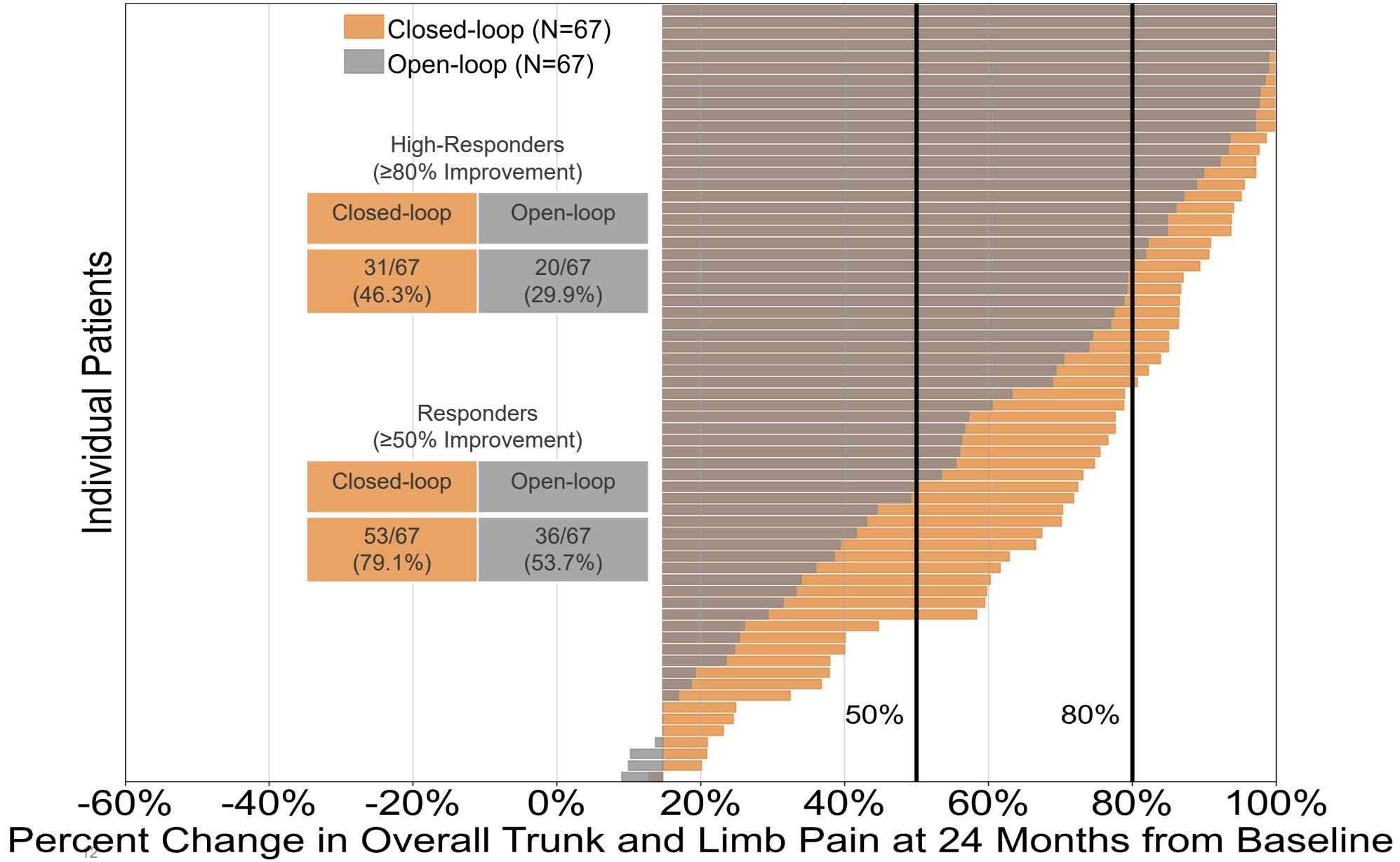
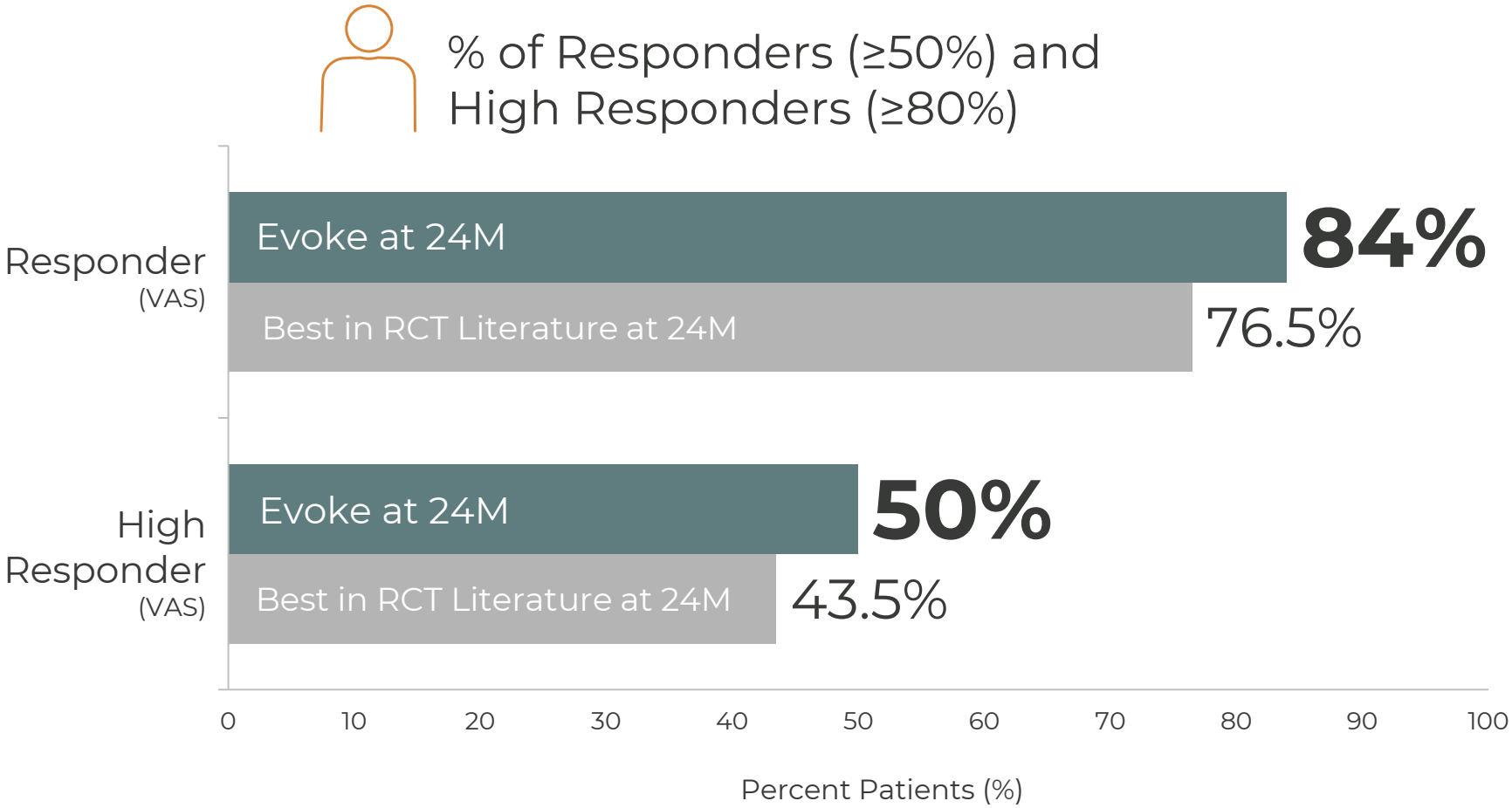
Change of the Overall Pain at 24 Months



Highest Responder and High Responder Rates in 24M RCT Literature



1. Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. Neurosurgery. 2016;79(5):667-677 2. Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): Senza Spinal Cord Stimulation (SCS) System 2015. Published online 2015. Accessed September 10, 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130022b.pdf

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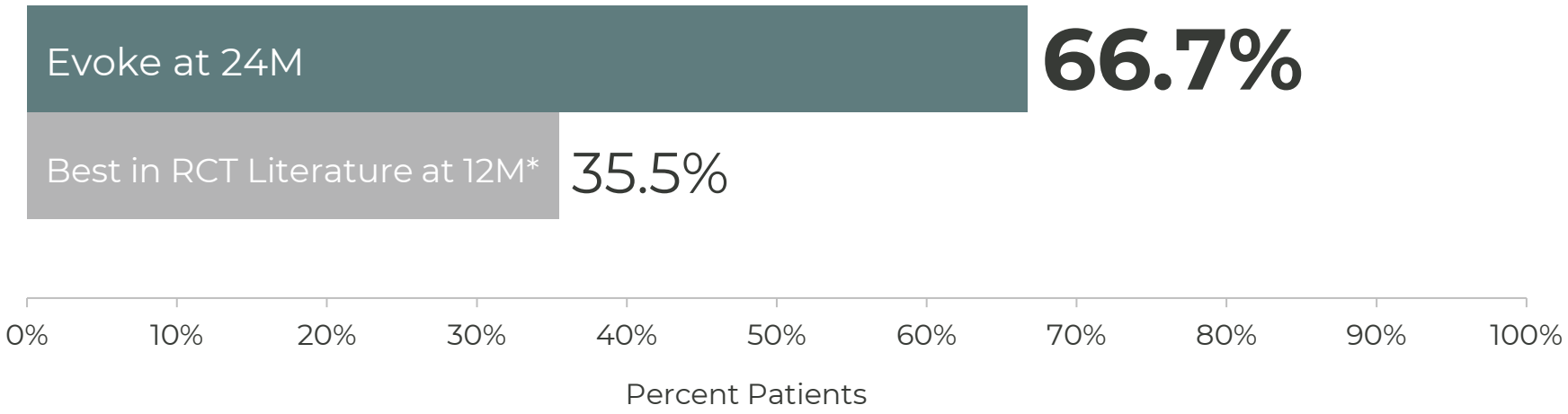
Consistent Pain Relief Enabled Compelling Opioid Reduction

% Patients who Reduced or Eliminated Opioids



*Not reported in RCT literature at 24 months.

Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): Senza Spinal Cord Stimulation (SCS) System 2015. Published online 2015. Accessed September 10, 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130022b.pdf

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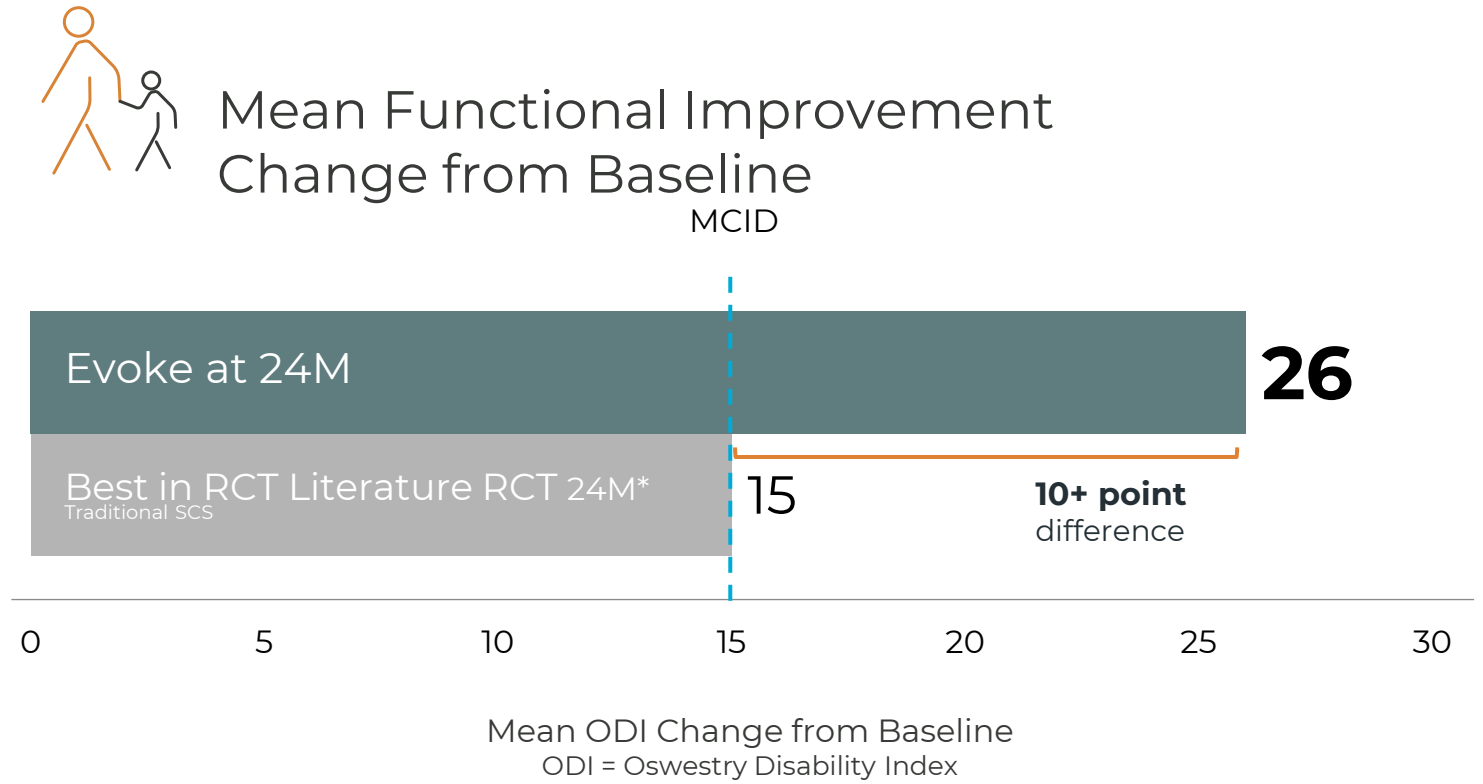
Evoke Enables a Return to a More Normal, Active Lifestyle



82% of Evoke patients demonstrated **clinically significant** functional improvements at 24M

*Kumar K, Taylor RS, Jacques L, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. Neurosurgery. 2008;63(4):762-770

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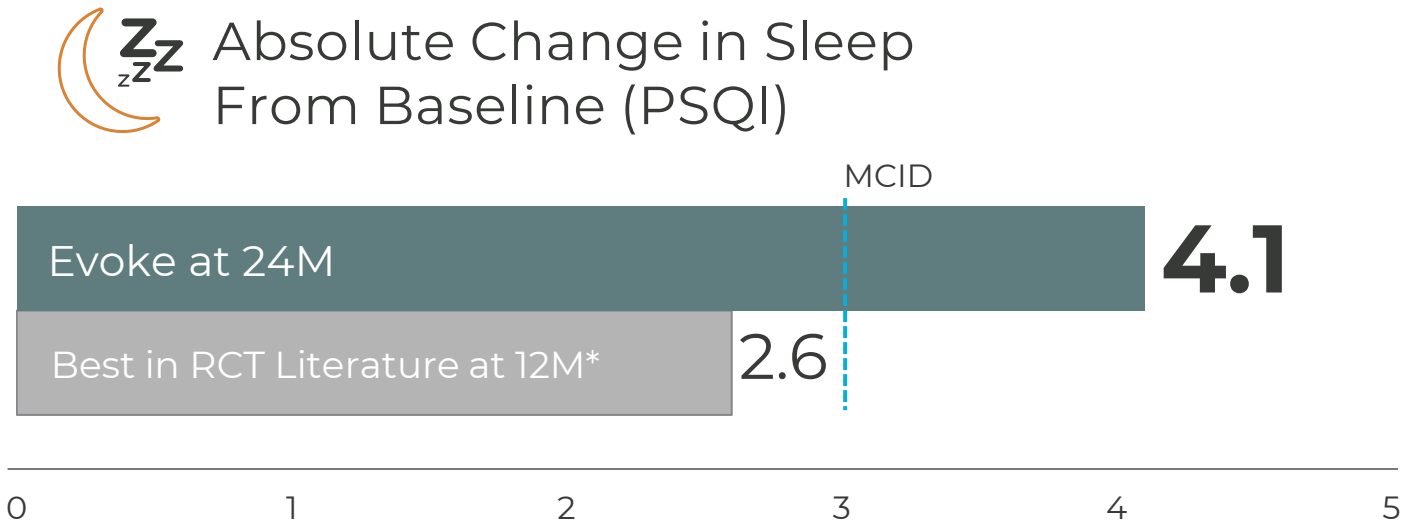
Evoke Patients Gain More Sleep and Improve Sleep Quality



Evoke patients gained an **additional 1.2 hours of sleep per night,** which is 54 extra full nights of sleep*

* Full night = 8 hours of sleep

1. 2021 ASPN Podium Presentation – EVOKE Real-Time ECAP-Controlled Closed-Loop SCS
2. Nevro Senza SCS System SSED P130022
3. Senza RCT -Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, Amirdelfan K, Morgan DM, Brown LL, Yearwood TL, Bundschu R, Burton AW, Yang T, Benyamin R, Burgher AH. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. Anesthesiology. 2015 Oct;123(4):851-60. doi: 10.1097/ALN.0000000000000774. PMID: 26218762.

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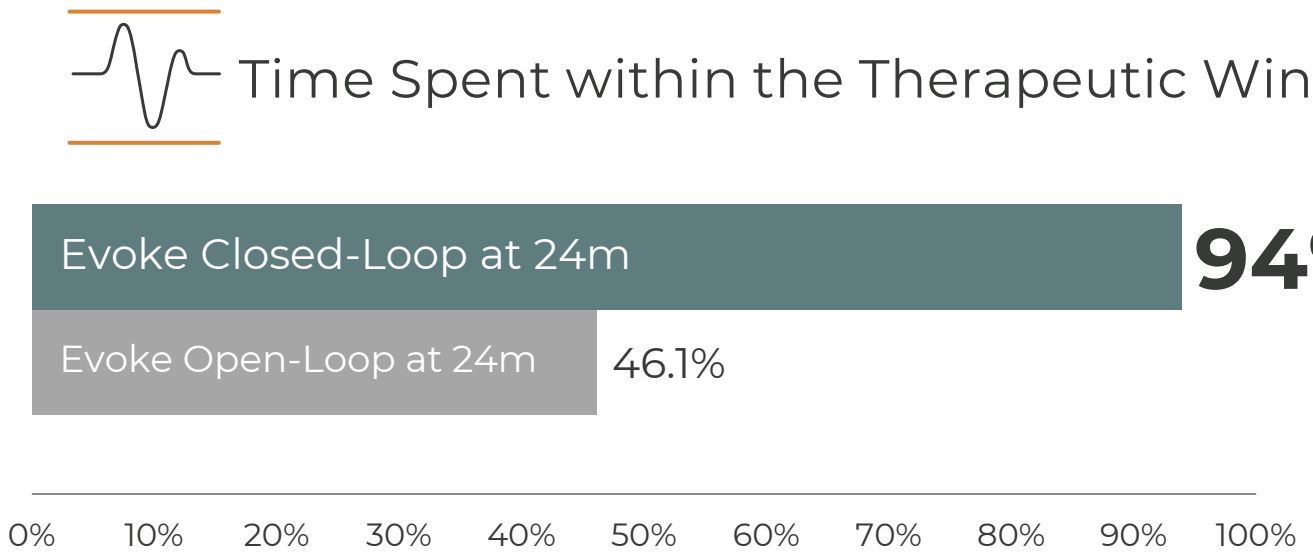
Precise Neural Activation Drives Superior Outcomes

Time Spent within the Therapeutic Window



Patients with ECAP-controlled therapy receive **>2x more therapeutic stimulation**

Mekhail N, Levy RM, Deer TR, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain; A Secondary Analysis of the Evoke Randomized Clinical Trial. JAMA Neurol. 2022;79(3):1-10

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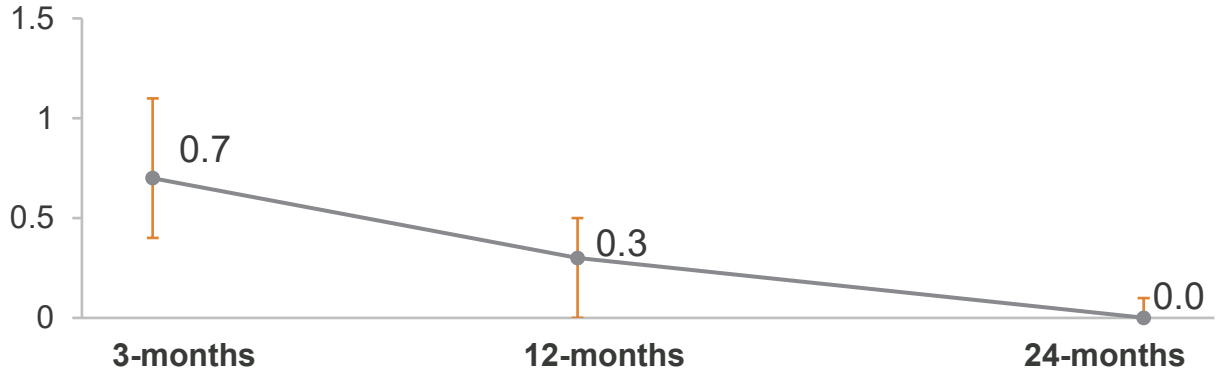
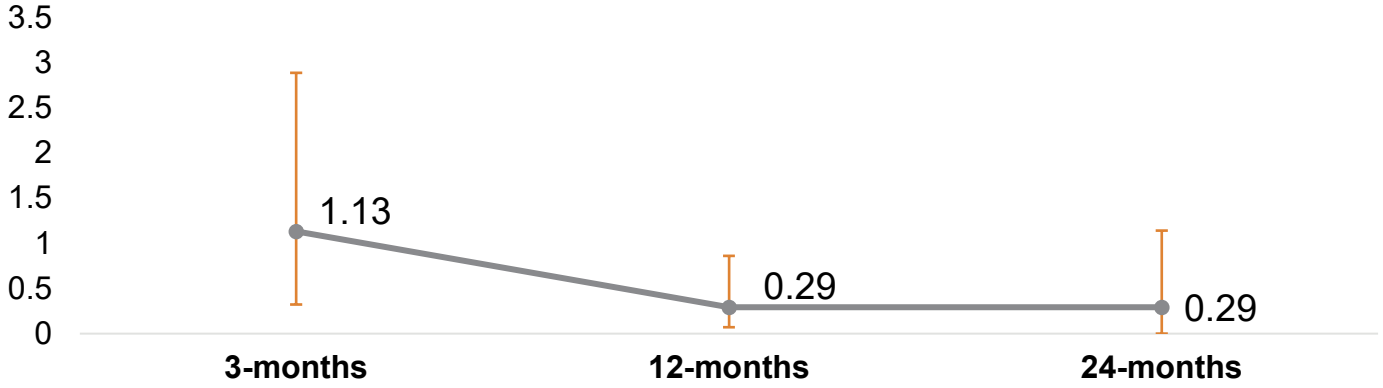
Durability and Consistency of Treatment

Near Elimination of Reprogramming and Patient Burden

Median Number of Interim Reprogramming Visits/Month/Patient



Median Daily Patient Button Presses to Adjust Stimulation Intensity



EVOKE Study

<1

Reprogramming Visit per patient per year
12 months & beyond

<1

Daily patient button presses to adjust Stimulation Intensity
12 Months & beyond

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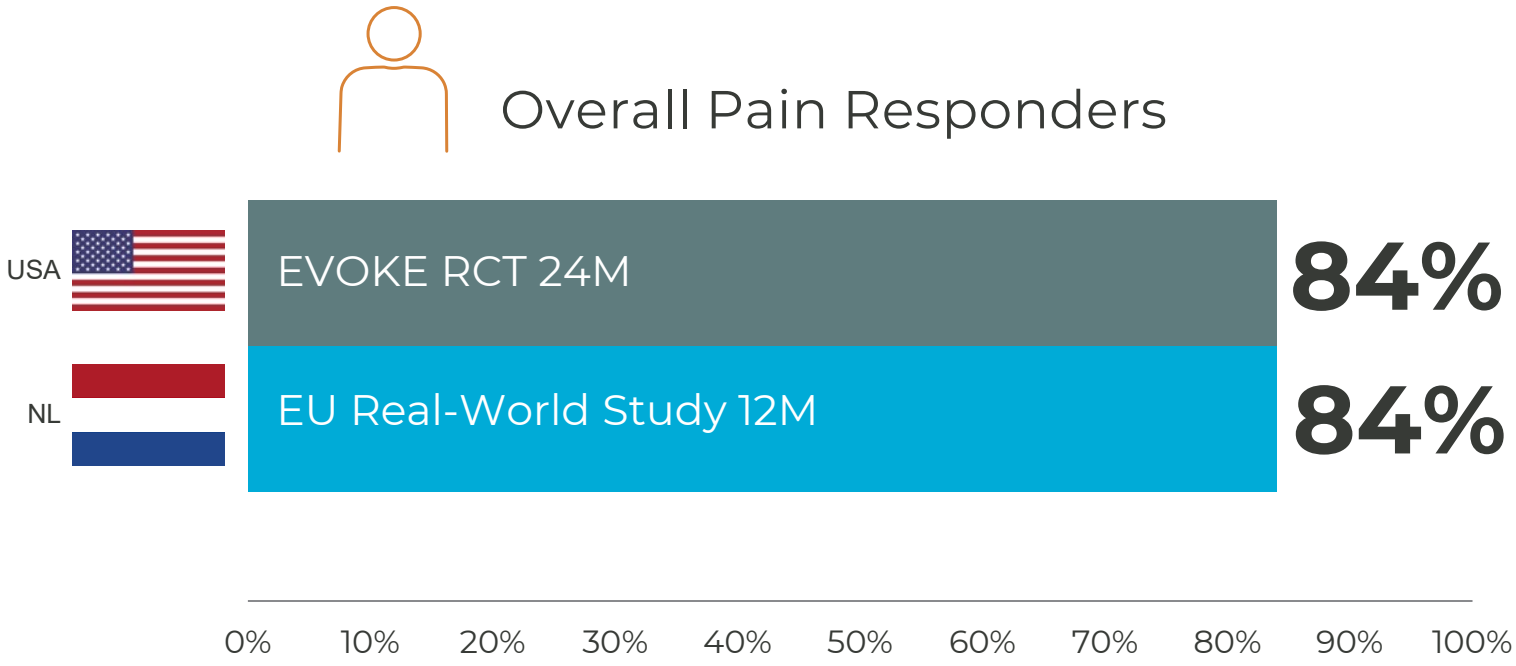
Commercial Outcomes Parallel RCT Evidence



Clinical Trial Results Paralleled by Real-World Results

1. Mekhail N, Levy RM, Deer TR, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain; A Secondary Analysis of the Evoke Randomized Clinical Trial. JAMA Neurol. 2022;79(3):1-10INS Barcelona Secondary Outcomes presentation citation 2. Nijhuis, et al. Long-Term Real-World Cohort of EVOKE Closed-Loop Spinal Cord Stimulation – European Prospective Study Experience, Presented at NANS 2022, Orlando, FL

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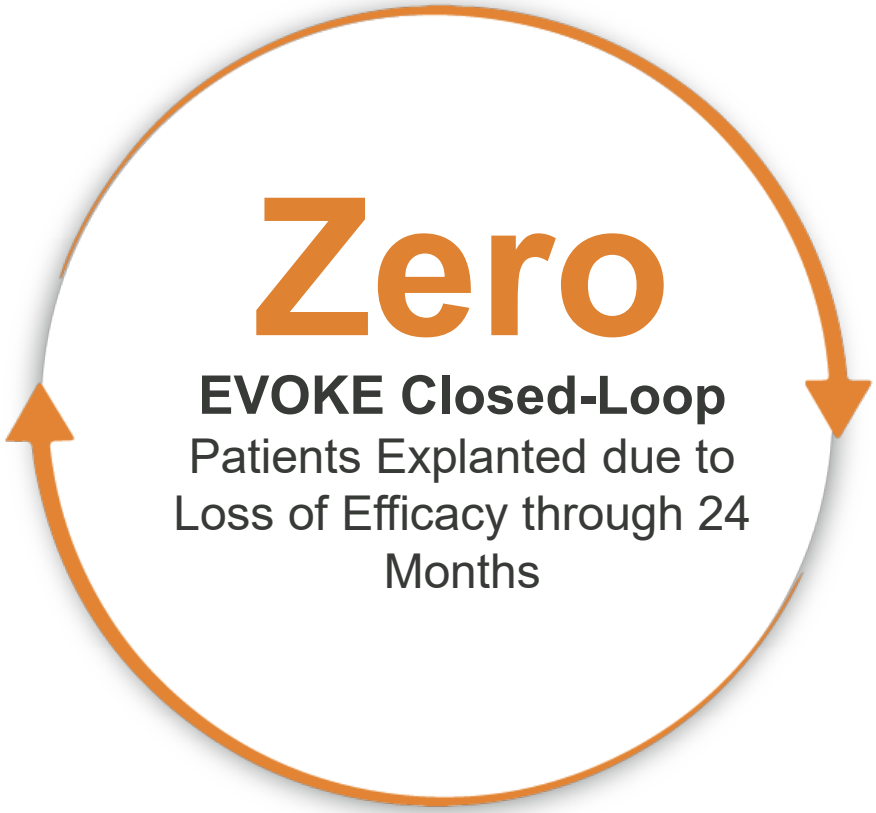
Safety Profile

No Difference between Closed-Loop and Open-Loop SCS

- All subjects received the same device and underwent the same procedure. Thus, the **true indicator of safety differences between groups are stimulation therapy-related adverse events.**
- **There were no differences in the safety profiles between treatment groups.**
  - 95% confidence interval (CI) for the rate difference between groups includes zero (see table).
- **Type, frequency, and severity of adverse events were similar to those reported in other SCS studies.**

Adverse Events (AEs)	Total N=134		Difference Between Groups
	Events n	Patients n (%)	Rate Difference (%) and 95% CI
Study-Related* AEs	42	28 (20.9%)	6.0 (-7.8, 19.7)
Procedure-Related AEs	28	21 (15.7%)	4.5 (-7.8, 16.8)
Device-Related AEs	18	17 (12.7%)	4.5 (-6.8, 15.7)
Stimulation Therapy- Related AEs	10	8 (6.0%)	3.0 (-5.0, 11.0)

*Adjudicated by the Clinical Events Committee (CEC) as possibly or probably related to the procedure, device and/or stimulation therapy.



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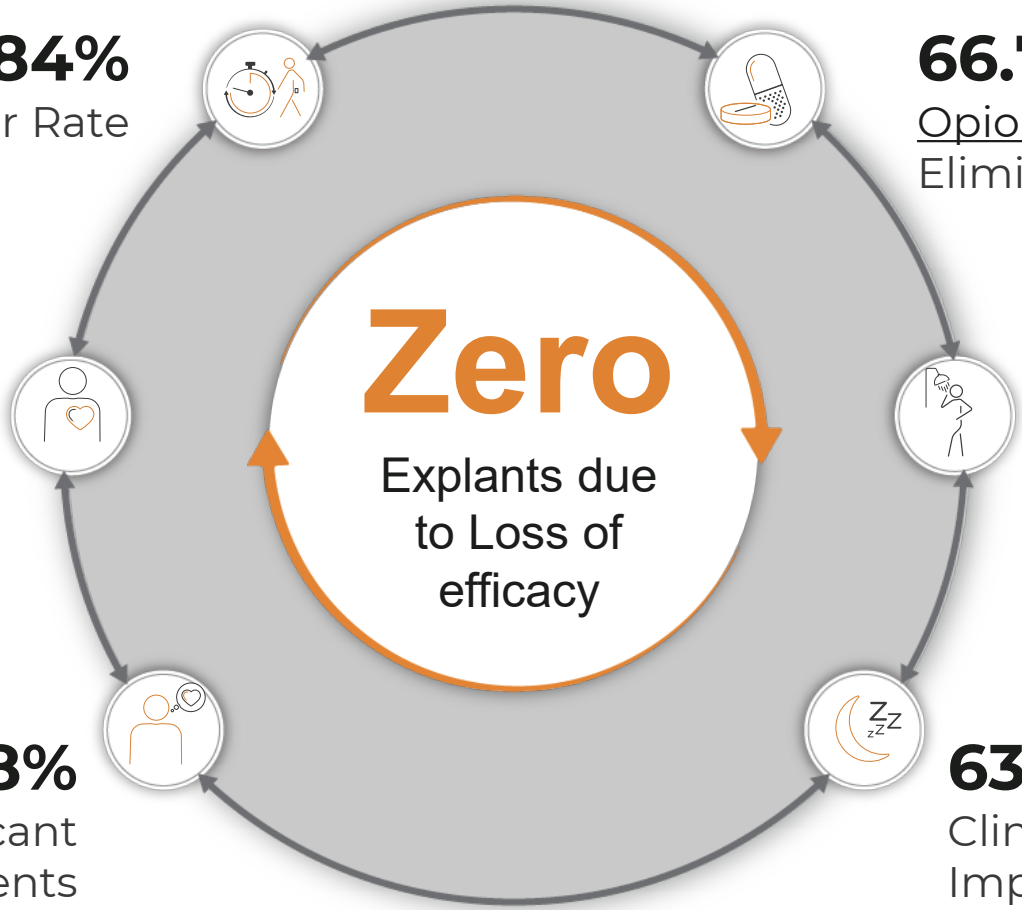
The EVOKE Study

Unprecedented, Restorative Clinical Outcomes at 24 Months



84%
Responder Rate

66.7%
Opioid Reduction or Eliminated Opioid Use

86%
Clinically Significant Quality of Life Improvements

82%
Clinically Significant Functional Improvements

68%
Clinically Significant Mood Improvements

63.3%
Clinically Significant Improvements in Sleep time & quality

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Better Understanding of the Mechanism of Action of SCS with Proper Neurophysiologic monitoring as well as Better patient's Selection Will Significantly Improve the Outcomes of Neuromodulation

Thank you…

1. Mekhail N, Levy RM, Deer TR, et al. 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. Lancet Neurology. 2020;19(2):123-134.
2. Mekhail N, et al. "Durability of Clinical and Quality of Life Outcomes of Closed0Loop Spinal Cord Stimulation for Chronic Back and Leg Pain (EVOKE Study) Accepted for publication, JAMA Neurology, 2022.