



## Upper Airway Stimulation for OSA 2018

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**Pittsburgh**

University of Pittsburgh / [CTSI](#) / Clinical + Translational Science Institute

### Disclosure: Patrick J Strollo, Jr., MD

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#### Research Support

- **Federal**
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  - PinMed
- **Industry Advisory:**
  - ResMed
  - Emmi Solutions
  - Jazz Pharmaceuticals
  - Itamar Medical
  - Inspire Medical Systems
  - Separation Design Group

## Outline

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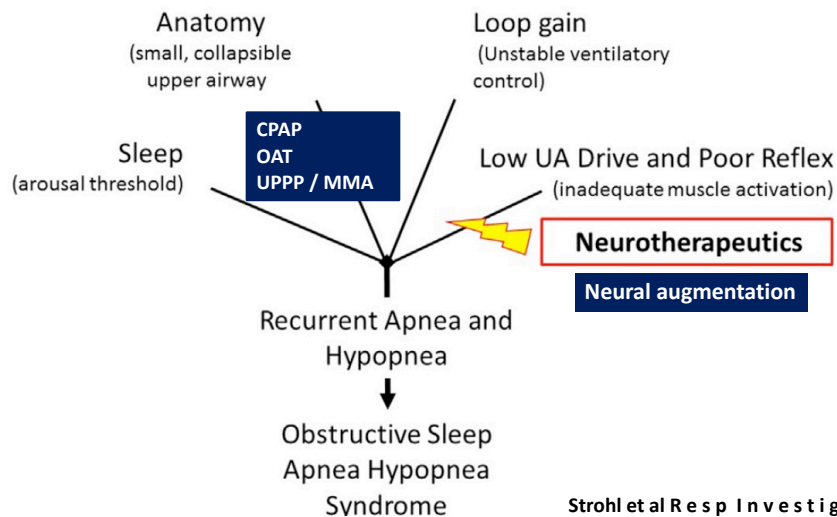
- **Upper Airway Stimulation**
- **STAR Trial**
- **Adhere Registry**
- **Conclusions**

## Outline

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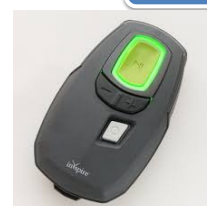
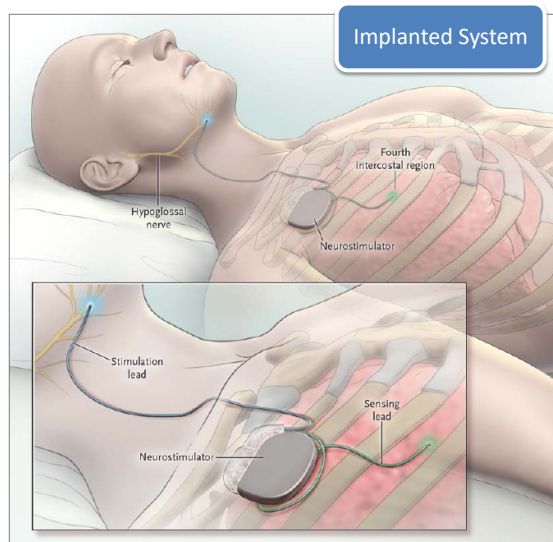
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## Upper Airway Stimulation: A new class of therapy



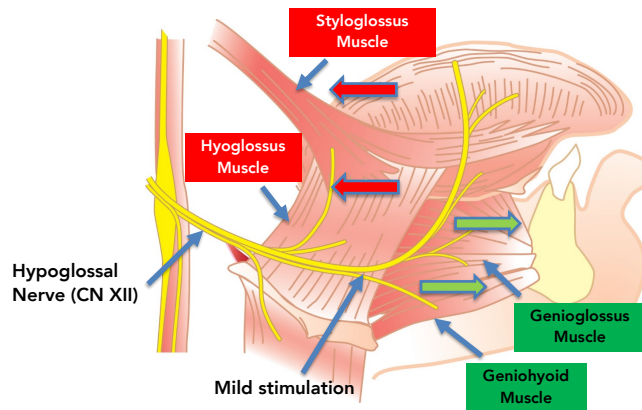
Strohl et al Res P Investigation  
2016 5 4:241 - 249

## Upper Airway Stimulation



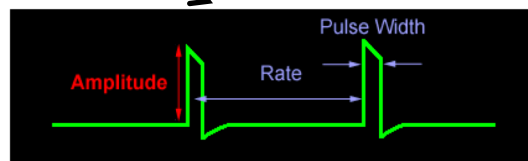
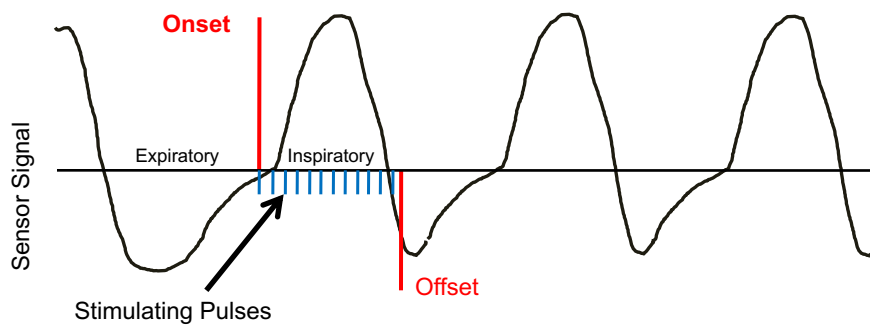
Strollo et al, N Engl J Med, 2014

## The Distal Hypoglossal Nerve



Heiser et al Sleep and Breathing 2016

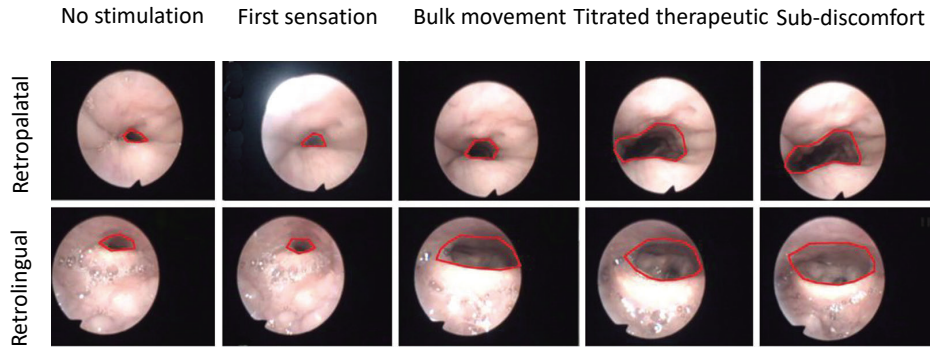
## Basic Therapy Parameters



- **Amplitude (V)** – primary stimulation strength adjustment
- **Rate (Hz)** – default 33 Hz
- **Pulse Width (µsec)** – default 90 µsec

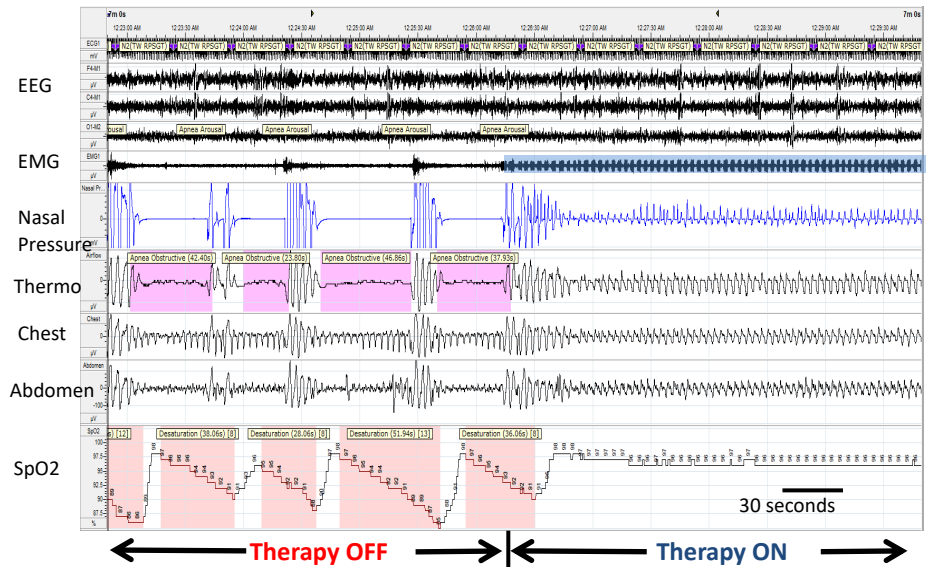


**Increases in retropalatal and retrolingual area comparing no stimulation with progressively higher levels of stimulation during DISE**



Safiruddin et al Eur Respir J 2015 45:129-138

**PSG: Effect of Stimulation**



## Outline

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## Stimulation Therapy for Apnea Reduction (STAR Trial) ClinicalTrials.gov NCT01161420

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***Hypothesis: Unilateral Stimulation of the Hypoglossal Nerve during sleep will safely and effectively treat Obstructive Sleep Apnea***

Strollo et al, NEJM 2014 370:139-49

## Outcome Measures: Baseline vs. 12-Months

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- **Co-Primary**
  - Apnea Hypopnea Index
  - Oxygen desaturation index (ODI<sub>4%</sub>)
- **Secondary**
  - Epworth Sleepiness Scale
  - Functional Outcomes of Sleep Questionnaire
  - SaO<sub>2</sub> < 90%

Strollo et al, NEJM 2014 370:139-49

## Methods

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- **Prospective, multicenter trial with a randomized therapy withdrawal arm in participants with moderate to severe OSA who had not accepted or had not tolerated CPAP.**
- **All underwent a screening polysomnographic (PSG) study, surgical consultation, and drug-induced sedation endoscopy (DISE).**

Strollo et al, NEJM 2014 370:139-49

## Inclusion / Exclusion Criteria

### Inclusion

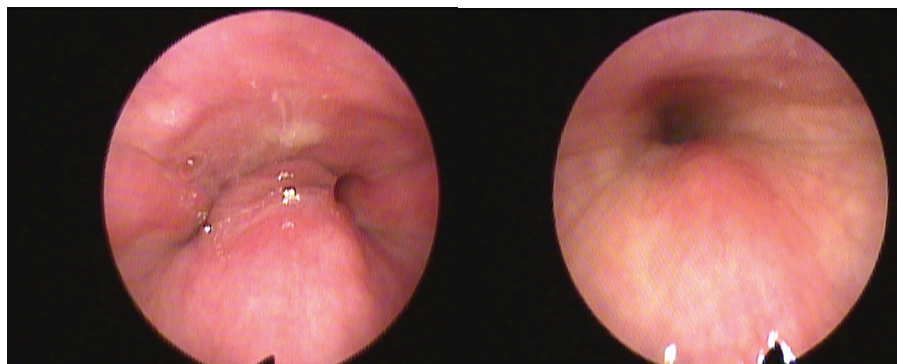
- AHI between 20 and 50
- Have not accepted or not tolerated CPAP
- Central and mixed sleep apnea accounted for < 25% of all AHI events
- Absence of significant apnea when sleeping in a non-supine position ( $AHI_{\text{non-supine}} > 10$ )

### Exclusion

- BMI > 32
- Neuromuscular diseases
- Severe Co-Morbid Cardiopulmonary Disease
- Other chronic sleep disorders
- Complete concentric collapse at the level of soft palate during drug-induced sedation endoscopy (DISE)

Strollo et al, NEJM 2014 370:139-49

## Examples collapse at the level of the palate during DISE



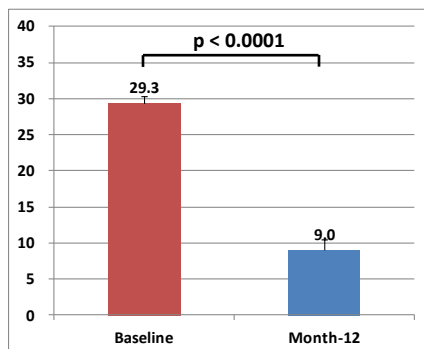
Anteroposterior collapse

Concentric collapse

JCSM 2013 9 (5) 433-438

## Primary Outcome Measures: AHI and ODI (n = 124)

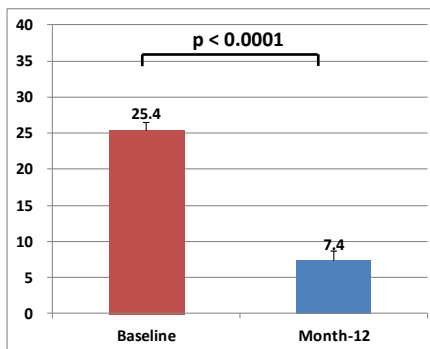
### AHI



• 68% reduction in AHI from baseline to Month-12

\*Median and error bar in standard error

### ODI

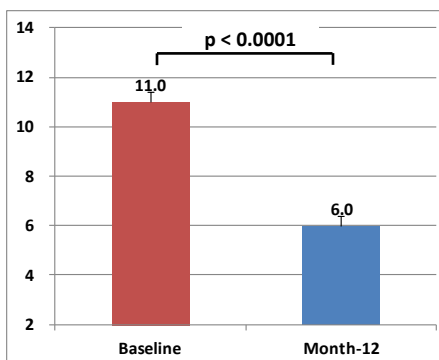


• 70% reduction in ODI from baseline to Month-12

Strollo et al, NEJM 2014 370:139-49

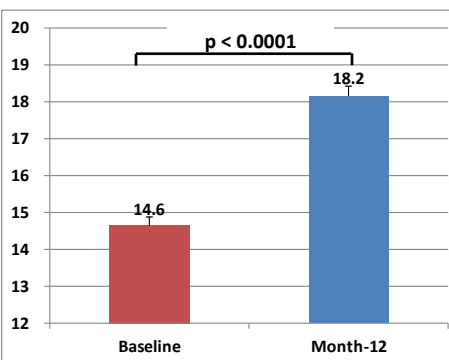
## Secondary Outcome Measures: FOSQ & ESS (n = 123)

### ESS Scale



\*Median and error bar in standard error

### FOSQ Score



Strollo et al, NEJM 2014 370:139-49

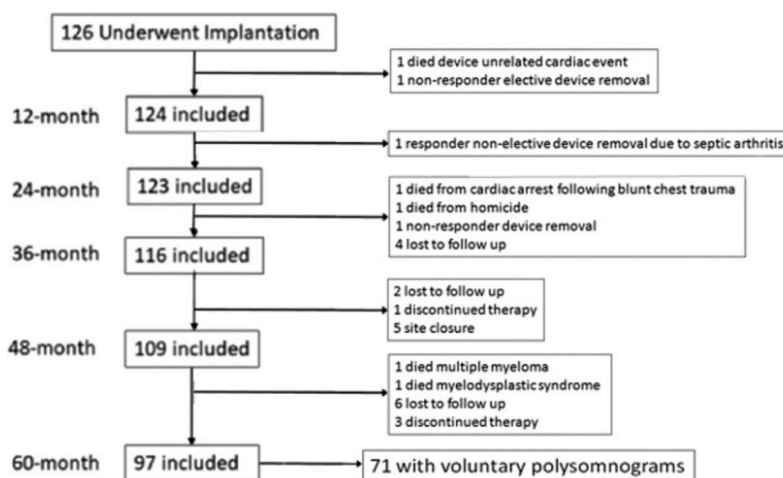
## 5 Year F/U: Summary of Outcome Measures



Outcome	Baseline N Mean ± SD Median	Month 12 N Mean ± SD Median	Month 36 N Mean ± SD Median	Month 60 N Mean ± SD Median
AHI	126 32.0 ± 11.8 29.3	124 15.3 ± 16.1 9.0	98 11.5 ± 14.0 6.0	71 12.4 ± 16.3 6.2
ODI	126 28.9 ± 18.2 25.4	124 14.0 ± 15.6 7.4	98 9.1 ± 11.7 4.8	71 9.9 ± 14.5 4.6
FOSQ	126 14.3 ± 3.2 14.6	123 17.3 ± 2.9 18.2	113 17.4 ± 3.5 18.8	92 18.0 ± 2.2 18.7
ESS	126 11.6 ± 5.0 11	123 7.0 ± 4.3 6	113 7.0 ± 5.0 6	92 6.9 ± 4.7 6

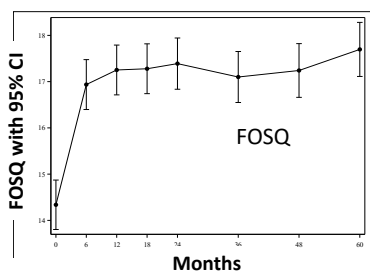
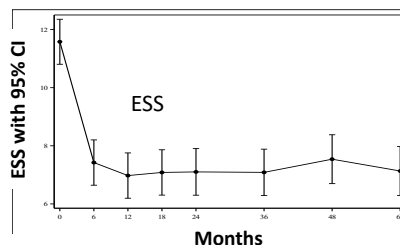
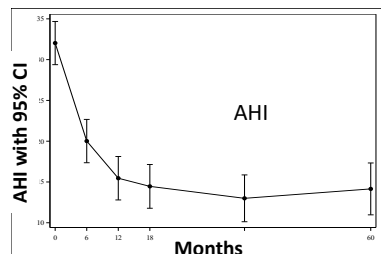
Woodson et al Otolaryngol Head Neck Surg. 2018 159:194-202

## Study Flow



Woodson et al Otolaryngol Head Neck Surg. 2018 159:194-202

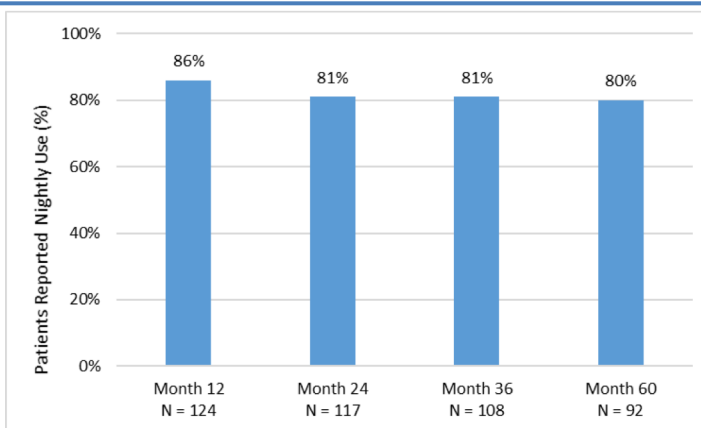
## 5 Year F/U: Sensitivity Analyses



Sustained therapeutic effects on AHI, FOSQ and ESS during the 5-year follow-up using a repeated measure model for estimated mean using all available data

Woodson et al Otolaryngol Head Neck Surg. 2018 159:194-202

## UAS Self-reported Nightly Device Use



Hours of use per night (mean ± SD)	≥ 4 hours of use/night n (%)	≥ 20 hours of use/week n (%)
4.7 ± 1.9	60 (67%)	72 (80%)

Woodson et al Otolaryngol Head Neck Surg. 2018 159:194-202

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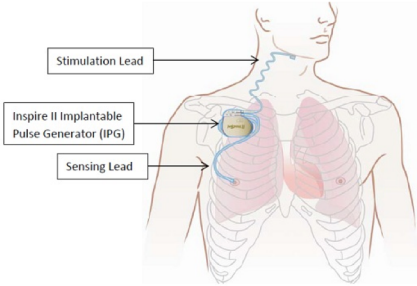
**Medical Devices**

Home > Medical Devices > Products and Medical Procedures > Device Approvals and Clearances > Recently-Approved Devices

**Products and Medical Procedures**

- Device Approvals and Clearances
- Recently-Approved Devices
- 2014 Device Approvals

## Inspire Upper Airway Stimulation - P130008



This is a brief overview of information related to FDA's approval to market this product. See the links below to the Summary of Safety and Effectiveness Data (SSED) and product labeling for more complete information on this product, its indications for use, and the basis for FDA's approval.

**Product Name:** Inspire® Upper Airway Stimulation (UAS)  
**PMA Applicant:** Inspire Medical Systems, Inc.  
**Address:** 9700 63rd Avenue North, Suite 200  
 Maple Grove, MN 55369  
**Approval Date:** April 30, 2014

## Outline

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- Upper Airway Stimulation
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- **Adhere Registry**
- Conclusions



## Adherence and Outcomes of UAS in OSA Registry (ADHERE Registry)

- **Study design:** International, multi-center registry of consecutive patients who have received an implanted UAS system (Inspire II, Inspire Medical Systems, Maple Grove MN).
- **Sample size:** Enrollment goal is a total of 2500 patients
- **Follow-up interval:** Implant through 12-months post-implant

[www.clinicaltrials.gov](http://www.clinicaltrials.gov) NCT02907398

### 14 Centers enrolled 508 patients

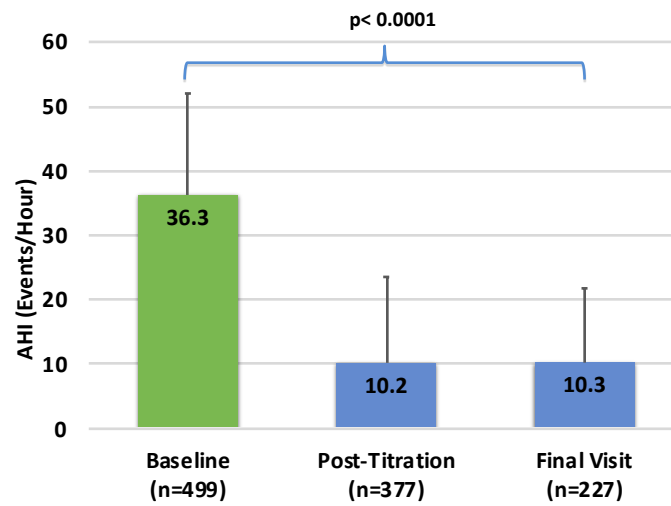
ID	Enrolling Center
1	Munich Technical University
2	University of Lubeck
3	Thomas Jefferson University
4	University-Hospital Mannheim*
5	<b>University of Pittsburgh*</b>
6	University of Pennsylvania
7	University of Alabama
8	Cleveland Clinic
9	Kansas University Medical Center
10	Keck School of Medicine of the University of Southern California
11	University of Minnesota Fairview Hospital
12	MedStar Washington Hospital Center
13	University of Florida Gainesville
14	University Hospital Cleveland*



\* STAR Trial sites

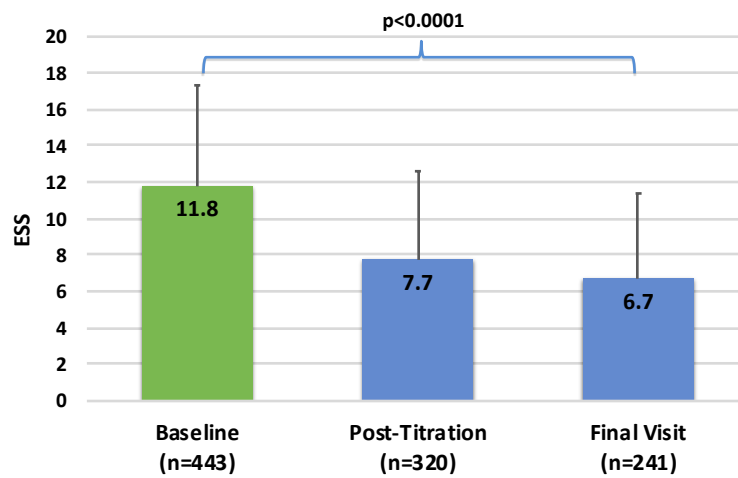
Heiser et al under review

## AHI Reduced at follow up visits



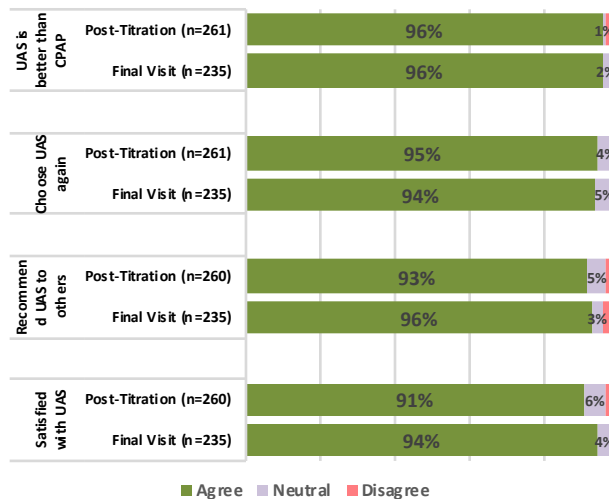
Heiser et al under review

## Daytime Sleepiness Reduced



Heiser et al under review

## Patient Experience with UAS at the Post-titration & Final Visit



Heiser et al under review

## Additional observations

### Therapy use was high at 12 months

Post Titration	6.4 ± 2.0 hours per night	n = 344
Final Visit	5.7 ± 2.2 hours per night	n = 229

### Post Hoc Analysis

- 4% increase in treatment success for each 1-year increase in age
- 9% reduced odds of treatment success for each one unit increase in BMI
- 3-fold higher odds of OSA treatment success in women vs men

Heiser et al under review

## CPAP adherence – SAVE trial



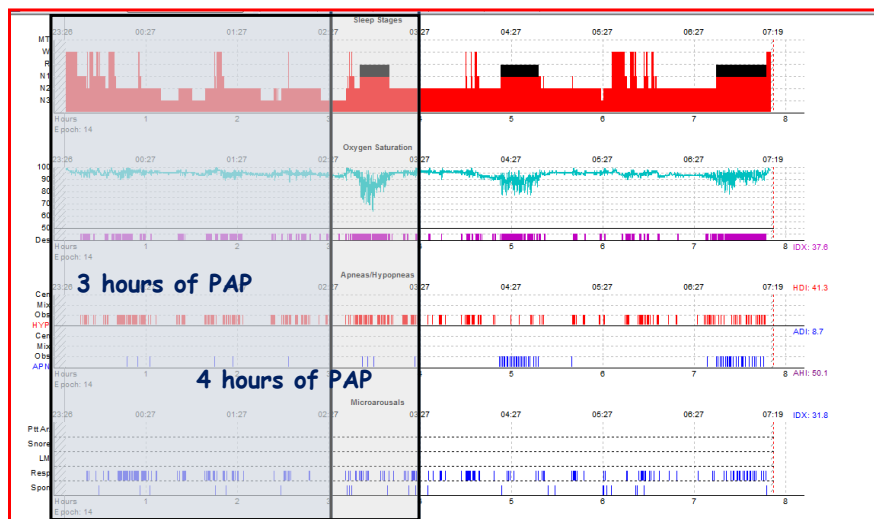
### Pre-randomization sham CPAP run-in

Potential participants were required to have at least 3 hr/day CPAP use during a 1-week run-in period using sham CPAP

Month	1	3	6	12	24	36	48
Number of patients	1284	1277	1260	1219	1035	710	481
Mean hr/day (SD)	4.4 (2.2)	4.1 (2.3)	3.9 (2.4)	3.5 (2.4)	3.4 (2.6)	3.3 (2.7)	3.2 (2.7)
Median (iqr)	4.8 (3.0-6.0)	4.5 (2.5-5.8)	4.2 (2.0-5.6)	3.6 (1.3-5.4)	3.4 (0.7-5.6)	3.5 (0.3-5.5)	3.3 (0.1-5.6)

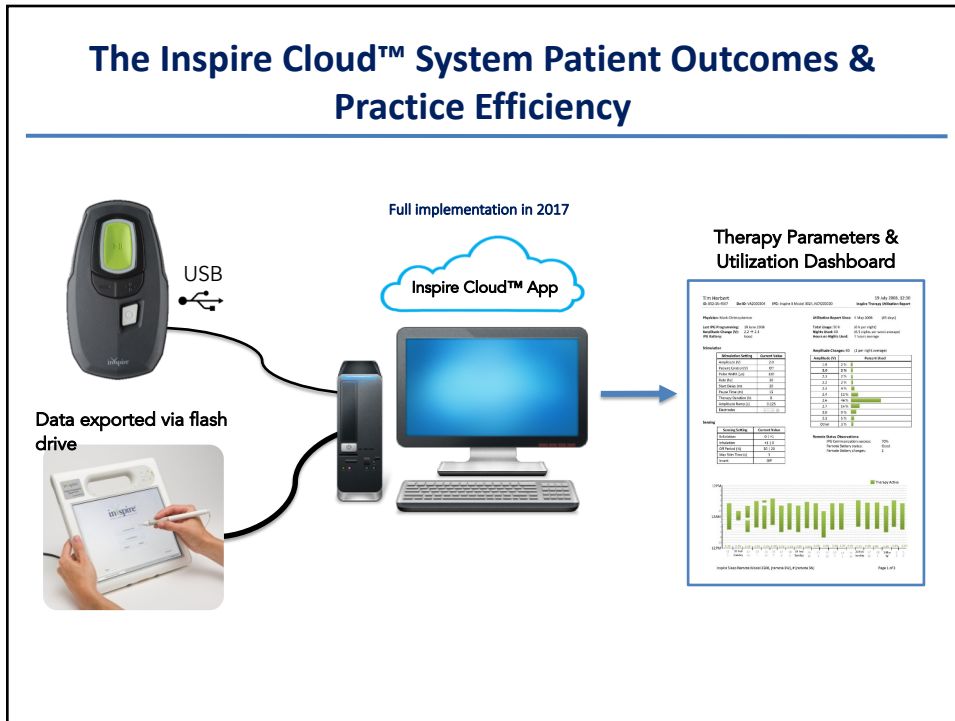
McEvoy, Antic et al N Engl J Med 2016;375(10):919-931

## PAP use for 3-4 Hours may be Inadequate



Babak Mokhlesi, MD, MSc (with permission)

## The Inspire Cloud™ System Patient Outcomes & Practice Efficiency



## Patient Adherence Report

19 July 2008, 12:30  
Inspire Therapy Utilization Report

ID: 652-55-4567 De-ID: VA2006304 IPG: Inspire II Model 3024, NCR200000

Physician: Mark Christopherson  
 Last IPG Programming: 19 June 2008  
 Amplitude Change (V): 2.2 → 2.3  
 IPG Battery: Good

Utilization Report Since: 4 May 2008 [65 days]  
 Total Usage: 50 h (6 h per night)  
 Nights Used: 60 (6.5 nights per week average)  
 Hours on Nights Used: 77-oars average

**Sensing and Stimulation Settings**

Stimulation Setting	Current Value
Amplitude (V)	2.0
Patient Control (V)	OFF
Pulse Width (µs)	320
Rate (Hz)	80
Start Delay (ms)	20
Pause Time (ms)	15
Therapy Duration (h)	8
Amplitude Ramp (s)	0.325
Biphasic	On

Sensing Setting	Current Value
Exhalation	0   13
Inhalation	12   20
Off Period (h)	3
Max Stim Time (s)	3
Invert	Off

**Amplitude Changes: 62 (1 per night average)**

Amplitude (V)	Percent Used
1.8	2%
2.0	2%
2.1	2%
2.2	2%
2.3	6%
2.4	11%
2.6	46%
2.7	14%
3.0	8%
3.3	5%
Other	3%

**Remote Status Observations:**  
 IPG Communications success: 70%  
 Remote Battery status: Good  
 Remote battery changes: 1

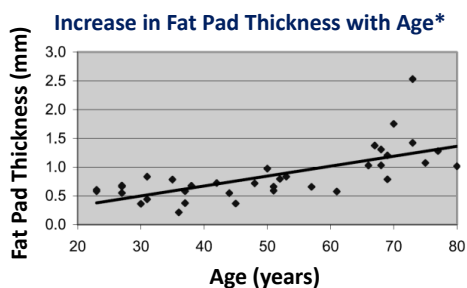
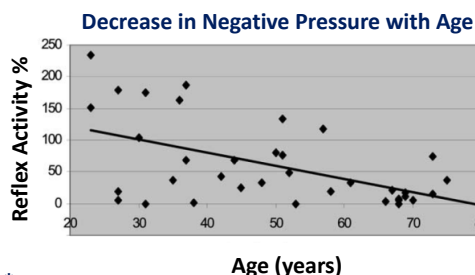
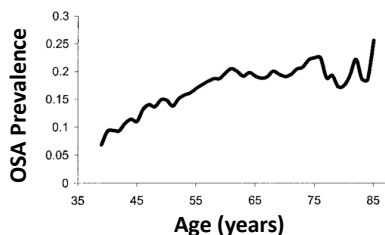
**Night to Night Adherence and Sleep History Analysis (on, pause, off times)**

**Energy Level Histogram**

Full implementation in 2018

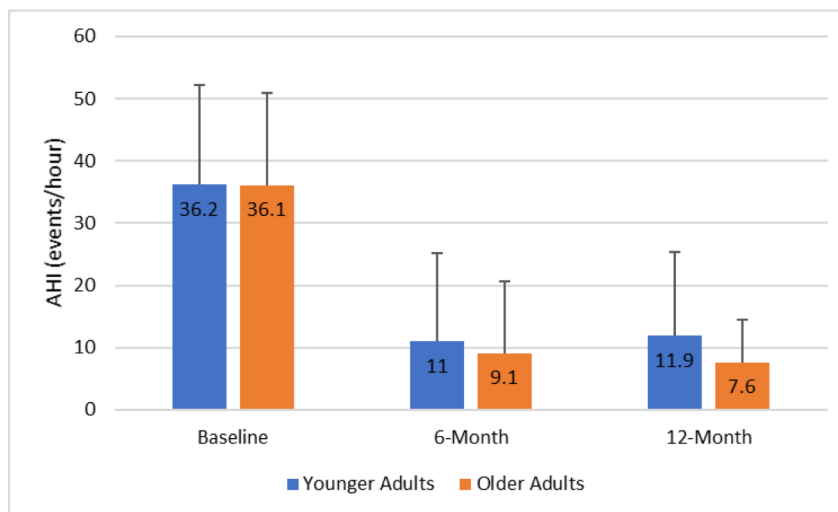
Inspire Sleep Remote Model 2500, (remote SW), # (remote SN)  
Page 2 of 3

## Impact of Age on OSA is not fully explained by BMI



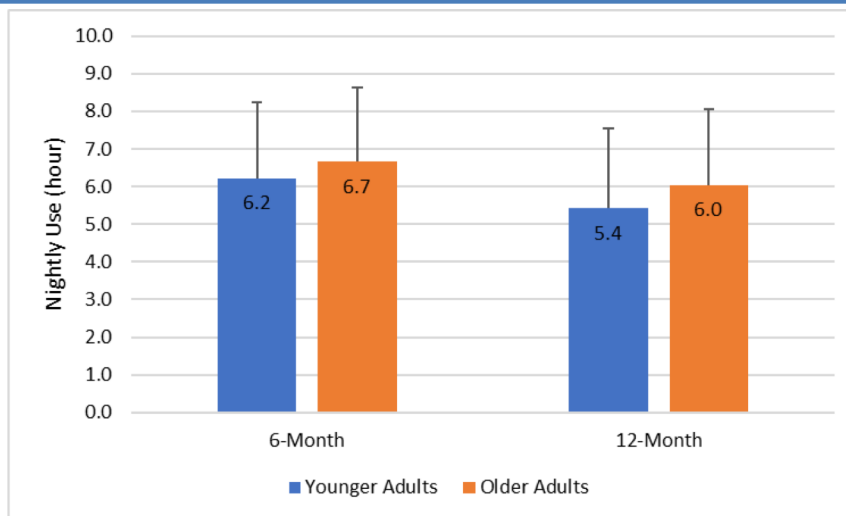
AJRCCM 2002 165:1217-1239  
Am J Med 2006 119:9-14

## Response to Upper Airway Stimulation in Older Adults with Moderate to Severe Obstructive Sleep Apnea



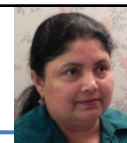
Strollo et al APSS 2018

### Adherence to Upper Airway Stimulation in Older Adults with Moderate to Severe Obstructive Sleep Apnea



Strollo et al APSS 2018

### ASSOCIATION BETWEEN ADHERENCE TO CPAP TREATMENT & COST AMONG MEDICARE ENROLLEES



- We identified 22,361 Medicare enrollees (mean age=67.2 years, sd=12.2) with a diagnosis of sleep apnea during 2007-2008.
- A diagnosis of sleep apnea was associated with higher costs (Odds Ratio (OR) =1.60; 95% Confidence Interval (CI)=1.58, 1.63) compared to those without a sleep apnea diagnosis after controlling for demographic characteristics and comorbidities.
- Almost half (47%) of those with a sleep apnea diagnosis were treated for sleep apnea using CPAP.
- We defined an episode of CPAP as at least one DME claim for CPAP in a 6-month period. Those who had four such episodes in the two year period since diagnosis were 'continuously adherent', and those with three episodes were 'partially adherent'.
- Continuous adherence with CPAP for two years was associated with 4-8% lower cost compared to those sleep apnea patients who did not receive CPAP treatment.

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## Conclusions

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- **Upper Airway Stimulation is an additional tool for the management of properly selected “at risk” patients who do not accept or adhere to positive pressure therapy**
- **The STAR Trial has provided robust evidence that upper airway stimulation is safe and effective in participants with moderate to severe OSA**
- **The treatment effect is maintained beyond the 12 month endpoint**
- **Preliminary data from the ADHERE Registry reveals favorable UAS adherence**





**FROM STEEL TO SCIENCE**

NATURE 2010 463: 258-259



**Thank You**

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