

Nyxoah Analyst Meeting

March 23, 2023



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KOL Speakers

Dr. Maurits S. Boon

Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

Maurits Boon is a Professor in Otolaryngology - Head and Neck surgery who is double boarded in Sleep Medicine. He has a practice that focuses on treatment of adult OSA. He researches and has extensive experience in sleep surgery and specifically using hypoglossal nerve stimulation. He is one of the authors and primary editors of the first textbook on hypoglossal nerve stimulation for treatment of OSA.



Dr. Maria V. Suurna

University of Miami Health Systems, Coral Gables, Florida

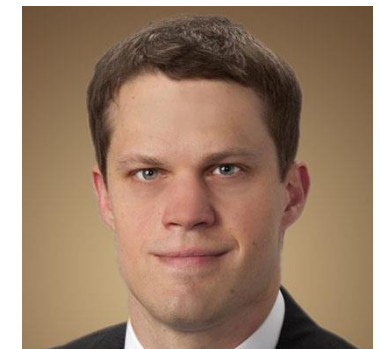
Maria V. Suurna, MD, FACS, is a Professor of Clinical Otolaryngology – Head and Neck Surgery Director of Sleep Surgery in the at the University of Miami Health and adjunct faculty at Weill Cornell Medicine. She is board certified in Otolaryngology and subspecialty board certified in Sleep Medicine. Dr. Suurna is nationally and internationally recognized as an expert in sleep surgery. She is dedicated to providing a comprehensive evaluation and treatment for snoring and obstructive sleep apnea, with the focus on sleep surgery including hypoglossal nerve stimulation implant.



Dr. David T. Kent

Vanderbilt University Medical Center, Nashville, Tennessee

Dr. David Kent is a surgeon-scientist with a clinical and academic career dedicated to the comprehensive management of sleep-disordered breathing, including obstructive sleep apnea (OSA). Dr. Kent was the first provider in Tennessee to offer hypoglossal nerve stimulation (Inspire) therapy as a treatment option for people with OSA. Dr. Kent's research focuses on the neurophysiology of the upper airway, especially mechanisms for control of breathing in OSA.



Nyxoah Analyst Meeting

Agenda

The Nyxoah Journey

*Olivier Taelman – Chief Executive Officer
Senior Management*

Hypoglossal Nerve Stimulation and The Genio Solution

Dr. Maurits S. Boon – Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

Addressing Complete Concentric Collapse

Dr. Maria V. Suurna – University of Miami Health Systems, Coral Gables, Florida

A Review of Ansa Cervicalis

Dr. David T. Kent – Vanderbilt University Medical Center, Nashville, Tennessee

Closing Remarks

Olivier Taelman – Chief Executive Officer

Q&A

Reception



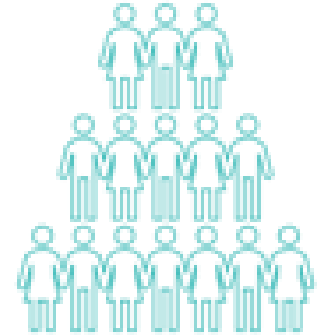
The Nyxoah Journey

Olivier Taelman – Chief Executive Officer

Blueprint for MedTech Success

Large & Underpenetrated Addressable Market

- 425M worldwide suffer from moderate to severe OSA requiring therapy
- Annual HGNS eligible population: US – 510,000 & Europe – 500,000
- < 50,000 HGNS implanted patients worldwide



Genio® Patient-Centric Solution

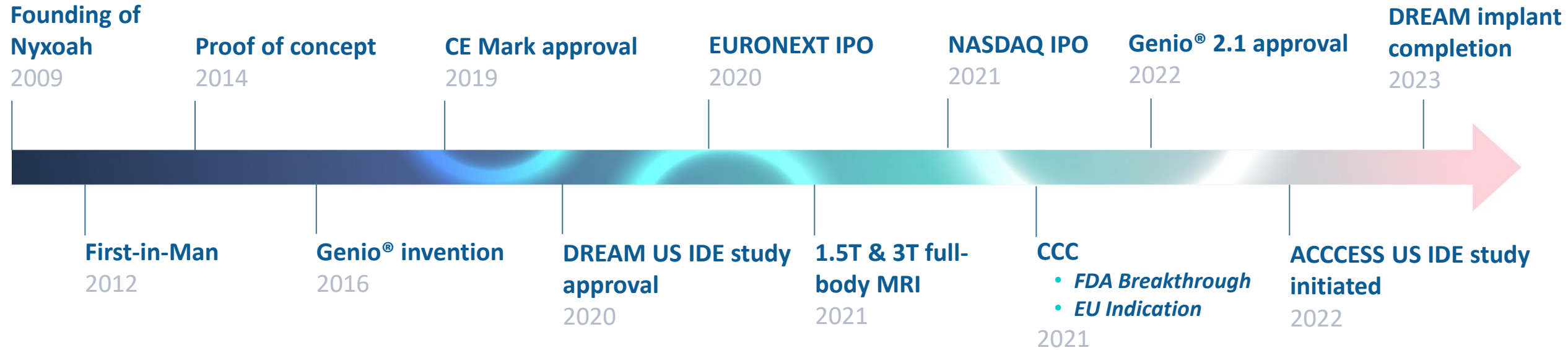
- Full-body MRI compatibility
- Scalable technology platform
- Single incision, leadless
- Bilateral stimulation
- External battery



Established Reimbursement

- HGNS fully covered by Medicare, Medicaid and Commercial payors in US
- DRG in Germany and Switzerland
- Germany commercial proof of concept





Nyxoah Is a Global Company

138 employees worldwide and expanding



Belgium

- Headquarter
- Finance, Clinical & Marketing
- Fully validated manufacturing site since 2023



Germany

- Dedicated Sales & Marketing
- Commercial proof of concept



United States

- Clinical, Regulatory & Market Access
- DREAM and ACCESS pivotal studies
- Commercial readiness



Israel

- R&D, Quality & Manufacturing



Australia

- Clinical





Hypoglossal Nerve Stimulation and The Genio Solution

Dr. Maurits S. Boon

Genio System From Nyxoah

Maurits S. Boon, MD
Professor
Vice Chairman of Education
Residency Program Director
Otolaryngology - Head and Neck Surgery
Thomas Jefferson University

Conflict of Interest Disclosures for Speakers

1. I do not have any relationships with any entities **producing, marketing, re-selling, or distributing** health care goods or services consumed by, or used on, patients, **OR**
2. I have the following relationships with entities **producing, marketing, re-selling, or distributing** health care goods or services consumed by, or used on, patients.

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	Inspire Medical Nyxoah Medical
Consultant	Inspire Medical Nyxoah Medical
Speakers' Bureaus	
Financial support	
Other	

3. The material presented in this lecture has no relationship with any of these potential conflicts, **OR**
4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

1. Upper Airway Stimulation for Obstructive Sleep Apnea. NEJM 2014
2. Upper Airway Stimulation for Obstructive Sleep Apnea: Results from the ADHERE Registry. Otolaryngology – Head and Neck Surgery. 2018
3. Bilateral hypoglossal nerve stimulation for treatment of adult obstructive sleep apnoea. Eur. Resp J. 2020

Which of the following is true?

- A Worldwide prevalence of at least mild OSA is greater than 900,000,000
- B Conventional treatment with CPAP is highly effective but poorly tolerated
- C Hypoglossal nerve stimulation is an alternative to CPAP therapy which is highly effective in select patients

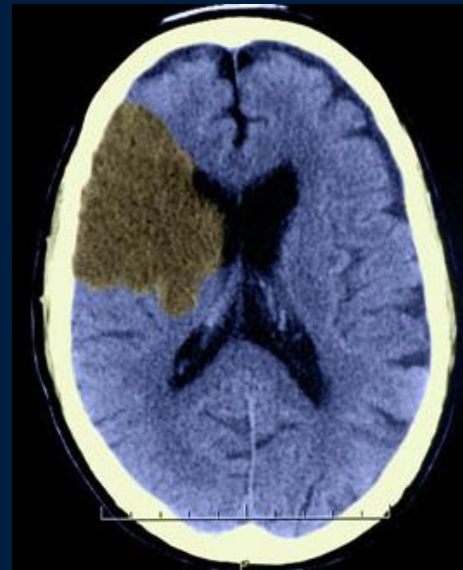
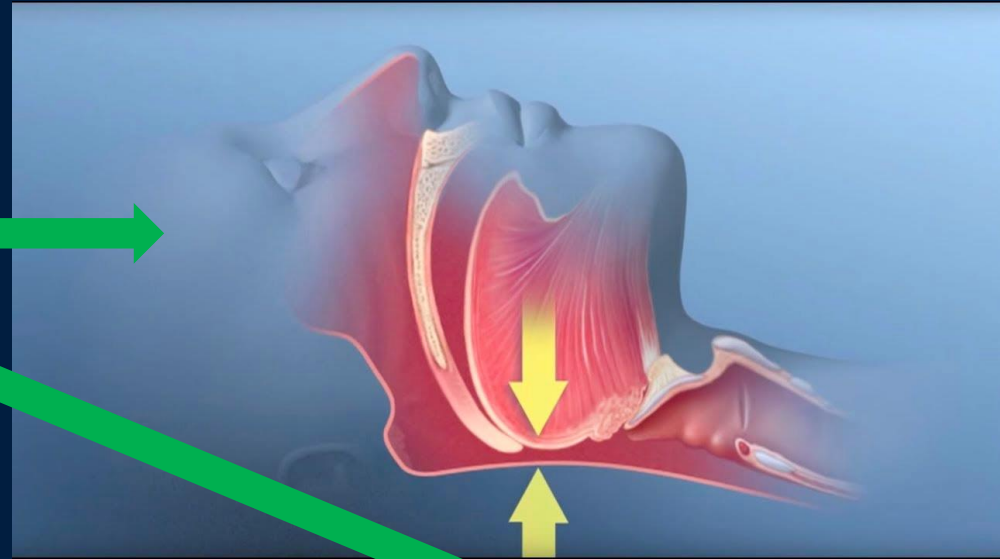
Objectives:

- Background of OSA
- Scope of the problem
- How hypoglossal nerve stimulation works
- Unique features of the Genio system
- Need for the Genio system from Nyxoah

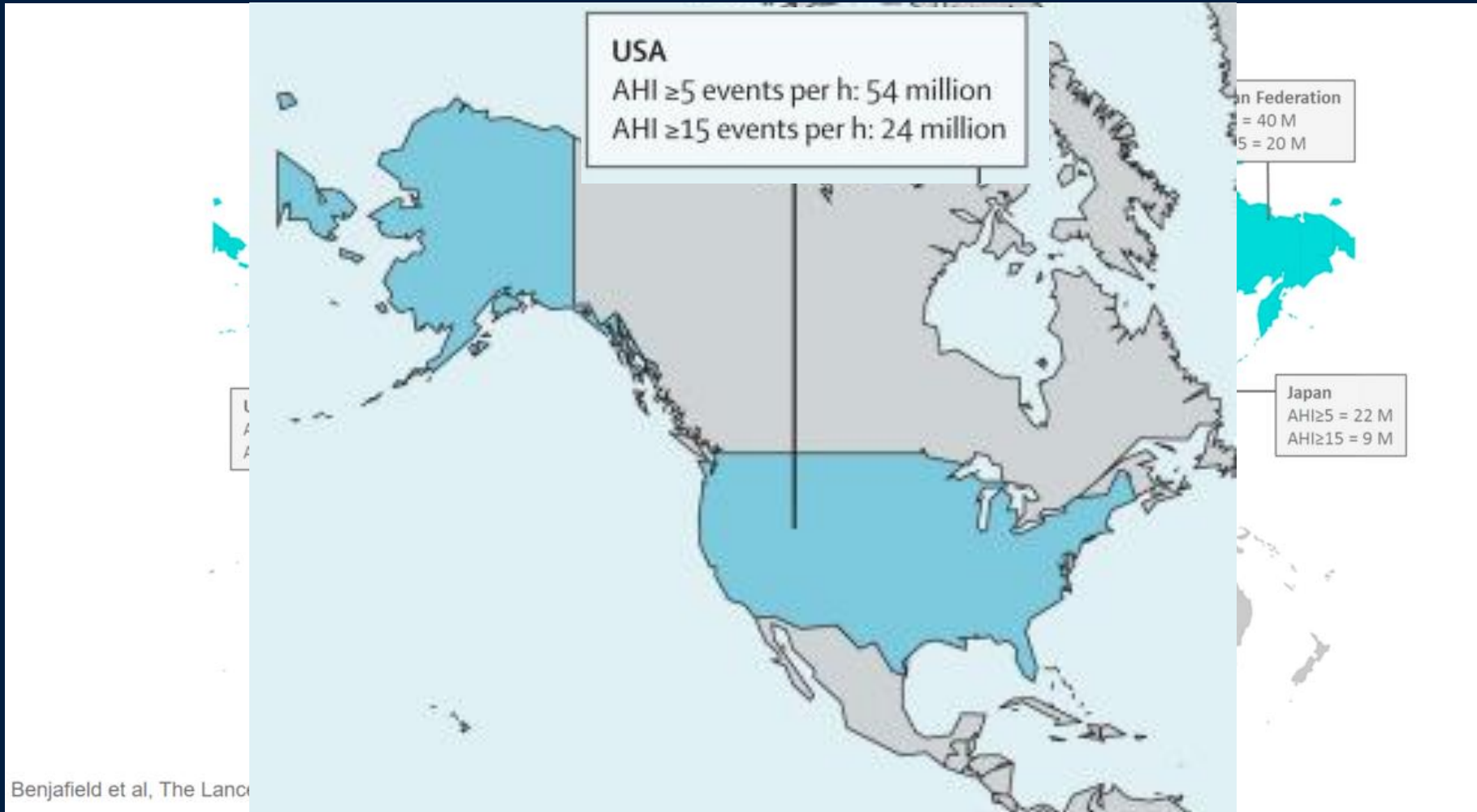


What is OSA?

- Repetitive episodes of airway obstruction that occur during sleep

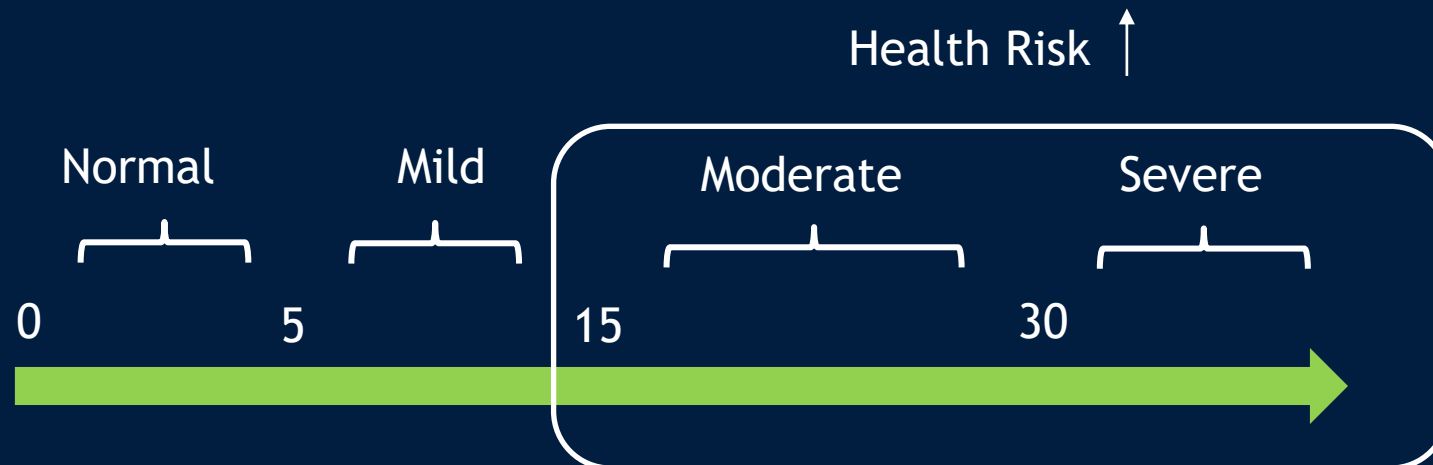


OSA is a Big Problem



Basics of OSA

- AHI primary measurement of disease severity
- AHI / REI: Measurement of number of episodes of airway obstruction that occur on average each hour during sleep



Treatment of OSA

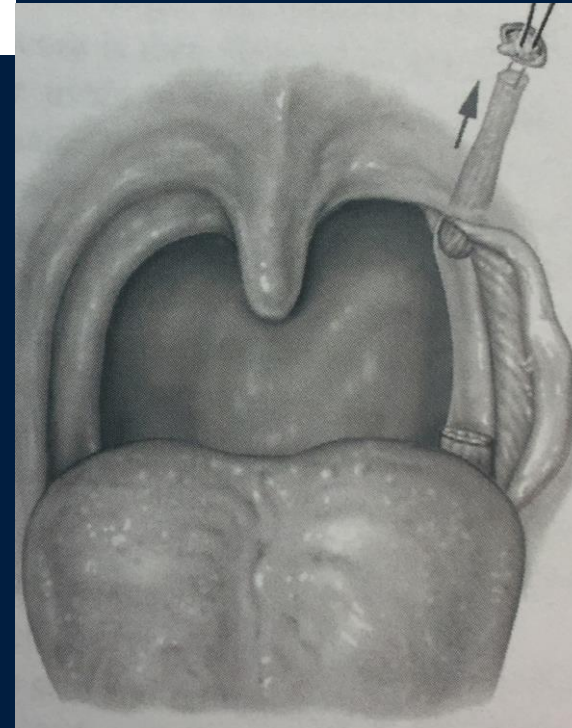
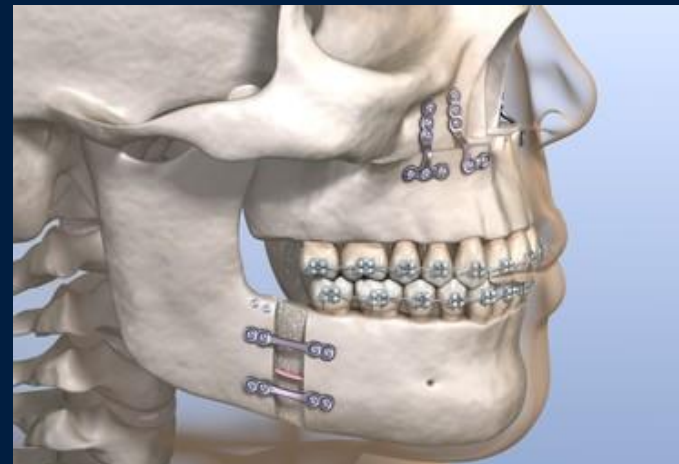


- CPAP first line treatment
- Pneumatic splint
- Highly effective at opening airway

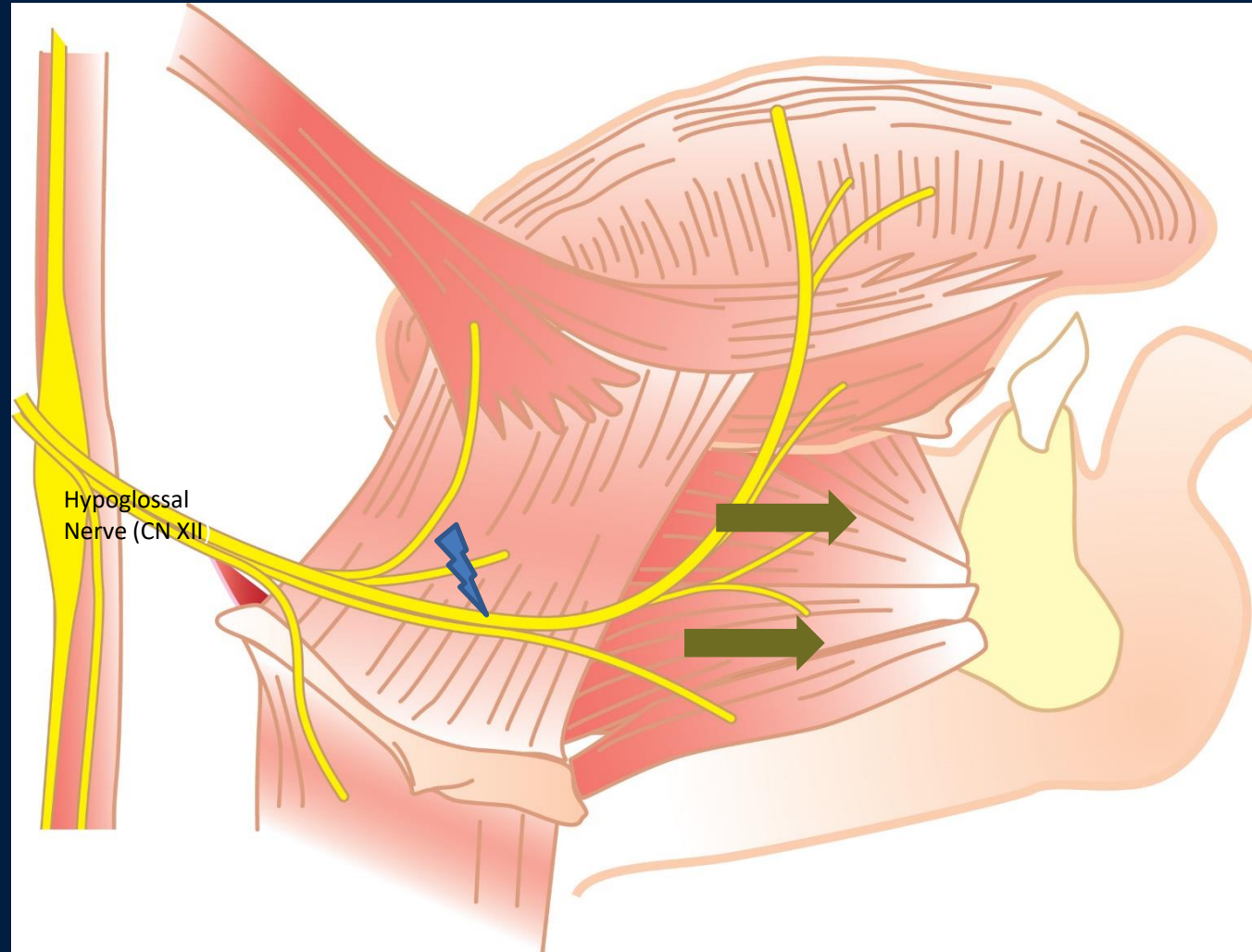
Tolerance Adherence <50%

Alternative Therapies

- EPAP
- Oral appliances
- Surgery

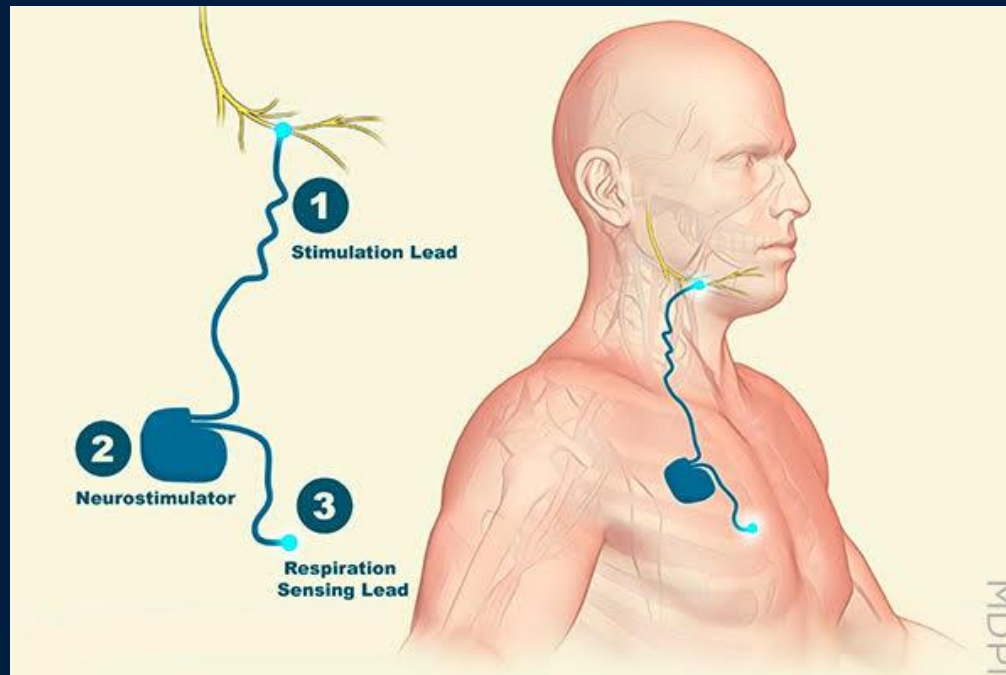


Hypoglossal Nerve Stimulation



Hypoglossal Nerve Stimulation

- Trials since the late 1990s
- Now an established therapy in multiple countries
- FDA approved Inspire system in 2014
- >36,000 implants as of February 2023

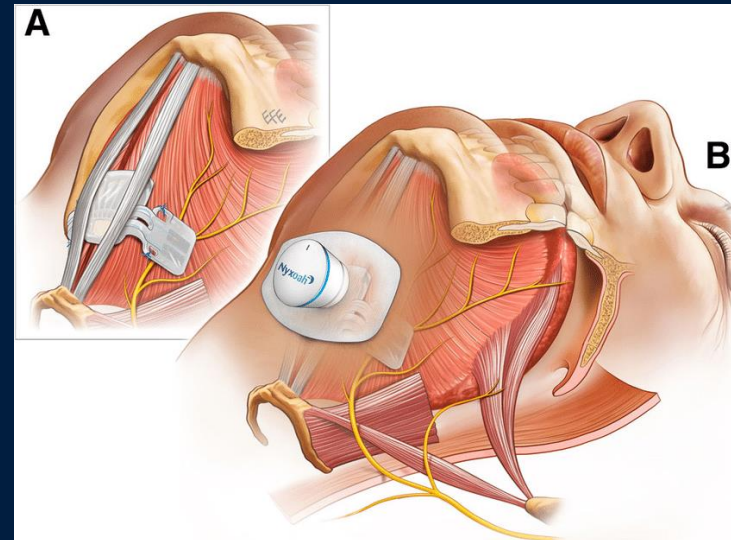


What's Different About The Genio System?

Single incision under the chin



Stimulation of both hypoglossal nerves

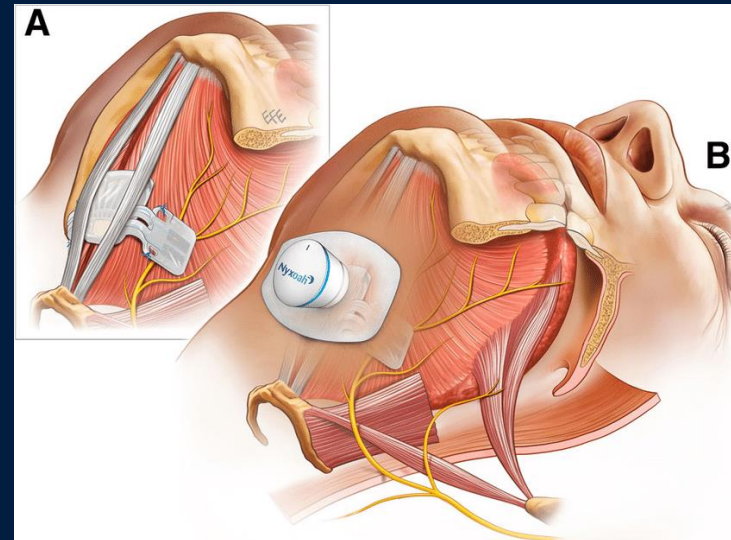


No implanted battery



What's Different About The Genio System?

Stimulation of both hypoglossal nerves



No implanted battery



What's Different About The Genio System?



Full-body, 1,5T and 3T MRI compatible

Genio technology

Safe, well-tolerated and effective

EU Approval - Safety & Efficacy

BLAST OSA - 27 patients

91% patients use the system more than 5 days/week
EU approval in 2019

Expand Genio® therapeutic indications

BETTER SLEEP - 42 patients

64% AHI responder rate after 6 months
CCC represented 43% of study cohort

FDA market authorization

DREAM - 115 patients

Implants completed

FDA - CCC Indication

ACCESS - 106 patients

First implants completed in Q1 2023



CCC label expansion in Europe
Breakthrough designation in the US > ACCESS

12-month data - Q1 2024
Abstract submission SLEEP June 2023

Implants completion - Q4 2024

Hypoglossal Nerve Therapy Need



- Burden of disease is huge with upwards of 50+ million people affected
- Conventional CPAP therapy is effective but poorly tolerated
- Huge need for this therapy
- >36,000 HGNS implants in US as of February 2023

Synopsis:

- Well tolerated / safe and effective therapy
- Huge patient need
- Established track record of efficacy



The Nyxoah Journey

David DeMartino – Chief Strategy Officer

Guidepoint Survey

- Sample size – 25 clinicians
- 12 US ENTs + 4 German ENTs
- 9 US Sleep Specialists

Physician Profile

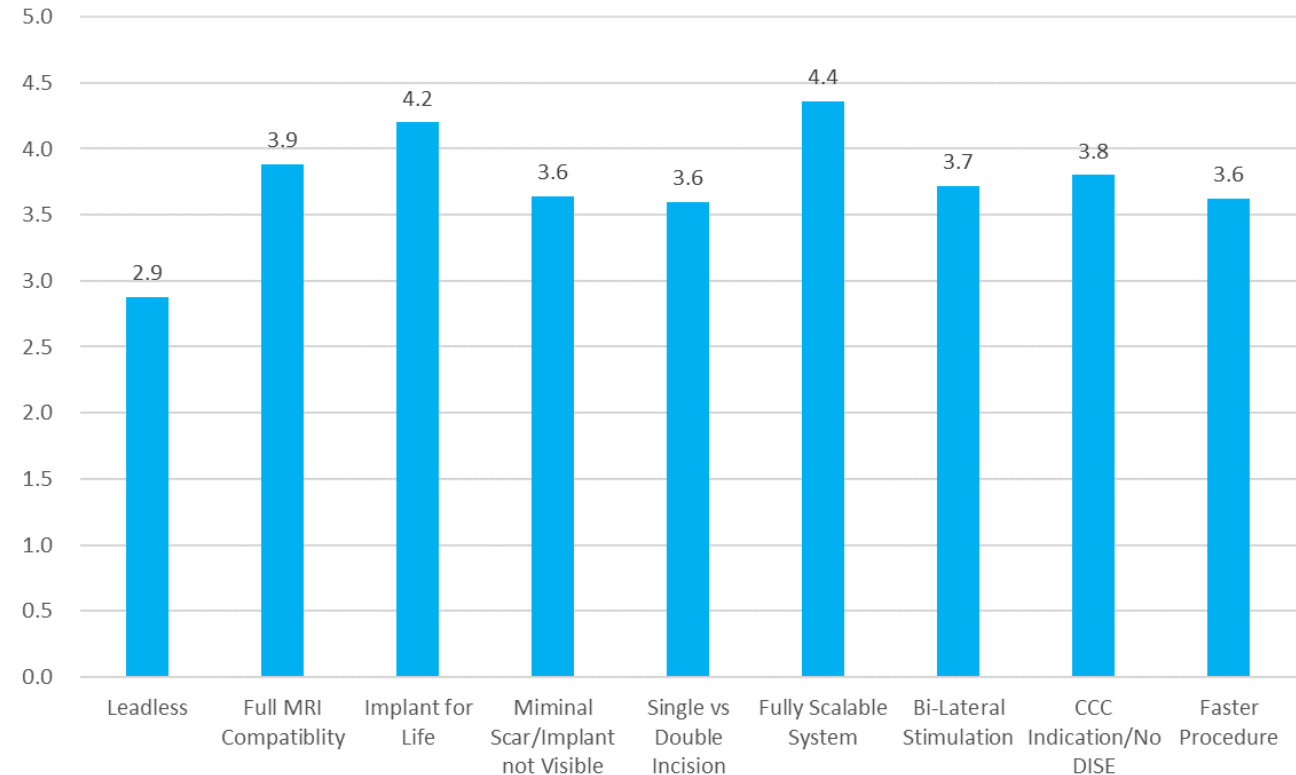
- Clinicians at least “somewhat familiar” with Genio and Inspire systems
- ENTs – Average annual HGNS implants = 40
- Sleep Specialists – Average annual HGNS referrals = 47

Genio's Patient-Centric Design Resonates with Clinicians

Importance of Genio's Key Features

From 1-5, with 5 being the highest

- **Scalability** – No need for additional surgery to receive the “latest-and-greatest” technology
- **No implantable battery** – No need to replace depleted battery
- **1.5T & 3T full-body MRI compatibility** – Peace of mind for patients and doctors
- **No CCC diagnosis required with CCC label expansion** – No need for DISE or alternatives

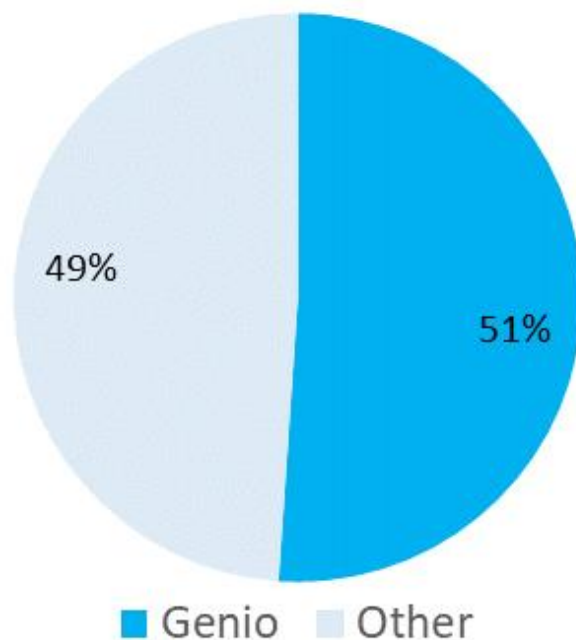


Note: n=25, aside from faster procedure data which only includes ENTs (n=16)

Genio is Well Positioned to Successfully Enter the Market

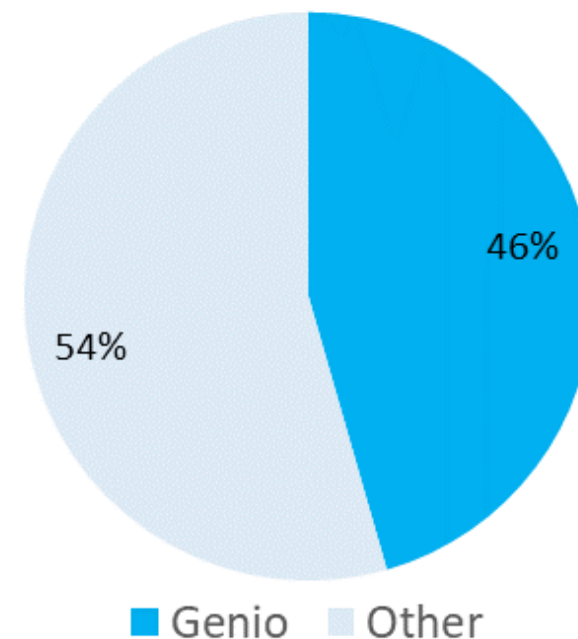
HGNS market share survey results

If Genio was available today, what percent of your HGNS implants would it represent?



ENTs

If Genio was available today, what percent of your HGNS referrals would it represent?



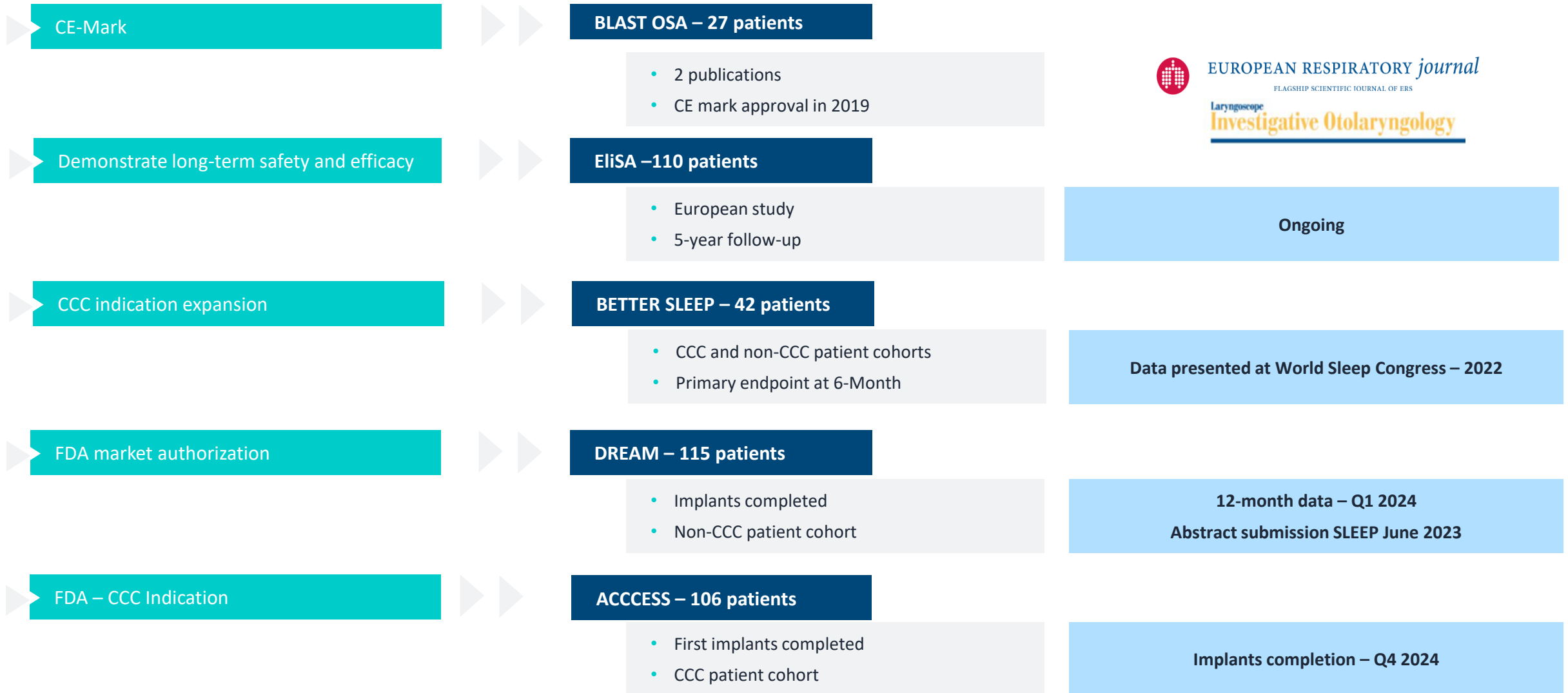
Sleep Specialists



The Nyxoah Journey

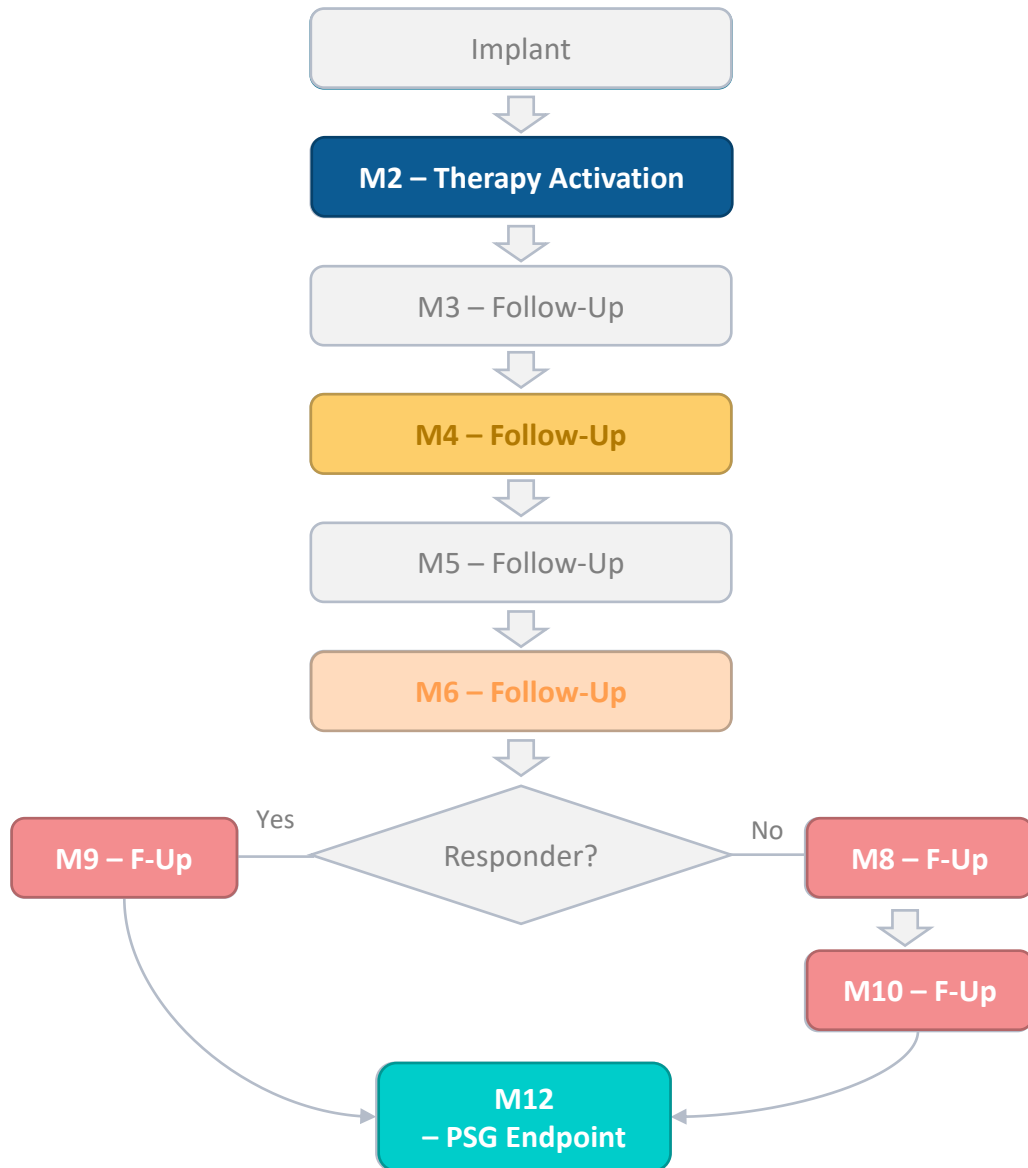
Jey Subbaroyan – VP Medical Affairs & Clinical Research

Clinical Strategy Overview



The Clinical Patient Journey With Genio

The "6 As"



ACQUIRE – Implant Technique

ACQUAINT – Setting Expectations

ACCLIMATE – Key to Success

ADAPT – Eliminate & Hone-In

ASCERTAIN – Dress rehearsal

ACHIEVE – Responder



Addressing Complete Concentric Collapse

Dr. Maria V. Suurna

Addressing Complete Concentric Collapse

Maria V. Suurna MD, FACS

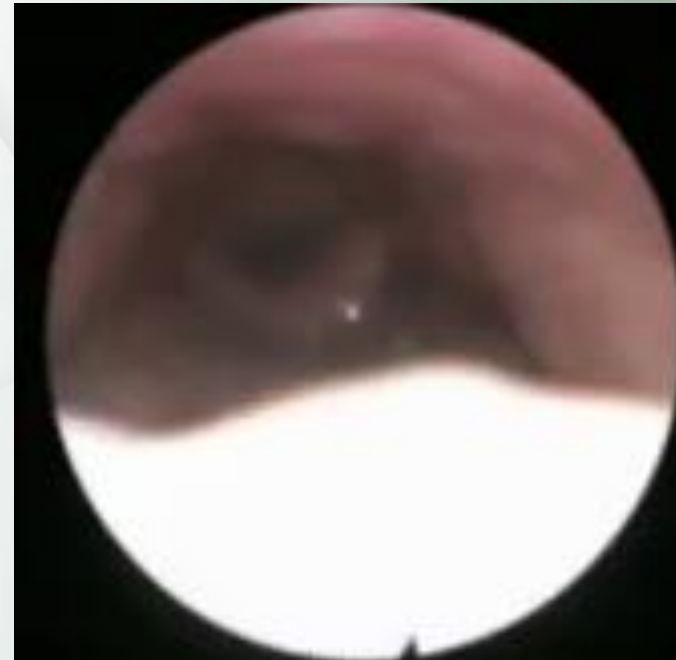
Director of Sleep Surgery
Department of Otolaryngology-Head and Neck
Surgery

Disclosures

- Inspire Medical - Consultant, Medical Advisory Board
- Medtronic - Consultant , Medical Advisory Board
- Nyxoah - Consultant, Scientific Advisory Board

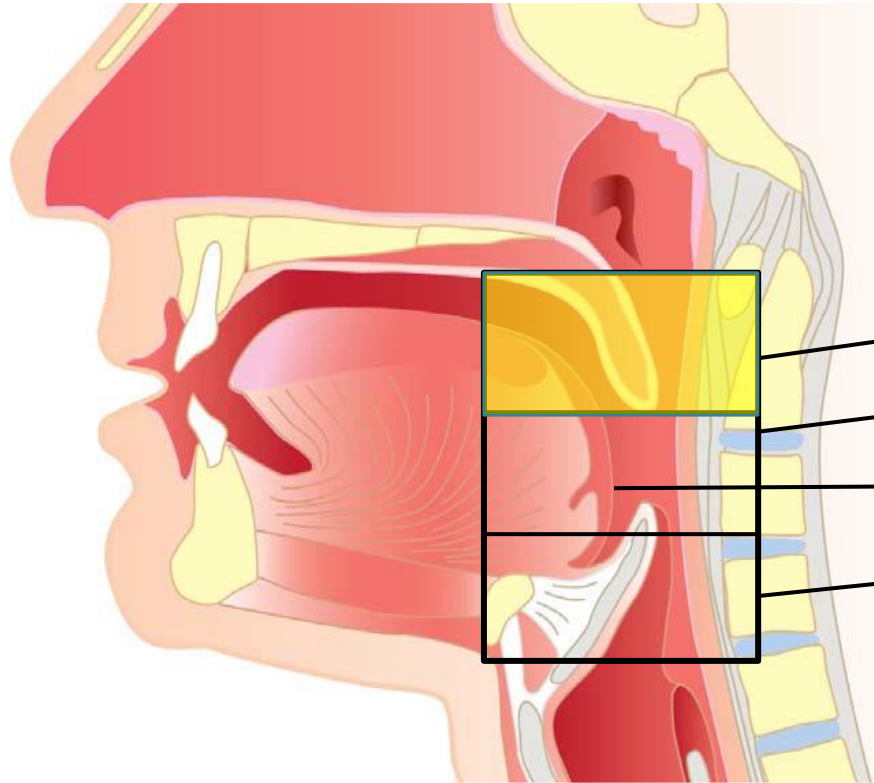
Drug Induced Sleep Endoscopy (DISE) Provides Structure-based, Dynamic Evaluation of the Upper Airway During Sedation

In 1991 Croft and Pringle described the technique of “**sleep nasendoscopy**” as the fiberoptic examination of the upper airway under conditions of spontaneous ventilation and pharmacologic sedation



VOTE Classification System can be Used to Report DISE Results

VOTE Classification System



Airway Level	Direction		
	Anterior-Posterior	Lateral	Concentric
Velopharynx			
Oropharynx			
Tongue base			
Epiglottis			

Degree of Obstruction:

None - (no to little obstruction, 0-25%)

Partial - (vibration, 25-75%)

Complete - (collapsed, >75%)

Patients with Anterior-Posterior Velopharyngeal Obstruction on DISE are Eligible for Implant



Complete AP collapse at palate

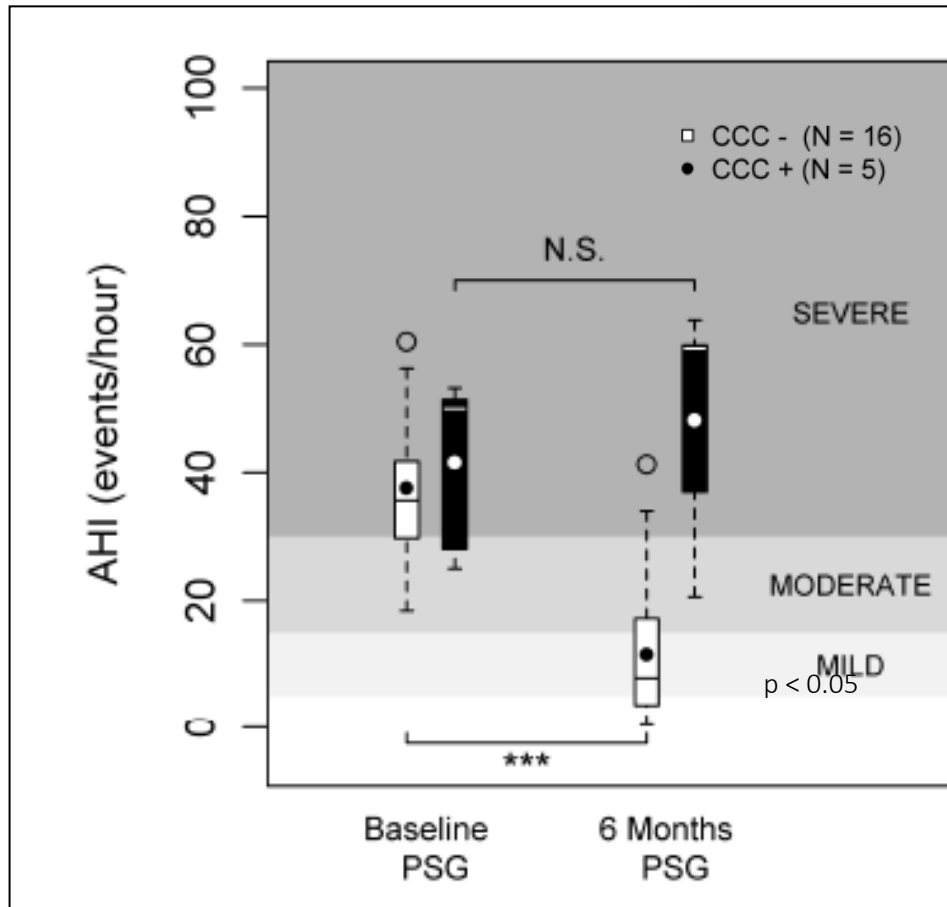
Good candidate



Complete concentric collapse at palate

Not a good candidate

DISE is an Important to Identify Upper Airway Stimulation Therapy Candidates



- Patients without complete concentric collapse (CCC) of velopharynx had significant improvements in AHI¹
- Patients with CCC did not have a significant change in AHI¹
- CCC on DISE was an exclusion criterion for the STAR pivotal trial²

¹Vanderveken O et al. *J Clin Sleep Med* 2013; 9:43-8.

²Strollo PJ, Soose RJ, Maurer JT, et al. *N Engl J Med* 2014; 370:139-49

Bilateral Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnea With and Without Complete Concentric Collapse (BETTER SLEEP)

 U.S. National Library of Medicine

ClinicalTrials.gov

- 8 Australian centers
- 42 patients implanted with Nyxoah bilateral hypoglossal nerve stimulation device
- 42.9% BETTER SLEEP patients had CCC

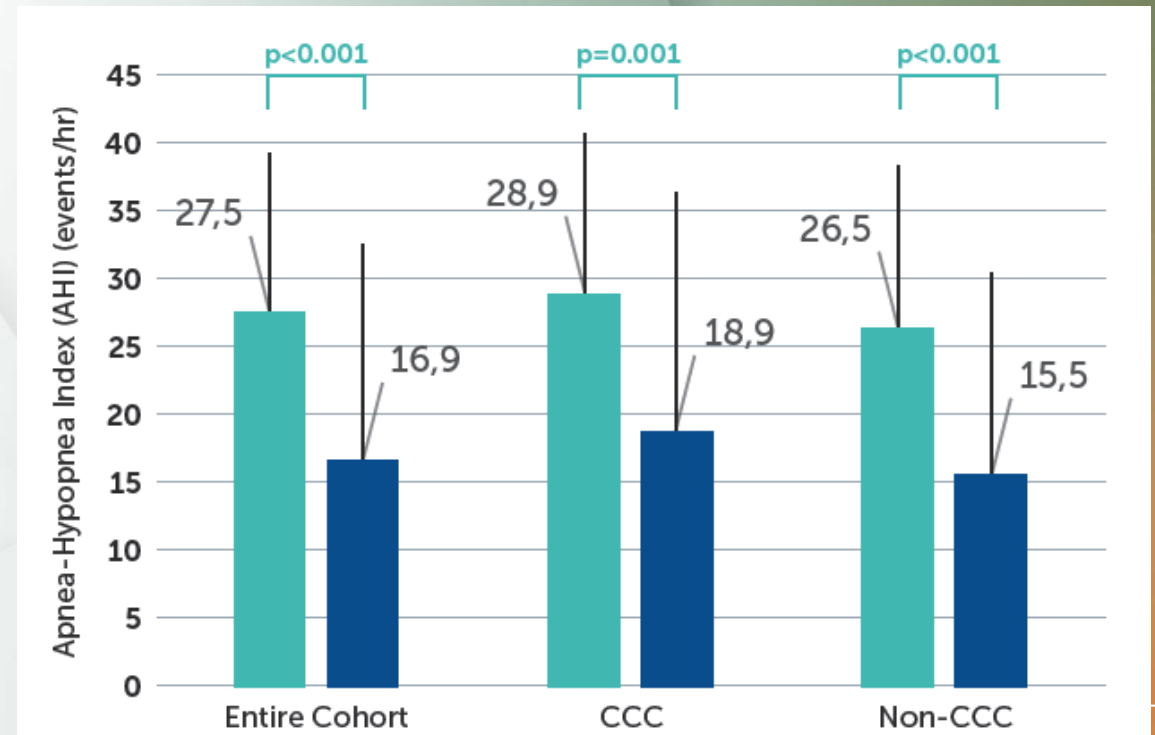
- 36 patients data available at 6 months
- 23/36 responders (64%) per Sher criteria
- CCC 9/15 (60%) and non-CCC 14/21 (67%)

Lewis R, et al. BETTER SLEEP Poster. Presented at World Sleep Congress May 4, 2022.

Bilateral Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnoea With and Without Complete Concentric Collapse (BETTER SLEEP)

Mean AHI change at 6 months of therapy use

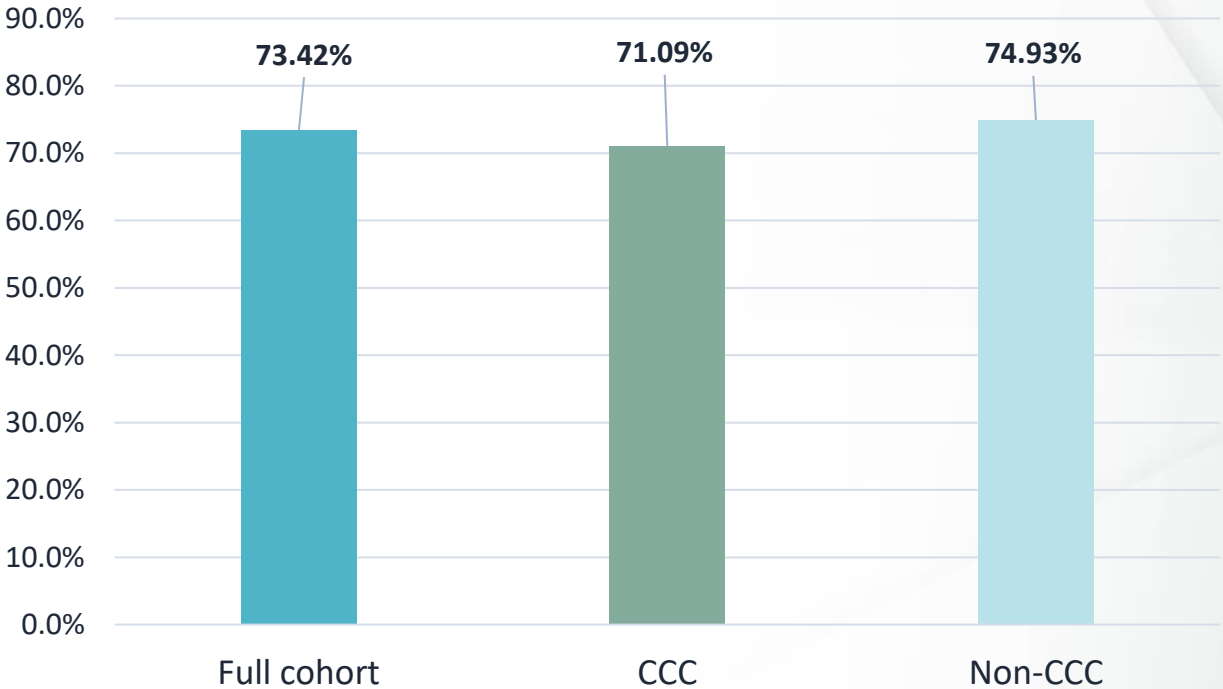
		Full Cohort – n=42	CCC – n=18	Non-CCC – n=24
Baseline	Mean ± SD	27.54 ± 11.91	28.93 ± 11.86	26.49 ± 12.10
Month 6	Mean ± SD	16.89 ± 16.00	18.86 ± 17.59	15.51 ± 15.00
Delta	Mean ± SD	-10.65 ± 11.57	-10.07 ± 12.25	-10.98 ± 11.28
	p-value	<0.001	0.001	<0.001



Bilateral Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnoea With and Without Complete Concentric Collapse (BETTER SLEEP)

- >70% reduction in AHI4 in responders in both CCC and non-CCC population at 6 months

AHI4 Responders – Mean AHI reduction



AHI responders	– AHI4 – Mean % reduction at 6 months
Full cohort	73.42%
CCC cohort	71.09%
Non-CCC cohort	74.93%

Lewis R, et al. BETTER SLEEP Poster. Presented at World Sleep Congress May 4, 2022.



BilatEral Hypoglossal Nerve StimulaTion for TreatmEnt of ObstRuctive SLEEP Apnoea With and Without Complete Concentric Collapse (BETTER SLEEP)

Conclusion:

- Statistically significant reduction in AHI and ODI across all cohorts
- Similar improvements in AHI4 and ODI4 for both CCC and non-CCC participants (not powered)

Hypoglossal Nerve Stimulation is likely an Acceptable Treatment for Patients with CCC

Europe

- CCC patients are indicated for the Genio® therapy in Europe
- CE-Mark Instructions for use: *The Genio® system is indicated to treat patients suffering from moderate to severe OSA with and without Complete Concentric Collapse (CCC) at the soft palate level*
- No DISE required to assess presence of CCC at the soft palate level

United States

- Genio® received "Breakthrough Device Designation" in the US for CCC patients
- Initiation of FDA ACCESS IDE clinical trial

Maria V. Suurna, M.D., F.A.C.S



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The Nyxoah Journey

Bruno Onkelinx – Chief Technology Officer

A glance into the future

Genio 2.1 2023 – 2024

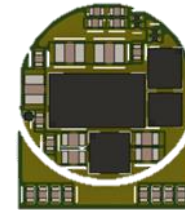


- Bilateral stimulation
- Battery-free / leadless
- Single incision procedure
- Full body MRI compatible



- Implant for life
- Ceramic housing
- Platform for next generation electronics
- Designed for manufacturing

Genio 3.0 2025



- Improved efficiency
- Independent Bilateral Stimulation
- Smart implant electronics
- Embedded sensors



- Improved ergonomics
- Greener and cost-effective DP



- Adaptive therapy
- Sensor algorithm implementation



- Patient APP
- Daily feedback on therapy usage
- Patient adjustable stimulation amplitude

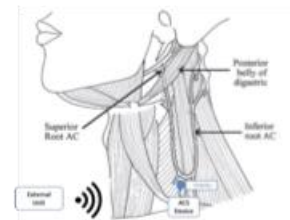
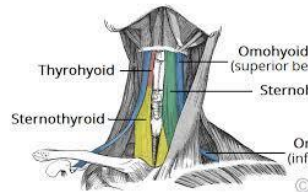


- HUB station
- Cloud connectivity
- Patient interface



- Remote care
- Cloud based data analysis

Genio 4.0 Ansa Cervicalis 2026



- Ansa Cervicalis stimulation
- Extended BMI indication
- Extended Responder Rate



A Review of Ansa Cervicalis

Dr. David T. Kent

Ansa Cervicalis Stimulation for OSA

David T. Kent MD

Assistant Professor of Otolaryngology-Head and Neck Surgery

Director of Sleep Surgery

Vanderbilt University Medical Center

Disclosures

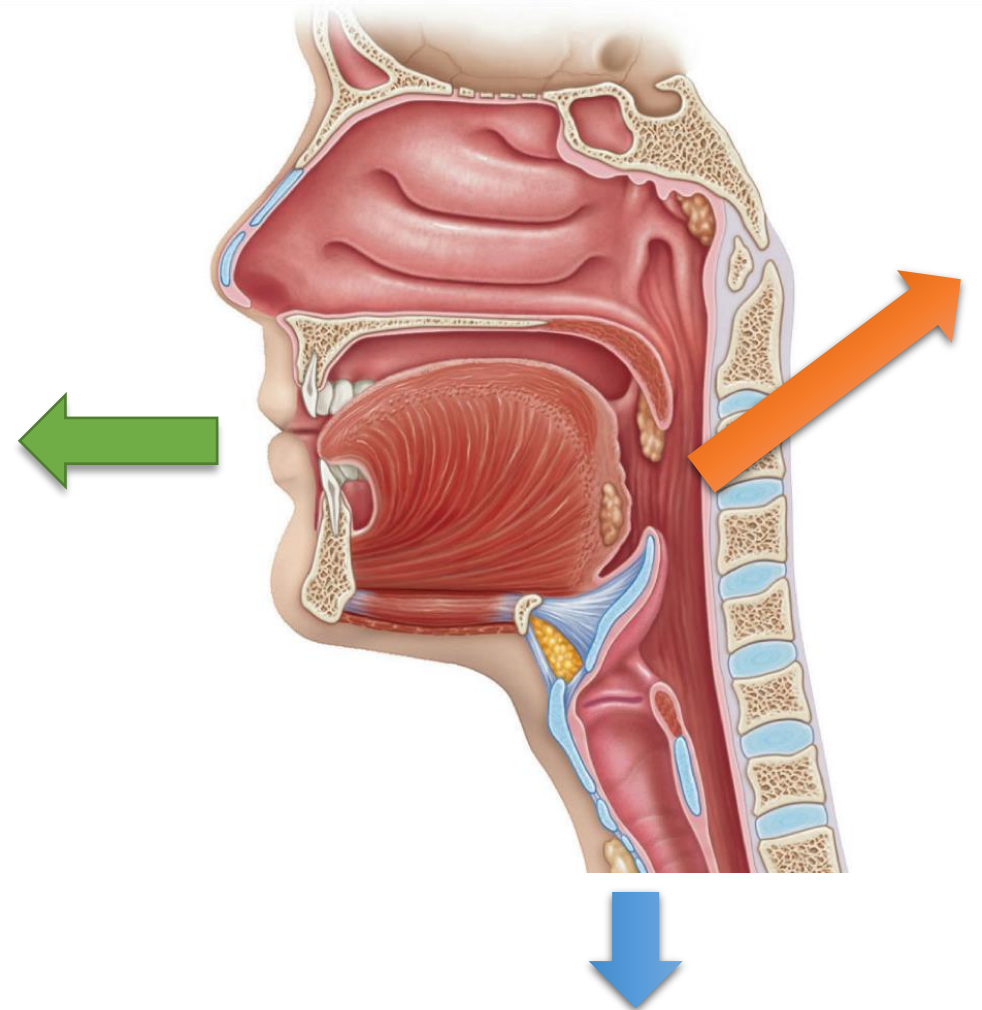
- Consultant
 - Invicta Medical, Inc
- Scientific Advisory Boards
 - Nyxoah SA
- Intellectual Property Interests
 - Listed as an inventor on US and international patents and applications owned by Vanderbilt University and licensed to Nyxoah SA
- Research Support
 - Inspire Medical Systems, Inc
 - Invicta Medical, Inc
 - Nyxoah SA

Funding Support

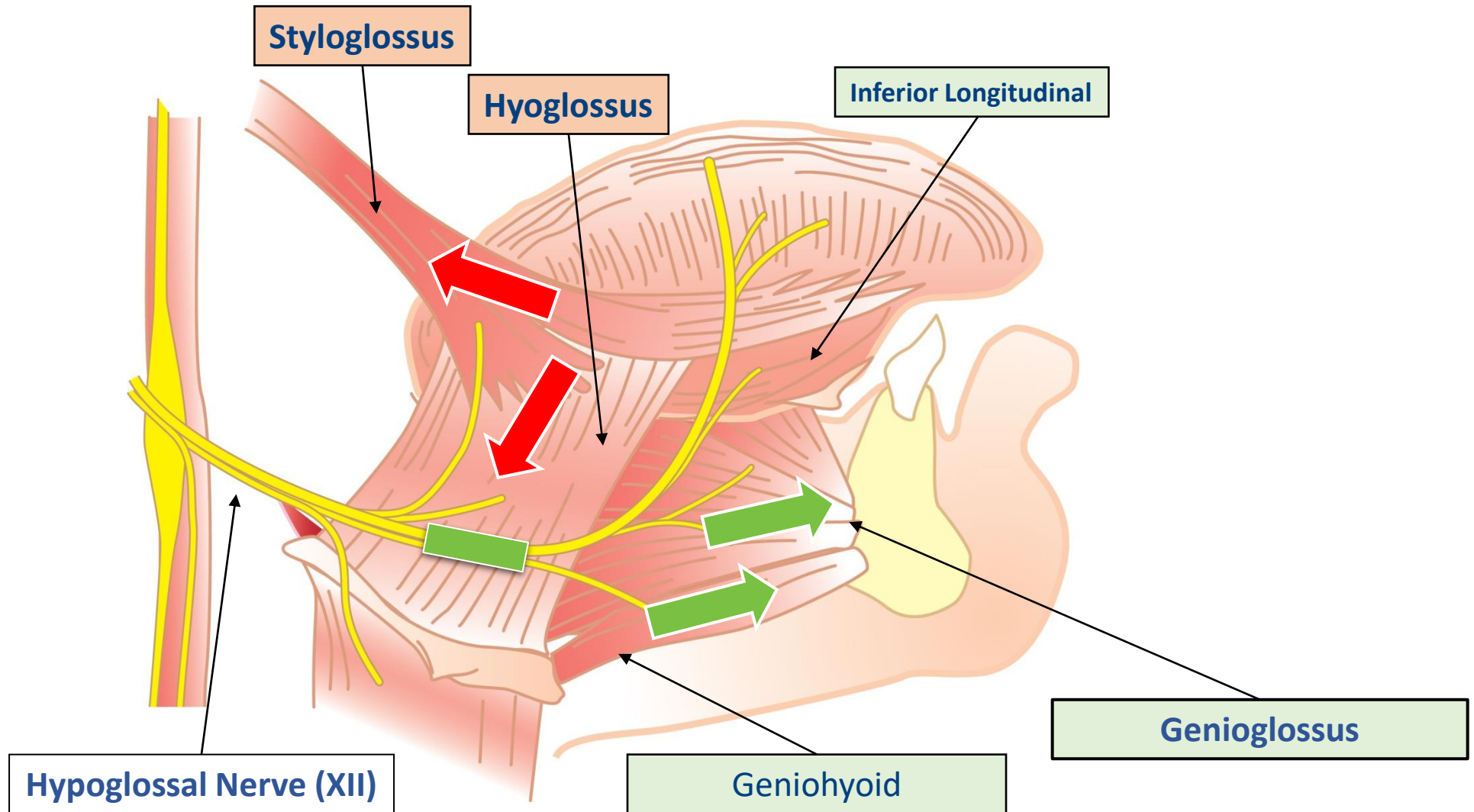
- AASM Foundation 2019 ABSM Junior Faculty Award
- NHLBI 1R01HL161635: The Effect of Ansa Cervicalis Neurostimulation on Airway Patency in Obstructive Sleep Apnea

Mechanisms Supporting Pharyngeal Airway

- Three physiologic supporting mechanisms
 1. Genioglossus (Tongue) tone
 2. Tracheal traction
 3. Intrinsic pharyngeal muscle tone
- Opposing forces may have synergistic effects



Hypoglossal Nerve Stimulation (HNS): Mechanism of Action

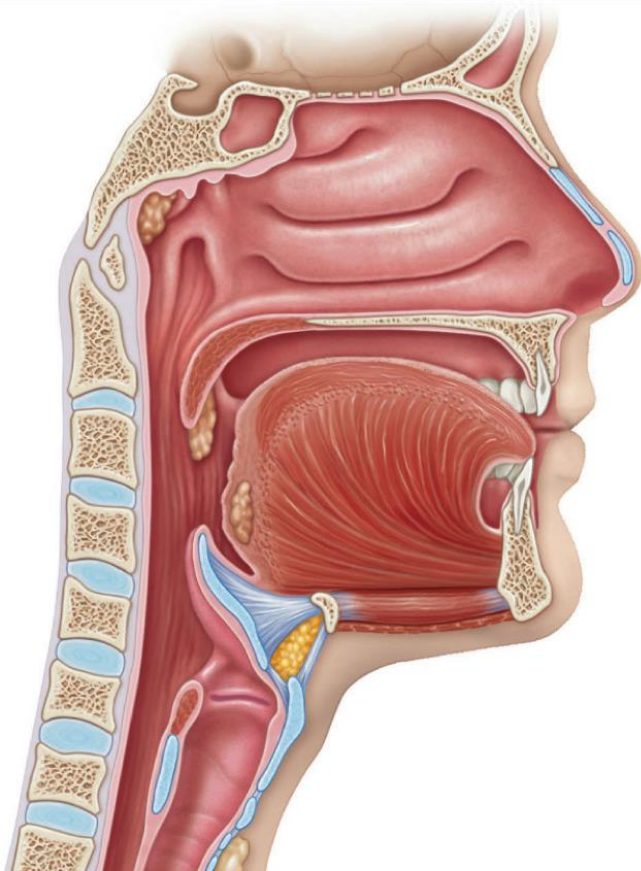


Medicare/Insurance HNS Indications (US)

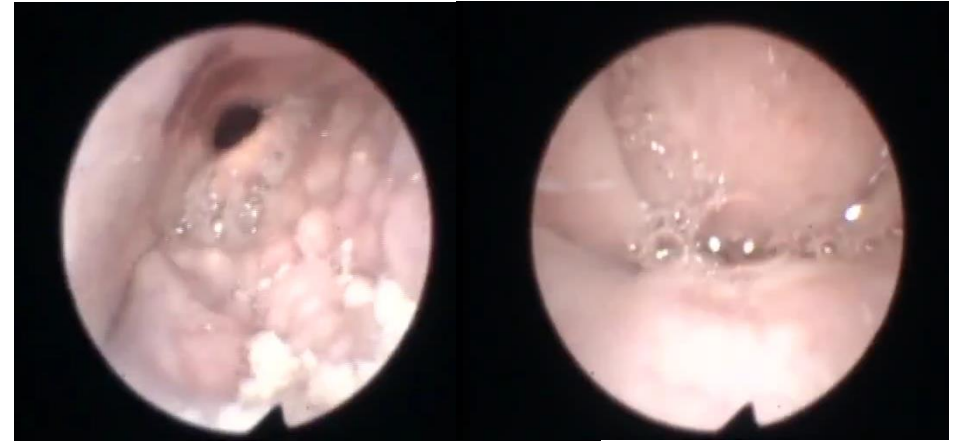
- 18+
- AHI range of 15-65* events per hour
- Failure or inability to tolerate CPAP

- **Body mass index < 32 kg/m²***
- **Appropriate airway anatomy**
 - **No complete circumferential collapse of the palate**

HNS: Mechanism of Action



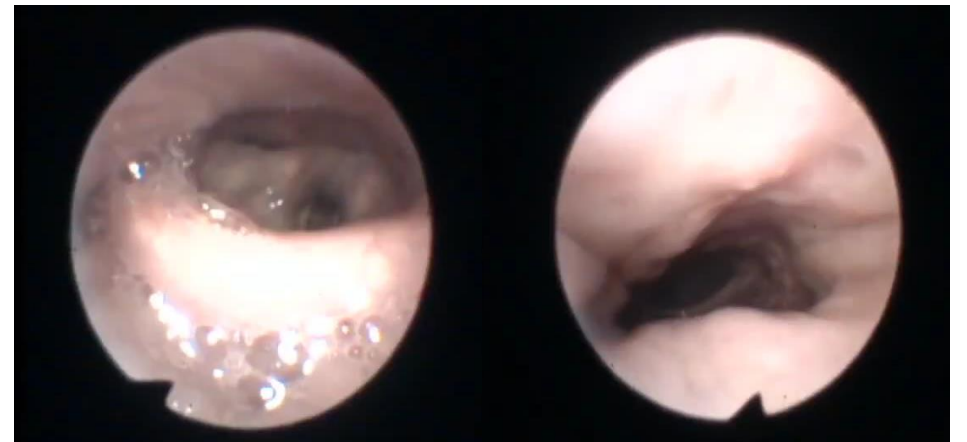
No Stimulation



Base of Tongue

Palate

Stimulation

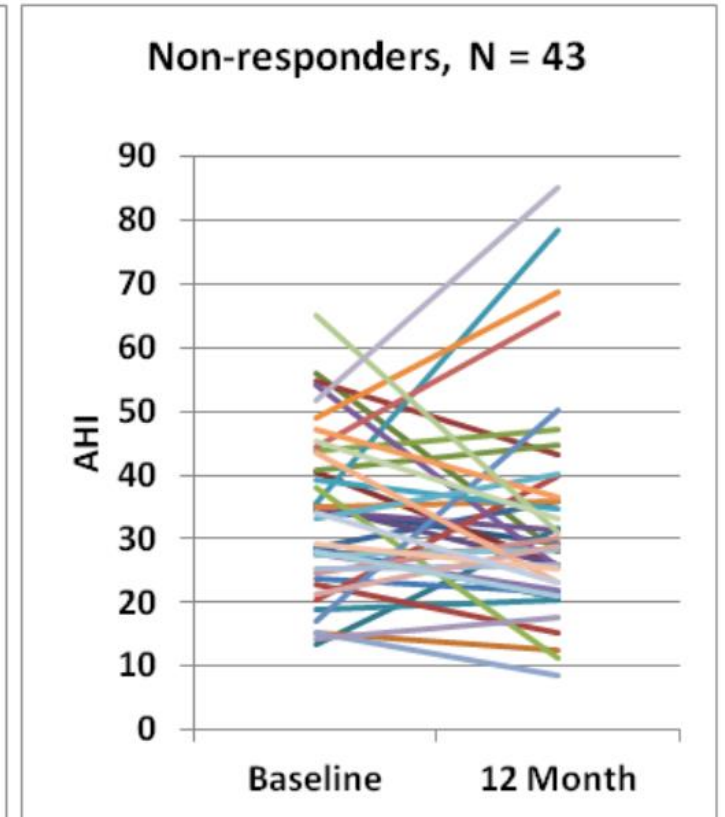
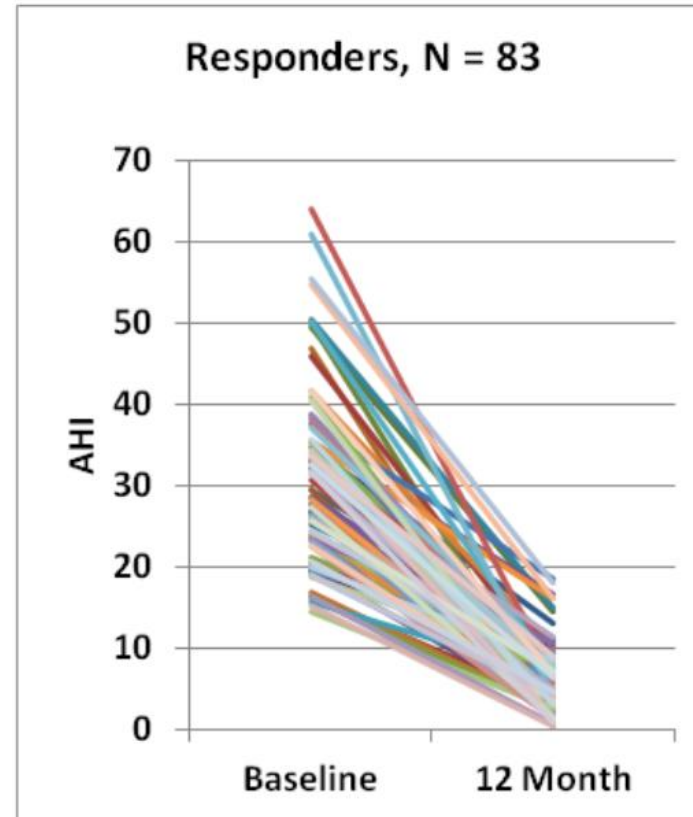


Base of Tongue

Palate

HNS Responders and Non-Responders

- 1y Responder Rate: 66%
 - AHI <5: 29%
- 5y
 - Follow up: 56.3%
 - Responder rate: 63%
 - AHI <5: 44%



HNS Failure: Residual Retropalatal and Lateral Wall Collapse

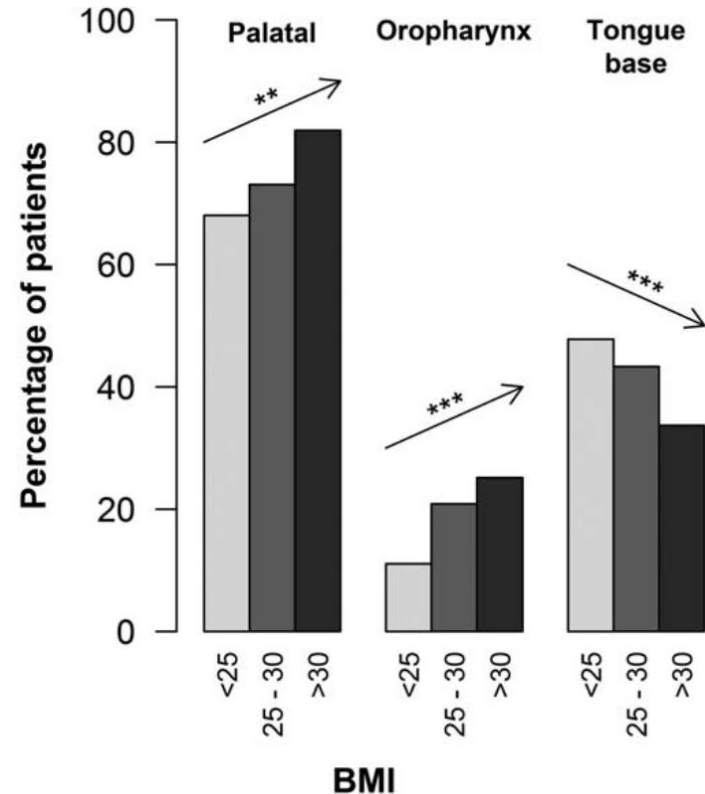
- Non-responders: **less retropalatal dilation**
- \pm LW collapse
 - Responder rate: **58% vs. 74%**
- Palate movement dependent on traction (“PG coupling”)
 - No direct stimulation



	Subjects n	Retropalatal area		
		No stimulation	Therapeutic stimulation	p-value
Responders	7	11 \pm 10	22 \pm 21	0.031
Nonresponders	7	15 \pm 6	19 \pm 10	0.109

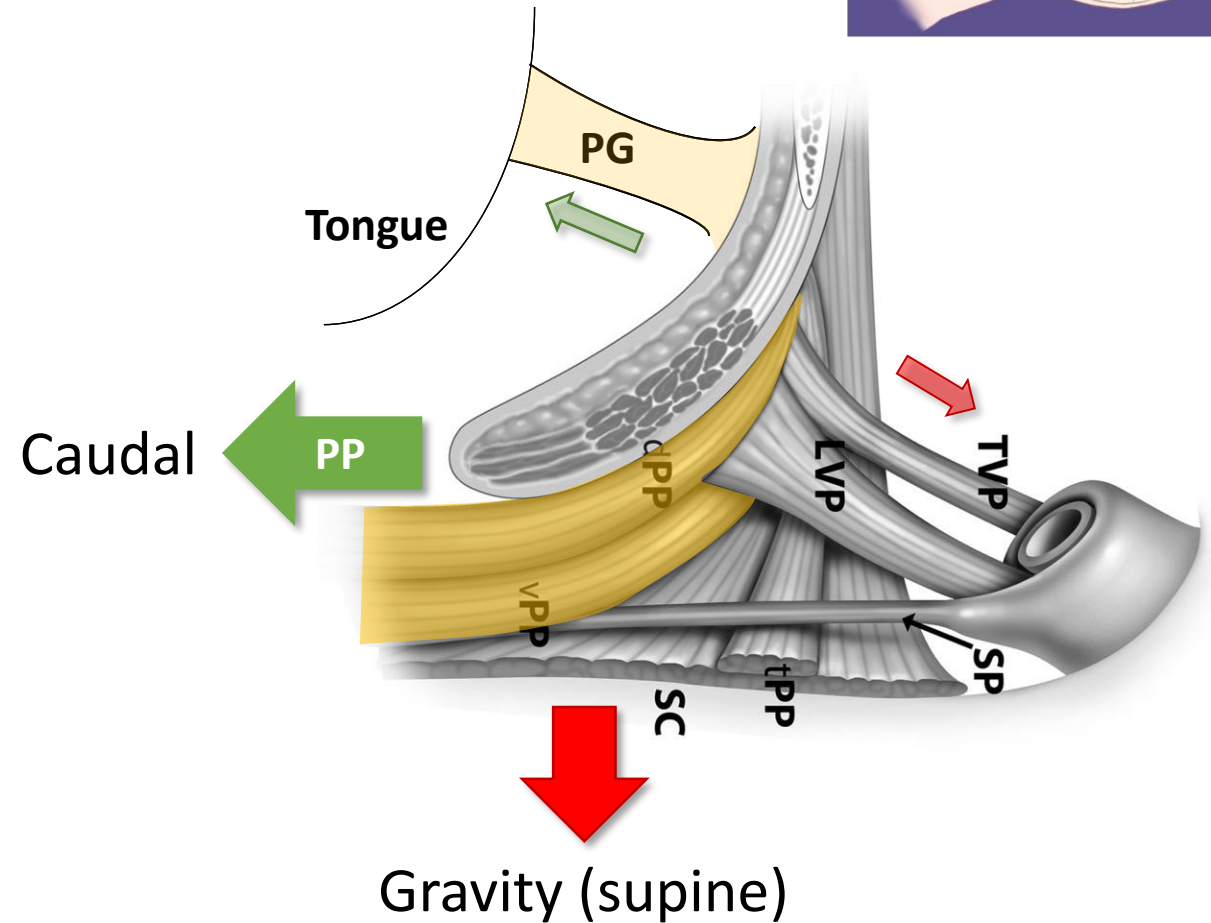
CCC and Lateral Wall Collapse

- 1,249 patients
- \nearrow BMI \rightarrow \nearrow CCC + LW, \searrow tongue
- \nearrow AHI \rightarrow \nearrow CCC + LW, \searrow tongue
- **Heavier and more severe OSA patients have more CCC, LW collapse**



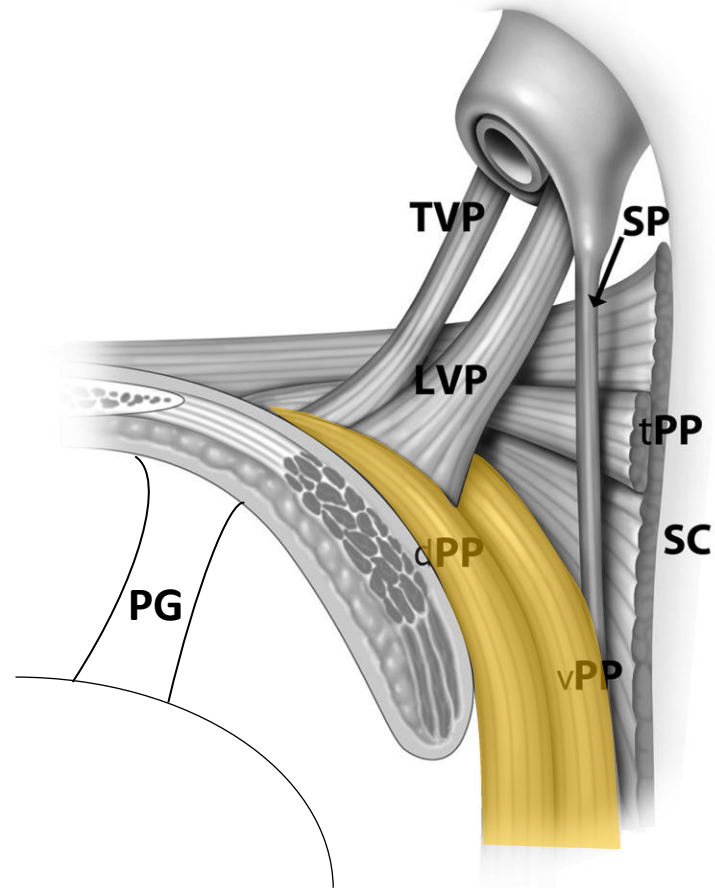
Why Does HNS Fail?

- Palatal “advancement” is not physiologic
- Palate hinges to open
 - Palatoglossus and palatopharyngeus are levers
- No extrinsic palatal musculature for **anterior** displacement
 - Displaces **caudally** (downwards) to open



Palatopharyngeus and Palatal Opening

- Real-time MRI of speech
- PP contraction
- Palate hinges caudally to open
- Requires **caudal anchor**

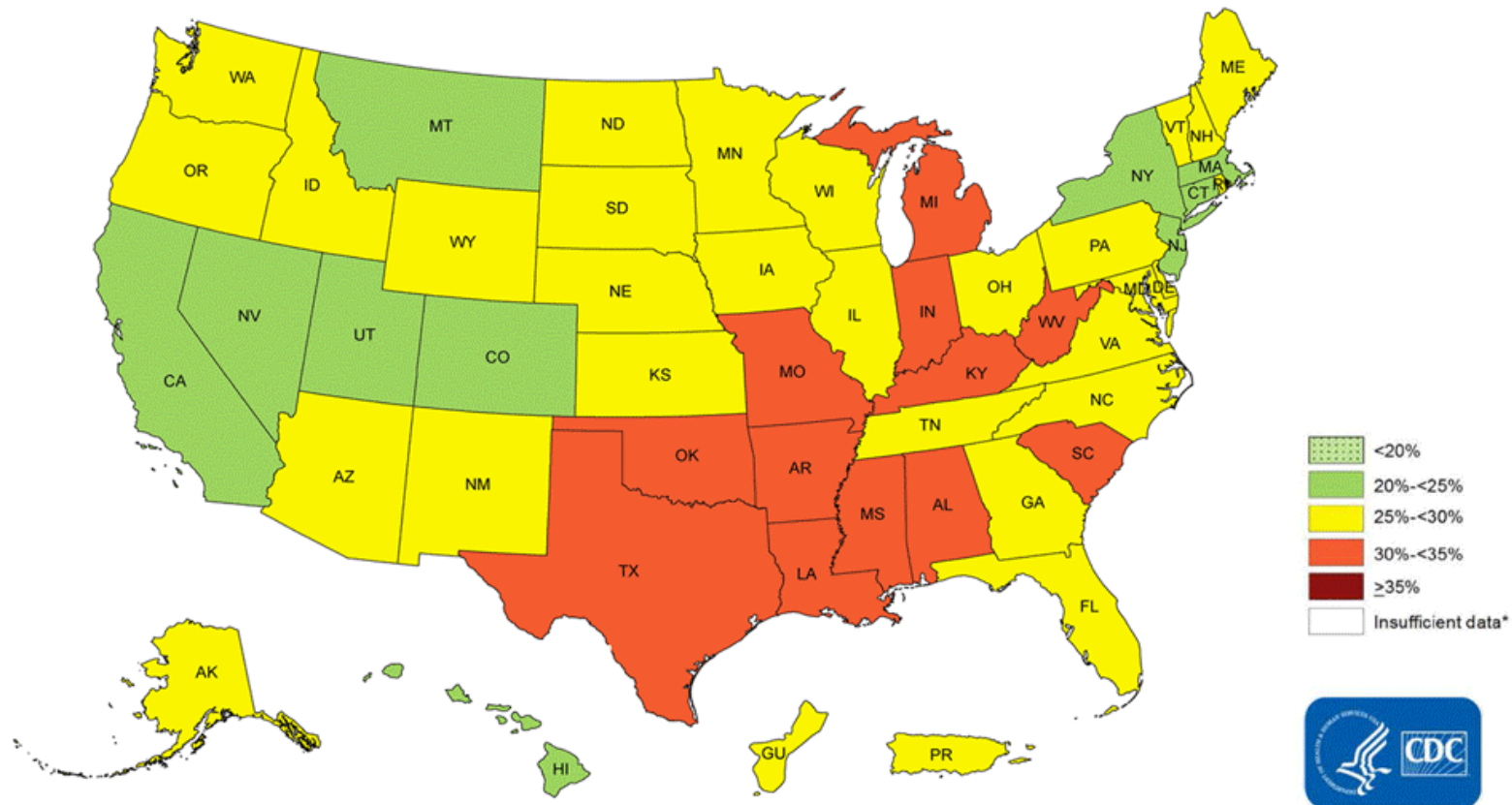


Olszewska E. Laryngoscope Investig Otolaryngol, 2019;
CineMRI: <https://youtu.be/wj7iM0BCWMQ>

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS

†Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

2011 2012 2013 2014 2015 2016 2017 2018



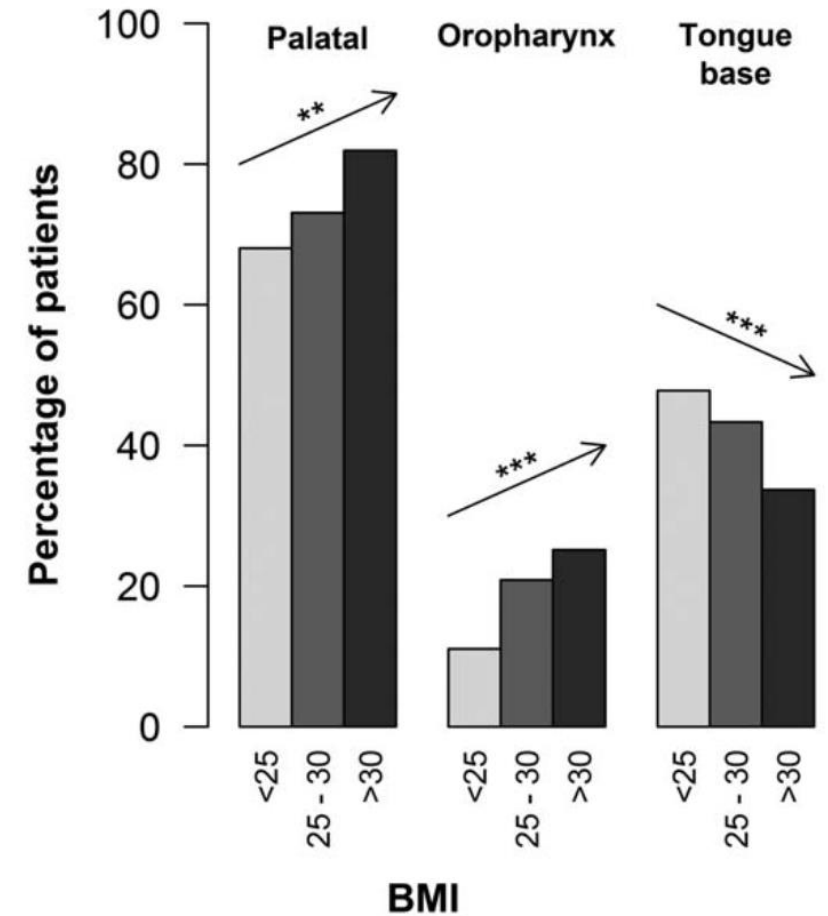
*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.



BMI and OSA in the US

- Increasing BMI → More OSA
 - But also increased: **CCC, LW collapse, BMI > 32**

US Men, 50-70y, Body Mass Index	AHI ≥ 15 Prevalence (%)
< 25	3.6
25-29.9	10.6
30-39.9	29.0
≥ 40	56.0



Worldwide: ~0.5 Billion With AHI ≥ 15

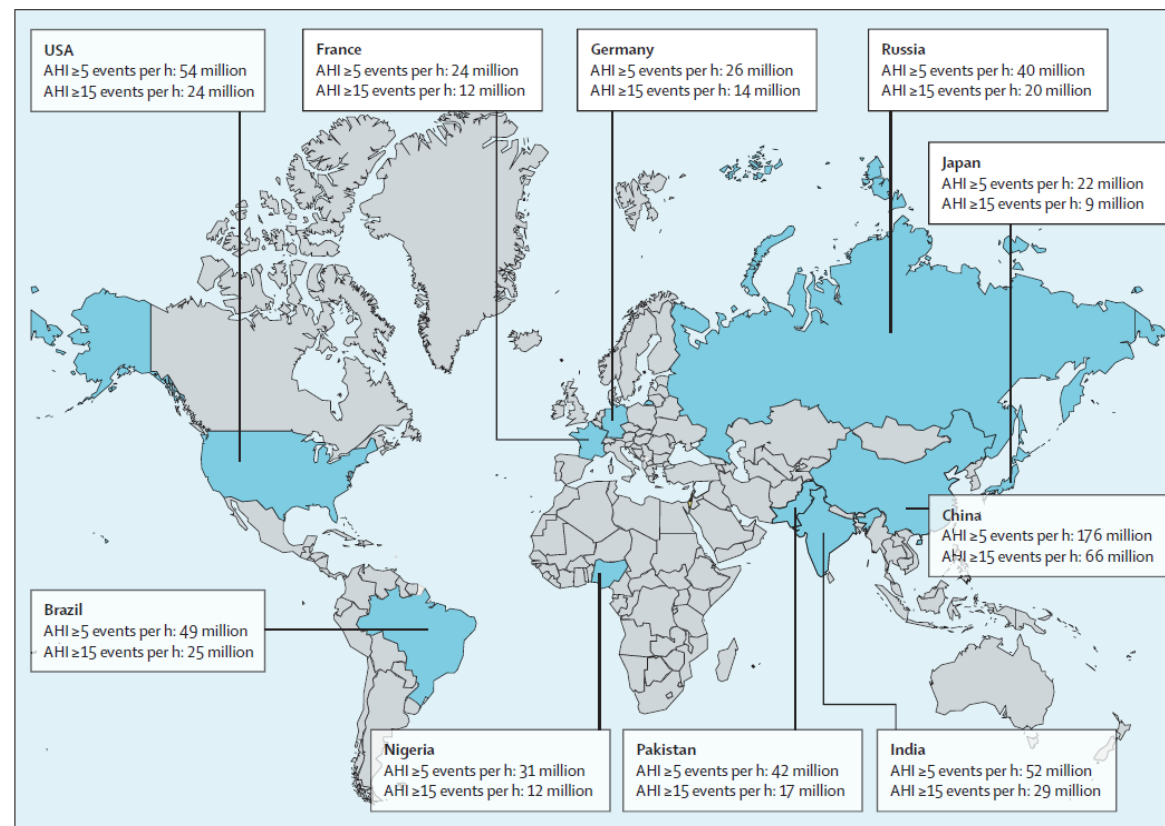
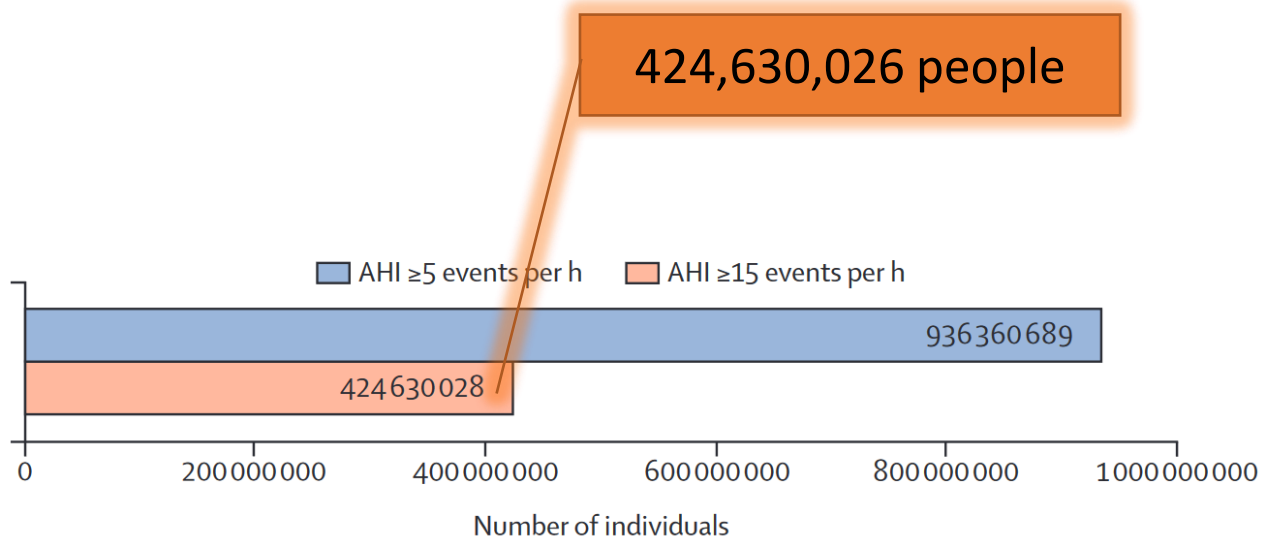
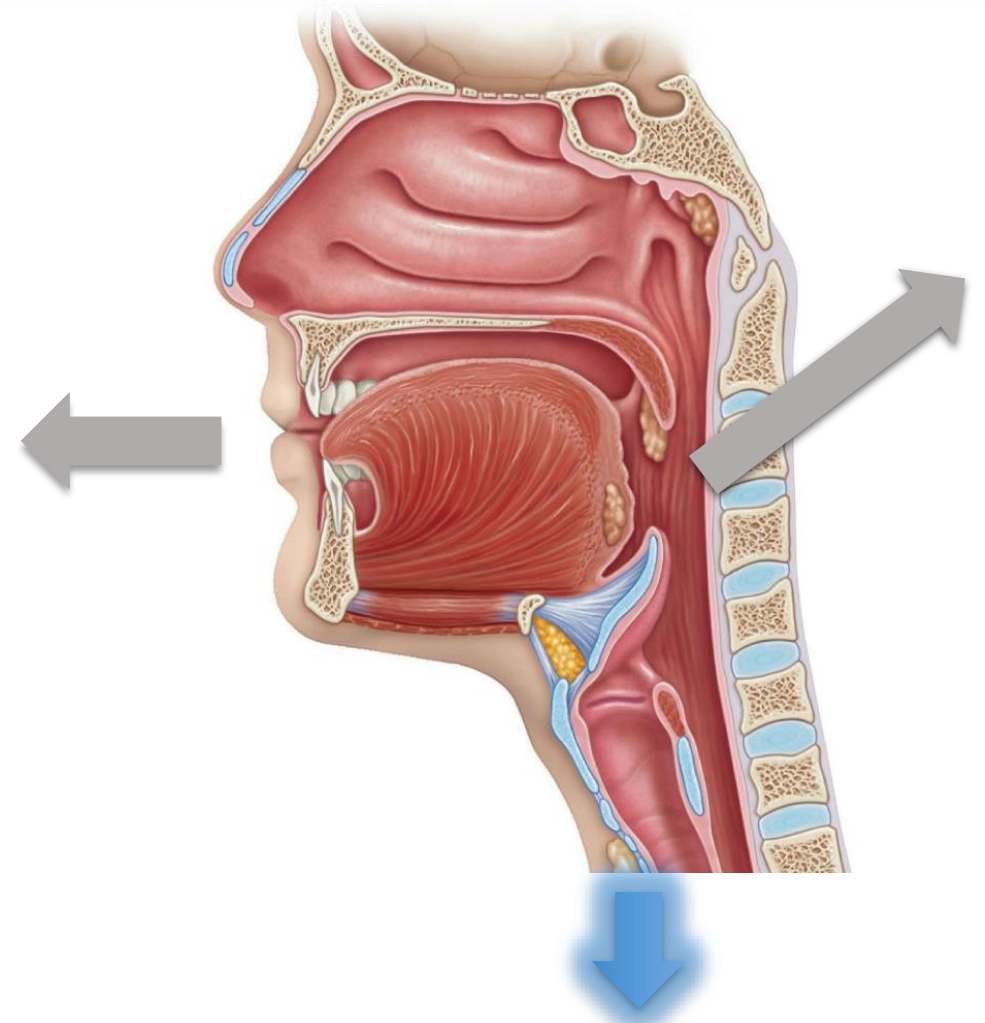


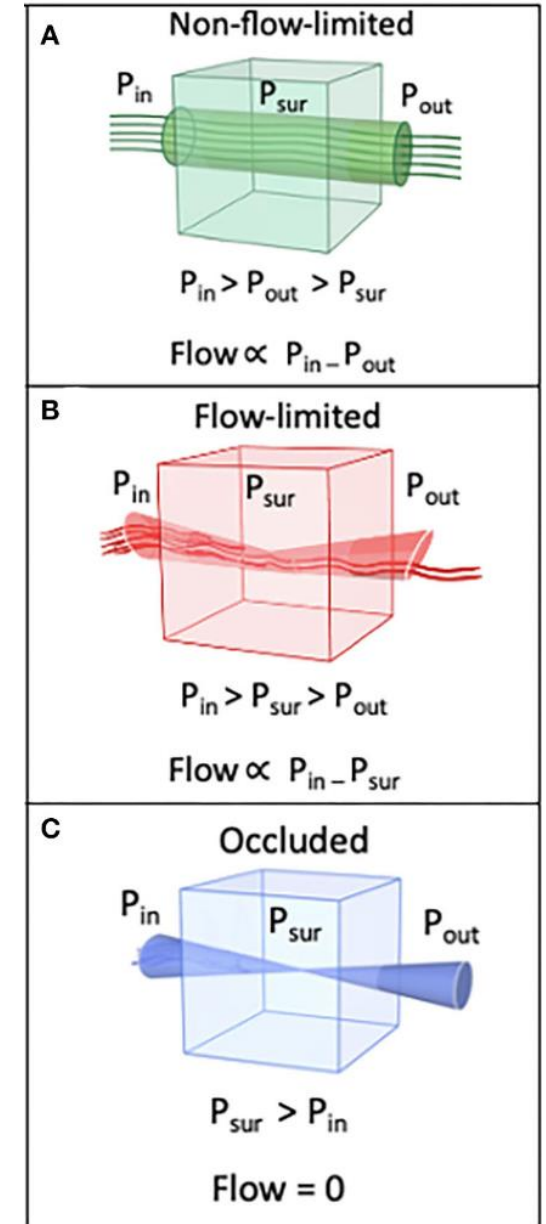
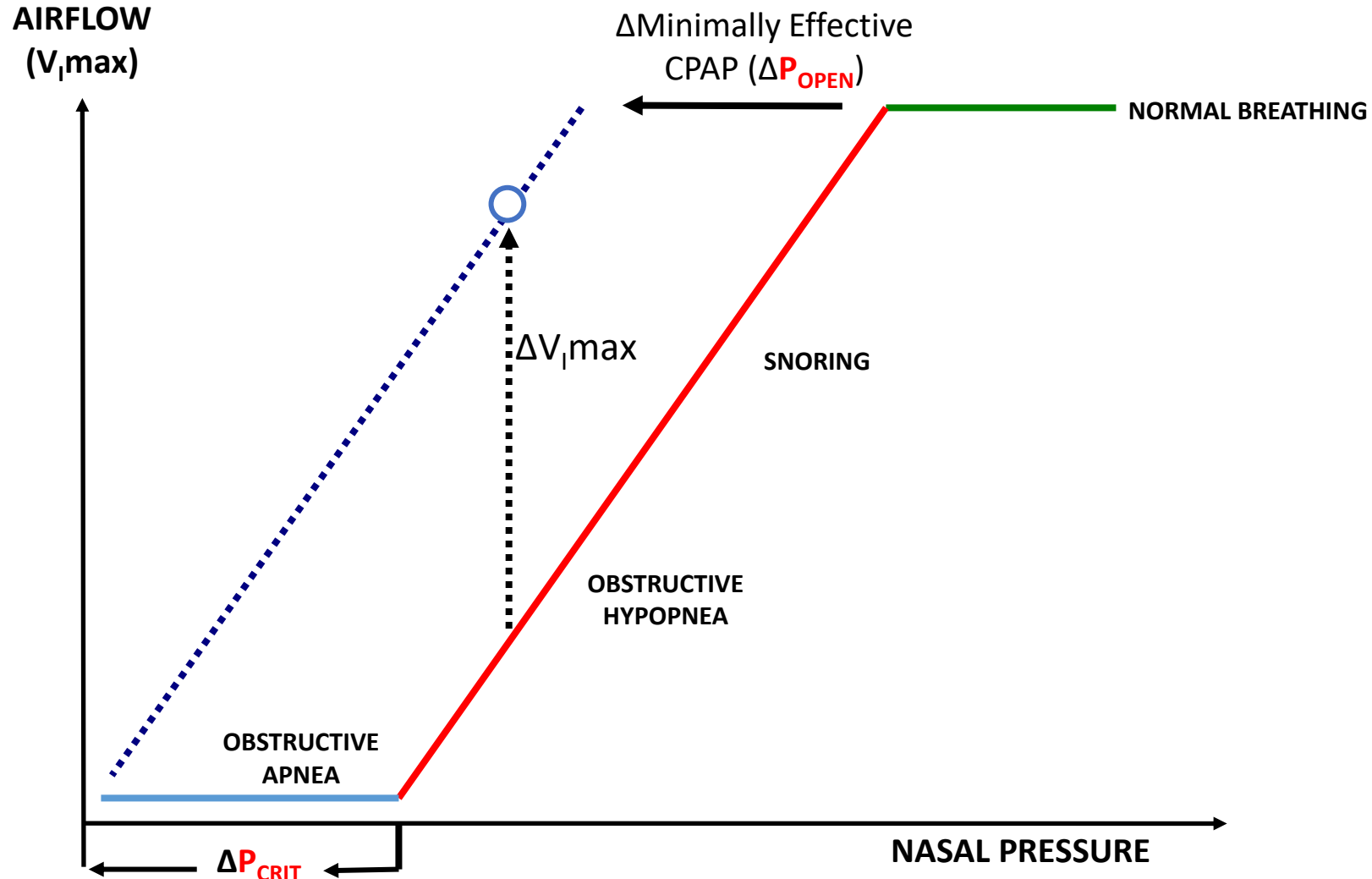
Figure 2: Top ten countries with the highest estimated number of individuals with obstructive sleep apnoea based on the American Academy of Sleep Medicine 2012 criteria⁴⁹

Mechanisms Supporting Pharyngeal Airway

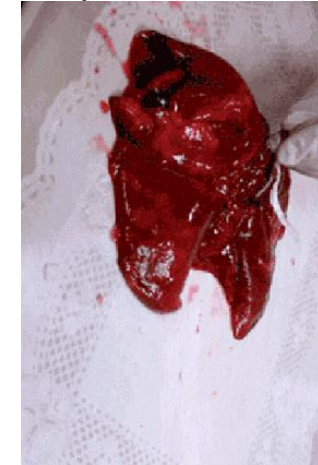
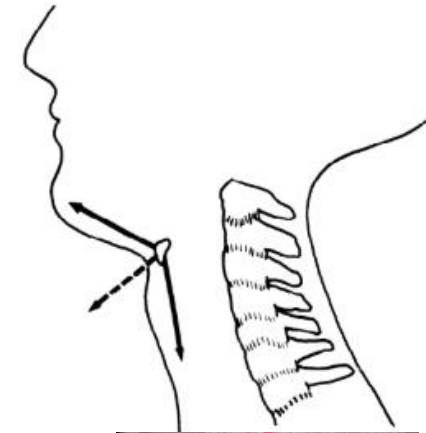
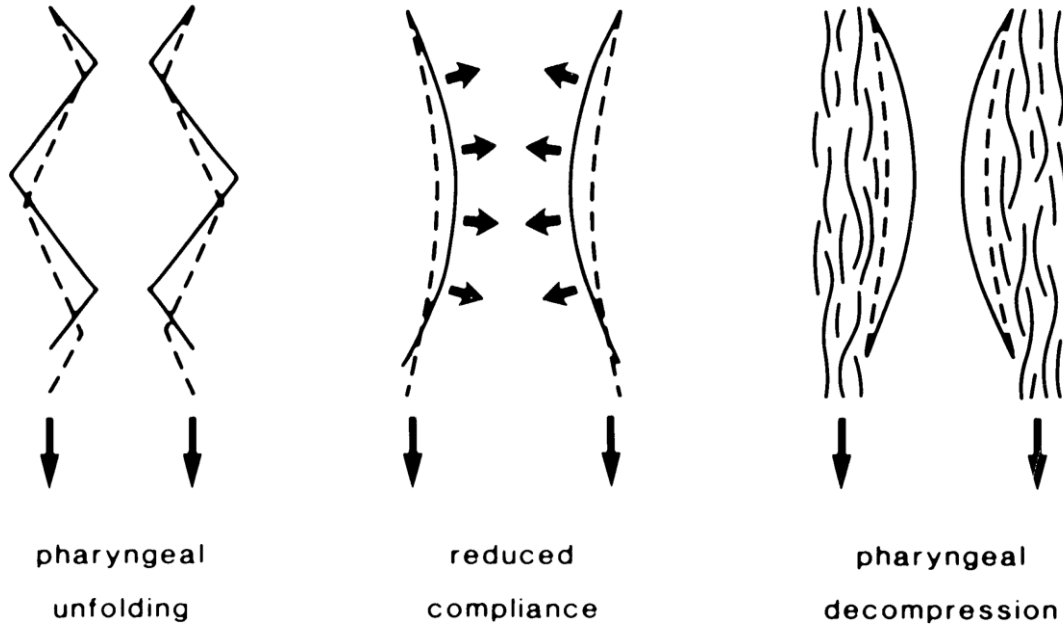
- The pharynx is modifiable in anterior-posterior **and caudal** directions
- Airway surgery (including HNS), primarily modifies anterior-posterior (back-to-front)
- Three supporting mechanisms
 1. Genioglossus (tongue) tone
 2. Intrinsic muscle tone
 3. **Tracheal Traction**
- Opposing forces may have synergistic effects



Modeling Pharyngeal Collapsibility



Tracheal Traction Is Determined by Lung Volume



1. Relieves airflow obstruction during sleep and anesthesia ($V_{I,max}$)
2. Decreases airway collapsibility (P_{CRIT})
3. Improves sleep apnea (AHI) and lowers CPAP requirement

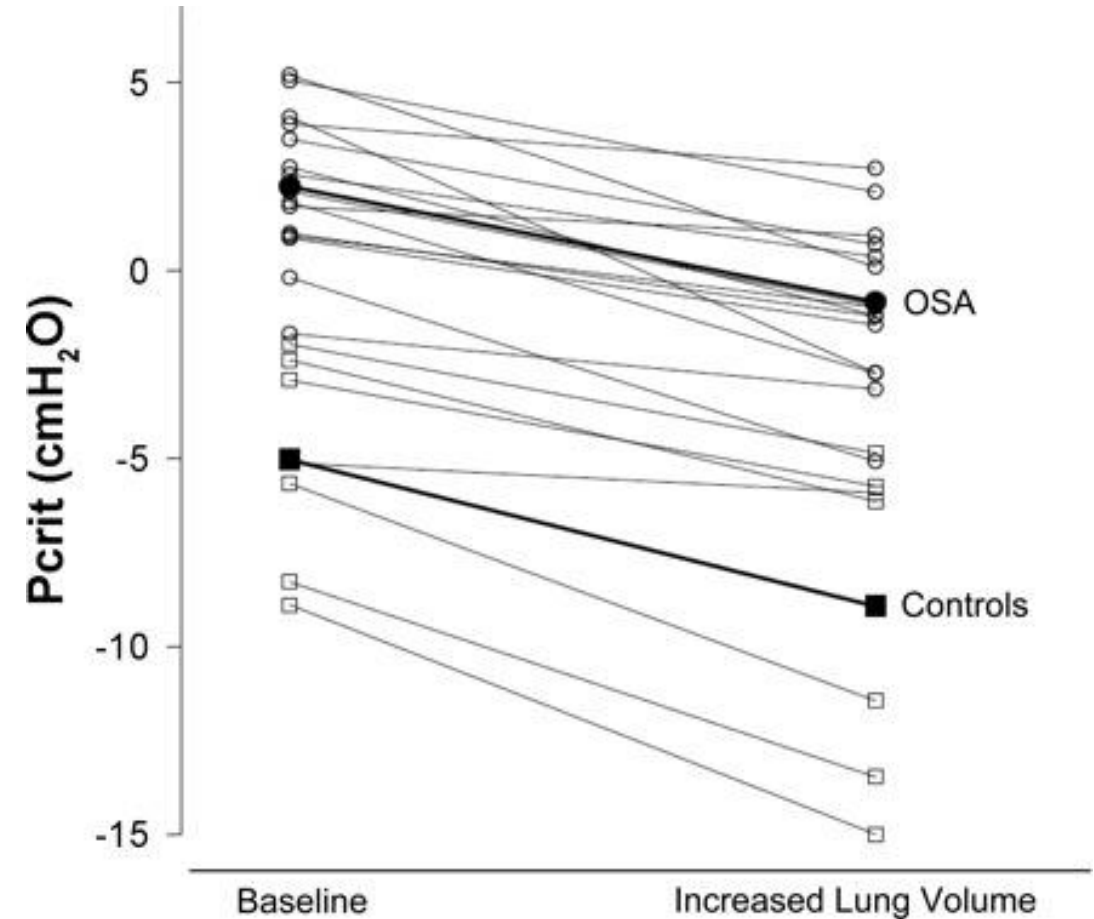
Thut DC et al. *J Appl Physiol* 75(5): 2084-90, 1993
Rowley JA et al. *J Appl Physiol*. 1996; 80(6):2171-2178

Squier SB et al. *J Appl Physiol* 109(4): 977-985, 2010
Hillman DR et al. *J Appl Physiol* 2013;115(3):337-45

Heinzer R et al. *Am J Respir Crit Care Med*. 2005 Jul 1; 172(1): 114-117
Heinzer et al. *Thorax*. 2006 May; 61(5): 435-439

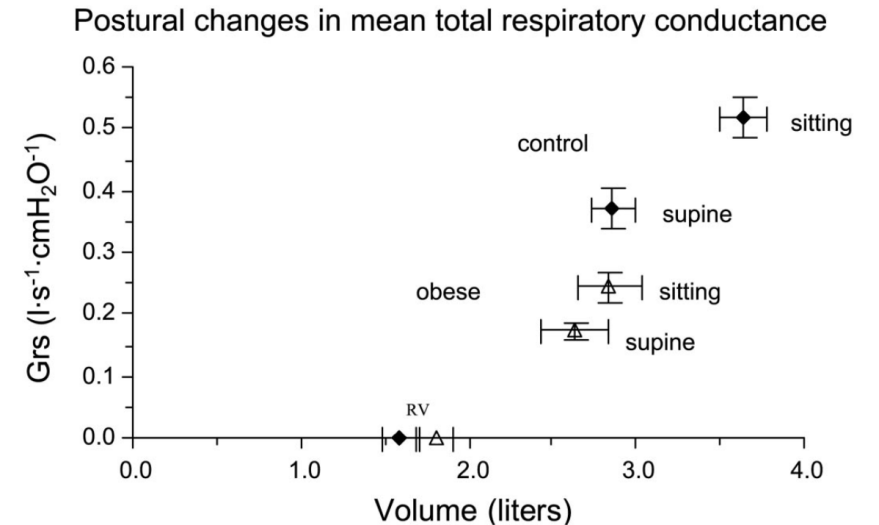
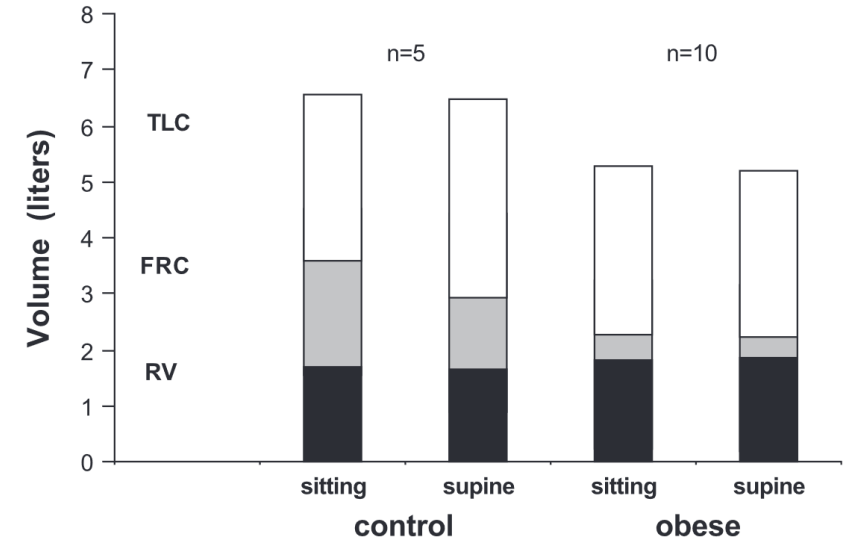
Increasing Lung Volume Decreases Airway Collapsibility (P_{CRIT})

- N=22, Controls and OSA
- **Increasing LV by ~500 mL decreased airway collapsibility (P_{CRIT})**
 - OSA: -3.1 ± 1.7 cmH₂O
 - Control: -3.9 ± 1.9 cmH₂O



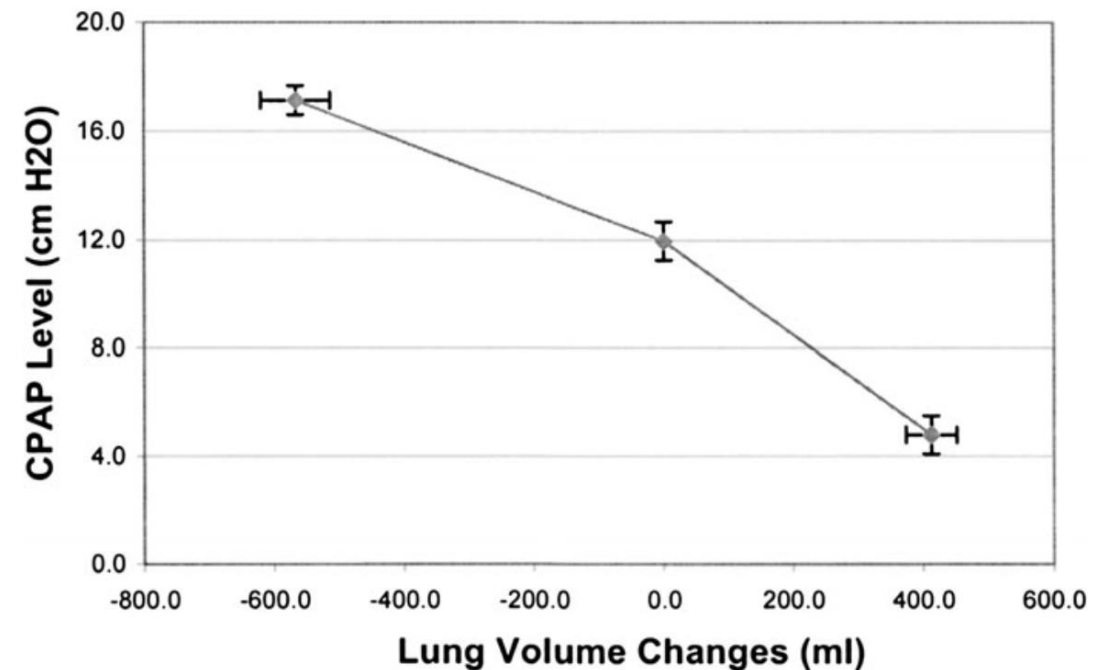
Obesity Decreases Lung Volumes

- 10 obese vs 13 control subjects
 - BMI: 44 ± 3 vs 23 ± 1 kg/m²
- Supine LV, control vs obese:
 - 2.69 ± 0.2 versus 2.22 ± 0.2 L
 - **Difference of ~500 mL**
- Obese airway resistance = 2x normal airway resistance

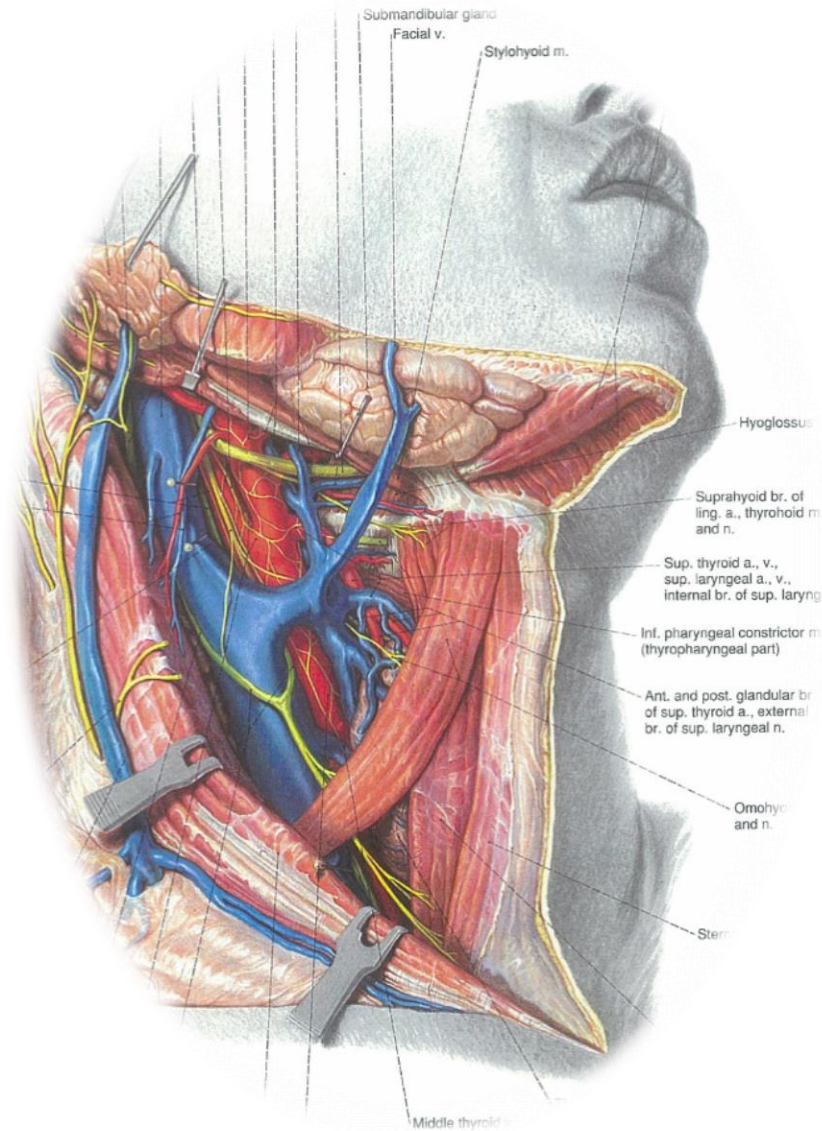


Increasing Lung Volume (LV) Changes CPAP Requirements

- N=17 patients with mod-sev OSA
- ↗ LV 421 ml ↘ CPAP from 11.9 to 4.8 cmH₂O
- ↘ LV 567 ml ↗ CPAP from 11.9 to 17.1 cmH₂O
- “Relatively small changes in LV [caudal traction] have an important effect on the upper airway in [OSA].”



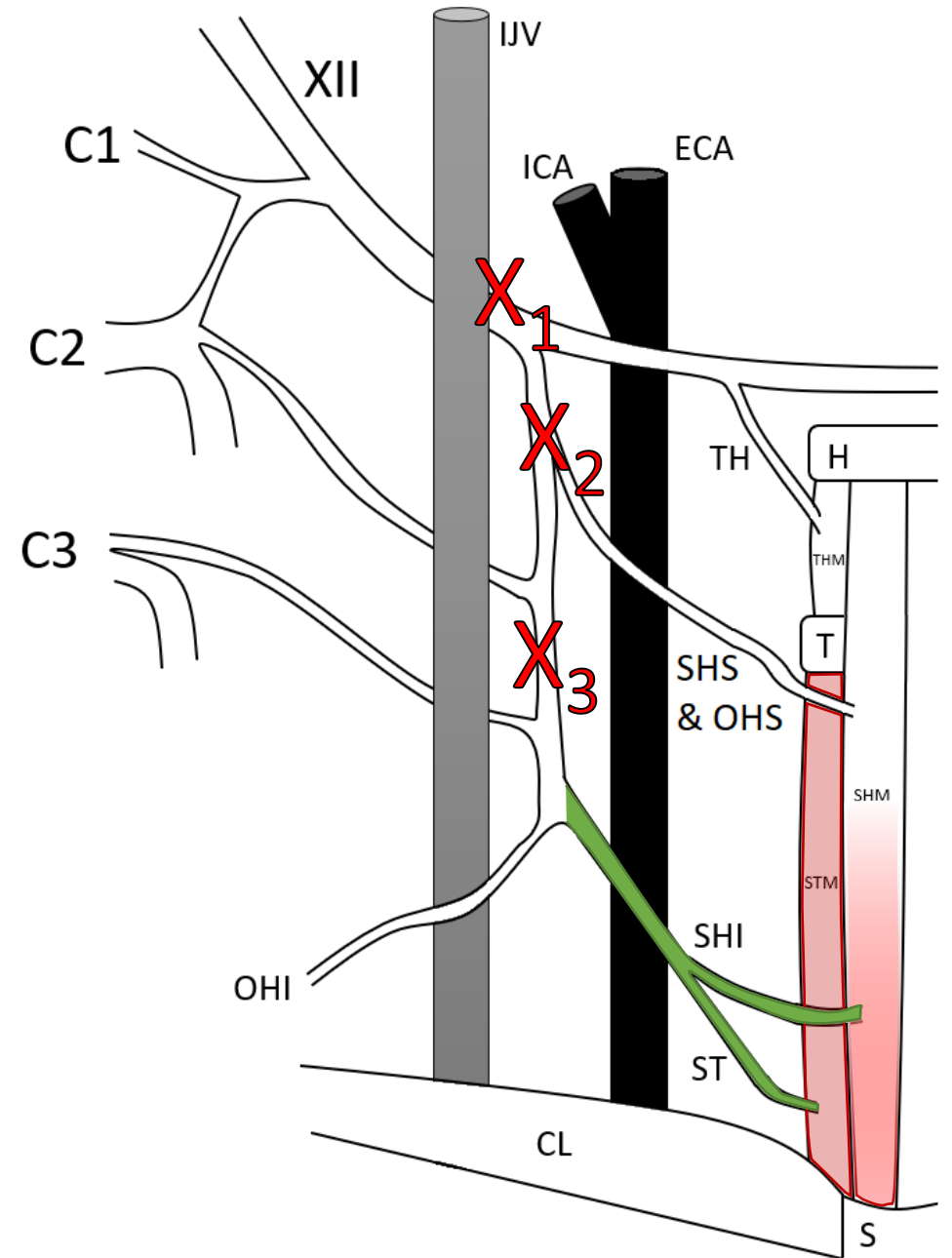
Infrahyoid Straps = Tracheal Traction?



- The human hyolaryngeal complex is highly mobile
 - Speech, swallowing adaptations
- Strap musculature enables a wide degree of control
 - Innervated by the **ansa cervicalis**
- **The sternoTHYROID muscle has multiple advantages**

Potential Stimulation Sites?

	X ₁	X ₂	X ₃	ST Trunk
Independent ansa control	X	✓	✓	✓
All anterograde fibers	✓	X	X	✓
Predictable, reliable anatomy	✓	✓	X	✓
No vagal nerve communication	X	X	X	✓
Complete sternothyroid innervation	X	X	X	✓



VUMC Evidence: Experimental Protocol

- DISE with percutaneous stimulation
 - Started 2017
- Wire electrodes placed under U/S
 - Custom design
- Hypoglossal Nerve Stimulation (HNS)
 - Distal medial branch
- Ansa Cervicalis Stimulation (ACS)
 - Sternothyroid trunk
- **Endoscopy and airflow measured during neurostimulation**



A Little Self-Experimentation



HNS



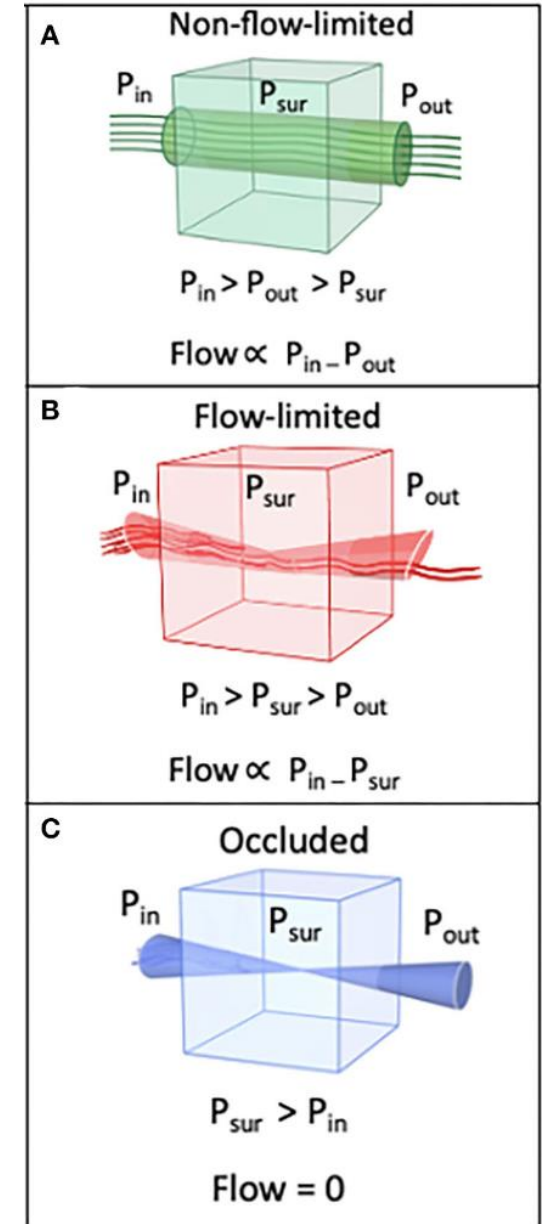
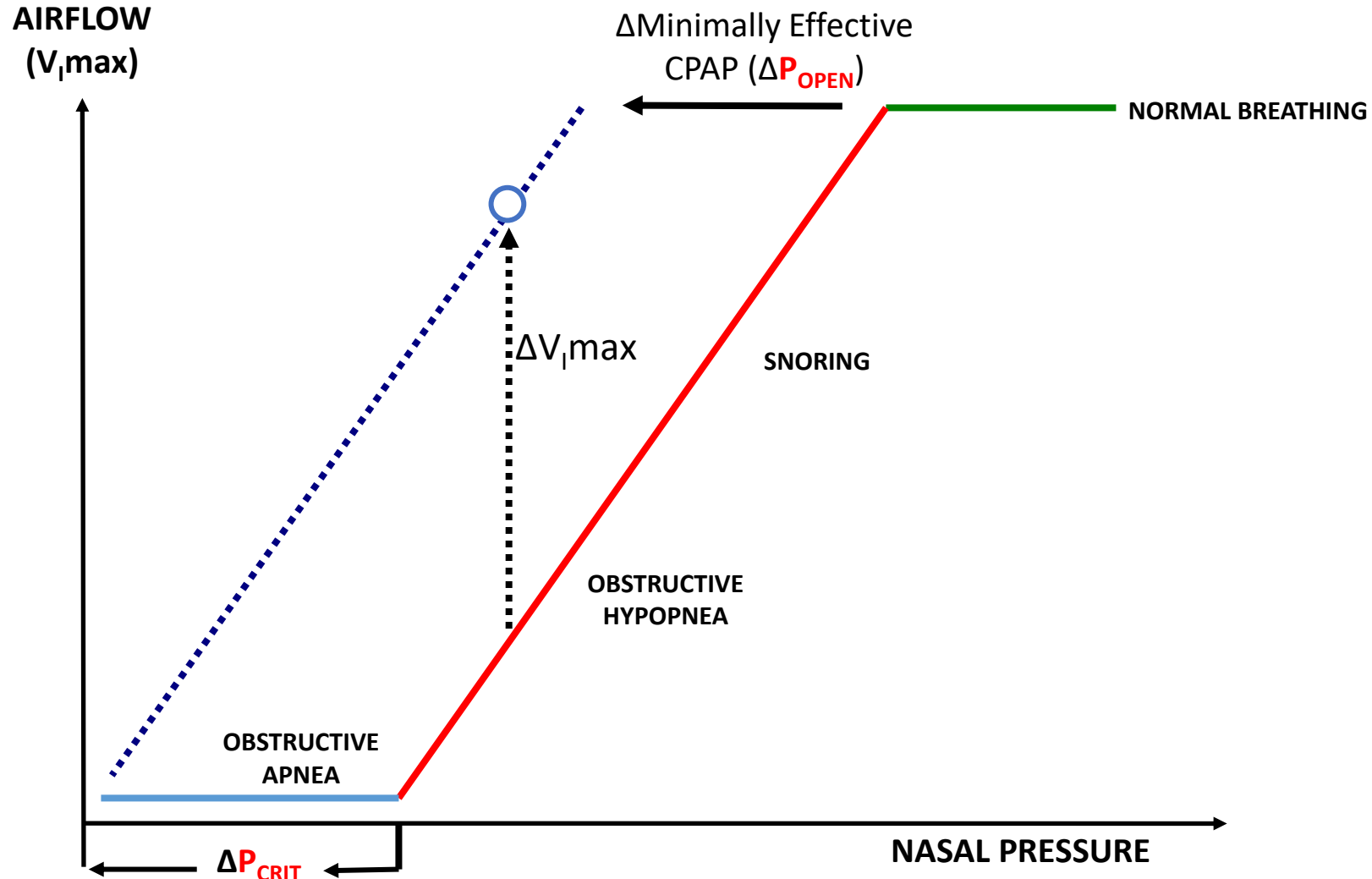
ACS

How Did We Figure Out HNS Works?

1. Increased peak inspiratory airflow ($V_{I,max}$) and pharyngeal cross-sectional area during sleep and anesthesia¹⁻³
2. Decreased pharyngeal collapsibility (P_{CRIT})⁴⁻⁶
3. Improves sleep apnea (AHI)^{7,8}

1: Schwartz et al. J Appl Physiol, 1996. 2: Eisele et al. Arch OTOHNS. 1997. 3: Isono et al. Eur Resp J, 1999. 4: Oliven et al. J Appl Physiol. 2003. 5: Oliven et al. Eur Resp J. 2007. 6: Oliven et al. J Appl Physiol 2009. 7: Schwartz et al. Arch OTOHNS. 2001. 8. Strollo et al. NEJM. 2014.

Modeling Pharyngeal Collapsibility

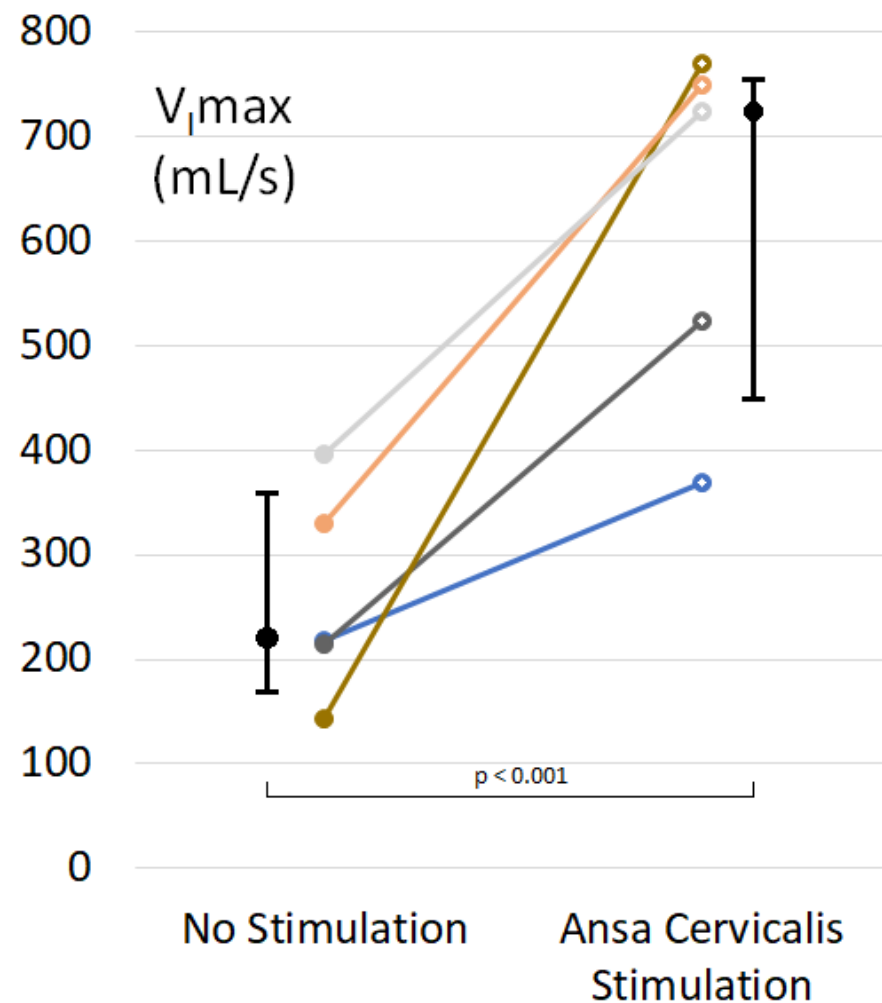
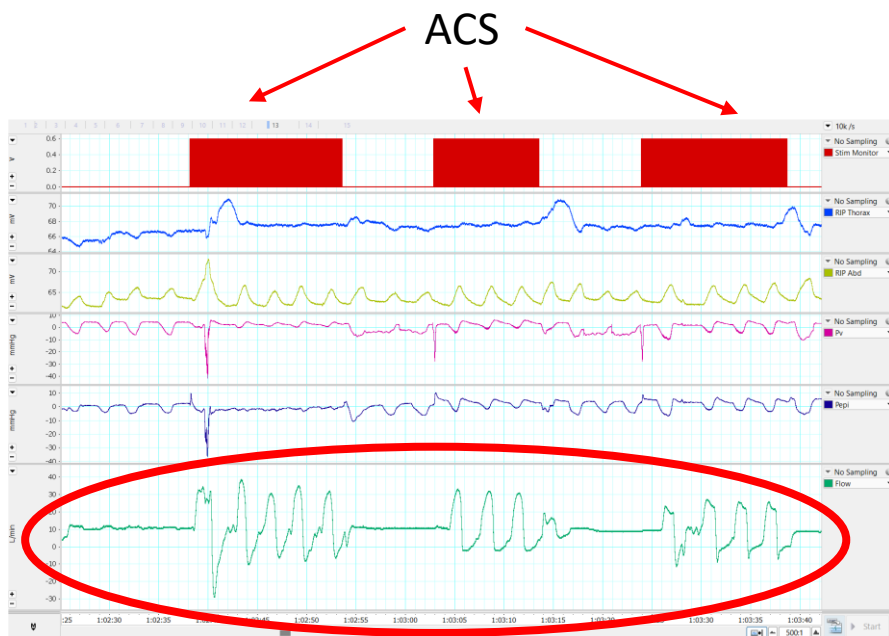


How Do We Figure Out if ACS Works?

1. Increased peak inspiratory airflow ($V_{I,max}$) and pharyngeal cross-sectional area during sleep and anesthesia^{1,2}
2. Decreased pharyngeal collapsibility (P_{CRIT})
3. Improves sleep apnea (AHI)

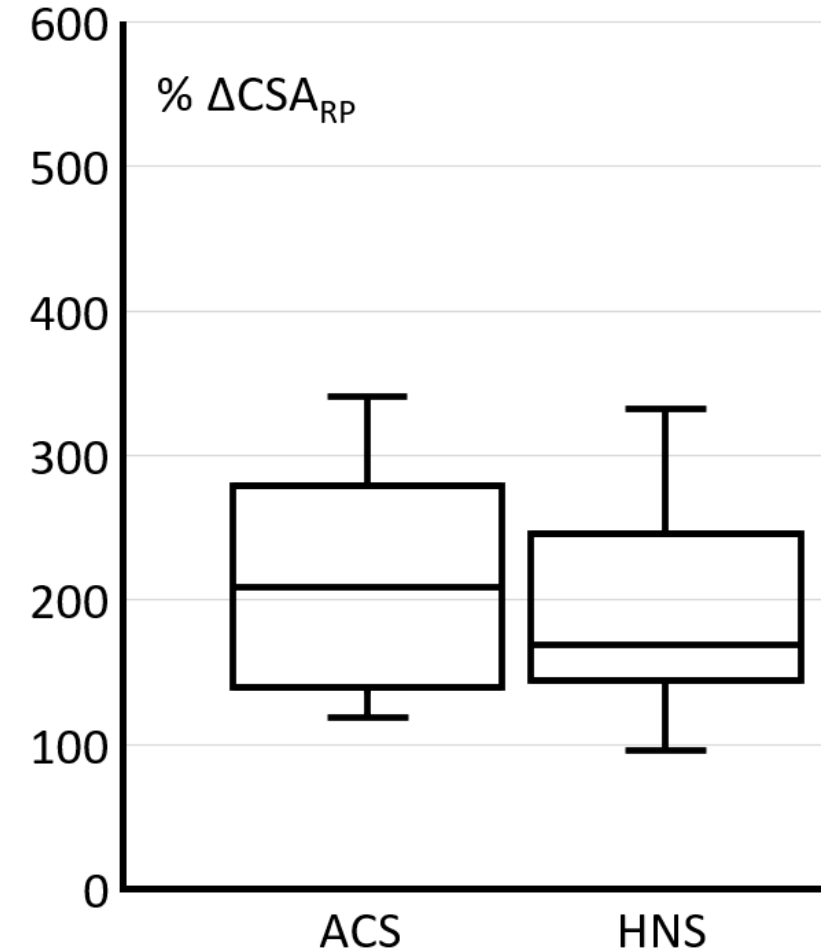
ACS Increases Peak Inspiratory Flow ($V_{I\max}$)

- 8 patients, severe OSA
 - AHI: 43.2 ± 8.9
 - BMI: 32.1 ± 2.5
- **ACS: Peak airflow increased 298% (473 mL/s)**
- CCC: 3/8, no significant effect

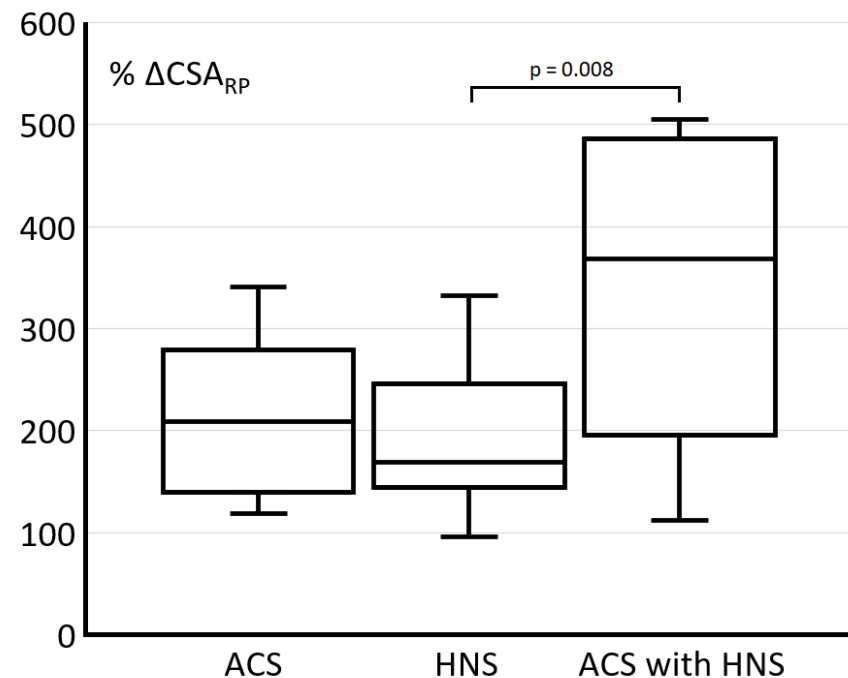
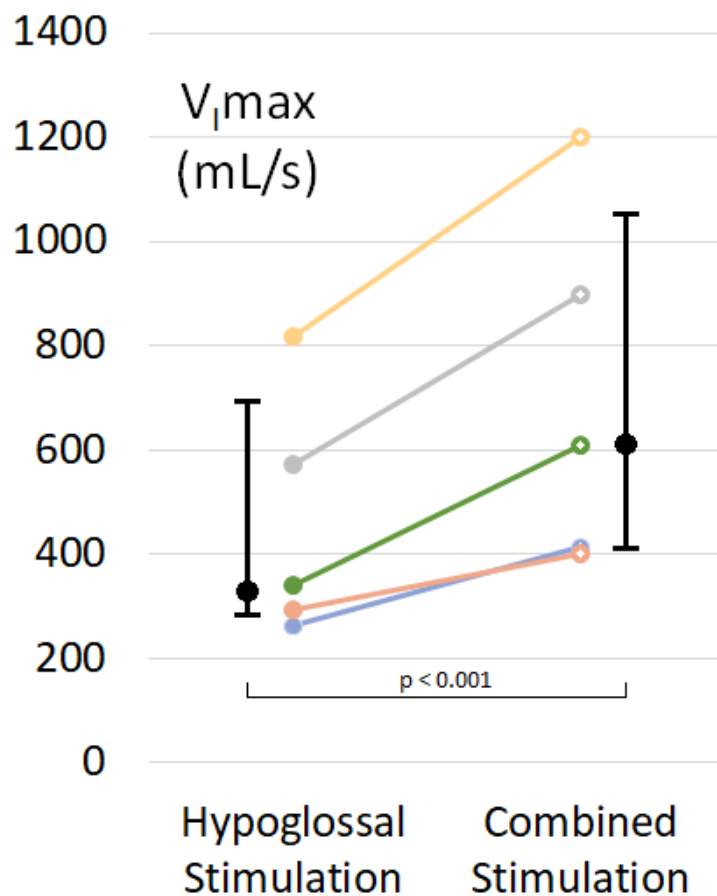


ACS Increased Retropalatal Cross-Sectional Area

- N=8
 - AHI: 43.4 ± 6.4
 - BMI: 31.4 ± 2.8
- Retropalatal cross-sectional area (CSA_{RP})
 - **ACS vs baseline: $211 \pm 75\%$**
 - HNS vs baseline: $192 \pm 70\%$



HNS+ACS Has Interactive Effects on $V_{i,max}$ and CSA_{RP}



- ACS+HNS vs HNS: Peak airflow increased by 151%
- CCC: no effect

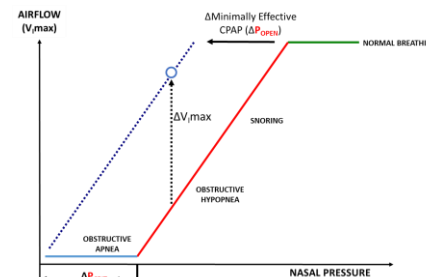
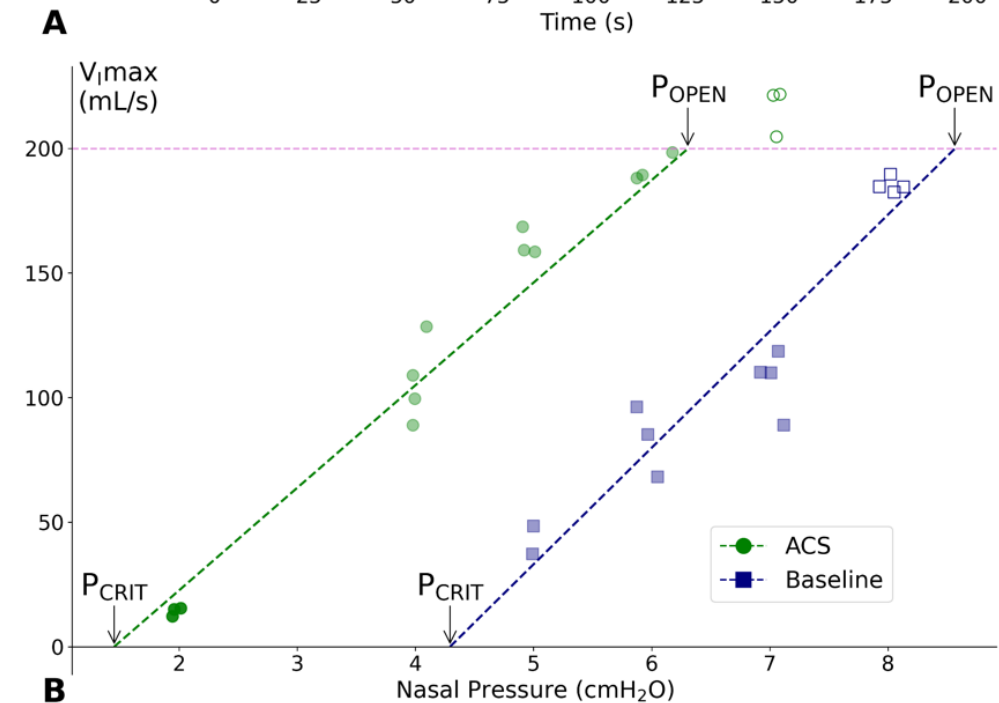
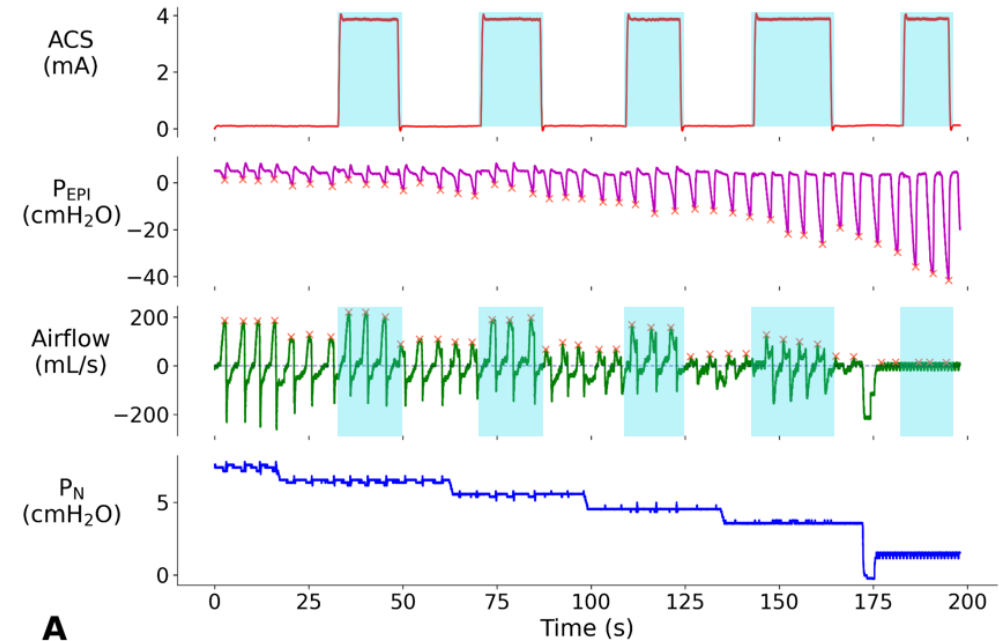
- ACS+HNS vs baseline: $341 \pm 141\%$
- ACS+HNS vs HNS: $180 \pm 68\%$
- CCC: no effect

How Do We Figure Out if ACS Works?

1. Increases peak inspiratory airflow ($V_{I,max}$) and pharyngeal cross-sectional area during sleep and anesthesia^{1,2}
2. Decreases pharyngeal collapsibility (P_{CRIT})
3. Improves sleep apnea (AHI)

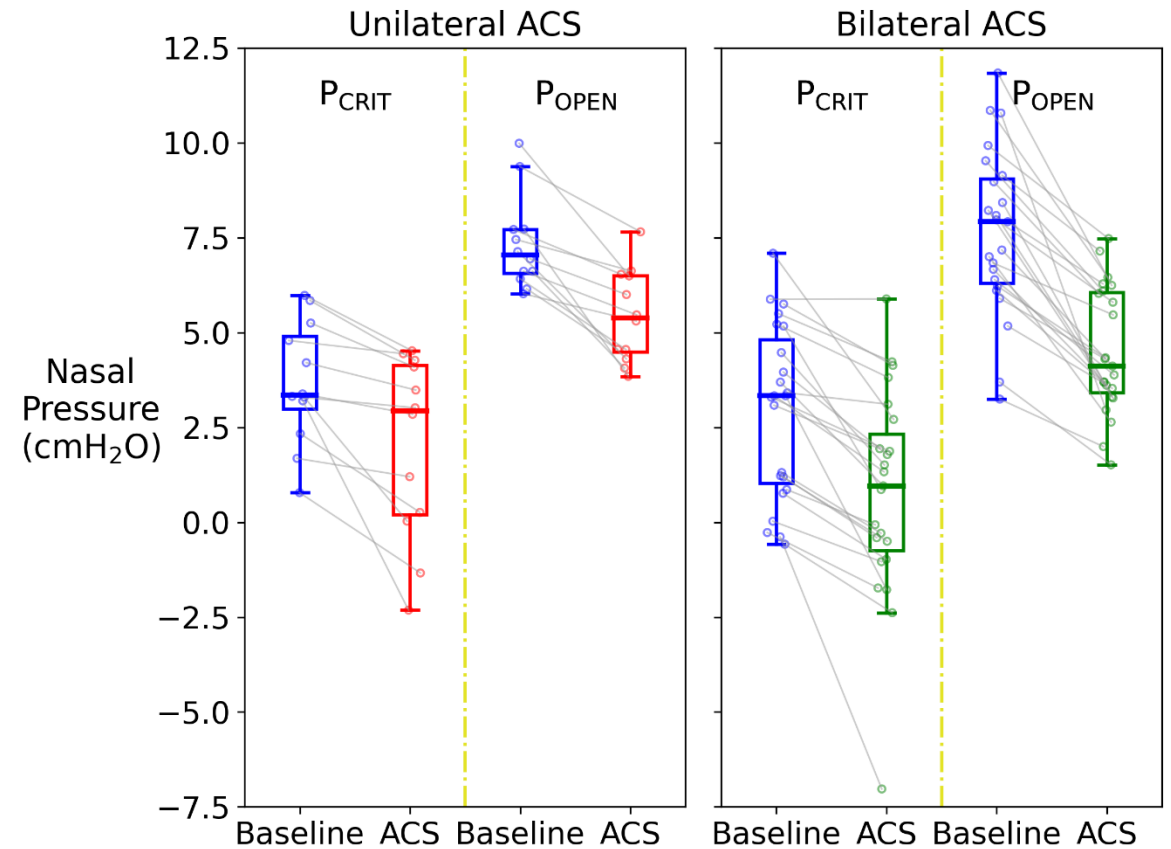
ACS Decreases Pharyngeal Collapsibility

- Bilateral (N=19) and unilateral (N=12) ACS
 - BMI: 31.6 ± 2.4
 - AHI: 43.1 ± 19.1
- Peak airflow changes assessed with ACS from P_{CRIT} to P_{OPEN}

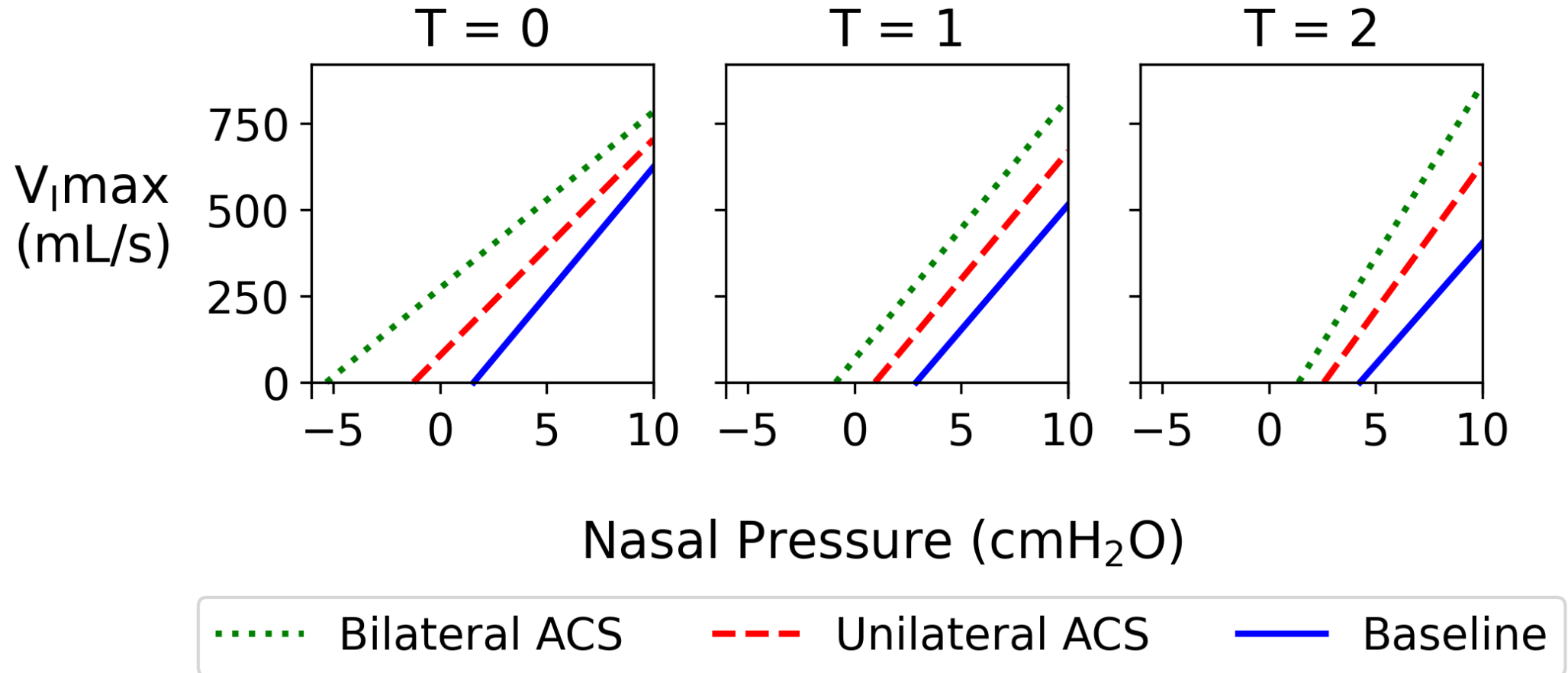


ACS Decreases Pharyngeal Collapsibility

- **Bilateral ACS**
 - ΔP_{CRIT} : -2.1 ± 1.6 cmH₂O
 - ΔP_{OPEN} : -3.1 ± 1.6 cmH₂O
- ΔP_{CRIT} Top 50%: -3.0 ± 1.6 cmH₂O
 - Lower AHI
 - 33.7 ± 12.8 vs. 53.5 ± 18.5 cmH₂O
 - **Greater BMI was more responsive**
 - 32.7 ± 1.7 vs. 30.3 ± 2.5 cmH₂O
- **CCC did not affect outcomes**

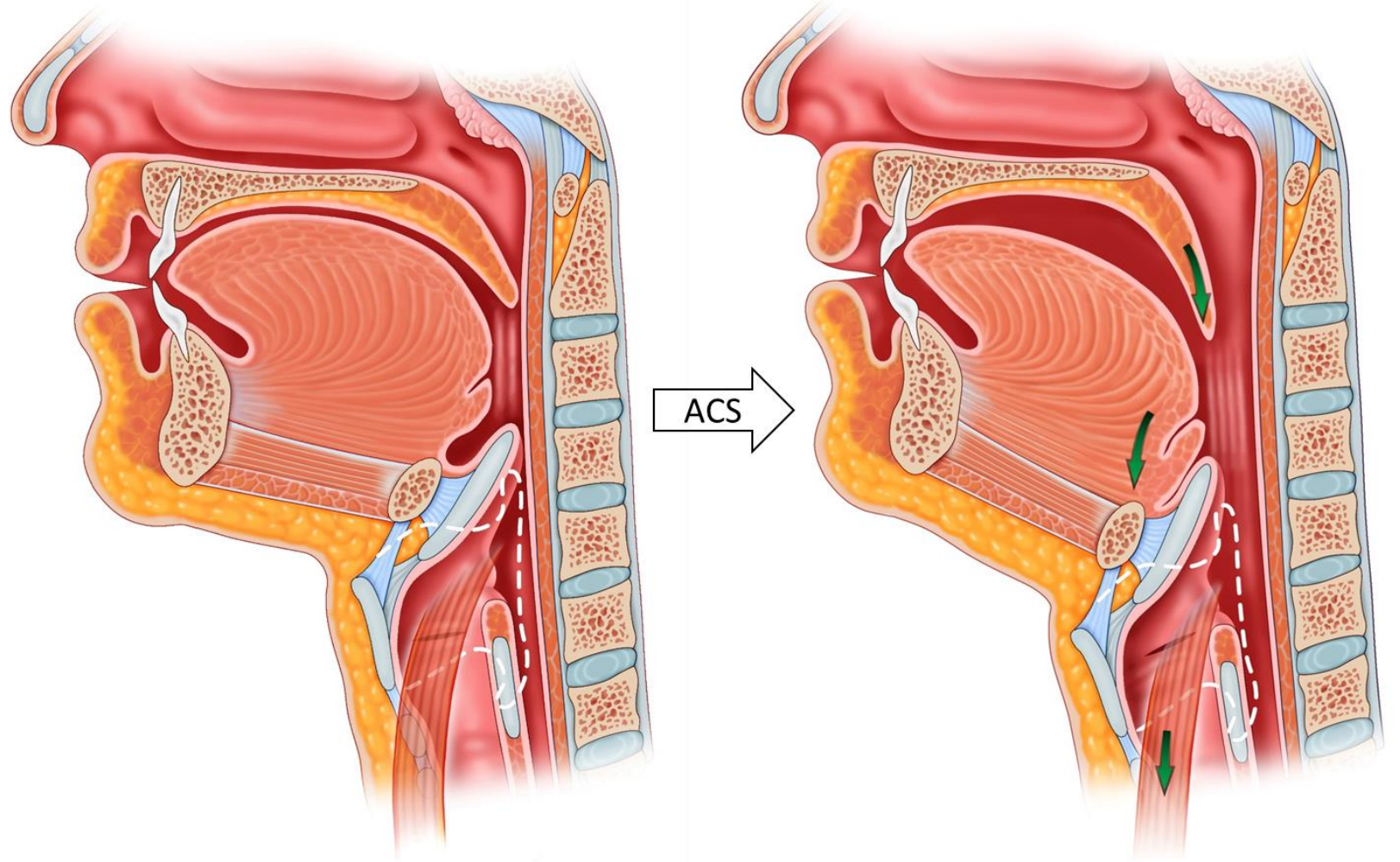


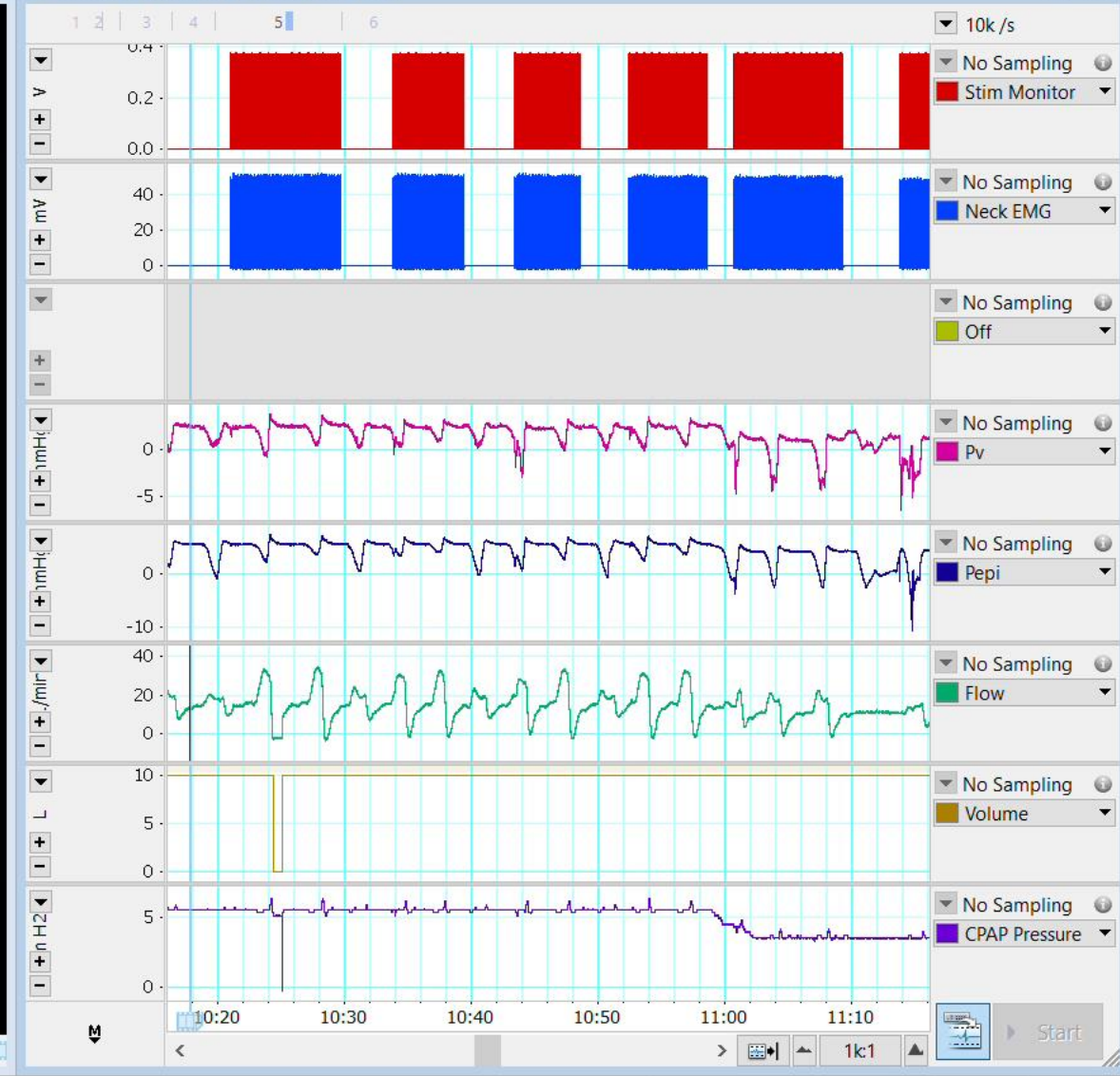
ACS Subtypes?

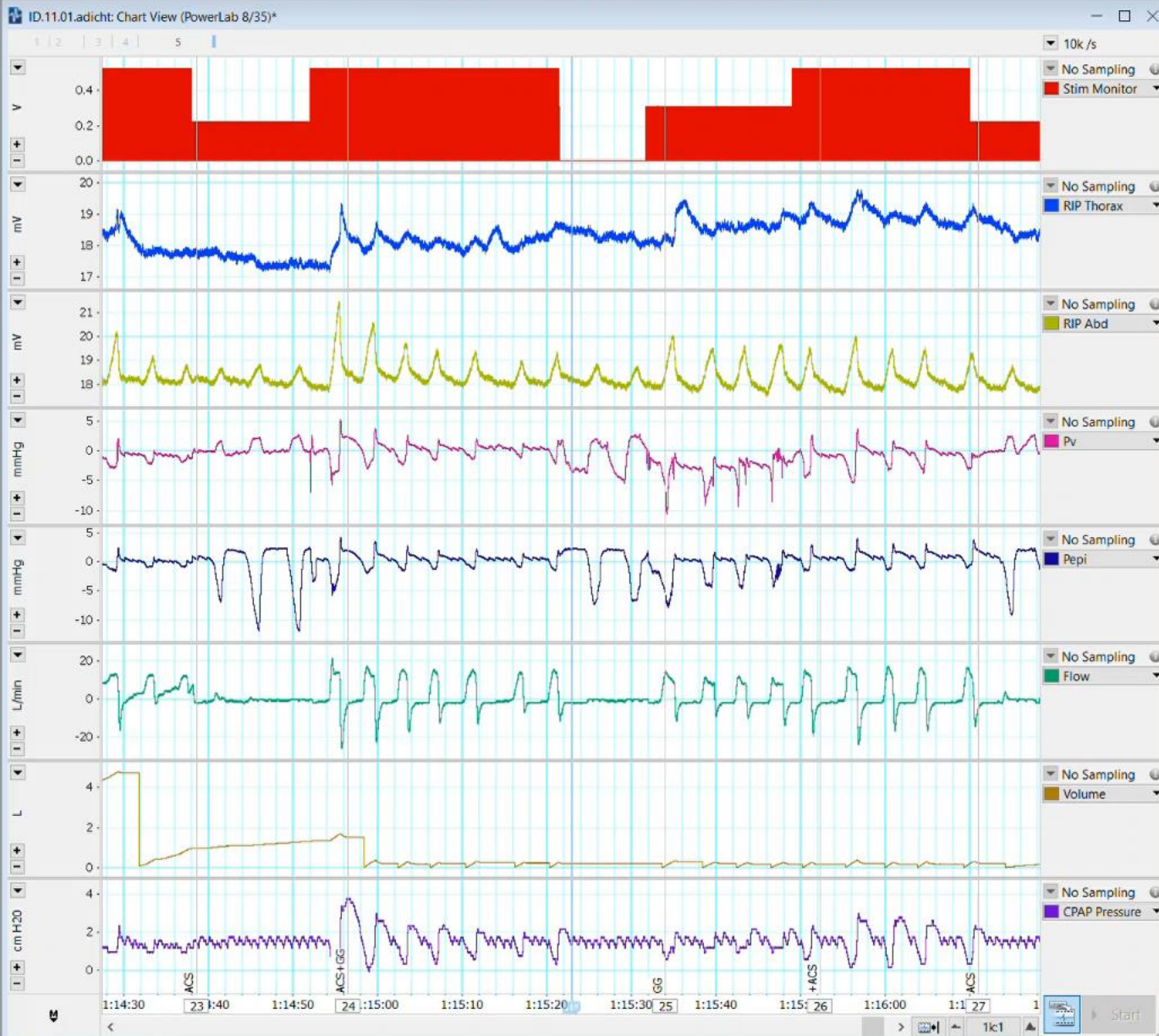


ACS: Proposed Mechanisms of Action

1. Palate tensioning/opening
2. Palate unloading
3. Lateral wall stabilization
4. Anterior epiglottic tilt







Conclusions

- OSA is not just an upper airway disease, it is an **upper body disease**
- **HNS is insufficient** for many OSA patients, especially \uparrow BMI, \uparrow AHI
 - A minority of OSA patients are eligible for therapy
- Ansa cervicalis stimulation is a **viable and surgically accessible neurostimulation target**
 - Single site activation of **sternothyroid trunk**
- Ongoing human research supports ACS as a potentially viable therapy

Conclusions

- ACS may complement HNS to yield *greater effects than either in isolation*
- Potential benefits?
 - **More comfortable therapy:** De-escalate single channel stimulation
 - **More effective therapy:** Reduced postoperative care burden
 - **More treatable patients:** Expanded indication (CCC, ↑BMI)

Thank You

- David Zealear
- Alan Schwartz
- Yike Li
- Kate VonWahlde
- Maryam Seirafi-Pour
- Katie Hartley
- Holly Budnick
- Many more...





Closing Remarks

Olivier Taelman – Chief Executive Officer

2023 Company Strategic Objectives

Clinical US

- DREAM – World class patient follow-up resulting in reaching primary endpoints
- ACCESS – Building US complete concentric collapse patient experience

US Market Readiness

- Regulatory PMA modular submissions
- CPT code confirmation by AMA
- Commercial launch preparedness

European Commercialization

- Germany as commercial proof of concept
 - Market Share gain in top HGNS accounts
 - Accelerate market penetration through DTC and referral programs
- Open new markets
 - Switzerland, Austria, Italy

We Are On Our Way...



GENIO[®]

Let's Make Sleep **Simple** Again

Thank you

Q&A



Nyxoah 