The New England Comparative Effectiveness Public Advisory Council

Public Meeting – December 6, 2012

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

Draft Report – November 16, 2012

Completed by:

The Institute for Clinical and Economic Review

ICER
INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

Table of Contents

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/m^2), 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; SaO_2: 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 (BiPAP) 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). Limitations to using an MAD include sufficient dentition for anchoring of the appliance and absence 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 (≥ 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 on 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. BiPAP 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 uvulva, 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.

While Aetna, Cigna, Humana and UnitedHealthcare provide coverage of split-night testing in patients undergoing full-night PSG, its use is restricted according to various thresholds of AHI (≥5-40) observed during the initial phase of full-night 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&

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&

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 (BiPAP) 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 ≥ 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, BiPAP 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, BiPAP 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 ≥ 4 hours/night, 6 nights/week or 70% of nights, generally during a 30-day period. Connecticare 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=gAAAABAAAAAA&

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=gAAAABAAAAAA&

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/m^2. 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 ≥ 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 ≥ 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 appoints 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≤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 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.

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
BiPAP (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 BiPAP 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 + PSG	Type III monitor 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 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 BiPAP 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.

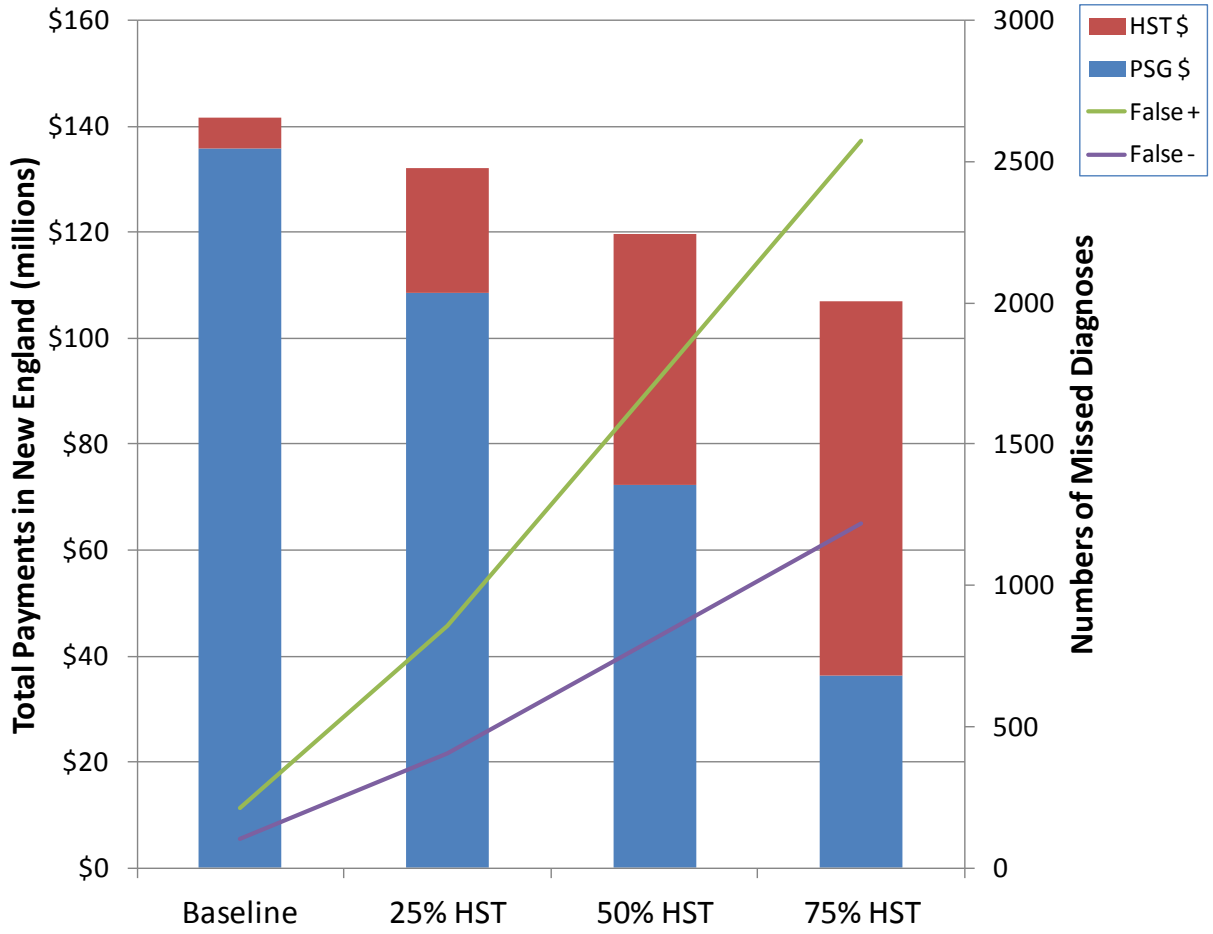
Estimates of the population age >16 years were obtained from 2011 Census data (Census.gov, 2012). This population was estimated to total 11.3 million individuals. The percentage of persons undergoing diagnostic testing in 2011 was estimated to be 1.03%, consistent with the rate observed in the HealthCore 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

Following the public CEPAC meeting on December 6, 2012, this section will be completed to capture the discussion of the Council members regarding the adaptation, specifically around these Questions to Guide 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.

About the Questions

Comparative Clinical Effectiveness
The general framework within which CEPAC discusses and votes on the evidence is shown below:

Given a health care "intervention A" for "patients with condition X," we will compare its clinical effectiveness for these patients to that of a "comparator B" by voting on the following question:

Is the evidence "adequate" to demonstrate that "intervention A" is equivalent or superior to "comparator B" for "patients with condition X"?

Discussion and voting will highlight the following issues:

1. The evidence on risks and benefits to determine the *comparative* clinical effectiveness of management options for specific patient populations. In judging comparative clinical effectiveness, there are two interrelated questions: the relative magnitude of differences in risks and benefits; and the relative confidence that the body of evidence can provide in the accuracy of estimates of risks and benefits. Considering these two issues together is required in order to make a judgment of whether the evidence is "adequate" to demonstrate that one intervention is equivalent to or superior than another.

2. Issues related to individual patient preferences and values, provider training, volume, or other factors that should be considered in judging the evidence on clinical effectiveness and value.
3. Weighing the evidence on cost-effectiveness and projected budgetary impact to determine the comparative value of various management options for key patient populations.
4. Comments or recommendations related to broader considerations of public health, equity, disparities, and access.

Comparative Value

When a majority of CEPAC votes that the evidence is adequate to demonstrate that an intervention produces patient outcomes as good as or better than a comparator, the Council will also be asked to vote on whether the intervention represents a "high," "reasonable," or "low" value. The value "perspective" that CEPAC will be 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 will be provided, CEPAC will not be given prescribed boundaries or thresholds for budget impact or incremental cost-effectiveness ratios to guide its judgment of high, reasonable, or low value.

For each vote, Council members will be asked to identify which element of the information provided to them on "value" was most influential in their judgment: 1) information on the incremental cost for an additional benefit (or for reduction in risk); or 2) information on the budget impact of different care/payment scenarios. Council members will also be asked to describe briefly the rationale for their rating of comparative value.

Questions for Obstructive Sleep Apnea (OSA)

Definitions:

1. 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.
2. 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.

3. 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.
4. Clinical prediction rules: Algorithm that uses various criteria, such as questionnaires and morphometric data, to predict the diagnosis of OSA.
5. 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™.
6. "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.
7. Mandibular Advancement Devices (MAD): Devices worn orally to treat OSA and snoring.

8. Adjunctive therapies: 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.

Comparative Clinical Effectiveness and Value: Diagnosis of OSA in Adults

Comparative Clinical Effectiveness

Note: Type II monitors are excluded from consideration in these voting questions due to the lack of studies assessing Type II monitors, though this in no way implies that Type II monitors are ineffective in diagnosing OSA.

Voting Questions:

1. Is the evidence adequate to demonstrate that Type III home monitors are equivalent to polysomnography in diagnosing OSA?

2. Is the evidence adequate to demonstrate that Type IV home monitors are equivalent to polysomnography in diagnosing OSA?

3. Is the evidence adequate to demonstrate that Type IV home monitors are equivalent to Type III monitors in diagnosing OSA?

4. Is the evidence adequate to demonstrate that a phased diagnostic approach using the Berlin questionnaire to identify candidates for polysomnography is equivalent to using polysomnography in all patients in which there is a clinical suspicion for the diagnosis of OSA?

5. Is the evidence adequate to demonstrate that a phased diagnostic approach using externally-validated clinical predication rules to identify candidates for polysomnography is equivalent to using polysomnography in all in which there is a clinical suspicion for the diagnosis of OSA?

Comment/Recommendation:

Are there any factors related to the following that should also be considered?

1. Patient characteristics or severity

2. Test-retest reliability and the diagnosis of OSA

3. Appropriate threshold of AHI for diagnosis of OSA

Comparative Value (TO BE ASKED IF >50% OF CEPAC VOTES IN FAVOR OF ADEQUACY OF EVIDENCE ON CLINICAL EFFECTIVENESS)

1. Based on reimbursement levels provided in this report, would you judge the comparative value of Type III home monitors compared to polysomnography to be: 1) high value; 2) reasonable value; or 3) low value?

2. Based on reimbursement levels provided in this report, would you judge the comparative value of Type IV home monitors compared to Type III monitors to be: 1) high value; 2) reasonable value; or 3) low value?

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

4. Based on reimbursement levels provided in this report, would you judge the comparative value of a phased diagnostic approach using externally-validated clinical prediction rule(s) compared to polysomnography alone to be: 1) high value; 2) reasonable value; or 3) low value?

Comparative Clinical Effectiveness and Value: Treatment of OSA in Adults

Comparative Clinical Effectiveness

Based on the findings of the AHRQ review, and time limitation of the CEPAC meeting, we will ask CEPAC for unanimous consent to the following stipulations. If there is dissent, then a formal vote will be taken.

- 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.

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

- There is insufficient evidence to demonstrate that any variation on CPAP (e.g. nasal, autotitrating, bilevel, etc.) notably improves adherence or outcomes in adults with OSA.

- 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.

Voting Questions

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

2. Is the evidence adequate to demonstrate that mandibular advancement devices (MAD) are superior to no treatment in treating OSA?

   Comment/Recommendation:

   Are there any factors related to patient characteristics or severity of OSA that should also be considered?

3. Is the evidence adequate to demonstrate that mandibular advancement devices (MAD) are equivalent or superior to CPAP in treating mild-to-moderate OSA (AHI 5-30 events/hour)?
   a. If yes, does the evidence suggest that:
      - Mandibular advancement devices are equivalent to CPAP?
      - Mandibular advancement devices are superior than CPAP?

   Comment/Recommendation:

   Are there any factors related to patient characteristics or severity of OSA that should also be considered?

Comparative Value (TO BE ASKED IF >50% OF CEPAC VOTES IN FAVOR OF ADEQUACY OF EVIDENCE ON CLINICAL EFFECTIVENESS)

1. Based on reimbursement levels provided in this report, would you judge the comparative value of MAD compared to no treatment to be: 1) high value; 2) reasonable value; or 3) low value?

2. Based on reimbursement levels provided in this report, would you judge the comparative value of MAD compared to CPAP for moderate OSA (AHI 15-30 events/hour) to be: 1) high value; 2) reasonable value; or 3) low value?

   Comment/Recommendation:

   Are there any factors related to patient characteristics or severity of OSA that should also be considered?

References

Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: a randomized, placebo-controlled trial. *Respiration*. 2011a;81(5):411-419.

Aarab G, Lobbezoo, Heymans MW, Hamburger HL, Naeije M. Long-term follow-up of a randomized controlled trial of oral appliance therapy in obstructive sleep apnea. *Respiration*. 2011;82(2):162-168.

Aetna. Clinical policy bulletin: Obstructive sleep apnea in adults. http://www.aetna.com/cpb/medical/data/1_99/0004.html. Accessed October/November, 2012.

Ahrens A, McGrath C, Hägg U. A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnoea. *Eur J Orthod*. 2011;33(3):318-324.

Amir O, Barak-Shinar D, Amos Y, MacDonald M, Pittman S, White DP. An automated sleep-analysis system operated through a standard hospital monitor. *J Clin Sleep Med*. 2010;6(1):59-63.

Anthem. Medical policy: Oral, pharyngeal and maxillofacial surgical treatment for obstructive sleep apnea (SURG.00129). http://www.anthem.com/medicalpolicies/policies/mp_pw_a050503.htm. Accessed October/November, 2012.

Aurora RN, Casey KR, Kristo D, et al. Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. *Sleep*. 2010;33(10):1408-1413.

Balk EM, Moorthy D, Obadan NO, et al. Diagnosis and treatment of obstructive sleep apnea in adults. Comparative effectiveness review no. 32. Rockville, MD: Agency for Healthcare Research and Quality; 2011; 11-EHC052-EF.

Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, et al. for the Spanish Sleep and Breathing Network. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *JAMA*. 2012;307(20):2161-2168.

Berry RB, Kryger MH, Massie CA. A novel nasal expiratory positive airway pressure (EPAP) device for the treatment of obstructive sleep apnea: a randomized controlled trial. *Sleep*. 2011;34(4):479-485.

BlueCross Blue Shield of Massachusetts. Medical policy: Diagnosis and medical management of obstructive sleep apnea syndrome (#293). http://www.bluecrossma.com/common/en_US/medical_policies/293_Diagnosis_and_Medical_Management_of_Obstructive_Sleep_Apnea_Syndrome_prn.pdf#page=1. Accessed October, 2012.

BlueCross Blue Shield of Massachusetts. Medical policy: Surgical treatment of snoring and obstructive sleep apnea syndrome (#130). http://www.bluecrossma.com/common/en_US/medical_policies/130%20Surgical%20Treatment%20of%20Snoring%20and%20Obstructive%20Sleep%20Apnea%20Syndrome%20prn.pdf#page=1. Accessed October, 2012.

BlueCross BlueShield of Rhode Island. Medical coverage policy: Minimally invasive surgery for snoring, obstructive sleep apnea syndrome/upper airway resistance syndrome. https://www.bcbsri.com/sites/default/files/polices/MinimallyInvasiveSurgeryforObstructiveSleepApneaSyndromeandUpperAirwayResistanceSyndrome.pdf. Accessed October, 2012.

BlueCross BlueShield of Rhode Island. Medical coverage policy: Oral appliances. https://www.bcbsri.com/sites/default/files/polices/OralAppliancesforSleepApnea.pdf. Accessed October, 2012.

BlueCross BlueShield of Rhode Island. Medical coverage policy: Sleep testing. https://www.bcbsri.com/sites/default/files/polices/SleepStudy.pdf. Accessed October, 2012.

BlueCross BlueShield of Vermont. Corporate medical policy: Oral appliances for obstructive sleep apnea. http://www.bcbsvt.com/export/sites/BCBSVT/provider/medicalpolicies/PDFs/Oral_Appliances_for_Obstructive_Sleep_Apnea_Medical_Policy.pdf. Accessed October, 2012.

BlueCross BlueShield of Vermont. Corporate medical policy: Sleep disorders diagnosis and treatment. http://www.bcbsvt.com/export/sites/BCBSVT/provider/medicalpolicies/PDFs/SleepDisordersDiagnosisandTreatment.pdf. Accessed October, 2012.

Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology*. 2008;108(5):812-821.

Cigna. Cigna medical coverage policy: Obstructive sleep apnea diagnosis and treatment services. http://www.cigna.com/assets/docs/health-care-professionals/coverage_positions/mm_0158_coveragepositioncriteria_obstructive_sleep_apnea_diag_trtment_svc.pdf. Accessed October/November, 2012.

Collop NA, Anderson WM, Boehlecke B, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adults patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2007;3(7):737-747.

ConnectiCare. Medical management: Medical pre-authorization criteria. http://www.connecticare.com/providers/medicalpolicycriteria.aspx. Accessed October, 2012.

Danzi-Soares N, Genta PR, Nerbass FB, et al. Obstructive sleep apnea is common among patients referred for coronary artery bypass grafting and can be diagnosed by portable monitoring. *Coron Artery Dis*. 2011;23(1):31-38.

Drager LF, Genta PR, Pedrosa RP, et al. Characteristics and predictors of obstructive sleep apnea in patients with systemic hypertension. *Am J Cardiol*. 2010;105(8):1135-1139.

Epstein LJ, Kristo D, Strollo Jr. PJ, et al. for the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*. 2009;5(3):263-276.

Friedman M, Hamilton C, Samuelson CG, et al. Transoral robotic glossectomy for the treatment of obstructive sleep apnea-hypopnea syndrome. *Otolaryngol Head Neck Surg*. 2012;146(5):854-862.

Gagnadoux F, Fleury B, Vielle B, et al. Titrated mandibular advancement versus positive airway pressure for sleep apnoea. *Eur Respir J*. 2009;34(4):914-920.

Goodday R, Bourque S. Subjective outcomes of maxillomandibular advancement surgery for the treatment of obstructive sleep apnea. *J Oral Maxillofac Surg*. 2012;70(2):417-420.

Guest, JF, Helter MT, Morga A, Stradling JR. Cost-effectivenss of using continuous positive airway pressure in the treatment of severe obstructive sleep apnoea/hypopnoea syndrome in the UK. *Thorax*. 2008;63(10):860-865.

Harvard Pilgrim Health Care. Medical review criteria: Obstructive sleep apnea surgeries. https://www.harvardpilgrim.org/pls/portal/docs/PAGE/PROVIDERS/MEDMGMT/MEDICAL_REVIEW_CRITERIA/OSA%20SURG-EFF102512.PDF. Accessed October/November, 2012.

Harvard Pilgrim Health Care. Sleep management criteria. http://www.carecorenational.com/content/pdf/11/10F894F484F54D369FF678ED8ACBF8D2.pdf. Accessed October, 2012.

Hayano J, Watanabe E, Saito Y, et al. Diagnosis of sleep apnea by the analysis of heart rate variation: a mini review. *Conf Proc IEEE Eng Med Biol Soc*. 2011;2011:7731-7734.

HealthNet. National medical policy: Obstructive sleep apnea, diagnosis and medical treatments (NMP28). https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/OSA_Diagnosis_and_Medical_Treatment_Mar_12.pdf. Accessed October, 2012.

HealthNet. National medical policy: Obstructive sleep apnea – surgical treatments (NMP146). https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/Obstructive_Sleep_Apnea_Surgical_Treatments_Mar_12.pdf. Accessed October, 2012.

Ho ML, Brass SD. Obstructive sleep apnea. *Neurol Int*. 2011;3(3):e15.

Huang T-W, Cheng P-W, Fang K-M. Concurrent palatal implants and uvulopalatal flap: safe and effective office-based procedure for selected patients with snoring and obstructive sleep apnea syndrome. *Laryngoscope*. 2011;121(9):2038-2042.

Humana. Medical coverage policies. http://apps.humana.com/tad/tad_new/Search.aspx?criteria=apnea&searchtype=freetext. Accessed October, 2012.

Institute for Clinical Systems Improvement. Health Care Guideline: Diagnosis and treatment of obstructive sleep apnea. http://www.icsi.org/sleep_apnea/sleep_apnea__diagnosis_and_treatment_of_obstructive_.html. Accessed October, 2012.

Jauhar S, Orchardson R, Banham SW, Livingston E, Sherriff A, Lyons MF. The Kushida Index as a screening tool for obstructive sleep apnoea-hypopnoea syndrome. *Br Dent J*. 2012;212(1):E2.

Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep*. 1991;14(6):540-545.

Kapur V, Blough DK, Sandblom RE, et al. The medical cost of undiagnosed sleep apnea. *Sleep*. 1999;22(6):749-755.

Kashyap R, Hock LM, Bowman TJ. Higher prevalence of smoking in patients diagnosed as having obstructive sleep apnea. *Sleep Breath*. 2001;5(4):167-172.

Kline CE, Crowley EP, Ewing GB, et al. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. *Sleep*. 2011;34(12):1631-1640.

Koyama RG, Esteves AM, Oliveira e Silva, et al. Prevalence of and risk factors for obstructive sleep apnea syndrome in Brazilian railroad workers. *Sleep Med*. 2012;13(8):1028-1032.

Kushida CA, Berry RB, Blau A, et al. Positive airway pressure initiation: a randomized controlled trial to assess the impact of therapy mode and titration process on efficacy, adherence, and outcomes. *Sleep*. 2011;34(8):1083-1092.

Kushida CA, Efron B, Guilleminault. A predictive morphometric model for the obstructive sleep apnea syndrome. *Ann Int Med*. 1997;127(8 Pt 1):581-587.

Kushida CA, Littner MR, Morgenthaler T, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep*. 2005;28(4):499-521.

Lee I-S, Bardwell W, Ancoli-Israel S, Loredo JS, Dimsdale JE. Effect of three weeks of continuous positive airway pressure treatment on mood in patients with obstructive sleep apnoea: a randomized placebo-controlled study. *Sleep Med*. 2012;13(2):161-166.

Marcos JV, Hornero R, Álvarez D, Aboy M, Del Campo F. Automated prediction of the apnea-hypopnea index from nocturnal oximetry recordings. *IEEE Trans Biomed Eng*. 2012;59(1):141-149.

Marcos JV, Hornero R, Álvarez D, Del Campo F, Aboy M. Automated detection of obstructive sleep apnoea syndrome from oxygen saturation recordings using linear discriminant analysis. *Med Biol Eng Comput*. 2010;48(9):895-902.

Martinez D, Breitenbach TC, Lumertz MS, et al. Repeating administration of the Epworth Sleepiness Scale is clinically useful. *Sleep Breath*. 2011;15(4):763-773.

Martinez D, daSilva RP, Klein C, et al. High risk for sleep apnea in the Berlin questionnaire and coronary artery disease. *Sleep Breath*. 2012;16(1):89-94.

Masa JF, Corral J, Pereira R, et al. Effectiveness of home respiratory polygraphy for the diagnosis of sleep apnoea and hypopnea syndrome. *Thorax*. 2011;66(7):567-573.

Mayo Foundation for Medical Education and Research. Healthy lifestyle: Obstructive sleep apnea. http://www.mayoclinic.com/health/obstructive-sleep-apnea/DS00968. Accessed November, 2012.

National Institute for Health and Clinical Excellence (NICE). Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. http://www.nice.org.uk/nicemedia/live/11944/40085/40085.pdf. Accessed October, 2012.

Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Int Med*. 1999;131(7):485-491.

Oktay B, Rice TB, Atwood Jr. CW, et al. Evaluation of a single-channel portable monitor for the diagnosis of obstructive sleep apnea. *J Clin Sleep Med*. 2011;7(4):384-390.

Pack AI, Gislason T. Obstructive sleep apnea and cardiovascular disease: a perspective and future directions. *Prog Cardiovasc Dis*. 2009;51(5):434-451.

Pietzsch JB, Garner A, Cipriano LE, Linehan JH. An integrated health-economic analysis of diagnostic and therapeutic strategies in the treatment of moderate-to-severe obstructive sleep apnea. *Sleep*. 2011;34(6):695-709.

Punjabi NM. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5(2):136-143.

Ronksley PE, Hemmelgarn BR, Heitman SJ, et al. Excessive daytime sleepiness is associated with increased health care utilization among patients referred for assessment of OSA. *Sleep*. 2011;34(3):363-370.

Rusu A, Todea D, Rosca L, Nita C, Bala C. The development of a sleep apnea screening program in Romanian type 2 diabetic patients: a pilot study. *Acta Diabetol*. 2012;49(2):105-109.

Sadatsafavi M, Marra CA, Ayas NT, Stradling J, Fleetham J. Cost-effectiveness of oral appliances in the treatment of obstructive sleep apnoa-hypopnoea. *Sleep Breath*. 2009;13(3):241-252.

Santos-Silva R, Sartori DE, Truksinas V, et al. Validation of a portable monitoring system for the diagnosis of obstructive sleep apnea syndrome. *Sleep*. 2009;32(5):629-636.

Sassani A, Findley LJ, Kryger M, Goldlust E, George C, Davidson TM. Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome. *Sleep*. 2004;27(3):453-458.

Sengul YS, Ozalevli S, Oztura I, Itil O, Baklam B. The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. *Sleep Breath*. 2011;15(1):49-56.

Sert-Kuniyoshi FH, Squires RW, Korenfeld YK, et al. Screening for obstructive sleep apnea in early outpatient cardiac rehabilitation: feasibility and results. *Sleep Med*. 2011;12(9):924-927.

Sert-Kuniyoshi FH, Zellmer MR, Calvin AD, et al. Diagnostic accuracy of the Berlin Questionnaire in detecting sleep-disordered breathing in patients with a recent myocardial infarction. *Chest*. 2011;140(5):1192-1197.

Servantes DM, Pelcerman A, Salvetti XM, et al. Effects of home-based exercise training for patients with chronic heart failure and sleep apnoea: a randomized comparison of two different programmes. *Clin Rehabil*. 2012;26(1):45-57.

Sharma SK, Agrawal S, Damodaran D, et al. CPAP for the metabolic syndrome in patients with obstructive sleep apnea. *N Engl J Med*. 2011;365(24):2277-2286.

Silva GE, Vana KD, Goodwin JL, Sherrill DL, Quan SF. Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales. *J Clin Sleep Med*. 2011;7(5):467-472.

Tan MCY, Ayas NT, Mulgrew A, et al. Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia. *Can Respir J*. 2008;15(3):159-165.

To K-W, Chan W-C, Chan T-O, et al. Validation study of a portable monitoring device for identifying OSA in a symptomatic patient population. *Respirology*. 2009;14(2):270-275.

Tomfohr LM, Ancoli-Israel S, Loredo JS, Dimsdale JE. Effects of continuous positive airway pressure on fatigue and sleepiness in patients with obstructive sleep apnea: data from a randomized controlled trial. *Sleep*. 2011;34(1):121-126.

Trikalinos TA, Ip S, Raman G, et al. Home diagnosis of obstructive sleep apnea-hypopnea syndrome. Technology assessment. Rockville, MD: Agency for Healthcare Research and Quality. http://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id48TA.pdf. Accessed October, 2012.

Tschopp K, Zumbrunn T, Knaus C, Thomaser E, Fabbro T. Statistical model for postoperative apnea-hypopnea index after multilevel surgery for sleep-disordered breathing. *Eur Arch Otorhinolaryngol*. 2011;268(11):1679-1685.

Tufts Health Plan. Medical necessity guidelines: Oral appliances for obstructive sleep apnea (#1035182). http://www.tuftshealthplan.com/providers/pdf/mng/Oral_Treatment_4_Obstructive_Sleep_Apnea.pdf. Accessed October, 2012.

Tufts Health Plan. Sleep management: Prior authorization program. http://www.tuftshealthplan.com/providers/pdf/mng/sleep_management_prior_authorization.pdf. Accessed October, 2012.

Tufts Health Plan. Medical necessity guidelines: UPPP and other procedures for OSA (#1044212). http://www.tuftshealthplan.com/providers/pdf/mng/Surgical_Treatment_for_Obstructive_Sleep_Apnea.pdf. Accessed October, 2012.

Tuomilehto HPI, Seppä JM, Partinen MM, et al. for the Kuopio Sleep Apnea Group. Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. *Am J Respir Crit Care Med*. 2009;179(4):320-327.

UnitedHealthcare®. Medical policy: Non-surgical treatment of obstructive sleep apnea. https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Assets/ProviderStaticFiles/ProviderStaticFilesPdf/Tools%20and%20Resources/Policies%20and%20Protocols/Medical%20Policies/Medical%20Policies/Nonsurgical_Treatment_of_Obstructive_Sleep_Apnea.pdf. Accessed October/November, 2012.

UnitedHealthcare®. Medical policy: Polysomnography and portable monitoring for evaluation of sleep related breathing disorders (2012T0334N). https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Assets/ProviderStaticFiles/ProviderStaticFilesPdf/Tools%20and%20Resources/Policies%20and%20Protocols/Medical%20Policies/Medical%20Policies/Polysomnography_and_Portable_Monitoring.pdf. Accessed October/November, 2012.

UnitedHealthcare®. Medical policy: Surgical treatment of obstructive sleep apnea (2012T0525E). https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Assets/ProviderStaticFiles/ProviderStaticFilesPdf/Tools%20and%20Resources/Policies%20and%20Protocols/Medical%20Policies/Medical%20Policies/Surgical_Treatment_of_Obstructive_Sleep_Apnea.pdf. Accessed October/November, 2012.

U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. Local coverage determination (LCD) for oral appliances for obstructive sleep apnea (L28603). 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=gAAAABAAAAAA&. Accessed October, 2012.

U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. Local coverage determination (LCD) for positive airway pressure (PAP) devices for the treatment of obstructive sleep apnea (L11528). 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&. Accessed October, 2012.

U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. Local coverage determination (LCD) for surgical treatment of obstructive sleep apnea (OSA) (L30731). 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=gAAAABAAAAAA&. Accessed October, 2012.

U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. National coverage determination (NCD) for continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (OSA) (240.4). 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&. Accessed October, 2012.

U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. National coverage determination (NCD) for sleep testing for obstructive sleep apnea (OSA) (240.4.1). 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&. Accessed October, 2012.

Weatherly HLA, Griffin SC, Mc Daid C, et al. An economic analysis of continuous positive airway pressure for the treatment of obstructive sleep apnea-hypopnea syndrome. *Int J Technol Assess Health Care*. 2009;25(1):26-34.

Weinstock TG, Wang X, Rueschman M, et al. A controlled trial of CPAP therapy on metabolic control in individuals with impaired glucose tolerance and sleep apnea. *Sleep*. 2012;35(5):617-625.

Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*. 1997;20(9):705-706.

Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, Hla KM. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort Study. *WMJ*. 2009;108(5):246-249.

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 alchohol	
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 ± SD) [range]	Baseline ESS (mean ± 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 ± 7	76%	27.6 (25.8 - 31.1) [median, range]	Sleep lab & on the ward (preoperative)	AHI ≥ 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 ± 5	48.7 ± 11.8	76%	31 ± 6.6	Sleep lab and home	nd	7 pts failed respiratory trial; 18 pts didn't have vaild HRP & PSG
Oktay, 2011	ApneaLink (Type IV)	Suspected OSA patients	USA (Jun. 2006 - Jul. 2007)	53	nd	nd	45.1 ± 11.3 [23-70]	55%	35.9 ± 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 ≥ 5	AHI ≥ 5	90	76.9	0.90
						RDI ≥ 10	AHI ≥ 10	82.1	80	0.91
						RDI ≥ 15	AHI ≥ 15	79	88.2	0.92
						RDI ≥ 20	AHI ≥ 20	100	92.5	0.99
						RDI ≥ 30	AHI ≥ 30	66.7	95.5	0.96
				ApneaLink - Home vs. PSG						
				95% CI	-3.1	RDI ≥ 5	AHI ≥ 5	67.5	76.9	0.82
						RDI ≥ 10	AHI ≥ 10	75	92	0.86
						RDI ≥ 15	AHI ≥ 15	73.7	85.3	0.92
						RDI ≥ 20	AHI ≥ 20	76.9	92.5	0.96
						RDI ≥ 30	AHI ≥ 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 ± SD) [range]	Baseline ESS (mean ± 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 ± 7	76%	27.6 (25.8 - 31.1) [median, range]	Sleep lab & on the ward (preoperative)	AHI ≥ 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 ± 22	10 ± 5.1 (ESS1)	46 ± 14	64%	27 ± 5.3	Sleep lab	nd	nd
Martinez, 2012	BQ	Patients w/angina, referred for angiography	Brazil (Mar. 2007 - Feb. 2008)	57	17 ± 14	nd	54 ± 6.9	46%	23 ± 11	Home	AHI ≥ 5	nd
Sert-Kuniyoshi, 2011	BQ	Recent MI (1-3 months previously)	USA (nd)	99	nd	nd	62 ± 13	81%	30 ± 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 ± 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 ± SD) [range]	Baseline ESS (mean ± 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 ± 15 [16 - 83]	82%	27 ± 5 [16 - 47]	Sleep lab	AHI ≥ 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 ± 5.4 [0-21]	46.6 ± 11.2 [21 - 78]	75%	32.5 ± 8.7 [19.4 - 64.3]	nd	ESS ≥ 10, ODI ≥ 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 ± 26.7	nd	52.19 ± 13.73	78%	29.83 ± 4.53	Sleep lab	AHI ≥ 5	nd
Marcos, 2010*	Algorithm based on SaO_2	Suspected OSA patients	Spain (nd)	129	nd	nd	53.47 ± 12.99	78%	29.88 ± 4.81	Sleep lab	AHI ≥ 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; SaO_2: 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 ≥ 5	nd	nd	0.84
						≥ 29, < 7	AHI ≥ 15	89	98	0.91
						≥ 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; SaO_2: 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 ≥ 15 with impaired glucose tolerance; 50% of patients had AHI ≥ 30	Glucose and insulin indices
		Sham first	25			53	40%	38		

AHI: apnea-hypopnea index; APAP: auto-titrating positive aiway 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; SaO_2: 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 aiway 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		CVD causes	1 (0.3%)
			Hospitalizations for UA/arrhythmia	17			
			Nonfatal stroke	3		Trauma	1 (0.3%)
			Heart failure	3			
			Nonfatal MI	2		Unknown	1 (0.3%)
			TIA	2			
			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			
			Nonfatal stroke	2		Unknown	1 (0.3%)
			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 1st: 18 (72%) CPAP 2nd: 13 (52%)	<0.0001
	Sham first				Sham 1st: 7 (28%) Sham 2nd: 4 (17%)	

APAP: auto-titrating positive aiway 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 advnacement 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 advnacement 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 advnacement 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	
Goodday, 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