

Hypoglossal Nerve Stimulation

Jordan Weiner, MD
Weiner Sleep Surgery

Overview

- History of HNS
- Mechanism of therapy
- Inspire vs. Genio – key differences
- Indications and contraindications
- Patient characteristics associated with HNS outcomes
- Surgical procedures – Inspire and Genio
- Postoperative device management
 - Postoperative activation
 - Therapy intensity escalation
 - Long-term follow up
- Outcomes data
 - National studies
 - My data
- My own thinking on these therapies after implanting more than 600 devices.

HISTORY OF HYPOGLOSSAL NERVE STIMULATION: 1990s – TODAY.

1990s: FIRST-GENERATION, FEASIBILITY.



1997 early implanted system

key investigators:

- DR. D. EISELE
- DR. P. SMITH

1997: DIRECT CN XII STIMULATION SHOWS REDUCTION.

TONGUE PROTRUSION



2000s: DEVELOPMENT & CHALLENGES.

FAILED CLINICAL TRIALS (APNEX MEDICAL)



ALTERNATIVE trunk cuff (IMTHERA MEDICAL)

Phase III

TECHNICAL LIMITATIONS & PATIENT SELECTION ARE KEY.

2010s: THE PIVOT: CLINICAL BREAKTHROUGH & APPROVAL.

STAR TRIAL

(Woodson et al., 2014)

AHI 29.3 → 9.0 (12 mo)

ESS 11.0 → 7.0

70% SUCCESS

2013: CE MARK (EUROPE)

2014: FDA APPROVAL (USA)

INSPIRE MEDICAL SYSTEMS

IMPLANTED GENERATOR



UNILATERAL (ONE-SIDE) PLACEMENT
STIMULATING CUFF

UNILATERAL VS BILATERAL MEDIAL BRANCH PLACEMENT

2020s: MODERN ERA: COMMERCIALIZATION, INNOVATION, & COMPETITION.

ESTABLISHED LEADER (INSPIRE)

- ADHERE REGISTRY >150,000 PATIENTS
- 2-INCISION APPROACH
- INSPIRE IV & V



PATENT LITIGATION & MARKET BATTLE.

NEW INNOVATION (NYXOAM)

- BILATERAL STIMULATION
- LESS INVASIVE
- GENIO SYSTEM (CE Mark: 2018)

LEADLATERAL STIMULATION
→ US FDA APPROVAL (2025)

Paddle-Electrode

EXTERNAL WEARABLE STIMULATOR

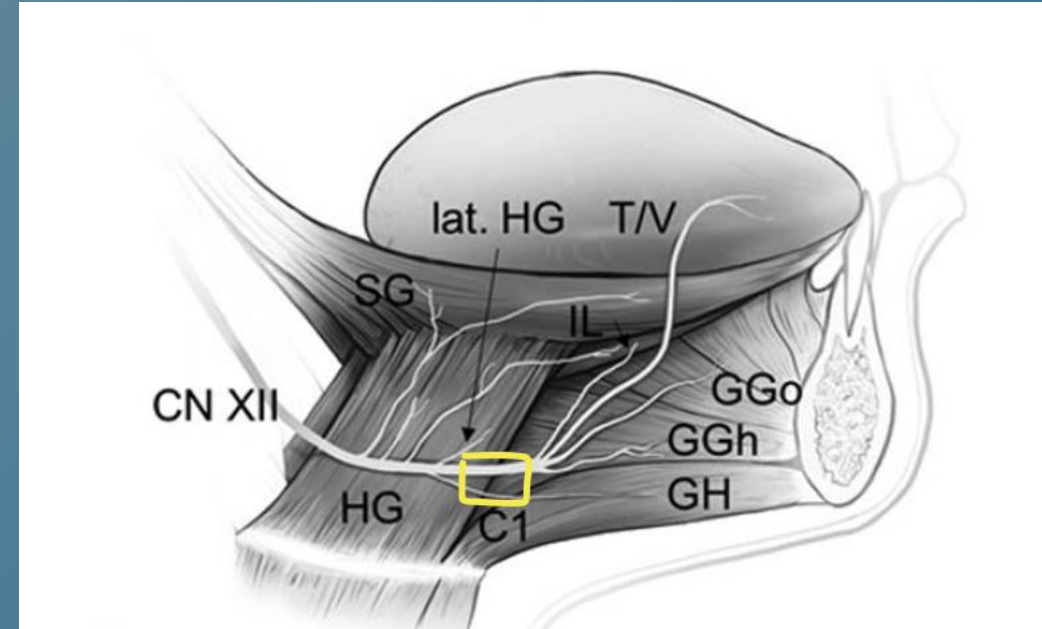


BILATERAL MEDIAL DIVISION PLACEMENT



Mechanism of therapy

- Hypoglossal nerve innervates tongue musculature
 - Pure motor nerve
 - Branches distally into medial and lateral divisions
 - Lateral division supplies tongue retractors (hyoglossus, styloglossus)
 - Medial division supplies tongue protrusor (genioglossus) and tongue stiffeners (transverse and vertical)
- HNS selectively stimulates the medial branch (Inspire and Genio)



Adapted from Heiser C, Thaler E, Boon M, Soose RJ, Woodson BT. Updates of operative techniques for upper airway stimulation. *The Laryngoscope*. 2016;126(S7). doi: [10.1002/lary.26158](https://doi.org/10.1002/lary.26158)

HNS mechanism



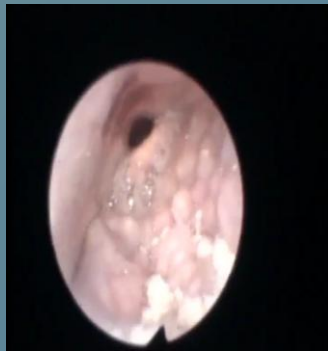
- Base of tongue pulled forward
- Pulls soft palate forward
- Turned on at bedtime
- Treats every breath, not apneic pauses
- Stiffening of airway dilators persists briefly after stimulation off
 - May keep airway less collapsible when off

Hypoglossal Nerve Stimulation Effect

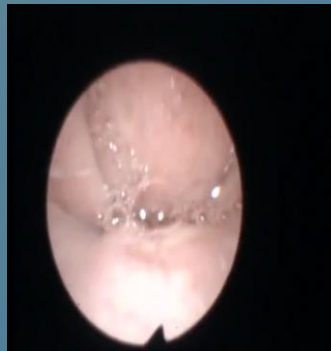
No Stimulation



Base of Tongue



Palate



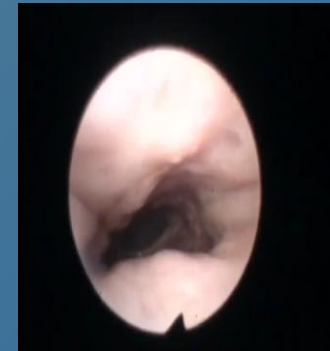
Stimulation



Base of Tongue



Palate



Inspire-Genio differences

Inspire

- Unilateral stimulation
- Breath sensing
- Stimulation timed with end-exhalation
 - End exhalation airway is most vulnerable to collapse



Genio

- Bilateral stimulation
- No breath sensing or synchronization
- Rate approximates breathing rate
- On for 70% of respiratory cycle
- Stimulation on for “most” inspirations at least partially



Inspire vs. Genio

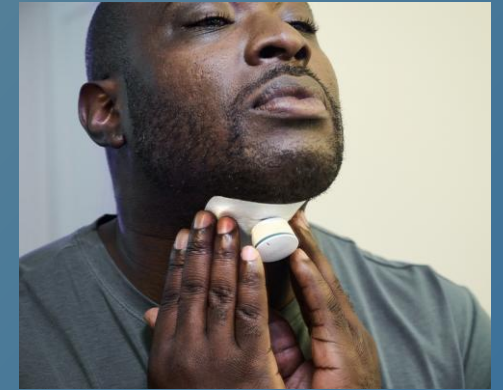
Inspire

- Fully implanted
 - Electrode
 - Lead wire
 - IPG with battery
- Turned on with handheld remote



Genio

- Partially implanted
 - Dual electrodes with antenna
- Pulse generator (“Activation Chip”) and battery not implanted
 - Placed on skin with adhesive patch over the implanted electrodes
 - Patches are disposable
 - AC charged on charging stand



Inspire vs. Genio

Inspire

- IPG battery lasts 10-12 years
 - Surgically replaced
- Full-body 1.5T MRI
- 3.0T MRI except shoulders and chest

Genio

- AC replaced as needed or with newer generation models
- No additional surgeries
- Full-body 3.0T MRI
- Men must keep upper central neck shaved

Indications



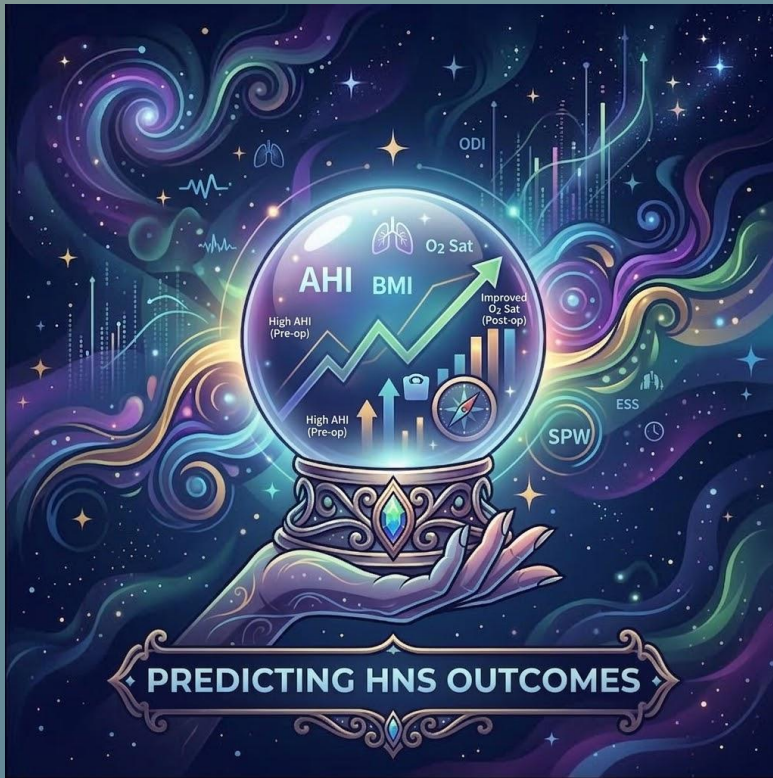
- Adults with CPAP intolerance or refusal
- Down's syndrome children (>13 years)
- Moderate to severe OSA
 - 15-100 non-Medicare, 15-65 Medicare
- No severe obesity
 - BMI < 40 non-Medicare, BMI < 35 Medicare

Contraindications

- Central sleep apnea
 - Central AHI > 25% of total AHI
- Large tonsils (3 or 4+)
- Complete concentric collapse
 - Inspire
 - Genio just announced results of ACCCESS
 - CCC patients
 - 77% Sher 20 responder rate
 - 88% ODI responder rate (>25% ODI reduction)
 - Results to be presented at upcoming ISSS
 - Nyxoah preparing submission to FDA to expand indications to include CCC
- Allergy to adhesive patch (Genio only)



Outcome predictors: what do we know?

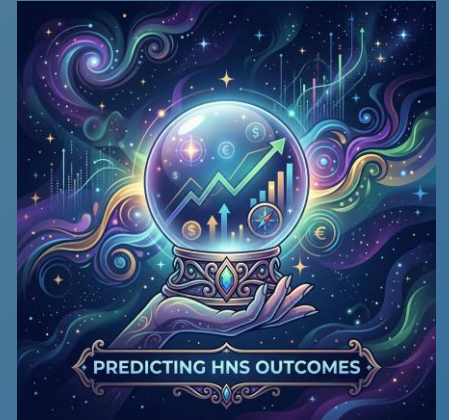


Better outcomes:

- Significant insomnia predicts poorer outcomes
 - Low arousal thresholds
 - Decreased tolerance
 - Therapeutic voltage causes arousals
 - Poor adherence
- Increasing obesity reduces AHI reduction
- Lateral and concentric collapse (pending publication of ACCCESS trial)

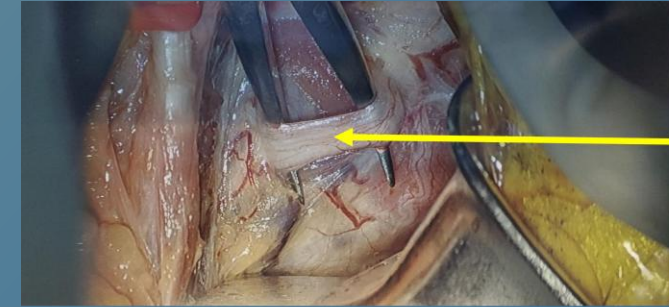
Better outcome predictors

- Large pharyngeal width (SPW)
 - HNS does not widen the oropharyngeal airway significantly
- Older age
- Lower BMI
- Lower tPAP pressure
- Females

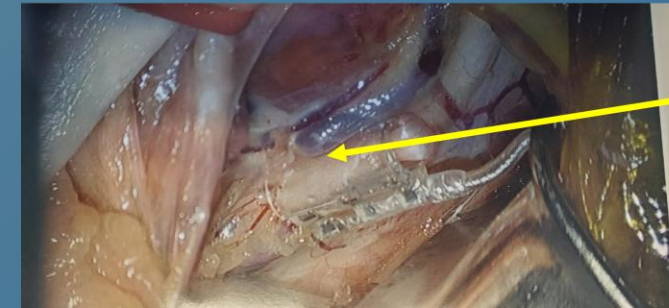


Surgical procedures – Inspire

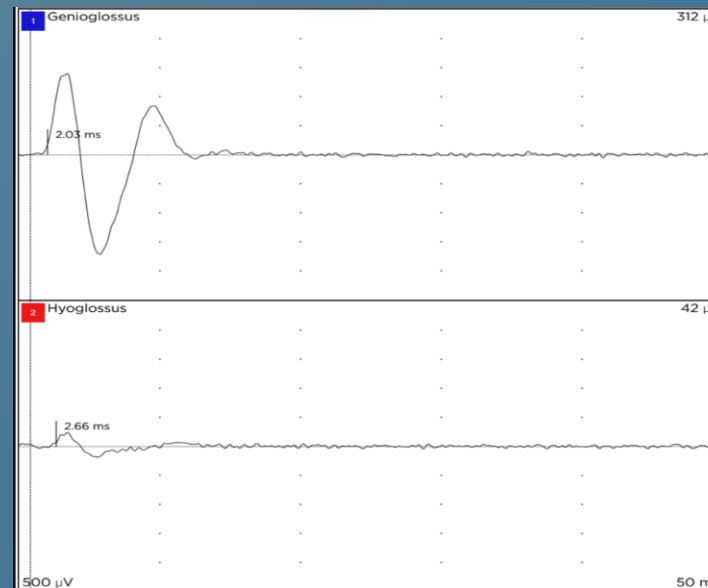
- Neck incision under mandible
- Electrode placed around medial HN
- Must ensure no retrusor branches included
 - Intraoperative EMG
 - Direct observation of muscle contractions
 - Genioglossus
 - Hyoglossus



Isolated and NIM tested inclusion branches

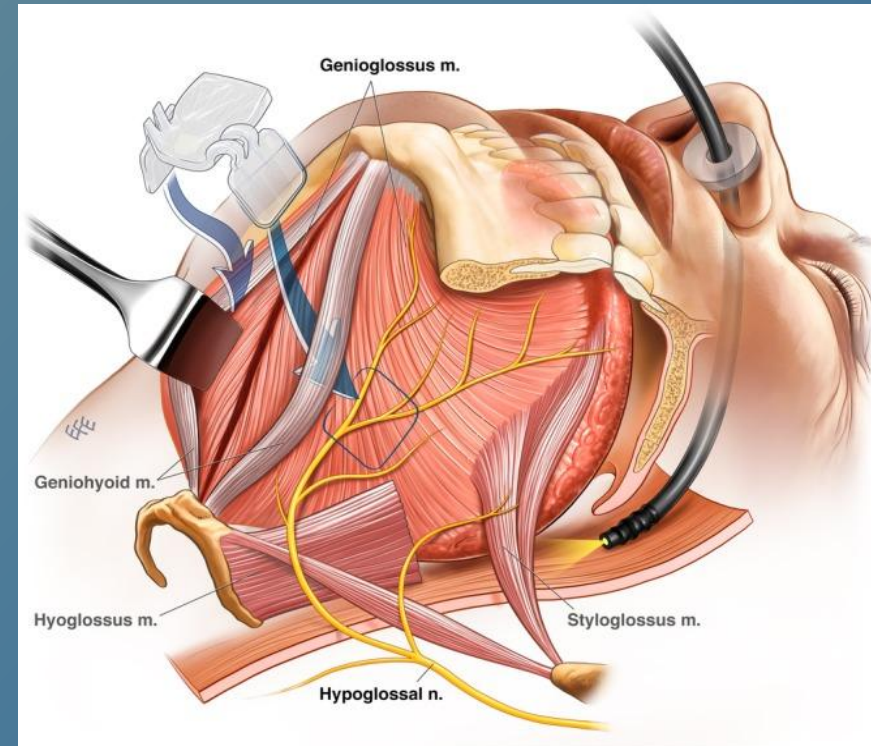


Stimulator lead around inclusion branches



Surgical procedures - Genio

- Midline neck incision under chin
- Implant placed deep to mylohyoid and geniohyoid muscles on top of genioglossus muscles
- Paddle electrodes (L and R) over distal branches of HN
- Visual confirmation of GG contraction and no HG contraction
- EMG signal confirmation



Postoperative device management

- Postoperative activation
 - Inspire in 4 weeks
 - Genio in 8 weeks

Inspire activation

- Start with program A
- Determine sensation threshold
- Determine functional threshold
 - Minimum voltage needed to cause some movement of tongue
- Run waveform
 - Evaluates sensing function



Inspire activation

- Set range based on the functional threshold
 - 0.5-0.1 V increments
- Can use ramp function
 - Starts therapy (after pause) at 80 or 90%
- Set start delay based on patient's needed time to fall asleep
- Set pause time
- Set therapy duration

Therapy is Off Turn On **John Doe** ID: 123456-78 De-ID: MPLS-062 Serial #: AIR----- Home

Stimulation Summary Initial Activation (3 of 3)

Review Recommendations and Configure Initial Therapy Settings

Stimulation Settings
Stimulation settings are based on saved stimulation levels and patient comfort during testing.

Recommended Stimulation Settings
Amplitude **1.8 V**
Lower Limit **1.8 V**
Upper Limit **2.8 V**

☒ Enable Patient Control

Amplitude V
1.8 ▼ ▲ Test Stimulation

Lower Limit V **1.8** ▼ ▲ (-0V)
Upper Limit V **2.8** ▼ ▲ (+1V)

Timing Settings
Recommended Timing Settings
Start Delay **30 m**
Pause Time **15 m**
Therapy Duration **8 h**

Start Delay m **30** ▼ ▲
Pause Time m **15** ▼ ▲
Therapy Duration h **8** ▼ ▲

Previous Step Test Connection Configure Done

Demonstration Mode 9 December 2020 01:44

Inspire post-activation



- Patient starts at functional threshold
- Remote used to increase 1 level every 1-2 weeks as tolerated
- Can decrease amplitude if needed for comfort
- Stop increasing once symptoms improved/resolved or maximum tolerated amplitude reached
- If still symptomatic but pt can't tolerate higher amplitude, consider comfort changes (reduced frequency, pulse width, ramp function) or change program (B-E)

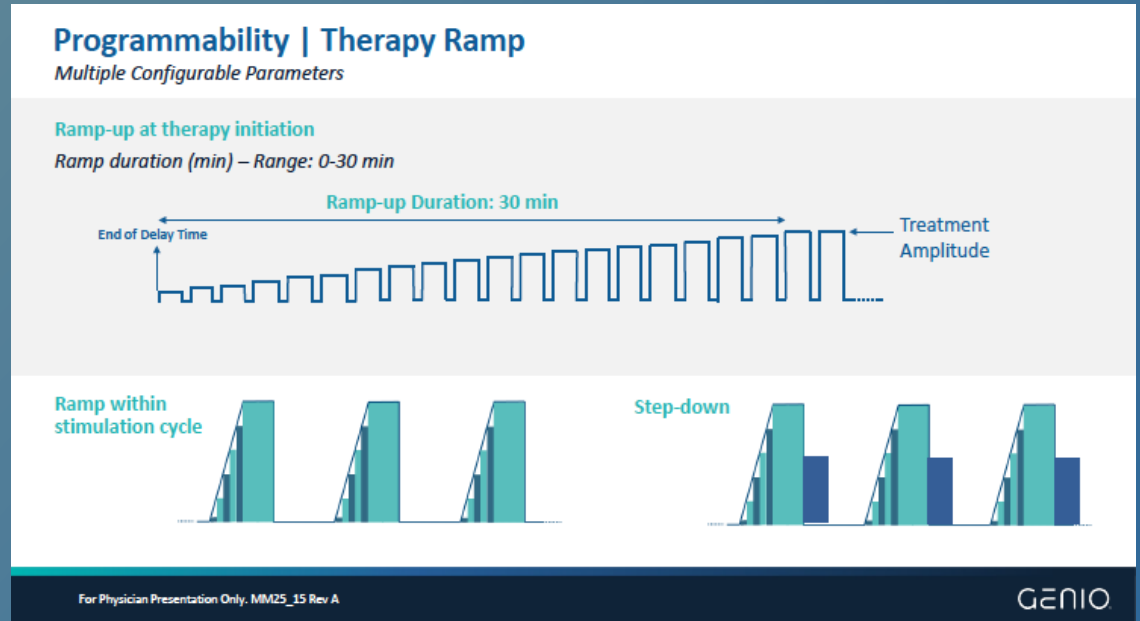
Genio activation

- Determine functional threshold
- Start therapy at FT
- Treatment amplitude is expressed as % of maximum (0-100%)
- Can adjust frequency (rate) and duration (width)



Genio comfort modifications

- Can ramp treatment *amplitude* over 0-30 min
- Can ramp within a stimulation cycle
- Can step down at end of stimulation
- Can reduce frequency or pulse duration similar to Inspire



Genio post-activation

- Therapy intensity is gradually increased as tolerated by pt using remote or by clinician at follow up



Troubleshooting: awake endoscopy

- Intolerance and/or inadequate apnea reduction
- Performed in office with awake pt
- Simultaneous viewing of retropalatal and retroglossal airway
- Programs A-E evaluated (Inspire)
- Allows visual assessment of movement of base of tongue and palate with stimulation
- Identify program/settings with best observed motion AND pt comfort

Awake endoscopy

- Can assess for over-titration
- Can assess for impact of nasal vs. oral breathing
 - If nasal breathing improves HNS effect:
 - Mouth tape or chin strap
 - Address nasal obstruction
- Can assess for cervical extension
 - If extension improves HNS effect, consider cervical pillow
- Can assess for jaw thrust
 - If improves HNS effect, consider dual therapy with MAD

Assessing efficacy

- During therapy progression:
 - nightly pulse oximetry (track ODI, T90, LSAT)
 - Periodic HSAT after adjustments
- Titration PSG
 - ONLY after symptomatic and objective improvements reached AND patient tolerating therapy
 - Titrated from just below home setting and above home setting as tolerated to identify optimal amplitude

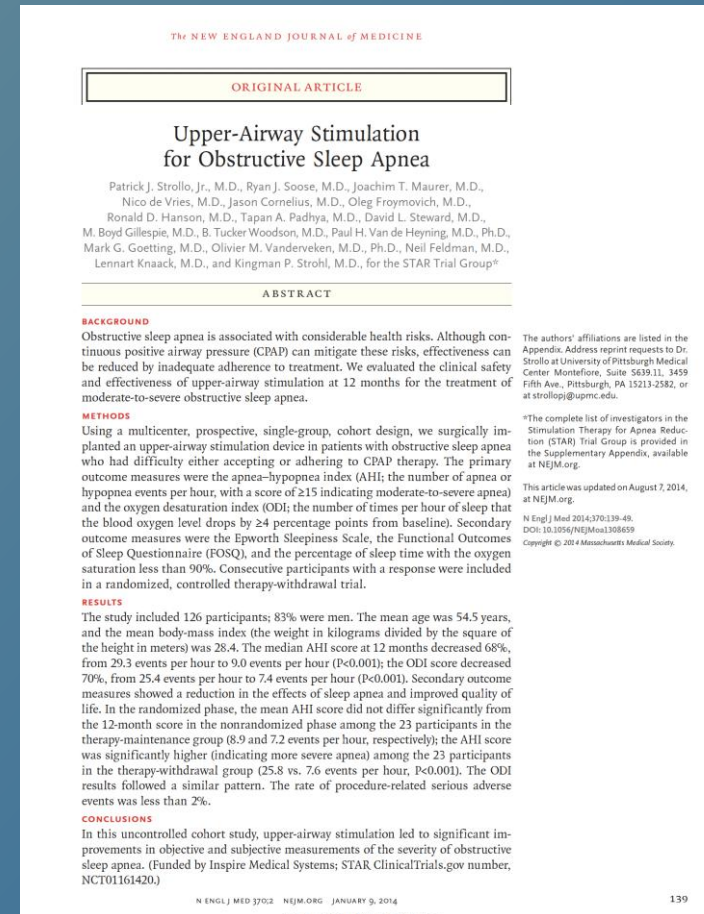


DISE with HNS

- *Performed if adequate apnea reduction not achieved*
- At maximal intensity tolerated for each program A-E (Inspire) preop
- Repeat baseline DISE to confirm site(s) of airway collapse
- Turn on HNS and test with each program
- Helps determine why HNS not opening airway with incoming program
- May identify a more effective program (Inspire)
- May suggest value of other surgical interventions

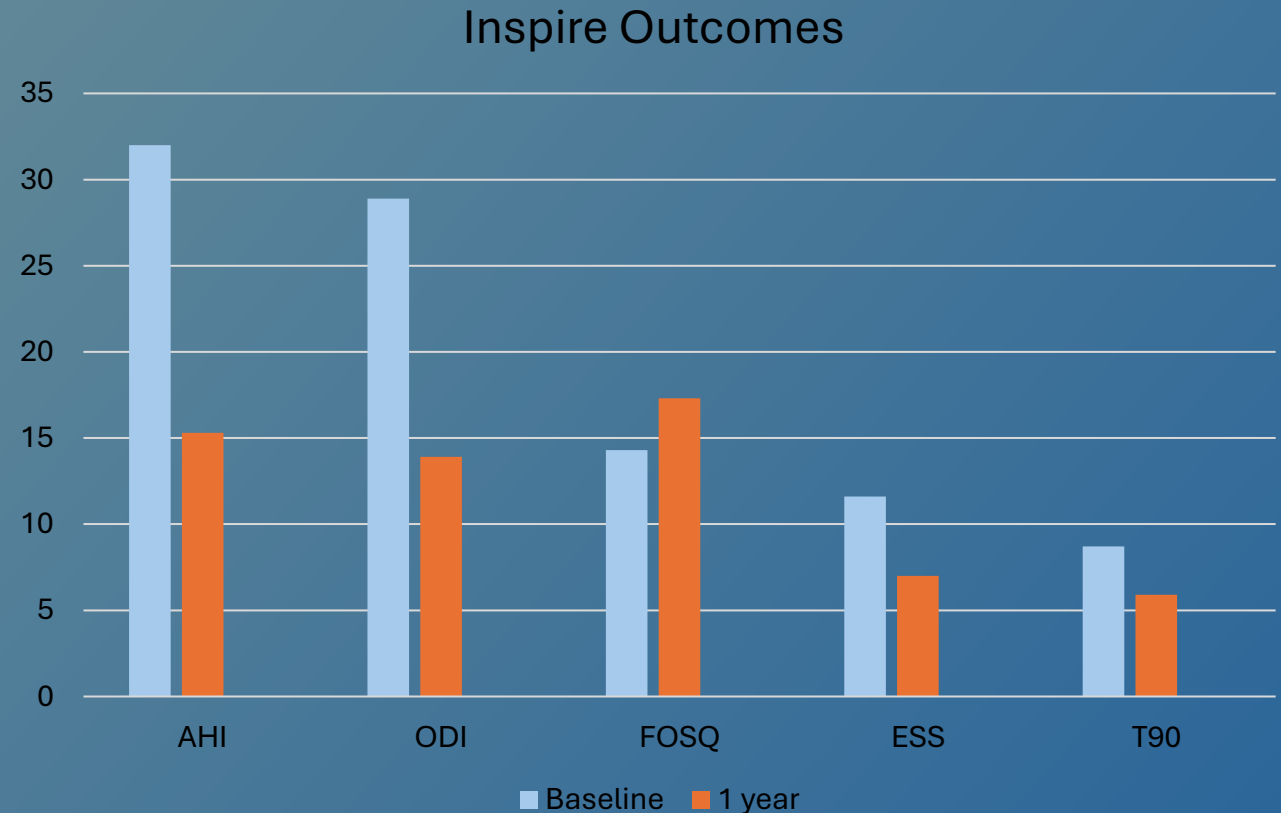
Outcomes: Inspire

- STAR trial, NEJM 2014
- AHI 20-50, mean 32.0
- BMI <32, mean 28.4
- No CCC
- 126 participants
- 124 completed study
 - 1 cardiac death
 - 1 explanted



Outcomes: Inspire

- 66% Sher20 response rate
- AHI decreased 68%
- ODI decreased 70%
- FOSQ increased 2.9
- ESS decreased 4.7
- T90 decreased 2.5%



Outcomes: Genio

- DREAM trial, JCSM 2025
- BMI < 32, mean 28.5
- AHI 15-65, mean 28.0
- ODI (4%) mean 27.0
- Minimum of 55 min supine sleep on PSG
- No CCC

JCSM | Journal of
Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Bilateral hypoglossal nerve stimulation for obstructive sleep apnea: a nonrandomized clinical trial
B. Tucker Woodson, MD¹; David T. Kent, MD²; Colin Huntley, MD³; Melyssa K. Hancock, MD⁴; Douglas J. Van Daele, MD⁵; Maurits S. Boon, MD⁶; Tod C. Huntley, MD⁷; Sam Mickelson, MD⁸; M. Boyd Gillespie, MD, MSc⁹; Maria V. Suuma, MD¹⁰; Ashutosh Kacker, MD, MBBS, MS¹⁰; Asim Roy, MD¹¹; Stuart MacKay, BSc(Med), MBBS, FRACS¹²; Kirk P. Withrow, MD¹³; Raj C. Dedhia, MD, MSCR¹⁴; Philip Huyett, MD¹⁵; Clemens Heiser, MD, PhD¹⁶; Sylvie di Nicola, MS¹⁷; Fatma Makori, MS¹⁸; Olivier M. Vanderveken, MD, PhD¹⁹; Tapan A. Padya, MD²⁰; Ulysses J. Magalang, MD²¹; Eugene Chio, MD²¹; Eric J. Kazian, MD, MPH²²; Richard Lewis, MBBS, FRACS²³
¹Medical College Wisconsin, Milwaukee, Wisconsin; ²Vanderbilt Univ. Medical Center, Nashville, Tennessee; ³Thomas Jefferson University, Philadelphia, Pennsylvania; ⁴ENT & Allergy Associates of Florida, Boca Raton, Florida; ⁵University of Iowa, Iowa City, Iowa; ⁶Center for ENT & Allergy, Carmel, Indiana; ⁷Advanced ENT Associates, Atlanta, Georgia; ⁸The University of Tennessee Health Science Center, Memphis, Tennessee; ⁹University of Miami Medical Center, Miami, Florida; ¹⁰West Coast Medicine, New York, New York; ¹¹Sleep Medicine Institute, Nebraska Ohio Medical University, Dublin, Ohio; ¹²Head & Neck Clinic, Illawarra ENT, Wollongong, New South Wales, Australia; ¹³University of Alabama at Birmingham, Birmingham, Alabama; ¹⁴University of Pennsylvania, Philadelphia, Pennsylvania; ¹⁵Harvard University, Mass Eye & Ear, Boston, Massachusetts; ¹⁶Technische Universität München, München, Germany; ¹⁷Inferential Premium Biometry, Paris, France; ¹⁸Faculty of Medicine, Translational Neurosciences, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium; ¹⁹University of South Florida, Tampa, Florida; ²⁰The Ohio State University Wexner Medical Center, Columbus, Ohio; ²¹Ohio ENT and Allergy Physicians, Columbus, Ohio; ²²Department of Head and Neck Surgery, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California; ²³Perth Head & Neck Surgery, Perth, Western Australia, Australia

Study Objectives: To evaluate the safety and efficacy of a novel bilateral hypoglossal nerve stimulation (HNS_{BL}) device for the treatment of obstructive sleep apnea.
Methods: Adult patients with moderate-to-severe obstructive sleep apnea who refused, failed, or did not tolerate positive airway pressure therapy underwent implantation and nightly use of HNS_{BL}. The coprimary endpoints at 12 months were (1) a minimum of 50% reduction in the 4% apnea-hypopnea index (AHI) from baseline with a final AHI of less than 20 events/h, and (2) a minimum of 25% reduction in the 4% oxygen desaturation index. Objective secondary endpoints included changes in mean AHI, oxygen desaturation index, and sleep time with blood oxygen saturation less than 90%. Self-reported secondary endpoints included changes in Epworth Sleepiness Scale, the short Functional Outcomes of Sleep Questionnaire score, the Symptoms of Nocturnal Obstruction and Related Events score, and bedpartner assessment of snoring.
Results: HNS_{BL} was implanted in 113 participants. Eleven serious adverse events occurred in 10 (8.7%) participants. The coprimary endpoints were completed by 89 (77.4%) participants. AHI and oxygen desaturation index responses were achieved in 63.5% (73/115, *P* = .002) and 71.3% (82/115, *P* < .001), respectively. Secondary endpoint analysis revealed significant changes in mean AHI (−18.3 ± 11.8 events/h, *P* < .001), oxygen desaturation index (−17.7 ± 14.6 events/h, *P* < .001), and sleep time with blood oxygen saturation less than 90% (6.9 ± 10.7%, *P* < .001). Significant changes were observed in all secondary endpoints (*P* < .001).
Conclusions: This pivotal clinical trial of HNS_{BL} demonstrated an acceptable safety profile with clinically significant improvements in obstructive sleep apnea severity and quality-of-life metrics. HNS_{BL} is a promising new treatment option for select patients with obstructive sleep apnea.
Clinical Trial Registration: Registry: ClinicalTrials.gov; Name: Dual-sided Hypoglossal NeRVe StimulAtion for the TreatMent of Obstructive Sleep Apnea (DREAM); URL: <https://clinicaltrials.gov/study/NCT03868618>; Identifier: NCT03868618.
Keywords: obstructive sleep apnea, hypoglossal nerve stimulation, sleep surgery
Citation: Woodson BT, Kent DT, Huntley C, et al. Bilateral hypoglossal nerve stimulation for obstructive sleep apnea: a nonrandomized clinical trial. *J Clin Sleep Med*. 2025;21(11):1883–1891.

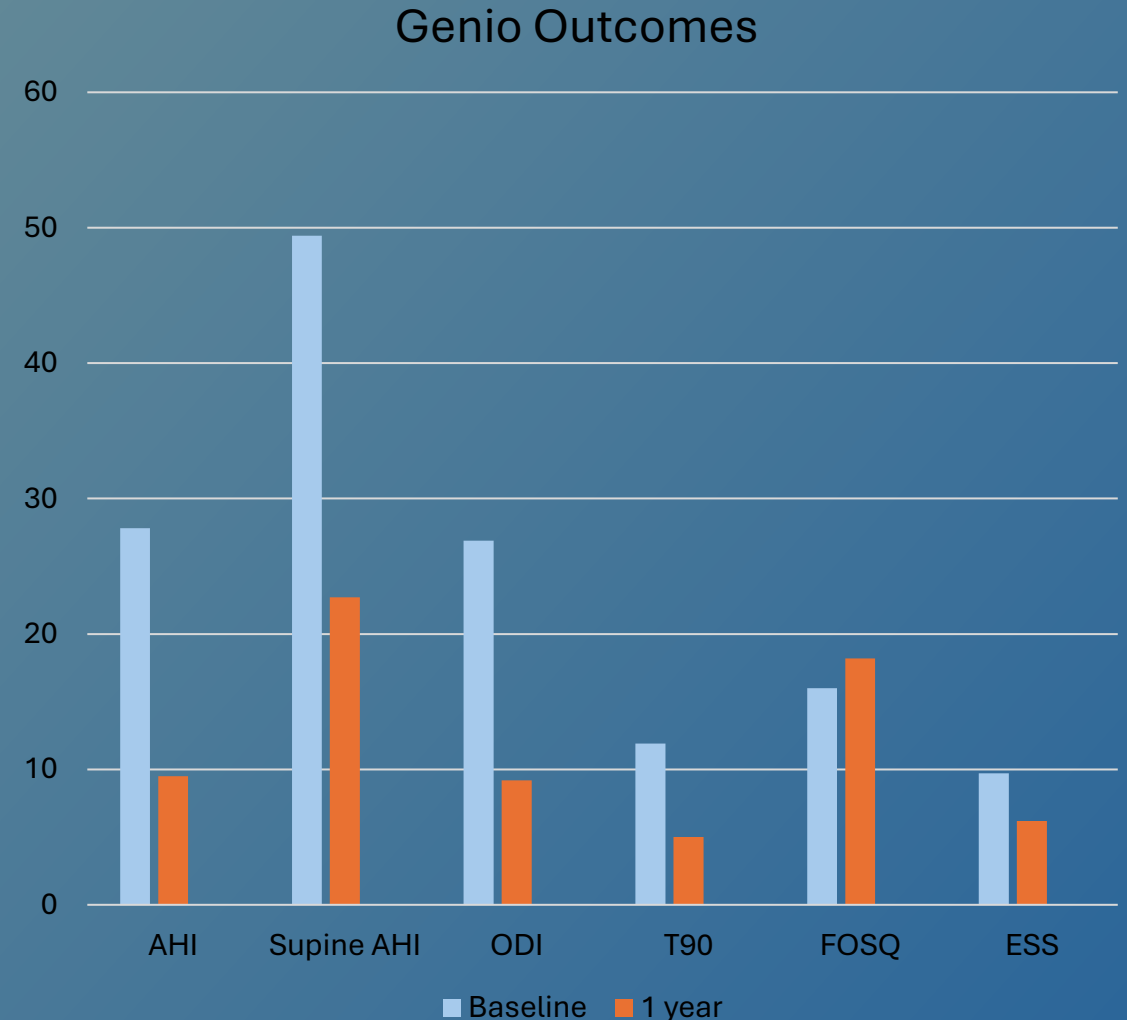
BRIEF SUMMARY
Current Knowledge/Study Rationale: Bilateral hypoglossal nerve stimulation is a novel approach to treat patients who have failed, refused, or not tolerated positive airway pressure or positional therapy. Therapy efficacy and safety were assessed over 12 months in 115 participants in a prospective, multicenter clinical trial.
Study Impact: The coprimary outcomes documented significant treatment response rates for decrease in the apnea-hypopnea index (63.5%; 73/115, *P* = .002) and the oxygen desaturation index (71.3%; 82/115, *P* < .001). Eleven serious adverse events occurred in 10 (8.7%) participants of which 3 (2.6%) were device related, 5 (4.3%) were procedure related, and 3 (2.6%) were unrelated to the device or the procedure.

INTRODUCTION
Obstructive sleep apnea (OSA) is a common disease characterized by recurrent episodes of upper airway obstruction during sleep.¹ Moderate-to-severe OSA affects nearly a half-billion people worldwide,² and has been associated with an increased risk of cardiovascular mortality and decreased quality of life.^{1,3–5} Positive airway pressure (PAP) is well established as the first-line treatment modality for OSA, but many patients struggle to maintain adherence due to myriad side effects.^{1,6,7}

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Outcomes Genio:

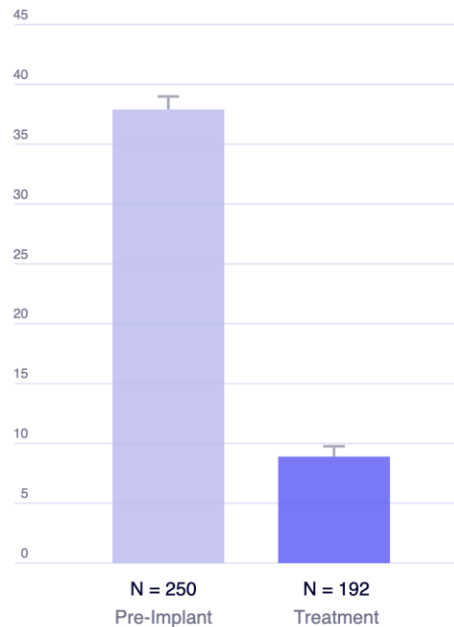
- 81.2% Sher20 responder rate (per protocol group), 63.5% (intention to treat group)
- AHI decreased 66.1%
- ODI decreased 65.8%
- Supine AHI decreased 55.1%
- T90 decreased 58%
- FOSQ increased 2.2
- ESS decreased 3.5



My outcomes

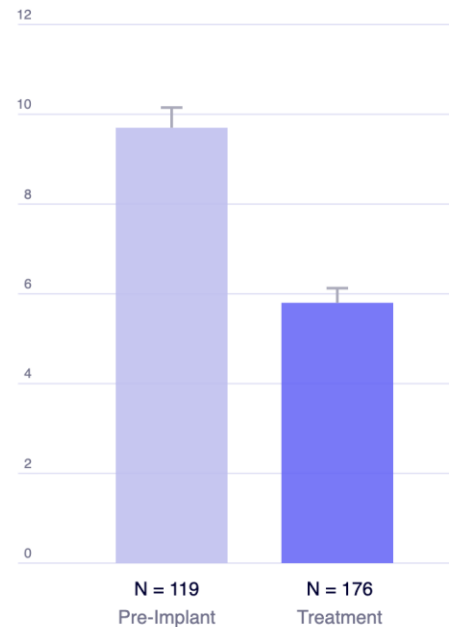
AHI outcomes

Mean treatment AHI: 8.9 (N=192)
Median treatment AHI: 5.3
Treatment AHI < 15: 86%



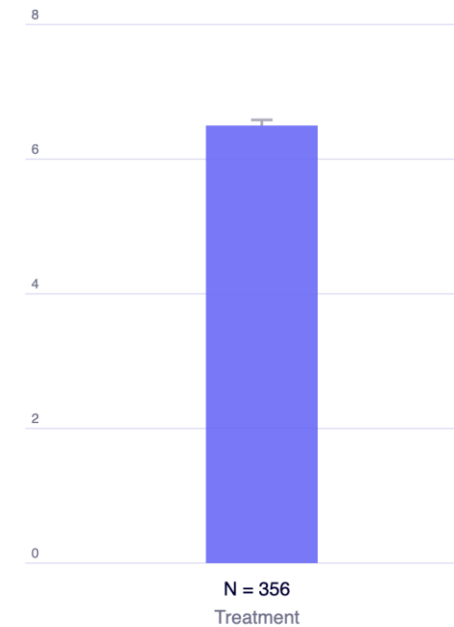
ESS outcomes

Mean treatment ESS: 5.8 (N=176)



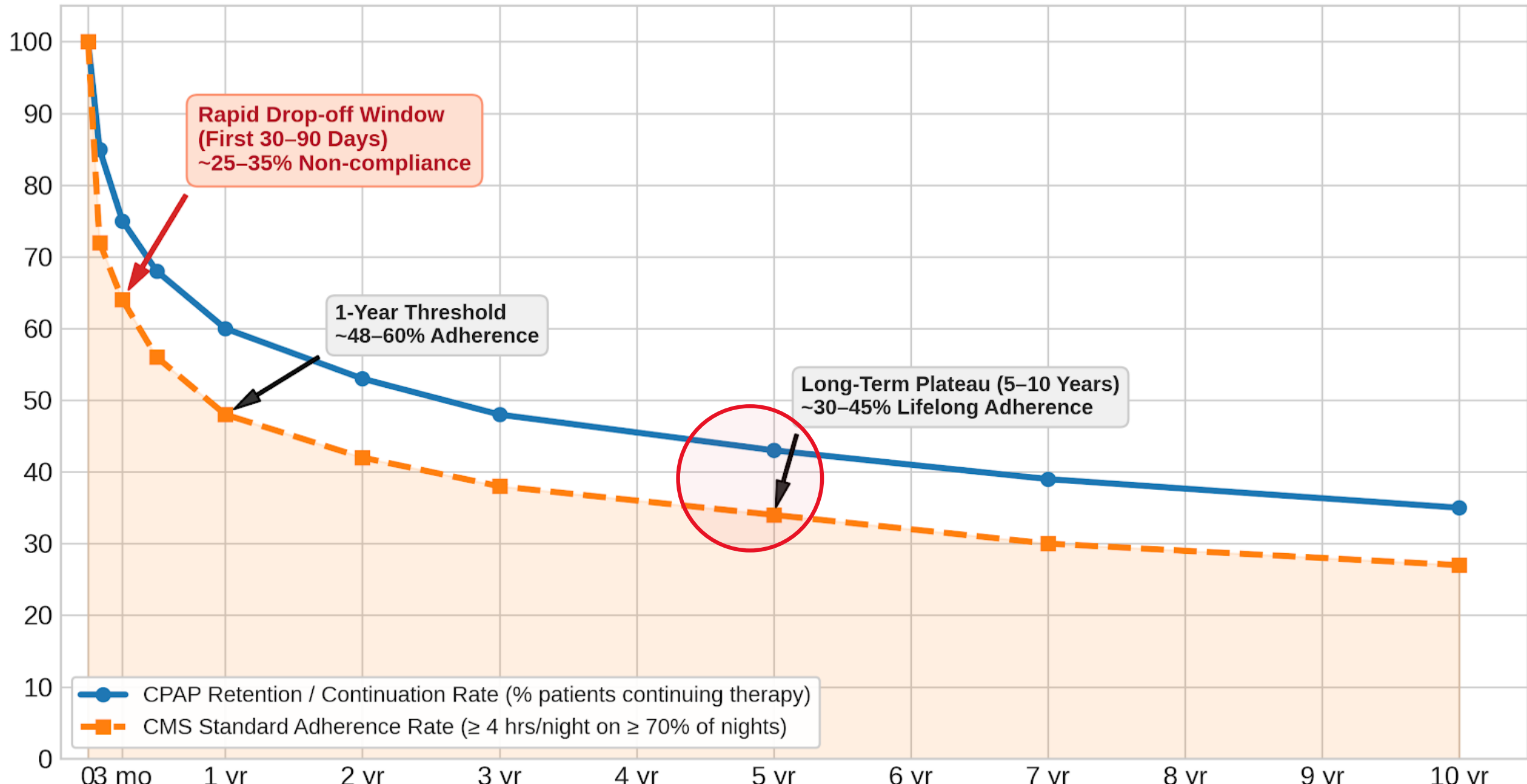
Practice utilization

Mean adherence: 6.5 (N=356)
Nights used $\geq$ 4 hours: 77.1%



My own thinking on these
therapies after implanting more
than 600 devices.

Longitudinal CPAP Adherence & Retention Rates Over Time (Synthesis of Published Clinical Trials & Real-World Registry Data)



My thoughts: CPAP



- CPAP remains the most efficacious therapy
- 1st line for most patients
- CPAP limited by low long-term adherence
- Highest efficacy is useless for patients not using therapy
 - 4 hours is *minimum* to confer benefit
 - > 6 hours is *ideal* for maximum benefit

My thoughts: HNS

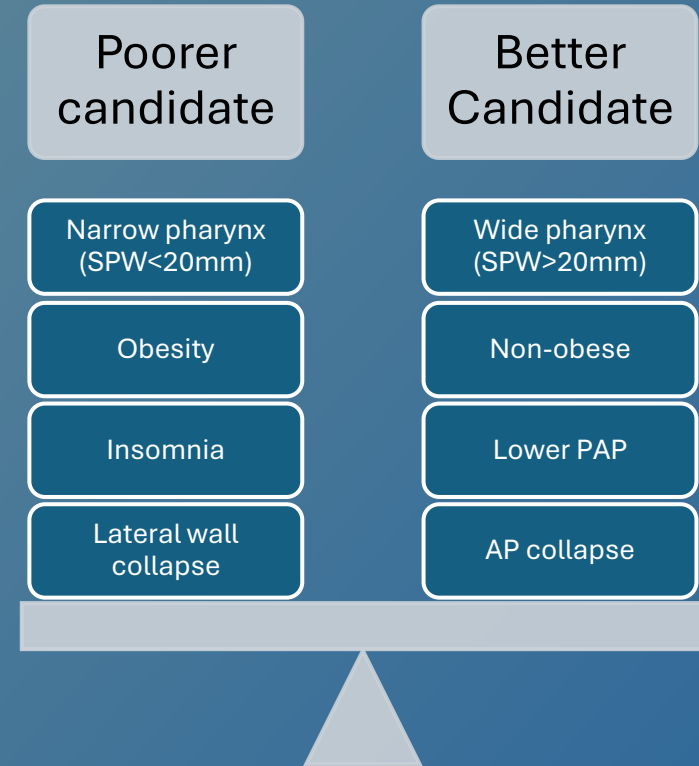
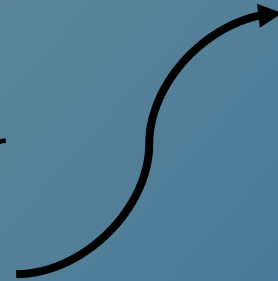
- HNS
 - Good option for non-adherent users
 - Safe
 - Well-tolerated
 - Acceptable AHI reduction
 - High adherence



Thoughts on HNS: patient selection

- **Patient selection is critical**

- FDA criteria is only first step
- Not all CPAP-intolerant patients are good candidates
- Patient selection is important for good outcomes
 - Think about prognostic indicators
- Meticulous surgical technique is also vital for better outcomes
 - Only protrusion branches are included
 - Even one tiny late exclusion branch will reduce optimal tongue motion



- **Weiner Sleep Surgery**
- www.weinersleepsurgery.com
- (c) 480-223-3185
- (p) 480-614-0499
- j.weiner@me.com

