Patrick J. Strollo, Jr., M.D. is Professor of Medicine and Clinical and Translational Science at the University of Pittsburgh. He is the Director of the UPMC Sleep Medicine Center. He received his undergraduate degree from Washington College and his MD from the Uniformed Services University of the Health Sciences. He is certified by the American Board of Internal Medicine in Internal Medicine, Pulmonary Diseases, and Sleep Medicine.

He has been an active member of the American Thoracic Society and the American Academy of Sleep Medicine for over 25 years. He served as President of the AASM 2010 -2011.

His research has involved team science with an emphasis on translational investigations. His work along with his collaborators has focused on three broad areas of investigation: 1) New strategies / tools for the diagnosis of sleep disordered breathing, 2) Management of sleep disordered breathing with positive pressure therapy and other novel treatments and 3) The impact of sleep disordered breathing on cardiovascular function. Dr. Strollo has over 100 publications that include 60 papers in peer reviewed journals in Sleep and Pulmonary Medicine and 60 book chapters and invited papers.

**OBJECTIVES:**

Participants should be better able to:

1. Review the patho-physiological basis for upper airway stimulation (UAS);
2. Discuss the feasibility trials related to UAS;
3. Understand the surgical selection and technique related to device implantation;
4. Discuss the STAR trial 18 month outcomes data.
Upper Airway Pacing for Obstructive Sleep Apnea

Patrick J Strollo, Jr, MD, FACP, FCCP, FAASM
Professor of Medicine and Clinical and Translational Science
Medical Director, UPMC Sleep Medicine Center

Disclosure: Patrick J Strollo, Jr., MD

Research Support
- Federal
  - R01 HL107370
  - RO1 DK096028-02
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  - PinMed
- Foundation
  - American Sleep Medicine Foundation

Industry advisory:
- ResMed
- Emmi Solutions
- Jazz Pharmaceuticals
Pathogenesis of Obstructive Sleep Apnea

Abnormal anatomy and the lack of neuromuscular compensatory mechanisms are the two major factors responsible for airway narrowing and closure during sleep.
Which of the following treatments for obstructive sleep apnea is associated with improved cardiovascular outcomes?

a. Uvulopalatopharyngoplasty  
b. Upper airway stimulation  
c. Continuous positive airway pressure  
d. Oral appliance therapy
Which of the following treatments for obstructive sleep apnea is associated with improved cardiovascular outcomes?

a. Uvulopalatopharyngoplasty
b. Upper airway stimulation
c. Continuous positive airway pressure
d. Oral appliance therapy

**Long-term cardiovascular outcomes in men with OSA**

**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.

*Lancet 2005 365: 1046–53*
The reported objective adherence to treatment with CPAP (defined as > 4 hrs./night) at 3 months is:

a. 80%
b. 50%
c. 20%
d. 10%
CPAP Therapy and Adherence

PAP 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

OSA Value of Selected Treatment Options

- Darker more valuable.

<table>
<thead>
<tr>
<th></th>
<th>Snoring</th>
<th>Mild Sleep Apnea</th>
<th>Moderate to Severe OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal decongestant</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Positional therapy</td>
<td></td>
<td></td>
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<tr>
<td>Surgery (adults)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Surgery (children)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral appliance</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PAP</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Outline

• Background
• Upper Airway Stimulation
• STAR Trial
• Conclusions

Upper Airway Stimulation

Upper Airway Anatomy & Stimulation Site

Stimulation Site: Medial branch of the hypoglossal nerve, activates only protrusors (genioglossus, geniohyoid), distal to retractors (styloglossus and hyoglossus)

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

Eur Respir J 2014; in press

Inspire UAS effect during DISE
PSG: Effect of Stimulation

**In-lab PSG Titration Algorithm**

- **Arousal Threshold**: ≥ 30 minutes in the patient’s preferred sleep position with minimum occurrence of events, preferably with REM sleep observed.

- **Therapeutic Amplitude Range**: Increase amplitude by 0.1 to 0.2 volts if ≥ 5 obstructive apneas or hypopneas or loud, unambiguous snoring.

- **Amplitude (volts)**: Reduce amplitude by 0.1 to 0.2 volts if stimulation causes persistent arousals or is poorly tolerated.

- **Time (minutes)**: Start: 0.2 V below Functional Threshold.

*Adapted from current practice guidelines established for CPAP titration by the American Academy of Sleep Medicine, ref: Journal of Clinical Sleep Medicine, Vol. 4, No 2, 2008*
Therapy Device Adjustments during PSG

Stimulation strength is adjusted in steps during sleep study until obstructive events are no longer observed.

Clinical Trial Experience

Proof of Principle Trial
- 8 patients
  - 4 Centers
- Completed in 2001
- Demonstrated therapy concept

Feasibility Trial
- 34 patients
  - 8 Centers
- Completed in 2010
- Demonstrated safety and patient selection

References:
2. Journal of Clinical Sleep Medicine 2013 9 (5) 433-438
3. The Laryngoscope 2012 122(7): 1626-33
Which of the following patient characteristics that are associated with a favorable treatment effect with upper airway stimulation for OSA?

a. AHI < 20
b. DISE with concentric collapse at the retropalatal level
c. BMI < 32
d. Excellent adherence to CPAP therapy
Examples collapse at the level of the palate during DISE

Outline

- Background
- Upper Airway Stimulation
- STAR Trial
- Conclusions
Stimulation Therapy for Apnea Reduction (STAR Trial)  
ClinicalTrials.gov NCT01161420

**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

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**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
  - SaO2 < 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 Criteria

- AHI between 20 and 50
- Have failed or have 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 ($AHI_{non-supine} > 10$)
Exclusion Criteria

- 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

Consort Flow Chart

Strollo et al, NEJM 2014 370:139-49
Baseline Characteristics of the Study Population (N = 126)

<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>

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

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AHI Changes in Responders and Non-responders

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
The change in polysomnography findings at 12 months compared to baseline (untreated) are:

a. Decreased Stage 2 Sleep
b. Decreased Arousal index
c. Decreased Stage REM Sleep
d. Decreased Deep (Stage III /IV) Sleep
**Upper Airway Stimulation effect on Sleep**

<table>
<thead>
<tr>
<th>Sleep Time, min</th>
<th>Baseline N = 126</th>
<th>12 Month N = 124</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean(SD) % of Total Sleep</td>
<td>Mean(SD) % of Total Sleep</td>
<td></td>
</tr>
<tr>
<td><strong>Total Sleep</strong></td>
<td>364.8 (68.0) 11.5</td>
<td>333.7 (69.3) 9.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>N1 Sleep</strong></td>
<td>42.0 (21.0)</td>
<td>31.1 (15.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>N2 Sleep</strong></td>
<td>234.5 (56.0) 64.3</td>
<td>214.3 (60.2) 64.2</td>
<td>0.0002</td>
</tr>
<tr>
<td><strong>N3 Sleep</strong></td>
<td>31.0 (27.6) 8.5</td>
<td>36.0 (31.5) 10.8</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>REM Sleep</strong></td>
<td>57.3 (27.4) 15.7</td>
<td>52.2 (33.8) 15.6</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Arousal Index</strong></td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.9 (20.5, 40.8)</td>
<td>14.8 (10.3, 24.8)</td>
<td>&lt;0.0001</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><strong>Heart Rate</strong></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><strong>Systolic Blood Pressure</strong></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><strong>Diastolic Blood Pressure</strong></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><strong>BMI</strong></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

![Graph showing AHI values for Maintenance Group (N=23) and Withdrawal Group (N=23)]

- **Baseline:**
  - Maintenance Group: 31.3
  - Withdrawal Group: 30.1

- **Month-12:**
  - Maintenance Group: 7.2
  - Withdrawal Group: 7.6

- **RCT:**
  - Maintenance Group: 8.9
  - Withdrawal Group: 25.8

*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
Results and pooled analysis of mean differences for the apnea-hypopnea index outcome at 3, 6, and 12 months

Change in polysomnographic measures of sleep disordered breathing and patient reported measures from baseline to 18 months
## 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

Under review

## 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

- Refine patient selection criteria using genioglossal stimulation (fine wire vs. transcutaneous approaches)
  - DISE
  - Awake Imaging with post hoc Computational Fluid Dynamics\(^1\)
- Explore complementary treatment in incomplete responders
- Understand alternative stimulation strategies (i.e. paced vs. tonic stimulation)

\(^1\)Sleep Med Rev 2008 12: 437-47
Acknowledgements

<table>
<thead>
<tr>
<th>STAR TRIAL CENTERS</th>
<th>STAR TRIAL INVESTIGATORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>St Lucas Andreas - Netherlands</td>
<td>DeVries</td>
</tr>
<tr>
<td>North Memorial - Minneapolis</td>
<td>Cornelius, Froymovich</td>
</tr>
<tr>
<td>UPMC</td>
<td>Strollo, Soose</td>
</tr>
<tr>
<td>University of South Florida</td>
<td>Padhya, Anderson</td>
</tr>
<tr>
<td>St Petersburg Sleep Disorders Center</td>
<td>Feldman</td>
</tr>
<tr>
<td>St Cloud ENT - Minnesota</td>
<td>Hanson, Payne</td>
</tr>
<tr>
<td>University of Mannheim - Germany</td>
<td>Maurer</td>
</tr>
<tr>
<td>University of Cincinnati</td>
<td>Steward, Surdulescu</td>
</tr>
<tr>
<td>Case Western</td>
<td>Strohl, Baskin</td>
</tr>
<tr>
<td>Medical University of South Carolina</td>
<td>Gillespie</td>
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<tr>
<td>Medical College of Wisconsin</td>
<td>Woodson</td>
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<tr>
<td>UZA - Belgium</td>
<td>VanderVeken, Verbracken, Van de Heyning</td>
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<tr>
<td>Borgess Kalamazoo</td>
<td>Goetting, Széles</td>
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<td>Intersom Köln - Germany</td>
<td>Knaack, Mockel</td>
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<td>California Sleep - Palo Alto</td>
<td>Roberson</td>
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<td>Swedish - Seattle</td>
<td>Stolz, Yang</td>
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<td>CHU de Bordeaux</td>
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<td>Foch Paris</td>
<td>Chabolle, Blumen, Hauser-Hauw</td>
</tr>
<tr>
<td>Bethanien Solingen - Germany</td>
<td>Randerath, Hohenhorst</td>
</tr>
</tbody>
</table>

FROM STEEL TO SCIENCE

Thank You
“I won’t lie to you. There’s some very risky paperwork involved with this procedure.”

WSJ 7/15/09

What is a QALY?

- A quality-adjusted life-year (QALY) takes into account both the quantity and quality of life generated by healthcare interventions. It is the arithmetic product of life expectancy and measure of the quality of the remaining life-years.
- A QALY places a weight on time in different health states.
- A year of perfect health is worth 1 and a year of less than perfect health is worth less than 1.
- Death is considered to be equivalent to 0; however, some health states may be considered worse than death and have negative scores.
## Health outcomes and incremental cost-effectiveness

<table>
<thead>
<tr>
<th>Lifetime</th>
<th>Risk of MI</th>
<th>Risk of Stroke</th>
<th>Expected number of MVC</th>
<th>Cost ($), discounted</th>
<th>Effectiveness (QALY), discounted</th>
<th>ICER ($/QALY), discounted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Treatment</td>
<td>0.481</td>
<td>0.249</td>
<td>1.030</td>
<td>243,543</td>
<td>9.54</td>
<td></td>
</tr>
<tr>
<td>UAS Treatment</td>
<td>0.389</td>
<td>0.240</td>
<td>0.367</td>
<td>286,497</td>
<td>10.63</td>
<td>39,471</td>
</tr>
<tr>
<td>Absolute Difference</td>
<td>0.092</td>
<td>0.009</td>
<td>0.663</td>
<td>42,953</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>Relative Risk</td>
<td>0.81</td>
<td>0.96</td>
<td>0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10-years</th>
<th>Risk of MI</th>
<th>Risk of Stroke</th>
<th>Expected number of MVC</th>
<th>Cost ($), discounted</th>
<th>Effectiveness (QALY), discounted</th>
<th>ICER ($/QALY), discounted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Treatment</td>
<td>0.136</td>
<td>0.067</td>
<td>0.473</td>
<td>90,487</td>
<td>5.44</td>
<td></td>
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<tr>
<td>UAS Treatment</td>
<td>0.086</td>
<td>0.050</td>
<td>0.160</td>
<td>115,218</td>
<td>5.87</td>
<td>57,773</td>
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<tr>
<td>Absolute Difference</td>
<td>0.050</td>
<td>0.017</td>
<td>0.313</td>
<td>24,731</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Relative Risk</td>
<td>0.63</td>
<td>0.75</td>
<td>0.34</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pietzsch et al SLEEP (in press)

## Cost-Effectiveness and Use of Selected Interventions in the Medicare Population

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost-Effectiveness (Cost/QALY)</th>
<th>Implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza vaccine</td>
<td>Cost saving</td>
<td>Cost saving^{24,25} 40–70%^{26-28}</td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>Cost saving</td>
<td>Cost saving^{29} 55–65%^{30}</td>
</tr>
<tr>
<td>Beta-blockers after myocardial infarction</td>
<td>Cost effective</td>
<td>$&lt;10,000^{31} 85–95%^{32}</td>
</tr>
<tr>
<td>Mammographic screening</td>
<td></td>
<td>$10,000–$25,000^{31} 50–70%^{26,28,32,33}</td>
</tr>
<tr>
<td>Colon-cancer screening</td>
<td>Cost saving</td>
<td>$10,000–$25,000^{34,35} 20–40%^{28,32,33}</td>
</tr>
<tr>
<td>Osteoporosis screening</td>
<td>Cost effective</td>
<td>$10,000–$25,000^{36} 35%^{34,35}</td>
</tr>
<tr>
<td>Management of antidepressant medication</td>
<td>Cost saving</td>
<td>Cost saving up to $30,000^{31} 40–55%^{33}</td>
</tr>
<tr>
<td>Hypertension medication (DBP &gt;105 mm Hg)</td>
<td>Cost effective</td>
<td>$10,000–$60,000^{31} 35%^{35}</td>
</tr>
<tr>
<td>Cholesterol management, as secondary prevention</td>
<td>Cost saving</td>
<td>$10,000–$50,000^{36,37} 30%^{38}</td>
</tr>
<tr>
<td>Implantable cardioverter-defibrillator</td>
<td></td>
<td>$30,000–$85,000^{39-41} 100,000 cases per year^{10,40}</td>
</tr>
<tr>
<td>Dialysis in end-stage renal disease</td>
<td>Dominated</td>
<td>$50,000–$100,000^{42} 90%^{43}</td>
</tr>
<tr>
<td>Lung-volume-reduction surgery</td>
<td></td>
<td>$100,000–$300,000^{44} 10,000–20,000 cases per year^{10}</td>
</tr>
<tr>
<td>Left ventricular assist devices</td>
<td>Dominated</td>
<td>$500,000–$1.4 million^{45,46} 5000–100,000 cases per year^{10}</td>
</tr>
<tr>
<td>Positron-emission tomography in Alzheimer’s disease</td>
<td>Cost effective</td>
<td>Dominated^{42} 50,000 cases per year^{47,48}</td>
</tr>
</tbody>
</table>

NEJM 2005 353:1516-22
Change in polysomnographic measures of sleep disordered breathing and patient reported measures from baseline to 18 months

![Graph A: Median AHI](image)

![Graph B: Median ODI](image)

![Graph C: Median FOSQ Score](image)

![Graph D: Median ESS Score](image)

Under review