



The New England Comparative Effectiveness Public Advisory Council

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Diagnosis and Treatment of Obstructive Sleep Apnea in Adults

Supplementary Data and Analyses to the Comparative Effectiveness Review of the Agency for Healthcare Research and Quality

Final Report – January 2013

Completed by:

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Introduction

To make informed healthcare decisions, patients, clinicians, and policymakers need to consider many different kinds of information. Rigorous evidence on the comparative clinical risks and benefits of alternative care options is always important; but along with this information, decision-makers must integrate other considerations. Patients and clinicians must weigh patients' values and individual clinical needs. Payers and other policymakers must integrate information about current patterns of utilization, and the impact of any new policy on access, equity, and the overall functioning of systems of care. All decision-makers, at one level or another, must also consider the costs of care, and make judgments about how to gain the best value for every healthcare dollar.

The goal of this initiative is to provide a forum in which all these different strands of evidence, information, and public and private values can be discussed together, in a public and transparent process. Initially funded by a three-year grant from the federal Agency for Healthcare Research and Quality (AHRQ), and backed by a consortium of New England state policymakers, the mission of the New England Comparative Effectiveness Public Advisory Council (CEPAC) is to provide objective, independent guidance on how information from supplemented AHRQ evidence reviews can best be used across New England to improve the quality and value of health care services. CEPAC is an independent body of 19 members, composed of clinicians and patient or public representatives from each New England state with skills in the interpretation and application of medical evidence in health care delivery. Representatives of state public health programs and of regional private payers are included as ex-officio members of CEPAC. The latest information on the project, including guidelines for submitting public comments, is available online: cepac.icer-review.org.

The Institute for Clinical and Economic Review (ICER) is managing CEPAC and is responsible for developing supplementary reports to AHRQ reviews for CEPAC consideration. ICER is an academic research group based at the Massachusetts General Hospital's Institute for Technology Assessment. ICER's mission is to lead innovation in comparative effectiveness research through methods that integrate evaluations of clinical benefit and economic value. By working collaboratively with patients, clinicians, manufacturers, insurers and other stakeholders, ICER develops tools to support patient decisions and medical policy that share the goals of empowering patients and improving the value of healthcare services. More information about ICER is available at www.icer-review.org.

ICER has produced this set of complementary analyses to provide CEPAC with information relevant to clinical and policy decision-makers in New England. This supplement is not meant to revisit the core findings and conclusions of the AHRQ review on "[Diagnosis and Treatment of Obstructive Sleep Apnea in Adults](#)," but is intended to augment those findings with: 1) updated information on the diagnosis and management options for obstructive sleep apnea (OSA) published since the AHRQ review; 2) regional and national data on utilization, existing clinical guidelines, and payer coverage policies; and 3) the results of budgetary impact and cost-effectiveness analyses developed to support discussion of the comparative value of different diagnosis and treatment approaches. This report is part of an experiment in enhancing the use of evidence in practice and policy, and comments and suggestions to improve the work are welcome.

1. Background

1.1 The Condition

Obstructive sleep apnea (OSA) is a chronic disorder, characterized by repetitive stops and starts in breathing during a night of sleep (Mayo Foundation, 2012). As muscles in the throat relax, partial (hypopnea) or complete (apnea) blockage of the airway occurs, leading to symptoms such as snoring, gasping or choking (Young, 2009). Other nighttime events associated with intermittent breathing interruptions include decreased oxygen saturation and arousals from sleep (Punjabi, 2008). Consequences of OSA include excessive daytime sleepiness, hypertension, chronic fatigue and insomnia (Mayo Foundation, 2012). Long-term health problems associated with OSA include cardiovascular disease (increased risk of heart failure and stroke), ocular disorders such as glaucoma, memory and cognitive problems, and changes in mood or development of depression (Mayo Foundation, 2012).

Documented prevalence of OSA in a worldwide general population ranges from 3 – 7% in adult men, and 2 – 5 % in adult women (Punjabi, 2008). Similar rates have been reported in pediatric populations (although the focus in the AHRQ review and in this supplemental report is on adults). Accurate estimation of the number of patients affected by OSA is difficult, as more than 80% of patients with moderate-to-severe disease may be undiagnosed (Young, 1997). Risk factors for development of OSA include obesity (body mass index (BMI) > 30 kg/m²), having a neck circumference ≥ 17 inches in men and ≥ 16 inches in women, being of male gender, age > 65 years, and having structural abnormalities related to the jaw, throat and nasal passages (Ho, 2011). In addition, other lifestyle factors may affect the development and/or severity of OSA. Smokers are more than twice as likely to develop OSA as nonsmokers (Kashyap, 2001), and excessive alcohol intake may also raise both the risk of OSA as well as the severity of breathing difficulties encountered during sleep (Koyama, 2012).

The economic burden of OSA is substantial. Direct medical costs have been estimated to total as much as \$3.4 billion in the U.S. (Kapur, 1999). In addition, findings from a recent Canadian study indicate that patients referred for sleep testing are 4 times more likely to be hospitalized than those not referred (Ronksley, 2011). Finally, the potential impact of OSA-related symptoms is substantial. For example, it has been estimated that more than 800,000 motor vehicle drivers in the U.S. are involved in OSA-related accidents each year, the estimated costs of which total nearly \$16 billion (Sassani, 2004).

1.2 Diagnostic Strategies

A multifaceted approach is typically taken to diagnose OSA. First, a comprehensive clinical evaluation is performed, including assessment of patient risk factors and a detailed sleep history (Epstein, 2009). The sleep history includes assessment of signs and symptoms of OSA such as presence of snoring or gasping during sleep, total sleep amount, morning headaches and memory complaints (Epstein, 2009).

Questionnaires

As part of a comprehensive clinical evaluation in a patient suspected of OSA, various screening questionnaires may be utilized to evaluate various symptoms. The most common instruments evaluate daytime sleepiness (the Epworth Sleepiness Scale [ESS]; Johns, 1991), snoring, blood pressure, and fatigue (the Berlin Questionnaire [BQ]; Netzer, 1999), and a variety of fatigue symptoms as well as demographic and anatomic information (the STOP-Bang questionnaire; Chung, 2008). The ESS asks a patient to evaluate his/her likelihood of dozing in 8 different daytime situations, with scores ranging from 0–24. The BQ separates patients into high risk/low risk stratification based on 10 questions related to snoring, feelings of fatigue, and blood pressure. The STOP-Bang questionnaire utilizes 4 questions related to snoring, tiredness, obstructive apnea and blood pressure along with clinical parameters (BMI, age, neck circumference and gender) to develop a summary risk score. The content of each of these questionnaires is shown in Appendix A.

Clinical Prediction Rules

In an effort to further simplify the screening process for OSA, clinicians and researchers have developed numerous algorithms to assist in risk stratification of patients suspected of OSA. Often, these tools are based on objectively-measured clinical parameters, along with clinical observations that are used as inputs in a statistical prediction model. Examples of input variables are BMI, age, presence of hypertension, morphometric parameters (e.g., palatal height, neck circumference), and results of pulmonary function testing.

Sleep Testing

Following initial assessment, patients judged to be at risk of OSA undergo objective sleep testing to measure the Apnea-Hypopnea Index (AHI): the sum of the number of apneas and hypopneas divided by the total hours of sleep (Ho, 2011). Hypopneas are defined as temporary reductions in breathing lasting at least 10 seconds; apneas are complete disruptions in breathing greater than 10 seconds, and lasting as long as one minute (Ho, 2011). An alternative measure of breathing disturbance severity is the Respiratory Disturbance Index (RDI) which includes respiratory event-

related arousals (RERAs) in addition to apneas and hypopneas (Ho, 2011); these are events that do not meet the definition of apneas or hypopneas but that involve definite arousal from sleep. While many clinicians and researchers equate the AHI with the RDI, the American Academy of Sleep Medicine (AASM) utilizes the RDI as the measure of OSA severity as detailed in Table 1 below (Epstein, 2009); these categories also apply to the AHI.

Table 1. OSA severity as defined by the AASM.

| OSA Severity | RDI Measurement (events/hour) |
|--------------|-------------------------------|
| Mild OSA | 5 - 14 |
| Moderate OSA | 15 - 30 |
| Severe OSA | >30 |

Polysomnography

A full-night sleep evaluation conducted in an accredited sleep facility and attended by a certified sleep technician is considered the gold standard for objective confirmation of OSA. Several “channels” (i.e., measurements of objective clinical parameters) are required during a polysomnography (PSG): cardiac activity (via ECG), brain activity (via EEG), visual movements (via electrooculogram), muscle activity (via electromyogram), airflow rate, oxygenation, respiratory movement, and body position (Ho, 2011). The measurement and clinical documentation of these physical parameters provides data to calculate the AHI and/or RDI by an experienced, board-certified clinician (Epstein, 2009). Patients spend an entire night undergoing evaluation of their sleep and breathing patterns during the PSG. Split-night testing may be undertaken in patients with a confirmed OSA diagnosis in the initial 2 hours of the PSG: following documentation of the AHI/RDI, titration of positive airway pressure therapy for treatment is conducted in the remaining hours (Kushida, 2005). While PSG is often the preferred test for OSA diagnosis, factors such as scoring methodology, inter-rater agreement in scoring, and night-to-night variability may affect the reliability and validity of the results (Trikalinos, 2007).

Home Sleep Testing

As an alternative to facility-based testing, different types of portable home sleep testing (HST) monitors may be used in combination with clinical evaluation for the diagnosis of OSA. The amount of clinical data collected with the various monitors differs: the AASM recommends that at a minimum, airflow, respiratory effort and blood oxygenation should be recorded (Collop, 2007). Full-night PSG utilizes Type I monitors; Type II monitors measure the same information as Type I but

are portable and/or unattended (Collop, 2007). Type III and IV devices utilize fewer channels and record less clinical data as detailed in Table 2 below (adapted from Balk, 2011).

Table 2. Sleep testing monitors.

| Type | Place of use | Number of channels | Clinical data collected |
|------|----------------|--------------------|--|
| I | Sleep facility | Usually 14-16 | ECG, EEG, EOG, EMG, airflow, SaO ₂ , effort |
| II | Home | ≥ 7 | May include all data listed for Type I |
| III | Home | ≥ 4 | Airflow +/- effort, ECG, SaO ₂ |
| IV | Home | At least 1-3 | Includes all monitors not fulfilling Type III criteria |

ECG: electrocardiogram; EEG: electroencephalogram; EMG: electromyogram; EOG: electrooculogram; SaO₂: oxygen saturation

1.3 Treatment Options

Several treatment options to alleviate obstruction of the airway are prescribed for patients with OSA. After consideration of lifestyle changes such as weight loss, smoking cessation and decreased alcohol consumption, first-line therapy typically involves positive airway pressure (PAP) devices (Epstein, 2009). For patients who do not respond to PAP, alternate approaches include dental appliances and surgery to alter the obstructive anatomy. Additional choices may include medication, atrial pacing and positional therapy, but were not the focus of the AHRQ report and as such will not be described in detail here. For all of the treatment options described, however, it is important to note that the evidence linking treatment to improvement in objective outcomes such as cardiovascular events is relatively weak (Pack, 2009); as such, effectiveness of these options is primarily described in terms of improvements in AHI and/or RDI alone.

Continuous Positive Airway Pressure (CPAP)

CPAP involves the continuous supply of pressurized air to a patient through a mask in order to keep the airway fully open during inhalation and exhalation. A titration process is undertaken to arrive at the maximum effective pressure able to be tolerated comfortably by the patient (Ho, 2011). Common side effects include claustrophobia, along with nasal and oral dryness (Balk, 2011), which may contribute to suboptimal compliance with therapy. Several modifications exist to decrease side effects of PAP such as heated humidification to combat dryness, and alternate modalities like auto-titrating PAP (APAP), bilevel PAP (BPAP) or variable PAP (VPAP). In patients who require very high pressures, these alternate modalities provide different inspiratory and expiratory pressures,

which may increase tolerance as well as compliance with therapy. Treatment with PAP is long-term with annual evaluation to assess therapy response as well as any equipment difficulties (Epstein, 2009).

Mandibular Advancement Devices (MADs)

Oral devices, custom-fitted by specialized dentists, may be used to treat patients with mild-to-moderate OSA. MADs are the most prescribed form of oral appliances and may also be used in patients intolerant to PAP therapy (Ahrens, 2011). These devices work by advancing the lower jaw, thereby increasing the airway space during sleep (Ho, 2011). MAD use may be limited by insufficient dentition for anchoring of the appliance and the presence of jaw dysfunction (Epstein, 2009). Side effects may include jaw or tooth pain, and potential aggravation of temporomandibular joint disease (Epstein, 2009). Annual appointments and periodic sleep testing are recommended following initial titration to evaluate continued successful management of OSA.

Surgical Procedures

Reserved predominantly for patients with moderate-to-severe OSA who have failed PAP therapy, surgical techniques designed to alter the anatomic space of the mouth and throat are also potential treatment options. For patients with enlarged tonsils, tonsillectomy and/or adenoidectomy may provide relief. Other common invasive procedures include uvulopalatopharyngoplasty (UPPP), in which the soft palate and surrounding tissue in the back of the mouth are removed to relieve airway obstruction, and maxillomandibular advancement (MMA), in which the upper and lower jaws are repositioned (Mayo Foundation, 2012). Tracheostomy, in which an opening in the windpipe is made, is a surgery typically reserved for patients who have failed all other treatment options. Following surgery, some patients may continue to require PAP therapy to effectively manage the symptoms of OSA. In addition to side effects that may occur with any surgical procedures (anesthesia risks, bleeding, infection risk and sudden death), other potential side effects of OSA surgery include speech or swallowing problems, taste alteration, and transient nerve paralysis (Balk, 2011).

Weight Loss Interventions

A less-invasive approach to the management of OSA involves the use of defined weight loss programs. As obesity is a significant cause of OSA in many patients, decreasing body fat may significantly improve AHI and associated symptoms of OSA. Potential interventions involve strict calorie control with or without structured physical exercise. Exercise alone may impact patients with OSA by decreasing AHI and improving sleep quality (Kline, 2011). Structured programs involve multiple weekly sessions with trainers and/or dieticians. Following

significant weight loss ($\geq 10\%$ of body weight), patients will require reassessment of their OSA along with continued monitoring for maintenance of weight reduction and any re-emergence of symptoms (Epstein, 2009).

2. Clinical Guidelines

2.1 Diagnosis

A. Polysomnography (PSG)

- **American Academy of Sleep Medicine (2009)**

http://www.aasmnet.org/Resources/clinicalguidelines/OSA_Adults.pdf

Full-night PSG is recommended to diagnosis OSA, but split-night studies may be an alternative to one full-night study if AHI/RDI ≥ 40 /hr, or 20 – 40/hr based on clinical judgment, during at least 2 hours of PSG. Diagnosis is confirmed when the number of obstructive events on PSG is > 15 events/hr or > 5 events/hour in patients presenting at least one symptom, such as insomnia. OSA severity is defined as mild for RDI ≥ 5 and < 15 , moderate for RDI ≥ 15 and ≤ 30 , and severe for RDI > 30 /hr.

- **Institute for Clinical Systems Improvement (2008)**

http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive_.html

When possible, a split-night study should be performed. Several definitions for the diagnosis of OSA are used, but for practical purposes the CMS definition is most useful, defining OSA as AHI or RDI ≥ 15 events/hour or >5 and ≤ 14 events/hour with at least one documented symptom. OSA severity is determined by the worst impairment rating of three domains: sleepiness, respiratory disturbance, and gas exchange abnormalities.

B. Home Monitors

- **American Academy of Sleep Medicine (2009)**

http://www.aasmnet.org/Resources/clinicalguidelines/OSA_Adults.pdf

The use of home monitors as an alternative to PSG should be restricted to patients with a high pretest likelihood of moderate-to-severe OSA, or to patients for whom PSG is impossible due to critical illness, immobility, or other safety concerns. Home monitors are not indicated for patients suspected of having a comorbid sleep disorder or other significant comorbidities that could weaken their accuracy (e.g. moderate-to-severe pulmonary disease). Home monitors should only be used in the diagnosis of OSA in conjunction with a comprehensive sleep evaluation performed by a board certified sleep specialist or individual who satisfies all criteria for the sleep medicine certification examination. An appropriately trained practitioner must apply the home monitor sensors or

directly train the patient in correct application of the sensors. Patients with high pretest probability of OSA who experience “technically inadequate” home testing or receive negative test results should receive PSG.

- **Institute for Clinical Systems Improvement (2008)**

- http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive.html

Unattended home testing, in conjunction with a comprehensive sleep evaluation, is an option for patients with high pretest probability of moderate-to-severe apnea when initiation of treatment is urgent and PSG is not readily available, patients are unable to be studied through PSG, and for patients with significant comorbid conditions, including comorbid sleep disorders. Home monitors should not be used in an unattended setting in patients with atypical or complicating symptoms. Patients suspected of having OSA that receive a negative home test result should receive follow-up PSG. Home tests should be interpreted by individuals qualified in the diagnosis of treatment sleep disorders.

- **National Institute for Health and Clinical Excellence (NICE) (2010)**

- <http://www.nice.org.uk/nicemedia/live/11944/40085/40085.pdf>

Moderate-to-severe OSA can be diagnosed from patient history and a sleep study using oximetry or through other monitoring devices unattended in the patient’s home. Additional evaluation in a sleep laboratory or in the home may be required to monitor further physiological variables, particularly when alternative diagnoses are being considered. OSA severity is determined through symptom severity and sleep study results.

2.2. Treatment

A. Positive Airway Pressure (PAP)

- **American Academy of Sleep Medicine (2009)**

- http://www.aasmnet.org/Resources/clinicalguidelines/OSA_Adults.pdf

CPAP is indicated for the treatment of moderate-to-severe OSA, mild OSA, improving self-reported sleepiness, and improving quality of life. Full-night PSG is the preferred titration approach, though split-night studies are usually sufficient to determine the optimal CPAP level. BPAP or APAP are treatment options for CPAP-intolerant patients.

- **Institute for Clinical Systems Improvement (2008)**

http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive_.html

PAP is among the most effective treatment options available for patients with OSA. The treatment success of PAP depends on patient adherence, which can be improved through patient education, proper mask fitting, and routine follow-up by clinician and DME providers. CPAP is the most commonly used PAP device. APAP is an alternative for patients intolerant to CPAP and may be used for an unattended CPAP titration following a positive sleep study or when there is a required change in CPAP pressure. Bi-level PAP is not recommended as initial treatment for OSA, but may be beneficial for patients with concurrent or more severe COPD or hyperventilation syndromes. A one-month follow-up evaluation to determine treatment acceptance and success is necessary, and routine follow-up thereafter should occur at least annually to ensure patient compliance.

- **National Institute for Health and Clinical Excellence (NICE) (2010)**

<http://www.nice.org.uk/nicemedia/live/11944/40085/40085.pdf>

CPAP is recommended as a treatment option for patients with moderate-to-severe symptomatic OSA. CPAP should only be used to treat patients with mild OSA if lifestyle advice and other treatment options have failed and symptoms impact the patient's quality of life. Masks should be replaced at least annually and long-term follow-up is important to ensure treatment compliance. The type of PAP utilized should depend on individual patient requirements.

B. Oral appliances

- **American Academy of Sleep Medicine (2009)**

http://www.aasmnet.org/Resources/clinicalguidelines/OSA_Adults.pdf

Oral appliances are indicated for use in patients with mild to moderate OSA who are inappropriate candidates for CPAP, who are unsuccessful with CPAP or other behavioral modifications, or prefer oral devices to CPAP. Candidates for oral appliances require adequate jaw range of motion, sufficient healthy teeth to seat the appliance, no important TMJ disorder, and adequate manual dexterity before initiating treatment. Qualified dental personnel should fit the oral device, and practitioners with training in sleep medicine or sleep related breathing disorders should oversee the patient's dental management. Following final adjustment and fitting, patients with OSA should receive PSG or a Type III sleep study with the oral appliance in place to ensure therapeutic benefit. Follow-up with a dental specialist is recommended every six months for the first year, and at least annually thereafter to assess symptoms and appropriate use.

- **Institute for Clinical Systems Improvement (2008)**

- http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive_.html

Oral devices are a recommended treatment option for patients with mild OSA who have failed to respond to behavioral modifications or who are intolerant of PAP. MADs may be successful for patients with mild OSA with an obstruction in the oropharynx and tongue base region. Follow-up evaluation to determine treatment acceptance and success is necessary.

C. Upper Airway Surgery

- **American Academy of Sleep Medicine (2010)**

- http://www.aasmnet.org/Resources/PracticeParameters/PP_SurgicalModificationsOSA.pdf

Most surgical interventions of the upper airway have low quality of evidence to support their use in treating OSA and therefore are not recommended as first-line treatments. MMA is a treatment alternative for patients with severe OSA who cannot tolerate or are unwilling to adhere to PAP, or in whom oral devices have been found ineffective or undesirable. RFA may be effective for patients with mild to moderate OSA who cannot tolerate or are unwilling to adhere to PAP, or in whom oral devices are ineffective or undesirable. LAUP and UPPP as a sole procedure are not routinely recommended as preferred treatment options.

- **Institute for Clinical Systems Improvement (2008)**

- http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive_.html

Patients with OSA should be referred to an ENT to consider surgical treatment options if significant anatomic problems exist. UPPP is typically considered a first-line surgical treatment of OSA when the uvula, palate and redundant pharynx are determined to be the major site of anatomic obstruction. MMA is indicated for patients with base tongue obstruction, severe OSA, morbid obesity, and failure of other treatments.

D. Behavioral Strategies

- **American Academy of Sleep Medicine (2009)**

- http://www.aasmnet.org/Resources/clinicalguidelines/OSA_Adults.pdf

Weight loss is recommended for all overweight OSA patients, but should not constitute the primary treatment for OSA due to low success rates of dietary programs and low cure rates for dietary approaches alone. Following significant weight loss, a follow-up PSG is indicated to determine whether PAP therapy is still beneficial or adjustments to the PAP level are required.

Positional therapy is a second-line treatment option or can complement primary treatment for OSA in patients with low AHI in the non-supine position. OSA correction by position adjustment should be documented with PSG before starting positional therapy as a primary therapy, and positional treatment should be initiated with a positioning device.

- **Institute for Clinical Systems Improvement (2008)**

http://www.icsi.org/sleep_apnea/sleep_apnea_diagnosis_and_treatment_of_obstructive_.html

Behavioral modifications, including weight loss, reduced alcohol consumption, sleep position, improved sleep hygiene, and integrated PAP preparation, may reduce the severity of OSA symptoms. Weight loss program should be encouraged as a treatment option for patients with OSA, including patients who are only moderately overweight. Patients who lose or gain weight should have their PAP settings reassessed.

- **National Institute for Health and Clinical Excellence (NICE) (2010)**

<http://www.nice.org.uk/nicemedia/live/11944/40085/40085.pdf>

Lifestyle management support, including helping people to lose weight, stop smoking, and decrease alcohol consumption should be considered as a primary therapy for adults with mild OSA. CPAP should only be used to treat patients with mild OSA if lifestyle advice and other treatment options have failed and symptoms impact the patient's quality of life.

3. Medicaid, Medicare, National and New England Private Insurer Coverage Policies

3.1 Diagnosis of OSA

Medicare

<http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=330&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAAAA&>

<http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=11528&ContrId=137&ver=62&ContrVer=1&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=Connecticut&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAAAA&>

A national coverage determination (NCD) was passed in 2009 providing coverage of sleep tests for the diagnosis of OSA in patients with clinical signs and symptoms of OSA. The following types of testing are included in the policy:

- Type I attended polysomnography (PSG) conducted in a sleep facility
- Type II or III devices with studies performed unattended in or out of a sleep facility, or attended in a sleep facility
- Type IV monitors, evaluating at least 3 channels (including airflow), performed unattended in or out of a sleep facility, or attended in a sleep facility
- Sleep testing monitors evaluating at least 3 channels (including actigraphy, pulse oximetry and peripheral arterial tone), conducted unattended in or out of a sleep facility, or attended in a sleep facility

A local coverage determination (LCD) regarding treatment of OSA in Medicare patients in the 6 New England states provides coverage of PSG and HST for the diagnosis of OSA. The HST must be unattended and utilized in the patient's home with instruction on appropriate use. The education may not be given by a durable medical equipment (DME) supplier. HST devices must meet the following criteria:

- Type II: measures and records ≥ 7 channels, including electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), heart rate, airflow, respiratory movement and oxygen saturation
- Type III: ≥ 4 channels, including heart rate, airflow, respiratory movement and oxygen saturation
- Type IV: ≥ 3 channels, including airflow

Medicaid

No publicly-available coverage policies for OSA diagnosis were available from Medicaid agencies in the 6 New England states.

National Private Payers

Among national payers, including Aetna, Cigna, Humana and UnitedHealthcare, portable home sleep testing (HST) is considered appropriate for patients utilizing Type II, III and IV devices that adhere to the characteristics described in the NCD listed above. HST is part of a comprehensive sleep evaluation in patients without a previous diagnosis of OSA, who are physically and cognitively capable of using a portable device, and who lack comorbidities that may impact the accuracy of testing, such as chronic obstructive pulmonary disease (COPD) or BMI > 45. Additionally, Cigna considers HST in patients with a high pre-test probability of OSA. In contrast, Humana does not require prior authorization for the use of HST.

Full-night PSG, conducted in a sleep facility, is medically necessary in patients with a low pre-test probability of OSA, who have one or more comorbidities (e.g. epilepsy, congestive heart failure) that may degrade the quality of HST, are unable to successfully use HST, or have previous negative or indeterminate HST results. Humana requires prior authorization for the use of PSG.

Aetna, Cigna, Humana and UnitedHealthcare provide coverage of split-night testing in patients undergoing full-night PSG who are diagnosed with OSA. Some policies restrict its use based on diagnosed OSA severity during the initial phase of testing.

Regional Private Payers

BlueCross BlueShield-MA (BCBS-MA), Harvard Pilgrim Health Care (HPHC), HealthNet and Tufts Health Plan provide policies for portable, unattended sleep testing in patients with a high pre-test probability of OSA (e.g., symptoms of excessive daytime sleepiness, duration of symptoms for at least 4 weeks), as well as additional criteria similar to national private payers. HPHC and Tufts Health Plan also require completion of a sleep questionnaire, such as the Epworth Sleepiness Scale

(ESS), prior to sleep testing. Approved Type III devices for HST include those measuring oxygen saturation, respiratory movement, airflow and heart rate with at least 4 recording channels (BCBS-MA and HPHC). HealthNet provides coverage of Type II, III and IV (at least 3 channels) devices, and Tufts Health Plan utilizes Type II and III devices.

The use of unattended, portable home testing is considered investigational and not medically necessary by BlueCross BlueShield-RI (BCBS-RI) and BlueCross BlueShield-VT (BCBS-VT).

Full-night PSG is considered to be medically necessary by regional payers for patients with multiple significant symptoms of OSA (e.g., ESS > 10), unexplained hypertension and obesity (BMI > 35), or in patients with key comorbidities. Tufts Health Plan requires documentation of a patient's BMI and ESS prior to full-night PSG, while HPHC requires completion of the ESS or Berlin Questionnaire (BQ). As with national payers, split-night testing is covered in select patients with AHI thresholds observed during full-night testing (≥ 5 -40).

3.2 Treatment of OSA – Positive Airway Pressure

Medicare

<http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=226&ncdver=3&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAAAA&AA&>

<http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=11528&ContrId=137&ver=62&ContrVer=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAAAA&AA&>

An NCD originally passed in 1986, provides coverage of continuous positive airway pressure (CPAP) in adults diagnosed with OSA, with an AHI/RDI ≥ 15 or AHI/RDI of 5-14 with at least one documented symptom (e.g., insomnia). CPAP is provided for an initial period of 12 weeks. Use beyond 12 weeks is covered in individuals with demonstrated benefit from CPAP therapy.

Patients with clinically identified risk-factors for OSA who do not qualify for CPAP therapy may be eligible for Coverage with Evidence Development (CED). Qualifying studies include those evaluating CPAP as a diagnostic tool or CPAP use without prior confirmatory sleep testing.

An LCD, affecting the 6 New England states, provides additional detail regarding PAP therapy in the treatment of OSA. Initial therapy with CPAP is covered in patients meeting the NCD criteria. In addition, patients must have had a clinical evaluation for OSA prior to a sleep test, and received education on device use and care from the provider. Bi-level PAP (BPAP) therapy (without back-up rate) is second-line treatment when CPAP is ineffective and the patient does not meet treatment goals during titration or home use. Continued use of PAP therapy beyond 3 months requires clinical evaluation by the treating physician, along with documentation of symptom improvement and patient adherence (use \geq 4 hours/night on 70% of nights over a 30-day period).

Medicaid

CPAP coverage policies were available from Medicaid agencies in Maine, New Hampshire, and Rhode Island. All three states require prior authorization for the use of CPAP. CPAP is covered in Rhode Island for adults with moderate-to-severe OSA, defined as documentation of at least 30 apneic episodes, each lasting a minimum of 10 seconds, during 6-7 hours of recorded sleep.

National Private Payers

In national payer policies from Aetna and UnitedHealthcare, CPAP is first-line therapy in patients diagnosed with OSA and AHI/RDI measurements as described by the NCD/LCD policies of CMS. Differences among the national payers arise in the tiering of alternate PAP modalities: CPAP and auto-titrating PAP (APAP) are first-line therapies for Aetna and Humana, while Cigna reserves use of APAP and flexible-CPAP for patients with demonstrated intolerance of CPAP, and variable PAP (VPAP) is second-line therapy with Aetna policy. Humana also tiers VPAP, BPAP and demand PAP (DPAP) as second-line therapy for patients who fail CPAP or APAP. Aetna and Humana consider flexible-CPAP to be experimental and do not cover it.

Regional Private Payers

As with national payers, CPAP is universally covered as first-line therapy in the treatment of OSA, defined using AHI/RDI criteria as described in the NCD/LCD policies of CMS. Mirroring the variations of national payer policies, differences arise in the tiering of PAP interventions. Groups such as Tufts Health Plan may cover APAP as first-line therapy; however many payers reserve coverage of APAP, BPAP or VPAP as second-line therapy. PAP therapy is covered initially over 3 months, with subsequent evaluation of symptom improvement and patient adherence. Compliance is defined as use \geq 4 hours/night, 6 nights/week or 70% of nights, generally during a 30-day period. Connecticut policies cover CPAP for OSA as described above, but do not address alternative versions of PAP.

3.3 Treatment of OSA – Oral Appliances

Medicare

<http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=28603&ContrId=137&ver=14&ContrVer=1&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=Connecticut&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAAABAAAA&>

While there is no NCD in place for the use of oral appliances, an LCD providing coverage policy for the 6 New England states allows the use of a custom-fabricated mandibular advancement devices provided by a licensed dentist in patients with: (a) an AHI/RDI ≥ 15 with a minimum of 30 events; or (b) an AHI/RDI = 5-14 with a minimum of 10 events and at least one documented symptom. If the AHI/RDI is > 30 , there should be documented intolerance of or contraindications to PAP therapy.

Medicaid

No publicly-available coverage policies for oral appliance use in OSA were available from Medicaid agencies in the 6 New England states.

National Private Payers

Custom-fitted and prefabricated oral appliances are covered therapeutic options for patients with OSA who are eligible for treatment with CPAP/APAP under Aetna, Cigna and Humana policies. For patients with severe OSA (AHI ≥ 30) who are unable to comply with PAP therapy, Cigna also provides coverage of oral appliances, while Humana recommends upper airway surgery before oral appliances in appropriate surgical candidates. UnitedHealthcare provides coverage of oral appliances in patients with mild OSA (AHI/RDI ≥ 5 , < 15) who are intolerant or who refuse PAP therapy. For patients with moderate-to-severe OSA (AHI/RDI ≥ 15), oral appliances may be used in combination with PAP therapy, or when patients are intolerant or refuse PAP. No coverage is provided for over-the-counter oral appliances.

Regional Private Payers

Most regional payers provide coverage for custom-fitted oral appliances. While the specific criteria regarding eligibility vary, included patients are diagnosed with mild-to-moderate OSA and are intolerant to or have failed CPAP therapy. HealthNet and Tufts Health Plan may also provide oral appliances to patients with severe OSA who have failed CPAP therapy. Some plans require patients to be free of temporomandibular dysfunction or pain, as well as periodontal disease (BCBS-MA,

BCBS-VT), and Connecticare's policy requires patients to be less than 150% of ideal body weight. Over-the-counter devices are generally not covered.

3.4 Treatment of OSA – Surgical Procedures

Medicare

<http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=30731&ContrId=268&ver=17&ContrVer=1&CoverageSelection=Local&ArticleType=All&PolicyType=Final&s=Connecticut&Keyword=sleep+apnea&KeywordLookUp=Title&KeywordSearchType=And&bc=gAAAABAAAA&>

The Centers for Medicare & Medicaid Services have not made an NCD for surgical procedures in the treatment of OSA, nor is there an LCD for New England. An LCD for Medicare patients in Wisconsin provides coverage criteria for uvulopalatopharyngoplasty (UPPP) and maxillomandibular advancement (MMA) (with or without supplementary procedures) in patients with an AHI/RDI ≥ 15 , primarily based on failure or intolerance of CPAP and other non-invasive treatment modalities, along with documented counseling and appropriate abnormal anatomy. Tracheostomy is reserved as a treatment option in patients with OSA that is unresponsive to other means of therapy. Non-covered procedures include laser-assisted uvulopalatoplasty (LAUP), palatal implants and radiofrequency ablation.

Medicaid

No publicly-available coverage policies for surgical procedures for OSA were available from Medicaid agencies in the 6 New England states.

National Private Payers

While all reviewed policies provide specific prior authorization criteria for surgical interventions, Humana explicitly requires review of all surgery requests by the Medical Director. Aetna, Cigna, Humana, UnitedHealthcare and Wellpoint/Anthem allow for coverage of UPPP and MMA in patients who meet criteria including intolerance to PAP and having the appropriate abnormal anatomy for the specific procedure. Tracheostomy is considered to be a procedure of last resort, appropriate for patients who have failed all other available treatment options. LAUP is considered investigational by Cigna, Humana, UnitedHealthcare and Wellpoint/Anthem; Aetna provides coverage in individual cases when patients are unable to undergo UPPP and have failed non-invasive therapies. Radiofrequency ablation of different parts of the tongue, mouth and throat is not covered by Aetna, Cigna, Humana and Wellpoint/Anthem, while UnitedHealthcare may cover

the procedure in patients with mild-to-moderate OSA (AHI/RDI ≥ 5 , ≤ 30). Palatal implants are not covered.

Regional Private Payers

Prior authorization of surgical treatment options is specifically mentioned in policies available from HPHC, Tufts Health Plan and BCBS- VT. Most regional payers provide coverage for UPPP in patients who may have failed or are intolerant to CPAP therapy or other non-invasive treatment options. Eligibility for the described surgical procedures requires patients to have documentation of abnormal anatomy. MMA is similarly covered by all regional payers except for BCBS-RI. Tracheostomy is exclusively reserved for patients who have failed, are intolerant of, or are not appropriate candidates for all other treatment options. Procedures that are not covered by regional payers include LAUP, radiofrequency ablation of the tongue, mouth and/or throat, and palatal implants.

Important prior authorization criteria also specified in surgical policies for the treatment of OSA include failure of weight loss (BCBS-VT); in addition, Connecticare, HPHC and HealthNet require diagnosis or documentation of OSA within the past 1-2 years. Eligibility for MMA by Connecticare and HealthNet includes failure of other surgical approaches (including UPPP).

4. New Evidence Following AHRQ Review

4.1 Updated Search

We conducted an updated systematic literature search of MEDLINE and Cochrane Central Register of Controlled Trials utilizing the search criteria defined by the AHRQ review. The search timeframe spanned from August 1, 2011 to September 14, 2012, with 1,026 records identified. The specific timeframe reflected the gap in current literature between an updated systematic review conducted by the Center for Evidence-based Policy at the Oregon Health & Science University (Gleitsmann, 2012) and this supplemental report (identical search criteria were used). The abstracts were screened using parameters designated by the AHRQ review (i.e., study type, patient population, comparators and outcomes evaluated). Following removal of duplicate citations and initial screening, full-text review was performed on 186 retrieved articles. Most of these were excluded (n=146) for a variety of reasons, including inappropriate study design (e.g., lack of separate validation cohort or retrospective study for diagnostic studies; not an RCT for treatment evaluation with CPAP), or no outcomes of interest.

Twenty-eight articles were evaluated for new evidence (Appendix B); findings from the major studies assessed are described in further detail below.

4.2 Diagnosis of OSA

Home Sleep Testing

One large, multicenter trial evaluating the use of a Type IV portable monitor versus PSG was identified (Appendix B, Table 1). Masa et al. examined adults (n=348) who were referred to pulmonary evaluation for suspected OSA across 8 centers in Spain (Masa, 2012). Patient baseline characteristics were similar to studies reported in the AHRQ review: mean age = 49, 76% male and average BMI = 31 kg/m². Following a randomized crossover design, each patient underwent PSG and HST within a 3-day period. Sensitivity and specificity of home testing (using AHI cutoffs on the home monitors) were estimated to be 87% and 86% respectively for mild OSA, 71% and 90% for moderate OSA, and 67% and 92% for severe OSA.

Questionnaires

Additional data regarding the use of questionnaires in the diagnosis of OSA were found in 2 large studies (Martinez, 2011; Silva, 2011). In the first of these, the use of the ESS measured before and after PSG was assessed in a cohort of patients (n=929) evaluated for OSA at a university-affiliated sleep clinic (Martinez, 2011). Patients were broadly similar in demographic composition to those found in the AHRQ-reviewed study of ESS (Drager, 2010) but with a more severe baseline AHI (24 versus 8 events/hour respectively). The sensitivity of an ESS score >10 to predict an AHI \geq 5 events/hour was estimated to be 54%; the corresponding specificity was 63%.

The second study involved a large cohort of patients enrolled in the Sleep Heart Health Study, and compared the ESS, STOP and STOP-Bang questionnaires, along with a 4-Variable screening tool (Silva, 2011). All patients (n=4,770) also underwent attended HST by trained technicians. Results were dichotomized by diagnosis of moderate-to-severe OSA (RDI 15-30) or severe OSA (RDI > 30). For patients with severe OSA, STOP and STOP-Bang had nearly identical diagnostic accuracy (sensitivity 69-70%, specificity 60%). The ESS showed lower sensitivity (46%) but higher specificity (70%) in comparison. The results with respect to STOP-Bang contrast with the findings of the single study evaluated by the AHRQ review, where Chung and colleagues documented a sensitivity of 100% in patients with severe OSA (AHI > 30) (Chung, 2008).

Clinical Prediction Rules

Four new studies detailing different algorithms and indices for the diagnosis of OSA were identified (Appendix B, Table 5). Similar to findings in the AHRQ review, each study evaluated a unique set of parameters to predict an elevated AHI as determined by PSG, and only 1 of the 4 algorithms was independently validated. One study of note (Hayano, 2011) assessed a large cohort of patients (n=862) utilizing an ECG-based detection algorithm. Sensitivity and specificity were estimated to be 89% and 98% respectively for detecting an AHI \geq 15.

Phased Testing

Two studies evaluated the sequential use of questionnaires as a screening tool, followed by further evaluation by a sleep specialist and/or PSG for OSA (Rusu, 2012; Sert-Kuniyoshi, 2011). Unfortunately, the studies lacked a control population or reference standard, so complete assessment of screening accuracy was not possible. However, findings regarding patient compliance with *testing* were described by Sert-Kuniyoshi et al. In this study, 383 patients attending cardiac rehabilitation at the Mayo Clinic were screened for risk of OSA using the Berlin Questionnaire. Those who completed cardiac rehabilitation and were considered to be high risk after screening (n=132) were referred for further evaluation; however, 21 patients (16%)

immediately declined further testing, and of the 111 patients who did receive appointments for sleep testing, only two-thirds attended and completed their evaluation.

4.3 Treatment of OSA

CPAP Therapy

A large (n=723) multicenter trial in Spain evaluated patients with moderate OSA (AHI ≥ 20) but without symptoms of daytime sleepiness (ESS ≤ 10), and focused on objective clinical events as a primary outcome (Barbé, 2012). Patients were randomized to CPAP therapy or no intervention and were followed over a median of 4 years. Incidence of systemic hypertension and/or cardiovascular events (i.e., nonfatal myocardial infarction or stroke) did not differ statistically between groups (9.2 vs. 11.0 per 100 person-years for CPAP and no intervention respectively, $p=0.20$).

CPAP Therapy and MADs

A small randomized controlled trial (n=57) of patients with mild-to-moderate OSA evaluated the efficacy, compliance and side effects associated with the use of nasal CPAP, MADs, or sham MADs (Aarab, 2011a). Over a 6-month period, patients using CPAP and an MAD experienced statistically-significantly ($p \leq 0.002$) larger declines in AHI from baseline (19.5 and 16.3 events/hr respectively) as compared to patients in the sham group (5.2), although the change in AHI between active treatment arms did not differ statistically. Interestingly, similar rates of compliance were found among the 3 arms (83%, 91%, and 94% for CPAP, MAD, and sham MAD respectively). In a 1-year follow-up of patients receiving active treatment (n=28), those receiving CPAP maintained a reduced AHI relative to baseline (-6.4) while patients on MAD did not (+0.1), a difference that was statistically-significant ($p=0.001$).

Surgical Interventions

Four new studies of different surgical procedures met the original inclusion criteria provided by the AHRQ review. Two of these studies were uncontrolled case series, and two were comparisons of different surgical procedures without a non-surgical control group.

Weight Loss Interventions

Three new studies assessing the impact of exercise programs were identified (Appendix B, Table 16). Patients in the exercise interventions received combined aerobic and/or strength-training

versus stretching or no training. Studies were generally small, ranging from 20 – 45 patients, with each lasting 3 months. Overall, patients in structured exercise programs experienced significant changes in AHI as compared to control arms (-4.2 to -8.5 for exercise vs. -0.6 to +4.5 for control, $p \leq 0.02$ for all comparisons). In contrast to the studies of weight loss interventions described in the AHRQ report, no significant changes in weight were observed in the newer studies (Kline, 2011; Servantes, 2011).

4.4 Combined Diagnosis and Treatment of OSA

An additional randomized controlled trial (RCT) evaluated home versus in-laboratory sleep testing followed by CPAP treatment (Kuna, 2011). While this trial did not meet the original inclusion criteria of the AHRQ review, which stipulated that sleep testing studies required confirmation of results via PSG in all subjects, the randomized design and focus on patient outcomes are an important contribution to the literature. In this study, 296 individuals (mean age: 53.4 years; 95% male) with suspected OSA were enrolled at 2 Veteran's Affairs medical centers. Those randomized to the home testing pathway performed an unattended sleep study using a Type III monitor. Those with an AHI ≥ 15 received 4-5 nights of titration using autotitrating CPAP until a satisfactory pressure was reached. To account for the possibility of false-negative results at lower levels of OSA severity, patients with an AHI < 15 received in-laboratory PSG followed by autotitrating CPAP if an OSA diagnosis was made. All patients in the in-laboratory pathway received PSG; if OSA was diagnosed during the first part of the night, fixed titration of CPAP was performed. All patients were followed for 3 months. The primary outcome of interest was the change from baseline in the Functional Outcomes of Sleep Questionnaire (FOSQ), which measures the impact of sleepiness and fatigue on work performance, chores, and leisure activities. The hypothesis tested was that the home testing approach was not clinically inferior to that of in-laboratory testing (i.e., a "noninferiority" study design).

A total of 113 and 110 home- and lab-tested individuals respectively were diagnosed with OSA and initiated CPAP treatment. Following 3 months of follow-up, statistically-significant ($p < .0001$) improvements in the total FOSQ score were noted for both groups (mean changes of 1.74 and 1.85 for home and in-lab respectively), with no difference between groups ($p = .77$). The median percentage of days with at least 4 hours of CPAP use was slightly greater than 50%, and on average, the number of AHI events per hour was less than 5 in both groups. The authors state that the relatively low rate of CPAP adherence may have been due to their conservative accounting of missing data (i.e., counted as no use) as well as social factors influenced by participants' low socioeconomic status.

4.5 Summary of Relevance of New Evidence

Diagnosis of OSA

Newly-obtained evidence includes a large multicenter study of the accuracy of Type IV home sleep testing, with results similar to reported values from the AHRQ review. Additional questionnaire studies provide a more complete and perhaps realistic picture of diagnostic accuracy in comparison to single studies evaluated for the AHRQ review; in the specific case of STOP-Bang, for example, sensitivity was 69-70% in newer studies vs. 100% in the single AHRQ-reviewed study. Four new studies of clinical prediction algorithms were identified; as with the studies evaluated in the AHRQ review, however, each algorithm was unique and only 1 was independently validated, making interpretation across studies problematic. Finally, new studies on phased testing approaches, while potentially valuable in terms of measuring compliance with sleep evaluation, were not designed to provide information on the diagnostic accuracy of such testing vs. facility-based PSG or some other reference standard.

Treatment of OSA

Similar to the findings of the AHRQ review, a new RCT found no statistically-significant differences in the risk of cardiovascular events for CPAP vs. no intervention. Other studies comparing CPAP and MAD are also consistent with the AHRQ review's findings—while both modalities appear to be effective, CPAP appears to better control AHI over the longer term. Recent studies of surgical interventions do not add materially to the evidence base, as 2 of these studies were uncontrolled and the other 2 studies compared different surgical interventions rather than to a non-surgical control arm.

Finally, new evidence on weight-control and/or exercise-based interventions appears to add to the original evidence base suggesting that some weight-loss interventions are effective in reducing OSA severity among obese patients; of note, results from the newer studies suggest that these benefits are independent of actual weight loss itself.

Combined Diagnosis and Treatment of OSA

A new RCT analyzed home- and laboratory-testing and treatment pathways, providing a “real-world” perspective on the 2 approaches. Improvement in functional outcomes, decreases in AHI, and CPAP adherence was found to be similar for both study arms, suggesting that a home-based pathway is comparable to a laboratory-based algorithm for diagnosis and treatment of OSA.

5. State-Specific Data

In order to gain further understanding regarding prevailing practice patterns in the region, data on sleep testing as well as CPAP utilization were obtained from selected New England payers. Information was provided by Medicaid agencies in Vermont and Massachusetts (MassHealth), as well as from the HealthCore Integrated Research Database™, which includes information on Wellpoint beneficiaries in Connecticut, Maine, and New Hampshire. All data obtained were for calendar year 2011.

5.1 Testing Frequency & Cost

Information on both numbers of patients tested and tests received is presented in Table 3 below for facility-based and home testing. For all payers, the proportion of patients tested in the population aged >16 was approximately 1%. Two of the 3 payers provide coverage for home testing (Vermont Medicaid does not); however, the vast majority of testing (94-99%) still appears to be facility-based, in contrast to anecdotal evidence provided by clinical experts. For the payers providing data on both numbers of testing claims and unique patients receiving tests, the number of tests per patient per year was in the range of 1.2-1.3.

Table 3. Frequency and type of sleep testing, by regional payer, calendar year 2011.

| Measure | Vermont Medicaid (n=68,000) | MassHealth (n=770,000) | HealthCore (n=1,500,000) |
|------------------------------|--------------------------------|---------------------------|-----------------------------|
| Patients Tested | 760 (1.1%) | 6,837 (0.9%) | 15,479 (1.0%) |
| In Facility | 760 (100%) | 6,800 (99.5%) | 14,522 (93.8%) |
| At Home | NC | 37 (0.5%) | 957 (6.2%) |
| Total Number of Tests | 974 | 8,487 | NR |
| Tests per Patient | 1.28 | 1.24 | NR |

NC: Not covered; NR: Not reported

NOTE: N=# of beneficiaries age >16 years in 2011

Payment data were provided by Vermont Medicaid. Testing costs totaled \$629,453 in calendar 2011, which equated to \$828 per patient tested and \$0.77 per member per month (PMPM) across all beneficiaries age >16 years.

5.2 CPAP Utilization & Cost

Data on CPAP utilization were provided by HealthCore and Vermont Medicaid. The proportion of individuals with at least one claim for a CPAP device or accessory was similar for the 2 payers: a total of 38,947 individuals had such claims in HealthCore (2.6% of all beneficiaries in the sample), while 1,390 Vermont Medicaid beneficiaries incurred CPAP claims (2.0%). Of note, these counts are higher than the counts of tested patients, as they reflect both newly-diagnosed patients initiating therapy *and* prevalent cases obtaining new devices or accessories.

As with testing, payment data for CPAP were available only from Vermont Medicaid. In calendar year 2011, a total of approximately \$1.4 million in CPAP-related payments were made, which equated to \$989 per CPAP user and \$1.69 PMPM across all beneficiaries in the sample. Nearly half of these expenses were related to claims for “oxygen concentrators”, devices to monitor and adjust the concentration of oxygen in airflow.

6. Analysis of Comparative Value

Analyses of comparative value focused on selected strategies for both testing and treatment of OSA. In analyses of diagnostic testing, the underlying prevalence of OSA (mild, moderate, and severe) among patients referred for testing was assumed to be 50%. In analyses of treatment, patients were assumed to have moderate OSA (i.e., AHI 15-30) consistent with baseline values in RCTs utilized for the model. The potential cost-effectiveness of competing strategies was compared. Selected strategies were also evaluated in region-focused budgetary impact analyses.

Methods and results are described in further detail below for each type of analysis. Surgery was not compared to other strategies due to differences in OSA severity in available surgical studies relative to other interventions. All input values for the model can be found in Tables 4 and 5 on the following page.

6.1 Cost-Effectiveness

Methods

1. Diagnostic Testing

Cost-effectiveness was evaluated in a hypothetical cohort of 1,000 Medicaid patients age >16 with suspected obstructive sleep apnea. The referent comparator for all strategies was PSG. Outcomes evaluated included total cost (payments), number of individuals diagnosed with OSA, number of false-negative results, and averted PSGs. It was assumed that no person required a repeat of any test in the model. Also, as the timeframe for this analysis ended at the point of diagnosis, we assumed no further clinical or economic sequelae for false-negative test results.

Three distinct strategies were compared to PSG alone, conducted in all 1,000 patients. The first involved screening with the Berlin Questionnaire, with only test-positive patients receiving PSG. The second strategy involved use of a clinical prediction algorithm based on morphometric (i.e., quantitative measurement of anatomy) characteristics of the head and neck, with patients defined as “high-risk” receiving PSG. The final strategy involved the use of Type III monitors for home testing; in this strategy, patients would be diagnosed based on home testing findings alone, and would *not* therefore receive confirmatory PSG. False-positive results were therefore also tallied for this strategy, while averted PSGs were not applicable. Sources of data for each strategy are described in further detail on page 30.

| Table 4. Input parameters for OSA models | | |
|--|----------------------|-----------------------|
| Variable | Input Value | Reference |
| Prevalence of OSA | 0.50 | Assumption |
| OSA severity | Moderate (AHI 15-30) | Assumption |
| Berlin questionnaire sensitivity | 0.93 | Drager et al, 2010 |
| Berlin questionnaire specificity | 0.59 | Drager et al, 2010 |
| Morphometric clinical prediction rules sensitivity | 0.98 | Kushida et al, 1997 |
| Morphometric clinical prediction rules specificity | 1.00 | Kushida et al, 1997 |
| Type III home monitor sensitivity | 0.97 | Amir et al, 2010 |
| Type III home monitor specificity | 0.94 | Amir et al, 2010 |
| Probability of tolerating CPAP | 0.97 | Gagnadoux et al, 2009 |
| Probability of tolerating MAD | 0.88 | Gagnadoux et al, 2009 |
| Probability of treatment success on CPAP | 0.73 | Gagnadoux et al, 2009 |
| Probability of treatment success on MAD | 0.43 | Gagnadoux et al, 2009 |

| Table 5. Costs for OSA models | | | |
|--|---|-------------|------------------------------------|
| Input parameter | CPT codes | Cost | Reference |
| Polysomnography (split night) | 95811 | \$652.83 | 2011 Vermont Medicaid |
| Berlin Questionnaire (one office visit) | 99214 | \$80.67 | CMS Physician Fee Schedule |
| CT for sinus/ maxilla/ mandible w/o contrast and office visit, for morphometric data | 70486, 99214 | \$356.04 | CMS Physician Fee Schedule |
| Type III home monitor | 95806 | \$200.70 | CMS Physician Fee Schedule |
| CPAP (one year rental and accessories) | E0601, A7030, A7031, A7035, A7036, A7037, A7038, A7046, E0562 | \$1184.15 | 2011 Vermont Medicaid |
| BPAP (one year rental and accessories) | E0470, A7030, A7031, A7035, A7036, A7037, A7038, A7046, E0562 | \$1925.73 | 2011 Vermont Medicaid |
| CPAP accessories (yearly) | A7030, A7031, A7035, A7036, A7037, A7038, A7046, E0562 | \$808.90 | 2011 Vermont Medicaid Data |
| MAD (device and inter-dental fixation) | E0486, 21110 | \$2011.94 | CMS Physician Fee Schedule, ResMed |

- *Berlin Questionnaire.* The AHRQ found the Berlin Questionnaire to have low evidence for use of diagnosing OSA; however, it remains one of the most frequently-studied questionnaires for this purpose. The sensitivity and specificity for the Berlin Questionnaire were obtained from a study of 99 individuals (Drager, 2010), the only high-quality study evaluated in the AHRQ report. The questionnaire was assumed to be given during a routine office visit, the cost for which (\$81) was estimated based on the Medicare fee schedule.
- *Morphometric data.* A study of 300 individuals by Kushida (1997) was used as the source for a study of screening with a clinical prediction algorithm based on morphometric measurements. The cost was estimated based on Medicare payments for a CT scan of the sinus/maxilla/mandible and a doctor's office visit to interpret the results.
- *Home monitor.* The phased testing approach using a type III home monitor was based on data from a quality A-rated study (Amir, 2010) of 53 individuals using the Morpheus Hx Type III monitor. The cost of the home monitor was estimated to be approximately \$200 based on data from the Medicare fee schedule.

Split-night PSG was assumed to be the “gold standard” test in all comparisons, and as such, to represent the true result for the patient. The cost of PSG was estimated to be approximately \$650 based on data from Vermont Medicaid.

2. Diagnostic Testing + CPAP Treatment

In these analyses, alternative test-and-treat strategies were analyzed for 1,000 hypothetical Medicaid patients, including (1) home sleep testing + autotitrating CPAP and (2) home sleep testing + split-night PSG for test-positive patients + fixed titration CPAP. Both strategies were compared to a “gold standard” of split-night PSG + fixed titration CPAP for all patients. Compliance with CPAP was assumed to be 100%. The model included 1 year of treatment with CPAP, although no clinical outcomes (other than those of testing) were evaluated. Because the test-and-treat analysis involved a treatment component, however, false-positive results were tallied.

- *Home monitor sleep study + auto-titrating CPAP.* Patients in this strategy would attend a home sleep study, and those who test positive for OSA would then undergo auto-titration of CPAP in order to begin treatment. Diagnostic accuracy and costs of home testing were estimated as in analysis 1 above. The cost of auto-titrating CPAP and related supplies (approximately \$1,200) was estimated from 2011 Vermont Medicaid data.
- *Home monitor sleep study + Split-night PSG + fixed titration CPAP.* Based on input from one of our clinical experts, a second strategy was included in which patients would first have a home sleep study, and those who test positive for OSA would then attend a split-night PSG. Those patients testing positive for OSA in the first part of the night would undergo fixed

titration of CPAP in order to begin treatment. Costs for all components were obtained from Vermont Medicaid data.

- *Split night PSG + fixed titration CPAP.* Patients in this strategy would attend a split-night sleep study with those testing positive for OSA in the first part of the night undergoing fixed titration of CPAP in order to begin treatment. The cost of the split night PSG and the fixed titration CPAP was estimated from 2011 Vermont Medicaid data.

All strategies were also evaluated with the cost for BPAP of treatment in place of CPAP (\$1,900 vs. \$1,200 annually). No differences other than cost were assumed.

3. MAD vs. CPAP Treatment

A 1-year time horizon was assumed for this analysis, beginning at the point of OSA diagnosis. All patients were assumed to be treated with either MAD or CPAP, except individuals who could not tolerate MAD calibration or CPAP titration respectively. Outcomes of interest included treatment cost and rates of treatment success, defined as achievement of an AHI <5 on subsequent sleep testing. Rates of treatment success and ability to tolerate treatment were obtained from a recent head-to-head crossover RCT of 59 patients diagnosed with OSA (Gagnadoux, 2009). We allowed compliance with treatment to vary in this analysis; however, the rates of treatment success in the RCT of interest were for all patients, and so incorporated compliance in the results. Compliance was varied in sensitivity analyses (see Results).

Costs of CPAP were defined as above. Costs of MAD included those of device creation and well as interdental fixation and calibration; estimates for the former were obtained from a regional Medicare contractor (ResMed), while those of the latter came from the Medicare fee schedule.

Results

1. Diagnostic Testing

Findings for analyses of various sleep-testing strategies compared to split-night PSG can be found in Table 6 on the following page. Of the 3 screening strategies, morphometric testing followed by PSG for test-positive patients was the most accurate, with 12 false-negative results per 1,000 patients tested, followed by home testing (14) and the Berlin questionnaire + PSG (35); home testing alone also produced 30 false-positive results. The morphometric strategy was more expensive than PSG alone, owing to the relatively high cost of the CT scan and PSGs conducted in nearly half of individuals. In contrast, the questionnaire and home monitor strategies were cost-saving. Savings in both strategies were driven by lower test costs in comparison to PSG alone. In addition, the questionnaire screening strategy avoided PSG in approximately one-third of tested patients.

Table 6. Outcomes and costs of multiple sleep-testing strategies among 1,000 hypothetical Medicaid patients referred for testing.

| Measure | PSG alone | Morphometric Type III monitor | | |
|---------------------------------|-----------|-------------------------------|-------------|----------------|
| | | + PSG | alone | Berlin Q + PSG |
| Total cost | \$652,830 | \$674,621 | \$200,700 | \$518,066 |
| Received PSG | 1000 | 488 | N/A | 670 |
| Dx with OSA | 500 | 488 | 516 | 465 |
| False negatives | N/A | 12 | 14 | 35 |
| False positives | | N/A | 30 | N/A |
| Averted PSGs | N/A | 512 | N/A | 330 |
| Difference vs. PSG alone | N/A | \$21,791 | (\$452,130) | (\$134,764) |

All numbers are for 1000 patients at moderate-to- high risk of OSA diagnosis

A sensitivity analysis was conducted in which the highest observed specificity for the Berlin questionnaire (95%) replaced the base case value (59%). Under this scenario, the number of PSGs avoided increased substantially (from 330 to 510), and as a result, cost savings nearly doubled to approximately \$250,000. Cost savings would diminish, however, as OSA prevalence rises; when OSA prevalence reaches 90% the costs of the Berlin questionnaire screening strategy would equal those of PSG alone. A second analysis was conducted in which the sensitivity and specificity of home testing were estimated to be 93% and 59% respectively (Santos-Silva, 2009) vs. base case estimates of 97% and 94%. Using these alternative estimates, the number of false positives increased markedly from 30 to 205 per 1000 patients tested, and the number of false negatives also increased (from 14 to 35).

2. Diagnostic Testing + CPAP Treatment

In analyses of various test-and-treat strategies for OSA, both home testing + CPAP strategies were cost-saving relative to split-night PSG+fixed CPAP titration (see Table 7 on the following page). Substantial cost savings (over \$400,000) were realized with a home testing + autotitrating CPAP strategy relative to the referent strategy, regardless of whether CPAP or BPAP was used as the treatment modality. However, this strategy also produced 44 patients per 1,000 with incorrect diagnoses (30 false positives and 14 false negatives). In contrast, use of home testing + PSG in positive patients followed by fixed CPAP had no false positives due to the presence of confirmatory PSG, but also produced lower cost savings (<\$150,000) due to the use of PSG for confirmation. Findings from a sensitivity analysis of home testing that assumed perfect specificity were not markedly different from base case analyses, as specificity was reported to be 94% in the trial report used for base case model input.

Table 7. Outcomes and costs of multiple test-and-treat strategies for OSA among 1,000 hypothetical Medicaid patients referred for testing and treated for 1 year if positive.

| Measure | Sleep lab PSG + fixed titration CPAP / BiPAP | Home monitor + autotitrating CPAP / BiPAP | Home monitor, PSG, fixed titration CPAP / BiPAP |
|--|--|---|---|
| Total cost | | | |
| CPAP | \$1,244,905 | \$811,129 | \$1,112,731 |
| BiPAP | \$1,615,695 | \$1,193,414 | \$1,473,139 |
| Diagnosed with OSA | 500 | 516 | 486 |
| True positives | 500 | 486 | 486 |
| True negatives | 500 | 471 | 471 |
| False positives | 0 | 30 | 0 |
| False negatives | 0 | 14 | 14 |
| Difference vs. sleep lab strategy | | | |
| CPAP | N/A | (\$433,776) | (\$132,174) |
| BiPAP | N/A | (\$422,281) | (\$142,556) |

All numbers are for 1000 patients at high risk of OSA diagnosis; difference in CPAP and BiPAP is cost only

3. MAD vs. CPAP Treatment

In analyses comparing MAD and CPAP treatment, the cost of creating and fixing the MAD device (~\$2,000) was estimated to be nearly twice that of the cost of CPAP device and accessory purchase over 1 year (~\$1,200). In addition, based on the trial results employed, there was an absolute difference of 30% in the rate of treatment success in favor of CPAP as well as a higher rate of successful titration/calibration (see Table 8 below). As a result, over 1 year of follow-up, CPAP was both more effective and less expensive than MAD in the base case comparison.

Table 8. Outcomes and costs of MAD vs. CPAP treatment among 1,000 hypothetical Medicaid patients diagnosed with OSA, over 1 year of follow-up.

| Measure | MAD | CPAP |
|-------------------------------------|-------------|-------------|
| Total cost | \$2,011,940 | \$1,184,150 |
| Failed calibration/titration | 120 | 30 |
| Patients treated | 880 | 970 |
| Number w/treatment success* | 378 | 689 |

All numbers are for 1000 patients with OSA diagnosis

*Treatment success calculated as success rate X probability of tolerating calibration/titration

Sensitivity analyses also were conducted to ascertain the impact of reduced CPAP compliance and longer-term follow-up on outcomes and costs. When compliance with MAD therapy in terms of

proportion of time on therapy per night was held constant at 100%, CPAP would be equally effective in comparison to MAD at a compliance rate of approximately 55%. This scenario is reasonably realistic, as compliance with CPAP has been reported to vary widely between 30-60% in published studies (Weaver, 2010).

MAD costs are incurred when the device is created and fixed in the mouth, while CPAP supply costs are ongoing. We also conducted sensitivity analyses to identify when MAD therapy would become cost-saving relative to CPAP. We assumed a lifespans of MAD and CPAP devices of 4 and 5 years respectively, and further assumed that CPAP costs after the first year of treatment would be for replacement supplies alone. Based on these assumptions, MAD therapy would become cost-saving relative to CPAP 25 months after treatment initiation.

6.2 Regional Budgetary Impact

The budgetary impact to New England of 2 potential changes in diagnostic testing patterns was also examined. In the first analysis, changes in the distribution of patients receiving home testing + autotitrated CPAP vs. split-night PSG + fixed titration of CPAP were examined. The assumed baseline distribution matched that presented in the HealthCore data (i.e., 94% facility-based vs. 6% home testing, see Section 5 for further details). The second analysis involved replacement of diagnostic testing using PSG alone with a phased approach using the Berlin Questionnaire. In this analysis, all patients were assumed to be tested with PSG at baseline, and all were assumed to convert to phased testing in the analysis.

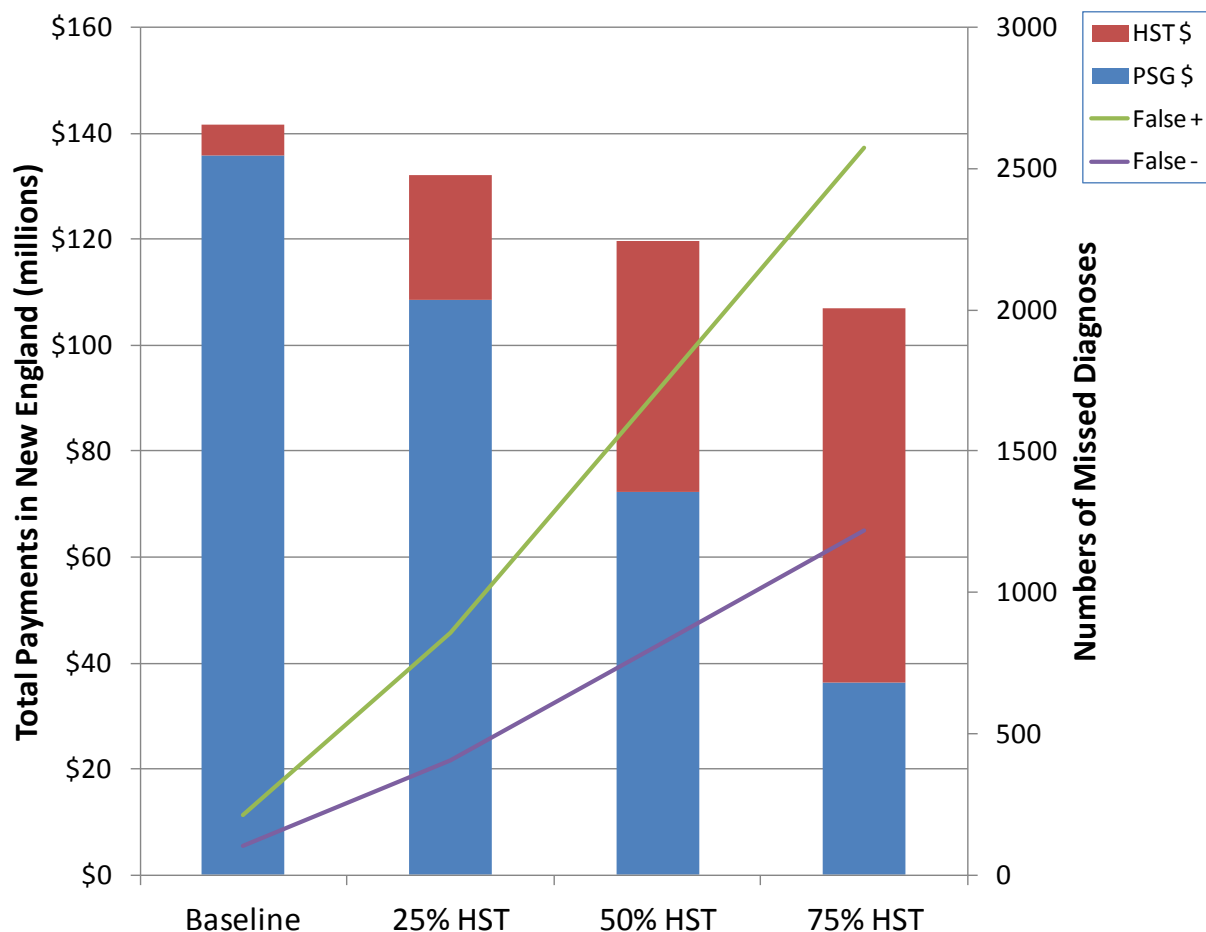
Estimates of the population age >16 years were obtained from 2011 Census data (Census.gov, 2012). This population was estimated to total 11.3 million individuals. The percentage of persons undergoing diagnostic testing in 2011 was estimated to be 1.03%, consistent with the rate observed in the HealthCore data (see Section 5). As with cost-effectiveness analysis, the prevalence of underlying OSA in the population referred for testing was assumed to be 50%. All cost estimates for the strategies of interest were identical to those used in cost-effectiveness analyses.

Findings from the analysis of changes in the mix of home vs. sleep testing are presented in Figure 1 on the following page. Approximately 116,000 patients were estimated to be referred for diagnostic testing across the region. Using the baseline estimates of the distribution of testing + treatment, total payments for these services across New England are estimated to total approximately \$142 million. The small amount of home testing assumed at baseline would generate 213 and 101 false-positive and false-negative results respectively.

When 25% of testing is assumed to occur in the home, approximately \$10 million in savings would be expected across New England; the number of false-positive and false-negative results would

increase to 858 and 407 respectively (1.1%). Expected savings would grow to over \$22 million for the region when equal proportions of home- vs. facility-based testing are assumed; in this scenario, an incorrect diagnosis would be made in approximately 2% of patients tested. Finally, when 75% of diagnostic testing is assumed to occur in the home setting, savings would approach \$35 million vs. baseline, while numbers of false-positive and false-negative results would grow to 2,574 and 1,221 respectively across New England, or slightly more than 3% of patients tested.

Figure 1. Estimated budgetary impact of changes in the distribution of home- vs. facility-based diagnostic sleep testing, among all patients age >16 tested in New England (n=116,328).



HST: Home sleep testing; PSG: Polysomnogram (facility-based)

In the second analysis, the estimated baseline costs of split-night PSG among 116,000 New Englanders referred for testing totaled \$75.9 million. Replacing this strategy with screening using the Berlin questionnaire with referral for split-night PSG in test-positive subjects avoided PSGs in over 38,000 individuals. Total costs for this strategy were estimated to be \$60.3 million across New England, or a savings of nearly \$16 million in comparison to baseline. Because screening would not

have perfect sensitivity, however, approximately 4,100 patients screened (3.5%) would be expected to have false-negative results.

6.3 Comparison of ICER Analysis to Published Cost-Effectiveness Analyses

A number of economic evaluations have focused on the management of OSA in recent years. In contrast to our analyses, these models attempted to link improvements in breathing indices to “hard outcomes” such as cardiovascular events and motor vehicle accidents. Effectiveness was reported in terms of life-years and quality-adjusted life years (QALYs) gained.

One recent report describes a simulation model examining the diagnosis and treatment of OSA over alternative 10-year and lifetime time horizons (Pietzch, 2011). Diagnostic strategies included Type III home sleep testing, split-night PSG, and full-night PSG. All patients receiving an OSA diagnosis were treated with CPAP. As in our analysis, autotitrating CPAP was assumed for home testing, and fixed titration was assumed with PSG testing. Full-night PSG generated an incremental cost-effectiveness ratio of \$17,131 per QALY gained in comparison to the universal comparator, undiagnosed and untreated OSA, and was also less costly and more effective than the other test-and-treat strategies due to its high specificity. Importantly, cost savings for full-night PSG vs. home testing in this study were driven in part by relatively high assumed rates of technical failure for both home monitoring and CPAP autotitration; neither issue has been raised as a major concern by clinical experts discussing the home testing experience in New England.

Four simulation models have evaluated the impact of CPAP therapy (at compliance rates of 70-75%) in patients with moderate-to-severe OSA. A simulation model comparing CPAP use to no active treatment in the UK found that, at an incremental cost-effectiveness ratio of approximately £25,000, CPAP would not meet traditional National Health Service thresholds for cost-effectiveness after 1 year of treatment (Guest, 2008). However, continued use of CPAP would reduce the ratio after 2 years, and would lead to overall cost savings after 11 years of therapy. A second study also evaluated the impact of CPAP vs. no treatment in Canada (Tan, 2008) over 5 years. The cost-effectiveness of CPAP was estimated to be \$3,626 per QALY gained.

A third model developed to support a National Institute of Health and Clinical Excellence (NICE) appraisal compared the costs and effects of CPAP to oral devices and lifestyle advice (Weatherly, 2009). Both CPAP and oral devices were found to be cost-effective in comparison to lifestyle advice among patients with moderate-severe OSA. CPAP also generated a cost-effectiveness ratio below traditional thresholds in comparison to oral devices, at £3,899 per QALY gained. CPAP cost-effectiveness ratios remained below these thresholds in a variety of sensitivity analyses, with the exception of an analysis focusing only on patients with mild disease. The final model compared CPAP, oral appliances, and no treatment using a third-party payer perspective in the US

(Sadatsafavi, 2009). As in the NICE analysis, CPAP was found to be the most costly and most effective strategy, at an incremental cost-effectiveness ratio of \$27,540 per QALY gained vs. oral appliances. The authors hypothesized that the higher ratio estimated in this study was due in part to the method they used for estimating cardiovascular event risk (i.e., use of relative risks to estimate the likelihood of MI and stroke vs. linkage of effects on blood pressure to reductions in cardiovascular event risk in the NICE analysis).

7. Questions and Discussion

Introduction

Each public meeting of CEPAC will involve deliberation and voting on key questions related to the supplementary analysis of the AHRQ review being presented by ICER. Members of CEPAC will discuss issues regarding the application of the available evidence to guide clinical decision-making and payer policies. The key questions are developed by ICER with significant input from members of the CEPAC Advisory Board to ensure that the questions are framed to address the issues that are most important in applying the evidence to practice and medical policy decisions. Definitions for key terms used in the voting questions are provided in Appendix C.

Summary of Votes and Recommendations

Following the outline of the AHRQ review, CEPAC members voted on questions concerning the comparative clinical effectiveness and comparative value of diagnostic and treatment options for adults with OSA. This summary includes the results of the votes of CEPAC on key evidence questions. In addition, we present policy considerations highlighted by CEPAC and by the roundtable of regional clinical experts and regional payers that discussed the implications of CEPAC votes for clinical practice, and payer policies. The meeting agenda and full attendance list, including roundtable panelists, are shown in Appendix D.

Comparative clinical effectiveness: Diagnostic Strategies

Based on the findings of the AHRQ review and time limitations of the CEPAC meeting, members of CEPAC were asked for their consent to the following stipulations.

- **There is insufficient evidence to distinguish the diagnostic accuracy of Type III vs. Type IV home monitors, and available evidence suggests their sensitivity and specificity largely overlaps.**

CEPAC Vote: 0 No

Voting Questions

- **Is the evidence adequate to demonstrate that Type III-IV home monitors are equivalent to polysomnography (PSG) in diagnosing OSA?**

CEPAC Vote: 2 No

- Is the evidence adequate to demonstrate that a phased diagnostic approach using the Berlin questionnaire to identify candidates for PSG is equivalent to using PSG alone in all patients in whom there is a clinical suspicion for the diagnosis of OSA?

CEPAC Vote: 3 Yes ☒ 10 No ☐ 1 Abstain

Comments: Although CEPAC voted that the evidence is inadequate to demonstrate that using a phased diagnostic approach with the Berlin questionnaire is equivalent to PSG alone, council members noted that questionnaires may still have utility in the diagnostic process, but not as a replacement for standard testing.

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- Is the evidence adequate to demonstrate that a phased diagnostic approach using externally-validated clinical prediction rules to identify candidates for PSG is equivalent to using PSG alone in all patients in whom there is a clinical suspicion for the diagnosis of OSA?

CEPAC Vote: 2 Yes ☒ 12 No ☐

Comparative clinical effectiveness: Treatment of OSA in Adults

Based on the findings of the AHRQ review and time limitations of the CEPAC meeting, members of CEPAC were asked for their consent to the following stipulations.

- There is insufficient evidence to demonstrate that other interventions (e.g. medication, palatal implants, bariatric surgery, acupuncture, nasal dilator strips, etc.) are better than continuous positive airway pressure (CPAP) in treating adults with OSA.

CEPAC Vote: ☒ 14 Yes ☐ 0 No

- There is insufficient evidence to demonstrate that any one form of mandibular advancement device (MAD) is more effective than any other in treating OSA in adults.

CEPAC Vote: ☒ 14 Yes ☐ 0 No

- There is insufficient evidence to demonstrate that any of the available intervention programs improve compliance with CPAP relative to usual CPAP care in adults with OSA.

CEPAC Vote: Yes No

Voting Questions

1. **Is the evidence adequate to demonstrate that surgery is equivalent or superior to CPAP in particular subpopulations with OSA?**

CEPAC Vote: 2 Yes No

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2. **Is the evidence adequate to demonstrate that MADs are superior to no treatment in treating adults with OSA?**

CEPAC Vote: Yes No

Comments: CEPAC votes are based on the patient inclusion criteria used for studies included in the AHRQ review. The council noted that certain patient subpopulations may benefit more than others from MADs. For example, patients with mild-to-moderate disease may experience improved outcomes with oral devices while patients with periodontal disease are contraindicated.

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3. **Is the evidence adequate to demonstrate that MADs are equivalent or superior to CPAP in treating mild-to-moderate OSA (AHI 5-30 events/hour)?**

CEPAC Vote: 3 Yes No

Comments: CEPAC members who voted “no” stated that even though the evidence is inadequate to demonstrate that MADs are equivalent or superior to CPAP, that it is important to consider higher compliance rates observed with oral devices.

Votes on Comparative Value

When a majority of CEPAC votes that the evidence is adequate to demonstrate that an intervention produces patient outcomes equivalent or superior to a reference option, the Council members are also asked to vote on whether the intervention represents a “high”, “reasonable”, or “low” value. The value perspective that members of CEPAC are asked to assume is that of a state Medicaid program that must make resource decisions within a fixed budget for care. While information

about hypothetical budget tradeoffs are provided, CEPAC is not given prescribed boundaries or thresholds for budget impact, PMPM changes, or incremental cost-effectiveness ratios to guide its judgment of high, reasonable, or low value. Typically only those CEPAC members who vote that the evidence is adequate to demonstrate equivalent or superior clinical effectiveness are asked to vote on comparative value. However, under certain circumstances when one intervention is particularly cost-saving compared to another and a value consideration is deemed important in spite of insufficient evidence to support clinical equivalency, CEPAC members who voted “no” may also be asked to vote on value.

Comparative Value: Diagnostic strategies

1. **Based on reimbursement levels provided with this report, would you judge the comparative value of a phased diagnostic approach using the Berlin questionnaire compared to PSG alone to be 1) high value; 2) reasonable value; or 3) low value compared to?**

No vote taken: majority of CEPAC voted “no” on comparative clinical effectiveness.

2. **Based on reimbursement levels provided with this report, would you judge the comparative value of a phased diagnostic approach using the externally-validated clinical prediction rules compared to PSG alone to be 1) high value; 2) reasonable value; or 3) low value?**

No vote taken: majority of CEPAC voted “no” on comparative clinical effectiveness.

3. **Based on reimbursement levels provided with this report, would you judge the comparative value of a home-based pathway (Type III-IV home monitor with auto-CPAP) compared to an in-lab pathway (split-night PSG plus CPAP) to be 1) high value; 2) reasonable value; or 3) low value?**

CEPAC Vote:

| | |
|--------|--------------|
| 6 High | 6 Reasonable |
|--------|--------------|

 2 Low

Comments: CEPAC members who voted that a home-based pathway had “high” value compared to an in-lab pathway emphasized the higher cost-benefit ratio for home-testing combined with autoCPAP. CEPAC members stated that since home-testing is less costly and functionally equivalent, a home-based paradigm represents “high” value and may increase access to services. CEPAC members noted the importance of considering the severity of the patient’s symptoms before determining the appropriate pathway, as home testing may be more effective for patients with high pre-test probability of OSA. One CEPAC member argued that in spite of variability of home testing accuracy, increasing access to home testing may result in improved studies and better standards for diagnosis and treatment of OSA.

CEPAC members who voted that a home-based pathway had “reasonable” value compared to an in-lab approach predominantly cited concerns for false positives and false negatives that may result in unnecessary treatment and increase costs. There was concern among CEPAC members that expanding access to home sleep testing may enlarge the scope of diagnostic testing to patients with lower risks of OSA, causing potential mis- or over-diagnosis. CEPAC members were also concerned with differences in outcomes that occur between clinical studies and a real world context, and that patients receiving home testing outside of a clinical trial may not experience the same quality of care and follow-up needed for successful diagnosis.

CEPAC members who voted that home-based pathways represent “low” value also voiced concerns with the specificity and sensitivity of portable monitors and felt that making home-testing more accessible may lead to over-screening that could potentially increase costs and result in a larger number of false positives.

Comparative Value: Treatment

1. **Based on reimbursement levels provided with this report, would you judge the comparative value of MADs compared to no treatment to be 1) high value; 2) reasonable value; or 3) low value for patients with mild-to-moderate OSA (AHI 5-30 events/hour)?**

CEPAC Vote: 1 High **8 Reasonable** 4 Low 1 Abstain

Comments: The CEPAC member who voted that MADs have “high” value stated that MADs are worth the cost to improve the quality of life for a patient with symptomatic OSA versus no treatment at all. CEPAC members who voted that MADs have “low” value discussed concerns with overtreatment of OSA, in particular patients with mild-to-moderate disease severity.

-
2. **Based on reimbursement levels provided with this report, would you judge the comparative value of MADs compared to CPAP to be 1) high value; 2) reasonable value; or 3) low value for patients with mild-to-moderate OSA (AHI 5-30 events/hour)?**

No vote taken: majority of CEPAC voted “no” on comparative clinical effectiveness.

Broader Considerations of Public Health, Equity, and Access

Are there any considerations related to public health, equity, disparities in access or outcomes for specific patient populations, or other social values that should be considered in medical policies related to the use of home monitors, PSG, or phased diagnostic approaches for patients in whom there is a clinical suspicion of OSA?

Comments: Some CEPAC members voiced concern for equitable access to home sleep testing for the Medicaid population, as some vendors are unwilling to travel to inner-city or rural areas to assist patients in the application and use of portable monitors. If home sleep testing is to be covered as a first-line option, council members suggested that programs should also be in place to help patients receive necessary guidance and follow-up when conducting a home sleep test to ensure equal access. Other CEPAC members feared that false negatives from home testing may prevent patients from further investigation even if they continue to have issues with sleep. In addition, patients who receive a false negative diagnosis through home testing may not have access to a sleep center for follow-up testing; senior populations are of particular concern.

Roundtable Discussion and Policy Implications

Following the CEPAC votes and deliberation, CEPAC engaged in a roundtable discussion with a panel composed of two representatives from the clinical expert community, one private payer, and one public payer (names shown in the meeting participant section of this report). A patient advocate was invited to serve on the roundtable but due to logistical reasons was unable to attend the in-person meeting. However, patient advocacy and support groups were contacted throughout the development of the supplementary report and CEPAC process to ensure that the patient perspective is represented. The goal of the roundtable was to explore the implications of CEPAC votes for clinical practice and payer policies. The topics discussed included:

Future Research Needs

CEPAC members identified the following research areas needed to fill the most important evidence gaps on the diagnosis and treatment of OSA:

- Clarification of the prevalence of OSA given increases in obesity
- Better definition of OSA to improve value of clinical prediction rules and other screening approaches
- Effectiveness of using screening tools to identify appropriate patients for sleep testing in primary care settings, including any barriers to their optimal use
- Long-term impact of shifting patients from PSG to home-testing on sensitivity and specificity of testing, clinical outcomes and costs
- Long-term impact of treatment on patient satisfaction and quality of life outcomes, including the impact of weight loss on OSA symptoms
- Long-term risks and harms associated with untreated OSA

- Issues surrounding patient compliance, management, and follow-up for long-term use of CPAP
- Further consensus on outcomes and compliance reporting in order to better draw comparisons across studies
- Sub-group analyses in order to understand the impact of diagnostic and treatment interventions on specific patient populations, in particular how effectiveness varies by disease severity
- Additional cost-effectiveness analyses, in particular to address impact of OSA on socioeconomic outcomes, including job retention, wages, income, etc.

Diagnosis of OSA

Home Sleep Testing vs. PSG

The majority of CEPAC supported the use of home testing over polysomnography for patients in whom there is a clinical suspicion for OSA and meet appropriate clinical criteria. Some CEPAC members remarked that the potential for false positives and false negatives from home testing requires quality standards to ensure that qualified providers interpret results and determine whether a patient should be referred for follow-up PSG.

There was concern among CEPAC members that expanding access to home sleep testing may have the unintended consequence of mis- or over-diagnosis as more patients with lower risks of OSA receive testing. However, panelists noted that this has not been the experience for payers with positive coverage for home sleep testing. Payers mentioned that there has been low rise in utilization of home sleep testing regardless of coverage for portable monitors, though decreased utilization may be a product of regulations in certain markets that require providers to rule out other sleep disorders or specific contraindications that may require a patient to receive PSG. Some providers are exploring innovative delivery models such as telemedicine to increase access to home testing services.

Role of Primary Care Physicians

CEPAC discussed with panelists the important role of primary care physicians in identifying patients at risk for OSA and referring patients for appropriate diagnostic testing. Providers noted that accreditation standards and quality benchmarking are important to ensure that providers administering home monitors are qualified to interpret results and appropriately refer patients to a sleep specialist for follow-up care. CEPAC also deliberated on the role of questionnaires and how screening tools can effectively be utilized by primary care providers to triage patients for further testing and improve quality of referrals. Clinical experts noted that questionnaires are not being used routinely in current practice but they represent a good starting point to ensure that patient

sleep patterns are being appropriately evaluated. Some CEPAC members felt that the benefit of early intervention should be further clarified before screening with questionnaires is endorsed. Other CEPAC members cautioned that many primary care providers are already constrained with limited time to spend with patients, and expanding their scope to include OSA screening may not be beneficial or feasible.

Treatment of OSA

Variations on CPAP

CEPAC discussed the available variations of CPAP therapy and cost differences among the various options. Panelists noted that most insurers require patients to fail therapy with autoCPAP or CPAP before receiving bi-level CPAP, so a patient using more expensive variations as a first-line treatment option is not a primary concern.

Compliance

CEPAC extensively discussed the issues surrounding patient compliance with various treatment interventions for OSA. Providers noted that patients who are symptomatic are typically more compliant, and that patients who are unaware of baseline sleeplessness or are asymptomatic may be unmotivated to adhere to treatment. The major reason patients fail on CPAP is due to poor compliance, and roundtable panelists and CEPAC agreed that patient education is lacking to increase awareness of the treatment benefits, thus improving adherence to CPAP and other treatment regimens. Physician and payer panelists provided examples of how compliance is being monitored in clinical practice, and how current data reveal that many patients are not using CPAP effectively.

Care Coordination

CEPAC members and panelists voiced concern that patients with OSA receive fragmented care and that further outreach with professional specialty societies is needed to develop new delivery models that improve care coordination. CEPAC recommended that reimbursement models shift to promote greater care coordination between primary care providers and specialists, and incentivize physicians to integrate care and track follow-up of patients receiving treatment for OSA. Clinical experts discussed how vendor contracts and other market dynamics for current practice are often barriers to care coordination.

Behavioral Modifications

CEPAC and the roundtable considered stronger levers to incentivize patients to lose weight to help moderate the effects of OSA and reduce costs of treatment. When discussing the current tools available, panelists mentioned new requirements through the Patient Protection and Affordable Care Act (PPACA) for insurers to reimburse counseling and other behavioral interventions to promote weight loss, as well as other health promotion programs including financial incentives for employees participating in wellness programs or who achieve other health targets.

CEPAC members suggested that requiring patients to attempt lifestyle modifications before undergoing sleep testing may be an option, but that this may not be reasonable for patients with moderate-to-severe apnea. CEPAC members cautioned that obesity is a psychological, hormonal, and metabolic disease often without a straightforward solution. CEPAC members agreed, however, that patients should be educated on sleep management and undergo counseling before they receive sleep testing and that behavioral modifications should be a concurrent mode of treatment.

Patient engagement

CEPAC generally supported the use of education campaigns to raise awareness of the symptoms and risks of OSA with information on how patients may communicate with their physician about testing. Some council members feared that widespread education campaigns could lead to overdiagnosis and overtreatment, and that patients may not change behavior on the basis of knowledge alone. Most CEPAC members agreed that patient education on behavioral modifications, treatment benefits, follow-up, and compliance should be a routine part of care.

Summary: Suggestions for Policy and Practice

For clinicians

- Use or develop innovative delivery models such as telemedicine to ensure that patients undergoing home testing have appropriate guidance on application and use of portable monitors, especially for patients where direct home services are not available.
- Collaborate with payers to pilot-test questionnaires to help primary care providers evaluate patients and appropriately identify patients for further sleep testing.
- Educate patients on the benefits of treatment and potential behavioral modifications, including positional therapy, weight loss, smoking cessation, reduced alcohol consumption, etc. Make behavioral interventions a concurrent mode of OSA treatment.
- Appropriately monitor and follow-up with patients to improve treatment compliance.
- Establish greater coordination between primary care providers and specialists to improve quality of care for patients with OSA.

For payers

- Reimburse home testing as a first-line treatment option with APAP. Only approve polysomnography for patients who meet certain clinical criteria, including conditions that prevent the use of portable monitors or comorbidities that diminish the accuracy of their results.
- Require that providers interpreting sleep testing results meet certain quality and accreditation standards to ensure quality of diagnosis and appropriate patient follow-up.
- Collaborate with providers to pilot-test questionnaires to help primary care providers and/or specialists conduct a comprehensive sleep evaluation and appropriately identify patients most likely to benefit from formal testing.
- Heighten efforts to reduce the administrative burden for clinicians referring patients for sleep testing for clinically appropriate reasons.
- Use global payment schemes and other innovative payment models that reward integrated care for patients with OSA.

For patients

- Patient advocacy groups should continue to provide resources to help patients understand OSA symptoms, improve treatment compliance, and modify behaviors that could improve outcomes. A high-profile education campaign may help raise awareness of the comparative effectiveness and value of the various diagnostic and treatment options available for OSA.
- Modify behaviors that improve OSA symptoms, including stopping use of sedatives, reducing alcohol use before bed, positional therapy, weight loss, smoking cessation, etc.

8. Public Comment

Members of the public were invited to submit public comment on the draft supplementary report during the period of November 15, 2012 to December 4, 2012. The following organizations submitted and/or presented public comments:

- Richard Justman, MD, National Medical Director, UnitedHealthCare
- Edward Grandi, Executive Director, American Sleep Apnea Association
- Stasia Wieber, MD, Physician, PriMed

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Appendix A

The Epworth Sleepiness Scale (Johns, 1991)

How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired? This refers to your usual way of life. Use the following scale to choose the *most appropriate* number for each situation:

- 0 = would never doze
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

| Situation | Chance of Dozing |
|---|------------------|
| Sitting and reading | |
| Watching TV | |
| Sitting, inactive in a public place (e.g., a theater) | |
| As a passenger in a car for an hour without a break | |
| Lying down to rest in the afternoon when circumstances permit | |
| Sitting and talking to someone | |
| Sitting quietly after a lunch without alcohol | |
| In a car, while stopped for a few minutes in traffic | |

Range of possible scores: 0 - 24

Normal score: ESS < 10

The STOP-Bang Scoring Model (Chung, 2008)

1. **S**noring: Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
2. **T**ired: Do you often feel tired, fatigued or sleepy during daytime?
3. **O**bserved: Has anyone observed you stop breathing during your sleep?
4. Blood **p**ressure: Do you have or are you being treated for high blood pressure?
5. **B**MI: BMI more than 35 kg/m²?
6. **A**ge: Age over 50 years?
7. **N**eck circumference: Neck circumference greater than 40 cm (16 inches)?
8. **G**ender: Gender male?

High risk of OSA: answering yes to 3 or more questions

Low risk fo OSA: answering yes to less than 3 questions

The Berlin Questionnaire (Netzer, 1999)

| Category 1 | Select appropriate response | | | | |
|--|--------------------------------|----------------------|-------------------------|---|-----------------------|
| 1. Do you snore? | Yes (*) | No | Don't know | | |
| 2. Your snoring is? | Slightly louder than breathing | As loud as talking | Louder than talking (*) | Very loud. Can be heard in adjacent rooms (*) | |
| 3. How often do you snore? | Nearly every day (*) | 3-4 times a week(*) | 1-2 times a week | 1-2 times a month | Never or nearly never |
| 4. Has your snoring ever bothered other people? | Yes (*) | No | | | |
| 5. Has anyone noticed that you quit breathing during your sleep? | Nearly every day (*) | 3-4 times a week (*) | 1-2 times a week | 1-2 times a month | Never or nearly never |

| Category 2 | Select appropriate response | | | | |
|--|-----------------------------|----------------------|------------------|-------------------|-----------------------|
| 1. How often do you feel tired or fatigued after your sleep? | Nearly every day (*) | 3-4 times a week (*) | 1-2 times a week | 1-2 times a month | Never or nearly never |
| 2. During your wake time, do you feel tired, fatigued or not wake up to par? | Nearly every day (*) | 3-4 times a week(*) | 1-2 times a week | 1-2 times a month | Never or nearly never |
| 3. Have you ever nodded off or fallen asleep while driving a vehicle? | Yes (*) | No | | | |

| Category 3 | Select appropriate response | | | | |
|-------------------------------------|-----------------------------|----|--|--|--|
| 1. Do you have high blood pressure? | Yes (*) | No | | | |

For scoring the questions: positive responses correspond to answers marked with a “ * ”

For scoring the categories:

- Category 1 is positive with 2 or more positive responses
- Category 2 is positive with 2 or more positive responses
- Category 3 is positive with a positive response and/or BMI > 30

Final evaluation:

2 or more positive categories indicates a *high* likelihood of sleep disordered breathing

Appendix B

Table 1. Home sleep testing versus polysomnography: Study characteristics.

| Study Author, Year | Index test (vs. PSG) | Participants | Country (enrollment years) | N | Baseline AHI (mean \pm SD) [range] | Baseline ESS (mean \pm SD) | Mean Age, year | Male (%) | Mean BMI (kg/m ²) | Setting | Sleep Apnea Definition | Patient Exclusions |
|--------------------|------------------------|-------------------------------|-------------------------------|-----|--------------------------------------|------------------------------|-------------------------|----------|------------------------------------|--|------------------------|--|
| Danzi-Soares, 2011 | Stardust II (Type III) | Severe CAD, referred for CABG | Brazil (nd) | 70 | nd | 7 (5-11) [median, range] | 58 \pm 7 | 76% | 27.6 (25.8 - 31.1) [median, range] | Sleep lab & on the ward (preoperative) | AHI \geq 5 | 4 pts withdrew; 5 pts excluded for technical problems |
| Masa, 2011 | BreastSC20 (Type IV) | Suspected OSA patients | Spain (Dec. 2008 - Dec. 2009) | 348 | nd | 11.6 \pm 5 | 48.7 \pm 11.8 | 76% | 31 \pm 6.6 | Sleep lab and home | nd | 7 pts failed respiratory trial; 18 pts didn't have valid HRP & PSG |
| Oktay, 2011 | ApneaLink (Type IV) | Suspected OSA patients | USA (Jun. 2006 - Jul. 2007) | 53 | nd | nd | 45.1 \pm 11.3 [23-70] | 55% | 35.9 \pm 9.1 [19.6-54.5] | Sleep lab and home | nd | 24 pts didn't have successful home tests and/or PSG |

AHI: apnea-hypopnea index; BMI: body mass index; CABG: coronary artery bypass grafting; CAD: coronary artery disease; ESS: Epworth Sleepiness Scale; HRP: home respiratory polygraphy; N: number; ND: no data; OSA: obstructive sleep apnea; PSG: polysomnography; SD: standard deviation

Table 2. Home sleep testing versus polysomnography: Study results.

| | | | | Bland-Altman | | ROC Analysis | | | | |
|--------------------|------------------------|-----|--|--------------|--------------------|----------------------------|--------------------------|-------------------------|-------------------------|------|
| Study Author, Year | Index test (vs. PSG) | N | Setting | Metric | Result (events/hr) | Threshold, events/hr Index | Threshold, events/hr PSG | Sensitivity, % (95% CI) | Specificity, % (95% CI) | AUC |
| Danzi-Soares, 2011 | Stardust II (Type III) | 70 | Sleep lab & on the ward (preoperative) | 95%CI | 5.3 (-23.9, 34.6) | ≥ 5 | AHI ≥ 5 | 92 (nd) | 67 (nd) | 0.90 |
| | Stardust II (Type III) | | | | | ≥ 15 | AHI ≥ 15 | 66 (nd) | 78 (nd) | 0.79 |
| | ESS | | | | | 10 | AHI ≥ 5 | 27 | 89 | nd |
| | ESS | | | | | 10 | AHI ≥ 15 | 21 | 71 | nd |
| | BQ | | | | | High vs. low risk | AHI ≥ 5 | 72 | 44 | nd |
| | BQ | | | | | High vs. low risk | AHI ≥ 15 | 74 | 34 | nd |
| Masa, 2011 | BreastSC20 (Type IV) | 348 | Sleep lab and home | nd | Graph | ≥ 5 | AHI ≥ 5 | 96 | 57 | 0.92 |
| | | | | | | ≥ 10 | AHI ≥ 5 | 87 | 86 | nd |
| | | | | | | ≥ 5 | AHI ≥ 10 | 97 | 39 | nd |
| | | | | | | ≥ 20 | AHI ≥ 10 | 71 | 90 | nd |
| | | | | | | ≥ 5 | AHI ≥ 15 | 94 | 60 | nd |
| | | | | | | ≥ 20 | AHI ≥ 15 | 67 | 92 | nd |
| | | | | | | ≥ 10 | AHI ≥ 10 | nd | nd | 0.88 |
| | | | | | | ≥ 15 | AHI ≥ 15 | nd | nd | 0.89 |

| Oktay, 2011 | ApneaLink (Type IV) | 53 | Sleep lab and home | ApneaLink - Lab vs. PSG | | | | | | |
|-------------|---------------------|----|--------------------|--------------------------|-------|---------------|---------------|------|------|------|
| | | | | 95% CI | -0.98 | RDI \geq 5 | AHI \geq 5 | 90 | 76.9 | 0.90 |
| | | | | | | RDI \geq 10 | AHI \geq 10 | 82.1 | 80 | 0.91 |
| | | | | | | RDI \geq 15 | AHI \geq 15 | 79 | 88.2 | 0.92 |
| | | | | | | RDI \geq 20 | AHI \geq 20 | 100 | 92.5 | 0.99 |
| | | | | | | RDI \geq 30 | AHI \geq 30 | 66.7 | 95.5 | 0.96 |
| | | | | ApneaLink - Home vs. PSG | | | | | | |
| | | | | 95% CI | -3.1 | RDI \geq 5 | AHI \geq 5 | 67.5 | 76.9 | 0.82 |
| | | | | | | RDI \geq 10 | AHI \geq 10 | 75 | 92 | 0.86 |
| | | | | | | RDI \geq 15 | AHI \geq 15 | 73.7 | 85.3 | 0.92 |
| | | | | | | RDI \geq 20 | AHI \geq 20 | 76.9 | 92.5 | 0.96 |
| | | | | | | RDI \geq 30 | AHI \geq 30 | 55.6 | 95.5 | 0.92 |

AHI: apnea-hypopnea index; AUC: area-under-the-curve; CI: confidence interval; N: number; ND: no data; PSG: polysomnography; RDI: respiratory disturbance index; ROC: receiver operating characteristic

Table 3. Questionnaires versus polysomnography: Study characteristics.

| Study Author, Year | Index test (vs. PSG) | Participants | Country (enrollment years) | N | Baseline AHI (mean \pm SD) [range] | Baseline ESS (mean \pm SD) | Mean Age, year | Male (%) | Mean BMI (kg/m ²) | Setting | Sleep Apnea Definition | Patient Exclusions |
|----------------------|---|---|--------------------------------|------|--------------------------------------|------------------------------|-----------------|----------|------------------------------------|--|------------------------|---|
| Danzi-Soares, 2011 | ESS & BQ | Severe CAD, referred for CABG | Brazil (nd) | 70 | nd | 7 (5-11) [median, range] | 58 \pm 7 | 76% | 27.6 (25.8 - 31.1) [median, range] | Sleep lab & on the ward (preoperative) | AHI \geq 5 | 4 pts withdrew; 5 pts excluded for technical problems |
| Martinez, 2011 | ESS1 (before PSG); ESS2 (after PSG) | Suspected OSA patients | Brazil (nd) | 929 | 24 \pm 22 | 10 \pm 5.1 (ESS1) | 46 \pm 14 | 64% | 27 \pm 5.3 | Sleep lab | nd | nd |
| Martinez, 2012 | BQ | Patients w/angina, referred for angiography | Brazil (Mar. 2007 - Feb. 2008) | 57 | 17 \pm 14 | nd | 54 \pm 6.9 | 46% | 23 \pm 11 | Home | AHI \geq 5 | nd |
| Sert-Kuniyoshi, 2011 | BQ | Recent MI (1-3 months previously) | USA (nd) | 99 | nd | nd | 62 \pm 13 | 81% | 30 \pm 5 | Sleep lab | nd | nd |
| Silva, 2011 * | ESS, STOP, STOP-Bang, 4-variable Screening Tool | Patients at risk for CVD/SDB | USA (nd) | 4770 | nd | nd | 62.4 \pm 10.3 | 52% | nd | Home | nd | nd |

* Patients from the Sleep Heart Health Study

AHI: apnea-hypopnea index; BMI: body mass index; BQ: berlin Questionnaire; CABG: coronary artery bypass grafting; CAD: coronary artery disease; CVD: cardiovascular disease; ESS: Epworth Sleepiness Scale; N: number; OSA: obstructive sleep apnea; PSG: polysomnography; SD: standard deviation; SDB: sleep disordered breathing

Table 4. Questionnaires versus polysomnography: Study results.

| | | | | Bland-Altman | | ROC Analysis | | | | |
|----------------------|-------------------------------------|-----|--|--------------|--------------------|----------------------------|--------------------------|-------------------------|-------------------------|------|
| Study Author, Year | Index test (vs. PSG) | N | Setting | Metric | Result (events/hr) | Threshold, events/hr Index | Threshold, events/hr PSG | Sensitivity, % (95% CI) | Specificity, % (95% CI) | AUC |
| Danzi-Soares, 2011 | Stardust II (Type III) | 70 | Sleep lab & on the ward (preoperative) | 95% CI | 5.3 (-23.9, 34.6) | ≥ 5 | AHI ≥ 5 | 92 (nd) | 67 (nd) | 0.90 |
| | Stardust II (Type III) | | | | | ≥ 15 | AHI ≥ 15 | 66 (nd) | 78 (nd) | 0.79 |
| | ESS | | | | | 10 | AHI ≥ 5 | 27 | 89 | nd |
| | ESS | | | | | 10 | AHI ≥ 15 | 21 | 71 | nd |
| | BQ | | | | | High vs. low risk | AHI ≥ 5 | 72 | 44 | nd |
| | BQ | | | | | High vs. low risk | AHI ≥ 15 | 74 | 34 | nd |
| Martinez, 2011 | ESS1 (before PSG); ESS2 (after PSG) | 929 | Sleep lab | nd | nd | ESS1 >10 | AHI > 5 | 54 (50-58) | 63 (55-71) | 0.61 |
| | | | | | | ESS1 >10 | AHI > 15 | nd | nd | 0.59 |
| | | | | | | ESS1 >10 | AHI > 30 | nd | nd | 0.59 |
| | | | | | | ESS2 >10 | AHI > 5 | 76 (73-79) | 50 (42-59) | 0.62 |
| | | | | | | ESS2 >10 | AHI > 15 | | | 0.60 |
| | | | | | | ESS2 >10 | AHI > 30 | | | 0.60 |
| Martinez, 2012 | BQ | 57 | Home | nd | nd | High vs. low risk | AHI ≥ 15 | 72 (52.4-85.7) | 50 (33.6-66.4) | nd |
| Sert-Kuniyoshi, 2011 | BQ | 99 | Sleep lab | nd | nd | High vs. low risk | AHI ≥ 5 | 68 (58-77) | 46 (36-56) | 0.58 |
| | | | | | | High vs. low risk | AHI ≥ 15 | 65 (55-74) | 36 (26-45) | 0.50 |
| | | | | | | High vs. low risk | AHI ≥ 30 | 71 (62-79) | 37 (27-46) | 0.54 |

AHI: apnea-hypopnea index; AUC: area-under-the-curve; BQ: Berlin Questionnaire; CI: confidence interval; ESS: Epworth Sleepiness Scale; N: number; ND: no data; PSG: polysomnography; ROC: receiver operating characteristic

Table 5. Clinical prediction rules versus polysomnography: Study characteristics.

| Study Author, Year | Index test (vs. PSG) | Participants | Country (enrollment years) | N | Baseline AHI (mean \pm SD) [range] | Baseline ESS (mean \pm SD) | Mean Age, year | Male (%) | Mean BMI (kg/m ²) | Setting | Sleep Apnea Definition | Patient Exclusions |
|--------------------|--|-----------------------------|-------------------------------|-----|--------------------------------------|------------------------------|---------------------------|----------|-------------------------------|-----------|---------------------------------|--|
| Hayano, 2011 | ECG-based algorithm (ACAT) | Suspected patients with SDB | Japan (Jan. 2005 - Dec. 2008) | 862 | 15 (19) [0 - 110] | nd | 49 \pm 15 [16 - 83] | 82% | 27 \pm 5 [16 - 47] | Sleep lab | AHI \geq 5 | 319 pts excluded due to technical problems; 12 had atrial fibrillation |
| Jauhar, 2012 | Kushida Index | Suspected OSA patients | Scotland (May - Nov. 2007) | 71 | nd | 11.1 \pm 5.4 [0-21] | 46.6 \pm 11.2 [21 - 78] | 75% | 32.5 \pm 8.7 [19.4 - 64.3] | nd | ESS \geq 10, ODI \geq 10/hr | 10 pts failed to attend sleep study; 4 didn't wear dentures at night |
| Marcos, 2012* | 2 algorithms based on SaO ₂ | Suspected OSA patients | Spain (nd) | 144 | 26.4 \pm 26.7 | nd | 52.19 \pm 13.73 | 78% | 29.83 \pm 4.53 | Sleep lab | AHI \geq 5 | nd |
| Marcos, 2010* | Algorithm based on SaO ₂ | Suspected OSA patients | Spain (nd) | 129 | nd | nd | 53.47 \pm 12.99 | 78% | 29.88 \pm 4.81 | Sleep lab | AHI \geq 10 | nd |

* Patient populations may overlap between the two studies.

AHI: apnea-hypopnea index; BMI: body mass index; ECG: electrocardiogram; ESS: Epworth Sleepiness Scale; N: number; ND: no data; ODI: oxygen desaturation index; OSA: obstructive sleep apnea; PSG: polysomnography; SaO₂: saturated oxygenation; SD: standard deviation; SDB: sleep disordered breathing

Table 6. Clinical prediction rules versus polysomnography: Study results.

| | | | | Bland-Altman | | ROC Analysis | | | | |
|--------------------|--|-----|-----------|--------------|--------------------|----------------------------|--------------------------|-------------------------|-------------------------|------|
| Study Author, Year | Index test (vs. PSG) | N | Setting | Metric | Result (events/hr) | Threshold, events/hr Index | Threshold, events/hr PSG | Sensitivity, % (95% CI) | Specificity, % (95% CI) | AUC |
| Hayano, 2011 | ECG-based algorithm (ACAT) | 862 | Sleep lab | 95% LOA | 0.5 (-18.6, 19.6) | nd | AHI \geq 5 | nd | nd | 0.84 |
| | | | | | | $\geq 29, < 7$ | AHI ≥ 15 | 89 | 98 | 0.91 |
| | | | | | | $\geq 38, < 27$ | AHI ≥ 30 | 71 | 99 | 0.96 |
| Jauhar, 2012 | Kushida Index | 71 | nd | nd | nd | > 70 | positive OSA diagnosis | 68 (50-81) | 71 (52-84) | nd |
| Marcos, 2012* | 2 algorithms based on SaO ₂ | 144 | Sleep lab | 95% CI | Graph‡ | MLR | AHI = 5 | 90 | 61.8 | nd |
| | | | | | | MLR | AHI = 10 | 89.6 | 77.1 | Nd |
| | | | | | | MLR | AHI = 15 | 96.2 | 80.3 | nd |
| | | | | | | MLP | AHI = 5 | 91.8 | 58.8 | nd |
| | | | | | | MLP | AHI = 10 | 89.6 | 81.3 | nd |
| | | | | | | MLP | AHI = 15 | 94.9 | 90.1 | nd |
| Marcos, 2010* | Algorithm based on SaO ₂ | 129 | Sleep lab | nd | nd | Positive OSA diagnosis | AHI ≥ 10 | 97 | 79.3 | 0.95 |

* Patient populations may overlap between the two studies.

‡ Data available in graph-form only.

AHI: apnea-hypopnea index; AUC: area-under-the-curve; CI: confidence interval; ECG: electrocardiogram; LOA: limit of agreement; MLP: multilayer perceptron; MLR: multiple linear regression; N: number; ND: no data; OSA: obstructive sleep apnea; PSG: polysomnography; ROC: receiver operating characteristic; SaO₂: saturated oxygenation

Table 7. Treatment with positive airway pressure vs. control: Study characteristics.

| Study Author, Year | Country (enrollment years) | Interventions | N | CPAP Pressure | Study Duration (trial design) | Mean Age (years) | Male (%) | Mean BMI (kg/m ²) | Other Patient Characteristics | Surrogate outcomes evaluated |
|--------------------|----------------------------|-----------------------------|-----|----------------|---|------------------|----------|-------------------------------|--|---|
| Barbé, 2012 | Spain (2004-2006) | CPAP | 357 | Auto or manual | 4 years (RCT) | 52.0 | 87.7% | 31.3 | AHI ≥ 20, ESS ≤ 10, some patients with history of hypertension | Incidence of hypertension |
| | | No treatment | 366 | | | 51.8 | 83.6% | 31.1 | | |
| Berry, 2011 | USA (nd) | EPAP | 127 | nd | 3 months (randomized, controlled, double blind) | 47.7 | 71.4% | 32.6 | AHI ≥ 10 | ESS, SaO ₂ , ODI, treatment success (≥ 50% reduction in AHI or AHI < 10) |
| | | Sham | 123 | | | 46.8 | 65.5% | 33.8 | | |
| Kushida, 2011 | USA and Germany (nd) | A-Flex with APAP | 56 | Auto | 6 months (randomized, controlled, double blind) | 49.1 | 75.9% | 33 | AHI ≥ 15 | ESS, FOSQ, blood pressure, SaO ₂ , arousal index |
| | | CPAP | 55 | | | 48.8 | 75.4% | 34.9 | | |
| | | APAP for 14 days, then CPAP | 57 | | | 48.3 | 75.5% | 35.6 | | |
| Lee, 2012 | USA (2004-2009) | CPAP | 26 | Manual | 3 weeks (randomized, controlled, double blind) | 48.3 | 84.6% | 29.8 | AHI ≥ 10 | Assessment of depressive symptoms, mood and anxiety |
| | | Sham | 30 | | | 48.2 | 83.3% | 28.6 | | |
| Sharma, 2011 | India (nd) | CPAP first | 43 | nd | 7 months (randomized, controlled, double blind) | 45 | 84% | 33.8 | AHI ≥ 15, ESS > 10; 75 of 86 patients (87%) had metabolic syndrome | ESS, arousal index, blood pressure, glucose and insulin indices, triglycerides, cholesterol |
| | | Sham first | 43 | | | 45 | 95% | 31.8 | | |
| Tomfohr, 2011 | USA (nd) | CPAP | 34 | Manual | 3 weeks (randomized, controlled, double blind) | 48.1 | 86.2% | 30.6 | AHI ≥ 10 | ESS, fatigue and vigor |
| | | Sham | 37 | | | 48.3 | 86.7% | 28.5 | | |

| | | | | | | | | | | |
|-----------------|----------|------------|----|--------|---|----|-----|----|--|-----------------------------|
| Weinstock, 2012 | USA (nd) | CPAP first | 25 | Manual | 16 weeks (randomized, double blind crossover) | 54 | 44% | 39 | AHI \geq 15 with impaired glucose tolerance; 50% of patients had AHI \geq 30 | Glucose and insulin indices |
| | | Sham first | 25 | | | 53 | 40% | 38 | | |

AHI: apnea-hypopnea index; APAP: auto-titrating positive airway pressure; BMI: body mass index; CPAP: continuous positive airway pressure; EPAP: expiratory positive airway pressure; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcomes of Sleep Questionnaire; N: number; ND: no data; ODI: oxygen desaturation index; OSA: obstructive sleep apnea; PSG: polysomnography; RCT: randomized controlled trial; SaO₂: saturated oxygenation; SD: standard deviation

Table 8. Treatment with positive airway pressure therapy vs. control: AHI.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Baseline AHI (SD) | Final AHI (SD) | Difference | 95% CI | P-value | Dropout (%) |
|--------------------|-----------------------------|--------------|---|----------------------|---------------------|---------------------------|-------------------------------|----------|-------------|
| Berry, 2011 | EPAP | 100 | 3 months (randomized, controlled, double blind) | 14.4 (IQR 5.5, 21.4) | 5.6 (IQR 2.1, 12.5) | Median of % change: -42.7 | nd | <0.0001 | 19 (16.0%) |
| | Sham | 95 | | 10.2 (IQR 3.4, 19.3) | 8.3 (IQR 4.2, 20.6) | Median of % change: -10.1 | | | 15 (13.6%) |
| Kushida, 2011 | A-Flex with APAP | 46 | 6 months (randomized, controlled, double blind) | 36.87 (30.0) | 1.26 (2.92) | nd | nd | 0.3 | 14.8% |
| | CPAP | 47 | | 41.08 (31.57) | 1.04 (1.28) | nd | | | 17.5% |
| | APAP for 14 days, then CPAP | 47 | | 37.29 (31.1) | 0.67 (0.93) | nd | | | 11.3% |
| Lee, 2012 | CPAP | 26 | 3 weeks (randomized, controlled, double blind) | 36.7 (21.8) | nd | -30.7* | 13.7-36.3 (of the difference) | <0.001 | 9 (25.7%) |
| | Sham | 30 | | 31.3 (18.6) | nd | -5.8* | | | 6 (16.7%) |
| Tomfohr, 2011 | CPAP | 29 | 3 weeks (randomized, controlled, double blind) | 38.6 (24.3) | 6.3 (6.5) | nd | nd | <0.01 | 4 (14.7%) |
| | Sham | 30 | | 31.7 (18.7) | 25.9 (19.7) | nd | | | 7 (18.9%) |
| Weinstock, 2012 | CPAP first | 24 | 16 weeks (randomized, double blind crossover) | 44 (27) | 3 (3) | nd | nd | <0.0001‡ | 1 (4%) |
| | Sham | | | | 31 (25) | | | | |
| | Sham first | 25 | | 32 (20) | 32 (24) | nd | | <0.0001‡ | 0 (0%) |
| | CPAP | | | | 2 (3) | | | | |

* As compared to baseline measurement.

‡ Significance between final AHI with CPAP as compared to sham.

AHI: apnea-hypopnea index; APAP: auto-titrating positive airway pressure; CPAP: continuous positive airway pressure; EPAP: expiratory positive airway pressure; IQR: inter quartile range; N: number; ND: no data

Table 9. Treatment with positive airway pressure therapy vs. control: Cardiovascular outcomes and mortality.

| Study Author, Year | Interventions | No. Analyzed | Cardiovascular Event | No. Events | Total deaths (%) | Mortality Event | No. Events (%) |
|--------------------|---------------|--------------|------------------------------------|------------|------------------|-----------------|----------------|
| Barbé, 2012 | CPAP | 357 | New hypertension | 68 | 8 (2.2%) | Cancer | 5 (1.4%) |
| | | | CVD events (all) | 28 | | | |
| | | | Hospitalizations for UA/arrhythmia | 17 | | CVD causes | 1 (0.3%) |
| | | | Nonfatal stroke | 3 | | | |
| | | | Heart failure | 3 | | Trauma | 1 (0.3%) |
| | | | Nonfatal MI | 2 | | | |
| | | | TIA | 2 | | Unknown | 1 (0.3%) |
| | | | CVD death | 1 | | | |
| | No treatment | 366 | New hypertension | 79 | 3 (0.8%) | Cancer | 2 (0.6%) |
| | | | CVD events (all) | 31 | | | |
| | | | Hospitalizations for UA/arrhythmia | 11 | | Unknown | 1 (0.3%) |
| | | | Nonfatal stroke | 2 | | | |
| | | | Heart failure | 5 | | | |
| | | | Nonfatal MI | 8 | | | |
| | | | TIA | 5 | | | |
| | | | CVD death | 0 | | | |

CPAP: continuous positive airway pressure; CVD: cardiovascular disease; MI: myocardial infarction; TIA: transient ischemic attack; UA: unstable angina

Table 10. Treatment with positive airway pressure vs. control: Compliance.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Compliance Definition | No. Compliant (SD) | P-value |
|--------------------|-----------------------------|--------------|---|--|--|-----------------------|
| Barbé, 2012 | CPAP | 357 | 4 years (RCT) | Use of CPAP ≥ 4 hours/night | 230 (64.4%) | nd |
| | No treatment | 366 | | | nd | |
| Berry, 2011 | EPAP | 127 | 3 months (randomized, controlled, double blind) | EPAP worn the entire night | 88.2% (IQR 67.5, 96.4) | nd |
| | Sham | 123 | | | 92.3% (IQR 84.0, 97.5) | |
| Kushida, 2011 | A-Flex with APAP | 54 | 6 months (randomized, controlled, double blind) | Mean hours worn/night | 4.44 (1.98) | 0.8 |
| | CPAP | 57 | | | 4.4 (2.02) | |
| | APAP for 14 days, then CPAP | 53 | | | 4.63 (1.75) | |
| Weinstock, 2012 | CPAP first | 25 | 16 weeks (randomized, double blind crossover) | Mean hours worn/night | 4.8 (CPAP) | Between arms: p<0.001 |
| | Sham first | | | | 3.4 (sham) | |
| | CPAP first | 25 | | Percent/day usage > 4 hours OR >70% sleep time | CPAP 1 st : 18 (72%) CPAP 2 nd : 13 (52%) | <0.0001 |
| | Sham first | | | | Sham 1 st : 7 (28%) Sham 2 nd : 4 (17%) | |

APAP: auto-titrating positive airway pressure; CPAP: continuous positive airway pressure; EPAP: expiratory positive airway pressure; IQR: inter quartile range; N: number; ND: no data; RCT: randomized controlled trial; SD: standard deviation

Table 11. Treatment with mandibular advancement devices vs. CPAP: Study characteristics.

| Study Author, Year | Country (enrollment years) | Interventions | N | CPAP Pressure | Study Duration | Mean Age (years) | Male (%) | Mean BMI (kg/m ²) | Other Patient Characteristics | Surrogate outcomes evaluated |
|--------------------|----------------------------|--------------------|----|---------------|---|------------------|----------|-------------------------------|-------------------------------|---|
| Aarab, 2011 | The Netherlands (nd) | MAD | 20 | Manual | 6 months (RCT with 18-month parallel-group follow-up) | 50.3 | 75% | 27.1 | AHI 5-45, ESS ≥ 10 | SF-36 evaluated along w/other sleep & wakefulness outcomes; side effects reported |
| | | nCPAP | 18 | | | 55.4 | 67% | 30.7 | | |
| | | Placebo (sham MAD) | 19 | | | 51.3 | 74% | 31.1 | | |

AHI: apnea-hypopnea index; BMI: body mass index; CPAP: continuous positive airway pressure; ESS: Epworth Sleepiness Scale; MAD: mandibular advancement device; N: number; nCPAP: nasal CPAP; ND: no data; RCT: randomized controlled trial; SF-36: short form health survey of 36 questions

Table 12. Treatment with mandibular advancement devices vs. control: AHI.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Baseline AHI (SD) | Final AHI (SD) | Difference (SD) | 95% CI | P-value | Dropout (%) |
|--|--------------------|--------------|--------------------------------------|-------------------|----------------|-----------------|---|--------------------|-------------|
| Aarab (a), 2011 | MAD | 20 | 6 months (RCT) | 22.1 (10.8) | nd | 16.3 (10.3) | nd | MAD vs. PL 0.000 | 5% |
| | nCPAP | 18 | | 20.9 (9.8) | nd | 19.5 (8.7) | nd | nCPAP vs. PL 0.002 | 18% |
| | Placebo (sham MAD) | 19 | | 20.1 (8.7) | nd | 5.2 (10.5) | nd | Among group 0.000 | 10% |
| Aarab (b), 2011 *long-term follow-up of Aarab (a) | MAD | 15 | 18 months (parallel-group follow-up) | nd | nd | 15.0 (10.5) | Mean difference between groups (MAD vs. nCPAP): -4.1 (-5.7, -2.5) | 0.3 | 29% |
| | nCPAP | 13 | | nd | nd | 20.2 (8.6) | | | 41% |

AHI: apnea-hypopnea index; CPAP: continuous positive airway pressure; MAD: mandibular advancement device; nCPAP: nasal CPAP; ND: no data; RCT: randomized controlled trial

Table 13. Treatment with mandibular advancement devices vs. control: Compliance.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Compliance Definition | Compliant % (SD) | P-value |
|--|--------------------|--------------|--------------------------------------|--|------------------|----------------------------|
| Aarab (a), 2011 | MAD | 20 | 6 months (RCT) | Percentage of nights per week usage, based on 6 months (self-report) | 90.6% (13.3) | Among the group p=0.228 |
| | nCPAP | 18 | | | 82.9% (27.2) | |
| | Placebo (sham MAD) | 19 | | | 93.9% (15.7) | |
| Aarab (b), 2011 *long-term follow-up of Aarab (a) | MAD | 15 | 18 months (parallel-group follow-up) | Percentage of nights per week usage, based on 6 months (self-report) | 85.8% (18.8) | NS |
| | nCPAP | 13 | | | 84.8% (20.6) | |

CPAP: continuous positive airway pressure; MAD: mandibular advancement device; nCPAP: nasal CPAP; ND: no data; NS: not significant; RCT: randomized controlled trial; SD: standard deviation

Table 14. Studies of surgical procedures: Study characteristics.

| Study Author, Year | Country (enrollment years) | Interventions | N | Study Duration (trial design) | Mean Age (years) | Male (%) | Mean BMI (kg/m ²) | Other Patient Characteristics |
|--------------------|---------------------------------|---|------|--|--------------------------------|----------|--------------------------------|--|
| Friedman, 2012 | USA (Mar. 2007 - Jun. 2011) | Transoral robotic surgery (TORS) | 27 | Mean follow-up: 88 days (retrospective cohort) | 43.8 | 89% | 32.3 | Concurrent z-palatoplasty done; AHI ≥ 15; Friedman tongue position 3 or 4; documented failure/refusal of conservative treatment (including CPAP); excluded patients with previous surgical treatment for OSA |
| | | Radiofrequency base-of-tongue reduction (RFBOT) | 24 | | 44 | 92% | 31.6 | |
| | | Submucosal minimally invasive lingual excision (SMILE) | 22 | | 41.7 | 91% | 31.5 | |
| Goodyday, 2012 | Canada (Feb. 2000 - Sept. 2010) | Maxillomandibular advancement (MMA) | 116 | 6 months (prospective cohort) | 45.6 | 68% | nd | 102/116 (88%) of patients used CPAP prior to surgery |
| Huang, 2011 | Taiwan (nd) | Palatal implant (PI) | 21 | 6 months (prospective cohort) | 43.2 | 81% | 27.2 | AHI ≥ 5, < 20; excluded Friedman palate position grade 3 or 4, tonsil size 3 or 4; excluded uvular size > grade 2; excluded BMI >30 |
| | | Uvulopalatal flap (UPF) | 20 | | 43.1 | 80% | 27.4 | |
| | | PI + UPF | 22 | | 42 | 73% | 27.6 | |
| Tschopp, 2011 | Switzerland (2007-2009) | Multilevel surgery, including UPPP, nasal surgery and tonsillectomy | 107* | 3 months (prospective cohort) | (median) 52.3 [IQR: 43.1-60.1] | nd | (median) 28.4 [IQR: 26.7-30.8] | OSA defined as pre-op AHI > 10; patients eligible for surgery if intolerant or refusing of CPAP therapy |

* Full analysis excluded as >20% of patients were diagnosed with upper airway resistance syndrome (UARS), a pre-specified criterion of the AHRQ review.

AHI: apnea-hypopnea index; BMI: body mass index; CPAP: continuous positive airway pressure; IQR: inter quartile range; N: number; ND: no data; OSA: obstructive sleep apnea; UPPP: uvulopalatopharyngoplasty

Table 15. Surgical trials: Outcomes.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Baseline AHI (SD) | Final AHI (SD) | Difference | 95% CI | P-value | Surgical Success (%) | P-value | Dropout (%) |
|--------------------|---|-------------------|--|-------------------|----------------|-------------|--------|---------|----------------------|---------|-------------------|
| Friedman, 2012 | Transoral robotic surgery (TORS) | 27 | Mean follow-up: 88 days (retrospective cohort) | 54.6 (21.8) | 18.6 (9.1) | 36.1 (21.6) | nd | --- | 18 (66.7%)‡ | --- | --- |
| | Radiofrequency base-of-tongue reduction (RFBOT) | 24 | | 54.7 (26.6) | 34.6 (22.5) | 20.0 (25.2) | nd | 0.022* | 5 (20.8%) | 0.001* | --- |
| | Submucosal minimally invasive lingual excision (SMILE) | 22 | | 53.7 (29.3) | 26.6 (23.9) | 27.2 (32.2) | nd | 0.254* | 10 (45.5%) | 0.135* | --- |
| Goodday, 2012 | Maxillomandibular advancement (MMA) | ESS ≤ 10 n=33 | 6 months (prospective cohort) | ESS: 7.3 | 4.5 (n=104) | nd | nd | <0.001§ | nd | nd | Overall: 31% |
| | | ESS 10-16 n=37 | | ESS: 12.9 | 4.4 (n=11) | nd | | | nd | nd | |
| | | ESS ≥ 16 n=46 | | ESS: 18.3 | 5.9 (n=1) | nd | | | nd | nd | |
| Huang, 2011 | Palatal implant (PI) | 21 | 6 months (prospective cohort) | 14.1 (5.1) | 9.0 (4.6) | nd | nd | <0.05# | nd | nd | nd |
| | Uvulopalatal flap (UPF) | 20 | | 14.2 (5.2) | 8.8 (4.0) | nd | | | nd | nd | |
| | PI + UPF | 22 | | 14.1 (5.9) | 6.1 (2.5) | nd | | | nd | nd | |
| Tschopp, 2011 | Multilevel surgery, including UPPP, nasal surgery and tonsillectomy | 107 | 3 months (prospective cohort) | nd | nd | nd | nd | nd | 50 (47%)^ | --- | At 12 months: 51% |

*Comparison vs. TORS

‡Surgical success defined as: AHI < 20, AHI reduction ≥ 50%

§Comparison of pre- and post-surgical ESS assessments

#P-value reported among treatment arms; PI + UPF vs. others: p<0.05

^ Treatment success defined as: AHI < 20, >50% reduction in pre-op AHI

AHI: apnea-hypopnea index; ESS: Epworth Sleepiness Scale; ND: no data; UPPP: uvulopalatopharyngoplasty

Table 16. Studies of exercise interventions: Study characteristics.

| Study Author, Year | Country (enrollment years) | Interventions | N | Study Duration (trial design) | Mean Age (years) | Male (%) | Mean BMI (kg/m ²) | Other Patient Characteristics |
|--------------------|--------------------------------|--|----|-------------------------------|------------------|----------|-------------------------------|---|
| Kline, 2011 | USA (nd) | Structured exercise training | 27 | 12 weeks (RCT) | 47.6 | 56% | 35.5 | AHI ≥ 15, BMI ≥ 25, no current OSA treatment, no active weight loss programs |
| | | Control (stretching) | 16 | | 45.9 | 56% | 33.6 | |
| Sengul, 2011 | Turkey (nd) | Structured breathing & exercise programs | 25 | 12 weeks (RCT) | 54.4 | 100% | 29.8 | Patients in good health, AHI 5-30 |
| | | Control (no treatment) | | | 48.0 | 100% | 28.4 | |
| Servantes, 2011 | Brazil (Mar. 2007 - Nov. 2008) | Aerobic training (home-based) | 18 | 3 months (RCT) | 51.8 | 47% | 26.9 | Patients with CHF (Class II-III, LVEF <40%), sleep apnea (not defined), stable medication therapy including β-blocker |
| | | Aerobic & strength training (home-based) | 18 | | 50.8 | 47% | 28.0 | |
| | | Control (no training) | 14 | | 53.0 | 45% | 27.7 | |

AHI: apnea-hypopnea index; BMI: body mass index; CHF: congestive heart failure; LVEF: left ventricular ejection fraction; OSA: obstructive sleep apnea; RCT: randomized controlled trial

Table 17. Treatment with exercise interventions: AHI.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Baseline AHI (SD) | Final AHI (SD) | Difference | 95% CI | P-value | Dropout (%) | Other Outcomes |
|--------------------|--|--------------|-------------------------------|-------------------|----------------|------------|--------|---------|--------------------------|---|
| Kline, 2011 | Structured exercise training | 27 | 12 weeks (RCT) | Graph* | Graph* | -7.6 | nd | <0.01 | 11% | Treatment success (AHI<20, reduction of ≥50% from baseline: 25% (exercise) vs. 7% (stretch), p=0.23) |
| | Control (stretching) | 16 | | Graph* | Graph* | +4.5 | | | 13% | |
| Sengul, 2011 | Structured breathing & exercise programs | 10 | 12 weeks (RCT) | 15.19 (5.43) | 11.01 (5.28) | nd | nd | 0.11 | Overall: 5/25 (20%) | For exercise group, AHI decreased (p=0.02); for control, change in AHI not significant (p=0.58); no significant changes in ESS between groups or change from baseline |
| | Control (no treatment) | 10 | | 17.92 (6.45) | 17.36 (11.18) | nd | | | | |
| Servantes, 2011 | Aerobic training (home-based) | 17 | 3 months (RCT) | 25.2 (24.7) | 16.7 (18.6) | nd | nd | 0.001 | 6% (1 death) | For Groups 1 & 2, significant changes from baseline (p≤0.001 for both); Group 3 was not significant; between Groups 1 & 2: no significant diff. in change, p=0.96 |
| | Aerobic & strength training (home-based) | 17 | | 26.4 (17.6) | 16.4 (11.1) | nd | | | 6% (1 MI) | |
| | Control (no training) | 11 | | 22.8 (17.4) | 25.9 (18.8) | nd | | | 21% (1 death, 2 strokes) | |

* Data available in graph-form only.

AHI: apnea-hypopnea index; ESS: epworth Sleepiness Scale; MI: myocardial infarction; ND: no data; RCT: randomized controlled trial; SD: standard deviation

Table 18. Treatment with exercise interventions: Weight changes.

| Study Author, Year | Interventions | No. Analyzed | Study Duration (trial design) | Baseline Weight, kg (SD) | Final Weight, kg (SD) | Change, kg | Difference | 95% CI | P-value | Dropout (%) |
|--------------------|--|--------------|-------------------------------|--------------------------|-----------------------|------------|------------|--------|---------|--------------------------|
| Kline, 2011 | Structured exercise training | 27 | 12 weeks (RCT) | 105.6 (3.0) | 104.7 | -0.9 | -0.3 | nd | NS | 11% |
| | Control (stretching) | 16 | | 99.3 (5.0) | 98.7 | -0.6 | | | | 13% |
| Servantes, 2011 | Aerobic training (home-based) | 17 | 3 months (RCT) | nd | nd | nd | nd | nd | 0.54* | 6% (1 death) |
| | Aerobic & strength training (home-based) | 17 | | nd | nd | nd | nd | | 0.55* | 6% (1 MI) |
| | Control (no training) | 11 | | nd | nd | nd | nd | | >1.0* | 21% (1 death, 2 strokes) |

* Versus baseline measurements

MI: myocardial infarction; ND: no data; NS: not significant; RCT: randomized controlled trial; SD: standard deviation

Appendix C



Key Definitions

1. **Adults:** Patients over 16 years of age.
2. **Obstructive sleep apnea:** According to the American Academy of Sleep Medicine (AASM), a diagnosis of OSA is established if a patient with polysomnography demonstrates an apnea/hypopnea index (AHI) of > 15 events/hour, or > 5 events/hours in patients who report any of the following: unintentional sleep episodes during wakefulness; daytime sleepiness; unrefreshing sleep; fatigue; insomnia; waking up breath holding, gasping, or choking; or the bed partner describing loud snoring, breathing interruptions, or both during the patient's sleep.
3. **Polysomnography:** Diagnostic test for obstructive sleep apnea that is performed overnight in a sleep laboratory whereby a technologist monitors the patient's patterns of physiological abnormalities during sleep.
2. **Home monitors:** Home monitors are portable machines used to diagnose OSA in the home environment without the attendance of a technologist. They are classified into 3 categories as described below:
 - a. Type II: have at least 7 channels for monitoring patients, including ECG-heart rate, EEG, airflow and respiratory effort.
 - b. Type III: minimum of 4 monitored channels, including airflow, heart rate and oxygen saturation.
 - c. Type IV: have 1-3 channels monitoring patients and do not meet the criteria of the other monitor types.
4. **Questionnaires:** The Berlin questionnaire, STOP, STOP-Bang, ASA Checklist, Epworth Sleepiness Scale, Hawaii Sleep questionnaires, and other questionnaires that focus on a patient's risk factors and chronic behaviors suggestive of OSA.
5. **Clinical prediction rules:** Algorithm that uses various criteria, such as questionnaires and morphometric data, to predict the diagnosis of OSA.
6. **Continuous Positive Airway Pressure (CPAP):** Machine used in patients with OSA to maintain a continuous level of positive airway pressure. Includes several variations, including: oral, nasal, autotitrating, bilevel, flexible bilevel, fixed, humidification, and C-Flex™.
7. **Usual care:** Control arms of studies have used a variety of interventions to classify usual care, including: no specific treatment, placebo therapy, optimal drug treatment, and conservative measures, which entail sleep hygiene counseling along with participation in a weight loss program.
8. **Surgery:** Any surgery to the airway designed to reduce airway obstruction. Specific surgical interventions include uvulopalatopharyngoplasty (UPPP), laser-assisted uvulopalatoplasty (LAUP), radiofrequency

ablation (RFA), and combinations of pharyngoplasty, tonsillectomy, adenoidectomy, or combination nasal surgery.

9. **Mandibular Advancement Devices (MADs):** Devices worn orally to treat OSA and snoring.
10. **Intervention Programs:** Specific therapies designed to improve CPAP compliance. Adjunctive therapies may include intensive support or literature, cognitive behavioral therapy, telemonitoring, and habit-promoting audio-based interventions.



New England Comparative Effectiveness Public Advisory Council

Public Meeting – Hartford, CT

December 6, 2012

10:00 AM – 4:00 PM

10:00 – 10:15 AM: Meeting Convened and Introductions (*Jeannette DeJesús, MPA, MSW and Steven Pearson, MD, MSc*)

10:15 – 11:00 AM: Presentation of the Evidence

11:00 AM – 12:00 PM: Q&A with ICER Staff and CEPAC Deliberation

12:00 – 1:00 PM: Lunch

1:00 – 1:30 PM: Public Comment

1:30 – 2:30 PM: Votes on Questions

2:30 – 3:50 PM: Roundtable Discussion on Implications of CEPAC Votes

3:50 – 4:00 PM: Close

MEETING PARTICIPANTS

| Name | State | Organization | Disclosures |
|----------------------------------|-------|--|---|
| Ellen Andrews, PhD | CT | CT Health Policy Project | |
| Robert Aseltine, PhD | CT | University of Connecticut Health Center | |
| R. William Corwin, MD | RI | Miriam Hospital | |
| D. Joshua Cutler, MD | ME | MaineHealth and Maine Heart Center | |
| Teresa Fama, MD | VT | Central Vermont Rheumatology | |
| Austin Frakt, PhD | MA | Boston University School of Medicine and Boston University School of Public Health | |
| Claudia Gruss, MD (Vice Chair) | CT | Arbor Medical Group, LLC | Wellpoint shares held jointly with spouse in excess of \$10,000 |
| Felix Hernandez, MD | ME | Eastern Maine Medical Center | |
| Joseph Kozachek, MD (ex-officio) | CT | Aetna | |
| Richard Lopez, MD (Chair) | MA | Atrius Health | |
| Lori Nerbonne, RN, BSN | NH | New Hampshire Patient Voices | |
| Sandhya Rao, MD | MA | Massachusetts General Physicians Organization | |
| Roger Snow, MD (ex-officio) | MA | Commonwealth of Massachusetts | |
| Keith A. Stahl, MD | NH | Family Health and Wellness Center | |
| Mitchell Stein, MBA | ME | Consumers for Affordable Health Care | |
| William Taylor, MD | MA | Harvard Medical School | Also employed by Harvard Pilgrim Health Care Institute (HPHCI), which receives funding from Harvard Pilgrim Health Care; Payments also received as a medical consultant to malpractice insurers |

Members not in attendance:

- Charles Eaton, MD, MS, Memorial Hospital of Rhode Island and Brown University
- William Cyrus Jordan, MD, MPH, Vermont Medical Society's Foundation for Research and Education
- Christopher Jones, PhD, University of Vermont College of Medicine

Roundtable Panelists

- **Mark D'Agostino, MD**
Section Chief, Otolaryngology
- **Lawrence Epstein, MD**
Chief Medical Officer, Sleep HealthCenters
- **Robert McDonough, MD, JD, MPP**
Head of Clinical Policy Research and Development, Aetna, Inc.
- **Robert Zavoski, MD, MPH**
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- Steve Pearson, MD, President
- Daniel Ollendorf, MPH, Chief Review Officer
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- Swetha Sitaram, MS, Research Associate
- Jessica Chubiz, MS, Research Associate
- Sarah Jane Reed, MSc, Program Coordinator

