Obstructive Sleep Apnea: Test and you will diagnose—But what does that mean? A PCP’s attempt to understand

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General Internal Medicine Grand Rounds
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Disclosures

• No financial disclosures
• I’m not trained in pulmonary or sleep medicine.
• My “hypothesis” when I started this was that we are over-diagnosing OSA...
Case Presentation

• HPI: 36 y/o male with c/o fatigue. No problems with falling asleep during the day (Epworth Score = 1). His wife has reported that he also snores and occasionally stops breathing at night.

• PMH: HTN, GERD

• Meds: Amlodipine, Losartan, Clonidine, Trazodone

• SH: Works full time as a floor manager in retail sales; 3 children; recently separated from his wife but now back together.

• PE: 97.8, 132/90, 85, BMI 31

• Labs: Testosterone 261 (low), LH and FSH normal. Other labs WNL.
Case Presentation

• Sleep Study
  – Apnea-Hypopnea Index = 31
  – CPAP titration done with a recommendation of 13 cm H20.

• Follow up
  – Tries CPAP for a time but does not like it and after a short time stops using.
Question 1: How do we define OSA?

- **Apnea-Hypopnea Index:** Number of apnea and hypopneas expressed as events per hour.
  - $> 5$ per hour is considered diagnostic for OSA with symptoms.
  - In the absence of symptoms $> 15$ per hour is considered diagnostic.
- **Mild OSA:** 5 – 15
- **Moderate OSA:** 16 – 30
- **Severe OSA:** $> 30$

- *All definitions are based on Expert Consensus.*

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Question 1: How do we define OSA?

- Apnea (Obstructive): Suspension of breathing
Question 1: How do we define OSA?

- Apnea (Central): Suspension of breathing
Question 1: How do we define OSA?

• Apnea (Mixed): Suspension of breathing

The apnea initially appears as a central apnea (without respiratory effort as evidenced by the constant esophageal pressure [Pes]). This is followed by a period of obstructive apnea (with respiratory effort as evidenced by changes in esophageal pressure).
Question 2: How do we do a sleep study?

<table>
<thead>
<tr>
<th>Parameters Measured:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Airflow: Thermistor/Nasal pressure X</td>
</tr>
<tr>
<td>2. Respiratory Effort: Esophageal pressure Piezo X</td>
</tr>
<tr>
<td>3. EKG X 4. EEG X 5. EOG X 6. EMG: Chin X Leg X</td>
</tr>
<tr>
<td>7. O2 Saturation: Finger X Ear X</td>
</tr>
</tbody>
</table>

1. **Airflow:** Generally measured through nasal pressure monitor

2. **Respiratory effort:** “Piezoelectric sensor” that detects changes in pressure, force in abdomen and chest.

3. **EKG** - Electrocardiogram
4. **EEG** – Electroencephalogram
5. **EOG** – Electrococulogram
6. **EMG** – Electromyogram
7. **O2 Saturation**

[Video Link](http://www.youtube.com/watch?v=q4FObhU06-U)

Question 2: How do we do a sleep study?

- Sleep lab versus in portable (home) sleep studies:
  - Respiratory disturbance index (RDI) 10% lower in portable studies (p < 0.05).
  - Mean low O2 saturation no different.
  - Sleep time 13% greater in portable studies (p < 0.05).
  - Poor recordings more common in portable than lab studies 14.6% versus 6.2% (p < 0.0001).
  - Cost of portable studies 35% to 88% lower.

Question 3: How often are our tests positive?

• Chart review
  – Four clinic based providers (myself and three others)
  – Patients seen between 07/01/13 to 10/31/13 with a sleep study done for diagnostic purposes.
  – Definitions
    • Apnea-Hypopnea Index $\geq 5 =$ Positive Sleep Study.
  – Exclusions:
    • Studies for CPAP titration
    • Use of oxygen at the time of study
Question 3:
How often are our tests positive?

- Polysomnography studies positive = 70/89 (78.7%)

<table>
<thead>
<tr>
<th>Provider</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Studies / All Studies (%)</td>
<td>34/42 (81.0%)</td>
<td>5/7 (71.4%)</td>
<td>14/19 (73.7%)</td>
<td>17/21 (81.0%)</td>
</tr>
</tbody>
</table>

- P-value = NS for comparison
Question 4:
Is this consistent with the general population?

- **Wisconsin Sleep Cohort Study.**
  - 6,947 survey sent to Wisconsin state employees starting in 1988
  - 5,901 completed (73%)
  - 2,884 randomly invited to participate in Study
  - *Excluded if pregnant, recent airway cancer, airway surgery or cardiopulmonary disease.*
  - 1,520 participants with $\geq$ 1 adequate sleep study.

- Young et al. The Occurrence of Sleep-Disordered Breathing Among Middle-Aged Adults. NEJM 1993;328:1230-1235.
Question 4:
Is this consistent with the general population?

- Prevalence of OSA in Wisconsin Sleep Cohort Study.

<table>
<thead>
<tr>
<th>Years of observation</th>
<th>Men (Age 30 – 70) AHI &gt; 5</th>
<th>Women (Age 30 – 70) AHI &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007 – 2010</td>
<td>33.9</td>
<td>17.4</td>
</tr>
</tbody>
</table>

- Young et al. The Occurrence of Sleep-Disordered Breathing Among Middle-Aged Adults. NEJM 1993;328:1230-1235.
Question 4: Is this consistent with the general population?

• Prevalence increases with age and BMI.

<table>
<thead>
<tr>
<th>Age 30 – 49</th>
<th>Men AHI &gt; 5</th>
<th>Women AHI &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 25</td>
<td>7.0</td>
<td>1.4</td>
</tr>
<tr>
<td>BMI 25 – 29.9</td>
<td>18.3</td>
<td>4.2</td>
</tr>
<tr>
<td>BMI 30 – 39.9</td>
<td>44.6</td>
<td>13.5</td>
</tr>
<tr>
<td>BMI ≥ 40</td>
<td>79.5</td>
<td>43.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age 50 – 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 25</td>
</tr>
<tr>
<td>BMI 25 – 29.9</td>
</tr>
<tr>
<td>BMI 30 – 39.9</td>
</tr>
<tr>
<td>BMI ≥ 40</td>
</tr>
</tbody>
</table>

Question 5: What does this imply at a US population level?

- US Population 2010 = 308,745,308
- % Population over age 18 = 76.5%
- % Female = 50.8%
- ≈ 60,270,000 adults in the US with AHI ≥ 5 in 2010.

- Calculation: $(308,745,308)(0.765)(0.508)(0.174) + (308,745,308)(0.765)(0.492)(0.339) = 60,271,005$

http://quickfacts.census.gov/qfd/states/00000.html

- Young et al. The Occurrence of Sleep-Disordered Breathing Among Middle-Aged Adults. NEJM 1993;328:1230-1235.
Question 6:
What is the cost of this?

• OSA diagnosis (Sleep study) = $  810.96
• CPAP titration = $  891.14
• Annual cost of CPAP rental = $ 1,341.12
• Total (assume no additional testing and used for 10 years...) = $ 15,113.30

Question 7:
Aside from Age and BMI can we predict who will test positive?

• Epworth Sleepiness Scale.
Question 7:
Aside from Age and BMI can we predict who will test positive?

- Epworth Sleepiness Scale. Epworth Scores by OSA Group (N)

<table>
<thead>
<tr>
<th>Group (N)</th>
<th>Normal</th>
<th>Mild OSA</th>
<th>Mod OSA</th>
<th>Severe OSA</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep 1991 (85)</td>
<td>2 – 10</td>
<td>4 – 16</td>
<td>5 – 20</td>
<td>8 – 23</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Chest 1993 (273)</td>
<td>0 – 15</td>
<td>2 – 22</td>
<td>5 – 22</td>
<td>10 – 23</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>UCH 2013 (38)</td>
<td>3 – 19</td>
<td>0 – 17</td>
<td>6 – 24</td>
<td>1 – 20</td>
<td>NS</td>
</tr>
</tbody>
</table>

Johns MW. Daytime Sleepiness, Snoring, and Obstructive Sleep Apnea. The Epworth Sleepiness Scale. Chest 1993;103:30-36.
Question 7: Aside from age and BMI can we predict who will test positive?

- Percentage of patients with positive sleep studies AND positive ESS

<table>
<thead>
<tr>
<th>Age</th>
<th>Men AHI &gt; 5 &amp; ESS &gt; 10 / All AHI &gt; 5</th>
<th>Women AHI &gt; 5 &amp; ESS &gt; 10 / All AHI &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI &lt; 25</td>
<td>BMI &lt; 25</td>
</tr>
<tr>
<td></td>
<td>38.5%</td>
<td>34.0%</td>
</tr>
<tr>
<td></td>
<td>BMI 25 – 29.9</td>
<td>BMI 25 – 29.9</td>
</tr>
<tr>
<td></td>
<td>37.2%</td>
<td>30.0%</td>
</tr>
<tr>
<td></td>
<td>BMI 30 – 39.9</td>
<td>BMI 30 – 39.9</td>
</tr>
<tr>
<td></td>
<td>42.4%</td>
<td>28.9%</td>
</tr>
<tr>
<td></td>
<td>BMI ≥ 40</td>
<td>BMI ≥ 40</td>
</tr>
<tr>
<td></td>
<td>66.5%</td>
<td>38.1%</td>
</tr>
<tr>
<td>Age 50 - 70</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI &lt; 25</td>
<td>BMI &lt; 25</td>
</tr>
<tr>
<td></td>
<td>40.7%</td>
<td>30.1%</td>
</tr>
<tr>
<td></td>
<td>BMI 25 – 29.9</td>
<td>BMI 25 – 29.9</td>
</tr>
<tr>
<td></td>
<td>37.7%</td>
<td>26.2%</td>
</tr>
<tr>
<td></td>
<td>BMI 30 – 39.9</td>
<td>BMI 30 – 39.9</td>
</tr>
<tr>
<td></td>
<td>40.6%</td>
<td>25.5%</td>
</tr>
<tr>
<td></td>
<td>BMI ≥ 40</td>
<td>BMI ≥ 40</td>
</tr>
<tr>
<td></td>
<td>51.9%</td>
<td>30.8%</td>
</tr>
</tbody>
</table>

A pause to gather my thoughts...

• Obstructive sleep apnea is a “Continuous variable disease.”

• Where on the spectrum of human sleep it becomes a disease has been defined as a AHI of ≥ 5.

• This definition includes about 25% of adults in the U.S.

• Who benefits?
Question 8:
What are the data for benefit of treating OSA?

Continuous Positive Airway Pressure (CPAP)
• Apnea-Hypopnea Index / Arousal Index
• Epworth Sleepiness Scale
• Hypertension
• Quality of Life
• Motor Vehicle Accidents
• Mortality (Cardiovascular)

Other Treatment Options
• CPAP versus Oxygen
• Exercise and Weight Loss
Question 8.1: What are the limitations of RCTs?

Randomized Control Trials

- Duration of follow-up
  - Most 12 weeks or less. Two years is the longest.
  - Surrogate end-points.
- Inclusion criteria
  - Mean AHI 10 - 60
- Controlled versus placebo controlled
  - Many studies did not have a placebo arm
- Difficulty of creating a true CPAP placebo
  - 55% of CPAP versus 33% of placebo patients believed they were on “Active Tx” (p < 0.0001)

Schwartz SW. CPAP or Placebo-Effect 2012;35:1593-1602.
Question 8.2:
What are the data for benefit of treating OSA with CPAP?

- **Apnea-Hypopnea Index**

Question 8.3:
What are the data for benefit of treating OSA with CPAP?

- **Arousal Index**

  ![Table of data](image)

Question 9.4: What are the data for benefit of treating OSA with CPAP?

- **Epworth Sleepiness Scale**

<table>
<thead>
<tr>
<th>Study</th>
<th>CPAP N</th>
<th>CPAP Mean(SD)</th>
<th>Control N</th>
<th>Control Mean(SD)</th>
<th>Weighted Mean Diff (Fixed)</th>
<th>Weight (%)</th>
<th>Weighted Mean Diff (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballester 1999</td>
<td>68</td>
<td>5.60 (4.12)</td>
<td>37</td>
<td>10.60 (6.08)</td>
<td>11.5</td>
<td>11.5</td>
<td>-5.00 [-7.19, -2.81]</td>
</tr>
<tr>
<td>Barbé 2001</td>
<td>29</td>
<td>8.00 (3.23)</td>
<td>25</td>
<td>8.00 (5.00)</td>
<td>10.5</td>
<td>10.5</td>
<td>0.00 [-2.29, 2.29]</td>
</tr>
<tr>
<td>Becker 2003</td>
<td>16</td>
<td>5.10 (3.80)</td>
<td>16</td>
<td>8.90 (5.00)</td>
<td>5.8</td>
<td>5.8</td>
<td>-3.80 [-6.88, -0.72]</td>
</tr>
<tr>
<td>Chakravorty 2002</td>
<td>32</td>
<td>8.00 (6.40)</td>
<td>21</td>
<td>11.00 (5.00)</td>
<td>5.8</td>
<td>5.8</td>
<td>-3.00 [-6.08, 0.08]</td>
</tr>
<tr>
<td>Henke 2001</td>
<td>27</td>
<td>11.00 (5.29)</td>
<td>18</td>
<td>15.00 (7.75)</td>
<td>3.3</td>
<td>3.3</td>
<td>-4.00 [-8.10, 0.10]</td>
</tr>
<tr>
<td>Jenkins 1999</td>
<td>54</td>
<td>7.50 (4.50)</td>
<td>53</td>
<td>12.30 (4.80)</td>
<td>17.7</td>
<td>17.7</td>
<td>-4.80 [-6.56, -3.04]</td>
</tr>
<tr>
<td>Mansfield 2004</td>
<td>21</td>
<td>6.90 (4.58)</td>
<td>19</td>
<td>9.90 (4.36)</td>
<td>7.2</td>
<td>7.2</td>
<td>-3.00 [-5.77, -0.23]</td>
</tr>
<tr>
<td>Monasterio 2001</td>
<td>66</td>
<td>9.60 (5.50)</td>
<td>59</td>
<td>11.80 (5.20)</td>
<td>15.6</td>
<td>15.6</td>
<td>-2.20 [-4.08, -0.32]</td>
</tr>
<tr>
<td>Montserrat 2001</td>
<td>24</td>
<td>6.65 (3.33)</td>
<td>23</td>
<td>14.59 (5.18)</td>
<td>8.8</td>
<td>8.8</td>
<td>-7.94 [-10.44, -5.44]</td>
</tr>
<tr>
<td>Pepperell 2002</td>
<td>53</td>
<td>6.80 (4.80)</td>
<td>51</td>
<td>11.30 (5.50)</td>
<td>13.9</td>
<td>13.9</td>
<td>-4.50 [-6.49, -2.51]</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

Test for heterogeneity chi-square=27.38 df=9 p=0.001 I²=67.1%
Test for overall effect z=10.12 p<0.00001

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Question 8.4:
What are the data for benefit of treating OSA with CPAP?

- **Epworth Sleepiness Scale**

- 29% of benefit is due to expectation of benefit...

Question 8.5:
What are the data for benefit of treating OSA with CPAP?

- Hypertension
  - SBP 2.6 and DBP 2.0 mmHg lower with CPAP than control.
Question 8.6:
What are the data for benefit of treating OSA with CPAP?

• Quality of Life

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>No. of studies</th>
<th>WMD</th>
<th>95% CI</th>
<th>HG $\chi^2$</th>
<th>HG p value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOSQ (absolute scores)</td>
<td>4</td>
<td>0.011</td>
<td>-0.040, 0.063</td>
<td>1.31</td>
<td>0.727</td>
<td>0.661</td>
</tr>
<tr>
<td>FOSQ (total score)</td>
<td>3</td>
<td>1.605</td>
<td>-2.421, 5.630</td>
<td>4.01</td>
<td>0.135</td>
<td>0.435</td>
</tr>
<tr>
<td>NHP</td>
<td>5</td>
<td>-1.657</td>
<td>-3.005, -0.308</td>
<td>2.11</td>
<td>0.716</td>
<td>0.016</td>
</tr>
<tr>
<td>SF-36</td>
<td>1</td>
<td>2.700</td>
<td>-0.913, 6.313</td>
<td>–</td>
<td>–</td>
<td>0.143</td>
</tr>
<tr>
<td>EuroQOL</td>
<td>1</td>
<td>2.000</td>
<td>-8.130, 12.130</td>
<td>–</td>
<td>–</td>
<td>0.699</td>
</tr>
<tr>
<td>SAQLI</td>
<td>1</td>
<td>0.900</td>
<td>0.625, 1.175</td>
<td>–</td>
<td>–</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Jing J, Huang T, Cui W, Shen H. Effect on QOL of CPAP in Patients with OSAS. Lung 2008;186:131-144.
Question 8.7: What are the data for benefit of treating OSA with CPAP?

- **Motor Vehicle Accidents**

  Comparison of MVA before and after CPAP. High rate of MVA before CPAP

  Mean AHI 37.9 – 60

  NNT = 5

Question 8.7: What are the data for benefit of treating OSA with CPAP?

- **Motor Vehicle Accidents**
  - Regression to the mean?
  - Changes in driving behavior after accidents?
    - OSA patients with baseline accident rates > controls; with CPAP OSA patients declined to that of the control group.
    - OSA patients starting with baseline accident rates = controls; with CPAP OSA patients declined at the same rate as controls.

George CFP. Reduction in MVA collisions following treatment of OSA with nCPAP. Thorax 2001;56:508-512.
Question 8.7: What are the data for benefit of treating OSA with CPAP?

- **Motor Vehicle Accidents**

  ![Publication Bias?](image)

Question 8.8: What are the data for benefit of treating OSA with CPAP?

- **Effect of CPAP on OSA and Cardiovascular Mortality**

*Figure 4*

HR and 95% CI from the included studies of continuous positive airway pressure treatment with cardiovascular mortality comparing OSA to the control.

Ge, et al. Is OSA Associated with Cardiovascular and All Cause Mortality? PLOS One 2013;8(7):e69432
Question 8.8: What are the data for benefit of treating OSA with CPAP?

• Is it the CPAP or the compliant patient?

Additional Reading:
Question 9: My patient hates CPAP... Is Oxygen alone of any benefit?

- Oxygen versus CPAP

**Figure 2**

Effect of CPAP versus oxygen on apnea hypopnea index (AHI)

**Figure 3**

Effect of CPAP versus oxygen on nocturnal mean oxyhemoglobin saturation (SpO₂)

Question 9: What impact does weight loss have on OSA?

- Weight loss and changes in AHI Index

“Although moderate-quality evidence showed that CPAP improves sleep measures compared with control or sham devices in patients with at least moderate OSA, there was little or no evidence on the effects of CPAP on other important clinical outcomes.”

So... What does it mean?
Or my take on it anyway...

- Recommend weight loss through diet and exercise to overweight patients.

- Patients benefiting from CPAP—Continue current therapy.
- Patients unsure or intolerant of CPAP—Discuss pros, cons and unknowns and respect patients’ choice.

- Who should we be testing?
  - Age > 50?
  - Epworth?

Questions, Comments, Rebuttals