Upper Airway Muscle Stimulation for Obstructive Sleep Apnea

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Staff Physician, John D. Dingell VA Medical Center.
Conflict of Interest Disclosure

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.

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Inspire Medical systems</td>
</tr>
<tr>
<td>Consultant</td>
<td></td>
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<tr>
<td>Speakers’ Bureaus</td>
<td></td>
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<tr>
<td>Financial support</td>
<td></td>
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<td>Other</td>
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</tbody>
</table>

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. Strollo et al, NEJM 2014 370:139-49
Outline

• Background
• Upper Airway Stimulation
• STAR Trial
• Conclusions
Sleep Disordered Breathing and Mortality: Eighteen-Year Follow-up of the Wisconsin Sleep Cohort (n = 1396)

![Graph showing survival rates and baseline AHI categories with mortality hazard ratios](image)

<table>
<thead>
<tr>
<th>Baseline AHI category</th>
<th>All-cause mortality Hazard Ratio (95% CI)</th>
<th>Cardiovascular mortality Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None: 0 - &lt; 5</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Mild: 5 - &lt; 15</td>
<td>1.4 (0.7, 2.6)</td>
<td>1.3 (0.4, 4.1)</td>
</tr>
<tr>
<td>Moderate: 15 - &lt; 30</td>
<td>1.7 (0.7, 4.1)</td>
<td>1.5 (0.3, 7.3)</td>
</tr>
<tr>
<td>Severe: ≥30</td>
<td>3.8 (1.6, 9.0)</td>
<td>5.2 (1.4, 19.2)</td>
</tr>
</tbody>
</table>

*Hazard ratios adjusted for age, age\(^2\), sex, body mass index, and body mass index\(^2\)*
**AIM:** Observational study to compare incidence of fatal and non-fatal cardiovascular events in simple snorers, patients with untreated OSA, patients treated with CPAP, and healthy men recruited from the general population.

**Design:** Prospective observational cohort. 264 healthy men, 377 simple snorers, 403 with untreated mild-moderate OSA (AHI 5-30), 235 with untreated severe OSA (AHI > 30), and 372 with OSA and treated with CPAP

**Conclusion:** In men, severe OSA significantly increases the risk of fatal and non-fatal cardiovascular events. CPAP treatment reduces this risk.

Marin et al Lancet 2005 365: 1046–53
CPAP Therapy and Adherence

CPAP therapy when used consistently results in decreased daytime sleepiness*, improved HRQOL, and decreased vascular risk.

Recent studies of CPAP therapy investigated adherence:

• **APPLES Study** – largest RCT in sleep medicine to date (1,516 subjects enrolled) and CPAP adherence rate was 39% at 6-months use of CPAP therapy (174 of 443)

• **Home PAP Study** – Evaluation of standard OSA care vs. home-base diagnostics and titration. Results of 3-month follow-up: CPAP adherence was 39% (Lab titration); CPAP adherence was 50% (Home titration)

**Conclusion:**

• CPAP is first-line therapy and effective when consistently used by OSA patients.

• Alternative therapy options for moderate or severe OSA patients who are nonadherent to PAP are desirable
CPAP Adherence: CPAP-only vs. CPAP + Motivational Enhancement

Bakker et al CHEST 2016; 150(2):337-345
In established coronary or cerebrovascular disease, CPAP failed to meet the primary composite endpoint.

CPAP did improve patient reported outcomes:
- ESS
- Anxiety / Depression
- Physical / Mental Health
- QOL
- Missed days of work

Cumulative Incidence %

Follow up Months

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>CPAP</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1346</td>
<td>1341</td>
</tr>
<tr>
<td></td>
<td>1222</td>
<td>1211</td>
</tr>
<tr>
<td></td>
<td>1118</td>
<td>1108</td>
</tr>
<tr>
<td></td>
<td>754</td>
<td>727</td>
</tr>
<tr>
<td></td>
<td>482</td>
<td>499</td>
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<tr>
<td></td>
<td>278</td>
<td>290</td>
</tr>
<tr>
<td></td>
<td>146</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td>146</td>
<td>103</td>
</tr>
<tr>
<td>Study</td>
<td>Population</td>
<td>Intervention</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>CANPAP</td>
<td>Systolic HF</td>
<td>CPAP vs UC</td>
</tr>
<tr>
<td>RICCADSA</td>
<td>Revascularized CAD</td>
<td>CPAP vs UC</td>
</tr>
<tr>
<td>SAVE</td>
<td>CAD</td>
<td>CPAP vs UC</td>
</tr>
<tr>
<td>ISAACC</td>
<td>CAD (ACS)</td>
<td>CPAP vs UC</td>
</tr>
<tr>
<td>SERVE-HF</td>
<td>Systolic HF</td>
<td>ASV vs UC</td>
</tr>
<tr>
<td>ADVENT-HF</td>
<td>Systolic HF</td>
<td>ASV vs UC</td>
</tr>
</tbody>
</table>

UC = Usual Care
Association of OSA in REM Sleep With Reduced Glycemic Control in Type 2 DM: Rx Implications

Adjusted for age, sex, race, BMI, years of Type 2 DM, and insulin use

Diabetes Care 2014 37:3555-363
Cumulative min of REM and NREM over 8 h of bedtime

Diabetes Care 2014 37:3555-363
Treatment Guideline

- Evaluate for other disorders
- OSA
  - AHI > 15
  - AHI ≥ 5 + Sx
- Discuss Treatment Options
- CPAP Offered
- Alternative Therapies
  - Behavioral
  - Oral Appliance
  - Surgical*
- Adjunctive
- Patient Education*

Outline

• Background
• **Upper Airway Stimulation**
• STAR Trial
• Conclusions
Pathways that in combination lead to recurrent OSA

- Anatomy (small, collapsible upper airway)
- Loop gain (Unstable ventilatory control)
- Sleep (arousal threshold)
- Low UA Drive and Poor Reflex (inadequate muscle activation)

Recurrent Apnea and Hypopnea

Obstructive Sleep Apnea Hypopnea Syndrome

Neurotherapeutics
Upper Airway Stimulation

Identifying the optimal site for cuff Placement for UAS

Hyoglossus Muscle
Styloglossus Muscle
Genioglossus Muscle
Geniohyoid Muscle

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

Stimulating Pulses

Onset

Offset

Sensor Signal

Expiratory

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

PSG: Effect of Stimulation

EEG
EMG
Nasal Pressure
Thermo
Chest
Abdomen
SpO2

30 seconds

Therapy OFF  Therapy ON
Outline

• Background
• Upper Airway Stimulation
• STAR Trial
• Conclusions
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

- **Co-Primary**
  - Apnea Hypopnea Index
  - Oxygen desaturation index (ODI$_{4\%}$)

- **Secondary**
  - Epworth Sleepiness Scale
  - Functional Outcomes of Sleep Questionnaire
  - SaO$_2$ < 90%

Strollo et al, NEJM 2014 370:139-49
Methods

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

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>• AHI between 20 and 50</td>
<td>• BMI &gt; 32</td>
</tr>
<tr>
<td>• Have not accepted or not tolerated CPAP</td>
<td>• Neuromuscular diseases</td>
</tr>
<tr>
<td>• Central and mixed sleep apnea accounted for &lt; 25% of all AHI events</td>
<td>• Severe Co-Morbid Cardiopulmonary Disease</td>
</tr>
<tr>
<td>• Absence of significant apnea when sleeping in a non-supine position</td>
<td>• Other chronic sleep disorders</td>
</tr>
<tr>
<td>( AHI_{\text{non-supine}} &gt; 10 )</td>
<td>• Complete concentric collapse at the level of soft palate during drug-induced sedation endoscopy (DISE)</td>
</tr>
</tbody>
</table>
Examples collapse at the level of the palate during DISE

Anteroposterior collapse

Concentric collapse

JCSM 2013 9 (5) 433-438
Propofol-induced sleep: Polysomnographic evaluation of patients with obstructive sleep apnea and controls

- 15 non-obese subjects (4 controls/11 OSA patients) were submitted to two diurnal polysomnograms (90-120 minutes of sleep), with and without the use of propofol.
- Propofol did not induce snoring in the control subjects, whereas 100 percent of the OSA patients snored.
- AHI and mean oxygen saturation (SaO2) did not differ significantly between examinations with and without sedation.
- Minimum SaO2 differed significantly with sedation, being lower during propofol sedation.
- Propofol also significantly changed the sleep architecture, with a significant increase in N3 sleep and total abolishment of rapid eye movement sleep during propofol sedation.

<table>
<thead>
<tr>
<th>Examination</th>
<th>No. of apneas</th>
<th>No. of hypopneas</th>
<th>AHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diurnal</td>
<td>10.1</td>
<td>25.6</td>
<td>13.7</td>
</tr>
<tr>
<td>Propofol</td>
<td>14.2</td>
<td>10.5</td>
<td>14.6</td>
</tr>
</tbody>
</table>

AH1, apnea-hypopnea index; ns, not significant. Comparison between examinations performed with Student paired t test.

Rabelo et al Otolaryngology–Head and Neck Surgery 2010 142:218-224
**Enrollment**
N = 929

**Screening**
N = 724

**Implant**
N = 126

- 1 unrelated participant death
- 1 participant with elective device removal

**Enrollment Exclusions (205)**
- Did not meet inclusion/exclusion criteria (108, 13.4%)
- Participant withdrawal of consent (60, 7.5%)
- Study implant limit complete – Participant withdrawn (21, 2.6%)
- Participants lost to follow-up prior to implant (13, 1.6%)
- Other withdrawals prior to implant (3, 0.4%)

**Screen Exclusions (598)**
- AHI < 20 (347, 43.2%)
- AHI > 50 (87, 10.8%)
- Central sleep apnea: (50, 6.2%)
- Positional OSA: (45, 5.6%)
- Tonsil size 3 or 4 (4, 0.5%)
- Other unfavorable anatomy (9, 1.1%)
- Complete concentric palatal collapse (54, 6.7%)
- Others (2, 2.5%)

Strollo et al, NEJM 2014 370:139-49
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± SD or N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>54.5 ± 10.2</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>83%</td>
</tr>
<tr>
<td>Caucasian race, no. (%)</td>
<td>97%</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>28.4 ± 2.6</td>
</tr>
<tr>
<td>Neck size, cm</td>
<td>41.2 ± 3.2</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>128.7 ± 16.1</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>81.5 ± 9.7</td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>38%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9%</td>
</tr>
<tr>
<td>Asthma</td>
<td>5%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2%</td>
</tr>
<tr>
<td>Prior UPPP, no. (%)</td>
<td>18%</td>
</tr>
</tbody>
</table>

Strollo et al, NEJM 2014 370:139-49
Primary Outcome Measures: AHI and ODI (n = 124)

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

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

*Median and error bar in standard error

Strollo et al, NEJM 2014 370:139-49
At 12-months, there were 37 (29% of 126) participants with AHI < 5/hr., 67 participants (53%) with AHI < 10, and 80 participants (63%) with AHI < 15
Secondary Outcome Measures: FOSQ & ESS (n = 123)

ESS Scale

FOSQ Score

*Median and error bar in standard error

Strollo et al, NEJM 2014 370:139-49
# Upper Airway Stimulation Effects on Sleep

<table>
<thead>
<tr>
<th></th>
<th>Baseline N = 126</th>
<th>12 Month N = 124</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep Time, min</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Sleep</td>
<td>364.8 (68.0)</td>
<td>333.7 (69.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>N1 Sleep</td>
<td>42.0 (21.0)</td>
<td>31.1 (15.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>N2 Sleep</td>
<td>234.5 (56.0)</td>
<td>214.3 (60.2)</td>
<td>0.0002</td>
</tr>
<tr>
<td>N3 Sleep</td>
<td>31.0 (27.6)</td>
<td>36.0 (31.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>REM Sleep</td>
<td>57.3 (27.4)</td>
<td>52.2 (33.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Arousal Index</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>28.9 (20.5, 40.8)</td>
<td>14.8 (10.3, 24.8)</td>
<td></td>
</tr>
</tbody>
</table>

Strollo et al, NEJM 2014 370:139-49
## Other Outcome Measures

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>Baseline Mean (SD), N</th>
<th>12 Month Mean (SD), N</th>
<th>Change (BL-12M) Mean (SD), N</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>74.8 (10.7), 126</td>
<td>75.0 (10.4), 124</td>
<td>-0.6 (11.7), 124</td>
<td>0.56</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>128.7 (16.1), 126</td>
<td>126.4 (13.9), 124</td>
<td>2.5 (16.3), 124</td>
<td>0.12</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>81.5 (9.7), 126</td>
<td>79.3 (9.5), 124</td>
<td>2.3 (10.6), 122</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI</td>
<td>28.4 (2.6), 126</td>
<td>28.5 (2.6), 119</td>
<td>-0.03 (1.3), 119</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Strollo et al, NEJM 2014 370:139-49
Randomized Controlled Therapy Withdrawal

Maintenance Group (N=23) Withdrawal Group (N=23)

AHI

Baseline

Month-12

RCT

*mean and error bar in standard error

Strollo et al, NEJM 2014 370:139-49
Relevant Adverse Events

• **Serious: Device related**
  – 1% *Device revision*

• **Non Serious: Procedure related**
  – ~25% *Pain* (minimal, most did not require narcotics - substantially less than UPPP)

• **Non-Serious: Device related**
  – ~33% *Tongue discomfort / abrasion* (time limited)
  – 1% *Mild or Mod Infection* (cellulitis)

* One Death Unrelated to the Trial

Strollo et al, NEJM 2014 370:139-49
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
### Star Trial 18 Month Follow Up: Stimulation Threshold

<table>
<thead>
<tr>
<th></th>
<th>1 Month (N=126)</th>
<th>12 Months (N=123)</th>
<th>18 Months (N=123)</th>
<th>P Value*</th>
<th>P Value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensation Threshold</td>
<td>1.15 ± 0.64</td>
<td>1.13 ± 0.62</td>
<td>1.07 ± 0.55</td>
<td>1.00</td>
<td>0.02</td>
</tr>
<tr>
<td>Functional Threshold</td>
<td>1.79 ± 0.79</td>
<td>1.80 ± 0.80</td>
<td>1.76 ± 0.73</td>
<td>0.51</td>
<td>0.38</td>
</tr>
<tr>
<td>Discomfort Threshold</td>
<td>2.47 ± 0.85</td>
<td>2.85 ± 1.02</td>
<td>2.69 ± 0.96</td>
<td>&lt;0.001</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Stimulation threshold unit in volts.
*1 month vs. 12 months; ** 12 months vs. 18 months

Strollo et al SLEEP 2015 38:1593-8
Star Trial 36 Month Follow Up

- AHI > 50% reduction to < 20
- ESS score < 10
- FOSQ score > 17.9
- Snoring self-report of no or soft snoring
- AHI not measured at 24 and 30 months (dotted line)

Star Trial 48 Month Follow Up

Baseline
- 126 received implant
- 1 death due to unrelated cause; 1 elective explant

12-mo
- 124 completed 12-mo follow-up
- 46 completed RCT withdrawal study

18-mo
- 124 completed 18-mo follow-up
- 1 explant due to septic arthritis

24-mo
- 123 completed 24-mo follow-up
- 2 deaths due to unrelated causes; 1 elective explant; 4 missed the visit

36-mo
- 116 completed 36-mo follow-up
- 98 completed voluntary PSG study
- 25 lost to follow up

48-mo
- 95 completed 48-mo follow-up

# Similarities and differences among XII nerve stimulators

<table>
<thead>
<tr>
<th>Type</th>
<th>Detection/Trigger</th>
<th>Selection</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnex Medical</td>
<td>Impedance sensing from chest electrode, with synchronization</td>
<td>Patient selection by BMI (≤ 35) and AHI (≥ 15)</td>
<td>Phase III trial suspended and company closed 2013</td>
</tr>
<tr>
<td>Inspire Medical Systems</td>
<td>Pressure sensing of effort from costal lead, with synchronization</td>
<td>Patient selection by BMI (≤ 32) and AHI (≥ 20 ≤ 65), DISE (absence of concentric collapse at palate)</td>
<td>FDA approved 2014</td>
</tr>
<tr>
<td>ImThera Medical</td>
<td>None</td>
<td>AHI (≥ 20) and BMI (≤ 35)</td>
<td>In Phase III FDA trial</td>
</tr>
</tbody>
</table>
Results and pooled analysis of mean differences for the apnea-hypopnea index outcome at 3, 6, and 12 months

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Eastwood 2011</td>
<td>19</td>
<td>10.7</td>
<td>21</td>
<td>43.1</td>
</tr>
<tr>
<td>Mwenge 2013</td>
<td>21.7</td>
<td>19.9</td>
<td>13</td>
<td>45.2</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>34</td>
<td></td>
<td>100.0%</td>
<td>-23.94 [-31.45, -16.43]</td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td>Chi² = 0.00, df = 1 (P = 0.94); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect</strong></td>
<td>Z = 6.26 (P &lt; 0.000001)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 months

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference IV, Fixed, 95% CI</th>
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<tr>
<td></td>
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<td>SD</td>
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<td>Mean</td>
</tr>
<tr>
<td>Eastwood 2011</td>
<td>19.5</td>
<td>16.7</td>
<td>21</td>
<td>43.1</td>
</tr>
<tr>
<td>Kezirian 2014</td>
<td>20.8</td>
<td>17.6</td>
<td>31</td>
<td>45.4</td>
</tr>
<tr>
<td>Van de Heyning 2012</td>
<td>10</td>
<td>11</td>
<td>8</td>
<td>38.9</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>60</td>
<td></td>
<td>100.0%</td>
<td>-25.60 [-31.18, -20.01]</td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td>Chi² = 0.60, df = 2 (P = 0.74); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect</strong></td>
<td>Z = 8.98 (P &lt; 0.000001)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

6 months

<table>
<thead>
<tr>
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<th>Control</th>
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<td></td>
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<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Kezirian 2014</td>
<td>25.3</td>
<td>20.6</td>
<td>31</td>
<td>45.4</td>
</tr>
<tr>
<td>Mwenge 2013</td>
<td>21</td>
<td>16.5</td>
<td>13</td>
<td>45.2</td>
</tr>
<tr>
<td>Strollo 2014</td>
<td>15.3</td>
<td>16.1</td>
<td>126</td>
<td>32</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>170</td>
<td></td>
<td>100.0%</td>
<td>-17.51 [-20.69, -14.34]</td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td>Chi² = 1.48, df = 2 (P = 0.46); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect</strong></td>
<td>Z = 10.81 (P &lt; 0.000001)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

12 months

Laryngoscope 2015 125:1254-64
Outline

• Background
• Upper Airway Stimulation
• STAR Trial
• Conclusions
Conclusions

- 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.
#### Future Directions

- Identify OSA Endotypes that benefit from treatment accounting for
  - Age, Disease Burden, Sleepiness & Cardiometabolic risk
- Respond to patient preference and its relationship to longitudinal care
- Understand the UAS responder endotype
  - More precise neural mapping
  - Limits of augmenting neural response
  - Impact of anatomy: $P_{crit}$, Imaging (wake and asleep)
- Value of complementary treatments in incomplete responders
  - Surgery, OAT, Medication?
- Understand alternative stimulation strategies (i.e. paced vs. tonic stimulation)