MANAGEMENT OF SLEEP APNEA: EVIDENCE BASED APPROACH

NEIL S. FREEDMAN, MD

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Dr. Freedman has previously served, and currently serves, in several educational and leadership roles in many professional societies. He was the previous chairman of the Annual Sleep Medicine course and is the current chairman of the Sleep Medicine Board Review course for CHEST. Within CHEST, he is chairman of the scientific program committee for the CHEST Annual Conference, a member of the education and joint finance committees, the current chair of the sleep network and a board member for the CHEST Foundation. In addition, he has developed and chaired a variety of courses for several professional societies including CHEST, ATS, AASM and APSS and has published extensively on the spectrum of sleep-disordered breathing.

OBJECTIVES:
Participants should be better able to:

1. Identify patients who are proper candidates for home sleep apnea testing;
2. Understand which outcomes are most likely to improve with CPAP therapy;
3. List alternative therapies to CPAP for patients with OSA.

THURSDAY, MARCH 3, 2016 11:45 AM
OSA Management: Evidence Based Approach

Neil Freedman, MD

Dr. Freedman has declared no conflicts of interest related to the content of his presentation.
Lecture Outline

• HST for the diagnosis of OSA
• Treatment of OSA:
  – PAP
  – Oral appliances
  – Surgery
  – Weight loss
  – Alternative therapies

Who is an Appropriate Candidate for Home Sleep Apnea Testing?

• Patients with a high clinical suspicion of moderate to severe OSA
  – Overweight or obese with snoring, witnessed apneas, daytime sleepiness +/- cardiovascular disease
• Contraindications based on AASM recommendations:
  – Low risk of moderate to severe OSA
  – Comorbid diseases
    • CHF, hypoventilation syndromes, neuromuscular disease, chronic lung disease, history of stroke
  – Comorbid sleep disorders
• Insurance and sleep benefit management companies may have their own policies

PSG Gravy Train is Over

HST Devices Valid for the Diagnosis of OSA

- WatchPAT is adequate for diagnosing OSA
  - Best supporting data of all devices (3 IA and 4 IIA studies)
- Devices that measure nasal pressure plus effort are adequate to diagnose OSA
  - Embletta and Stardust II
- Devices that measure nasal pressure without effort are adequate to diagnose OSA
  - Apnea link (1 IA) and ARES (2 IA and 1 IIA studies)
- Thermal sensing device alone without effort measurement is inadequate for diagnosing OSA

RCTs Outcomes Data Supporting HST for OSA

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>HST Device</th>
<th>Treatment</th>
<th>Similar Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mulgrew</td>
<td>68</td>
<td>Overnight oximetry</td>
<td>In lab CPAP vs CPAP set via APAP</td>
<td>ESS, SAQLI, AHI *Better compliance with APAP</td>
</tr>
<tr>
<td>Berry</td>
<td>106</td>
<td>WatchPAT</td>
<td>In lab CPAP vs CPAP set via APAP</td>
<td>ESS, FOSQ, Compliance</td>
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<tr>
<td>Skomro</td>
<td>102</td>
<td>Embletta</td>
<td>In lab CPAP vs CPAP set via APAP</td>
<td>ESS, SF-36, PSQI, SAQLI, BP, Compliance</td>
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<td>Kuna</td>
<td>213</td>
<td>Embletta</td>
<td>In lab CPAP vs CPAP set via APAP</td>
<td>ESS, FOSQ, PVT, SF-12, Compliance</td>
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<td>Rosen</td>
<td>197</td>
<td>Embletta</td>
<td>In lab CPAP vs CPAP set via APAP</td>
<td>ESS, FOSQ, SF-36, SAQLI compliance, * Nightly use &gt; APAP</td>
</tr>
<tr>
<td>Berry</td>
<td>156</td>
<td>Embletta</td>
<td>In lab CPAP vs APAP</td>
<td>ESS, FOQS, AHI, Compliance, PAP satisfaction scores</td>
</tr>
</tbody>
</table>

HST for OSA is Here to Stay

- Data supports it in the proper patient populations
  - High clinical suspicion of moderate to severe OSA
- Payers want it
- Patients will demand it
- Technology will improve to continue to expand diagnostic options
- Sleep community should embrace and champion this approach
Continuous Positive Airway Pressure (CPAP)

- Initially described by Sullivan in 1981
- Currently the mainstay of therapy for OSAS

Does CPAP Treatment Make A Difference?
Perceived CPAP Benefits: Reality or Wishful Thinking?

<table>
<thead>
<tr>
<th>AHI</th>
<th>Sleep Architecture</th>
<th>Subjective Sleepiness</th>
<th>Objective Sleepiness</th>
<th>Neurocognitive and Mood</th>
<th>Quality of Life</th>
<th>Cardiovascular Disease</th>
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</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Question

Which one of the following outcomes is most likely to improve with CPAP treatment?

A) Hypertension  
B) Daytime sleepiness  
C) Obesity  
D) Depression
QUESTION
Which one of the following outcomes is most likely to improve with CPAP treatment?

A. Hypertension
B. Daytime sleepiness
C. Obesity
D. Depression

CPAP Outcomes Summary:
Patients with Daytime Symptoms

<table>
<thead>
<tr>
<th></th>
<th>AHI</th>
<th>Sleep Architecture</th>
<th>Subjective Sleepiness</th>
<th>Objective Sleepiness</th>
<th>Neurocognitive and Mood</th>
<th>Quality of Life</th>
<th>Cardiovascular Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe/Moderate OSAS</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Mild OSAS</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>NA</td>
</tr>
</tbody>
</table>
The Effect of CPAP Treatment on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

- CPAP improved:
  - Diurnal SBP \(-2.58 \text{ mm Hg}\)
    - (95% CI \(-3.57 \text{ to } -1.59 \text{ mm Hg}\))
  - Diurnal DBP \(-2.01 \text{ mm Hg}\)
    - (95% CI \(-2.84 \text{ to } -1.18 \text{ mm Hg}\))
  - Similar improvements in nocturnal BP

- Improvements associated with:
  - More severe disease
  - Daytime sleepiness
  - Greater PAP adherence
  - Younger age

- Improvements predicted by:
  - Baseline BP and Epworth

- Conclusions:
  - CPAP is associated with modest, but significant, improvements in BP


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Improvements in Less Severe Disease
Inconsistent & Debatable

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Severity</th>
<th>Intervention</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>APPLES 2012</td>
<td>1105</td>
<td>Mild 14%</td>
<td>CPAP vs Sham CPAP x 6 months</td>
<td>Transient improvement in working memory at 2 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate 31%</td>
<td></td>
<td>No improvements in neurocognitive function across spectrum of dx at 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe 55%</td>
<td></td>
<td>Improved MWT and Epworth in severe dx at 6 months</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Improved Epworth in moderate &amp; severe dx at 2 &amp; 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mild dx without improvement in MWT/Epworth at 2 &amp; 6 months</td>
</tr>
<tr>
<td>CATNAP 2012</td>
<td>223</td>
<td>Mild (63%)</td>
<td>CPAP vs Sham CPAP x 8 weeks</td>
<td>CPAP significantly improved FOSQ vs sham CPAP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate (37%)</td>
<td></td>
<td>CPAP improved ESS better than sham (baseline ESS = 15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epworth &gt; 10</td>
<td></td>
<td>- CPAP (\downarrow) mean ESS by 2.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Sham (\uparrow) ESS by 0.5 (NS)</td>
</tr>
</tbody>
</table>

*** APPLES used 3% or arousal hypopnea definition
*** CAPTNAP used 3% hypopnea definition

Kushida, C et al. SLEEP 2012;35(12):1593-1602
Weaver, T et al. Amer J Respir Crit Care Med 2012;186:677-683
CPAP Effects on BP in NonSleepy Severe OSA with HTN Limited and Delayed

Adjusted Mean Differences (95% CI)
CPAP vs Control

<table>
<thead>
<tr>
<th></th>
<th>3 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>P = 0.2008</td>
<td>P = 0.2852</td>
</tr>
<tr>
<td>DBP</td>
<td>P = 0.1275</td>
<td>*P = 0.0021</td>
</tr>
</tbody>
</table>

Adjusted Mean BP (mm Hg)

Overall, CPAP Does Not Reduce the Incidence of HTN or CV Disease in OSA without Daytime Sleepiness

Barbe, F et al. AJRCCM 2010;181:718-726

Barbe, F et al. JAMA 2012;307:2161-2168
OSA, CV Disease and Treatment (CPAP): The Bottom Line: Data is Inconclusive

- CPAP may reduce cardiovascular mortality
  - Prospective observational studies
- CPAP can reduce blood pressure, but reductions in BP are small and results are inconsistent across studies
  - EDS and uncontrolled HTN may predict a more robust BP response
  - Better adherence = Better BP response
  - Antihypertensive medication better than CPAP
  - CPAP may improve BP in patients with resistant HTN and OSA
  - CPAP better than oxygen in patients with CV disease or CV risk factors
- CPAP does not reduce the incidence of HTN or cardiovascular diseases in patients with OSA and no daytime sleepiness
- Limited data for reductions of arrhythmias with CPAP
- CPAP improves LVEF in patients with CHF with systolic dysfunction and OSAS
- Minimal to no data concerning:
  - Mild OSAS
  - Long-term RCTs on other cardiovascular outcomes

Other CPAP Outcomes

- CPAP use associated with reductions in motor vehicle accidents
- CPAP use not associated with weight loss
  - May be associated with mild weight gain
- CPAP use may improve lipid profile
  - Reduction in total cholesterol and LDL
  - Increase in HDL
  - No affect on triglycerides
- Improvements in DM and metabolic syndrome debatable
  - Weight loss better than CPAP for improving these outcomes
- CPAP can improved daytime sleepiness in patients with REM related OSA
  - No data on other outcomes in this group
- Benefits for patients without symptoms not clear across spectrum of disease severity
AASM Practice Parameter and Clinical Guideline Recommendations Still Supported by the Data

- **CPAP Indications** (Standards):
  - Treatment of moderate - severe OSAS
  - Improving subjective sleepiness

- **CPAP Recommendations** (Options):
  - Treatment of mild OSAS
  - Improving quality of life
  - As an adjunctive anti-hypertensive therapy

Kushida, C et al. Sleep 2006; 29:375-380
Gay, P et al. Sleep 2006;29:381- 401

How Much CPAP is Enough?
More CPAP = Less Sleepiness

![Graph showing the relationship between hours of nightly CPAP use and % with normal values for FOSQ, ESS, and MSLT.](image)

Weaver, T et al. Sleep 2007;30:711-19

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How Much CPAP is Enough?

- Depends on the outcome
- Depends on the individual
- Not all individuals will demonstrate improvements in all outcomes
- Some CPAP use is good, more is probably better
Determining CPAP Prescription

- AASM recommends full-night in-lab titration (Guideline)
- AASM 2008 Guidelines for manual titration
- Goal CPAP pressure
- Minimal pressure required to resolve:
  - All apneas, hypopneas, snoring and arousals related to these events
  - In all stages of sleep
  - In all positions
- Repeat titration only for new symptoms or significant weight change

Kushida, C et al. Sleep 2006; 29:375-80

Split-night Studies

- Indications:
  - An AHI of ≥ 40 events per hour during the initial 2 hours of the PSG; and
  - At least 3 hours to conduct an adequate CPAP titration
- Consider for:
  - AHI of 20 to 40 events/hour during the initial 2 hours of a sleep study
  - Data less supportive
- Disadvantages:
  - Sub-optimal CPAP titrations

Kushida, C et al. Sleep 2006; 29:375-80
Many Patients May Not Achieve an Optimal CPAP Titration

- **Quality of Titration:**
  - **Optimal:**
    - AHI < 5 with supine REM
  - **Good:**
    - AHI < 10 with supine REM
  - **Adequate:**
    - AHI < 75% of baseline or
    - No supine REM
  - **Inadequate:** Other


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Insurance Companies Will Dictate Out of Center OSA Treatment as well as Diagnosis

- United Healthcare is “excited” to inform you about the proactive approach we are taking for our enrollees with possible and confirmed OSA. United Healthcare is working with our provider network to help our members get tested for OSA more comfortably in their own homes, when appropriate.
- Preauthorization required for all sleep studies as of 10/1/11
- Requests for in-laboratory polysomnography will be denied if the patient is eligible for home sleep testing.
  - Contracted with IDTF VirtuOx to perform home sleep testing nationwide as of 1/1/12
- **Home sleep testing followed by the use of APAP (auto-adjusting positive airway pressure) devices in the self-adjusting mode for unattended treatment is an alternative to in-laboratory titration of CPAP (continuous positive airway pressure).**

AutoCPAP (APAP): What is it?

- Aka: Automatic, automated, autotitrating, autoadjusting, selftitrating
- Detects and responds to changes in upper airway flow or resistance patterns
- Potential applications:
  - Diagnosis
    - No Data
    - Not Recommended
  - Treatment:
    - In place of, or as an adjunct to, conventional CPAP

### APAP Devices and Technologies

<table>
<thead>
<tr>
<th>Company</th>
<th>Device</th>
<th>Snore</th>
<th>FL</th>
<th>Hypopnea</th>
<th>Apnea</th>
<th>Flow Based</th>
<th>FOT</th>
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</thead>
<tbody>
<tr>
<td>Resmed</td>
<td>Autoset S8 S9 S10</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Phillips Respironics</td>
<td>Remstar Auto M Series Auto</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Paykel</td>
<td>Icon Auto Sleepstyle 254 Auto</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>DeVilbiss</td>
<td>Sleepcube Auto</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Weiman</td>
<td>Somnosmart</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
Question

Which of the following OSA patients would be the most appropriate candidate for APAP therapy?

A) 55 year old male with congestive heart failure and an AHI = 30 events/hour.
B) 60 year old male with COPD and an AHI = 40 events/hour.
C) 35 year old male with BMI = 35 and an AHI = 35 events/hour.
D) 32 year old male with obesity hypoventilation syndrome and AHI = 43 events/hour.
Who is a Potential Candidate for APAP?

- **Clear Candidates**
  - Uncomplicated moderate to severe OSAS

- **Unclear Groups**
  - REM-related OSAS
  - Position dependent
  - High pressures (>10)
  - CPAP intolerant

- **Not APAP Candidates** (AASM Standard)
  - Congestive heart failure
  - COPD and chronic lung disease
  - Obesity Hypoventilation Syndrome
  - Other hypoventilation syndromes
  - Lack of snoring

How does APAP Compare to Conventional CPAP for the Treatment of OSAS?

Morgenthaler, TI et al. Sleep 2008;31:141-47
APAP vs CPAP Conclusions

• Lower mean pressures with APAP
• Similar outcomes to CPAP:
  – Adherence
  – AHI
  – Subjective sleepiness (EPWORTH)
  – Note: No outcomes data on BP with APAP
• APAP is as effective as CPAP for uncomplicated moderate to severe OSA

Unattended APAP P95/P90 to Determine Fixed CPAP:
APAP Outcomes = PSG Determined CPAP

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Device</th>
<th>Duration (wks)</th>
<th>Similar Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>West 2006</td>
<td>98</td>
<td>Resmed Autoset Spirit</td>
<td>26</td>
<td>ESS, OSLER, SF-36, SAQLI, Compliance, AHI</td>
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<tr>
<td>Cross 2006</td>
<td>204</td>
<td>Resmed Autoset Spirit</td>
<td>12</td>
<td>ESS, OSLER, SF-36, FOSQ, Compliance</td>
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<tr>
<td>Mulgrew 2007</td>
<td>68</td>
<td>Resmed Autoset Spirit</td>
<td>12</td>
<td>ESS, SAQLI, AHI *Better compliance with APAP P95</td>
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<td>Berry 2008</td>
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<td>Resmed Autoset Vantage</td>
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<td>ESS, FOSQ, Compliance</td>
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<td>Skomro 2010</td>
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<td>Kuna 2011</td>
<td>213</td>
<td>Philips Respironics RemStar Auto</td>
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<td>ESS, FOSQ, PVT, SF-12, Compliance</td>
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<td>Rosen 2012</td>
<td>197</td>
<td>Philips Respironics RemStar Auto Pro</td>
<td>12</td>
<td>ESS, FOSQ, SF-36, SAQLI Adherence, * Nightly use &gt; APAP</td>
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RCTs of Unattended APAP: APAP = CPAP

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</tr>
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<tr>
<td>Planes 2003</td>
<td>35</td>
<td>SEFAM REM+ Auto</td>
<td>52</td>
<td>AHI, ESS, Compliance</td>
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<td>Hukins 2004</td>
<td>58</td>
<td>Resmed Autoset T</td>
<td>16</td>
<td>ESS, SF-36, Compliance</td>
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<td>Masa 2004</td>
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<td>AHI, ESS, QOL, Pressure,</td>
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<td>Douglas 2010</td>
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<td>Side effects, Compliance</td>
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<td>Compliance, PAP</td>
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<td></td>
<td></td>
<td></td>
<td>satisfaction</td>
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</table>

APAP Modifications Don’t Improve Outcomes

- APAP with AFLEX = CPAP at 6 months
  - Similar:
    - Compliance
    - AHI, Epworth
    - QOL, BP

- APAP w/ SensAwake = APAP w/o SensAwake (Fisher & Paykel)
  - Similar
    - AHI
    - P90
    - Mean pressure
    - Sleep architecture

Kushida, C et al. Sleep 2011;34:1083-92
Dungan, G et al. JI Clin Sleep Med 2011;7:261-7
APAP for OSA: The Bottom Line

• Recommended for the treatment of patients with moderate to severe uncomplicated OSA
  – As stand alone therapy or to set a fixed CPAP setting
  – Should be considered as first line therapy
• Not recommended for:
  – OSA with comorbidities:
    • CHF, hypoventilation syndromes, COPD
    • Non-snorers or s/p UPPP
  – OSA diagnosis or split-night studies
• Similar outcomes to CPAP
• Should be considered as first line therapy

PAP Adherence

• Definition: > 4 hours per night on 70% of the observed nights

Objective Measurement of Patterns of Nasal CPAP Use by Patients with Obstructive Sleep Apnea


American Review of Respiratory Disease, Vol. 147, No. 4 (1993), pp. 887-895
CPAP Adherence

- Subjective adherence 60% to 90%
- Objective adherence 40% – 84%
- Patients tend to overestimate adherence
  - ≈ 60 minutes per night
  - Pattern observed in CPAP naïve and long term users
- Adherence patterns determined early

Question

Which one of the following has been associated with lower adherence to PAP therapy?

A) Severe OSA (AHI > 30)
B) Excessive daytime symptoms
C) Pressures < 12 cm H₂O
D) Lower socioeconomic status
QUESTION
Which one of the following has been associated with lower adherence to PAP therapy?

A. Severe OSA (AHI > 30)
B. Excessive daytime symptoms
C. Pressures < 12 cm H₂O
D. Lower socioeconomic status

Predictors of Adherence Inconsistent:
The Bottom Line

- Possibly daytime sleepiness and more severe disease associated with improved adherence
- African American race and/or lower socioeconomic class associated with lower adherence
- Pressure level not predictive
Question

Which one of the following interventions has been associated with improved PAP adherence?

A) AutoPAP  
B) Education  
C) Nasal steroids  
D) PSG titration

QUESTION

Which one of the following interventions has been associated with improved PAP adherence?

A. AutoPAP  
B. Education  
C. Nasal steroids  
D. PSG titration
AASM Practice Parameters and Clinical Guideline Adherence Recommendations

• Interventions to Improve Adherence:
  - Heated humidification (*Standard*)
  - Education (*Standard*)

• Follow up:
  - CPAP usage should be objectively monitored (*Standard*)
  - Initial follow up in first few weeks (*Standard*)
  - Yearly and as needed follow-up thereafter (*Option*)

Kushida, C et al. Sleep 2006; 29:375-80
Gay, P et al. Sleep 2006;29:381- 401

Impact of Supportive, Educational and Behavioral Therapies on CPAP Compliance

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Interventions</th>
<th>Evidence Quality</th>
<th>Mean Improvements in Nightly CPAP Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supportive</td>
<td>• Increased practical support</td>
<td>Low to moderate</td>
<td>.85 hours</td>
</tr>
<tr>
<td></td>
<td>• Encouragement</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Telemedicine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Relaxation prior to CPAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>• Video</td>
<td>Low to moderate</td>
<td>.6 hours</td>
</tr>
<tr>
<td></td>
<td>• Face-to-face sessions</td>
<td></td>
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<tr>
<td></td>
<td>• Group sessions</td>
<td></td>
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<tr>
<td></td>
<td>• Written material</td>
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<tr>
<td></td>
<td>• Phone calls</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Home follow up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioral therapies</td>
<td>• Motivational interviewing</td>
<td>Very low to low</td>
<td>1.44 hours</td>
</tr>
<tr>
<td></td>
<td>• Written feedback</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CBT with education</td>
<td></td>
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</tr>
</tbody>
</table>

Wozniak D et al. Cochrane Database Review 2014
Heated Humidification May Improve Adherence for Some Patients

- AASM Practice Parameters and Clinical Practice Guidelines (Standard)
  - Improved compliance
  - More effective for:
    - Nasal complaints
    - Rhinitis
- Role of heated tubing unclear
  - Limited data suggests no improvement in adherence

Haniffa, M et al. Cochrane Databases of Syst. Rev. 2004
Kushida, C et al. Sleep 2006; 29:375-80
Gay, P et al. Sleep 2006;29:381- 401

Data on Heated Humidification and PAP Adherence: Inconsistent and Not Very Strong

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Interventions</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Massie 1999 | 38 | • CPAP with heated, cold pass and no humidification  
  • Duration: 3 weeks | • Heated humidification improved adherence  
  • No difference in adherence with cold pass or no humidification  
  • Reduced upper airway dryness with HH  
  • No differences in Epworth between groups |
| Neill 2003  | 42 | • CPAP with and without heated humidification  
  • Duration: 3 weeks | • Small increase in adherence  
  • Reduced upper airway symptoms  
  • No change in sleepiness or satisfaction |
| Mador 2005  | 98 | • CPAP with and without heated humidification  
  • Durations: 12 months | • No differences in adherence  
  • No differences in daytime sleepiness, QOL  
  • Reduced upper airway dryness with HH |
| Salgado 2008| 39 | • APAP with and without heated humidification  
  • Durations: 30 days | • No differences in adherence  
  • No differences in nasal symptoms |
| Worsnop 2010| 54 | • Heated vs no humidification  
  • Durations: 12 weeks | • No differences on adherence  
  • Reduced nasal symptoms |

Salgado S et al. J Bras Pneumol. 2008;34:690-4
Optimum form of CPAP delivery interface remains unclear

The best mask is the one the patient will wear
Changing Mask Type May Change Therapeutic CPAP Pressure

Teo, M et al. Sleep 2011;34:951-5

Adherence Interventions and Outcomes
Summary: The Bottom Line

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Education/Supportive Care           | Beneficial| • Various interventions helpful in most patients  
• Best intervention, or combination, not clear                                           |
| Behavioral Therapies                | Beneficial| • Various interventions improve adherence  
• Low quality supporting data data                                                     |
| Heated humidification               | Inconsistent/Controversial | • Some, but not the majority of data support improved adherence  
• Nasal congestion or rhinitis may be associated with improved adherence with heated humidification |
| Advanced PAP (Flex, Bilevel and APAP) | No benefit | • Not associated with improved adherence or other outcomes  
• Bilevel, may be the exception, in CPAP nonadherent                                    |
| Nasal Steroids                      | No Benefit | • Not associated with improved adherence or nasal symptoms                             |
Adherence Interventions and Outcomes Summary: The Bottom Line

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Mask Type                     | Unclear  | • Best mask type is not clear and is patient dependent  
                                |          | • Changing mask type may alter effective PAP pressure                                           |
| Hypnotics                     | Controversial | • Eszopiclone may improve PAP titration efficacy and 6 month adherence  
                                |          | • Data do not support other hypnotics                                                           |
| Telemedicine                  | Unclear  | • Limited data suggest benefit, other not supportive  
                                |          | • More data required                                                                            |
| Compliance Monitoring         | Unclear  | • No clear data to guide therapy or determine which patients may benefit from this intervention |
| Sleep Specialist Care         | Unclear  | • Observational studies support  
                                |          | • RCTs show mixed results in uncomplicated moderate/severe OSA                                  |

What is the Best Follow-up Strategy?

• Short term:  
  – AASM recommends initial follow up in first few weeks *(Standard)*  
  – Most payers require office follow up between 31 and 91 days  
  – Not clear if either strategy improves adherence
• Long term:  
  – AASM recommends annual follow up and as needed *(Option)*  
  – Some payers will require annual follow up  
  – Recent data suggest little objective benefit from face-to-face office follow up in patients without subjective complaints  
    • Without subjective complaints, the likelihood of a therapeutic intervention was 0.07 (95% CI = 0.03-0.15, p < 0.001)
• Conclusion: The value and optimal timing of routine follow up for all patients with OSA is yet to be determined

Nannapaneni S et al. J Clin Sleep Med 2014;10:919-
Oral Appliances for OSA

Oral Appliance Mechanisms of Action

• Mandibular advancement

and/or

• Maintains tongue in a more anterior position
Indications for Oral Appliance (OA) Therapy for OSA

• 2006 AASM Practice Parameters
  – Indicated for use in mild to moderate OSA (Guideline) in patients who:
    • Prefer OAs to CPAP
    • Do not respond to CPAP
    • Are not appropriate CPAP candidates
    • Fail CPAP or behavioral measures

• 2014 AADSM Definition of an Effective Oral Appliance
  – Work best for mild to moderate OSA
  – May be used in patients with severe OSA who do not respond to, or are unwilling or unable to, tolerate CPAP therapy

Predictors of Success

• Less severe disease
• Supine dependent OSA
• Younger age
• Female gender
• Lower BMI
• Smaller neck circumference
• CPAP failures with lower pressure requirements
• Problem:
  - Ability to accurately predict success prior to initiating therapy is only approximately 50%
Advances in OA Titration:
Remote Controlled In-lab Titration

- Remotely titrates oral appliance during a full night PSG

Remmers J et al. Sleep 2013;36:1517-25

MATRx May Predict Outcomes with OA Therapy

- Success definition:
  - AHI <10/hr and ≥ 50% reduction in baseline AHI
- Able to predict:
  - Success in 87%
  - Failure in 83%
- Overall PPV = 87%

Figure 4—Response to therapy at final protrusive position for the two predictive groups, predicted success and predicted failure.
Do Oral Appliances Improve Important Patient Outcomes

and

Which Patient Groups Benefit the Most?

Oral Appliance AASM Practice Parameters Summary

• OAs indicated for mild-to-moderate OSA (Guideline)
• Severe OSA should have initial trial with CPAP (Guideline)
• CPAP more effective for reducing AHI and improving oxygenation
• OAs = CPAP for improving sleepiness

Kushida, C et al. Sleep 2006;29:240-43
Ferguson, K et al. Sleep 2006;29:244-62
Effect of Oral Appliances on Blood Pressure in OSA: A Systematic review and Meta-analysis

- 7 studies with n = 399 (2 RCTs, n = 146)
- Results:

<table>
<thead>
<tr>
<th></th>
<th>Overall Mean Changes BP mm Hg (95% CI)</th>
<th>P Value</th>
<th>Mean Changes Nocturnal BP mm Hg (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>-2.7 (0.8 to -4.8)</td>
<td>0.04</td>
<td>-2.0 (1.1 to -5.3)</td>
<td>0.212</td>
</tr>
<tr>
<td>DBP</td>
<td>-2.7 (-0.9 to -4.6)</td>
<td>0.004</td>
<td>-1.7 (-0.1 to -3.2)</td>
<td>0.03</td>
</tr>
<tr>
<td>MAP</td>
<td>-2.4 (-0.08 to -4.01)</td>
<td>0.003</td>
<td>-1.9 (1.3 to -5.1)</td>
<td>0.255</td>
</tr>
</tbody>
</table>

- Conclusions: Pooled estimates suggest a favorable effect on many parameters of BP
- Limitations: Most studies observational. More RCT data needed


Surgery for OSA

Upper Airway

Bariatric

HGNS
AASM Practice Parameters Upper Airway Surgery for OSA: All Recommended as Options

- Tracheostomy:
  - Effective single intervention to treat OSA. Should be considered only when other options do not exist, have failed, or when this operation is deemed clinically urgent.

- Maxillomandibular advancement (MMA):
  - Indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to use other treatments.

- UPPP:
  - Should only be offered when PAP or OA are not tolerated or effective.

- Multi-level or stepwise surgery (MLS):
  - Acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed UPPP as a sole treatment.

- Radio frequency ablation (RFA):
  - Considered in mild to moderate OSA who cannot tolerate or who are unwilling to adhere to CPAP or OA therapy.

- Palatal implants:
  - May be effective in mild OSA who cannot tolerate or who are unwilling to adhere to CPAP or OA therapy.

Aurora, R et al. SLEEP 2010;33(10):1408-1413

Upper Airway Surgery for OSA

- Typically not first line therapy for OSA.
- Little rigorous data to support most upper airway surgical procedures:
  - Data are inconsistent or incomplete.
  - Difficult to predict success prior to surgery.
  - Laser assisted uvuloplasty (LAUP) not recommended.
- Upper airway surgical options supported by best data/outcomes:
  - Maxillomandibular advancement (MMA) for adults.
  - Adenotonsillectomy for pediatric population.

Aurora, R et al. SLEEP 2010;33(10):1408-1413
“What a glorious day to begin a short-lived diet and exercise program.”

Weight Loss Improves OSA: Best Data Based on Bariatric Surgery

- BMI improves
  - 55.3 to 37.7 Kg/m²
- AHI improves
  - 54.7 to 15.8
- Residual disease in majority
  - AHI < 10 in 44%
  - AHI < 5 in 25%
- Objective testing recommended after weight loss to determine ongoing need for treatment

Surgical vs Conventional Therapy for Weight Loss Treatment of Obstructive Sleep Apnea

- RCT of 60 obese patients (BMI > 35 and < 55)
- Recently diagnosed OSA AHI ≥ 20 on CPAP therapy
- Randomized to:
  - Conventional weight loss program with regular counseling and very low calorie diet
  - Bariatric surgery: Adjustable gastric banding
- Follow up: 2 years
- Outcomes:
  - Primary: Change in AHI
  - Secondary: Change in weight, CPAP adherence and functional status

Dixon et al. JAMA. 2012;308(11):1142-1149

Surgical vs Conventional Weight Loss for OSA

- Results:
  - Bariatric surgery patients lost more weight compared to conventional weight loss
    • 27.8 kg vs 5.1 kg (p < 0.001)
  - Bariatric surgery led to a non-significant reduction in the AHI compared to conventional weight loss
    • 25.5 vs 14.0 (p = 0.18)
    • Most patients had residual severe OSA
    • Mild OSA (AHI < 15) achieved by minority of patients
  - No difference in PAP adherence between groups
    • Only 60% to 66% adherence in both groups at 2 year follow up
- Conclusions:
  - Bariatric surgery (adjustable gastric banding) does not lead to greater reductions in AHI despite greater reductions in weight

Dixon et al. JAMA. 2012;308(11):1142-1149
Hypoglossal Nerve Stimulation Devices

- Relatively recently approved by the FDA (May 1, 2014)
- Exclusions:
  - BMI > 32 kg/m², AHI < 20 or > 50, central apneas, concentric upper airway collapse on DISE
- Current supporting data:
  - Overweight and mildly obese (BMI < 32 kg/m²) patients with moderate to severe OSA who are CPAP intolerant
  - Improved OSA, daytime sleepiness and QOL with up to a year follow up
    - Mean 68% reduction in AHI over a year (AHI 29.3 to 9)
  - Low complication rate: < 2%
- Role in OSA therapy yet to be determined
  - Cost will be the major barrier
- All data specific to the INSPIRE device
HGNS Therapy Effective Over 1 Year

** P < 0.001

Up to 33% of Patients Do Not Respond to INSPIRE Therapy

Responder Definition:
- AHI < 20
- ≥ 50% reduction in AHI from baseline
- 53% with AHI < 10
- 63% with AHI < 15
Not All Patients Will Respond to INSPIRE HGNS Treatment: 18 Month Data

19 of 83 (23%) responders at 12 months were non-responders at 18 months

Table S2—Characteristics of responders and non-responders at 18 mo.

<table>
<thead>
<tr>
<th></th>
<th>Responder</th>
<th>Non-responder</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>80</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>55.1 ± 10.0</td>
<td>52.4 ± 10.5</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex (male %)</td>
<td>83%</td>
<td>85%</td>
<td>0.59</td>
</tr>
<tr>
<td>BMI</td>
<td>28.6 ± 2.5</td>
<td>28.0 ± 2.8</td>
<td>0.19</td>
</tr>
<tr>
<td>Neck size (cm)</td>
<td>41.2 ± 3.2</td>
<td>41.1 ± 3.3</td>
<td>0.83</td>
</tr>
<tr>
<td>Baseline AHI</td>
<td>30.9 ± 11.2</td>
<td>32.3 ± 11.7</td>
<td>0.52</td>
</tr>
<tr>
<td>Baseline ODI</td>
<td>27.3 ± 11.3</td>
<td>30.0 ± 12.0</td>
<td>0.23</td>
</tr>
<tr>
<td>Prior UPPP (%)</td>
<td>20.0%</td>
<td>14.6%</td>
<td>0.47</td>
</tr>
<tr>
<td>Baseline FOSQ</td>
<td>14.7 ± 3.2</td>
<td>13.3 ± 3.1</td>
<td>0.10</td>
</tr>
<tr>
<td>Baseline ESS</td>
<td>11.5 ± 4.9</td>
<td>11.8 ± 5.2</td>
<td>0.77</td>
</tr>
</tbody>
</table>

AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; ODI, oxygen desaturation index; UPPP, uvulopalatopharyngoplasty

Strollo P et al. SLEEP 2015;38:1593-1598

Alternatively, Some Non-responders at 12 Months Were Responders at 18 Months

- Of the 43 non-responders at 12 months
  - 16 of the 43 (37%) met criteria for response at 18 months
- Overall response rate similar at 12 and 18 months

Strollo P et al. SLEEP 2015;38:1593-1598
Real World Observations

• Most patients won’t be candidates for HGNS
  – Mostly BMI and AHI related
• Many patients won’t want to undergo implantation
• Many patients can be made PAP adherent with some education and attention to details
• Major barrier to therapy = Cost and payers
  – Device cost to institution ≈$21,000
  – Having a multidisciplinary team approach in an integrated system may facilitate approval for procedures

Other Alternative Therapies

• Nasal EPAP and oral negative pressure therapy
  – May have a role for patients with less severe disease
  – Residual OSA common
  – Typically not covered by insurance

• Positional therapy
  – Definition of positional OSA not standardized
  – Data mostly from small, uncontrolled, short term studies
  – Long term adherence typically poor
  – Recommended as a secondary or supplemental treatment

Berry R et al. Sleep 2011;34:479-85
Colrain I et al. Sleep Medicine 2013;14:830-37
Oxygen Treatment for OSA

- Cardiovascular risk related to OSA is dependent on severity (AHI) and degree of oxygen desaturation
  - CV risk tied more to degree of oxygen desaturation than AHI
- Oxygen therapy for COPD:
  - Improves survival in patients with resting hypoxemia (PaO2 < 60 mm Hg)
  - More (duration) = Better outcomes
- JCSM systematic review and meta-analysis 2013:
  - No long term outcomes data
  - Oxygen improves oxygen saturation similar to CPAP
  - CPAP improves AHI > oxygen
    - Oxygen may increase the duration of apneas and hypopneas
- CPAP is better than oxygen for reducing BP
- Oxygen not recommended as a primary therapy for OSA

Gottlieb D et al. NEJM 2014;370:2276-2285

Not Ready for Prime Time Interventions

- Medications
  - Increase upper airway tone
  - Affect arousal threshold
- Genetic and biomarker testing
- Upper airway muscle exercises/training
- Telemedicine
Summary

• HST and APAP should be the first line management approach for patients with uncomplicated OSA

• CPAP is indicated for the treatment of the spectrum of OSA severity
  – Best data for patients with moderate to severe OSA
  – Subjective sleepiness responds best to PAP therapy
  – PAP can improve BP, but improvements tend to be small
  – The role of PAP for other cardiovascular outcomes is not clear
  – Role in mild OSA and in those without daytime sleepiness is not clear

• Oral appliances best for patients with mild to moderate disease
  – Effects on BP not clear

Summary: Other Therapies for OSA

• Upper airway surgery:
  – Typically not first line therapy
  – MMA may be best choice for adults

• Weight loss
  – Can reduce AHI
  – Significant residual OSA typical
  – Bariatric surgery does not lead to greater reductions in AHI despite greater reductions in weight

• Nasal EPAP and oral negative pressure therapy
  – May have a role in mild to moderate disease
  – Residual OSA common
Summary: Other Therapies for OSA

• Hypoglossal nerve stimulation
  – Role in the management of OSA yet to be determined
  – Up to 1/3 of patients non-responders

• Positional therapy:
  – Typically second line therapy

• Oxygen:
  – No role as a primary therapy
  – CPAP better for decreasing blood pressure

• Medications:
  – None currently approved as primary therapies

Thank You