Results of the ADHERE Upper Airway Stimulation Registry and Predictors of Therapy Efficacy

ADHERE Registry Summary (n=1,017 enrolled)

E Thaler, R Schwab, J Maurer, et al

Laryngoscope, Sept 2019

Publication Link [open access]

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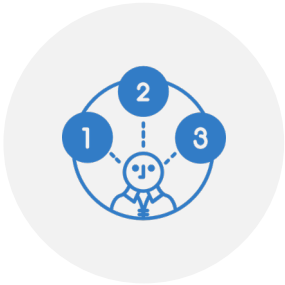
OSA Treatment Background

While CPAP is the gold standard treatment of OSA, 30-50% cannot tolerate CPAP[1]

Untreated OSA associated with daytime sleepiness, higher cardiovascular risk



There is a need for treatment options for CPAP-intolerance

Upper Airway Stimulation – surgical option, shown to be safe and effective in multiple studies

1. Rose, SLEEP 2012, Home-PAP study

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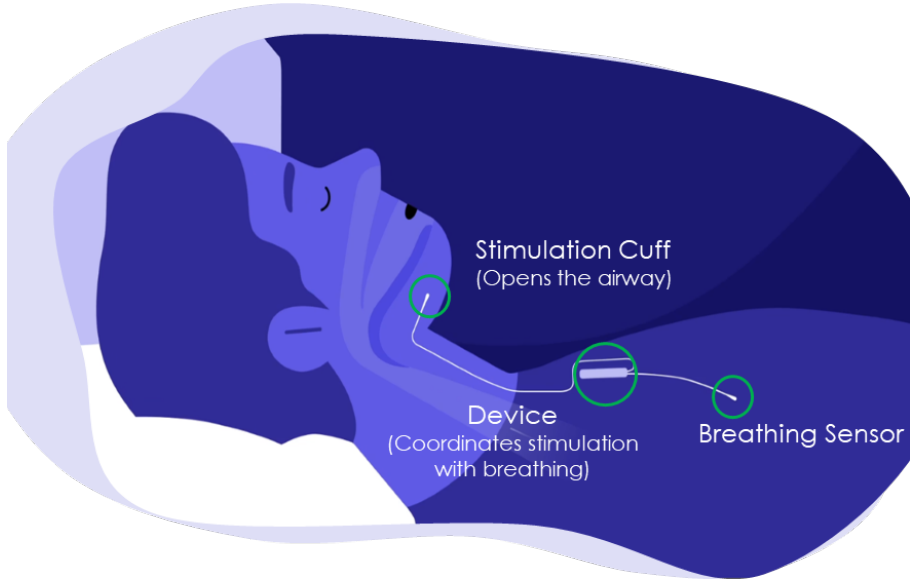
Inspire Therapy

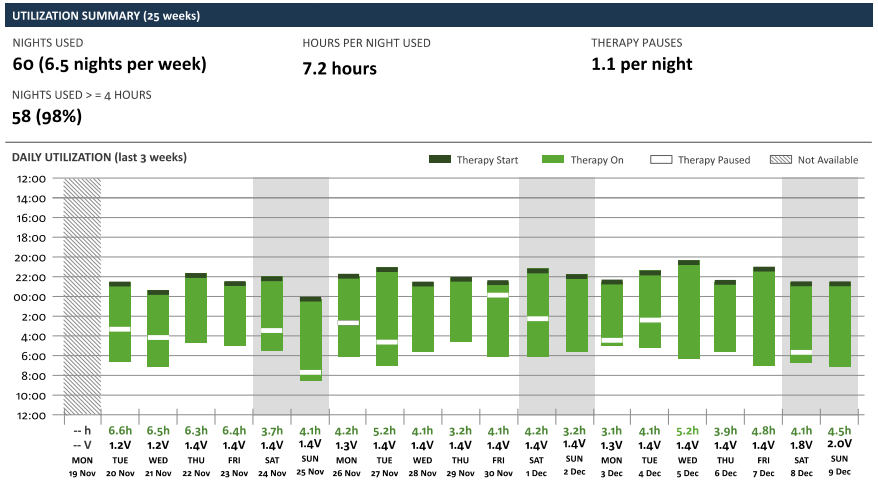
A Treatment for Obstructive Sleep Apnea Patients Who Are Unable to Use CPAP

Safe Outpatient Procedure



Sleep Remote

Nightly Adherence Monitoring (Quality Measures)



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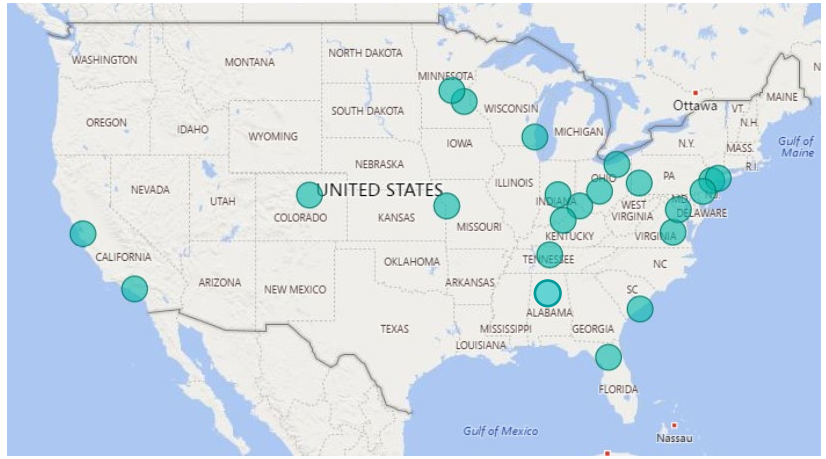
ADHERE Registry

- Goal: Collect **real-world outcomes** data
- International multi-center, standard-of-care registry
- Eligibility – prospective patients receiving UAS for OSA
  - CPAP intolerant or non-compliant
  - AHI between 15-65, and fewer than 25% central apneas
  - Absence of velum complete concentric collapse on DISE

1,400 enrollments as of Sept 2019

Enrollment Goal: 2,500 patients

36 SITES IN THE US & EUROPE



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Registry Data Collection
Follows Clinical Protocol

Baseline

Medical Record

- Demographics
- OSA History
- AHI
- ESS

Implant

- Implant Time
- Adverse Events

Post-Titration (6mo.)

- Titration PSG (AHI)
- ESS
- Therapy Usage
- Clinical Global Impression
- Patient Experience

Annual Visit (12mo.)

- HSAT / PSG AHI
- ESS
- Therapy Usage
- Clinical Global Impression
- Patient Experience

AHI: apnea-hypopnea index (4%);
ESS: Epworth sleepiness scale;
AE: adverse event;
PSG: in-lab polysomnography;
HSAT: home sleep apnea test

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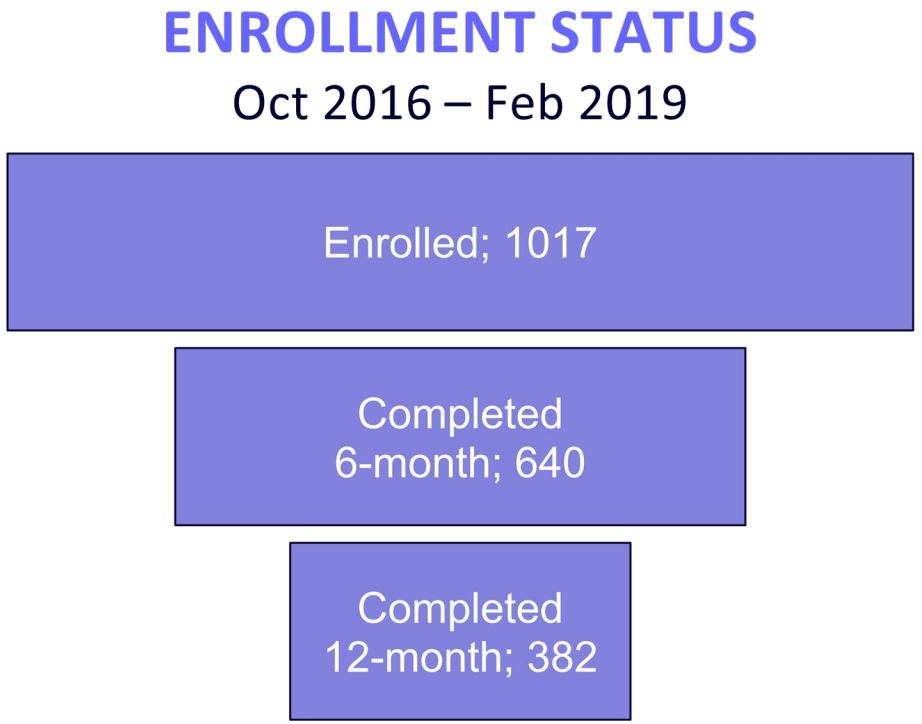
Study Enrollment Status
At Manuscript Completion

- Study is on-going, continues to capture data through patient follow-up

- This paper (n=1,017) extends the work from ADHERE-500[1]



1. Heiser, Eur Resp J 2019

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ADHERE Registry Goals

Report outcomes and new findings

UPDATE CLINICAL OUTCOMES (AHI, ESS, USAGE) AND SAFETY

DISSEMINATE NEW FINDINGS AS ENROLLMENTS PROGRESS

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ADHERE Registry

Demographics: middle aged, male, severe OSA (n=1,017)

Patient Characteristics	Value
Age	60 ± 11 (22-86)
Sex	74% Male
Ethnicity	96% Caucasian
Body Mass Index	29.3 ± 3.9
Baseline AHI	36 ± 15

Baseline Co-morbidities	Value
Hypertension	47%
Depression	22%
Diabetes	13%
Atrial Fibrillation	6%
Heart Attack	4%
Stroke	3%

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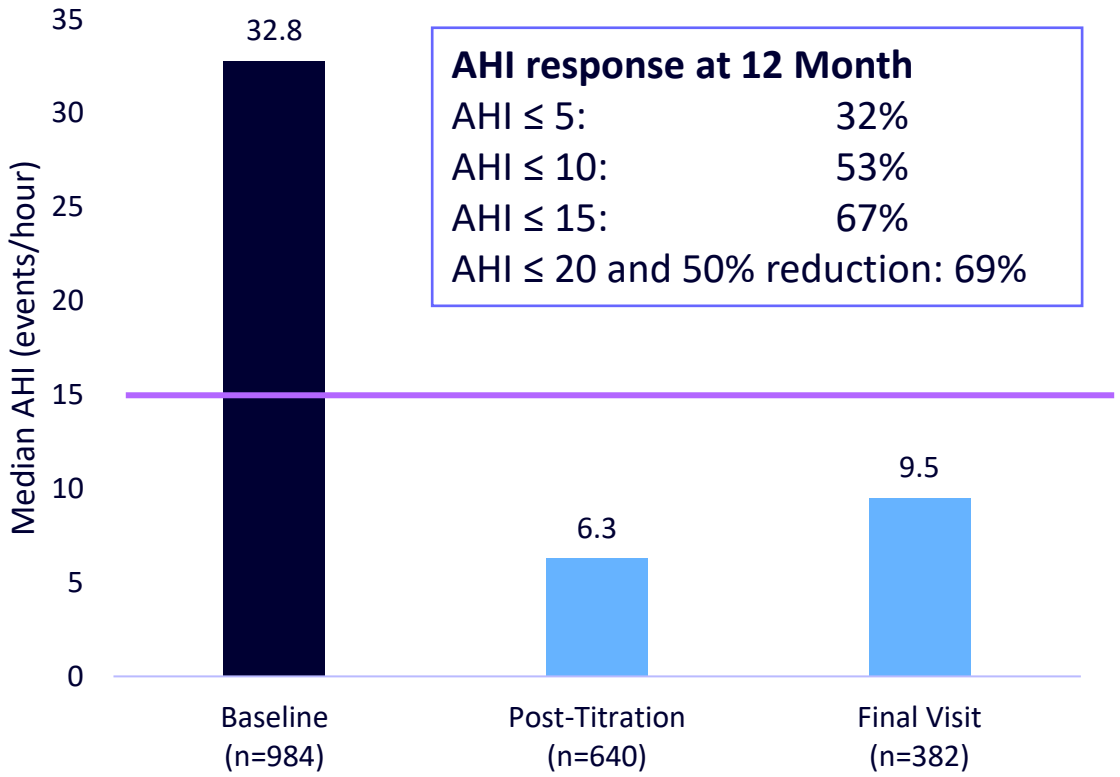
ADHERE Registry: Consistent effectiveness

Apnea Hypopnea Index (AHI)

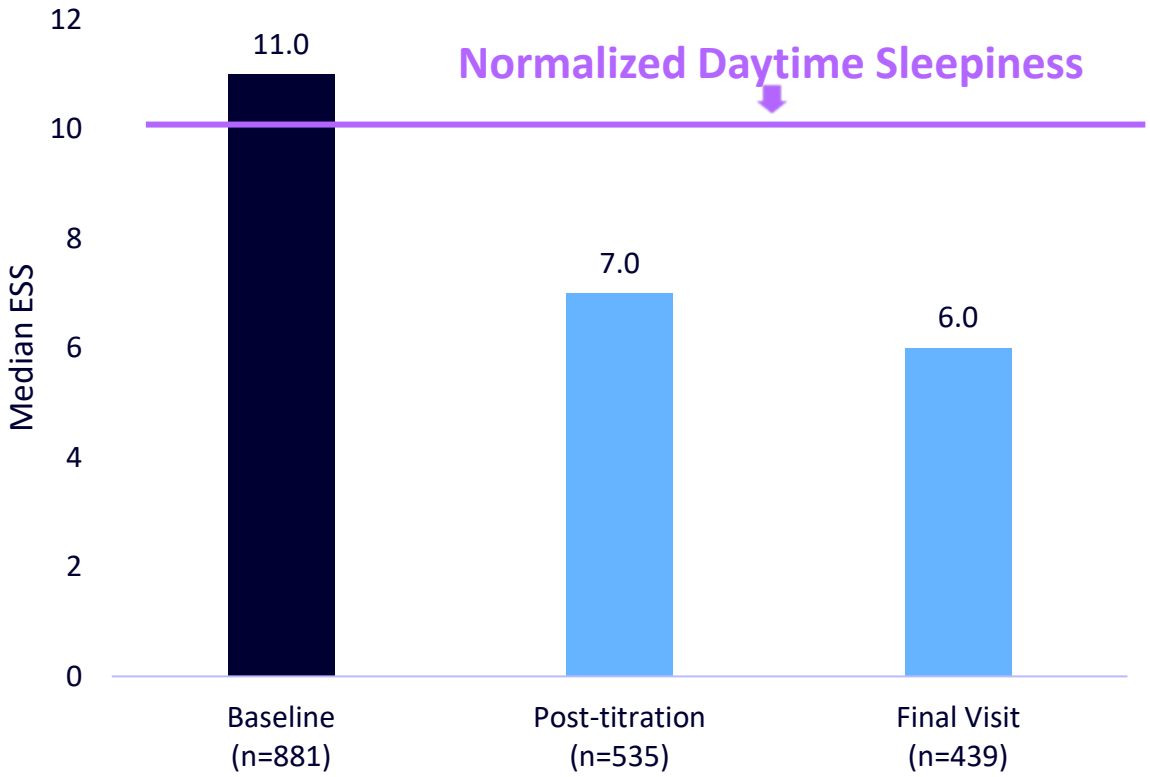


AHI response at 12 Month

AHI ≤ 5:	32%
AHI ≤ 10:	53%
AHI ≤ 15:	67%
AHI ≤ 20 and 50% reduction:	69%

Mean AHI reduced from baseline of 35.8 ± 15.4 to 14.2 ± 15.0 at 12 months ($p < 0.001$)

Epworth Sleepiness Scale (ESS)



Mean ESS reduced from baseline of 11.4 ± 5.6 to 7.2 ± 4.8 at 12 months
Reference: ESS < 10 considered free of symptoms for excessive daytime sleepiness

Thaler, et al. Laryngoscope 2019

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ADHERE Registry: Strong safety profile

Type	Post-Titration		Final Visit	
	# of Events	% of Patients	# of Events	% of Patients
Tongue Weakness	3	<1%	0	-
Swallowing or speech related	4	1%	1	<1%
Discomfort (incision/scar)	14	4%	8	2%
Discomfort (device)	10	3%	5	1%
Infection	2	<1%	0	-
Post-Op – Other	14	4%	6	2%
Stimulation related discomfort	41	12%	28	8%
Tongue abrasion	12	3%	14	4%
Insomnia/Arousal	10	3%	17	5%
Revision interventions (including explant)	1	<1%	2	<1%
Other Discomfort	12	3%	8	2%
Activation - Other	37	3%	23	7%
Total	161	46%	113	32%

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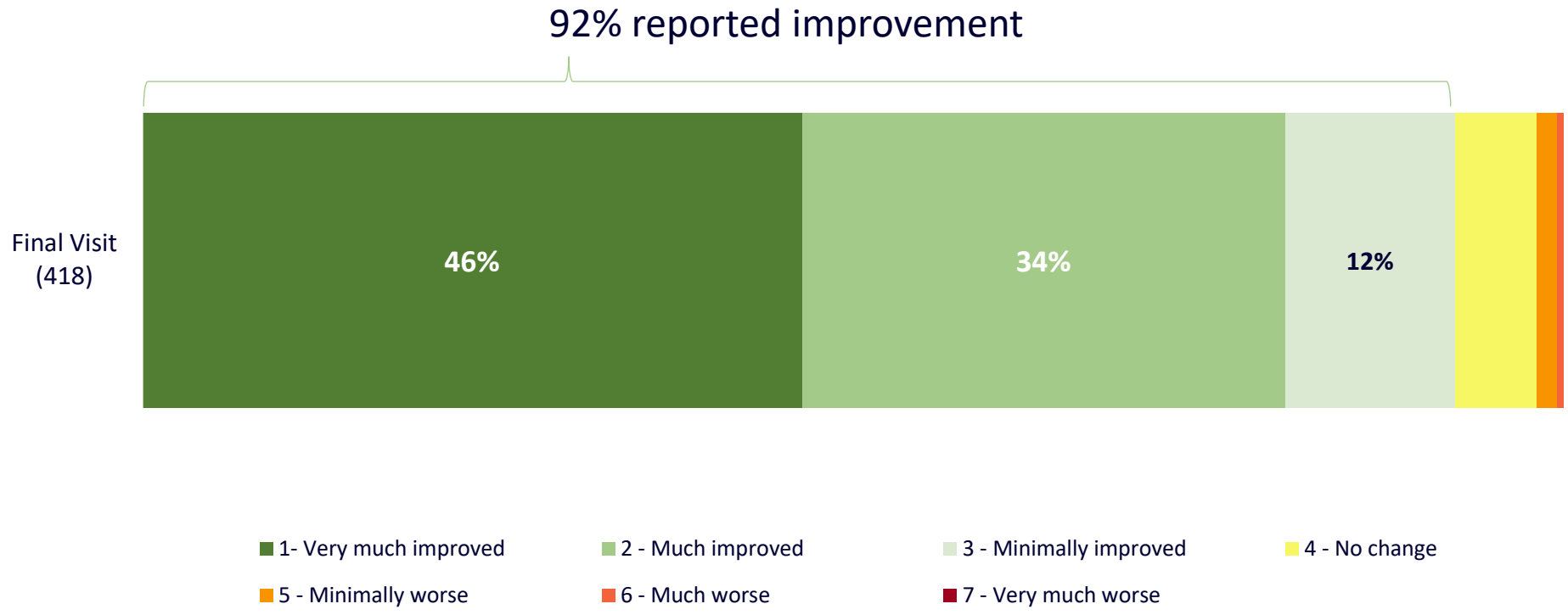
Adhere Registry Physician Global Impression:
92% of patients had improvement at 12-months



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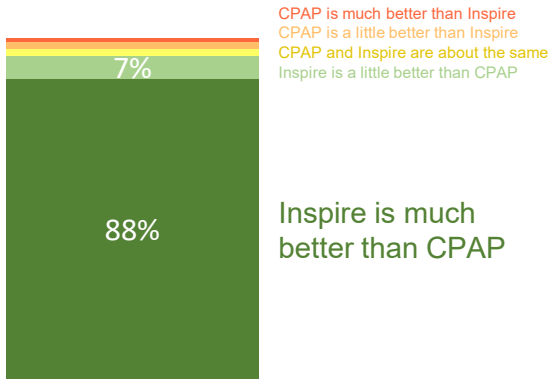
High Patient Satisfaction

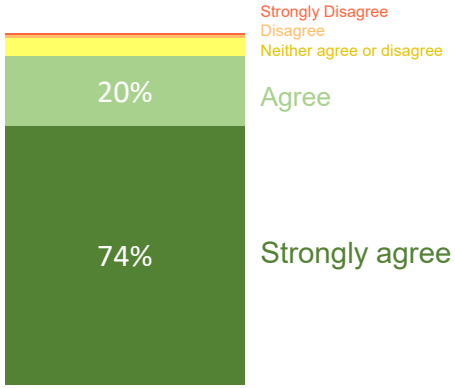
How does Inspire compare against your previous experience with CPAP? (n=378)

95%



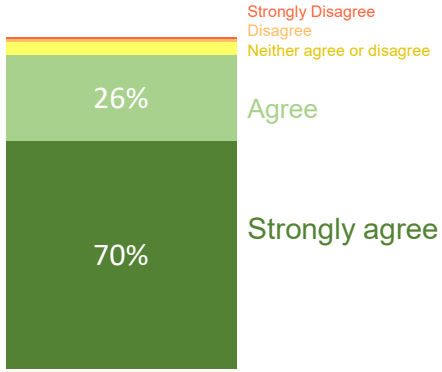
Given the chance, I would choose to receive Inspire again (n=390)

94%



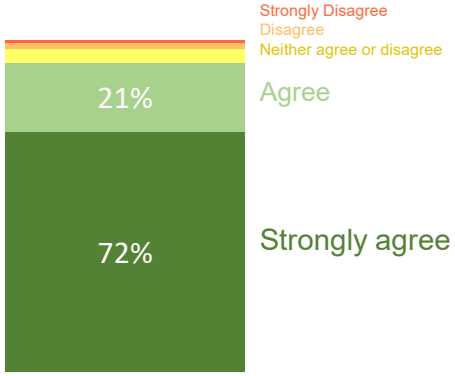
I would recommend Inspire to a friend or family member (n=390)

96%



Overall, how satisfied are you with Inspire? (n=391)

93%



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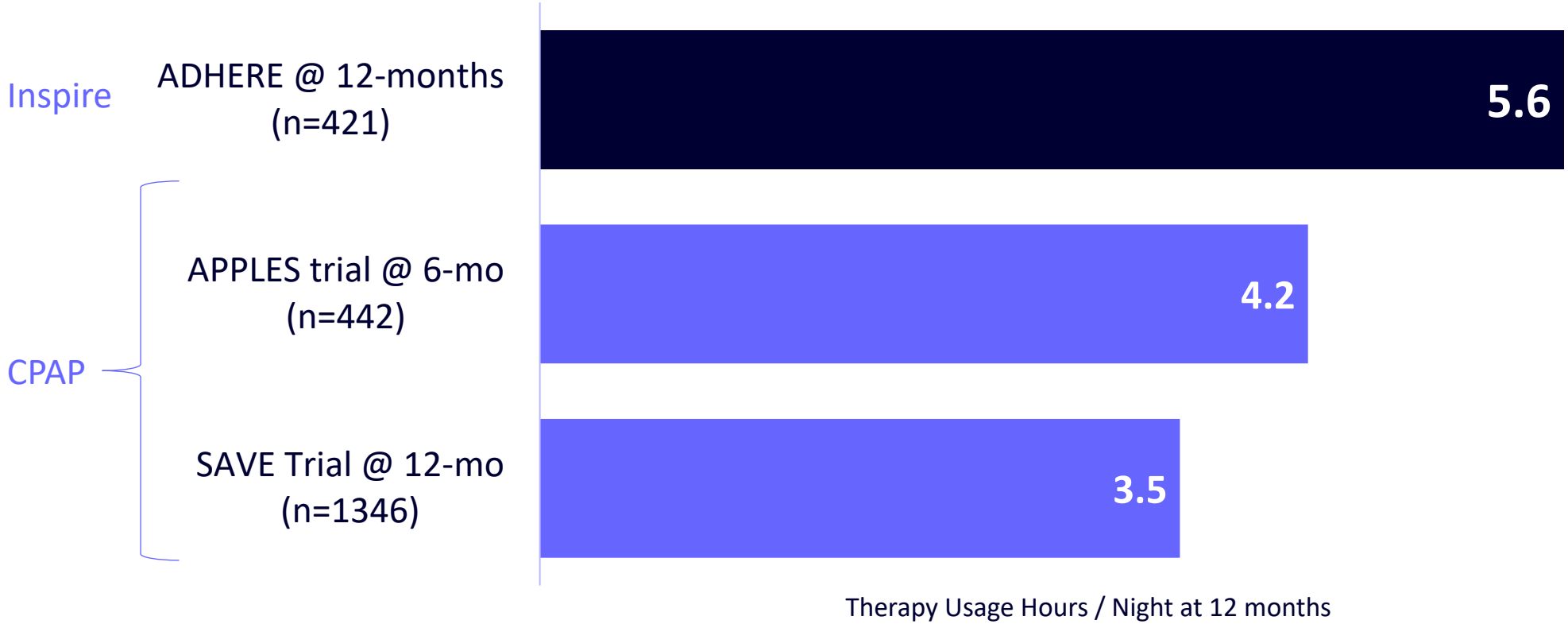
High Patient Adherence

Usage of 5.6 hr/night is higher than CPAP clinical trials



1. ADHERE-1000: Thaler, Laryngoscope 2019
2. APPLES: Kushida, Sleep 2012
3. SAVE: McEvoy, NEJM 2016
4. Medicare PAP "guideline" is 4 hours / night, 5 nights per week, within a 30 consecutive day period

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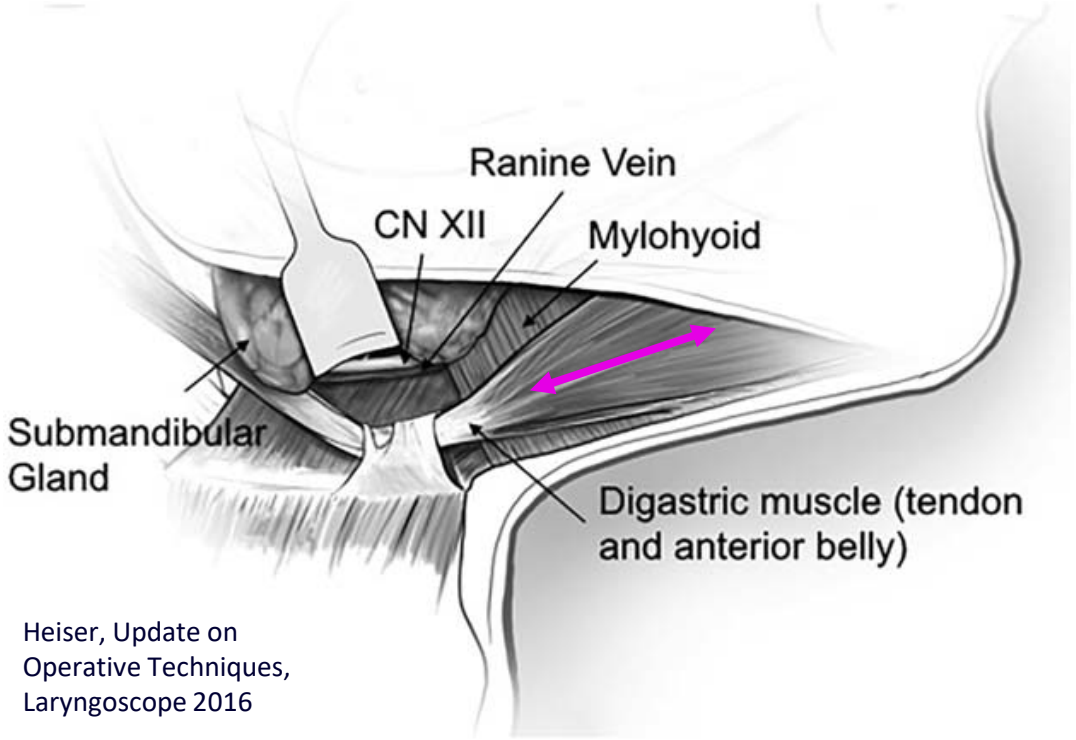
Improved understanding of approaching the hypoglossal nerve

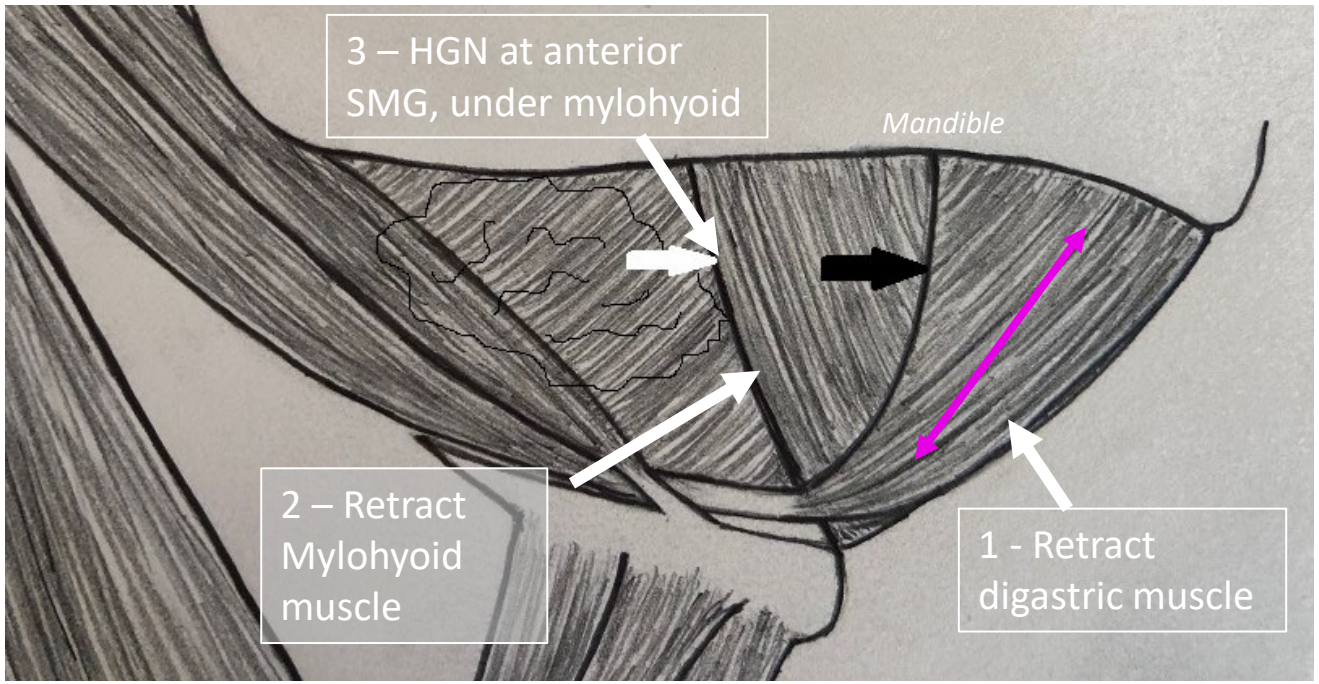
Locating digastric & mylohyoid can prevent "mistaken identity" of mylohyoid nerve vs. hypoglossal nerve

Previous understanding – digastric runs horizontal



Heiser, Update on Operative Techniques, Laryngoscope 2016

Current understanding –digastric fibers run more vertical



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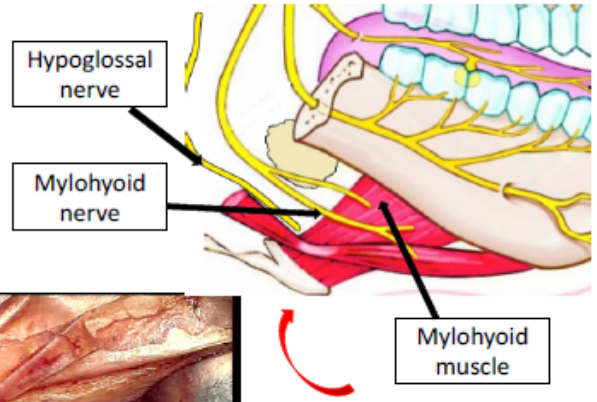
Example: Clinica Navarra Case Report of mistaken nerve

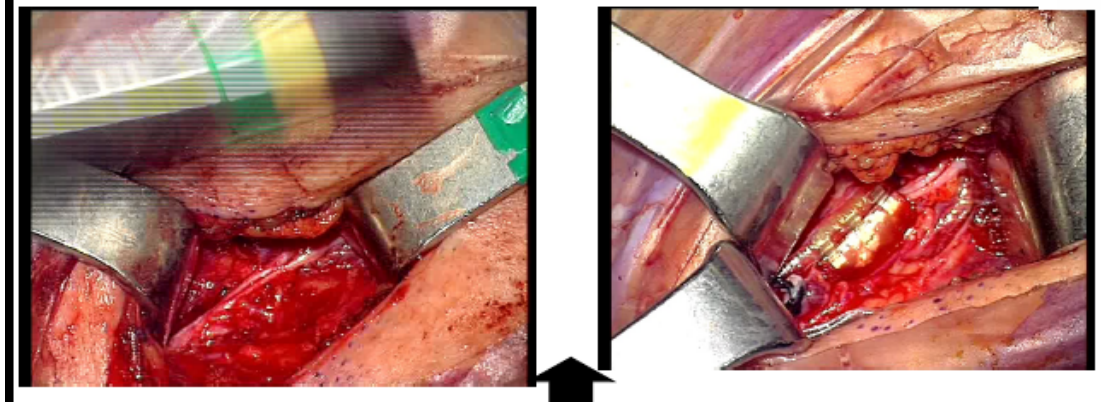
Introduction

Surgical challenges during hypoglossal nerve stimulation surgery aren´t common and they are usually related to identification of the medial division branches. We report an unusual case of an undescribed setback in which the mylohyoid nerve was confused for the hypoglossal nerve.

Clinical Case

62-year old man with a five-year history of OSA, with CPAP intolerance. A body mass index (BMI) of 24, an Epworth Sleepiness Scale 9/24, and AHI of 47/hour, and history of tonsillectomy during childhood. Physical examination, awake endoscopy and drug-induced sleep endoscopy (DISE) revealed an antero-posterior soft palate and tongue base collapse. Having met surgical implantation criteria, upper airway stimulation surgery and an Inspire system implant were indicated.





This lustration represents where we found the mylohyoid nerve, normally it is located more superiorly, it runs forward and inferiorly along the inner aspect of the mandibular ramus and curves anteriorly to travel within the mylohyoid ridge.

- Mylohyoid nerve (MHN) runs along the mylohyoid muscle, similar path as HGN, but is smaller in caliber
- NIM testing of mylohyoid can also appear to have tongue protrusion
- Hypoglossal nerve (HGN) is deep to the mylohyoid muscle
- Clear identification of muscle layers can avoid ‘mistaken identity’ of MHN for HGN

Baptista, et al. ISSS 2019 [poster]

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Post-hoc predictors of therapy response

- **Multiple ways to define response to therapy**
  (AHI, ESS, usage, or combination of these)

- **Sleep surgeons measure success by the "Sher Response Rate"**
  - 50% decrease in AHI, and $\leq$ 20 events/hour

- **STAR** 1-year responder rate: **66%**
- **ADHERE-1000** 1-year responder rate: **69%**

- **Can we identify potential predictors of increased response?**

Sher, Sleep 1996

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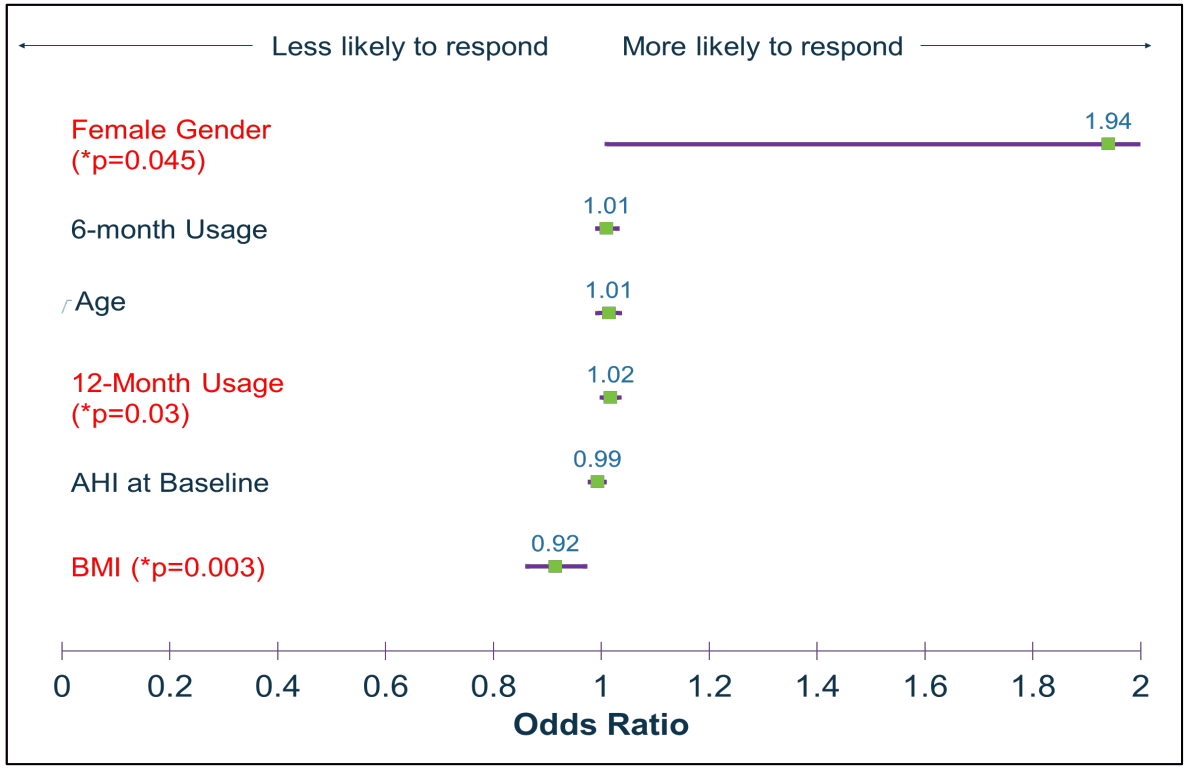
All subpopulations showed significant success

Females, and lower BMI had greater magnitude improvement

- Univariate / multi-variate regression of demographics vs. AHI response (Sher Criterion)
- Predictors of highest success were:
  - Female Gender - 94% increased odds of favorable response vs males (ie, 80% vs 67% Response)
  - Lower BMI - every 1pt. decrease in BMI associated with 8% higher odds of favorable AHI response
- Age nor baseline AHI did not predict response
- Suggests a biological mechanism or phenotype that is more sensitive to UAS

These are retrospective findings and not intended to change patient selection

Univariate model for therapy response



Therapy response is defined as at least 50% reduction of AHI to less than 20.

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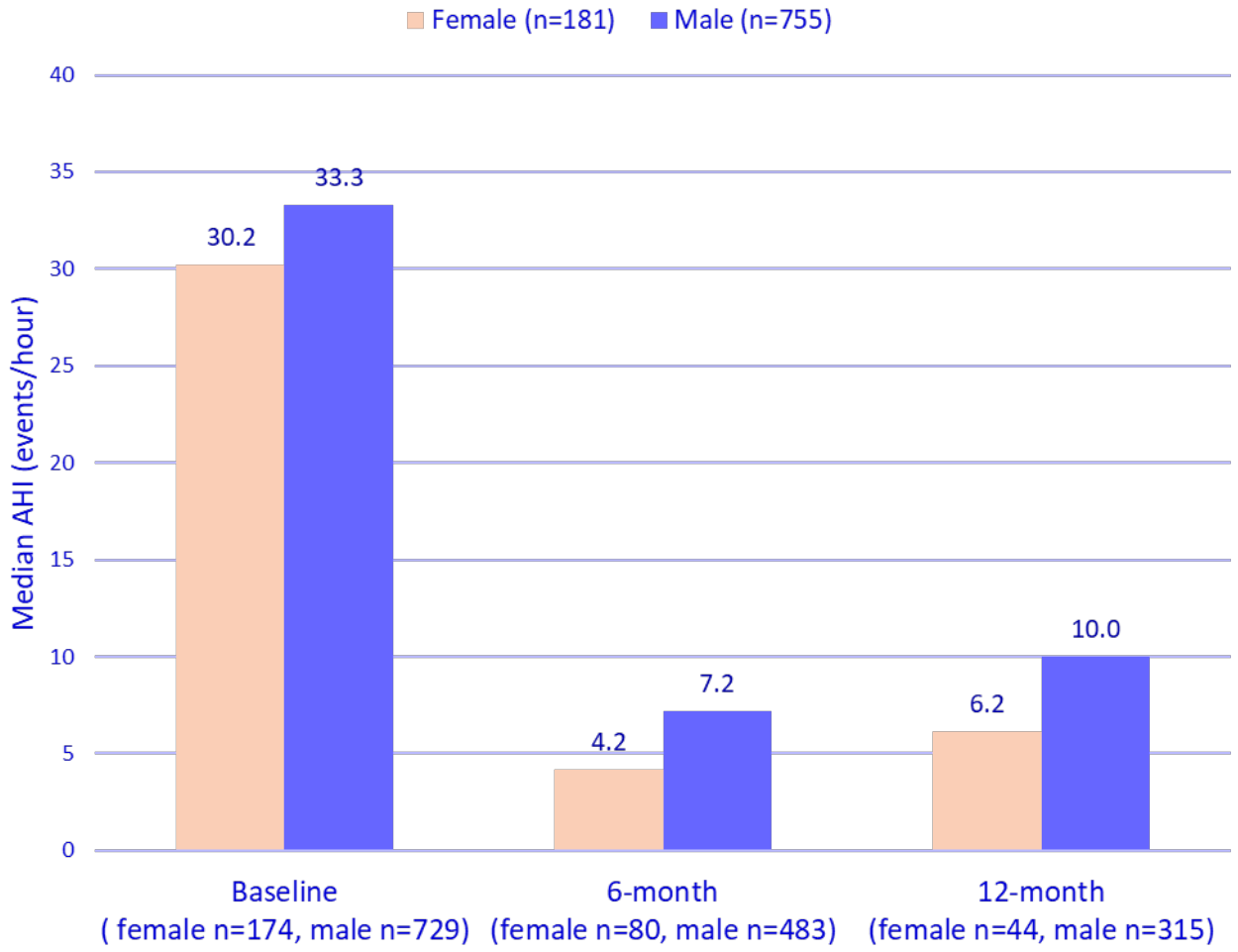
Both genders had significant reduction in AHI



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ADHERE Registry Update Summary

Largest real-world data collection of upper airway stimulation for treatment of OSA to date

Reduced OSA severity, sustained through 12-months, **consistent** with multiple other studies

Improved patient symptoms, and **high satisfaction**

Maintained high therapy **adherence** after 12 months

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Supplementary Details

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Multi-variate model with stepwise selection – gender and BMI were retained as predictors

	Univariable Results		Multivariable Results Full Model		Multivariable Results Reduced Model	
Parameter	**OR (p-value)**	**95% CI for OR**	**OR (p-value)**	**95% CI for OR**	**OR (p-value)**	**95% CI for OR**
Sex (Female vs Male)	1.943 (0.0457)	1.013, 3.729	3.634 (0.0041)	1.505, 8.772	3.413 (0.0049)	1.452, 8.019
Age at consent	1.014 (0.1862)	0.993, 1.034	1.000 (0.9998)	0.976, 1.025		
BMI at baseline	0.915 (0.0028)	0.863, 0.970	0.913 (0.0108)	0.851, 0.979	0.909 (0.0050)	0.851, 0.972
Baseline AHI	0.993 (0.2914)	0.979, 1.006	1.006 (0.5198)	0.988, 1.024		
Tongue motion	P = 0.6414		P = 0.3795			
Bilateral protrusion vs. Right protrusion	1.312 (0.3488)	0.743, 2.318	1.554 (0.1645)	0.835, 2.894		
Bilateral or right protrusion vs. Other	0.963 (0.9244)	0.442, 2.100	-	-		
Other vs. Right protrusion	1.284 (0.5843)	0.525, 3.141	1.339 (0.6320)	0.406, 4.415		
Therapy hours per week at 6-mo	1.011 (0.2457)	0.993, 1.029	1.004 (0.8103)	0.971, 1.038		
<28 hours vs ≥28 hours at 6-months	0.726 (0.3864)	0.352, 1.498	1.130 (0.8362)	0.355, 3.592		
Therapy hours per week at 12-mo	1.017 (0.0390)	1.001, 1.033	1.001 (0.9668)	0.969, 1.034		
<28 hours vs ≥28 hours at 12-months	0.622 (0.0769)	0.367, 1.053	0.651 (0.3732)	0.254, 1.673		

- Gender, baseline BMI, and binary therapy use (<28 hours vs ≥28 hours) at final follow-up were entered into the model in the first, second, and third step. No other variable met the chi-square score of 0.2 significance level for entry into the model.

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