Effective Health Care Program

Comparative Effectiveness Review
Number 32

Diagnosis and Treatment of Obstructive Sleep Apnea in Adults

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Diagnosis and Treatment of Obstructive Sleep Apnea in Adults

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The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (http://www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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Diagnosis and Treatment of Obstructive Sleep Apnea in Adults

Structured Abstract

Background. Methods for diagnosing and treating obstructive sleep apnea (OSA) are cumbersome, resource-intensive, and often inconvenient for the patient.

Purpose. Systematically review the evidence on OSA diagnosis and treatment in adults. The Key Questions focus on OSA screening and diagnosis, treatments, associations between apnea- hypopnea index (AHI) and clinical outcomes, and predictors of treatment compliance.

Data Sources. MEDLINE®, Cochrane Central Register of Controlled Trials, and existing systematic and narrative reviews.

Study selection. Primarily prospective comparative studies of different tests, randomized controlled trials of treatments, and multivariable association studies. Only published, peer-reviewed, English-language articles were selected and manually screened based on predetermined eligibility criteria.

Data extraction. A standardized protocol was used to extract details on design, diagnoses, interventions, outcomes, and quality.

Data synthesis. In total, 234 studies met eligibility criteria (46 on diagnostic tests, 17 predictor studies, 190 on treatments). We found moderate evidence that portable monitors are accurate in diagnosing OSA (as defined by polysomnography), but retain a variable bias in estimating AHI; low strength of evidence that the Berlin Questionnaire is able to prescreen patients with OSA with moderate accuracy; and insufficient evidence to evaluate other questionnaires or clinical prediction rules. No study adequately addressed phased testing for OSA. There was insufficient evidence on routine preoperative testing for OSA. High strength of evidence indicates an AHI >30 events/hr is an independent predictor of death; lesser evidence for other outcomes. We found moderate evidence that continuous positive airway pressure (CPAP) is an effective treatment for OSA; moderate evidence that autotitrating and fixed CPAP have similar effects; insufficient evidence regarding comparisons of other CPAP devices; moderate evidence that oral devices are effective treatment for OSA; moderate evidence that CPAP is superior to oral devices; and insufficient trial evidence regarding the relative value of most other OSA interventions, including surgery. We found high and moderate evidence, respectively, that AHI and Epworth Sleepiness Scale are independent predictors of CPAP compliance, and low evidence that some treatments improve CPAP compliance.

Limitations. Very few trials evaluated objective clinical outcomes. Data were meager for many specific questions. Studies were generally of moderate to poor quality, and often had short followups, high dropout rates, and poor analyses and reporting.

Conclusions. Portable monitors and questionnaires may be effective screening tools, but assessments with clinical outcomes are necessary to prove their value over polysomnography. CPAP is highly effective in minimizing AHI and improving sleepiness. Oral devices are also effective, although not as effective as CPAP. Other interventions, including those to improve compliance, have not been adequately tested.

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Executive Summary[a]

Background

Obstructive sleep apnea (OSA) is a relatively common disorder in the United States that affects people of all ages, but is most prevalent among the middle-aged and elderly. Affected individuals experience repeated collapse and obstruction of the upper airway during sleep, which results in reduced airflow (hypopnea) or complete airflow cessation (apnea), oxygen desaturation, and arousals from sleep. Adverse clinical outcomes associated with OSA include: cardiovascular disease, hypertension, non-insulin-dependent diabetes, and increased likelihood of motor vehicle and other accidents due to daytime hypersomnolence. Studies estimate the prevalence of OSA at approximately 10 to 20 percent of middle-aged and older adults. Evidence also indicates that these rates are rising, likely due to increasing rates of obesity.

Based on the considerable mortality and morbidity associated with it and its attendant comorbidities, OSA is an important public health issue. Complicating diagnosis and treatment, however, is the great degree of clinical uncertainty that exists regarding the condition, due in large part to inconsistencies in its definition. Ongoing debate surrounds what type and level of respiratory abnormality should be used to define the disorder as well as what is the most appropriate diagnostic method for its detection. In addition, there is no current established threshold level for the apnea-hypopnea index (AHI) that would indicate the need for treatment. By consensus, people with relatively few apnea or hypopnea events per hour (often <5 or <15) are not formally diagnosed with OSA. Also of concern are the high rates of perioperative and postoperative complications among OSA patients, as are the numbers of asymptomatic and symptomatic individuals who remain undiagnosed and untreated.

Three main categories of outcomes of interest in comparative effectiveness research are clinical (or health) outcomes (i.e., events or conditions that the patient can feel, such as disability or quality of life or death), intermediate or surrogate outcomes (such as laboratory measurements), and adverse events. Objective clinical outcomes relevant to patients with OSA include comorbidities found to be associated with untreated sleep apnea, primarily cardiovascular disease (including congestive heart failure, hypertension, stroke, and myocardial infarction) and non-insulin-dependent diabetes. In addition, mortality due to cardiovascular disease, diabetes, motor vehicle accidents, and other causes represent important adverse outcomes of OSA. Intermediate outcomes of interest in the management of patients with OSA include sleep study measures (e.g., AHI), blood pressure (an intermediate outcome for cardiovascular disease), and hemoglobin A1c (a measure of control of diabetes mellitus).

All interventions have the potential for adverse events. Therefore, it is important to gather information on both the benefits and harms of interventions in order to fully assess the net comparative benefits. Compliance with continuous positive airway pressure (CPAP) and other devices is an important issue related to the effective treatment of OSA. Interventions that have better compliance or that may improve compliance are clearly of interest. Also of relevance is establishing definitive diagnostic standards and measures that would more clearly identify OSA patients, both symptomatic and asymptomatic. Such standards would serve to reduce OSA-related morbidities as well as related health care costs. Studies have found that prior to diagnosis, OSA patients have higher rates of health care use, more frequent and longer hospital stays, and

[a] Please refer to the main report for references.

greater health care costs than after diagnosis. Therefore, this review is of additional interest to the requesting organizations and broadly for the identification of diagnostic tests that would contribute to the early and definitive diagnosis of patients with OSA.

Objectives

In response to several nominations received through the Effective Healthcare Web site, which were evaluated and found to meet program criteria, the Agency for Healthcare Research and Quality (AHRQ) requested that the Tufts Evidence-based Practice Center (Tufts EPC) conduct a Comparative and Effectiveness Review (CER) of studies regarding the diagnosis and treatment of OSA.[b] Key Questions that are clinically relevant for the diagnosis and treatment of OSA were developed with input from domain experts and other stakeholders and from comments received in response to public review. Seven Key Questions are addressed in this report. Three pertain to diagnosis of and screening for OSA (Key Questions 1-3), two address the comparative effectiveness of treatments (Key Questions 5 and 7), and two address associations between baseline patient characteristics and long-term outcomes and treatment compliance (Key Questions 4 and 6).

Key Questions

Diagnosis

1. How do different available tests compare in their ability to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep? How do these tests compare in different subgroups of patients, based on: race, sex, body mass index, existing non-insulin-dependent diabetes mellitus, existing cardiovascular disease, existing hypertension, clinical symptoms, previous stroke, or airway characteristics?
2. How does phased testing (screening tests or battery followed by full test) compare to full testing alone?
3. What is the effect of preoperative screening for sleep apnea on surgical outcomes?
4. In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index or oxygen desaturation index and other patient characteristics with respect to long-term clinical and functional outcomes?

Treatment

5. What is the comparative effect of different treatments for obstructive sleep apnea in adults?
    a. Does the comparative effect of treatments vary based on presenting patient characteristics, severity of obstructive sleep apnea, or other pretreatment factors? Are any of these characteristics or factors predictive of treatment success?
        - Characteristics: Age, sex, race, weight, bed partner, airway, other physical characteristics, and specific comorbidities

[b] Criteria for selecting topics for systematic review include appropriateness, importance, lack of duplication, feasibility, and potential value. See http://www.effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.

- Obstructive sleep apnea severity or characteristics: Baseline questionnaire (and similar tools) results, formal testing results (including hypoxemia levels), baseline quality of life, positional dependency
- Other: Specific symptoms

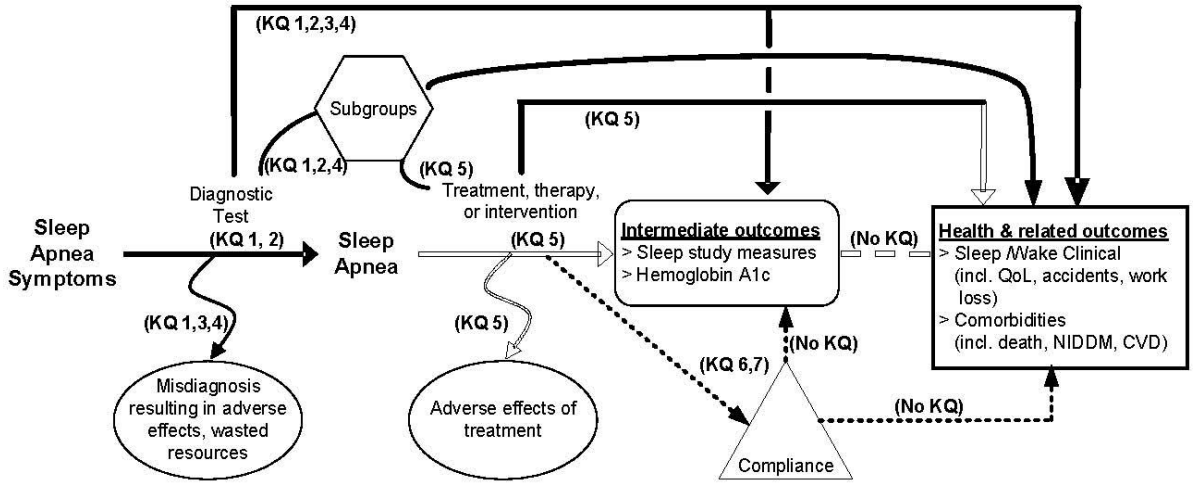
b. Does the comparative effect of treatments vary based on the definitions of obstructive sleep apnea used by study investigators?

6. In obstructive sleep apnea patients prescribed nonsurgical treatments, what are the associations of pretreatment patient-level characteristics with treatment compliance?
7. What is the effect of interventions to improve compliance with device use (positive airway pressure, oral appliances, positional therapy) on clinical and intermediate outcomes?

Analytic Framework

To guide the development of the Key Questions for the diagnosis and treatment of OSA, we developed an analytic framework (Figure A) that maps the specific linkages associating the populations and subgroups of interest, the interventions (for both diagnosis and treatment), and outcomes of interest (intermediate outcomes, health-related outcomes, compliance, and adverse effects). Specifically, this analytic framework depicts the chain of logic that evidence must support to link the interventions to improved health outcomes.

Figure A. Analytic framework for the diagnosis and treatment of obstructive sleep apnea in adults



CVD=cardiovascular disease; KQ=Key Question; NIDDM=non-insulin-dependent diabetes mellitus; QoL=quality of life.

Methods

Input from Stakeholders

During a topic refinement phase, the initial questions were refined with input from a panel of Key Informants. The Key Informants included experts in sleep medicine, general internal medicine, and psychiatry; a representative from Oregon Division of Medical Assistance

programs; a person with OSA; a representative of a sleep apnea advocacy group; and the AHRQ Task Order Officer.

After a public review of the proposed Key Questions, the clinical experts from among the Key Informants were reconvened to form the Technical Expert Panel, which served to provide clinical and methodological expertise and input to help refine Key Questions, identify important issues, and define parameters for the review of evidence, including study eligibility criteria.

Data Sources and Selection

We conducted literature searches of studies in MEDLINE® (inception—September 2010) and the Cochrane Central Register of Controlled Trials (through 3rd quarter 2010). All English-language studies with adult human subjects were screened to identify articles relevant to each Key Question. The search strategy included terms for OSA, sleep apnea diagnostic tests, sleep apnea treatments, and relevant research designs.

The reference lists of related systematic reviews and selected narrative reviews and primary articles were also reviewed, and relevant articles were screened. After screening of the abstracts, full-text articles were retrieved for all potentially relevant articles and rescreened for eligibility.

Data Extraction and Quality Assessment

Study data were extracted into customized forms. Together with information on study design, patient and intervention characteristics, outcome definitions, and study results, the methodological quality of each study was rated from A (highest quality, least likely to have significant bias) to C (lowest quality, most likely to have significant bias).

Data Synthesis and Analysis

For all Key Questions or specific comparison of interventions with at least two studies, summary tables present the study and baseline patient characteristics, the study quality, and the relevant study results. For each comparison, separate tables include all the studies that reported specific outcomes. For Key Question 1 (diagnosis), we graphically display the Bland-Altman limits of agreement and the sensitivity and specificity of studies comparing portable monitors to polysomnography (PSG). For Key Question 5 (treatment), when there were three or more similar studies evaluating the same outcome, we performed random effects model meta-analyses of the following: the sleep study measures AHI, arousal index, and minimum oxygen saturation; the standard measure of sleepiness, the Epworth Sleepiness Scale (ESS); the quality-of-life measure Functional Outcomes Sleep Questionnaire (FOSQ); and compliance. We performed subgroup meta-analyses based on study design (parallel or crossover), minimum AHI threshold to diagnose OSA, specific intervention (when appropriate), and other factors. Of note, where interventions (either diagnostic tests or treatments) are not discussed, this does not imply that the interventions were excluded from analysis (unless explicitly stated); instead, no studies of these interventions met eligibility criteria.

As per the AHRQ updated methods guide series, we assessed the evidence for each question (or comparison of interventions) based on the risk of bias, study consistency, directness of the evidence, and degree of certainty of the findings. Based on these factors, we graded the overall strength of evidence as high, moderate, low, or insufficient.

When there were substantial differences in conclusions for different outcomes within the same comparison, we also described the evidence supporting each outcome as sufficient, fair, weak, limited, or no evidence.

Results

Key Question 1. How do different available tests compare in their ability to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep? How do these tests compare in different subgroups of patients based on: race, sex, body mass index, existing non-insulin-dependent diabetes mellitus, existing cardiovascular disease, existing hypertension, clinical symptoms, previous stroke, or airway characteristics?

Comparison of Portable Devices and Polysomnography

PSG devices are classified as Type I monitors. Portable monitors are classified as either Type II, which record all the same information as PSG; Type III, which do not differentiate between whether the patient is asleep or awake, but have at least two respiratory channels (two airflow channels or one airflow and one effort channel); or Type IV, which fail to fulfill criteria for Type III monitors but usually record more than two bioparameters.

The strength of evidence is moderate, among 15 quality A, 45 quality B, and 39 quality C studies, that Type III and Type IV monitors may have the ability to accurately predict AHI suggestive of OSA with high positive likelihood ratios and low negative likelihood ratios for various AHI cutoffs in PSG. Type III monitors perform better than Type IV monitors at AHI cutoffs of 5, 10, and 15 events/hr. Analysis of difference versus average analyses plots suggest that substantial differences in the measured AHI may be encountered between PSG and both Type III and Type IV monitors. Large differences compared with in-laboratory PSG cannot be excluded for all portable monitors. The evidence is insufficient to adequately compare specific monitors to each other.

No recent studies compared Type II monitors with PSG. A prior Technology Assessment of home diagnosis of OSA concluded that ~~–b~~based on [three quality B studies], type II monitors [used at home] may identify AHI suggestive of OSA with high positive likelihood ratios and low negative likelihood ratios," though ~~–s~~ubstantial differences in the [measurement of] AHI may be encountered between type II monitors and facility-based PSG."

Comparison of Questionnaires and Polysomnography

Of the six studies reviewed (one quality A, one quality B, four quality C), *the strength of evidence is low* among three studies supporting the use of the Berlin questionnaire in screening for sleep apnea because of the likely selection biases. *The strength of evidence is insufficient* to draw definitive conclusions concerning the use of the STOP, STOP-Bang, ASA Checklist, Epworth Sleepiness Scale, and Hawaii Sleep questionnaires to screen for sleep apnea because each questionnaire was assessed in only a single study.

Clinical Prediction Rules and Polysomnography

The strength of evidence is low among seven studies (three quality A, three quality B, and one quality C) that some clinical prediction rules may be useful in the prediction of a diagnosis of OSA. Ten different clinical prediction rules have been described. Nine clinical prediction rules have been used for the prediction of a diagnosis of OSA (using different criteria). The oropharyngeal morphometric model gave near perfect discrimination (area under the curve

[AUC] = 0.996) to predict the diagnosis of OSA, and the pulmonary function data model had 100 percent sensitivity with 84 percent specificity to predict diagnosis of OSA. The remaining models reported lower diagnostic sensitivities and specificities. Each model was deemed useful to predict the diagnoses of OSA by the individual study authors. However, while all the models were internally validated, external validation of these predictive rules has not been conducted in the vast majority of the studies.

Key Question 2. How does phased testing (screening tests or battery followed by full test) compare to full testing alone?

The strength of evidence is insufficient to determine the utility of phased testing, followed by full testing when indicated, to diagnose sleep apnea, as only one study that met our inclusion criteria investigated this question. This prospective quality C study did not fully analyze the phased testing, thus the sensitivity and specificity of the phased strategy could not be calculated due to a verification bias; not all participants received PSG (full) testing.

Key Question 3. What is the effect of preoperative screening for sleep apnea on surgical outcomes?

The strength of evidence is insufficient regarding postoperative outcomes with mandatory screening for sleep apnea. Two quality C prospective studies assessed the effect of preoperative screening for sleep apnea on surgical outcomes. One study found no significant differences in outcomes between patients undergoing bariatric surgery who had mandatory PSG or PSG based on clinical parameters. The second study found that general surgery patients willing to undergo preoperative PSG were more likely to have perioperative complications, particularly cardiopulmonary complications, possibly suggesting that patients willing to undergo PSG are more ill than other patients.

Key Question 4. In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index or oxygen desaturation index, and other patient characteristics with respect to long-term clinical and functional outcomes?

The strength of evidence is high from four studies (three quality A, one quality B) indicating that an AHI >30 events/hr is an independent predictor of all-cause mortality; although one study found that this was true only in men under age 70. All other outcomes were analyzed by only one or two studies. Thus, only a *low strength of evidence* exists that a high AHI (>30 events/hr) is associated with incident diabetes. This association, however, may be confounded by obesity, which may result in both OSA and diabetes. *The strength of evidence is insufficient* regarding the association between AHI and other clinical outcomes. The two studies of cardiovascular mortality did not have consistent findings, and the two studies of hypertension had unclear conclusions. One study of nonfatal cardiovascular disease found a significant association with baseline AHI (as they did for cardiovascular mortality). One study each found no association between AHI and stroke or long-term quality of life.

Key Question 5. What is the comparative effect of different treatments for obstructive sleep apnea in adults?

a. Does the comparative effect of treatments vary based on presenting patient characteristics, severity of obstructive sleep apnea, or other pretreatment factors? Are any of these characteristics or factors predictive of treatment success?
   - Characteristics: age, sex, race, weight, bed partner, airway, other physical characteristics, and specific comorbidities
   - Obstructive sleep apnea severity or characteristics: baseline questionnaire (and similar tools) results, formal testing results (including hypoxemia levels), baseline quality of life, positional dependency
   - Other: specific symptoms

b. Does the comparative effect of treatments vary based on the definitions of obstructive sleep apnea used by study investigators?

With some exceptions for studies of surgical interventions, we reviewed only randomized controlled trials (RCT) of interventions used specifically for the treatment of obstructive sleep apnea (OSA).

Comparison of Continuous Positive Airway Pressure and Control

There are 22 trials (11 each of quality B and C) that provide sufficient evidence supporting large improvements in sleep measures with continuous positive airway pressure (CPAP) compared with control. There is only weak evidence that demonstrated no consistent benefit in improving quality of life, neurocognitive measures, or other intermediate outcomes. Despite no evidence or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes AHI and ESS, the strength of evidence that CPAP is an effective treatment to alleviate sleep apnea signs and symptoms was rated *moderate*.

Comparison of CPAP and Sham CPAP

There are 24 trials (5 quality A, 13 quality B, 6 quality C) that provide sufficient evidence supporting large improvements in sleep measures with CPAP compared with sham CPAP, but weak evidence of possibly no difference between CPAP and sham CPAP in improving quality of life, neurocognitive measures, or other intermediate outcomes. Despite no evidence or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI, ESS, and arousal index, the strength of evidence that CPAP is an effective treatment for the relief of signs and symptoms of sleep apnea was rated *moderate*.

Comparison of Oral and Nasal CPAP

Three small trials (one quality B, two quality C) with inconsistent results preclude any substantive conclusions concerning the efficacy of oral (or full face mask) versus nasal CPAP in improving compliance in patients with OSA. Largely due to small sample size, the reported effect estimates in the studies reviewed were generally imprecise. Thus, overall, *the strength of evidence is insufficient* regarding differences in compliance or other outcomes between oral and nasal CPAP.

Comparison of Autotitrating CPAP and Fixed CPAP

The strength of evidence is moderate that autotitrating CPAP (autoCPAP) and fixed pressure CPAP result in similar levels of compliance (hours used per night) and treatment effects for

patients with OSA. Twenty-one studies (1 quality A, 10 quality B, 10 quality C) comprising an experimental population of over 800 patients provided evidence that autoCPAP reduces sleepiness as measured by ESS by approximately 0.5 points more than fixed CPAP. The two devices were found to result in similar compliance and changes in AHI from baseline, quality of life, and most other sleep study measures. However, there is also evidence that minimum oxygen saturation improves more with fixed CPAP than with autoCPAP, although by only about one percent. Evidence is limited regarding the relative effect of fixed CPAP and autoCPAP on blood pressure. There were no data on objective clinical outcomes.

Comparison of Bilevel CPAP and Fixed CPAP

The strength of evidence is insufficient regarding any difference in compliance or other outcomes between bilevel CPAP and fixed CPAP. Five small, highly clinically heterogeneous trials (one quality B, four quality C) with largely null findings did not support any substantive differences in the efficacy of bilevel CPAP versus fixed CPAP in the treatment of patients with OSA. Largely due to small sample sizes, the studies mostly had imprecise estimates of the comparative effects.

Comparison of Flexible Bilevel CPAP and Fixed CPAP

The strength of evidence is insufficient regarding the relative merits of flexible bilevel CPAP and fixed CPAP as there was only one quality B study that investigated this comparison. This study found that flexible bilevel CPAP may yield increased compliance (use ≥4 hr/night) compared with fixed CPAP.

Comparison of C-Flex™ and Fixed CPAP

No statistically significant differences in compliance or other outcomes were found between C-Flex and fixed CPAP. *The strength of evidence is low* for this finding because of the mixed quality (Bs and Cs) of the four primary studies.

Comparison of Humidification in CPAP

The strength of evidence is insufficient to determine whether there is a difference in compliance or other outcomes between positive airway pressure treatment with and without humidification. Five trials examined different aspects of humidified CPAP treatment for patients with OSA. While some studies reported a benefit of added humidity in CPAP treatment in improving patient compliance, this effect was not consistent across all the studies. Overall, the studies were clinically heterogeneous, small, and of quality B (three studies) or C (two studies).

Comparison of Mandibular Advancement Devices and No Treatment or Inactive Oral Devices

The strength of evidence is moderate to show that the use of mandibular advancement devices (MAD) improves sleep apnea signs and symptoms. Five trials (four quality B, one quality C) compared MAD with no treatment, using a variety of different types of MAD, and found significant improvements with MAD in AHI, ESS, and other sleep study measures. Any differences in quality of life measures or neurocognitive tests were equivocal between treatment

groups. No trial evaluated objective clinical outcomes. Another five trials (four quality B, one quality C) compared the effects of MAD with inactive oral devices and reported similar findings.

Comparison of Different Oral Devices

The strength of evidence is insufficient to draw conclusions with regard to the relative efficacy of different types of oral MAD in patients with OSA because the reviewed studies were generally small, and each was concerned with a unique comparison. Five studies (four quality B, one quality C) with unique comparisons found little to no differences between different types and methods of use of MAD or other oral devices in sleep study or sleepiness measures. No study evaluated objective clinical outcomes. Only one study evaluated compliance; no significant differences were observed. One trial found that a greater degree of mandibular advancement resulted in an increased number of patients achieving an AHI <10 events/hr; however, the mean AHI was similar between treatment groups.

Comparison of Mandibular Advancement Devices and CPAP

The strength of evidence is moderate that CPAP is superior to MAD in improving sleep study measures. Ten mostly quality B trials overall found that CPAP resulted in greater reductions in AHI and arousal index, and increases in minimum oxygen saturation. The evidence regarding the relative effects on ESS were too heterogeneous to allow conclusions. In a single study, patients were more compliant with MAD than CPAP (hours used per night and nights used). No study evaluated objective clinical outcomes. *The strength of evidence is insufficient* to address which patients might benefit most from either treatment.

Comparison of Surgery and Control

The strength of evidence is insufficient to evaluate the relative efficacy of surgical interventions for the treatment of OSA. Six trials and one nonrandomized prospective study with unique interventions compared surgery with control treatment for the management of patients with OSA. Three studies were rated quality A, one quality B, and three quality C. The results were inconsistent across studies as to which outcomes were improved with surgery compared with no or sham surgery.

Comparison of Surgery and CPAP

The strength of evidence is insufficient to determine the relative merits of surgical treatments versus CPAP. Of 12 studies (1 quality A, 11 quality C) comparing surgical modalities with CPAP, only two were RCTs, and they compared CPAP with uvulopalatopharyngoplasty (UPPP), removal of the soft tissue at the back of the throat, the uvula, and soft palate. While one of these trials found that CPAP resulted in a higher mortality benefit, the other found no difference between groups. Due to the heterogeneity of interventions and outcomes examined, the variability of findings across studies, and the inherent bias of all but one study regarding which patients received surgery, it is not possible at this time to draw useful conclusions comparing surgical interventions with CPAP in the treatment of patients with OSA. The quality A trial was the only unbiased comparison of surgery and CPAP (patients had previously received neither treatment). It did not find statistically significant differences in ESS and quality of life measures between patients with mild to moderate OSA who had temperature-controlled radiofrequency tissue volume reduction of the soft palate and those who had CPAP at 2 months followup.

Likewise, the other trial, comparing maxillomandibular advancement osteotomy and CPAP, did not find statistically significant differences in AHI and ESS in patients with severe OSA. For the nonrandomized studies, comparisons between surgery and CPAP are difficult to interpret since baseline patient characteristics (including sleep apnea severity) differed significantly between groups, particularly in regards to what previous treatments patients had. The reported findings on sleep study and quality of life measures were heterogeneous across studies.

Comparison of Surgery and Mandibular Advancement Devices

The strength of evidence is insufficient regarding the relative merit of MAD versus surgery in the treatment of OSA, as there was only one study (quality B) that examined this question. A statistically significant improvement in AHI was observed in the MAD group compared with the surgery group. No study evaluated objective clinical outcomes.

Comparison of Other Treatments

The strength of evidence is low to show that some intensive weight loss programs may be effective treatment for OSA in obese patients. Three trials (one quality A, two quality B) compared weight loss interventions with control interventions. All three trials found significant relative reductions in AHI with diet. Other outcomes were inconsistent.

The *strength of evidence is insufficient* to determine the effects of other potential treatments for OSA. Twenty-one studies evaluated other interventions including atrial overdrive pacing, eight different drugs, palatal implants, oropharyngeal exercises, a tongue-retaining device, a positional alarm, combination tongue-retaining device and positional alarm, bariatric surgery, nasal dilator strips, acupuncture, and auricular plaster. All of these interventions were evaluated by one or two studies only. The findings were heterogeneous. No study evaluated objective clinical outcomes.

Key Question 6. In OSA patients prescribed nonsurgical treatments, what are the associations of pretreatment patient-level characteristics with treatment compliance?

Across five studies (one quality A, one quality B, three quality C), *the strength of evidence is moderate* that more severe OSA as measured by higher AHI is associated with greater compliance with CPAP use. Each study measured compliance differently, including thresholds of 1, 2, or 3 hours of use per night or as a continuous variable, and undefined "objective compliance" measured by the device. *The strength of evidence is moderate* that a higher ESS score is also associated with improved compliance. *There are low strengths of evidence* that younger age, snoring, lower CPAP pressure, higher BMI, higher mean oxygen saturation, and the sleepiness domain on the Grenoble Sleep Apnea Quality of Life test are each possible independent predictors of compliance. It is important to note, however, that selective reporting, particularly of nonreporting of nonsignificant associations, cannot be ruled out. The heterogeneity of analyzed and reported potential predictors greatly limits these conclusions. Differences across studies as to which variables were independent predictors may be due to the adjustment for different variables, in addition to differences in populations, outcomes, CPAP machines, and CPAP training and followup. One quality C study of mandibular advancement devices failed to identify potential predictors of compliance.

Key Question 7. What is the effect of interventions to improve compliance with device (positive airway pressure, oral appliances, positional therapy) use on clinical and intermediate outcomes?

The strength of evidence is low that some specific adjunct interventions may improve CPAP compliance, but studies are heterogeneous and no general type of intervention (e.g., education, telemonitoring) was more promising than others. The 18 trials (two quality A, eight quality B, and eight quality C) had inconsistent effects across a wide variety of interventions. Studies generally had small sample sizes with less than 1 year of followup. Compared with usual care, several interventions were shown to significantly increase hours of CPAP use per night in some studies. These included intensive support or literature (designed for patient education), cognitive behavioral therapy (given to patients and their partners), telemonitoring, and a habit-promoting audio-based intervention. However, the majority of studies did not find a significant difference in CPAP compliance between patients who received interventions to promote compliance with device use and those who received usual care. No study of nurse-led care (which was not focused primarily on compliance) showed an effect on compliance rates.

Discussion

The findings of the systematic review have been summarized in **Table A**. Interventions (either diagnostic tests or treatments) that are not discussed lack studies meeting eligibility criteria. Interventions were not excluded from analysis unless explicitly stated as such.

Diagnosis

In theory, obstructive sleep apnea (OSA) is relatively simple to diagnose. However, PSG, the standard diagnostic test, is inconvenient, resource-intensive, and may not be representative of a typical night's sleep (particularly the first night the test is given). Furthermore, there are variations across laboratories in the definitions of OSA (using different thresholds of AHI, from 5 to 15 events/hr) and in the way that the PSG results are read and interpreted. Moreover, AHI, which is used as the single metric to define OSA, can vary from night to night and does not take into account symptoms, comorbidities, or response to treatment.

Two approaches have been taken to reduce the resources involved in diagnosing OSA, including tests (questionnaires and clinical prediction rules) to screen for OSA and portable monitors to be used instead of sleep-laboratory PSG. Five questionnaires and 10 validated clinical prediction rules have been compared with PSG. However, very few of the screening tests have been evaluated by more than one set of researchers, and few have been directly compared with each other. Thus, *the strength of evidence is low* that the Berlin questionnaire is accurate in its ability to screen for OSA; the commonly used STOP and STOP-Bang questionnaires have not been adequately tested. For such tests to be of clinical value, apart from having very high sensitivity and specificity, they should be easy to administer and require only information from symptoms and signs easily obtainable during a physical examination. The evaluated clinical prediction models were all internally validated, but definitive conclusions on the external validity (i.e., generalizability) of these predictive rules in independent populations cannot be drawn from the available literature. *The strength of evidence is low* that some clinical prediction rules may be useful in the prediction of a diagnosis of OSA. No study examined the potential clinical utility of applying the questionnaires or prediction rules to clinical practice.

Numerous portable monitors (evaluated in 99 studies) have been developed for use in nonlaboratory settings; these use fewer "channels" (specific physiologic measures) than typical 16-channel PSG. The more recent studies do not substantially change the conclusions from the Tufts Evidence-based Practice Center's (Tufts EPC) 2007 Technology Assessment on *Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*.[c] Although most of the tested portable monitors fairly accurately predict OSA, it is unclear whether any of these monitors can replace laboratory-based PSG. The evidence suggests that the measured AHI from portable monitors is variable compared with PSG-derived AHI, but the source of this variability is unclear. So far, no studies have evaluated the predictive ability for clinical outcomes or response to treatment by portable monitors. Furthermore, no available studies have evaluated the impact of patient triage via screening tests and/or portable monitors.

The value of preoperative screening for OSA remains poorly defined. The only study that directly addressed this question was a retrospective study of patients undergoing bariatric surgery. It showed better perioperative outcomes from routine PSG. There are also no adequate studies that compared phased testing (simple tests followed by more intensive tests in selected patients) with full evaluation (by PSG).

Apnea-Hypopnea Index as a Predictor of Clinical Outcomes

The strength of evidence is high that high baseline (>30 events/hr or range) AHI is a strong and independent predictor of all-cause mortality over several years of followup, with the association being strongest among people with severe OSA (AHI >30 events/hr). However, the strength of evidence for the association between baseline AHI and other long-term clinical outcomes is generally insufficient, and thus the association between reductions in AHI by OSA treatment and improvements in long-term outcomes remains theoretical.

Treatment

The strength of evidence is moderate that fixed CPAP is an effective treatment to minimize AHI and improve sleepiness symptoms, as supported by more than 40 trials of patients treated with CPAP or no treatment. However, no trial reported long-term clinical outcomes, and compliance with CPAP treatment is poor. Because patients frequently do not tolerate CPAP, many alternative treatments have been proposed. First, several alternative CPAP machines have been designed to vary the pressure during the patient's inspiratory cycle or to titrate the pressure to a minimum necessary level. Other modifications include different masks, nasal pads, and added humidification. The large majority of relevant trials have compared autotitrating CPAP (autoCPAP) with fixed CPAP and the strength of evidence of no clinical differences between them is *moderate*. The strength of evidence is insufficient for other device comparisons and, overall, the evidence does not support the use of one device for all patients, since such decisions should be individualized.

The second alternative to CPAP therapeutic option is the use of oral devices, which have been designed with the goal of splinting open the oropharynx to prevent obstruction. The most commonly tested are the mandibular advancement devices (MAD), for which the strength of evidence for their efficacy in sleep outcomes is *moderate*. Based on direct and indirect

[c] Tufts-New England Medical Center EPC. Home diagnosis of obstructive sleep apnea-hypopnea syndrome. Health Technology Assessment Database www cms gov/determinationprocess/downloads/id48TA pdf. 2007;2010.

comparisons, CPAP appeared to be more effective than MAD. However, given the issues with noncompliance with CPAP, the decision as to whether to use CPAP or MAD will likely depend on patient preference.

The third major alternative to OSA treatment includes surgical interventions to alleviate airway obstruction. Given the very few randomized trials and the differences in the populations that choose to undergo surgery versus conservative treatment, the strength of evidence is insufficient to determine the relative value of surgery to no treatment, to CPAP, to MAD, or to alternative types of surgery. Additional interventions were also evaluated in randomized trials, (including weight loss programs, atrial overdrive pacing, eight different drugs, and other interventions) but in general the strength of evidence is insufficient to determine the effects of these potential treatments.

For all the treatment comparisons, it is important to identify which subgroups of patients may benefit most from specific treatments. Unfortunately, the trials are nearly silent on this issue. Very few trials reported subgroup analyses based on baseline characteristics, and for most comparisons there were too few studies or the interventions examined were too heterogeneous to analyze potential differences. Such analyses were feasible for the comparison between CPAP and control, where subgroup meta-analyses based on definitions of OSA (different minimum AHI thresholds) failed to demonstrate any difference in effectiveness of CPAP in reducing AHI or ESS. Though statistical heterogeneity existed across the trials, this was primarily attributed to study design factors that have no clinical implications. Despite statistical heterogeneity, and based on the consistency of findings that support CPAP as effective to minimize AHI in all patients with OSA, it is reasonable to conclude that the relative effectiveness in different populations is a moot point. The one exception to this may be patients with mild OSA (with AHI <15 events/hr), since people with low AHI cannot have as large an improvement in their AHI as people with severe OSA. Notably, across interventions there is little evidence supporting the hypothesis that any OSA treatment improves quality of life or neurocognitive function.

The strength of evidence is insufficient regarding the effect of interventions to improve CPAP compliance. The studies were very heterogeneous in their interventions and each evaluated different interventions. Higher baseline AHI and increased sleepiness as measured by the Epworth Sleepiness Scale are both predictors of improved compliance with CPAP (high strength and moderate strength of evidence, respectively). The unsurprising interpretation of this finding is that patients with more severe symptoms are more likely to accept the discomfort or inconvenience of using CPAP overnight.

Limitations

The most important limitations in the evidence were the lack of trials that evaluated long-term clinical outcomes, the sparseness of evidence to address several Key Questions, and the fact that no study of diagnostic tests or treatments attempted to assess how results may vary in different subgroups of patients. In general, the intervention trials were of quality B or C, with few quality A studies. Followup durations tended to be very short, and study dropout rates were frequently very high. Other frequent methodological problems with studies included incomplete reporting and/or inadequate analyses, which required estimations of pertinent results by the authors of this systematic review. The heavy reliance on industry support for trials of devices may lead to the concern of publication bias. However, this concern may be reduced since most of our conclusions were that the strength of evidence is either low or inadequate for interventions. Furthermore, the effects of CPAP and MAD on sleep measures are sufficiently large that

conclusions about the effectiveness of these devices would be unlikely to change with the addition of unpublished trials.

Implications for Future Research

General Recommendation

- The recurrent problem of high dropout rates as evidenced in the literature we reviewed bears further investigation and is crucial for the conduct of future trials. It is important to understand whether this a problem peculiar to this field, whether patients' symptoms interfere with their desire to fulfill their obligations as research participants, whether patients are not well informed about the serious consequences of sleep apnea and therefore are less motivated to comply with followup, or whether the treatments are so onerous that patients are refusing to continue with them.

Diagnostic Tests

- The most clinically useful evaluation of prediction rules and questionnaires (to screen for or diagnose OSA) would be trials to evaluate whether use of the tests improves clinical outcomes. Individual patient-data meta-analysis of measurements with portable monitors would provide insights on the diagnostic information contributed by different neurophysiologic signals. Future studies of the accuracy or bias of diagnostic tests should focus more on head-to-head comparisons of portable monitors, questionnaires, and prediction rules, to determine the optimal tool for use in a primary care setting to maximize initial evaluation of OSA and triage high-risk patients for prompt PSG. Direct comparisons among existing alternatives to PSG are more important than the current focus on developing new diagnostic tests.
- Trials are needed comparing potential phased testing strategies with direct PSG or addressing the value of preoperative screening for OSA. Studies of appropriate tests for patients, based on the type or severity of their symptoms, would be useful.

Treatments

- Only 3 of the 190 studies of treatments reported clinical outcomes; comparative studies focusing on long-term followup and clinical outcomes are needed.
- Fixed CPAP is clearly an effective treatment for OSA, and no further trials are needed to assess its efficacy, with the exception of trials assessing long-term clinical outcomes. All other interventions should either be:
  - directly compared with fixed CPAP, among patients naïve to CPAP, or
  - compared with no treatment or alternative treatment among patients who have failed to comply with CPAP treatment.
- Treatment effect heterogeneity should be investigated.
- The benefit from different degrees of mandibular advancement has to be determined.
- Head-to-head comparisons are needed of alternative treatments for patients who do not tolerate CPAP.
- Rigorously conducted head-to-head comparisons of surgical interventions versus CPAP are needed to overcome limitations of existing observational evidence.

- More studies are needed on the various additional interventions (including weight loss, drugs, and specific exercises), and their incremental benefit to accepted treatments for OSA should be examined.
- Interventions to improve compliance to CPAP and MAD should be tested in direct comparisons.

Predictors of Clinical Outcomes and Compliance

- The question of whether OSA severity is associated with long-term outcomes (beyond all-cause mortality) may be informed by patient-level meta-analyses of available large cohorts.
- Predictive models of compliance and response to treatment are needed.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 1: Diagnosis Portable monitors vs. PSG	Low (Type II monitors); Moderate (Types III & IV monitors)	• No recent studies have compared Type II portable monitors to PSG. [d] A prior systematic review concluded that "based on [3 quality B studies], Type II monitors [used at home] may identify AHI suggestive of OSA with high positive likelihood ratios and low negative likelihood ratios," though "substantial differences in the [measurement of] AHI may be encountered between Type II monitors and facility-based PSG." • There were 29 studies that compared Type III portable monitors [e] with PSG. 7 of these are new since a previous report. 18 Type III monitors have been evaluated. • There were 70 studies that compared Type IV portable monitors [f] to PSG. 24 of these are new since a previous report. 23 Type IV monitors have been evaluated. • Overall, 15 studies were graded quality A, 45 quality B, and 39 quality C. The studies were applicable to the general population of patients being referred to specialized sleep centers or hospitals for evaluation of suspected sleep apnea. It is unclear if the studies are applicable to patients with comorbidities or who may have central sleep apnea. Most of the studies were conducted either in the sleep laboratory setting or at home. • Studies measured either concordance (comparisons of estimates of AHI), test sensitivity and specificity (to diagnose OSA as defined by PSG), or both. • Type III monitors had a wide range of mean biases (difference in AHI estimate from PSG), from -10 to +24 events/hr, with wide limits of agreements within studies. • Type IV monitors had a wide range of mean biases, from -17 to +12 events/hr, with wide limits of agreements within studies. • To diagnose OSA defined as a PSG AHI ≥5 events/hr, Type III monitors had sensitivities of 83–97% and specificities of 48–100%. Type III monitors commonly less accurately diagnosed OSA with AHI ≥15 events/hr, with sensitivities 64–100% and specificities 41–100%. • Evaluation of positive and negative likelihood ratios, and available ROC curves, suggest that Type III monitors are generally accurate in diagnosing OSA (as measured by PSG), with high positive likelihood ratios, low negative likelihood ratios, and high AUC. • To diagnose OSA, Type IV monitors had a very wide range of sensitivities and specificities. • Across studies (by indirect comparison), the range of sensitivities and specificities of both Type III and Type IV monitors largely overlapped, thus not demonstrating greater accuracy with either type of monitor. • **Conclusion**: The strength of evidence is low that Type II monitors are accurate to diagnose OSA (as defined by PSG), but have a wide and variable bias in estimating the actual AHI. • **Conclusion**: The strength of evidence is moderate that Type III and IV monitors are generally accurate to diagnose OSA (as defined by PSG), but have a wide and variable bias in estimating the actual AHI. The evidence is insufficient to adequately compare specific monitors to each other.

[d] Type II monitors are portable devices that record all the same information as PSG (Type I monitors).
[e] Type III monitors are portable devices that contain at least two airflow channels or one airflow and one effort channel.
[f] Type IV monitors comprise all other devices that fail to fulfill criteria for Type III monitors. They include monitors that record more than two physiological measures as well as single channel monitors.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 1: Diagnosis Questionnaires vs. PSG	Low / Insufficient	• There were 6 studies that compared 6 questionnaires with PSG diagnosis of OSA. Overall, these studies are applicable to patients visiting preoperative clinics, sleep laboratories, and primary care centers for evaluation of sleep apnea. • There were 1 quality A and 3 quality C studies that evaluated the Berlin Questionnaire (based on snoring, tiredness, and blood pressure), with OSA defined as AHI ≥5 events/hr; sensitivity ranged from 69–93%, specificity ranged from 56–95%. With an AHI ≥15 events/hr definition, sensitivity was somewhat lower and specificity was similar. To predict severe OSA (AHI ≥30 events/hr), sensitivity and specificity were generally lower. • Each of the following 4 questionnaires was evaluated in a single study (1 quality B, 2 quality C): STOP, STOP-Bang, ASA checklist, Hawaii Sleep Questionnaire), which all had relatively low specificity for OSA (AHI thresholds of 5, 10, or 30 events/hr), ranging from 37–67%. STOP, ESS, and the Hawaii Questionnaire had sensitivities <80%. STOP-Bang had high sensitivity to predict diagnosis of OSA, particularly those with AHI ≥15 or ≥30 events/hr (93 and 100%, respectively). The American Society of Anesthesiologists Checklist had a sensitivity of 87% to predict severe OSA, but lower sensitivity to predict those with lower AHI. In 1 quality A study, ESS had a low sensitivity (49%) and higher specificity (80%) to predict OSA with AHI ≥5. • **Conclusion**: The strength of evidence is low that the Berlin Questionnaire is moderately accurate (sensitivity and specificity generally <90%) to screen for OSA. The strength of evidence is insufficient to evaluate other questionnaires, but 1 study found that STOP-Bang may have high enough sensitivity to accurately screen for OSA.
Key Question 1: Diagnosis Clinical Prediction, Rules vs. PSG	Low	• There were 7 studies that compared 10 validated clinical prediction rules with PSG (3 quality A, 3 quality B, 1 quality C). Only 1 model has been externally validated (by independent researchers); thus the applicability of the studies to the general population is unclear. Of the models, 8 include variables obtainable through routine clinical history and examination. • A single morphometric model and a model that included pulmonary function test data had near perfect discrimination (AUC=0.996) or sensitivity (100%), but neither was independently validated. The other clinical prediction rules had variable accuracy for predicting OSA (AHI ≥5, 10, or 15 events/hr) or severe OSA (AHI ≥30 events/hr). • **Conclusion**: Thestrength of evidence is low that some clinical prediction rules may be useful in the prediction of a diagnosis of OSA.
Key Question 2: Diagnosis Phased testing	Insufficient	• A single quality C study partially addressed the value of phased testing, but had substantial verification bias due to implementation of the phased testing. • **Conclusion**: The strength of evidence is insufficient to determine the utility of phased testing.
Key Question 3: Diagnosis Preoperative screening	Insufficient	• There were 2 quality C studies that assessed the effect of preoperative screening for OSA on surgical outcomes, though only 1 of these was designed to address the question. • The retrospective study that compared mandatory prebariatric-surgery PSG with PSG performed based on clinical parameters (performed during different time periods) did not find significant differences in outcomes. The other study found only that those patients who volunteered for preoperative PSG were more likely to suffer cardiopulmonary perioperative complications than patients who refused PSG. • **Conclusion**: The strength of evidence is insufficient to determine the utility of preoperative sleep apnea screening.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 4: Predictors AHI as a predictor of long-term clinical outcomes	Variable (High for all-cause mortality; Low for diabetes; Insufficient for other long-term clinical outcomes)	• There were 11 studies (of 8 large cohorts) that performed multivariable analyses of AHI as an independent predictor of long-term clinical outcomes. • There were 4 studies (3 quality A, 1 quality B) that evaluated all-cause mortality. All found that AHI was a statistically significant independent predictor of death during 2–14 years of followup. The association was strongest among people with an AHI >30 events/hr. There was 1 study, however, that found an interaction with sex and age such that AHI was associated with death only in men ≤70 years of age. The evidence on mortality is applicable to the general population, with and without OSA, and also more specifically to men with OSA symptoms or evidence of OSA. • There were 2 quality A studies that evaluated cardiovascular mortality. There was 1 study that found that only AHI >30 events/hr predicted cardiovascular death; the other study found no association. • A single quality A study evaluated nonfatal cardiovascular disease and similarly found that only AHI >30 events/hr was an independent predictor. • A single quality B study suggested that the association between AHI and stroke may be confounded by obesity. • There were 2 studies (1 quality A, 1 quality B) that came to uncertain conclusions regarding the possible association between AHI and incident hypertension. • There were 2 studies (1 quality A, 1 quality B) that suggested an association between AHI and incident type 2 diabetes, though 1 study found that the association was confounded by obesity. • A single quality A study found no significant association between AHI and future quality of life (SF-36 after 5 years). This conclusion appears to be applicable for both the general population and specifically for patients diagnosed with sleep disordered breathing. • **Conclusion:** The strength of evidence is high that an AHI >30 events/hr is an independent predictor of all-cause mortality; although one study found that this was true only in men under age 70. The strength of evidence is low that a higher AHI is associated with incident diabetes, though possibly confounded with obesity. The strength of evidence is insufficient to determine the association between AHI and other clinical outcomes.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments CPAP vs. control	Moderate	• There were 43 trials that compared CPAP devices with either no treatment or sham CPAP. All but 2 evaluated fixed CPAP. Of the 43 trials, 4 were rated quality A, 22 quality B, and 17 quality C. Overall, the studies are applicable to a broad range of patients with OSA. • Only 1 study evaluated a clinical outcome, namely heart failure symptomatology, and found no significant effect after 3 months. • By meta-analysis, CPAP results in a statistically significant large reduction in AHI (-20 events/hr compared with no treatment and -46 events/hr compared with sham CPAP). All studies found statistically significant effects, though there was statistical heterogeneity across studies that could not be fully explained. There were no clear, consistent relationships across studies between definition of OSA (by minimum threshold AHI) or other clinical features and effect size. • By meta-analysis, CPAP results in a statistically and clinically significant improvement in sleepiness as measured by ESS (-2.6 compared with no treatment and -2.7 compared with sham CPAP). The studies were statistically significant and most, but not all, found significant improvements in ESS. No factors clearly explained the heterogeneity. • CPAP also generally resulted in improvements in other sleep study measures, but had inconsistent effects on other sleepiness tests, quality of life tests, neurocognitive tests, and blood pressure. • All adverse events related to CPAP treatment were potentially transient and could be alleviated with either stopping treatment or with ancillary interventions. Generally about 5-15% of patients in trials had specific adverse events they considered to be a major problem while using CPAP. These included claustrophobia, oral or nasal dryness, epistaxis, irritation, pain, and excess salivation. No adverse event with potentially long-term consequences was reported. • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS, and other sleep study measures, the strength of evidence is moderate that CPAP is an effective treatment for OSA. However, the strength of evidence is insufficient to determine which patients might benefit most from treatment.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments Different CPAP devices vs. each other	Variable (Moderate for autoCPAP vs. CPAP; Low for C-Flex™ vs. CPAP; Insufficient for others)	• No study evaluated clinical outcomes. • There were 21 trials that compared autoCPAP with fixed CPAP. Of these, 1 trial was rated quality A; 10 trials each were rated quality B or C. These studies are applicable mainly to patients with AHI more than 15 events/hr and BMI more than 30 kg/m^2. By meta-analysis there was statistically significant, but clinically nonsignificant better improvement in ESS (-0.5), minimum oxygen saturation (1%), and compliance (11 minutes) with autoCPAP than fixed CPAP, and no statistically significant differences in AHI or arousal index. • There were 4 trials comparing C-Flex™ to fixed CPAP. No statistically significant differences were found for compliance, sleep study measures, or other tested outcomes. • There were 14 trials comparing bilevel or flexible bilevel CPAP with fixed CPAP, humidification with no humidification (with fixed CPAP), or oral with nasal fixed CPAP. The studies had either inconsistent results, were sparse, or had imprecise results. • **Conclusion**: Despite no or weak evidence on clinical outcomes, overall, there is moderate strength of evidence that autoCPAP and fixed CPAP result in similar compliance and treatment effects for patients with OSA. • **Conclusion**: The strength of evidence is low of no substantial difference in compliance or other outcomes between C-Flex and CPAP. • **Conclusion**: The strength of evidence is insufficient regarding comparisons of different CPAP devices (or modifications).
Key Question 5: Treatment OSA treatments MAD vs. control	Moderate	• There were 10 trials comparing various MADs with either no treatment or with sham devices (without mandibular advancement). No studies were rated quality A, 8 quality B, 2 quality C. The studies are generally applicable to patients with AHI ≥15 events/hr, though less so to patients with comorbidities or excessive sleepiness. All studies excluded edentulous patients or those with periodontal diseases. • No study evaluated clinical outcomes. • By meta-analysis, MAD results in a statistically significant reduction in AHI (-12 events/hr). All studies found statistically significant improvements in AHI, ranging from -6 to -25 events/hr, without statistical heterogeneity. • By meta-analysis, MAD results in a statistically and clinically significant improvement in sleepiness as measured by ESS (-1.4). Of 8 studies, 5 found statistically and clinically significant improvements in ESS, ranging from -1 to -4.5, without statistical heterogeneity. • MAD also generally resulted in improvements in other sleep study measures, but had inconsistent effects on or inadequate evidence for other outcomes of interest. • There was insufficient evidence to address whether study heterogeneity could be explained by different definitions of OSA or other clinical factors, particularly in light of the clinical heterogeneity across studies due to the difference in MADs. • In 2 studies about 5% of patients had tooth damage (or loosening). Substantial jaw pain was reported in about 2–4% of patients, but no study reported on the long-term consequences of any adverse events. • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS, and other sleep study measures, overall, the strength of evidence is moderate that MAD is an effective treatment for OSA in patients without comorbidities (including periodontal disease) or excessive sleepiness. However, the strength of evidence is insufficient to address which patients might benefit most from treatment.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments Oral devices vs. each other	Insufficient	• There were 5 trials comparing different oral devices; 3 compared different MADs; 2 compared different tongue devices. Of these 5 trials, 4 were rated quality B and 1 quality C. These studies are applicable mostly to patients with AHI of15 to 30 events/hr and BMI less than 30 kg/m^2. All studies were restricted to patients with a sufficient number of teeth to anchor the mandibular devices in place. • No study evaluated clinical outcomes. In general, the studies found no differences among devices in sleep study or other measures. Only 1 study (comparing 2 tongue-retaining devices) evaluated compliance and found no difference. • **Conclusion**: The strength of evidence is insufficient regarding comparisons of different oral devices.
Key Question 5: Treatment OSA treatments CPAP vs. MAD	Moderate	• There were 10 trials comparing different MADs with CPAP. A single study of an extraoral device vs. autoCPAP was rated quality C; 9 studies of oral MAD vs. fixed CPAP were rated quality B. The studies are generally applicable to patients with AHI >5-10 events/hr. • No study evaluated clinical outcomes. • A single study compared compliance rates, finding that patients used MAD significantly more hours per night and nights per week than CPAP. • There were 2 studies that found that CPAP was significantly more likely to result in 50% reductions in AHI and achieved AHI <5 events/hr, but 1 study found no difference in achieving <10 events/hr. By meta-analysis, CPAP resulted in significantly greater reductions in AHI (-8 events/hr); 7 of 9 studies found statistically significant differences. By meta-analysis, CPAP results in a statistically significant greater improvement in AHI than MAD (-8 events/hr). • The studies had inconsistent findings regarding the relative effects of MAD and CPAP on ESS. • The studies generally found superior effects of CPAP over MAD for other sleep study measures, but no differences in quality of life or neurocognitive function. • A single study found no differences with either device in achieving an AHI of either <5 or <10 events/hr based on baseline severity of OSA (at an AHI threshold of 30 events/hr). • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, overall the strength of evidence is moderate that the use of CPAP is superior to MAD. However, the strength of evidence is insufficient to address which patients might benefit most from either treatment.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments Surgery vs. control	Insufficient	• There were 7 studies comparing 7 different surgical interventions to sham surgery, conservative therapy, or no treatment. Of these, 3 studies were rated quality A, 1 quality B, and 3 quality C. • No study evaluated clinical outcomes. • Of these 7 studies, 4 found statistically significant improvements in AHI, other sleep study measures, and/or sleepiness measures. The remaining studies found no differences in these outcomes or quality of life or neurocognitive function. • Adverse events from surgery (also evaluated from large surgical cohort studies) were generally due to perioperative complications, including perioperative death in about 1.5% in two studies of UPPP – though most studies reported no deaths, hemorrhage, nerve palsies, emergency surgical treatments, cardiovascular events, respiratory failure, and rehospitalizations. Long-term adverse events included speech or voice changes, difficulties swallowing, airway stenosis, and others. In smaller studies, when these adverse events were reported they occurred in about 2–15% of patients. However the largest 2 studies (of 3,130 UPPP surgeries and 422 RFA surgeries) reported no long-term complications (not including perioperative death or cardiovascular complications). • **Conclusion**: Overall, the strength of evidence is insufficient to evaluate the relative efficacy of surgical interventions for the treatment of OSA.
Key Question 5: Treatment OSA treatments Surgery vs. CPAP	Insufficient	• Of 12 eligible studies comparing surgery with CPAP (1 quality A, 11 quality C), only 2 were RCTs. • There were 2 retrospective studies that evaluated mortality in UPPP vs. CPAP. Of these, 1 study found higher mortality over 6 years among patients using CPAP (HR = 1.31; 95% CI 1.03, 1.67) and 1 study found no difference in 5-year survival. • Both trials found no difference in outcomes either between RFA and CPAP after 2 months or between maxillomandibular advancement osteotomy and CPAP at after 12 months. The remaining studies were heterogeneous in their conclusions. • **Conclusion**: The strength of evidence is insufficient to determine the relative merits of surgical treatments versus CPAP.
Key Question 5: Treatment OSA treatments Surgery vs. MAD	Insufficient	• A single trial (quality B) compared UPPP and MAD treatment. • The trial did not evaluate clinical outcomes. The study found that significantly more patients using MAD achieved 50% reductions in AHI at 1 year and significantly lower AHI at 4 years. • **Conclusion**: The strength of evidence is insufficient to determine the relative merits of surgical treatments versus MAD.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments/ Other treatments	Variable (Low for weight loss vs. control; Insufficient for others)	• There were 3 trials (1 quality A, 2 quality B) comparing weight loss interventions with control interventions. The studies were heterogeneous in terms of baseline OSA severity, presence of comorbidities, and severity of obesity. The studies are generally applicable to people with BMI >30 kg/m^2. • No study evaluated clinical outcomes. • A single study found increased odds of achieving an AHI <5 events/hr after 1 year of a very low calorie diet compared with no treatment (OR=4.2, 95% CI 1.4, 12). All 3 trials found significant relative reductions in AHI with diet, from -4 to -23 events/hr. Other outcome data are inconsistent or sparse. • A total of 19 studies evaluated 21 other interventions including atrial overdrive pacing, 8 different drugs, palatal implants, oropharyngeal exercises, a tongue-retaining device, a positional alarm, combination tongue-retaining device and positional alarm, bariatric surgery, nasal dilator strips, acupuncture, and auricular plaster. All of these interventions were evaluated by 1 or 2 studies only. No study evaluated clinical outcomes. • **Conclusion**: The strength of evidence is low to show that some intensive weight loss programs are effective treatment for OSA in obese patients. • **Conclusion**: The strength of evidence is insufficient to determine the effects of other potential treatments for OSA.
Key Question 6: Predictors Predictors of treatment compliance	Variable (see Conclusions)	• There were 5 large cohort studies that conducted multivariable analyses of potential predictors of compliance with CPAP treatment. Of these, 1 study was rated quality A, 1 quality B, and 3 quality C. In general, the studies are applicable to patients initiating CPAP whose AHI is greater than 30 events/hr. • Of these 5 cohort studies, 4 studies all found that higher baseline AHI was associated with greater compliance. Also, 2 of 3 studies found that higher baseline ESS was a predictor of greater compliance. And 2 of 3 studies found that age was not a predictor of compliance. Only 1 or 2 studies evaluated other potential predictors, with no consistent findings. • A single quality C cohort study evaluated potential predictors of compliance with newly initiated MAD. The study did not identify any statistically significant predictors. • **Conclusion**: The strength of evidence is moderate that more severe OSA as measured by higher AHI is associated with greater compliance with CPAP use. The strength of evidence is moderate that higher ESS is also associated with improved compliance. • **Conclusion**: The strength of evidence is insufficient regarding potential predictors of compliance with MAD.

Table A. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 7: Treatment Treatments to improve compliance	Low	• There were 18 trials evaluating interventions to improve CPAP compliance. Of these, 2 were rated quality A, 8 quality B, and 8 quality C. These studies are mostly applicable to patients initiating CPAP with AHI >30 events/hr and BMI greater than 30 kg/m^2. No study evaluated interventions to improve compliance with other devices. • There were 9 studies evaluating extra support or education. These studies had inconsistent findings regarding the effect of the interventions on compliance. Only 3 of 7 studies found increased number of hours of CPAP use; only 1 of 3 studies found persistent improved compliance (and that was of compliance with followup visits). • There were 3 studies evaluating telemonitoring. No study found a statistically significant increase in CPAP usage (hours per night). • A single study evaluated the effect of cognitive behavioral therapy, and showed that the behavioral intervention significantly increased hours of CPAP use per night compared with usual care (difference = 2.8 hours; 95% CI 1.8, 3.9; P<0.0001). • There were 2 studies evaluating 2 other interventions: the hypnotic zolpidem and nasal pillows. No intervention was found to be effective to improve compliance. • There were 3 studies evaluating nursing care models. None improved compliance. • **Conclusion**: The strength of evidence is low that some specific adjunct interventions may improve CPAP compliance among overweight patients with more severe OSA who are initiating CPAP treatment. However, studies are heterogeneous and no general type of intervention (e.g., education) was more promising than others.

AHI = apnea-hypopnea index, AUC = area under the ROC curve, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, HR = hazard ratio, MAD = mandibular advancement device, OSA = obstructive sleep apnea, PSG = polysomnography (sleep-laboratory based), RFA = radiofrequency ablation, ROC = receiver operating characteristics, SF-36 = Short Form Health Survey 36, UPPP = uvulopalatopharyngoplasty.

Introduction

Obstructive sleep apnea (OSA) is a relatively common disorder in the United States that affects people of all ages, but is most prevalent among the middle-aged and elderly. Affected individuals experience repeated collapse and obstruction of the upper airway during sleep, which results in reduced airflow (hypopnea) or complete airflow cessation (apnea), oxygen desaturation, and arousals from sleep. Hypopneas and apneas are thought to have similar pathophysiologies and bear the same clinical significance, resulting in chronic overnight oxygen desaturation.[4]

Airway obstruction results in repeated cycles of loud snoring, disruption of rapid eye movement (REM) sleep, and frequent arousals throughout the night followed by hypersomnolence and daytime fatigue serious enough to affect concentration at work and while driving.[5] OSA has been associated with a variety of adverse clinical outcomes, such as cardiovascular disease,[6-9] including specifically cardiac disease and stroke, hypertension,[10-12] and non-insulin-dependent diabetes and other metabolic abnormalities,[7,13-16] increased likelihood of motor vehicle and other accidents,[17,18] and decreased quality of life.[19] These comorbidities combined with the inability to function at a normal level during the day are of considerable clinical concern.

The prevalence of OSA appears to be high, but it is not clear how common the condition is. The Wisconsin Sleep Cohort Study, a prospective natural history study of adults 30-60 years old reported that about 10 percent had clear evidence of OSA in 1988, when the study began.[1] The Sleep Heart Health Study, another prospective cohort study, of adults over age 40 years who were not being treated for sleep-disordered breathing, found that about 17 percent had clear evidence of OSA when they were recruited into the study in the late 1990s.[2] The National Sleep Foundation poll in 2005 found that as many as one in four American adults are at high risk of OSA and could benefit from an evaluation for OSA.[3]

OSA is an important public health issue due to associated morbidity and mortality rates; attendant comorbidities, such as hypertension and diabetes; and the adverse effects on daily quality of life. One study of general population volunteers in the U.S. found steadily increasing prevalence from under 10 percent at age 40 to approximately 20 percent among those over 60 years old.[20] Evidence also indicates that these rates are rising, most probably due to increasing rates of obesity.[21] The prevalence of OSA among those aged 65 and older (Medicare beneficiaries) is believed to be higher. In the population-based Sleep Heart Health Study, the prevalence of an apnea-hypopnea index (AHI; a measure of the presence and severity of OSA) of $\geq$15 events/hr was 1.7-fold higher in people older than 60 years, compared with people between 40 and 60 years of age.[20] Similar observations were made in cohort studies that used population-based samples and a wide range of ages.[22-25]

Complicating the diagnosis and treatment of OSA is the great degree of clinical uncertainty regarding the condition, due in large part to inconsistencies in its definition. According to a recent technology assessment, controversy regarding which type of sleep monitoring device is most appropriate for diagnosing sleep apnea continues to be ongoing.[26] Disagreement also exists about the type and level of respiratory abnormality that should be used to define sleep apnea, particularly for patients who have hypopneic episodes, rather than apnea. Moreover, no current established threshold level for AHI exists that indicates the need for treatment. By consensus, people with relatively few apnea or hypopnea events per hour (often <5 or <15) are not formally diagnosed with OSA. Notably, there is evidence to suggest that patients with relatively mild

sleep apnea (fewer apnea-hypopnea events per hour) may have substantially increased cardiovascular disease risk compared with the general population, despite the fact that the AHI values in these patients can be within the range considered normal or only slightly elevated. In addition, the symptom of excessive daytime sleepiness is highly variable and not always present in patients with OSA. In fact, a majority of patients are asymptomatic and may be unaware of the occurrence and frequency of their nocturnal arousals, and, therefore, fail to seek timely medical attention.[5] Thus, most patients remain undiagnosed and untreated.[5,19,27,28]

Given the increasing prevalence of OSA among middle-aged and elderly adults in the U.S., its important effects on mortality and morbidity, and the continued variability in standards used to diagnose and treat the disorder, the present systematic review is timely and may be of potential value in the development of clinical practice guidelines and Medicare coverage decisions regarding OSA.

It should be noted that this report focuses on OSA in adults and does not discuss other sleep apneas, such as central or mixed sleep apnea. Central sleep apnea is associated with conditions caused by damage to the brain stem (such as a stroke or encephalitis), neurological disorders, such as Parkinson's and Alzheimer's disease, and congestive heart failure. Patients with central sleep apnea do not have the obstructive characteristics of OSA. Mixed sleep apnea involves events with features of both central and obstructive apneas. Thus symptoms, diagnosis, treatments, and the natural histories of the two types differ, and therefore lie outside the scope of this review.

OSA in children also differs from adult OSA in its etiology, symptomatology, sleep study findings, and consequences. OSA in the pediatric population is largely caused by increased upper airway resistance during sleep due to soft tissue hypertrophy, craniofacial abnormalities, and/or neuromuscular deficits. The general symptoms of OSA in children are similar to that of adults (snoring and excessive daytime sleepiness), but also manifest as hyperactivity, aggressive behavior, poor school performance, and/or morning headaches. While pediatric patients with OSA do have increased risk of hypertension, insulin resistance, and hypercholesterolemia, they do not seem to suffer the same degree of cardiovascular consequences as adults.[29] Neurocognitive sequelae, such as poor school performance and attention deficit, are the most obvious consequences. Due to these important differences between adult and pediatric patients this review is restricted to the evaluation and treatment of adult OSA. Thus, this report's applicability to the pediatric population is uncertain.

Diagnosis

In general, individuals with OSA experience repetitive cycles of upper airway obstruction and frequent nighttime arousals. Upper airway obstruction during sleep is most often due to anatomical anomalies of the nasopharyngeal or mandibular areas that cause narrowing of the respiratory passages, decreased pharyngeal muscle tone that reduces the cross-sectional area of the upper airway, and insufficient neuromuscular responses to airway obstruction.[5] This narrowing is often exacerbated by obesity-related peripharyngeal fat.[5] AHI, the count of the hourly apnea and hypopnea events during sleep, when combined with determinations of obstruction, is the primary measurement used for the diagnosis of OSA. It (or variations that measure oxygen desaturations or other measures of respiratory disturbance instead of apnea) can by measured by polysomnography (PSG) in a sleep laboratory or by (portable) monitors in other settings. Notably, though, AHI can vary from night-to-night or between settings and does not take into account symptoms, comorbidities, or response to treatment.[30]

The severity of sleep apnea is typically quantified by the number of apneas and hypopneas per hour of sleep, defined as the AHI, measured during overnight monitoring. The American Academy of Sleep Medicine uses a threshold to define OSA of 15 events/hr (with or without OSA symptoms) or 5 events/hr with OSA symptoms (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).[31,32] However, as we found during our review, the minimum thresholds to diagnose sleep apnea in research studies vary from 5 to 20 events per hour by PSG.

Polysomnography

The current diagnostic standard used in clinical practice is PSG. The formal diagnosis of sleep apnea requires a comprehensive, technologist-attended sleep study with multichannel PSG performed in specialized sleep laboratories.[4,33] Laboratory-based PSG records a variety of neurophysiologic and cardiorespiratory signals that are read by trained technologists and interpreted by sleep physicians after a diagnostic sleep study has been completed. The sleep study incorporates a number of assessments and measurements including: recordings of rapid eye movements, electroencephalogram to detect arousals, chest and abdominal wall monitors to evaluate respiratory movements, electrocardiogram, electromyogram, oximetry, and nasal and oral air flow measurements.[5] This process of diagnosing OSA by PSG in a sleep lab has some constraints including cost, inconvenience, and interlaboratory variation in hardware and assessment methods. Additionally, the current clinical standard, which is the 16-channel, in-laboratory PSG has never been validated, and its true sensitivity and specificity in diagnosing OSA is not well documented.[26]

Portable Monitors

Since in-laboratory PSG is costly, resource-intensive, and potentially inconvenient for the patient, other diagnostic tools have been developed, including portable testing and questionnaires for prescreening patients. Portable monitors vary in the type of neurophysiologic and respiratory information collected, and each synthesizes the accumulated data differently.[34] There are different types (classes) of portable monitors. Each gathers different neurophysiologic and respiratory information and may synthesize the accumulated data differently. Portable monitors can be used in the home setting or sleep units.

The American Sleep Disorders Association has classified the different monitors that have been used in sleep studies into four categories, depending on which channels they record and evaluate.[34] As we did in the *2007 Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*,[26] we used the operational rules described in Table 1 to classify sleep monitors. Briefly:

- Type I is facility-based PSG.
- Type II monitors are portable and record the same information as Type I (perhaps with fewer channels). Type II monitors record signals that allow the reliable identification of (micro) arousals from sleep (e.g., electro-oculography, chin electromyography, electroencephalography) ***and*** at least two respiratory channels (two airflow channels or one airflow and one effort channel).

- Type III monitors are portable, but do not record the channels that differentiate between sleep and wake, but have at least two respiratory channels (two airflow channels or one airflow and one effort channel).
- Type IV are all other portable monitors that fail to fulfill criteria for Type III monitors. Therefore Type IV channels may include monitors that record more than two bioparameters.

Thus, portable monitors are classified as either Type II, III or IV. Please refer to our previous report for a more complete discussion of portable monitors.[26]

Table 1. Delineation of operational rules used to classify monitors in sleep studies

Type	Portability	Number of Channels	Indicative signals	≥2 airflow/ effort channels	Identifies sleep/ wake	Measures AHI
I	Facility-based	~14-16	EEG, EOG, EMG, ECG/HR, airflow, effort, SaO2	Yes	Yes	Yes
II	Portable	≥7	May have EEG, HR*, EOG, chin EMG, ECG/HR, airflow, effort, SaO2	Yes	Yes	Yes
III	Portable	≥4	Airflow and/or effort, ECG/HR, SaO2	Yes	No	No
IV	Portable	~1-3†	[All monitors not qualifying for Type III]	No	No‡	No

AHI = apnea-hypopnea index, ECG = electrocardiography, EEG = electroencephalography, EMG = electromyography, EOG = electro-oculography, HR = heart rate, SaO2 = arterial O2 saturation.
* Heart rate is allowed instead of EEG in Type II monitors. Essentially, many Type II monitors gather the same signals as Type I monitors.
† May have more than three channels, provided that criteria for Type III are not met
‡ May include monitors that measure signals that are in principle able to identify arousals from sleep.

Pretesting Questionnaires and Other Tests

Questionnaires are used to prescreen patients for further testing or treatment. The most commonly used screening questionnaire in clinical practice is the Epworth Sleepiness Scale (ESS).[35] This questionnaire asks patients to rate how likely they are to fall asleep in certain situations, such as riding in the car on a long trip. The ESS focuses solely on sleepiness and not other signs and symptoms of OSA, thus is not specific to OSA. Another questionnaire commonly used in practice is the STOP questionnaire from the University of Toronto.[36] In addition, researchers have created models to predict OSA based on demographic features, symptoms, head and neck anatomy, and other variables.

The value of the various questionnaires and other screening tools remains unclear. It is also unknown whether the tests can be accurately used to predict the clinical severity of patients' sleep apnea and the likelihood of clinically important sequelae. If the screening tests are found to be sufficiently predictive of the results of full sleep testing, the question arises of how best to determine which patients should be prescreened (or sent directly for a sleep study), and, after screening, which should be treated for OSA, tested further, or considered to not have OSA.

Preoperative Testing

The occurrence of both perioperative and postoperative complications in OSA patients has been documented with respect to either surgical intervention for OSA or other procedures.[37-39] In

a study of patients undergoing hip or knee replacement surgery, 24 percent of 101 patients with OSA had major postoperative complications (respiratory or cardiac) compared with 9 percent of matched controls.[39] Other studies have highlighted the risk of anesthesia and analgesia-related adverse outcomes, such as perioperative airway collapse and postoperative oxygen desaturation.[37,39] Many surgical patients with OSA, however, remain undiagnosed at the time of surgery,[37-39] and may benefit from some type of preoperative assessment for OSA.[37] Finding patients with undiagnosed sleep apnea who are undergoing surgery could, in theory, allow for optimization of perioperative care to minimize problems with intubation, extubation, and other respiratory events. At present, the value of screening all or selected surgical patients, and what method of screening would be most effective and efficient, is unclear.

Treatment

Irrespective of the cause of OSA, the defining characteristic is obstruction of the airway during sleep. The most common first line therapy is use of continuous positive airway pressure (CPAP) devices during sleep. However, the machines are not well-tolerated by many patients and may not fully resolve the OSA. Other commonly used treatments include dental and mandibular devices to improve oral airway obstruction, and a range of surgical treatments, including implanted structural supports, to reduce obstruction. Other interventions include devices to alter sleep position, physical therapy to improve oropharyngeal muscle tone, atrial overdrive pacing for patients with nocturnal bradycardia, complementary and alternative medicine, and interventions to achieve weight loss, including bariatric surgery.

Continuous Positive Airway Pressure

CPAP is the standard first-line therapy for most patients diagnosed with OSA.[40] The CPAP machine directly relieves the obstruction by counteracting airway narrowing through the delivery of compressed air to the oropharynx, thereby splinting the airway (keeping it open with increased air pressure). When used properly and consistently, CPAP results in improved sleep patterns and quality of life due to decreased daytime somnolence. However, many patients refuse the offer of CPAP therapy, do not tolerate it, or fail to use the portable machine properly.[41] These patients remain essentially untreated and receive little or no benefit from the device.

In addition, patients commonly fail to fully comply with CPAP use, either using the device for only part of the night or only on some nights. There are many reasons why patients do not comply with CPAP therapy including, discomfort with the mask or tubing; nasal congestion; poor mask fit with either leakage of air, skin irritation, or claustrophobia; the complexity of the machines, their noise, and the general inconvenience of their use.[42,43] Numerous interventions have been proposed to improve compliance with CPAP including training, nursing followup, and ancillary devices to improve comfort. The value of such measures, however, remains unclear.

The issue of adherence to therapy has also resulted in many technological modifications to the machine and the interface (mask) with the goal of improving adherence. Standard CPAP provides continuous fixed pressure during the entire sleep time. Therefore the patient has to both inhale and exhale with the same positive pressure being delivered into the airway. For some patients, especially those with obstructive lung disease, exhaling against this fixed pressure can be quite uncomfortable. One of the first modifications to address this issue was the introduction of bilevel pressure machines. Such devices deliver a higher pressure on inhalation and then a lower pressure during exhalation. A recently introduced flexible bilevel machine allows for a slight reduction in the positive airway pressure at the end of inspiration and at the beginning of

expiration. The inspiratory pressure and expiratory pressure changes are determined in part by the patient's own respiratory efforts. The impetus behind this feature is to promote an increased breathing synchrony with the machine and therefore increase patient comfort. Other CPAP machines have also been designed to improve comfort with the goal of improving compliance. These include C-Flex™ (Respironics, Inc.) where there is a very brief release of the positive airway pressure at the beginning of the expiratory phase of the respiratory cycle, and autotitrating CPAP (autoCPAP) where the machine can sense airflow resistance and increase the positive pressure in response. (Other companies make similar devices, including the Expiratory Pressure Relief™ device by ResMed, Inc., but since we found no eligible studies of other such devices, we do not discuss them further.) The value of the modifications to CPAP, however, remains unclear.

Regardless of the most effective method, improving compliance may require health care resources, and the time and effort of both health care professionals and patients. Thus, it would be helpful if health care providers could determine which patients are at greatest risk of poor compliance and what pretreatment, patient-level characteristics may best predict noncompliance. Efforts to improve compliance could then be focused on those individuals who would most benefit.

Current recommendations for determining the settings for CPAP are for a full night in laboratory CPAP titration.[44] The goal of CPAP titration is to obtain the minimal pressure at which all apneas, hypopneas, snoring and arousals from respiratory events in all stages of sleep and in all body positions are eliminated.[45] Some patients however undergo a split night study and have both the diagnostic polysomnogram and the CPAP titration done all in one night in the sleep laboratory. The use of a split-night study is meant to reduce wait-time from diagnosis to treatment. However, some studies indicate that split-night CPAP titrations are suboptimal.[46]

Other methods of determining the optimal CPAP level have been tried with moderate success. In patients with uncomplicated OSA and no significant comorbidities the following methods: a clinical prediction formula, adjusting CPAP for symptoms of snoring, and the use of autoCPAP have all been shown to adequately determine a starting pressure for OSA.[47-49] The patients may require an adjustment of the pressure based on symptoms if the optimal pressure is determined with these methods.[47] Close followup and monitoring of CPAP pressures is important in all patients regardless of how the CPAP level was determined.

Dental and Mandibular Devices

Oral and mandibular appliances, generally fitted by a dentist, can be worn overnight. Mandibular advancement devices, which are generally worn in the mouth, advance the mandible and usually maintain an opening between the incisors. Other oral devices ~~"r~~etain" or splint the tongue away from the airway, or otherwise mechanically splint the oropharynx and increase upper airway patency during sleep. Current recommendations are to test the oral device for efficacy of treating OSA by either an in-laboratory polysomnogram or home sleep test.[50] The American Academy of Sleep Medicine recommends oral appliances for patients with mild to moderate OSA who prefer the oral appliance to CPAP, do not respond to CPAP, cannot have CPAP for various reasons, or who fail CPAP.[51]

Surgery

For patients with clearly defined anatomic airway obstruction or prior treatment failures with noninvasive techniques (MAD or CPAP), oropharyngeal surgery may be an option. In general,

the goal of surgery is to remove the anatomic obstruction and to relieve symptoms. The specific surgery used depends on the patient's anatomy and the location and cause of the airway obstruction. The most common surgery is uvulopalatopharyngoplasty (UPPP) in which the soft tissue at the back of the throat and uvula (soft palate) are removed to increase width and improve the opening ability of the airway. The tonsils and adenoids may also be removed, if present. Removal techniques used in UPPP include conventional scalpel or laser-assisted procedures. Genioglossal advancement with hyoid myotomy/suspension may also be used to relieve obstruction at the base of the tongue. Another technique, maxillary-mandibular advancement osteotomy, involves moving the jaw forward to enlarge the oropharynx. Recently, radiofrequency ablation, primarily of the base of the tongue and/or nasal turbinates, has also been used to remove or shrink as well as scar redundant tissue to eliminate or otherwise minimize obstruction. Implants that provide structural support to the palate are sometimes also used to improve breathing. All of these surgical interventions may be used alone or in combination, depending on the patient's anatomy and tolerance for surgery (some procedures require several stages) and the surgeon's discretion.

Miscellaneous Treatments

Positional therapy involves the use of devices that maintain the patient in a preferred position during sleep. Most prevent the patient from sleeping in a supine position, which in many patients exacerbates airway obstruction. These devices include backpacks or balls strapped to the back. Other devices include wedge pillows to elevate the head and shoulders. Physical therapy of the oropharynx has also been advocated to strengthen the musculature, thus reducing obstruction.

Atrial overdrive pacing is a potential treatment for patients who already have implanted dual-chamber pacemakers. The pacemaker is set to pace the atrium at a rate higher than either the basal atrial rate or the lowest spontaneous rate. This intervention is based on the incidental finding that patients with OSA who received atrial overdrive pacing for atrial tachyarrhythmias reported a reduction in breathing disorders.[52] Atrial pacing may maintain sympathetic activity and counteract increases in vagal tone.[53]

Several pharmacologic agents have been studied for the treatment of OSA. The goals of these agents fall into two categories: ventilatory stimulants or REM sleep suppressants. As an example, selective serotonin reuptake inhibitors may stimulate ventilation and increase upper airway muscle tone. REM suppressant agents theoretically should be effective treatment for patients in whom the majority of the respiratory events occur during REM sleep. Other miscellaneous agents, such as opioid antagonists and nicotine, have also been studied.

Weight Loss

For many patients, obesity is the principle cause of their OSA due to excess fat in the oropharynx and upper airway resulting in poor muscle tone and obstruction. Thus weight loss can be an effective definitive treatment for these patients. The treatments for weight loss in this population are the same as for the general population, including lifestyle changes and bariatric surgery. However, individuals with OSA may be at increased surgical and anesthesia-related risk, due in part to decreased pharyngeal tone and depressed ventilatory responses to hypoxia and hypercapnia.[54]

Statement of Work

The Medicaid Evidence-based Decisions Project (MED) group, the Medicaid Medical Directors Learning Network, and the American College of Physicians (ACP) requested that the Agency for Healthcare Research and Quality (AHRQ) conduct an assessment of the diagnostic and treatment procedures for OSA. The ACP guidelines committee has expressed an interest in a full review of screening, diagnosis, and treatment of OSA for the purpose of developing a new guideline on the management of the disorder. MED is a collaboration of state Medicaid programs with the goal of making evidence available to states to support benefit design and coverage decisions made by state programs. The present Comparative Effectiveness Review (CER) was requested so that it may be used by the group to support benefit design and state coverage decisions. The AHRQ commissioned the Tufts Evidence-based Practice Center to conduct a CER of studies related to the diagnosis and treatment of OSA.

Three main categories of outcomes of interest in comparative effectiveness research are clinical (or health) outcomes (i.e., events or conditions that the patient can feel, such as disability, quality of life, or death), intermediate or surrogate outcomes (such as laboratory measurements), and adverse events.[55] Clinical outcomes relevant to patients with OSA include comorbidities found to be associated with untreated sleep apnea, primarily cardiovascular disease (including congestive heart failure, hypertension, stroke, and myocardial infarction) and non-insulin-dependent diabetes. In addition, mortality due to cardiovascular disease, diabetes, motor vehicle accidents, and other causes represent important adverse outcomes of OSA. Intermediate outcomes of interest in the management of patients with OSA include sleep study measures (e.g., AHI), measures of cardiovascular status (e.g., blood pressure), and measures of diabetes status (e.g., hemoglobin A1c).

All interventions have the potential for adverse events. Therefore, it is important to gather information on both the benefits and harms of interventions in order to fully assess the net comparative benefit. As discussed earlier, compliance with CPAP (or other devices) is an important issue to effectively treat OSA. Interventions that have better compliance or that may improve compliance are clearly of interest. Also of relevance is establishing definitive diagnostic standards and measures that would more clearly identify OSA patients, both symptomatic and asymptomatic. Such standards would serve to markedly reduce OSA-related morbidities as well as related health care costs. Studies have found that prior to diagnosis, OSA patients have higher rates of health care use, more frequent and longer hospital stays, and greater health care costs than after diagnosis.[4,39] Therefore, this review is of additional interest to the requesting organizations as well as broadly for the identification of diagnostic tests that would contribute to the early and definitive diagnosis of patients with OSA.

Key Questions

Diagnosis

1. How do different available tests compare in their ability to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep? How do these tests compare in different subgroups of patients, based on: race, sex, body mass index, existing non-insulin-dependent diabetes mellitus, existing cardiovascular disease, existing hypertension, clinical symptoms, previous stroke, or airway characteristics?

2. How does phased testing (screening tests or battery followed by full test) compare to full testing alone?
3. What is the effect of preoperative screening for sleep apnea on surgical outcomes?
4. In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index or oxygen desaturation index and other patient characteristics with respect to long-term clinical and functional outcomes?

Treatment

5. What is the comparative effect of different treatments for obstructive sleep apnea in adults?
    a. Does the comparative effect of treatments vary based on presenting patient characteristics, severity of obstructive sleep apnea, or other pretreatment factors? Are any of these characteristics or factors predictive of treatment success?
        - Characteristics: Age, sex, race, weight, bed partner, airway, other physical characteristics, and specific comorbidities
        - Obstructive sleep apnea severity or characteristics: Baseline questionnaire (and similar tools) results, formal testing results (including hypoxemia levels), baseline quality of life, positional dependency
        - Other: specific symptoms
    b. Does the comparative effect of treatments vary based on the definitions of obstructive sleep apnea used by study investigators?
6. In obstructive sleep apnea patients prescribed nonsurgical treatments, what are the associations of pretreatment patient-level characteristics with treatment compliance?
7. What is the effect of interventions to improve compliance with device use (positive airway pressure, oral appliances, positional therapy) on clinical and intermediate outcomes?

Methods

The present Comparative Effectiveness Review (CER) evaluates various diagnostic and treatment modalities for the management of obstructive sleep apnea (OSA). The Tufts Evidence-based Practice Center (Tufts EPC) reviewed the existing body of evidence on the relative benefits and possible harms of different interventions used to diagnose and treat OSA. The comparisons are based on a systematic review of the published scientific literature using established methodologies as outlined in the Agency for Healthcare Research and Quality's (AHRQ) *Methods Guide for Comparative Effectiveness Reviews* (Agency for Healthcare Research and Quality. Methods Guide for Comparative Effectiveness Reviews [posted November 2008]. Rockville, MD.), which is available at: http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60.

AHRQ Task Order Officer

The Task Order Officer (TOO) was responsible for overseeing all aspects of this project. The TOO facilitated a common understanding among all parties involved in the project, resolved ambiguities, and fielded all Tufts EPC queries regarding the scope and processes of the project. The TOO and other staff at AHRQ reviewed the report for consistency, clarity, and to ensure that it conforms to AHRQ standards.

External Expert Input

During a topic refinement phase, the initial questions were refined with input from a panel of Key Informants. Key Informants included experts in sleep medicine, general internal medicine and psychiatry, a representative from Oregon Division of Medical Assistance programs, an individual with OSA, a representative of a sleep apnea advocacy group, and the assigned TOO. After a public review of the proposed Key Questions, the clinical experts among the Key Informants were reconvened to form the TEP, which served to provide clinical and methodological expertise and input to help refine Key Questions, identify important issues, and define parameters for the review of evidence. Discussions among the Tufts EPC, TOO, and Key Informants, and, subsequently the TEP occurred during a series of teleconferences and via email. In addition, input from the TEP was sought during compilation of the report when questions arose about the scope of the review. See Preface for the list of Key Informants and members of the TEP, and title page for our local domain expert.

Key Questions

Key Questions, developed and refined in cooperation with the Key Informants and TEP, take into account the patient populations, interventions, comparators, outcomes, and study designs (PICOD) that are clinically relevant for diagnosis and treatment of OSA. Seven Key Questions are addressed in the present report. Three pertain to screening for and diagnosis of OSA (Key Questions 1-3), two address the comparative effectiveness of treatments for OSA (Key Questions 5 & 7), and two address associations between baseline patient characteristics and long-term outcomes and treatment compliance (Key Questions 4 & 6). The Key Questions are listed at the end of the Introduction.

Analytic Framework

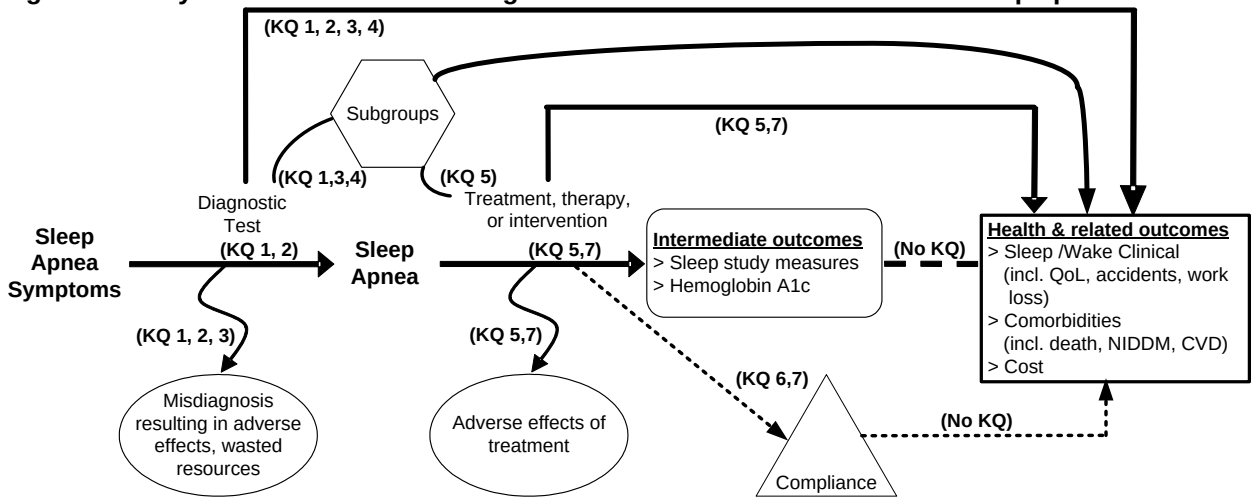
To guide the development of the Key Questions for the diagnosis and treatment of OSA, we developed an analytic framework (Figure 1) that maps the specific linkages associating the populations and subgroups of interest, the interventions (for both diagnosis and treatment), and outcomes of interest (intermediate outcomes, health-related outcomes, compliance, and adverse effects). Specifically, this analytic framework depicts the chain of logic that evidence must support to link the interventions to improved health outcomes.

Literature Search

We conducted literature searches of studies in MEDLINE® (inception—September 2010) and both the Cochrane Central Trials Registry®, and Cochrane Database of Systematic Reviews® (through 3rd Quarter, 2010). All English language studies with adult human subjects were screened to identify articles relevant to each Key Question. The reference lists of related systematic reviews as well as selected narrative reviews and primary articles were also reviewed for relevant studies. Our search included terms for OSA, sleep apnea diagnostic tests, sleep apnea treatments, and relevant research designs (see Appendix A for complete search strings). In addition, with input from the TEP, a separate search was conducted for cohort studies addressing Key Question 4 (the assessment of the relationship between sleep indices or patient characteristics with outcomes) and Key Question 6 (associations of pretreatment patient-level characteristics with treatment compliance in nonsurgical treatments). This additional search was also conducted through September 2010. TEP members were also invited to provide additional citations. All articles suggested by TEP members were screened for eligibility using the same criteria as for the original articles. The consensus of the TEP was not to include unpublished data, based primarily on the balance between the large volume of trial data and limited time and resources.

The literature search was supplemented by solicited Scientific Information Packets. A sister organization, also under contract with AHRQ, solicited industry stakeholders, professional societies, and other interested researchers for research relevant to the Key Questions. A Web site was also available for anyone to upload information. Studies from this source were screened using the same eligibility criteria as for the primary search.

Figure 1. Analytic framework for the diagnosis and treatment of obstructive sleep apnea in adults



CVD = cardiovascular disease, KQ = Key Question, NIDDM = non-insulin-dependent diabetes mellitus, QoL = quality of life.

Study Selection and Eligibility Criteria

The Tufts EPC has developed a computerized screening program, *Abstrackr*, to automate the screening of abstracts to include eligible articles for full-text screening.[56] The program uses an active learning algorithm to screen for articles most relevant to the Key Questions. Relevance was established by manually double-screening 1,000 abstracts to train the program. Subsequently, abstracts selected by the program were screened by one researcher. The results of each group of abstracts that were manually screened (and classified as accept or reject) were iteratively fed into the program for further training prior to generation of the next group of abstracts to be manually screened. This process continued until the program was left with only abstracts it rejected. Using *Abstrackr,* we reduced by 50 percent the number of abstracts we needed to manually screen prior to starting the subsequent steps of the systematic review. While the review was subsequently being conducted, all abstracts rejected by the program were also manually screened. (All abstracts rejected by *Abstrackr* were also rejected by manual screening.) Full-text articles were retrieved for all potentially relevant articles. These were rescreened for eligibility. The reasons for excluding these articles were tabulated in Appendix B.

Eligible studies were further segregated using the following selection criteria: population and condition of interest; interventions, predictors, and comparators of interest; outcomes of interest; study designs; and duration of followup. Of note, where interventions are not discussed (either diagnostic tests or treatments), this does not imply that the interventions were excluded from analysis (unless explicitly stated); instead, no studies of these interventions met eligibility criteria.

Population and Condition of Interest

We included studies conducted only in adults (>16 years). By consensus with the TEP, we excluded studies in which more than 20 percent of the participants had neuromuscular disease, Down syndrome, Prader-Willi syndrome, major congenital skeletal abnormalities, narcolepsy, narcotic addiction, Alzheimer's disease, epilepsy, or who had experienced a disabling stroke. This threshold (20 percent) was chosen arbitrarily to avoid excluding potentially relevant small studies that included some patients with conditions not of interest to the current report. This

turned out to be a moot point since no eligible studies explicitly included patients with any of these conditions.

Diagnostic testing (Key Questions 1 & 2). We included studies of adults with symptoms, findings, history, and comorbidities that indicated an increased risk of sleep apnea. Studies conducted in only asymptomatic or healthy general-population participants, as well as those in patients with known sleep apnea, were excluded.

Preoperative screening (Key Question 3). We included studies of all preoperative patients, irrespective of the surgery to be performed, as long as they were scheduled to receive general anesthesia. We excluded studies in which all patients were known to have sleep apnea. There were no other restrictions based on patient symptoms or existing diagnoses.

Predictors of long-term outcomes (Key Question 4). We included studies of adults, regardless of health status, who had a baseline sleep study performed for any reason.

Treatment of OSA (Key Question 5) and treatment compliance (Key Questions 6 & 7). We included studies of adults with a confirmed diagnosis of OSA, whether associated with symptoms or not, and with formal sleep study testing demonstrating an apnea-hypopnea index (AHI) ≥5 events/hr. We excluded studies with >20 percent of study subjects without OSA, unless a subgroup analysis of OSA patients was reported. This restriction included patients with central sleep apnea or snoring without OSA.

Interventions, Predictors, and Comparators of Interest

Diagnostic testing (Key Question 1). We evaluated two types of comparisons: portable monitoring devices (used at home or setting other than a sleep laboratory) versus facility-based polysomnography (PSG); and questionnaires or prediction models versus PSG or portable monitors. Generally, portable devices (and PSG) are categorized by the number and type of ~~"c~~channels" measured. Each channel separately monitors and measures indicators of the physiological status of organs. Combinations of these channels are used in different types of devices for the diagnosis of sleep apnea. For example, a sleep-facility-based PSG includes at least the following channels: electroencephalography, electrooculography, electromyography, heart rate or electrocardiography (ECG), airflow, breathing/respiratory effort, and arterial oxygen saturation. Some portable devices have four monitored channels with at least two channels measuring respiratory movement, or one measuring respiratory movement combined with a channel measuring airflow, in addition to heart rate or ECG, and oxygen saturation. Other portable devices measure one, two, or three physiological indicators.

We followed the construct of our 2007 technology assessment on PSG.[26] With the TEP, we came to agreement that PSG is an accurate measure of AHI and other (obstructive and nonobstructive) apnea measures, but is not a definitive test for OSA (syndrome) since the definition of the syndrome includes clinical judgment and arbitrary thresholds.

We excluded studies with verification bias in which not everyone had PSG as the comparator.

We included all portable devices with any combination of two or more channels and those that measured the following single channels: pulse transit time, peripheral arterial tone, and pulse oximetry. We excluded studies on devices that used other single channel tests, specifically those

that measured only heart rate, heart rate variability, or actigraphy alone. For the first analysis (portable versus PSG) we included only studies that performed an overnight PSG.

For the second analysis (questionnaires, etc. versus standard testing), we included studies that evaluated screening and other questionnaires, scales that included clinical criteria (e.g., signs, symptoms, history, and comorbidities), and other clinical decisionmaking tools. These tests could be compared to either overnight PSG or portable testing. We excluded studies that assessed only single patient characteristics or risk factors. We also excluded tests that were not validated in a group of participants separate from the sample used to develop the test. Accepted studies either validated their models in a separate subgroup of study participants or had their models evaluated in subsequent studies.

Phased testing (Key Question 2). We included any study that directly compared phased testing (a series of tests performed dependent on the results of initial tests) with full testing (overnight PSG) alone.

Preoperative screening (Key Question 3). We included studies that assessed any test or predictor of sleep apnea.

Predictors of long-term outcomes (Key Question 4). We included studies that assessed AHI (or similar sleep study measures) together with other potential predictors of long-term outcomes.

Treatment of OSA (Key Question 5) and treatment compliance (Key Questions 6 & 7). We included studies that assessed almost any proposed intervention or combination of interventions to treat (or manage) OSA or to improve compliance with OSA treatment (listed below). However, for nonsurgical interventions, the patients must have used the intervention at home (or equivalent). Thus studies in which the patients received the intervention only in the sleep laboratory (primarily studies of positive airway pressure devices) were excluded. The included interventions, alone or in combination, were:

- Positive airway pressure devices (continuous positive airway pressure [CPAP], bilevel positive airway pressure, autotitrating continuous positive airway pressure, other similar devices, and device modifications designed to improve comfort or compliance)
- Oral appliances and dental devices (mandibular advancement devices, tongue-retaining devices, and other similar devices)
- Devices designed to alter sleep positions (positional therapy)
- Weight loss interventions (where the goal was improvement of OSA)
- Physical therapy, training, or strengthening of the airway
- Surgical implants in the oropharynx
- Any surgery to the airway designed to reduce airway obstruction
- Medications of current interest for possible treatment of OSA
- Based on decisions of the TEP, we excluded drugs that treat sleepiness, sleep quality, or bruxism, but not OSA, drugs used only in highly selected patients with OSA (e.g., those with Alzheimer's disease). The excluded drugs include: armodafinil, bromocriptine, donepezil, eszopiclone, and modafinil.
- Miscellaneous interventions (including, but not limited to, drugs, complementary and alternative medicine, and atrial overdrive pacing).

In studies relevant to Key Question 6, patients must have received a nonsurgical treatment (a treatment with which they would need to comply). In studies relevant to Key Question 7, patients must have received either CPAP (or a variation), an oral or dental device, or a positional therapy device, in addition to an intervention whose purpose was to improve the compliance with the device.

Outcomes of Interest

Diagnostic testing (Key Questions 1 & 2). We included all studies reporting concordance or agreement among tests, predictive value (sensitivity, specificity) for diagnosis, change in clinical management, and clinical outcomes.

Preoperative screening (Key Question 3). We included studies reporting all intraoperative events, surgical recovery events, surgical recovery time, postsurgical events, length of intensive care or hospital stay, and intubation or extubation failures.

Predictors of long-term outcomes (Key Question 4). We included analyses of long-term clinical outcomes of interest, including all-cause mortality, cardiovascular death, nonfatal cardiovascular disease, incident hypertension, quality of life measures, incident stroke, and incident type 2 diabetes mellitus.

Treatment of OSA (Key Question 5). We included all studies reporting the following apnea-related outcomes of interest (see below for descriptions of selected OSA-related outcomes):

- Sleep/wakefulness clinical outcomes
  - Quality of life outcomes, both disease specific (e.g., Functional Outcomes of Sleep Questionnaire [FOSQ], Calgary questionnaire) as well as general (e.g., Short Form survey instrument 36 [SF-36]).
  - Sleepiness / somnolence measures, including validated subjective (e.g., Epworth Sleepiness Scale) and objective measures (e.g., Multiple Sleep Latency Test, Maintenance of Wakefulness Test).
  - Neurocognitive tests, as reported by studies
  - Accidents ascribed to somnolence (e.g., motor vehicle, home accidents)
  - Productivity outcomes (e.g., work days lost)
- Objective clinical outcomes
  - Mortality
  - Cardiovascular events, including categorical changes in hypertension diagnosis or stage
  - Non-insulin-dependent diabetes (diagnosis, resolution, start or end treatment)
  - Depression events (diagnosis, recurrence, etc.).
- Intermediate or surrogate outcomes
  - Sleep study measures (from a minimum of 6 hour sleep studies)
    - Apnea-hypopnea index (AHI, continuous or categorical). If AHI not reported, we captured respiratory disturbance index or oxygen desaturation index
    - Arousal index
    - Time in deeper sleep stages (stages 3-4 and rapid eye movement sleep)
    - Sleep efficiency (percent of time spent asleep)
    - Minimum (nadir) oxygen saturation

    - Comorbidities surrogate outcomes
        - Hemoglobin A1c
        - Blood pressure (systolic, diastolic, and mean arterial pressures)
- Compliance (adherence), either categorically (whether adhering or not) or quantitatively (time using device)
- Adverse events, complications, and harms

Description of OSA-related outcomes.

- Epworth Sleepiness Scale (ESS): A self-administered questionnaire which asks the patients the chances of their dozing in eight situations often encountered in daily life. Each item is rated on a 4-point scale, with a total score that can range from 0 to 24.[35] It measures―sleep propensity" as it asks about actual dozing, not―subjective sleepiness." Based on a study of normal subjects, the reference range is defined as ≤10. [57,58] Domain experts consider a 1 point change in ESS to be clinically significant.
- Multiple sleep latency test (MSLT): A measurement of how quickly a subject falls asleep (when asked to) lying down in a quiet, darkened room. Sleep onset is monitored by electrodes and other wires.[59] Though a reference range is not used in clinical practice, based on several studies of normal volunteers, a plausible reference range is 3.2 to 20 minutes.[58]
- Maintenance of wakefulness test (MWT): A measurement of how long a subject can stay awake (when asked to) sitting in bed, resting against pillows, in a quiet, dimly lit room. Sleep onset is monitored by electrodes and other wires.[60] Using a 20 minute protocol, a plausible reference range is approximately 12 to 20 minutes (staying awake).[58]
- Apnea-hypopnea index (AHI): The number of episodes of apnea (complete airflow cessation) plus the number of hypopneas (reduced airflow) per hour of monitored sleep. Only PSG and portable monitors that measure airflow directly measure AHI. As noted above, the American Academy of Sleep Medicine uses a threshold of 15 events/hr (with or without OSA symptoms) or 5 events/hr with OSA symptoms to define OSA.[31,32] Portable monitors that do not measure airflow may measure an oxygen desaturation index (ODI), the frequency of predefined oxygen desaturations (usually decreases of 3 or 4 percent). A related measure is the respiratory disturbance index (RDI), the frequency of respiratory events that disrupt sleep (in addition to apneas and hypopneas).
- Arousal index: The frequency per hour of arousals from sleep measured by electroencephalography as sudden shifts in brain wave activity.
- Slow wave sleep (stage 3 or 4 sleep): The percentage of time while asleep that the subject is in stage 3 or 4 sleep, measured by electroencephalography.
- Sleep efficiency: The percentage of time that a subject is asleep while in bed.
- Minimum oxygen saturation: The minimum oxygen saturation measured during sleep.

Treatment compliance (Key Questions 6 & 7). We included studies reporting adherence or compliance outcomes that were measured categorically as well as continuously (time spent using device per each time period).

Study Designs

We included only English-language, published, peer-reviewed articles. We did not include abstracts, conference proceedings, or other unpublished "grey" literature. Sample size thresholds were chosen based primarily on practical consideration of available resources and time balanced with the likely amount of available literature.

Diagnostic testing and screening (Key Questions 1-3). We included all prospective cross-sectional or longitudinal studies of any followup duration. At least 10 study participants had to be analyzed with each test of interest. For studies pertaining to Key Question 1, we did not reevaluate studies included in the 2007 Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome, also written by the Tufts EPC.[26] The findings of relevant studies from the previous report are summarized briefly in the appropriate sections of the Results section. These studies were also included in relevant figures; however, they are not presented in the summary tables of the present review.

Predictors of long-term outcomes (Key Question 4). We included longitudinal studies enrolling ≥500 participants with a followup ≥1 year. Included studies had to report a multivariable analysis.

Treatment of Sleep Apnea (Key Question 5) and treatment compliance (Key Question 7). We included longitudinal studies that analyzed ≥10 patients per intervention. Nonsurgical studies were restricted to randomized controlled trials (RCTs). We also included retrospective and nonrandomized prospective studies that compared surgery (including bariatric surgery) to other modes of intervention. Furthermore, we included prospective or retrospective noncomparative cohort studies of surgical interventions. However, these studies were restricted to those with at least 100 patients who received a given type of surgery. From these surgical cohort studies we evaluated only adverse events (complications). For Key Question 5, studies of any duration were accepted as long as the interventions were used in the home setting (or equivalent). Studies for Key Question 7 were restricted to those with ≥2 weeks followup.

Treatment compliance (Key Question 6). We included longitudinal studies that analyzed ≥100 patients who were followed for ≥1 month. For analyses of compliance with CPAP, we included only prospective studies that reported multivariable analyses. We included any analysis of compliance with other devices.

Data Extraction and Summaries

Two articles were extracted simultaneously by all researchers for training, after which approximately a dozen articles were double data extracted for further training. Subsequently, each study was extracted by one experienced methodologist. Each extraction was reviewed and confirmed by at least one other methodologist. Data were extracted into customized forms in Microsoft Word, designed to capture all elements relevant to the Key Questions. Separate forms were used for questions related to diagnosis (Key Questions 1-3), treatment (Key Questions 5 & 7), surgical cohort treatment studies (Key Question 5), and predictors (Key Questions 4 & 6) (see Appendix C for the data extraction forms). The forms were tested on several studies and revised before commencement of full data extraction.

Items common to the diagnosis and treatment forms included first author, year, country, sampling population, recruitment method, whether multicenter or not, enrollment years, funding source, study design, inclusion, and exclusion criteria, specific population characteristics including demographics such as age and sex, blood pressure, and baseline severity of OSA as measured by PSG and subjective scales like ESS.

For Key Questions related to diagnosis, information extracted about the test included the setting, the scoring system, the definitions of apnea and hypopnea, time period of the test, whether total sleep time or the total recording time was used as the denominator for calculation of the indices, and cutoffs used in comparisons. If the index test was a device, then additional details on the type of device, channels, and the synchronicity with polysomnographic testing were also extracted. Data used to develop the questionnaire were ignored; only data from validation samples were extracted.

For the Key Questions related to treatment, details regarding the interventions, including type of positive airway pressure device, surgical techniques, dental or oral devices were also extracted, as well as those of adjunct interventions. Extracted information included definitions, followup time periods, and type of outcome (sleep/wakefulness clinical outcomes; general and disease-specific quality of life outcomes; sleepiness/somnolence measures; general symptom scales; psychological, cognitive, or executive function, and physical function scales; somnolence-related accidents; sleep quality; objective clinical outcomes; and intermediate or surrogate outcomes like sleep study or clinical measures). Compliance was also recorded as an outcome.

For each outcome of interest, baseline, followup, and change from baseline data were extracted, including information of statistical significance. For most outcomes, only data from the last reported time point was included. When outcome data were reported as overall outcomes, without a specific time point, the mean or median time of followup was used. All adverse event data were extracted.

For studies that reported analyses of predictors of outcomes (related to Key Question s 4 & 6), full data were extracted for each predictor of interest when analyses were performed from the perspective of the predictor (i.e., baseline age as a predictor of death, not the mean age of those who lived and died). Multivariable analyses that included the most pretreatment predictors were preferred over other reported analyses.

Quality Assessment

We assessed the methodological quality of studies based on predefined criteria. We used a three-category grading system (A, B, or C) to denote the methodological quality of each study as described in the AHRQ methods guide (see this chapter's introductory paragraph). This grading system has been used in most of the previous evidence reports generated by the Tufts EPC. This system defines a generic grading scheme that is applicable to varying study designs including RCTs, nonrandomized comparative trials, cohort, and case-control studies. For RCTs, we primarily considered the methods used for randomization, allocation concealment, and blinding as well as the use of intention-to-treat analysis, the report of dropout rate, and the extent to which valid primary outcomes were described as well as clearly reported. For treatment studies, only RCTs could receive an A grade. Nonrandomized studies and prospective and retrospective cohort studies could be graded either B or C. For all studies, we used (as applicable): the report of eligibility criteria, the similarity of the comparative groups in terms of baseline characteristics and prognostic factors, the report of intention-to-treat analysis, crossovers between interventions,

important differential loss to followup between the comparative groups or overall high loss to followup, and the validity and adequacy of the description of outcomes and results.

A (good). Quality A studies have the least bias, and their results are considered valid. They generally possess the following: a clear description of the population, setting, interventions, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; clear reporting of dropouts and a dropout rate less than 20 percent dropout; and no obvious bias. For treatment studies, only RCTs may receive a grade of A.

B (fair/moderate). Quality B studies are susceptible to some bias, but not sufficiently to invalidate results. They do not meet all the criteria in category A due to some deficiencies, but none likely to introduce major bias. Quality B studies may be missing information, making it difficult to assess limitations and potential problems.

C (poor). Quality C studies have been adjudged to carry a substantial risk of bias that may invalidate the reported findings. These studies have serious errors in design, analysis, or reporting and contain discrepancies in reporting or have large amounts of missing information.

Data Synthesis

We summarized all included studies in narrative form as well as in summary tables (see below) that condense the important features of the study populations, design, intervention, outcomes, and results. For questions regarding comparisons of diagnostic tests (Key Questions 1-3), we used Bland-Altman plots, which graph the differences in measurements against their average.[61,62] This approach is recommended for analyses in which neither test can be considered a reference (gold) standard, as is the case with sleep apnea diagnostic tests. For each study with available information (either reported in the paper or after figure digitizing), we visually depicted the average difference between the two measurements and the spread of the 95 percent limits of agreement the boundaries that include 95 percent of the differences between the two measurements). We conducted analyses of sensitivity and specificity in studies that did not report Bland-Altman plots. Briefly, the sensitivity and specificity were derived and visually depicted in receiver operating characteristics space. Studies that yielded high positive likelihood ratio and/or low negative likelihood ratio were identified. For operational cutoffs for a high positive likelihood ratio and a low negative likelihood ratio we used the values 10 and 0.1, respectively.[63] We did not attempt to meta-analyze the diagnostic test studies.

For Key Questions 5 & 7 that evaluate the effect of an intervention on intermediate and clinical outcomes, we performed DerSimonian & Laird[64] random effects model meta-analyses of differences of continuous variables between interventions where there were at least three unique studies that were deemed to be sufficiently similar in population and had the same comparison of interventions and the same outcomes. Based on available data and clinical importance, we performed meta-analyses for AHI, ESS, arousal index, minimum oxygen saturation, multiple sleep latency test, the quality of life measure FOSQ, and compliance.

During data extraction we found that about half of the RCTs had a parallel design (separate groups of patients received separate interventions for the duration of the trial) and half had a crossover design (where all patients received all interventions for a given duration, in random order). For parallel trials, we evaluated the net change (the difference between the change from

baseline between the intervention of interest and the control intervention). Almost all crossover studies analyze the difference in final values after treatment with the different interventions. The concept is that, by definition, there is only one set of baseline values for the cohort of patients, and these, thus, cancel out. Therefore, for crossover studies, differences of final values are evaluated.

However, a large number of studies did not report full statistical analyses of the net change or difference of final values. Where sufficient data were reported, we calculated these values and estimated their confidence intervals (CI). These estimates were included in the summary tables and were used for meta-analyses. In the summary tables we include only the P values reported by the studies (not estimated P values). If a study reported an exact P value for the difference, we calculated the CI based on the P value. When necessary, standard errors of the differences were estimated from reported standard deviations (or standard errors) of baseline and/or final values. For parallel trials, we assumed a 50 percent correlation of baseline and final values in patients receiving a given intervention. Likewise for crossover trials, we assumed a 50 percent correlation between final values after interventions (among the single cohort of patients). Thus in both cases we used the following equation to estimate the standard error (SE):

$$SE^2_{difference} = (SE_A)^2 + (SE_B)^2 - 2 \cdot r \cdot (SE_A) \cdot (SE_B)$$

where r=0.5 and A & B are the correlated values.

For our primary meta-analyses, we combined the net changes from the parallel trials and the difference of final values from the crossover trials. However, we also performed (and include in the figures) subgroup analyses based on study design.

For Key Questions 4 & 6, the reported associations are presented in summary tables and described and discussed in narrative form. We did not attempt any metaregression for these studies.

Summary Tables

All summary tables are located in Appendix D. Summary tables succinctly report measures of the main outcomes evaluated. The decision about which data to include in the summary tables was made in consultation with the TEP. We included information regarding sampling population, country, study design, interventions, demographic information on age and sex, body mass index, the study setting, information on severity of sleep apnea (based on AHI and ESS), number of subjects analyzed, mean study duration and range, years of intervention, dropout rate, and study quality. For continuous outcomes, we included the baseline values, the within-group changes (or final values for crossover studies), the net difference (or difference between final values) and its 95 percent CI and P value. For categorical (dichotomous) outcomes, we report the number of events and total number of patients for each intervention and (usually) the risk difference and its 95 percent CI and P value. After consideration of the reported data across studies, and with the agreement of the TEP, we entered results for quality of life outcomes (except FOSQ) and for all neurocognitive test outcomes into a highly summarized table which does not provide all reported data. In these tables, for each test (or scale or subscale, etc.) we report which intervention statistically significantly favored the patient (e.g., resulted in better quality of life). If neither intervention was favored, we report no further data. If one intervention was statistically significantly better than another, we report the net (or final) difference for the test (or subscale), its estimated 95 percent CI and P value, and the "worst" and "best" possible scores for the test.

Each set of tables includes a study and patient characteristics table (which is organized in alphabetical order by first author). Results are presented in separate summary tables for each outcome. Within these tables, the studies are ordered by quality (A to C), then number of patients analyzed for that outcome (largest to smallest). It should be noted that the P value column includes the P value reported in the articles for the difference in effect between the two interventions of interest. The table also includes the 95 percent CI about the net difference (or difference in final values, from crossover studies); however, in the large majority of cases, these numbers were estimated by the Tufts EPC based on reported standard deviations, standard errors, and P values. This is noted in each table.

Grading a Body of Evidence for Each Key Question

We graded the strength of the body of evidence for each analysis within each Key Question as per the AHRQ methods guide,[65] with modifications as described below. Risk of bias was defined as low, medium, or high based on the study design and methodological quality. We assessed the consistency of the data as either "no inconsistency" or "inconsistency present" (or not applicable if only one study). The direction, magnitude, and statistical significance of all studies were evaluated in assessing consistency, and logical explanations were provided in the presence of equivocal results. We also assessed the relevance of evidence. Studies with limited relevance either included populations which related poorly to the general population of adults with OSA or that contained substantial problems with the measurement of the outcome(s) of interest. We also assessed the precision of the evidence based on the degree of certainty surrounding an effect estimate. A precise estimate was considered an estimate that would allow a clinically useful conclusion. An imprecise estimate was one for which the CI is wide enough to preclude a conclusion.

We rated the strength of evidence with one of the following four strengths (as per the AHRQ methods guide): High, Moderate, Low, and Insufficient. Ratings were assigned based on our level of confidence that the evidence reflected the true effect for the major comparisons of interest. Ratings were defined as follows:

High. There is high confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.

No important scientific disagreement exists across studies. At least two quality A studies are required for this rating. In addition, there must be evidence regarding objective clinical outcomes.

Moderate. There is moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

Little disagreement exists across studies. Moderately rated bodies of evidence contain fewer than two quality A studies or such studies lack long-term outcomes of relevant populations. Upon reviewing the evidence, we decided that when there was no or weak evidence for clinical outcomes but sufficient evidence (see further below on this page) of a large clinical and highly statistically significant effect on the relatively important sleep study and sleepiness measures (i.e., AHI, arousal index, minimum oxygen saturation, ESS, and FOSQ), we would rate the overall strength of evidence as moderate, despite the weak evidence on clinical outcomes.

Low. There is low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.

Underlying studies may report conflicting results. Low rated bodies of evidence could contain either quality B or C studies.

Insufficient. Evidence is either unavailable or does not permit a conclusion.

There are sparse or no data. In general, when only one study has been published, the evidence was considered insufficient, unless the study was particularly large, robust, and of good quality.

These ratings provide a shorthand description of the strength of evidence supporting the major questions we addressed. However, they by necessity may oversimplify the many complex issues involved in appraising a body of evidence. The individual studies involved in formulating the composite rating differed in their design, reporting, and quality. The strengths and weaknesses of the individual reports, as described in detail in the text and tables, should also be considered.

When there were disagreements on effect estimates across different outcomes within the same comparison or when a large amount of evidence existed for only an important surrogate outcome (e.g., AHI), we also rated the strength of evidence for particular outcomes within a comparison. Similar rating categories and criteria were used; however, the descriptors were altered to delineate between rating the comparison and rating the individual outcomes within a comparison. These descriptors are modifications of the standard AHRQ approach:

Sufficient. There is sufficient assurance that the findings of the literature are valid with respect to the outcome of interest within a comparison. No important scientific disagreement exists across studies. Further research is unlikely to change our confidence in the estimate of effect for this outcome.

Fair. There is fair assurance that the findings of the literature are valid with respect to the outcome of interest within a comparison. Little disagreement exists across studies. Further research may change our confidence in the estimate of effect and may change the estimate for this outcome.

Weak. There is weak assurance that the findings of the literature are valid with respect to the outcome of interest within a comparison. Underlying studies may report conflicting results. Further research is likely to change our confidence in the estimate of effect and may change the estimate for this outcome.

Limited or no evidence. Evidence is either unavailable or does not permit estimation of an effect due to lacking or sparse data for the outcome of interest within a comparison.

Overall Summary Table

To aid discussion, we summarized all studies and findings into one table in the Summary and Discussion. Separate cells were constructed for each Key Question and subquestion. The table also includes the strength of evidence to support each conclusion.

Peer Review and Public Commentary

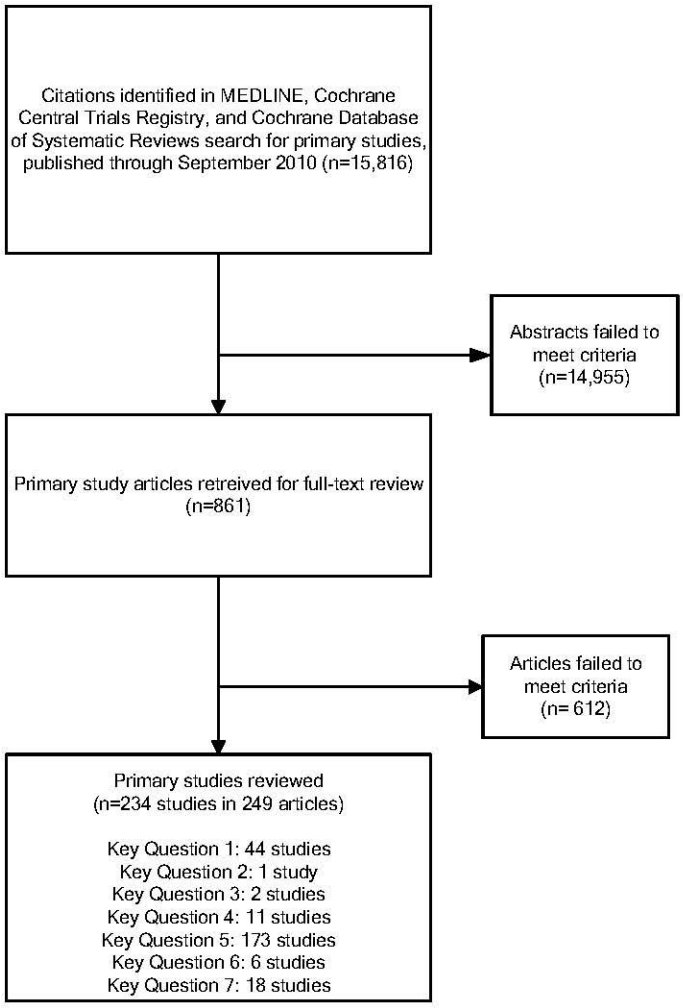
As part of a newly instituted process at AHRQ, the initial draft report was prereviewed by the TOO and an AHRQ Associate Editor (a senior member of a sister EPC). Following revisions, the draft report was sent to invited peer reviewers and was simultaneously uploaded to the AHRQ Website where it was available for public comment for 30 days. All reviewer comments (both invited and from the public) were collated and individually addressed. The authors of the report had final discretion as to how the report was revised based on the reviewer comments, with oversight by the TOO and Associate Editor.

Results

The literature search in MEDLINE®, the Cochrane Central Trials Registry®, and Cochrane Database of Systematic Reviews® yielded 15,816 citations. From these, 861 articles were provisionally accepted for review based on the abstracts and titles (Figure 2). After screening their full texts, 612 articles were rejected for not meeting eligibility criteria (see Appendix B for the list of rejected articles and their reasons for rejection). The most common reasons for article rejection were: inclusion in the 2007 *Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*;[26] analysis of too few study participants; no interventions, outcomes, predictors, or analyses of interest; and retrospective, noncomparative, or cross-sectional study design. In total, 234 studies (in 249 articles) met criteria and are reviewed. All relevant studies found in previous systematic reviews, selected narrative reviews, and by domain experts had already been captured by our literature search.

Due to the large quantity of evidence reviewed, Summary Tables are in Appendix D.

Figure 2. Literature flow



Note that the numbers of studies for each Key Question do not sum to the total number of studies because some studies addressed multiple Key Questions.

Key Question 1. How do different available tests compare in their ability to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep? How do these tests compare in different subgroups of patients, based on: race, sex, body mass index, existing non-insulin-dependent diabetes mellitus, existing cardiovascular disease, existing hypertension, clinical symptoms, previous stroke, or airway characteristics?

The American Sleep Disorders Association classified the different monitors that have been used in sleep studies into four categories, depending on which channels they record and evaluate.[34] Type I monitors are facility-based polysomnography (PSG). Type II monitors record the same information as Type I with fewer channels, and record signals that allow for the reliable identification of arousals from sleep (electroencephalography, electrooculography, electromyography, electrocardiography), and have at least two airflow channels or one airflow and one effort channel. Type III monitors contain at least two airflow channels or one airflow and one effort channel. Type IV monitors comprise all other devices that fail to fulfill criteria for Type III monitors. They include monitors that record more than two physiological measures as well as single channel monitors. We evaluate Type III monitors separately from Type IV monitors.

To address this Key Question, we evaluated three types of comparisons: portable monitoring devices (Types II, III, and IV) versus PSG, questionnaires versus PSG or portable monitors, and clinical prediction models versus PSG or portable monitors.

We searched for prospective cross-sectional or longitudinal studies of any followup duration with at least 10 study participants analyzed with each test of interest. We did not reevaluate studies included in the 2007 *Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome* conducted by the Tufts Evidence-based Practice Center.[26] We briefly summarize the findings of the previous report. We do not present studies included in the 2007 Technology Assessment in our summary tables, but we include them in graphs, when applicable.

Comparison of Portable Devices and Polysomnography

Type II Monitors

The 2007 Technology Assessment identified three quality B studies that compared two different Type II monitors in the home setting to either the same monitor in the laboratory setting (two studies) or full laboratory PSG (one study). Difference versus average (mean bias) analyses of the apnea-hypopnea index (AHI) ranged from 0 to -2 events/hr. However, based on the 95 percent limits of agreement between portable and laboratory AHI measurements, discrepancies between the monitors and PSG were as wide as -36 to 36 events/hr. In one study, the difference between the two measurements was dependent on their average value; the portable monitor overestimated laboratory-based measurements for AHI<20 events/hr, but underestimated it in more severe cases. One study assessed the ability of a Type II monitor to predict an AHI>15 events/hr with laboratory-based PSG. Sensitivity was 81 percent, specificity 97 percent, and positive likelihood ratio >10.

No Type II monitors were identified in the update.

Type III Monitors

Findings of the 2007 Technology Assessment

The 2007 Technology Assessment included 22 studies that compared 13 different Type III monitors with facility-based PSG in various settings. In all studies, difference versus average analyses suggested that measurements of AHI with facility-based PSG and respiratory disturbance index (RDI) with portable monitors can differ substantially. The mean difference of AHI-RDI ranged from -10 to 24 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -39 to 54 events/hr. Such large discrepancies can affect clinical interpretation in some patients. For example, a discrepancy of 30 events/hr is important when the measurements are 4 and 34 events/hr by PSG and the device, respectively, but it may be irrelevant if the measurements are 40 and 70 events/hr. In most studies, the difference versus average analyses plots showed that the discordance between facility-based PSG and portable monitors increases as the AHI or RDI values get higher. None of the studies accounted for this in their analyses of concordance, and this makes the interpretation of the above findings difficult.

Analysis of sensitivity and specificity found that Type III monitors may have the ability to predict an elevated AHI (as determined by PSG) with high positive likelihood ratios and low negative likelihood ratios for various AHI cutoffs in laboratory-based PSG.

Description of Studies Published After the Completion of the 2007 Technology Assessment (Appendix D Tables 1.1.1 & 1.1.2)

We identified seven studies[66-72] published after the completion of our previous Technology Assessment (Appendix D Table 1.1.1). Three studies were performed in the sleep laboratory setting,[68,70,71] with simultaneous recording of physiological parameters by both the device and the PSG machine, three studies were performed both in the sleep laboratory as well as at home[66,67,69] and one study was performed in the home setting.[72] When studies were performed at home, the measurements taken by the device and the PSG machine are on different nights. The seven different Type III monitors that were included were Apnoescreen II respiratory polygraph, Stardust II, Apnea Risk Evaluation System (ARES™) Unicorder, Morpheus Hx (bedside computerized analysis system), Embletta portable diagnostic system, CID102L8 Type II device and SOMNOcheck® (SC), resulting in a total of 20 unique Type III monitors when pooled with the studies in the 2007 Technology Assessment (Appendix D Table 1.1.2). Twelve of the 20 monitors are assessed in only a single study, 7 are evaluated in 2 studies each, and one monitor is assessed in 3 studies. Therefore there is inadequate evidence to perform indirect comparisons of diagnostic efficacy between the monitors.

The number of analyzed participants in these studies ranged from 45 to 149. Three studies were graded quality A and four were graded quality B due to potential bias, the reasons for which varied across studies—incomplete reporting of population, unclear reporting of concordance results and unclear analytical strategy.

Participants were referral cases for the evaluation of suspected sleep apnea and were recruited from sleep centers or respiratory clinics. The population of subjects in the sleep laboratory setting was not different from the population of subjects assessed outside the sleep laboratory. In all studies, the majority of the participants were males. The mean ages of patients ranged from 45 to 63 years. Patients had mean Epworth Sleepiness Scale (ESS) scores (a standard measure of sleepiness symptoms) ranging from 8 to 12. At PSG, patients' mean AHI

ranged from 15 to 39.9 events/hr. The data loss, or the proportion of participants who did not complete the study, ranged from 2 to 23 percent.

Concordance (Appendix D Table 1.1.2)

Six of the seven new studies provided enough information to perform analyses of the concordance between AHI readings from Type III monitors and PSG.[66,67,69-72]} In the seventh study, the difference versus average analyses plots were not interpretable from the figure provided.[68] The Apnoescreen II, Stardust II, ARES, Morpheus Hx (bedside computerized analysis system), Embletta portable diagnostic system, CID102L8 Type II device and SOMNOcheck monitors were used in these studies.

The mean bias is the average difference between the AHI (or RDI or ODI) estimated with the portable device and the AHI measured by PSG. The mean difference of AHI-RDI ranged from -4 to 3 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -31 to 36 events/hr. Among studies that were conducted using the same monitor in both the laboratory (simultaneous recording of signals by device and PSG) and home setting (nonsimultaneous recording of signals by device and PSG), there was no major difference in the range of mean bias reported in both settings.

When we considered all studies, including the 22 studies from the 2007 Technology Assessment, the results pointed to the same direction. The mean difference of AHI-RDI ranged from -10 to 24 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -39 to 54 events/hr.

Sensitivity and Specificity (Tables 2a and 2b; Appendix D Table 1.1.3; Figure 3)

All seven studies assessed the sensitivity and specificity of portable monitor recordings to identify AHI suggestive of obstructive sleep apnea (OSA).[66-72] Two studies used a cutoff of AHI of 5 events/hr[68,69] and one study used a cutoff of AHI of 15 events/hr[70] in facility-based PSG to diagnose OSA. The other four studies did not report an AHI cutoff.[66,67,71,72] They reported the sensitivity and specificity for a cutoff range of 5 to 30 events/hr.

Garcia-Diaz 2007 reported sensitivity and specificity pairs for three cutoffs of RDI derived from the Type III monitor (10, 15, and 30 events/hr), recorded independently by two observers. The sensitivity for these three cutoffs ranged from 94.6 to 100 percent, and the specificity ranged from 88 to 100 percent. To 2009 used three different cutoffs for oxygen desaturation with the ARES Unicorder (drops of 4, 3, and 1 percent). A single cutoff for diagnosing sleep apnea (≥5 events/hr) was used for all desaturation levels. The best sensitivity was found with 1 percent oxygen desaturation (sensitivity 97 percent, specificity 63 percent).

Among studies that were conducted using the same monitor in both the laboratory (simultaneous recording of signals by device and PSG) and home setting (nonsimultaneous recording of signals by device and PSG), there was no major difference in the range of sensitivity and specificity reported in both settings. Across all 29 studies, including the 22 studies from the 2007 Technology Assessment, the range of sensitivity of Type III devices for predicting OSA with an AHI cutoff of 5 was 83 to 97 percent, and the range of specificity was 48 to 100 percent (Appendix D Table 1.1.3). When the AHI cutoff was increased to 15, the range of sensitivity was 64 to 100 percent and the range of specificity was 41 to 100 percent. Raising the AHI cutoff to 30, the range of sensitivity was 75 to 96 percent and the range of specificity was 79 to 97 percent.

Across all 29 studies, including the 22 studies from the 2007 Technology Assessment, the positive and negative likelihood ratios were calculated and plotted on graphs for each AHI cutoff of 5, 10, 15, 20, 30, and 40 events/hr. These graphs are presented as a matrix of plots in Figure 3, illustrating the diagnostic ability of Type III portable monitors to predict an elevated AHI, at various AHI cutoffs as determined by PSG. Each cutoff of AHI is depicted in a separate plot in receiver operating characteristics (ROC) space. Each circle represents one study, and sensitivity/specificity pairs from the same study (from different cutoffs or a different device setting) are connected with lines. Studies to the left of the near-vertical thin diagonal line have a positive likelihood ratio ≥10, and studies above the near-horizontal thin diagonal line have a negative likelihood ratio ≤0.1. A high positive likelihood ratio and a low negative likelihood ratio indicate that testing with a portable monitor can accurately predict an elevated AHI (as determined by PSG).

With an AHI cutoff of 5 events/hr, most of the studies have a positive likelihood ratio ≥10 and a negative likelihood ratio close to 0.1. At the AHI cutoff of 10 events/hr, most of the studies have a positive likelihood ratio of ≥10, with some studies having a positive likelihood ratio ≥10 and a negative likelihood ratio ≤0.1. This is also seen with a cutoff of 15 events/hr. There are fewer studies evaluating the cutoff of 20 and 30 events/hr, but the results indicate a trend towards better prediction of OSA. (Figure 3)

The ROC space plots indicate that Type III monitors generally accurately diagnose OSA (determined by full PSG), and also predict different severities of OSA (defined by having AHI above different thresholds) with high positive likelihood ratios and low negative likelihood ratios for various AHI cutoffs in PSG.

Table 2a. Range of sensitivity and specificity of Type III monitors (n=7)

AHI cutoff by PSG (events/hr)	Sensitivity (%)	Specificity (%)
5	83 – 97	48 – 100
15	64 – 100	41 – 100
30	75 – 96	79 – 97

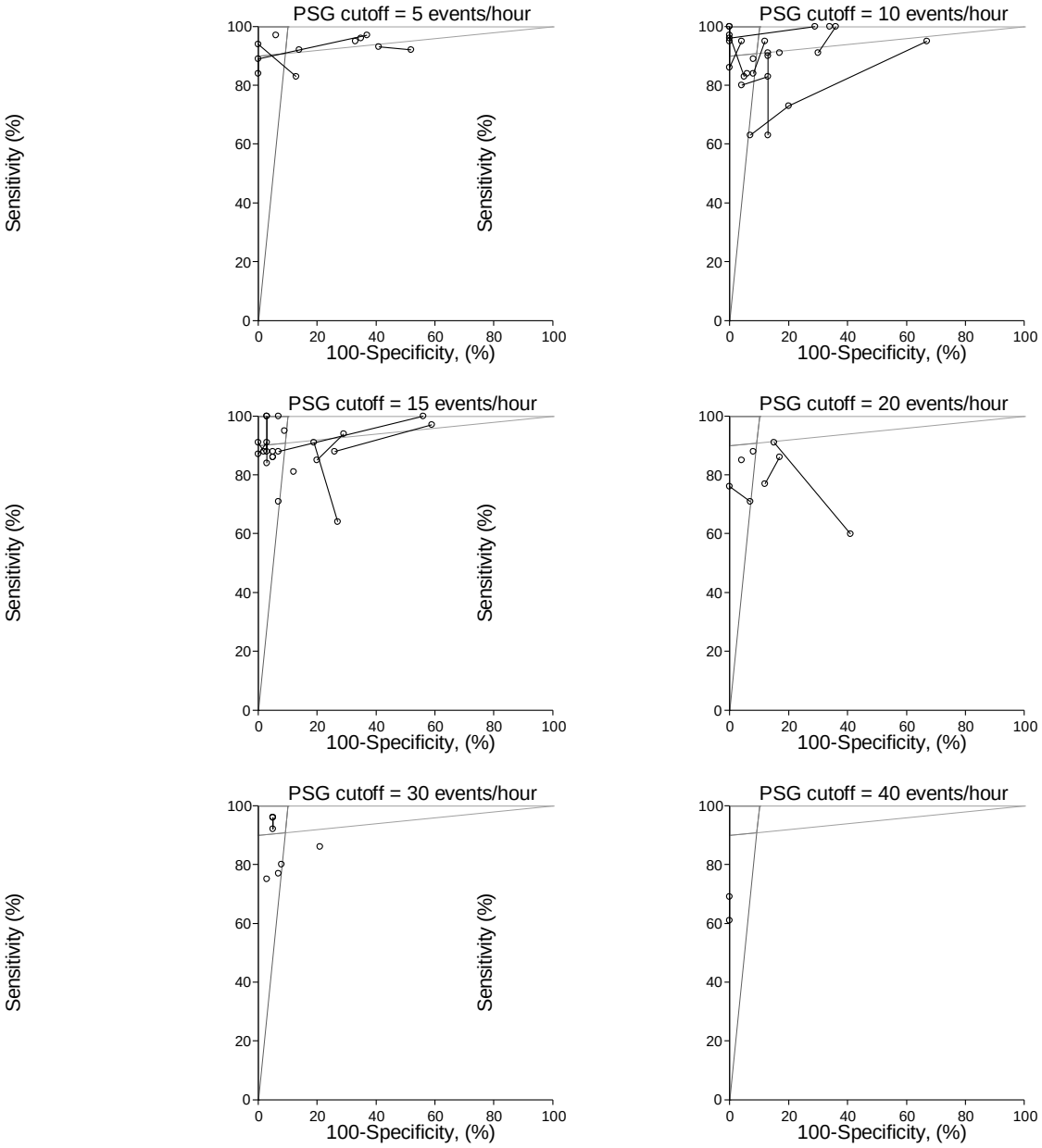
AHI = apnea-hypopnea index, nd = no data, PSG = polysomnography.

Table 2b. Range of sensitivity and specificity of Type IV monitors with ≥3, 2, and 1 channels (n=24)

AHI cutoff by PSG (events/hr)	≥3 channels (n=6) Sensitivity (%)	≥3 channels (n=6) Specificity (%)	2 channels (n=6) Sensitivity (%)	2 channels (n=6) Specificity (%)	1 channel (n=12) Sensitivity (%)	1 channel (n=12) Specificity (%)
5	85 – 100	67 – 100	92 – 98	50 – 100	85 – 96	50 – 100
15	75 – 92	50 – 100	67 – 91	78 – 96.4	43 – 100	42 – 100
30	88	100	Nd	nd	18 – 100	50 – 100

AHI = apnea-hypopnea index, nd = no data, PSG = polysomnography.

Figure 3. Diagnostic ability of Type III monitors to identify AHI cutoffs suggestive of diagnosis of OSA, and its severity, as per laboratory-based polysomnography



Sensitivity and specificity of Type III monitors in receiver operating characteristics space. Each circle represents one pair of sensitivity/specificity measurements for a given Type III monitor. Circles connected by lines represent the same monitors being tested at different thresholds within a study. The thin diagonal lines represent the thresholds for a positive likelihood ratio >10 (to the left of the near-vertical line) and negative likelihood ratio ≤0.1 (above the near-horizontal line). A high positive likelihood ratio and a low negative likelihood ratio indicate that the portable monitor has very good ability to predict the results of PSG. AHI = apnea-hypopnea index, PSG = polysomnography.

Type IV Monitors

Findings of the 2007 Technology Assessment

The 2007 Technology Assessment included 46 studies that compared 11 different Type IV monitors with facility-based PSG in various settings. In all studies, difference versus average analyses suggested that measurements of AHI with facility-based PSG and of RDI with portable monitors can differ greatly. The mean difference of AHI-RDI ranged from -17 to 12 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -49 to 61 events/hr.

Analysis of sensitivity and specificity found that studies of Type IV monitors that record at least three bioparameters showed high positive likelihood ratios and low negative likelihood ratios. Studies of Type IV monitors that record one or two bioparameters also had high positive likelihood ratios and low negative likelihood ratios for selected sensitivity and specificity pairs from ROC curve analyses.

Description of Studies Published After the Completion of the 2007 Technology Assessment (Appendix D Tables 1.1.2; 1.2.1-1.2.3)

We identified 24 new studies[73-96] that compared Type IV monitors with facility-based PSG in various settings. Their description and findings, stratified based on their number of channels, i.e., the number of different physiological parameters that were being measured, are presented in Appendix D Table 1.2.1 (≥3 channels), Appendix D Table 1.2.2 (2 channels), and Appendix D Table 1.2.3 (1 channel). Fifteen studies were performed only in the sleep laboratory setting,[74,75,77-81,83-86,89,91,93,96] six were performed in both the sleep laboratory as well as the home setting,[73,87,88,92,94,95] two were performed in the home setting,[76,82] and one in a community setting.[90] The different Type IV monitors included were, ApneaLink™, ARES Unicorder, Apnomonitor, FlowWizard®, Holter Monitor, Oximetry devices, Embletta™ PDS (portable diagnostic system), ClearPath System Nx 301, Lifeshirt®, MESAM 4, RUSleeping™ RTS, SOMNIE, and WatchPAT™, resulting in a total of 23 unique monitors when pooled with the studies in the 2007 Technology Assessment (Appendix D Table 1.1.2). In one study, we reclassified a device from a Type III to a Type IV because of the particular channels used in the ARES Unicorder.[73] Six devices had more than three channels,[73,79,87,88,93,96] six had two channels,[74,80,81,85,89,95] and 12 had only a single channel.[75-78,82-84,86,90-92,94] Oximetry (either alone or in combination with snoring sound recording), ECG, or actigraphy was assessed in 22 studies. Among the remaining monitors, 14 of the 23 monitors were assessed in a single study, four (ARES, Holter ECG, Oxiflow, Sleep Strip) were assessed in two or three studies, and four (ApneaLink, Autoset, MESAM IV, WatchPAT 100) were assessed in five to eight studies. Given the heterogeneity of studies and monitors, we determined it was not appropriate to perform indirect comparisons of diagnostic efficacy between specific monitors.

The number of analyzed participants in these studies ranged from 14 to 366. Seven studies were graded quality A. Eleven studies were graded quality B due to potential bias, the reasons for which varied across studies – multiple sites with difference between sites, incomplete reporting of population, unclear reporting of results, and incomplete reporting of test blinding protocols. Six studies were graded quality C due to significant bias, with varying reasons across different studies – nonblinding of portable device tests results from PSG results, unclear reporting of results and population characteristics, and more than 50 percent dropout rate.

Participants in 19 studies were referral cases for the evaluation of suspected sleep apnea and were recruited from sleep centers or hospitals.[73,75-77,79-87,89,92-96] One study enrolled commercial

motor vehicle drivers,[90] two studies recruited patients with heart failure,[74,88] one study recruited diabetic patients,[78] and one study was conducted in patients referred for uvulopalatopharyngoplasty.[91] In all studies, the proportion of male participants ranged from 32 to 100 percent. The mean ages of patients ranged from 37 to 61 years. Patients had mean ESS scores (a standard measure of sleepiness symptoms) ranging from 5.8 to 13.3. At PSG, patients' mean AHI ranged from 14 to 44 events/hr. The data loss, or the proportion of participants who did not complete the study ranged, from 0 to 78 percent. In one study among commercial truck drivers, the high rate of data loss was explained by reasons unrelated to the device performance, including termination of employment and previous history of PSG diagnosis.[90] Excluding this study, the range of data loss was 0 to 18 percent.

Concordance (Appendix D Tables 1.3.1-1.3.3)

Fifteen of the 24 studies provided enough information to perform analyses of the concordance between AHI readings from Type IV monitors and PSG.[73,75,77-79,81,82,85,86,88,89,92,94-96] In the other nine studies, Bland-Altman analyses were either not conducted or the Bland-Altman plots were not interpretable.

The mean difference of AHI-RDI ranged from -10 to 12 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -32 to 49 events/hr. Among studies that were conducted using the same monitor in both the laboratory (simultaneous recording of signals by device and PSG) and home setting (nonsimultaneous recording of signals by device and PSG), there was no major difference in the range of mean bias reported in both settings.

When we considered all studies, including the 46 studies from the 2007 Technology Assessment, the mean difference of AHI-RDI ranged from -17 to 12 events/hr. Based on the 95 percent limits of agreement between AHI and RDI measurements, discrepancies between the monitors and PSG varied from -49 to 61 events/hr., affecting clinical interpretation. As seen in the 2007 Technology Assessment, the difference versus average analyses plots showed that the discordance between facility-based PSG and portable monitors increases as the AHI or RDI values get higher. None of the studies accounted for this in their analyses of concordance, and this makes the interpretation of the above findings difficult.

Sensitivity and Specificity (Tables 2a and 2b; Appendix D Tables 1.1.3; 1.3.1-1.3.3, 1.1.3; Figure 4)

All of the studies reported the sensitivity and specificity of portable monitor recordings to identify AHI suggestive of OSA. They reported the sensitivity and specificity for a range of cutoffs from 5 to 30 events/hr.

Among the devices with three or more channels,[73,79,84,87,88,93,96] the range of sensitivity of these devices for predicting OSA with an AHI cutoff of 5 events/hr was 85 to 100 percent, and the range of specificity was 67 to 100 percent (Appendix D Table 1.3.1). When the AHI cutoff was increased to 15 events/hr, the range of sensitivity was 75 to 96 percent and the range of specificity was 50 to 100 percent. Raising the AHI cutoff to 30, one study reported a sensitivity of 88 percent and specificity of 100 percent.[79]

When evaluating devices with only two channels[74-76,81,85,89,91,95] the range of reported sensitivity of these devices for predicting OSA with an AHI cutoff of 5 events/hr was 91.8 to 97.7 percent, and the range of reported specificity was 50 to 100 percent. When the AHI cutoff was increased to 15 events/hr, the range of sensitivity was 67 to 90.6 percent and the range of specificity was 78 to 96.4 percent. (Appendix D Table 1.3.2)

In studies that assessed devices with only one channel the range of reported sensitivity of these devices for predicting OSA with an AHI cutoff of 5 events/hr was 85.4 to 96 percent and the range of reported specificity was 50 to 100 percent.[77,78,80,82,83,86,90-92,94] When the AHI cutoff was increased to 15 events/hr, the range of sensitivity was 42.5 to 100 percent and the range of specificity was 42 to 100 percent. Raising the AHI cutoff to 30 events/hr, the range of sensitivity was 18 to 100 percent and range of specificity was 50 to 100 percent (Appendix D Table 1.3.3).

Table 2 summarizes the range of sensitivity and specificity of Type IV devices with different channels.

Among studies that were conducted using the same monitor in both the laboratory (simultaneous recording of signals by device and PSG) and home setting (nonsimultaneous recording of signals by device and PSG), there was no major difference in the range of sensitivity and specificity reported in both settings.

Across all studies, including the 46 studies from the 2007 Technology Assessment, the range of sensitivity of Type IV devices for predicting OSA with an AHI cutoff of 5 was 85 to 100 percent, and the range of specificity was 50 to 100 percent. When the AHI cutoff was increased to 15, the range of sensitivity was 7 to 100 percent and the range of specificity was 15 to 100 percent.

There were 22 of 24 studies that had information that could be extracted for analysis.[73-85,87-92,94-96] Across all studies, including the 46 studies from the 2007 Technology Assessment, the positive and negative likelihood ratios were calculated and plotted on graphs for each AHI cutoff of 5, 10, 15, 20, 30 and 40 events/hr. These graphs are presented as a matrix in Figure 4, illustrating the diagnostic ability of Type IV portable monitors to predict an elevated AHI at different thresholds (as determined by PSG). With an AHI cutoff of 5 events/hr, most of the studies have a negative likelihood ratio close to 0.1. At the AHI cutoff of 10 events/hr, the studies are equally distributed in regions that indicate either a positive likelihood ratio $\geq$10 or a negative likelihood ratio $\leq$0.1. With a cutoff of 15 events/hr, the studies are spread out in regions that indicate a positive likelihood ratio $\geq$10 or a negative likelihood ratio $\leq$0.1, as well as the intersection of these regions. The studies that fall into the intersection region have the best ability to predict an elevated AHI. Similar trends are seen when cutoffs of 20 and 30 events/hr are used (Figure 4).

The ROC space plots indicate that Type IV monitors generally accurately predict an elevated AHI (as determined by PSG), though the positive likelihood ratios are lower, and negative likelihood ratios are higher, than is seen with Type III monitors.

Summary

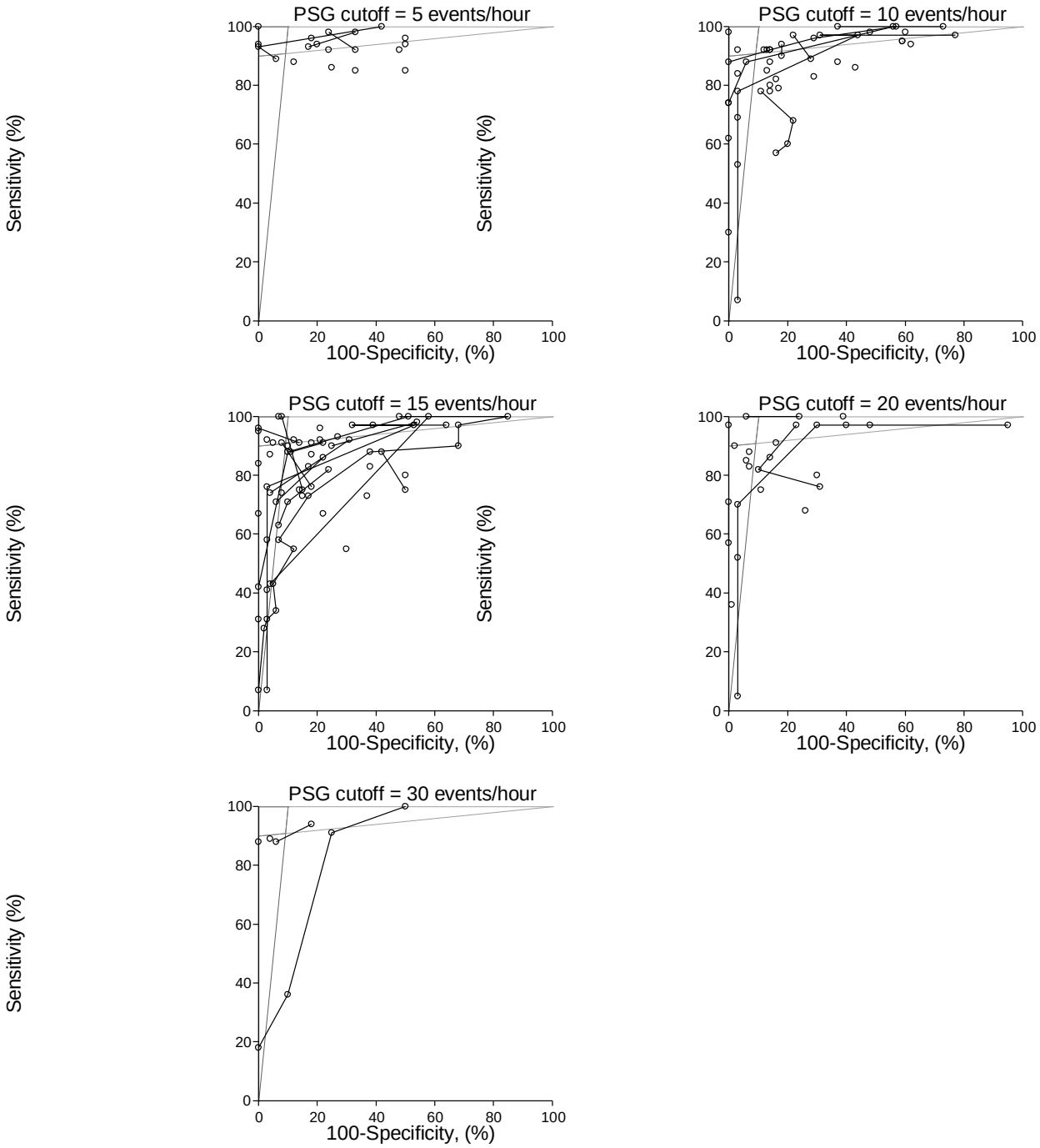
Analysis of difference versus average analyses plots suggest that substantial differences in the measured AHI may be encountered between both Type III and Type IV monitors, and PSG. Large differences compared with PSG cannot be excluded for all monitors. These studies on Type III and Type IV monitors are applicable to the general population referred to specialized sleep centers or hospitals for evaluation of suspected sleep apnea. Most of the studies are conducted either in the sleep laboratory setting or at home. Fifteen studies were graded quality A (six evaluating Type III monitors, nine assessing Type IV monitors), 45 studies were graded quality B (13 evaluating Type III monitors, 32 assessing Type IV monitors), and 39 studies were graded quality C (10 evaluating Type III monitors, 29 assessing Type IV monitors). No specific Type III monitor was evaluated by more than three studies. Among Type IV monitors, oximetry

was evaluated by different monitors in 22 studies; no other monitor was evaluated by more than eight studies. No study directly compared different portable monitors to each other.

The strength of evidence is moderate that Type III and Type IV monitors may have the ability to accurately predict an elevated AHI (as determined by PSG) with high positive likelihood ratios and low negative likelihood ratios for various AHI cutoffs in PSG. Type III monitors perform better than Type IV monitors at AHI cutoffs of 5, 10 and 15 events/hr. The evidence is insufficient to adequately compare specific monitors to each other.

Based on a prior systematic review, the strength of evidence is low that Type II monitors are accurate to diagnose OSA (as defined by PSG), but have a wide and variable bias in estimating the actual AHI. The prior review concluded that ~~–b~~based on [three studies], type II monitors [used at home] may identify AHI suggestive of OSA with high positive likelihood ratios and low negative likelihood ratios," though ~~–s~~ubstantial differences in the [measurement of] AHI may be encountered between type II monitors and facility-based PSG."

Figure 4. Diagnostic ability of Type IV monitors to identify AHI cutoffs suggestive of diagnosis of OSA, and its severity, as per laboratory-based polysomnography



Sensitivity and specificity of Type IV monitors in receiver operating characteristics space. Each circle represents one pair of sensitivity/specificity measurements for a given Type IV monitor. Circles connected by lines represent the same monitors being tested at different thresholds within a study. The thin diagonal lines represent the thresholds for a positive likelihood ratio >10 (to the left of the near-vertical line) and negative likelihood ratio ≤0.1 (above the near-horizontal line). A high positive likelihood ratio and a low negative likelihood ratio indicate that the portable monitor has very good ability to predict the results of PSG. AHI = apnea-hypopnea index, PSG = polysomnography.

Comparison of Questionnaires and Polysomnography

We identified six studies that compared sleep questionnaires with facility-based PSG in various settings (Appendix D Table 1.4.1). Three papers described studies performed in sleep laboratory settings,[36,97,98] one in a home setting,[99] and two in a hospital, but not in a sleep clinic or sleep laboratory.[100,101]

Two of the five studies were conducted in the same group of patients visiting a preoperative clinic;[36,97] one study was carried out among adult sleep disorder clinic patients;[98] one study was done in patients visiting their primary care physician;[99] one other study was conducted among patients attending a medical outpatient department in a tertiary care medical center;[100] and, one study was conducted among patients attending a hypertension clinic of a hospital.[101] The number of analyzed participants in these studies ranged from 53 to 211. The validated questionnaires that were administered in these studies included Berlin, STOP (Snoring, Tiredness during daytime, Observed apnea, and high blood Pressure), the STOP-Bang (STOP with body mass index [BMI], age, neck circumference, and sex variables), the American Society of Anesthesiologists (ASA) screening checklist for OSA in surgical patients, Hawaii Sleep Questionnaire, and the Epworth Sleepiness Scale. In all the studies, the cutoff of AHI in facility-based PSG that were considered suggestive of OSA was 5 events/hr.

One study was graded quality A as it had no issues in reporting of the study.[101] However, the study was not primarily designed to evaluate the two instruments (Berlin questionnaire and the Epworth Sleepiness Scale), and it assessed the association of various clinical factors with the risk for OSA. It was included because the sensitivity and specificity for the index tests were reported. One study was graded quality B due to inadequate reporting of the results of the PSG, and four were graded quality C either due to selection bias or a dropout rate higher than 40 percent. These studies are applicable to patients visiting preoperative clinics, sleep laboratories, and primary care centers for evaluation of sleep apnea.

Berlin Questionnaire (Appendix D Table 1.4.2)

Four studies assessed the sensitivity and specificity of the Berlin questionnaire in identifying AHI suggestive of OSA.[97,99-101] The Berlin questionnaire predicts the risk of OSA as high or low based on a score in three categories of questions related to snoring, tiredness, and blood pressure.

The number of subjects enrolled in the three studies ranged from 53 to 2,127, but the number of subjects analyzed ranged from 53 to 211. The subjects were either patients from preoperative clinics,[97] or from the population visiting their primary care physician,[99] or a department in a hospital.[100,101] The percentage of male subjects ranged from 42 to 80 percent, with the average age ranging from 46 to 55 years and average BMI ranging from 28 to 30 kg/m2. The mean baseline AHI ranged from 5 events/hr to 21 events/hr.

Chung 2008 reported sensitivity and specificity pairs for three cutoffs of the AHI index (5, 15, and 30 events/hr). With an AHI cutoff of 5 events/hr, sensitivity was 69 percent and specificity 56 percent. At the AHI cutoff of 15 events/hr, the sensitivity was higher (79 percent) the specificity was lower (51 percent). At an AHI cutoff of 30 events/hr, regarded as diagnostic of severe sleep apnea, the sensitivity was higher still (87 percent) and specificity lower (46 percent). The area under the receiver operating characteristics curve (AUC) for ability of the Berlin questionnaire to predict an AHI above 5, 15, and 30 events/hr ranged from 0.67 to 0.69. In Netzer 1999, with an AHI cutoff of 5 events/hr, the sensitivity of OSA prediction per the Berlin questionnaire was 86 percent and specificity was 77 percent. Changing the AHI cutoff to 15 events/hr decreased the sensitivity (54 percent) and increased the specificity (97 percent). At

AHI cutoffs of 30 events/hr, the sensitivity further decreased (17 percent) and specificity remained the same (97 percent). In Sharma 2006, a cutoff of 5 events/hr resulted in a sensitivity of 86 percent and specificity of 95 percent. In Drager 2010, with an AHI cutoff of 5 events/hr, the sensitivity of OSA prediction per the Berlin Questionnaire was 93 percent and specificity was 59 percent. Figure 5 plots the sensitivity and specificity in the receiver operating characteristics space, illustrating the diagnostic ability of the Questionnaire to identify AHI cutoffs suggestive of diagnosis of OSA.

In summary, using an AHI cutoff of 5 events/hr, sensitivity ranged was from 69 to 93 percent and specificity from 56 to 95 percent. Using an AHI cutoff of 15, the range of sensitivity was 54 percent to 79 percent, and specificity was 51 percent to 97 percent. For the definition of severe sleep apnea using a cutoff of 30, the range of reported sensitivity was 17 percent to 87 percent and specificity was 46 percent to 77 percent. The two studies were inconsistent as to whether the Berlin Questionnaire had a high positive likelihood ratio of ~~d~~diagnosing" OSA or a low negative likelihood ratio of rejecting the diagnosis of sleep apnea.

STOP Questionnaire (Appendix D Table 1.4.2)

Chung 2008 (Pubmed identifier 18431116) a quality C study, reported the sensitivity and specificity of the STOP Questionnaire to identify AHI suggestive of OSA.[36] The STOP questionnaire predicts the risk of OSA as high or low based on answers to questions related to snoring, tiredness, witnessed apneas, and blood pressure. With an AHI cutoff of 5 events/hr, the sensitivity was 66 percent and specificity was 60 percent. Changing the AHI cutoff to 15 events/hr increased the sensitivity (74 percent) and decreased the specificity (53 percent). At AHI cutoffs of 30 events/hr, sensitivity increased (80 percent) and specificity decreased (49 percent). The AUC for the ability of the STOP questionnaire to predict an AHI above 5, 15, and 30 events/hr ranged from 0.703 to 0.769.

STOP-Bang Questionnaire (Appendix D Table 1.4.2)

Chung 2008 (Pubmed identifier 18431116) a quality C study, assessed the sensitivity and specificity of the STOP-Bang questionnaire to identify AHI suggestive of OSA.[36] The STOP-Bang questionnaire predicts the risk of OSA as high or low based on answers to questions related to snoring, tiredness, witnessed apneas, and blood pressure (as in the STOP questionnaire) in combination with anthropometric data, namely BMI (whether >35 kg/m^2), age (>50 years), neck circumference (>40 centimeters), and sex. With an AHI cutoff of 5 events/hr, sensitivity was 84 percent and specificity was 56 percent. Changing the AHI cutoff to 15 events/hr sensitivity increased to 93 percent and specificity decreased to 43 percent. At AHI cutoffs of 30 events/hr, sensitivity further increased to 100 percent and specificity decreased to 37 percent. The AUC for ability of the STOP-Bang questionnaire to predict an AHI above 5, 15 and 30 events/hr ranged from 0.782 to 0.822.

American Society of Anesthesiologists Checklist (Appendix D Table 1.4.2)

Chung 2008 (Pubmed identifier 18431117) a quality C study assessed the sensitivity and specificity of the ASA screening checklist to identify AHI suggestive of OSA in surgical patients.[97] The ASA checklist predicts the risk of OSA as high or low based on results from three categories: predisposing physical characteristics (including BMI, neck circumference, craniofacial abnormalities, nasal obstruction, and tonsillar position), history of apparent airway obstruction during sleep, and reported or observed somnolence. With an AHI cutoff of 5

events/hr the sensitivity was 69 percent and specificity was 56 percent. An AHI cutoff of 15 increased the sensitivity to 79 percent and decreased specificity to 51 percent. Using an AHI cutoff of 30 events/hr increased sensitivity to 87 percent and decreased to specificity 46 percent. The AUC for the ability of the ASA Checklist to predict an AHI above 5, 15, and 30 events/hr ranged from 0.617 to 0.783.

Hawaii Sleep Questionnaire (Appendix D Table 1.4.2)

Kapuniai 1988 (quality B) assessed the sensitivity and specificity of the apnea score derived from the Hawaii Sleep Questionnaire to identify an AHI suggestive of OSA.[98] The questionnaire included queries about characteristics in sleep apnea patients including, stopping breathing during sleep, loud snoring, and waking from sleep gasping for or short of breath. Additional questions on sex, age, height, weight, sleep history, and history of tonsillectomy or adenoidectomy were also collected. The final model included self-reports of loud snoring, breathing cessation during sleep, and adenoidectomy in a regression model to calculate an Apnea Score. An apnea score ≥3 as per the model was considered high risk for sleep apnea. Additionally, an apnea score ≥2 without details about adenoidectomy was used as a cutoff to indicate a high risk of sleep apnea. With an AHI cutoff of 5 events/hr, the sensitivity of OSA prediction per an apnea score of ≥3 was 59 percent and the specificity 69 percent. When the apnea score cutoff of ≥2 was used, sensitivity was 70 percent and specificity was 65 percent. Using an AHI cutoff of 10, the sensitivity was 78 percent and specificity was 67 percent.

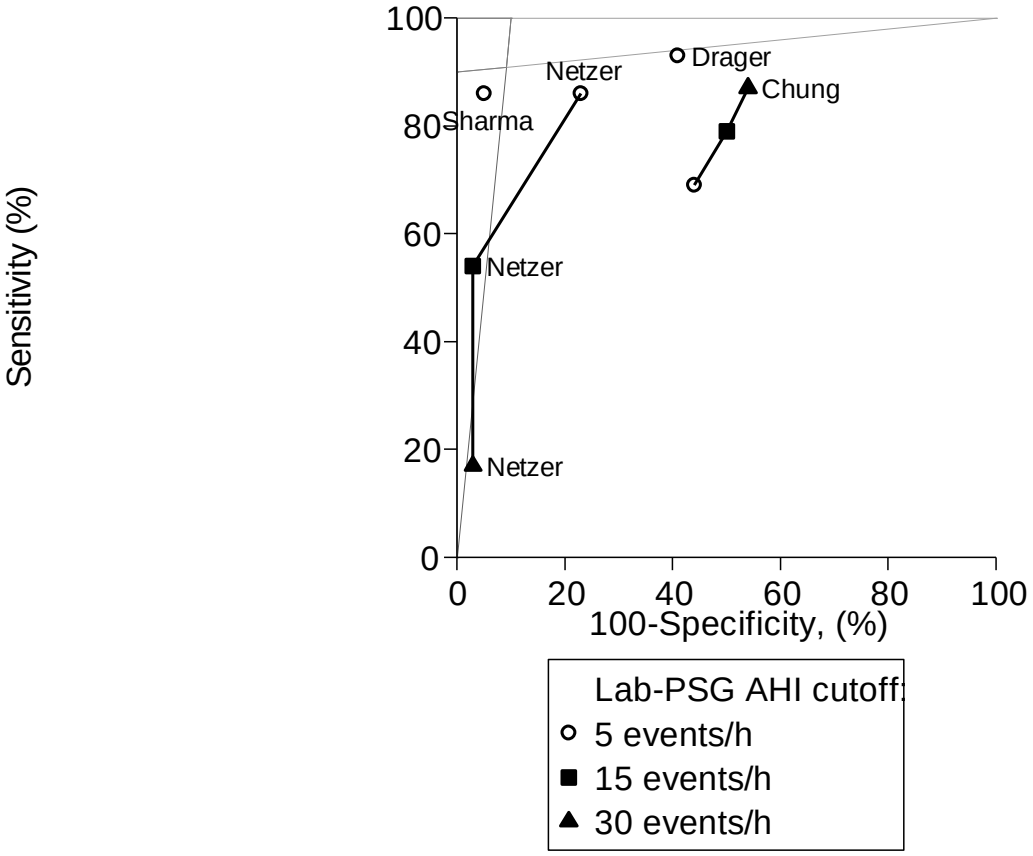
Epworth Sleepiness Scale (Appendix D Table 1.4.2)

Drager 2010 (quality A) assessed the sensitivity and specificity of ESS to identify an AHI suggestive of OSA.[101] With an AHI cutoff of 5 events/hr, the sensitivity of OSA prediction per an ESS score >10 (defined as excessive daytime sleepiness) was 49 percent and the specificity 80 percent.

Summary

Overall, largely because of the likely selection biases in the quality C studies, the strength of evidence is low supporting the use of the Berlin questionnaire in screening for sleep apnea. Only one study each investigated the use of the STOP, STOP-Bang, ASA Checklist, Hawaii Sleep questionnaire, and ESS each. The strength of evidence is insufficient to draw definitive conclusions concerning these questionnaires.

Figure 5. Diagnostic ability of the Berlin questionnaire to identify AHI cutoffs suggestive of diagnosis of OSA and its severity as per laboratory-based polysomnography



AHI = apnea-hypopnea index, PSG = polysomnography.

Clinical Prediction Rules and Polysomnography

Overall Description of Studies Using Clinical Prediction Rules (Table 3; Appendix D Table 1.5.1)

We identified seven studies that compared clinical prediction rules with facility-based PSG in various settings (Appendix D Table 1.5.1).[102-108] All studies had either validated their models in a separate subgroup of study participants or had their models evaluated in subsequent studies. Thus, all examined clinical prediction rules are considered internally or externally validated. Six papers described studies performed in sleep laboratory settings[102-104,106-108] and one[105] in a hospital or nursing home setting.

The populations enrolled in these studies included patients referred for sleep-disordered breathing and suspected sleep apnea. The number of analyzed participants in these studies ranged from 101 to 425. The mean age of patients ranged from 47 to 79 years; the study by Onen 2008 limited enrollment to elderly individuals (≥70 years). With regard to overall methodologic quality, three studies were graded as quality A,[103,106,107] three quality B,[102,105,108] and one quality

C.[104] The main methodological concerns in the quality C study were the high risk for selection bias and the high dropout rate (29 percent).

The definition of sleep apnea was based on AHI in five studies (≥5 events/hr in one study, ≥10 in one study, and ≥15 in three studies) and on RDI in two studies (≥5 events/hr). The 10 predictive models utilized questionnaire items and clinical variables in two studies,[102,103] morphometric parameters in one study,[104] standardized nurse observations during the sleep study in one study,[105] clinical variables and observations during the sleep study in two studies[106,107] and pulmonary functional data in one study[108] (Table 3).

Detailed Description of Clinical Prediction Rules (Appendix D Table 1.5.2)

Gurubhagavatula 2001 developed two clinical prediction rules based on a combination of a multivariable apnea prediction questionnaire score and oximetry results in 359 patients. The clinical prediction rules were developed for two separate objectives: first, to predict the diagnosis of OSA, defined as RDI ≥5 events/hr and, second, to predict the diagnosis of severe OSA, defined as RDI ≥30 events/hr, and thus select appropriate patients for split night studies. The multivariable apnea prediction questionnaire score rates apnea risk between zero and one, with zero representing low risk and one representing high risk. The authors separated the subjects into three groups based on predefined threshold scores. Those who had high scores were predicted to have OSA, those with low scores were predicted to be free of OSA, and those with intermediate scores underwent nocturnal pulse oximetry. Among these subjects, those with oxygen desaturation index (ODI) above predefined thresholds were predicted to have OSA. The optimal model parameters for each of the two clinical prediction rules were obtained by the bootstrapping technique.

The optimal model for prediction of OSA (RDI ≥5 events/hr) was determined to use the following parameters: lower score threshold = 0.14, upper score threshold = 0.58, and ODI threshold = 5.02 events/hr. This model displayed a sensitivity of 94.1 percent and a specificity of 66.7 percent.

The optimal model for the prediction of severe OSA (RDI ≥30 events/hr) was defined using the following parameters: lower score threshold = 0.38, upper score threshold = 0.9, and ODI threshold = 21 events/hr. This model displayed a sensitivity of 83.3 percent and a specificity of 94.7 percent.

Kushida 1997 developed a prediction rule based only on morphometric parameters. These parameters included the palatal height, the maxillary intermolar distance between the mesial surfaces of the crowns of the maxillary second molars, the mandibular intermolar distance between the mesial surfaces of the crowns of the mandibular second molars, the horizontal overlap of the crowns of the maxillary and mandibular right central incisors, BMI, and neck circumference measured at the level of the cricothyroid membrane. By using a morphometric-calculated value of 70 as a threshold (range of calculated values 40-160), the model predicted the diagnosis of OSA (AHI ≥5 events/hr) with a sensitivity of 97.6 percent (95 percent CI 95.0, 98.9), a specificity of 100 percent (95 percent CI 92.0, 100), and an AUC of 0.996. The authors proposed the use of their model as a screening tool rather than a substitute for PSG.

Onen 2008 developed the Observation-based Nocturnal Sleep Inventory, a set of nurse observations performed in the patient's hospital room and made in five standardized hourly bedside visits over the course of one night. As designed, at each visit, approximately 5 minutes of listening and observation is required to detect three nocturnal conditions that characterize sleep-disordered breathing: interrupted breathing (apnea), gasping, or choking; snoring; and

awakening. The authors examined three different combinations of thresholds of snoring episodes and apnea to predict diagnosis of OSA, defined as AHI ≥15 events/hr. The test accuracy of these sets of observations were: ≥2 snoring episodes or ≥1 apnea episode produced a sensitivity of 89.7 percent and a specificity of 81.4 percent; ≥3 snoring episodes or ≥1 apnea episode produced a sensitivity of 74 percent and a specificity of 93 percent; and ≥5 snoring episodes or ≥1 apnea episode produced a sensitivity of 56 percent and a specificity of 100 percent.

Rodsutti 2004 developed a clinical prediction rule based on three clinical variables (age, sex, and BMI) and two items from a self report questionnaire (reported snoring, and reported cessation of breathing during sleep). Each of these variables was stratified into two or more categories and scores were assigned to each category. The sum of the individual scores for the five variables was then calculated to obtain a summary score that could range from 0 to 7.3. The calculated sensitivities and specificities for the three categories of the summary score were: <2.5—sensitivity 0 percent, specificity 89 percent; 2.5-4.2—sensitivity 44 percent, specificity 85 percent; ≥4.2—sensitivity 76 percent, specificity 60 percent.

Crocker 1990 developed a statistical model to predict the probability of a patient having an AHI >15 events/hr, based on logistic regression of data from a 24-item questionnaire and clinical characteristics on 105 patients. The regression equation that was developed included witnessed apneas, hypertension, BMI, and age. The model displayed relatively high sensitivity (92 percent), but low specificity (51 percent). The same model was examined by Rowley 2000 in an independent set of patients.

Rowley 2000 tested the performance of Crocker's model to predict either the presence of OSA (defined as AHI ≥10 events/hr) or prioritize patients for a split-night protocol (defined as AHI ≥20 events/hr). In this dataset, the model displayed a sensitivity of 84 percent and a low specificity (39 percent) with a relatively low discrimination (AUC=0.669) for the prediction of OSA. For prioritizing patients for a split-night protocol (AHI ≥20 events/hr), the model had a sensitivity of 33 percent and a specificity of 90 percent with an AUC = 0.7.

In addition to the model developed by Crocker 1990, Rowley 2000 examined three other clinical prediction rules for the presence of OSA (defined as AHI ≥10 events/hr) or prioritizing patients for a split-night protocol (defined as AHI ≥20 events/hr). The models utilized different combinations of clinical, morphometric, and sleep observation variables. The second clinical prediction formula was based on snoring, BMI, age, and sex. This formula had a sensitivity of 96 percent with a specificity of 13 percent for the prediction of OSA, and a sensitivity of 34 percent and a specificity of 87 percent for prioritizing patients for a split-night protocol.

The third clinical prediction formula utilized snoring, gasping or choking, hypertension, and neck circumference. The performance characteristics of this prediction rule were: prediction of AHI ≥10 events/hr—sensitivity 76 percent, specificity 54 percent; prediction of AHI ≥20 events/hr—sensitivity 34 percent, specificity 89 percent.

Finally, the fourth clinical prediction formula using snoring, gasping, witnessed apneas, BMI, age, and sex predicted AHI ≥10 events/hr with a sensitivity of 87 percent and a specificity of 35 percent. With regards to the prediction of AHI ≥20 events/hr, the model had a high specificity (93 percent) with a low sensitivity (39 percent). The authors examined the predictive performance of these models in subgroups by sex, which was used as a variable in the second and the fourth clinical prediction formulas. In general, higher AUC values were attained in men (range 0.761-0.801) compared with women (range 0.611-0.648).

Zerah-Lancner 2000 developed a predictive index for OSA based on pulmonary function data obtained through spirometry, flow–volume curves, and arterial blood gas analysis. This model

calculated probabilities of having a PSG positive for OSA based on specific respiratory conductance (derived from respiratory conductance and functional reserve capacity) and daytime arterial oxygen saturation. Using a threshold index of 0.5, the model predicted the presence of OSA (defined as AHI ≥15 events/hr) with 100 percent sensitivity and 84 percent specificity.

Summary

In summary, 10 different clinical prediction rules have been described in seven papers. The strength of evidence is low that some clinical prediction rules may be useful in the prediction of a diagnosis of OSA. Nine of the clinical prediction rules have been used for the prediction of diagnosis of OSA (using different criteria, AHI or RDI-based), while five of these models have been either specifically developed or also tested for the prediction of severe OSA (defined as AHI ≥20 or ≥30 events/hr), a diagnosis used for prioritizing patients for a split-night protocol. With the exception of the model by Zerah-Lancner 2000, which requires pulmonary function data, and the model by Onen 2008, which requires direct observation of patients' sleep, all other models are parsimonious, utilizing easily attainable variables through clinical interview and examination (including oximetry and morphometric measurements) and items collected from questionnaires. Only Rowley 2000 examined different prediction rules in the same patients. In this study, no predictive rule with desirable performance characteristics (both high sensitivity and specificity) was found for the prediction of OSA (range of sensitivities 76-96 percent, range of specificities 13-54 percent) or severe OSA (ranges of sensitivities 33-39 percent, range of specificities 87-93 percent). Of the remaining models, the morphometric model by Kushida 1997 gave near perfect discrimination (AUC= 0.996), and the pulmonary function data model by Zerah-Lancner 2000 had 100 percent sensitivity with 84 percent specificity. However, while all the models were internally validated, definitive conclusions on the applicability to the population at large of these predictive rules in independent populations cannot be drawn from the available literature. It should be further noted that no study examined the potential clinical utility of applying these prediction rules to clinical practice.

Table 3. Descriptions of clinical prediction rules

Study PMID	Clinical Prediction Rule	Description
Crocker, 1990[102] 2368960	Statistical model	Derived by logistic regression on data from a 24-item questionnaire and clinical features.
Gurubhagavatula, 2001[103] 11734444	Clinical prediction rule, derived	Combination of Multivariable Apnea Prediction (MAP) questionnaire score and oximetry results. MAP score predicts apnea risk using a score between 0 and 1, with 0 representing low risk and 1 representing high risk. Oximetry desaturation index (ODI) using a 3% drop (ODI3) as well as a 4% drop (ODI4) in oxygen saturation. Optimal model parameters obtained by the bootstrapping technique.
Kushida, 1997[104] 9341055	Morphometric model	Model: P + (Mx - Mn) + 3 X OJ + 3 X [Max (BMI -25, 0)] X (NC / BMI) P = palatal height (in millimeters), Mx is the maxillary intermolar distance (in millimeters) between the mesial surfaces of the crowns of the maxillary second molars, Mn is the mandibular intermolar distance (in millimeters) between the mesial surfaces of the crowns of the mandibular second molars, OJ is the overjet (in millimeters) or the horizontal overlap of the crowns of the maxillary and mandibular right central incisors, BMI is the body mass index (kg/m2; ideal BMI <25), Max (BMI -25, 0) refers to the larger of the two quantities: BMI - 25, or zero. If BMI is <= 25, then [Max (BMI - 25, 0)] is zero; if BMI >25, then BMI - 25 is inserted into the formula; NC is neck circumference (in centimeters) measured at the level of the cricothyroid membrane.
Onen, 2008[105] 18775037	Observation-based Nocturnal Sleep Inventory (ONSI)	Nurse observations made in five standardized hourly bedside visits over the course of one night.
Rodsutti, 2004[106] 15283004	Clinical prediction rule, derived	Sum of the individual scores for age, sex, snoring, stops breathing, and BMI; range = 0 -7.3.
Rowley, 2000[107] 11083602	Model #1	Clinical prediction model #1: Probability of predicting AHI ≥10 = $1/ (1 + e^{-(-13.9+0.06a+2.98b+0.23c+1.35d)})$ where a = age; b= I if witnessed apneas present, 0 if witnessed apneas absent; c = BMI; d = 1 if patient has hypertension, 0 if hypertension absent.
	Model #2	Clinical prediction model #2: Probability of predicting AHI ≥10 = $e^x/ (1+e^x)$ where, x = -10.5132 + 0.9164*sex + 0.0470*age + 0.1869*BMI+1.932*snoring; where sex = 1 for male, 0 for female, snoring = 1 for present, 0 for absent.
	Model #3	Clinical prediction model #3: Probability of predicting AHI ≥10 = $(10^{(-2.132 + 0.069*NC + 0.31*H+ 0.206'*HS+0.224*PR)} + 1)$ where NC=neck circumference, H=1 if hypertension, 0 if hypertension absent, HS=1 if habitual snorer, 0 if not, PR = 1 if reports nocturnal choking/gasping, 0 if no nocturnal choking/gasping.
	Model #4	Clinical prediction model #4: Probability of predicting AHI ≥10 = $e^x/ (1+e^x)$ where, x = -8.160+1.299*Index1+O.163*BMI-0.025*BMI*Index1+0.032*age +1.278*sex where, sex=1 if male, 0 if female, index1 = the mean of nonmissing values for frequency of snorting/gasping, loud snoring, breathing stops/chokes.
Zerah-Lancner, 2000[108] 11112139	Based on Pulmonary function data	Probability (p) of having a polysomnography positive for sleep apnea: logit (p)= -136 sGrs + 2.5 (100 - SaO_2) + 4.2 where specific respiratory conductance (sGrs) (in $cmH_20^{-1} * s^{-1}$) = respiratory conductance (Grs) / functional reserve capacity (FRC) SaO_2 = daytime arterial oxygen saturation in %. The estimated value of p was derived from logit (p)= $\log_e(p/1-p)$, from 0 to 1 range.

Key Question 2. How does phased testing (screening tests or battery followed by full test) compare to full testing alone?

To address this question, our literature search included any study that directly compared phased testing (a series of tests performed dependent on the results of initial tests) with full testing (overnight polysomnography [PSG]) alone. We included all prospective cross-sectional or longitudinal studies of any followup duration. At least 10 study participants had to be analyzed with each test of interest to warrant inclusion. Only one study met our inclusion criteria.[109]

Gurubhagavatula 2004 assessed the accuracy of phased testing with full testing among 1,329 respondents from a pool of 4,286 randomly selected commercial driver's license holders in Pennsylvania.[109] Those respondents with an existing diagnosis of obstructive sleep apnea (OSA) or obesity-hypoventilation syndrome, or using supplemental oxygen were excluded. The respondents were mostly male (94 percent) with a mean age of 44 years, and a mean body mass index (BMI) of 28.4 kg/m^2. The study suffered from verification bias as only the participants considered to be at high risk for OSA in early testing phases were followed up with PSG. The study received a quality rating of C.

To assess the presence of sleep apnea, the study compared five case-identification strategies with PSG. Of the five strategies, one assessed a two-stage testing strategy that involved the calculation of a multivariable clinical prediction rule score (from a multivariable apnea prediction questionnaire) for all participants (Stage I). The prediction score ranged from zero (no risk) to one (maximal risk for OSA), and was calculated by combining a symptom score (symptoms included self-reported frequency of gasping or snorting, loud snoring, and the frequency of breathing stops, choking, or struggling for breath) with BMI, age, and sex. A score between 0.2 and 0.9 was defined as an intermediate risk score. Participants in this category received subsequent nocturnal pulse oximetry testing (Stage II) and those with ODI ≥5 events/hr underwent PSG. OSA was defined as an ODI ≥5 events/hr and severe OSA as ≥10 events/hr. Of the 1,329 respondents, 406 (31 percent) underwent oximetry and PSG testing.

Of the 1,329 respondents, 551 subjects had a multivariable apnea prediction score above 0.436 (considered a high-risk stratum), and 247 subjects (45 percent) were enrolled from that group for oximetry and PSG testing. From the group with a prediction score below 0.436 (considered a low-risk stratum), 159 participants (20 percent) were randomly enrolled for oximetry and PSG testing. From the pooled sample of 406 subjects, OSA was diagnosed in 28 percent of the subjects. In the low risk stratum, 11 percent of the subjects had sleep apnea as compared to 52 percent of those in the high risk stratum.

The proportion of patients with OSA among those who were classified as intermediate risk by the multivariable apnea prediction score (between 0.2 and 0.9) and had further oximetry was not reported. The proportion of OSA in patients who were considered either high risk (score >0.9) or low risk (score <0.2) were also not reported.

Summary

The strength of evidence is insufficient to determine the utility of phased testing followed by full testing when indicated to diagnose sleep apnea, as only one study investigated this question. This prospective quality C study did not fully analyze the phased testing, thus the sensitivity and specificity of the phased strategy could not be calculated due to a verification bias because not all

participants had PSG testing. The methodological problems with this study also limit the applicability to the general population of people with OSA.

Key Question 3. What is the effect of preoperative screening for sleep apnea on surgical outcomes?

To address this question, our literature search included any prospective, cross-sectional or longitudinal study of any followup duration that compared use of routing screening with no or limited screening and reported all intraoperative events, surgical recovery events, surgical recovery times, postsurgical events, length of intensive care or hospital stays, and intubation or extubation failures among patients with no previous OSA diagnosis undergoing surgical procedures.

Two studies met selection criteria (Appendix D Table 3.1).[97,110] Both studies were rated quality C as they had different selection criteria for enrolling subjects in the two comparative arms, indicating a substantial risk of selection bias.

Hallowell 2007, in a retrospective chart review of patients who had undergone bariatric surgery, compared 576 patients who had a PSG based on results from a clinical and physical examination (a positive, but undefined, Epworth Sleepiness Scale score, symptoms of loud snoring or daytime sleepiness, or clinical suspicion by the surgeon or pulmonologist) with 318 patients who underwent a mandatory PSG. The reported outcomes included intensive care unit (ICU) admission, respiratory-related ICU admission, duration of hospital stay, and mortality. The mean age of the patients (13 percent male) was 43 years and mean body mass index (BMI) of 51 kg/m^2. The followup period was restricted to the immediate postoperative interval.

Chung 2008 was a study designed to compare different screening tools with polysomnography (PSG) in a cohort of preoperative patients (and is discussed under *Key Question 1*). Only about half their enrolled patients consented to PSG. The study thus compared patients who did or did not have preoperative screening with polysomnography (PSG) for complication rates (respiratory, cardiac, or neurological complications), use of prolonged oxygen therapy, requirement of additional monitoring, intensive care unit (ICU) admissions, hospital stay after surgery, readmission, and emergency department visits. The study included 416 patients scheduled to undergo elective procedures in general surgery, gynecology, orthopedics, urology, plastic surgery, ophthalmology, or neurosurgery. Subjects were 51 percent male with a mean age of 55 years and a mean BMI of 30.1 kg/m^2. The followup period was 30 days. Though included in this review, the value of this study to address this Key Question is dubious as there was a systematic difference between those patients who did and did not have PSG. It is highly likely that those who underwent testing were (or considered themselves to be) sicker and at higher risk of having sleep apnea.

Duration of Hospital Stay (Appendix D Table 3.2)

The duration of stay in the hospital was evaluated in both studies. In Hallowell 2007, among bariatric surgery patients, those who underwent mandatory testing with PSG were released on average 9.6 hr earlier than those who underwent PSG based on criteria from the physical and clinical examinations. No data were reported as to whether this difference was statistically significant. In Chung 2008, among patients who had elective general surgery procedures, those who volunteered for PSG had a nonsignificantly longer median hospital stay than those who refused PSG (difference of medians 15.5 hr)

Intensive Care Unit Admission (Appendix D Table 3.3)

Both studies evaluated ICU admission. In Hallowell 2007, among bariatric surgery patients, those who underwent mandatory PSG testing had a somewhat lower risk of being admitted to the ICU (relative risk [RR] = 0.62; 95 percent confidence interval [CI] = 0.32, 1.22), as compared with those who underwent selective PSG testing. In Chung 2008, among patients who had elective general surgery procedures, a greater percentage of patients who volunteered for PSG were admitted to the ICU than those who refused preoperative PSG (RR = 3.16; 95 percent CI 1.05, 9.52) [The RR's and 95 percent CI's were calculated from reported data].

Other Postoperative Outcomes (Appendix D Table 3.3)

In Hallowell 2007, among bariatric surgery patients, those who underwent mandatory PSG testing had a substantially, but nonsignificantly lower risk of respiratory complications leading to ICU admission (RR = 0.16; 95 percent CI 0.02, 1.27), as compared with those who underwent selective PSG testing. In Chung 2008, those who volunteered for PSG testing had significantly more total complications, and nonsignificantly more respiratory complications, cardiac complications, prolonged oxygen therapy, and additional monitoring, but nonsignificantly fewer emergency department visits within 30 days. There were no apparent differences in neurological complications, or hospital readmission within 30 days.

Summary

Two quality C prospective studies assessed the effect of preoperative screening for sleep apnea on surgical outcomes among patients with no prior OSA diagnosis. One study found that patients undergoing bariatric surgery who had mandatory PSG possibly had somewhat shorter hospital stays and, possibly, fewer respiratory-related ICU admissions than those patients who had (in a previous era) PSG based on clinical parameters. However, these differences were not statistically significant. The second study found that general surgery patients willing to undergo preoperative PSG were more likely to have perioperative complications, particularly cardiopulmonary complications, possibly suggesting that patients willing to undergo PSG are more ill than patients not willing to undergo the procedure. The methodological problems with the studies and their restricted eligibility criteria limit their applicability to the general population of people with OSA.

Overall, the strength of evidence is insufficient regarding postoperative outcomes with mandatory screening for sleep apnea.

Key Question 4. In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index or oxygen desaturation index and other patient characteristics with respect to long-term clinical and functional outcomes?

To address this question, our literature search was restricted to longitudinal studies of at least 500 participants who were assessed with formal sleep testing at baseline and followed for at least 1 year. Outcomes of interest included incident clinical events, quality of life, and psychological or neurocognitive measures. Analyses of interest were restricted to multivariable analyses of apnea-hypopnea index (AHI) (or similar sleep study measure) and demographic and clinical variables. We preferentially included analyses of baseline variables only.

Eleven articles met eligibility criteria. Four evaluated predictors of all-cause mortality,[1,2,111,112] two cardiovascular death,[1,6] one each nonfatal cardiovascular events[6] and

stroke,[113] two hypertension,[11,114] two type 2 diabetes mellitus,[115,116] and one quality of life.[117] Three articles each evaluated the Sleep Heart Health Study (SHHS)[2,114,117] and the Wisconsin Sleep Cohort Study.[1,11,115]

All-Cause Mortality (Appendix D Tables 4.1 & 4.2)

Four studies evaluated AHI as a predictor of all-cause mortality in multivariable analyses.[1,2,111,112] Among these studies, three enrolled participants primarily during the 1990s; the smallest study enrolled participants during the 1970s and 1980s (Lavie 1995). The two studies by Lavie (2005 & 1995) were restricted to adult men with sleep apnea symptoms or evidence of sleep apnea. The two other studies (SHHS [Punjabi 2009] and Wisconsin [Young 2008]) were large, prospective cohort studies of adults from the general population. Three of the four studies were rated quality A; the SHSS article was deemed to be quality B as a stratified analysis with cross-product terms was used instead of a full multivariable regression.

All four studies found that higher baseline AHI was predictive of increased mortality over about 2 to 14 years of followup. Three of the studies evaluated categories of AHI. Each found that people with AHI >30 events/hr had a statistically significant risk of death compared with those with a low AHI (<5-10 events/hr); hazard ratios ranged from about 1.5-3.0. People in these studies with an AHI of between approximately 5 to 10 and 30 events/hr had a nonsignificantly increased risk of death. The oldest study (Lavie 1995) evaluated AHI as a continuous variable and found a significant linear association (OR = 1.012 per unit of AHI).

The SHHS analysis (Punjabi, 2009) found an interaction between AHI and both age and sex such that the association between AHI and death was seen only in men up to age 70 years. In older men (>70 yr) and in women, no significant association was found. Both SHHS and Lavie 1995 reported no substantial changes in the associations between AHI and death with the iterative addition of other predictors.

Summary

Four studies (three quality A, one quality B) found that AHI was a statistically significant independent predictor of death with long-term followup (2-14 years). The association was strongest among people with an AHI >30 events/hr. The SHHS study, however, found an interaction with sex and age such that AHI was associated with death only in men ≤70 years old.

Cardiovascular Mortality (Appendix D Tables 4.3 & 4.4)

Two studies evaluated AHI as a predictor of cardiovascular mortality in multivariable analyses.[1,6] Both enrolled participants primarily in the 1990s. Marin 2005 was restricted to otherwise healthy men with sleep disordered breathing. The Wisconsin Sleep Cohort Study included adults from the general population. Both studies were rated quality A.

Marin 2005 found a statistically increased risk of cardiovascular death during 10 years of followup among those with a baseline AHI ≥30 events/hr who were not treated with continuous positive airway pressure (CPAP). Those with a lower AHI or who were treated with CPAP were found to not be at an increased risk of cardiovascular death. Addition of the statistically significant predictor of existing cardiovascular disease, and the nonsignificant predictor of hypertension, did not substantially alter the association between AHI and cardiovascular death risk. The Wisconsin study found no association between AHI and cardiovascular death after 14 years of followup.

Summary

One of two studies (both quality A) found a significant independent association between an AHI ≥30 events/hr and the risk of cardiovascular death, but not lower baseline AHI, after long-term followup (10 years). The relationship was not altered by adjustment for existing cardiovascular disease or hypertension. In addition, an association was not seen in those treated with CPAP. No association was noted in the second study.

Nonfatal Cardiovascular Disease (Appendix D Tables 4.3 & 4.4)

Marin 2005,[6] a study of men with sleep disordered breathing, also evaluated the risk of nonfatal cardiovascular disease (myocardial infarction, stroke, or acute coronary insufficiency requiring an invasive intervention), and was also rated quality A for this outcome. The study found a similar association with nonfatal cardiovascular disease as for cardiovascular death. Only those participants with an AHI ≥30 events/hr who were not treated with CPAP were at a statistically significant increased risk of nonfatal cardiovascular disease. Adjustment for existing cardiovascular disease or hypertension did not substantially change the observed association.

Stroke (Appendix D Tables 4.3 & 4.4)

One study (Arzt 2005) evaluated the risk of stroke in adults aged 30 to 60 years without a previous history of stroke.[113] The participants were enrolled beginning in 1988. The study was rated quality B due to questions concerning the ascertainment of stroke. No statistically significant association was found between AHI and incident stroke during 12 years of followup. The low event rate (14/1,475) and the wide confidence intervals of the odds ratios, though, suggest that the study was highly underpowered to evaluate this outcome. However, in an analysis adjusted only for age and sex (not for body mass index [BMI]), the association between an AHI ≥20 events/hr and incident stroke was statistically significant (OR = 4.48; 95 percent CI 1.31-15.3; P=0.02), thus suggesting that AHI and stroke are confounded with elevated BMI.

Hypertension (Appendix D Tables 4.5 & 4.6)

The association between AHI and risk of developing hypertension was evaluated in the two large cohort studies (SHHS and the Wisconsin Sleep Cohort Study).[11,114] The Wisconsin study excluded people with cardiovascular disease (but not hypertension). SHHS was rated quality A and the Wisconsin study was rated quality B for reasons discussed below.

In an overall analysis AHI was not an independent, significant predictor of incident hypertension in the SHHS at 5 years. However, AHI and hypertension were confounded by BMI. When BMI was not included in the model, an AHI of 15-30 events/hr and an AHI ≥30 events/hr were both significantly associated with incident hypertension (AHI = 15-30 events/hr: OR = 1.54, 95 percent CI 1.12-2.11; AHI ≥30 events/hr: OR = 2.19, 95 percent CI 1.39, 3.44).

Several subgroup analyses were also performed. Although the AHI x sex interaction term was not statistically significant (P=0.09), a significant association was found between an AHI≥30 events/hr and hypertension in women but not men. Similarly the AHI x BMI interaction term was not significant (P=0.36) but an AHI>30 events/hr was in those with a BMI less than, but not above, the median 27.3 kg/m^2. No consistent difference was found in associations of AHI and incident hypertension between those younger or older than the median age of 59 years, or with or without clinically significant sleepiness (defined as ESS ≤or >11, respectively).

The Wisconsin Sleep Cohort Study analyzed the risk of having hypertension at 4 and 8 years among people without cardiovascular disease. However, it should be noted that 28 percent of the

participants had hypertension at baseline. Although the analysis adjusted for baseline hypertension, inclusion of these participants makes interpretation of the analysis unclear. Nevertheless, any AHI above 0 events/hr was found to be a statistically significant independent predictor of hypertension at 4 and 8 years of followup. Across AHI categories, it was observed that the higher the AHI the stronger the association. No interaction terms with other predictors were significant, and the results did not substantially change with the addition of sets of predictors.

Summary

In two studies, the association between AHI and future hypertension is unclear. One study found no overall independent association with incident hypertension, but found that BMI may have been a confounding factor. There were associations in subgroups of men and those with less than the median BMI, although the interaction terms were not statistically significant. The other study found that AHI was an independent predictor of future hypertension; however, the analysis included (and adjusted for) 28 percent of participants having hypertension at baseline.

Type 2 Diabetes (Appendix D Tables 4.7 & 4.8)

Two studies evaluated AHI as a predictor of incident type 2 diabetes mellitus in multivariable analyses.[115,116] The Wisconsin Sleep Cohort Study enrolled participants in 1988 while Botros 2009 recruited subjects with sleep disordered breathing in the early 2000s. Both excluded people with diabetes at baseline. The Wisconsin study was rated quality B due to unclear and incomplete reporting of the description of those included in the longitudinal analysis and of the results. The other study was rated quality A.

The Wisconsin study found no association between baseline AHI and the incidence of diabetes after 4 years. However, the association was confounded by waist girth. In an analysis without waist girth, a strong association was observed (AHI 5-15 events/hr: OR = 2.81, 95 percent CI 1.51-5.23, P=0.001; AHI ≥15 events/hr: OR = 4.06, 95 percent CI 1.86-8.85, P=0.0004). Botros 2009 found that AHI ≥8 events/hr was significantly associated with incident diabetes after a mean of 2.7 years in an analysis controlled for BMI and change in BMI over the 2.7 years. The association was similar both with and without adjustment for other predictors.

Summary

Two studies suggest an association between higher AHI and incident type 2 diabetes. However, the Wisconsin study suggests that the association may be confounded by obesity, as measured by waist girth.

Quality of Life (Appendix D Tables 4.9 & 4.10)

The SHHS evaluated AHI as a predictor of quality of life as assessed with SF-36 after 5 years.[117] This analysis was rated quality A. The study found no statistically significant association between baseline AHI and changes in either the Physical or Mental Component Summaries.

Overall Summary

Three publications derived each from the Sleep Heart Health Study and the Wisconsin Sleep Cohort Study, and five other large cohort studies performed multivariable analyses of AHI as a predictor of long-term clinical outcomes.

A high strength of evidence indicates that an AHI >30 events/hr is an independent predictor of all-cause mortality; although one study found that this was true only in men under age 70 years. The evidence on mortality is applicable to the general population, with and without OSA, and also more specifically to men with OSA symptoms or evidence of OSA. All other outcomes were analyzed by only one or two studies. Thus only a low strength of evidence exists that a higher AHI is associated with incident diabetes. This conclusion appears to be applicable for both the general population and specifically for patients diagnosed with sleep disordered breathing. This association, however, may be confounded with obesity, which may result in both OSA and diabetes. The strength of evidence is insufficient regarding the association between AHI and other clinical outcomes. The two studies of cardiovascular mortality did not have consistent findings, and the two studies of hypertension had unclear conclusions. One study of nonfatal cardiovascular disease found a significant association with baseline AHI (as they did for cardiovascular mortality). One study each found no association between AHI and stroke or long-term quality of life.

Key Question 5. What is the comparative effect of different treatments for obstructive sleep apnea in adults?

a. Does the comparative effect of treatments vary based on presenting patient characteristics, severity of obstructive sleep apnea, or other pretreatment factors? Are any of these characteristics or factors predictive of treatment success?
   - Characteristics: Age, sex, race, weight, bed partner, airway, other physical characteristics, and specific comorbidities
   - Obstructive sleep apnea severity or characteristics: Baseline questionnaire (and similar tools) results, formal testing results (including hypoxemia levels), baseline quality of life, positional dependency
   - Other: Specific symptoms

b. Does the comparative effect of treatments vary based on the definitions of obstructive sleep apnea used by study investigators?

With some exceptions for studies of surgical interventions, we reviewed only randomized controlled trials (RCT) of interventions used specifically for the treatment of obstructive sleep apnea (OSA). RCTs had to analyze at least 10 patients per intervention and the intervention had to be used for some period of time in the home setting (or equivalent). We also included prospective or retrospective studies that compared surgical interventions (including bariatric surgery) to nonsurgical treatments (with the same sample size restriction). In addition, we reviewed cohort (noncomparative) studies of surgical interventions with at least 100 patients with OSA that reported adverse event (or surgical complication) rates.

To address the subquestions to this Key Question, we sought within-study subgroup or regression analyses and, when the evidence base was sufficient and appropriate, looked for explanations of differences (heterogeneity) across studies.

In total, we found 155 eligible studies, reported in 167 articles. Of these, 132 were RCTs, 6 were prospective nonrandomized comparative studies, 5 were retrospective nonrandomized comparative studies, 2 were prospective surgical cohort studies, and 10 were retrospective surgical cohort studies.

Each section below focuses on a specific comparison between categories of interventions, with a final section focusing on adverse events. Most sections include a summary table

describing the patient and study characteristics for all studies included in that section, and separate results summary tables for each outcome. We did not compile summary tables for comparisons evaluated by only one study.

Comparison of CPAP and Control

We identified 22 studies (reported in 23 articles) that compared a variety of CPAP devices with a control treatment. Twelve trials had a parallel design[118-130] and 10 were crossover trials.[131-140] One study[120] used C-Flex™ (a proprietary technology that reduces the pressure slightly at the beginning of exhalation) and the remaining trials used fixed continuous positive airway pressure (CPAP) devices. CPAP pressure was chosen manually in 13 studies, automatically determined in five, and was undefined in four. In 17 studies, it was reported that CPAP was introduced on a separate night than the diagnostic sleep study. The CPAP intervention was compared to no specific treatment in four studies, to placebo treatment (e.g., lactose tablets) in nine studies, to optimal drug treatment in one study, and to conservative measures (e.g., advice on sleep hygiene measures, weight loss) in seven studies. In four of these studies, the conservative measures were also applied to the CPAP arm.[118,127,129,130]

Mean baseline AHI ranged from 10 to 65 events/hr; nine trials included patients with an AHI ≥5, one with an AHI ≥10, seven with an AHI ≥15, two with an AHI ≥20, one with an AHI ≥30, and two did not report a lower AHI threshold. Most trials had unrestrictive eligibility criteria with the exception of Barbe 2010, which included hypertensive patients, Drager 2007, which included patients with severe OSA (mean baseline AHI = 65 events/hr), and two others (Kaneko 2003 and Mansfield 2004), which included only patients with symptomatic, stable, and optimally-treated congestive heart failure. The sample size of the studies ranged from 12 to 359 (total = 1,116 across studies). Eleven studies were rated quality B and 11 studies were rated quality C. The primary methodological concerns included small sample sizes with multiple comparisons, the lack of a power calculation, high dropout rates, incomplete reporting and, for certain crossover trials, the lack of a washout period. Overall, the studies are applicable to a broad range of patients with OSA.

Objective Clinical Outcomes

Mansfield 2004 evaluated the impact of CPAP treatment on heart failure symptomatology, as assessed by the New York Heart Association class.[126] No statistically significant improvement was found after 3 months of treatment with CPAP compared with no specific treatment for OSA. No studies evaluated other objective clinical outcomes.

Apnea-Hypopnea Index (Appendix D Table 5.1.2; Figure 6)

Seven trials provided data on apnea-hypopnea index (AHI) during treatment.[119,121,123,126,127,129,140] All reported that AHI was statistically significantly lower in patients on CPAP than those on no treatment. Meta-analysis found that the difference in AHI between CPAP and control was statistically significant, favoring CPAP (difference = -20 events/hr; 95 percent CI -26, -14; P<0.001). Subgroup meta-analysis by minimum threshold AHI for study eligibility revealed that the single study with a minimum threshold of 20 events/hr found a larger difference in effect (Kaneko 2003: -28 events/hr) than the other studies that included patients with a lower AHI (range -10 to -22 events/hr); although, this difference did not fully account for the observed heterogeneity.

Epworth Sleepiness Scale (Appendix D Table 5.1.3; Figure 7)

Fourteen trials provided data on the Epworth Sleepiness Scale (ESS).[118-120,126-131,135-138,140] Thirteen studies examined the comparison of CPAP versus control and one study of C-Flex versus control.[120] Nine studies reported statistically significant differences in ESS between CPAP and control, whereas the remaining five found no significant difference. Meta-analysis of all 12 studies with available data on the comparison of CPAP versus control revealed a statistically significant difference between CPAP and control, favoring CPAP (difference = -2.4; 95 percent CI -3.2, -1.5; P<0.001). However, the results were statistically heterogeneous.

Subgroup analysis by study design showed that synthesis of parallel trials (n=7) provided a significantly larger estimate of summary effect compared with crossover trials (n=5) (differences = -2.7 and -2.1, respectively, P for interaction = 0.04). A smaller effect was seen in the seven studies that included patients with an AHI as low as 5 events/hr (-2.2) as compared with the three studies that included only patients with at least 15 AHI events/hr (-4.4), but, again, this difference was not statistically significant. The single study that tested C-Flex versus no treatment (Drager 2007) demonstrated the biggest absolute reduction in ESS for the intervention arm (difference = -7.0; 95 percent CI -10.2, -3.7; P<0.001) compared with all other studies in this group.

Other Sleep Study Measures (Appendix D Table 5.1.4a-e; Figures 8 & 9)

Six studies evaluated arousal index.[119,121,123,129,139,140] All studies found greater reductions in arousal index for the CPAP arm; although in one study,[119] this difference was not statistically significant. Meta-analysis of the five studies with sufficient data for analysis (Figure 8) revealed that arousals were significantly lower using CPAP compared with control interventions (difference = -15 events/hr; 95 percent CI -22, -7; P<0.001). Study results were found to be significantly heterogeneous. No significant difference in effect was found in the parallel design and crossover studies.

Five studies, all testing CPAP, evaluated minimum oxygen saturation (Figure 9).[121,123,126,129,140] Meta-analysis revealed the studies were heterogeneous and a statistically significant greater increase in minimum oxygen saturation while using CPAP compared with control (difference = 12 percent; 95 percent CI 6.4, 17.7; P<0.001). All studies found a statistically significant effect, although the small study by Ip 2004[121] detected a more pronounced increase of minimum oxygen saturation in favor of CPAP (difference = 27 percent; 95 percent CI 17.4, 35.8; P<0.001). Notably, this study enrolled severely hypoxemic patients (baseline minimum oxygen saturation was 65 percent in the patients randomized to the CPAP arm), which demonstrated a dramatic improvement when receiving CPAP treatment. The remaining studies were statistically homogeneous.

Sleep efficiency (measured as percent of total sleep time) was evaluated by two studies, neither of which detected a significant effect of CPAP treatment.[119,140] Five studies examined whether CPAP treatment increased the time in slow wave sleep (in absolute number of minutes or as a percentage of total sleep time) compared with control interventions.[119,123,126,139,140] Three studies found no significant differences. McArdle 2001 found a statistically significant difference of 18 minutes more when on CPAP and Mansfield 2004 reported a marginally significant net increase in the percentage of total sleep time with CPAP (4 percent, P=0.046). The same five studies found no significant differences for the outcome of rapid eye movement (REM) sleep (expressed in absolute number of minutes or as a percentage of total sleep time).

Objective Sleepiness and Wakefulness Tests (Appendix D Table 5.1.5a,b)

Six trials evaluated the Multiple Sleep Latency Test.[127,128,131,133,135,136] Four trials found no significant difference between CPAP and control, while Engleman 1998 and Engleman 1994 reported a statistically significant result favoring CPAP (respective net differences of 2.40 and 1.10 minutes). Meta-analysis of the six trials did not show a statistically significant difference between the interventions, but may suggest (nonsignificant) improvement with CPAP (difference = 0.78; 95 percent CI -0.07, 1.63; P=0.072).

Only Engleman 1999 evaluated the Maintenance of Wakefulness test sleep onset latency; no difference between CPAP and placebo intervention was found.

Quality of Life (Appendix D Table 5.1.6a,b)

Four studies evaluated results from the Functional Outcomes of Sleep Questionnaire (FOSQ).[127,131,138,140] The studies generally did not provide information on the exact FOSQ subscales that were analyzed, and the scores reported were generated by different methodologies (total summed score of responses, weighted average of subscale scores, or ratio of total summed score over maximum possible score). Thus, the reported FOSQ results appeared to be highly inconsistent (with baseline values ranging from 0.8 to 101 across studies) and a meta-analysis could not be performed. Regardless, none of the studies reported a statistically significant difference between CPAP and no treatment.

Ten studies reported on quality of life measures; five used the Short Form Health Survey 36 (SF-36),[126,129,131,137,140] four used various components of the Nottingham Health Profile,[118,127,136,137] three used the General Health Questionnaire-28,[133,135,136] two used the energetic arousal score of the University of Wales mood adjective list,[136,137] two used the sleep apnea hypopnea syndrome-related symptoms questionnaire,[118,127] and one used the Calgary sleep apnea quality of life index (SAQLI).[129]

Overall, 29 comparisons of different quality of life measures were reported. In six trials, 11 quality of life measures reached statistical significance. In the studies that used SF-36, CPAP showed favorable results for the vitality scale in two studies,[126,137] the physical scale in two studies,[129,137] and the bodily pain in one study.[129] Among the various subscales of the Nottingham Health Profile, statistically significant differences in favor of CPAP for the physical scale were found only in one study.[118] Of the three studies using the General Health Questionnaire-28 scale, significant results were shown in only one study.[133] No significant findings were recorded for the University of Wales mood adjective list energetic arousal score in two studies, whereas one study reported significant differences for the SAQLI summary score.[129]

In summary, the impact of CPAP on quality of life is uncertain due to inconsistent findings across studies and the methodological issue of multiple testing of various quality of life subscales within these studies.

Neurocognitive and Psychological Tests (Appendix D Table 5.1.7)

Eight studies evaluated neurocognitive and psychological tests.[125,127,131,133,135-137,140] Of the 56 comparisons between CPAP and control, significant differences were detected in 10 comparisons across four studies; all significant differences were in favor of CPAP.[131,133,135,137] The tests with significant results included examinations of cognitive performance (intelligence quotient, digit symbol test), executive function (trailmaking), anxiety and depression scores, processing speed (Paced Auditory Serial Addition Test), and semantic fluency (the controlled oral word association test).

Blood Pressure and Hemoglobin A1c (Appendix D Table 5.1.8a,b)

Comparisons of daytime or nighttime blood pressure measurements between CPAP-treated patients and patients on control interventions were reported by seven studies.[120,123,127,130-132,134] No statistically significant differences were reported. Only one crossover trial (Comondore 2009) evaluated hemoglobin A1c; no difference was found between CPAP and no treatment.

Study Variability

For the main sleep study outcomes of interest (AHI, ESS, minimum oxygen saturation, and arousal index), the included studies were generally consistent in their findings, showing a beneficial effect of CPAP intervention. However, meta-analysis showed that the magnitude of the detected effects in the studies were heterogeneous. In subgroup meta-analyses by study design, there was evidence of larger effect magnitudes in parallel compared with crossover trials for the ESS outcome. The baseline severity of hypoxemia (for the minimum oxygen saturation outcome) were detected as factors influencing the magnitude of effect size for CPAP. No study reported subgroup analyses for the sleep outcomes of interest.

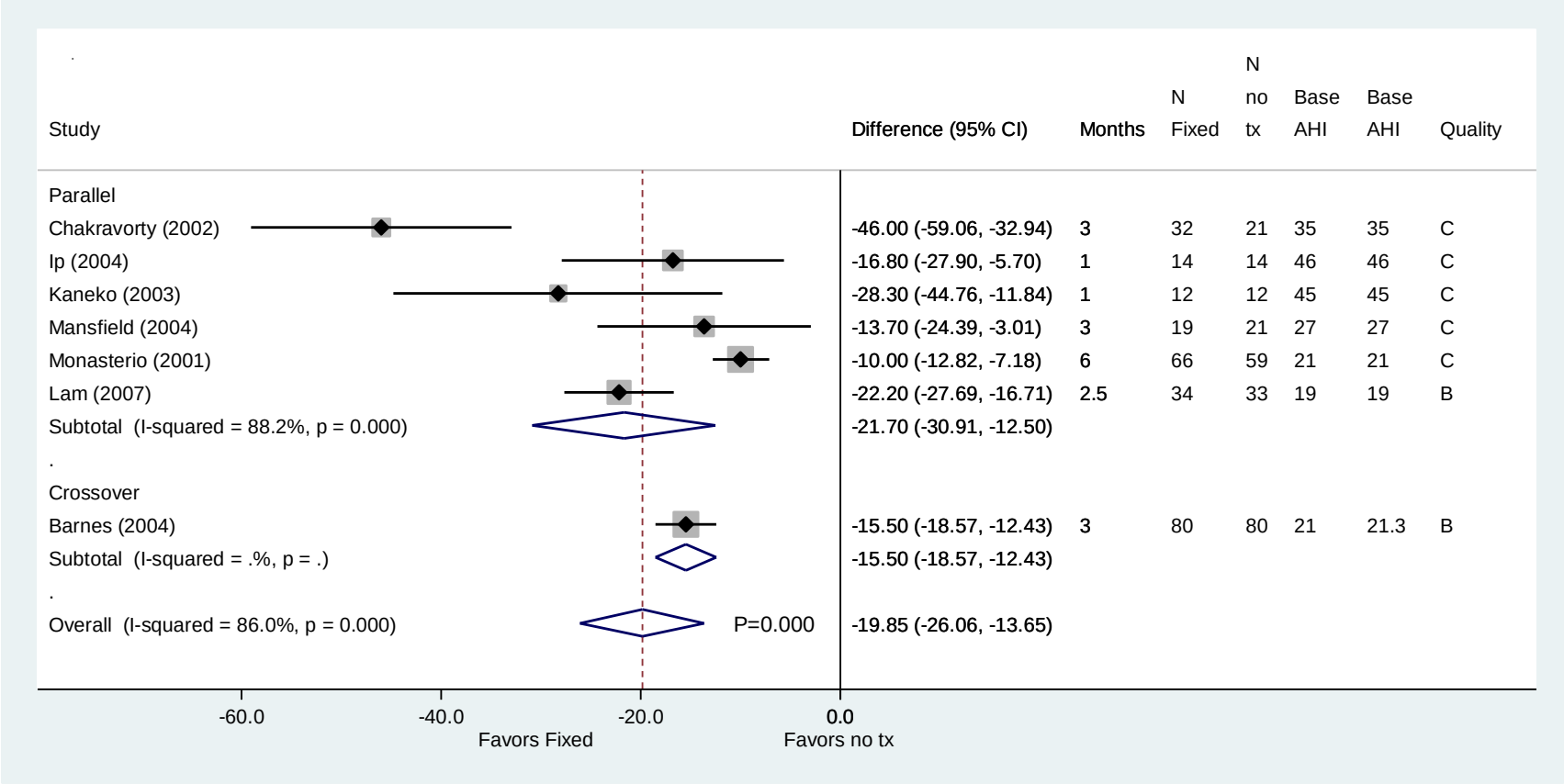
A wide range of measures were used in a small number of studies to assess quality of life, neurocognitive, and psychological outcomes. Most of these outcomes were explored as secondary endpoints. The majority of the comparisons did not report statistically significant differences in these assessments.

Summary

Eleven quality B trials and 11 quality C trials compared CPAP with control interventions. Most studies used fixed CPAP devices with manual choice of pressure. The studies reviewed generally found that CPAP was superior in reducing AHI, improving ESS, reducing arousal index, and raising the minimum oxygen saturation. These findings were confirmed by meta-analysis, although results were statistically heterogeneous. There was evidence that the magnitude of the demonstrated efficacy of CPAP treatment may have been influenced by study design (parallel trials showed larger effect sizes), type of device, or baseline severity of disease. No consistent effect of CPAP versus control in improving other sleep study measures (slow wave and REM sleep or Multiple Sleep Latency Test) was observed. Most studies found no significant difference in quality of life or neurocognitive measures, although certain studies reported statistically significant results in favor of CPAP for the physical and vitality scales of SF-36 and various indices of cognitive performance. Generally, no consistent results were found for these measures. The wide variability in the quality of life and neurocognitive outcomes examined, and the multiple testing performed by small-sized studies, warrant cautious interpretation of any positive findings. A single study evaluated the impact of CPAP on the severity of symptoms of congestive heart failure and reported nonsignificant results. Similarly, no benefit from CPAP was found for lowering blood pressure.

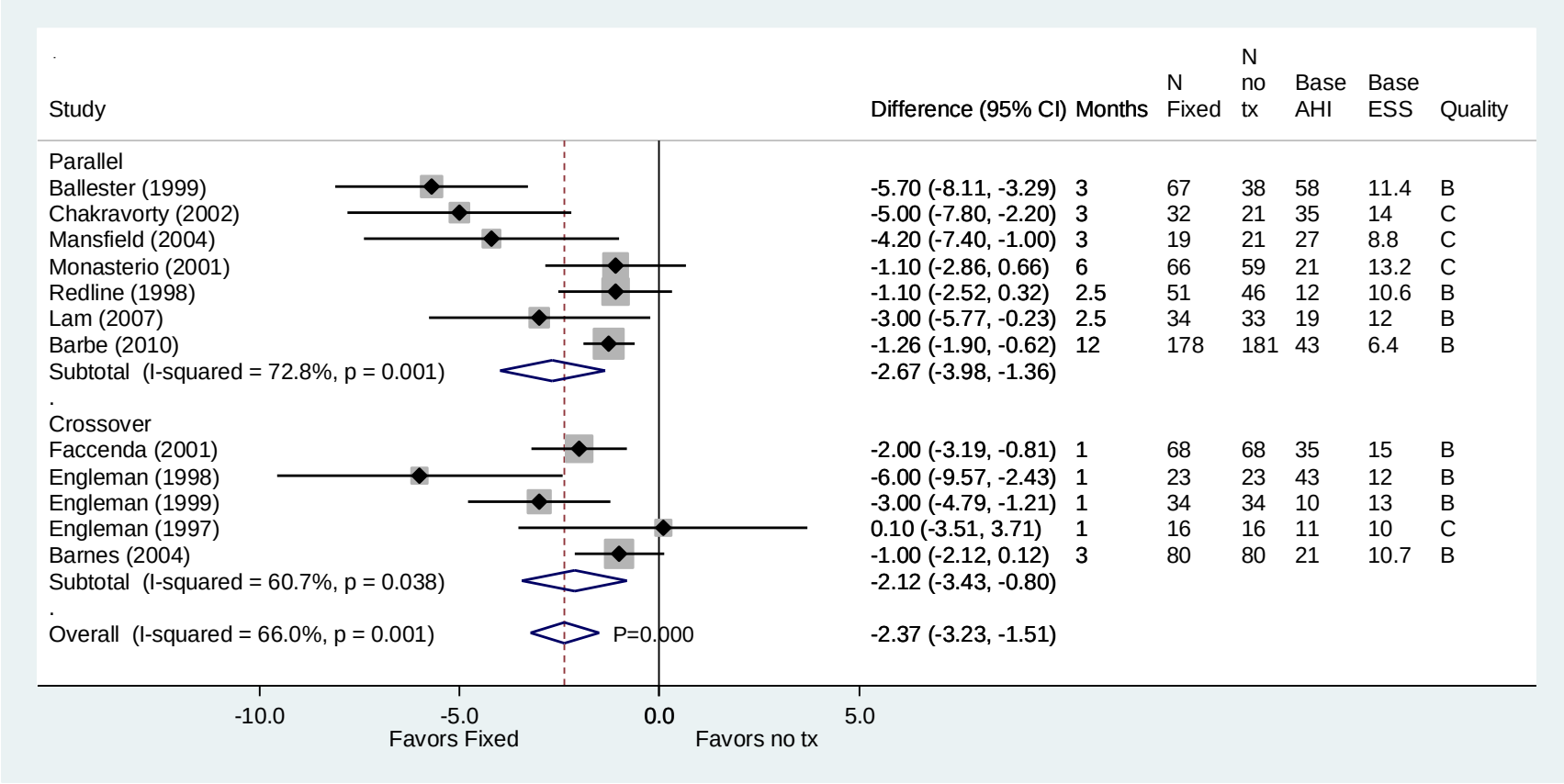
The reviewed studies report sufficient evidence supporting large improvements in sleep measures with CPAP compared with control. There is only weak evidence that demonstrated no consistent benefit in improving quality of life, neurocognitive measures or other intermediate outcomes. Despite no or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI and ESS, the strength of evidence that CPAP is an effective treatment to alleviate sleep apnea signs and symptoms was rated moderate.

Figure 6. Meta-analysis of AHI (events/hr) in randomized controlled trials of CPAP vs. control, by study design



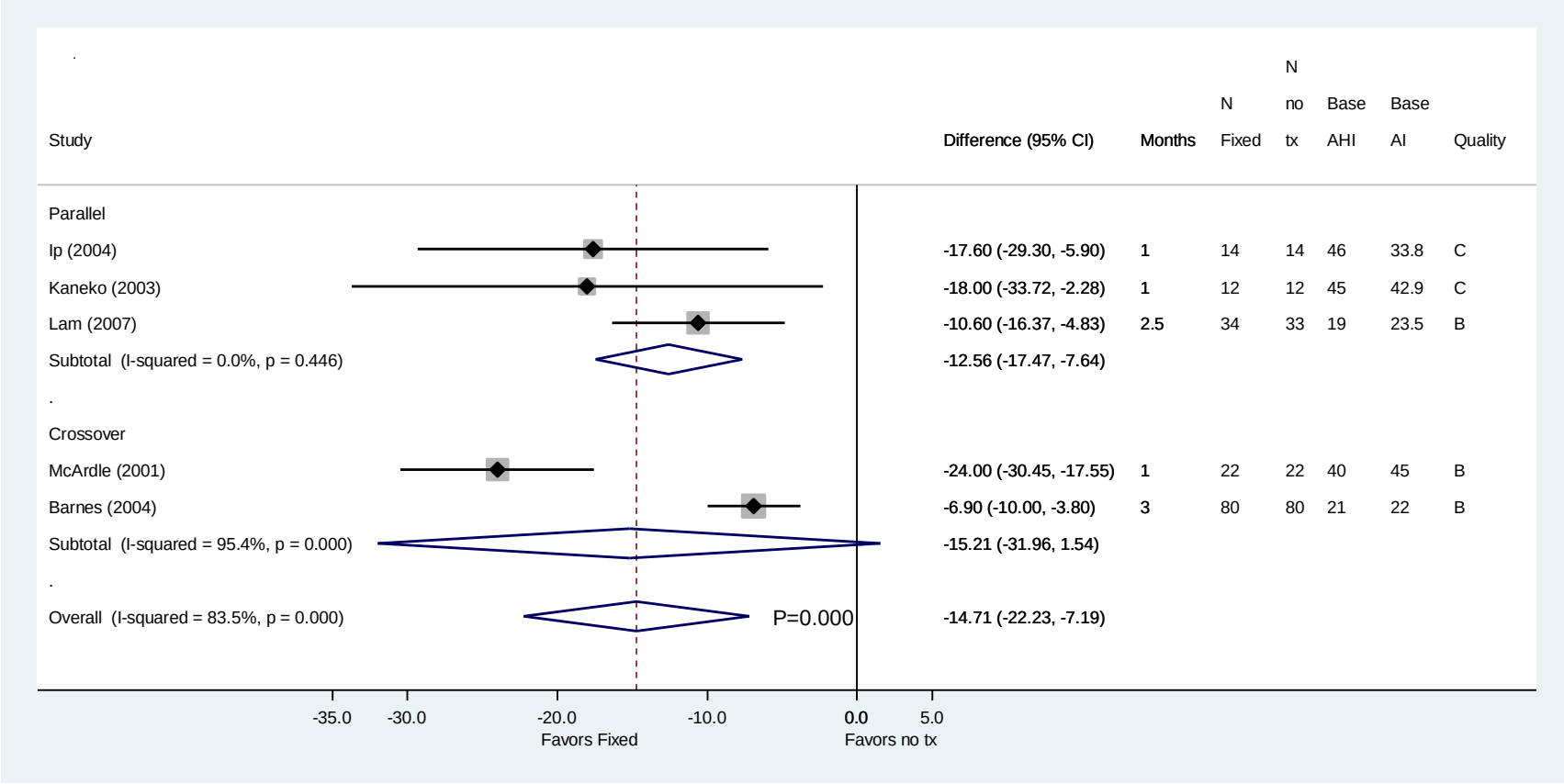
AHI = apnea-hypopnea index; CI = confidence interval; Fixed = fixed CPAP (continuous positive airway pressure); tx = treatment.

Figure 7. Meta-analysis of ESS in randomized controlled trials of CPAP vs. control, by study design



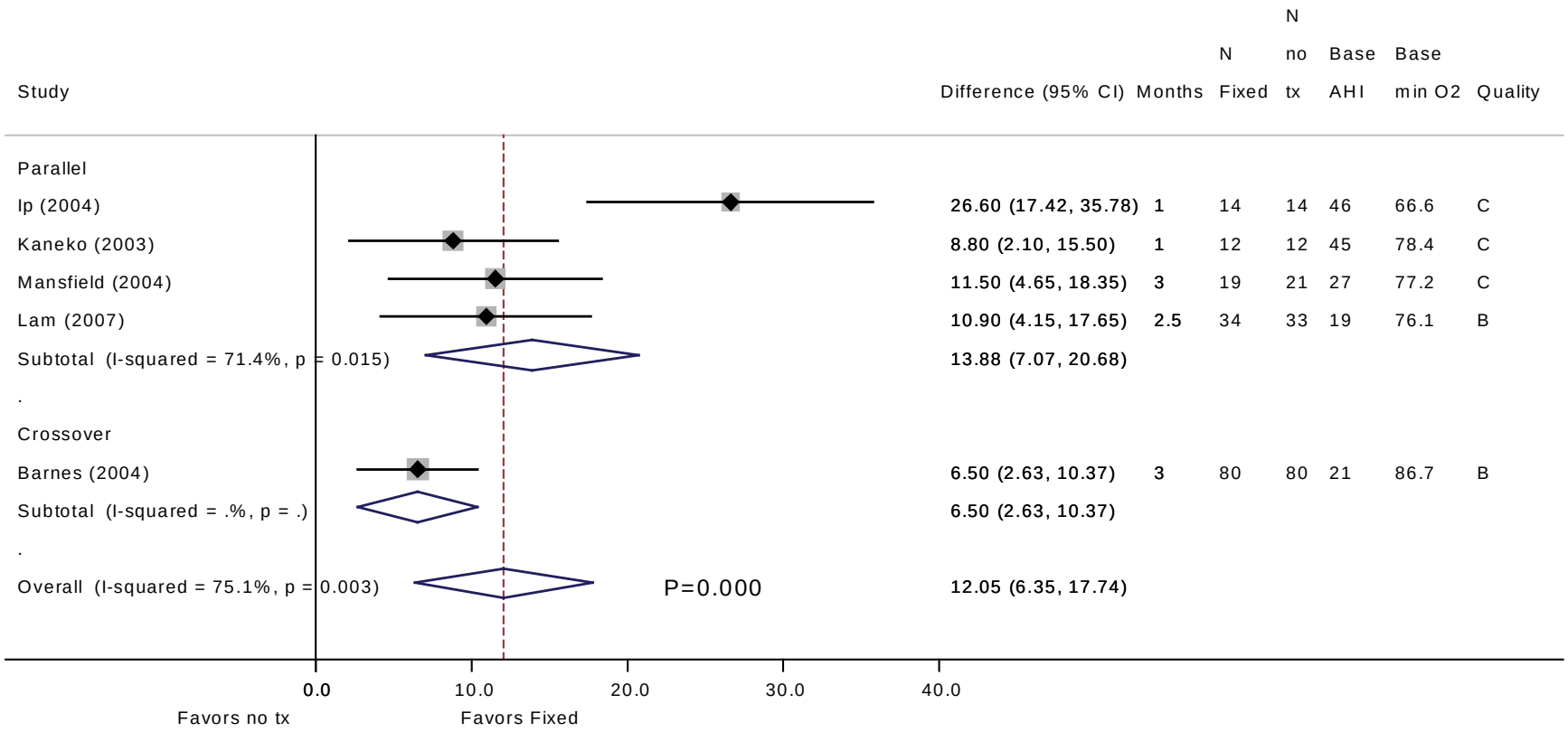
AHI = apnea-hypopnea index, CI = confidence interval, ESS = Epworth Sleepiness Scale, Fixed = fixed CPAP (continuous positive airway pressure), tx = treatment.

Figure 8. Meta-analysis of arousal index (events/hr) in randomized controlled trials of CPAP vs. control, by study design



AHI = apnea-hypopnea index, AI = arousal index, CI = confidence interval, Fixed = fixed CPAP (continuous positive airway pressure), tx = treatment.

Figure 9. Meta-analysis of minimum oxygen saturation (%) in randomized controlled trials of CPAP vs. control, by study design



AHI = apnea-hypopnea index, CI = confidence interval, Fixed = fixed CPAP (continuous positive airway pressure), min O2 = minimum oxygen saturation, tx = treatment.

Comparison of CPAP and Sham CPAP

There were 24 trials (reported in 30 articles) that compared CPAP devices with sham CPAP treatment (Appendix D Table 5.2.1).[141-170] Eighteen trials had a parallel design and six were crossover trials. The patients in these trials were treated with either fixed CPAP (8 trials[141,145,146,150,152,153,165,167]) or autoCPAP (16 trials[142-144,147-149,151,153-164,166,168-170]). In 19 of the 24 studies reviewed, it was reported that the CPAP was introduced on a separate full night from the night of the diagnostic sleep study.

Mean baseline AHI ranged from 22 to 68 events/hr; three trials included patients with an AHI ≥5 events/hr, five with an AHI ≥10, eight with an AHI ≥15, one with an AHI ≥20, one with an AHI ≥30, and six did not report a lower AHI threshold. Most trials had unrestrictive eligibility criteria. Exceptions were two studies (Egea 2008 and Smith 2007) that included only patients with stable and optimally-treated congestive heart failure, one study (Campos-Rodriguez 2006) that included only patients with primary hypertension and on hypertension treatment, and a final study (Robinson 2006) that included only hypertensive patients with significant OSA, but without sufficient daytime hypersomnolence. The reviewed studies were generally small with sample sizes ranging from 25 to 101 (total = 1,076 across studies), followed for 1 week to 3 months. Five studies were rated quality A, 13 studies quality B, and six studies quality C. The primary methodological concerns included small sample sizes with multiple comparisons, the lack of power calculations, high dropout rates, and incomplete reporting. Overall, the studies are applicable to a broad range of patients with OSA.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Apnea-Hypopnea Index (Appendix D Table 5.2.2; Figure 10)

Nine trials provided data on AHI comparing CPAP with sham CPAP.[143,147,148,153,157,160,163,167,169] All trials had a parallel design, all except one (Lam 2010) evaluated fixed CPAP, and reported that AHI was statistically significantly lower in patients on CPAP than those on sham treatment. The one RCT that evaluated autoCPAP[169] did not report sufficient data to estimate the effect size; thus it was not included in meta-analysis. Meta-analysis revealed that the difference in AHI between CPAP and control was statistically significant, favoring CPAP (difference = -46 events/hr; 95 percent CI -57, -36; P<0.001). However, the results were statistically heterogeneous. Subgroup meta-analysis by minimum threshold AHI for study eligibility revealed that there was no statistical heterogeneity among four studies (Haensel 2007, Mills 2006, Loredo 2006, Norman 2006) that included patients with an AHI of at least 15 events/hr (difference = -58; 95 percent CI -68, -49; P<0.001). This difference was significantly larger than one study (Egea 2008) that included patients with an AHI of at least 10 events/hr (-25; P<0.0001), and another study (Loredo 1999) that included patients with an AHI of at least 20 events/hr (-37; P=0.02). Similarly, subgroup meta-analysis of two studies (Becker 2003 and Spicuzza 2006) that included patients with an AHI of at least 5 events/hr showed a lower net difference of AHI (difference = -43; 95 percent CI -65, -21); however, this effect was not statistically significant in difference compared with the five studies that included patients with an AHI of at least 15 events/hr.

Epworth Sleepiness Scale (Appendix D Table 5.2.3; Figures 11 & 12)

Sixteen trials comparing CPAP with sham CPAP reported ESS data.[142-145,147,150,151,157,159,162,164-166,168-170] Eleven trials had a parallel design, and the remaining five had a crossover design. Five of the six trials comparing autoCPAP versus sham autoCPAP reported statistically significant differences on the ESS, while only six of the 10 trials comparing fixed CPAP versus sham CPAP reported statistically significant findings. Meta-analysis of all 16 studies showed a statistically significant difference between CPAP and sham control, favoring CPAP (difference = -2.5; 95 percent CI -3.5, -1.5; P<0.001). However, the results were statistically heterogeneous.

Subgroup meta-analyses by study designs (Figure 11), by types of CPAP (Figure 12), and by minimum threshold ESS for study eligibility were conducted to explore possible factors that could explain the heterogeneity. We found that the same pooled estimates by trial designs (parallel versus crossover: -2.5 versus -2.5) but significant different pooled estimates by types of CPAP (autoCPAP versus CPAP: -1.9 versus -2.8; P=0.05). Subgroup meta-analysis by minimum threshold AHI for study eligibility showed significant net differences on the ESS among three studies including patients with an AHI of at least 10 events/hr (difference = -3.6; 95 percent CI -6.4, -0.9; P=0.01), among four studies including patients with an AHI of at least 15 events/hr (difference = -1.2; 95 percent CI -3.5, -0.3; P=0.02). The difference between the two subgroups (AHI ≥10 versus AHI ≥15) was marginally significant (P=0.08). However, the subgroup meta-analysis did not show significant differences on the ESS in two studies (Hui 2006 and Becker 2003) that included patients with an AHI of at least 5 events/hr (difference = -2.1; 95 percent CI -6.1, 1.9)

Other Sleep Study Measures (Appendix D Tables 5.2.4-5.2.7; Figure 13)

Three trials evaluated arousal index.[143,153,157] All three had a parallel design and evaluated fixed CPAP, and all three studies found greater reductions in arousal index for the CPAP arm. In one study (Becker 2003), however, this difference was not statistically significant. Meta-analysis revealed that arousals were significantly more reduced while using CPAP as compared with sham CPAP (difference = -27 events/hr; 95 percent CI -42, -12; P<0.001). Study results were significantly heterogeneous.

Only one trial evaluated minimum oxygen saturation; no significant difference in minimum oxygen saturation was observed in a comparison of CPAP with sham CPAP.[143] This trial was rated quality C due to a small sample size without a power calculation and a high dropout rate.

Sleep efficiency (measured as percent of total sleep time) was evaluated by two studies, neither of which detected a significant effect of CPAP treatment.[148,153] Four studies examined whether CPAP treatment increased the time in slow wave sleep (in absolute number of minutes or as a percentage of total sleep time) compared with sham CPAP, and all found no significant effect.[143,147,153,157] The same four studies also evaluated the outcome of REM sleep (expressed in absolute number of minutes or as a percentage of total sleep time). Three of the four studies did not find a significant effect of CPAP treatment; the other (Loredo 2006) reported that CPAP treatment significantly increased the time in REM sleep (difference = 7.5 percent of total sleep time; 95 percent CI 3.5, 11.5; P<0.05).

Objective Sleepiness and Wakefulness Tests (Appendix D Table 5.2.8)

One study evaluated the Multiple Sleep Latency Test outcome and found no significant difference in sleep latency test score comparing CPAP with sham CPAP.[142] Four studies evaluated the Maintenance of Wakefulness Test outcome,[151,159,168,170] with two reporting a statistically significant result, favoring autoCPAP. The remaining study (Marshall 2005) also showed a marginally significant increase in time maintaining alertness during the day in comparing CPAP with sham CPAP (P=0.09).

Quality of Life (Appendix D Tables 5.2.9 & 5.2.10)

Three studies administered the Functional Outcomes of Sleep Questionnaire (FOSQ), and all found no significant difference in test scores comparing CPAP with sham CPAP.[142,159,162]

Six studies (two using autoCPAP and four CPAP) measured quality of life using SF-36.[142,147,159,162,165,166] Five of the six studies did not find significant differences in physical and mental health component summary scores. The remaining study (Siccolli 2008) reported that patients who received autoCPAP treatment had significantly increased physical and mental health component summary scores compared with those who received sham treatment (differences = 8.2 and 10.8; P=0.01 and P=0.002, respectively) This study also found a similar result for the SAQLI summary score (difference = 0.9; P=0.001).

Neurocognitive and Psychological Tests (Appendix D Table 5.2.11)

Seven studies evaluated neurocognitive and psychological tests,[142,148,149,153,157,159,160] Of the 26 comparisons between CPAP and sham CPAP, a significant difference was detected only in one comparison of the digit vigilance test (measure of sustained attention and psychomotor speed) in one study, favoring CPAP.[160]

Blood Pressure (Appendix D Table 5.2.12)

Comparisons of daytime or nighttime blood pressure measurements between CPAP-treated patients and patients on sham CPAP were reported by 12 studies.[141-147,150,160,163,163,164,169] Six of these studies reported mean arterial pressure, and 10 reported systolic and diastolic blood pressure. The results were inconsistent across studies. About half of the studies reported significant blood pressure reduction favoring CPAP, and the other half reported no significant differences.

Study Variability

One study conducted a subgroup analysis of patients who had good compliance to CPAP use (≥3.5 hr/night) and found similar outcomes on the ESS and in blood pressure, favoring autoCPAP as compared with sham CPAP.[145] Trends toward larger reductions in blood pressure outcomes among this subgroup of patients were observed; however, the study did not perform a statistical analysis to test the differences between patients with good compliance and those with poor compliance.

For the main sleep study outcomes of interest (AHI, ESS, minimum oxygen saturation, and arousal index), the studies reviewed were generally consistent in their findings, showing a beneficial effect of CPAP intervention. However, our meta-analysis showed that the results of the studies were heterogeneous in terms of the magnitude of their detected effects. In subgroup meta-analyses by study designs, by types of CPAP, and by minimum threshold AHI for study eligibility to explore possible factors that may explain the heterogeneity, only minimum

threshold AHI for study eligibility could account for some of the observed heterogeneity. However, no consistent patterns were seen with regard to the impacts of minimum threshold AHI for study eligibility on the main sleep study outcomes.

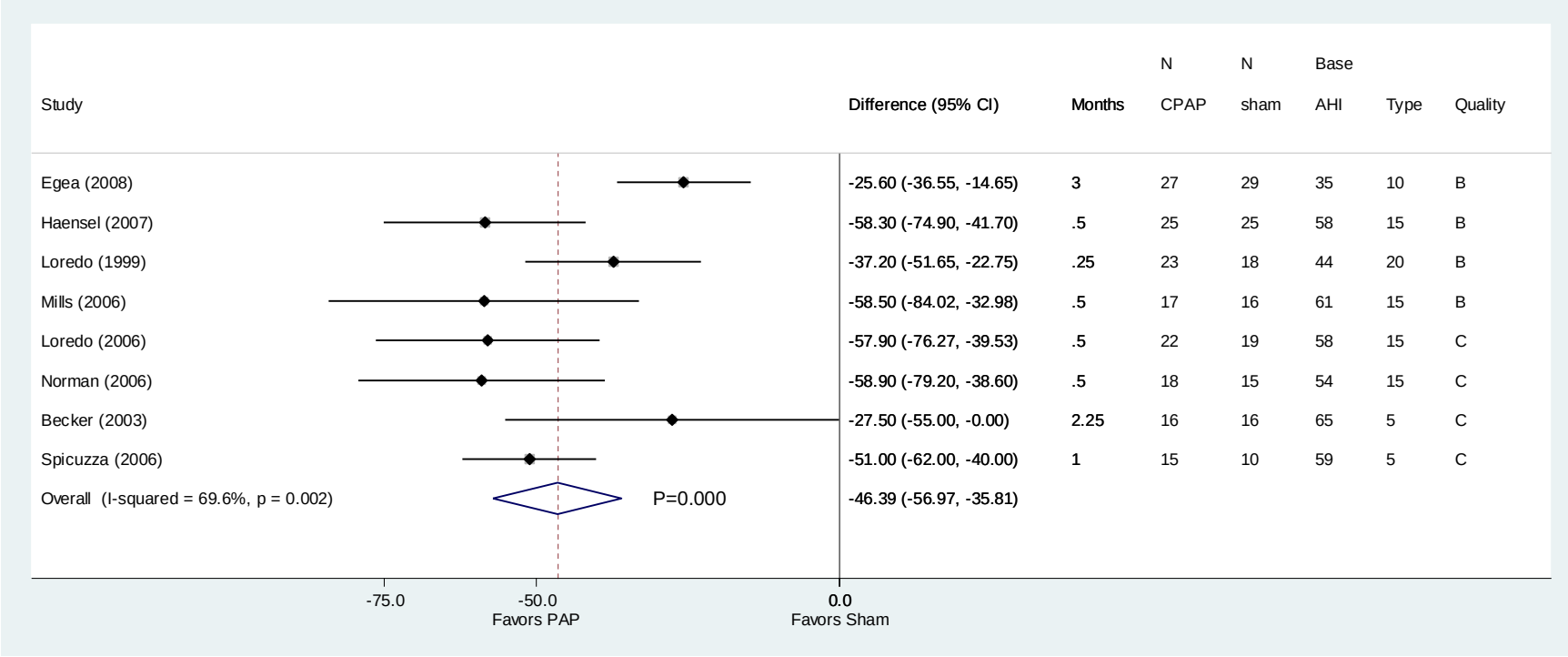
Regarding quality of life and neurocognitive outcomes, few studies used a wide range of tests and outcomes. In most cases, these outcomes were explored as secondary endpoints. Most of the comparisons performed did not reach statistical significance.

Summary

Five quality A, 13 quality B, and six quality C trials compared autoCPAP (16 trials) or fixed CPAP (8 trials) with sham treatments. The reviewed studies generally found that CPAP was superior in reducing AHI, improving ESS, and reducing arousal index. These findings were confirmed by meta-analysis, although the studies' results were statistically heterogeneous. There was evidence that the magnitude of the demonstrated efficacy of CPAP treatment may have been influenced by baseline severity of disease, although no consistent patterns were observed regarding the impacts of baseline severity of disease on the main sleep study outcomes. Most studies did not find a significant effect of CPAP versus sham in improving other sleep study measures (slow wave and REM sleep, Multiple Sleep Latency Test), but a small number of studies did show CPAP to significantly improve Maintenance of Wakefulness Test measures. Most studies also found no significant difference in effects on quality of life or neurocognitive function. The effects of CPAP on blood pressure outcomes were mixed. About half of the studies reported significant blood pressure reduction, favoring CPAP, and the other half reported no significant differences. No study evaluated objective clinical outcomes.

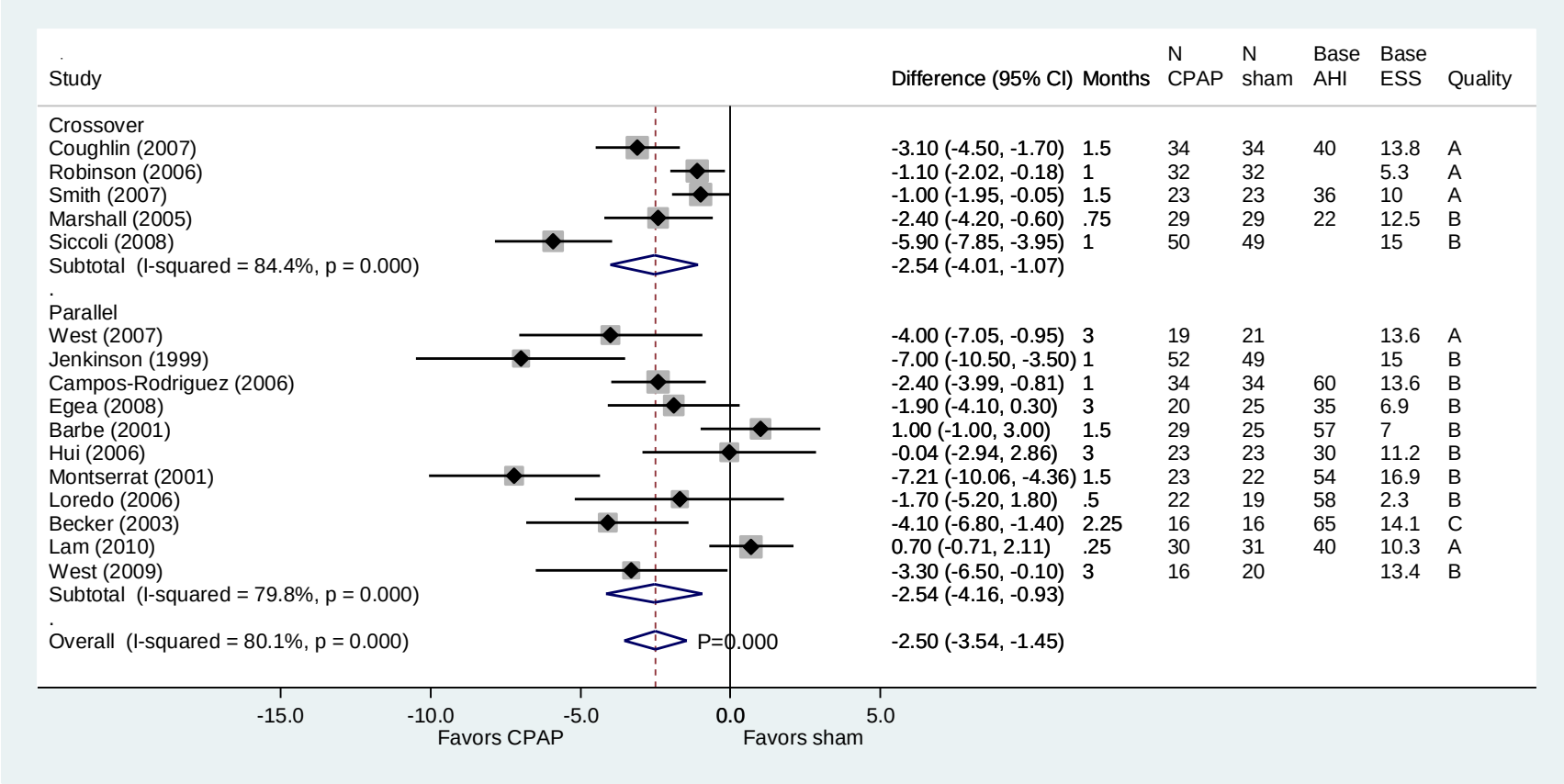
There was sufficient evidence supporting large improvements in sleep measures with CPAP compared with sham CPAP, but weak evidence that there is no difference between CPAP and sham CPAP in improving quality of life, neurocognitive measures, or other intermediate outcomes. Despite no or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI, ESS, and arousal index, the evidence that CPAP is an effective treatment for the relief of signs and symptoms of sleep apnea was rated moderate.

Figure 10. Meta-analysis of AHI (events/hr) in randomized controlled trials of CPAP vs. sham CPAP



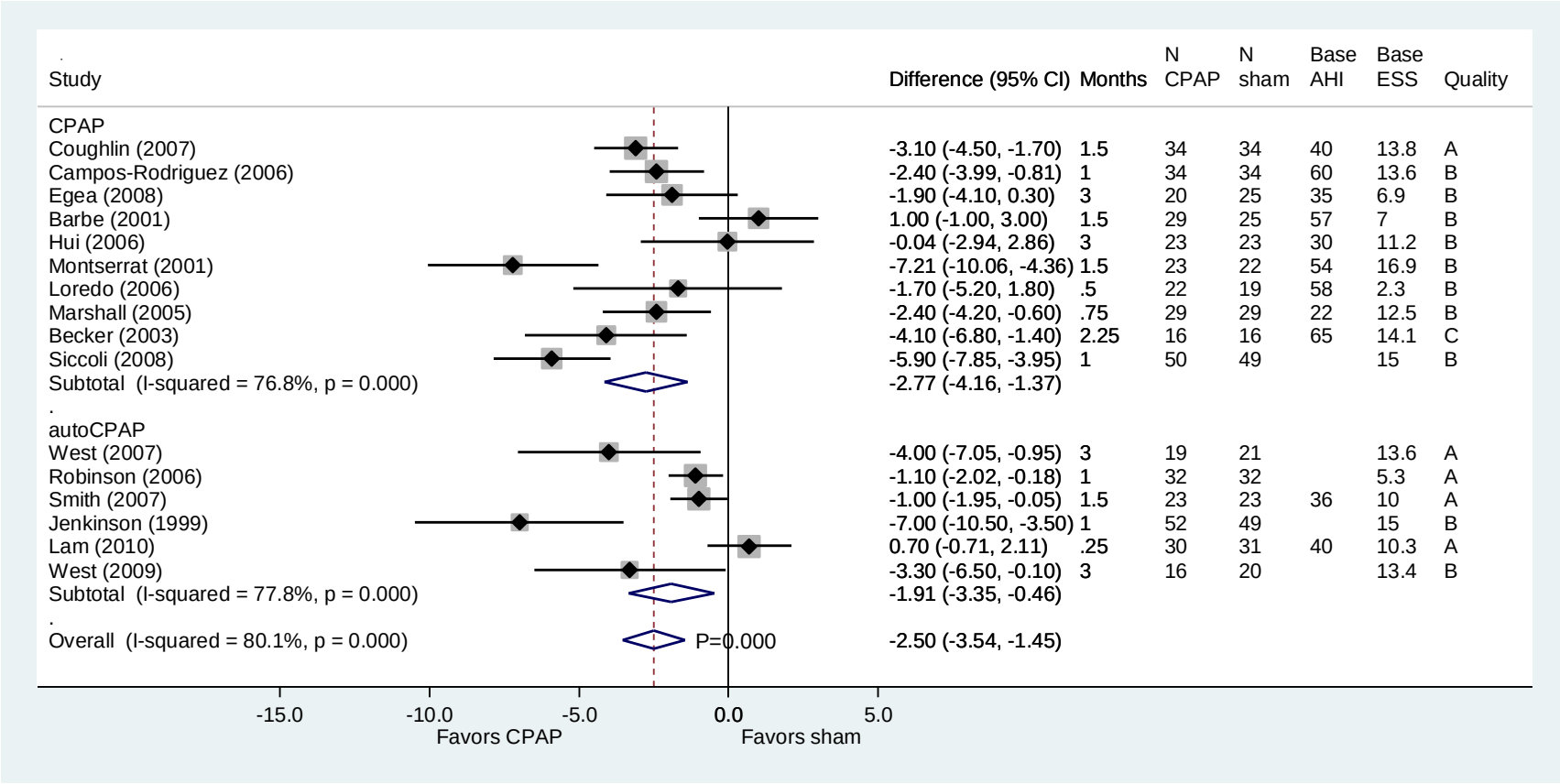
AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure.

Figure 11. Meta-analysis of ESS in randomized controlled trials of CPAP vs. sham CPAP, by study design



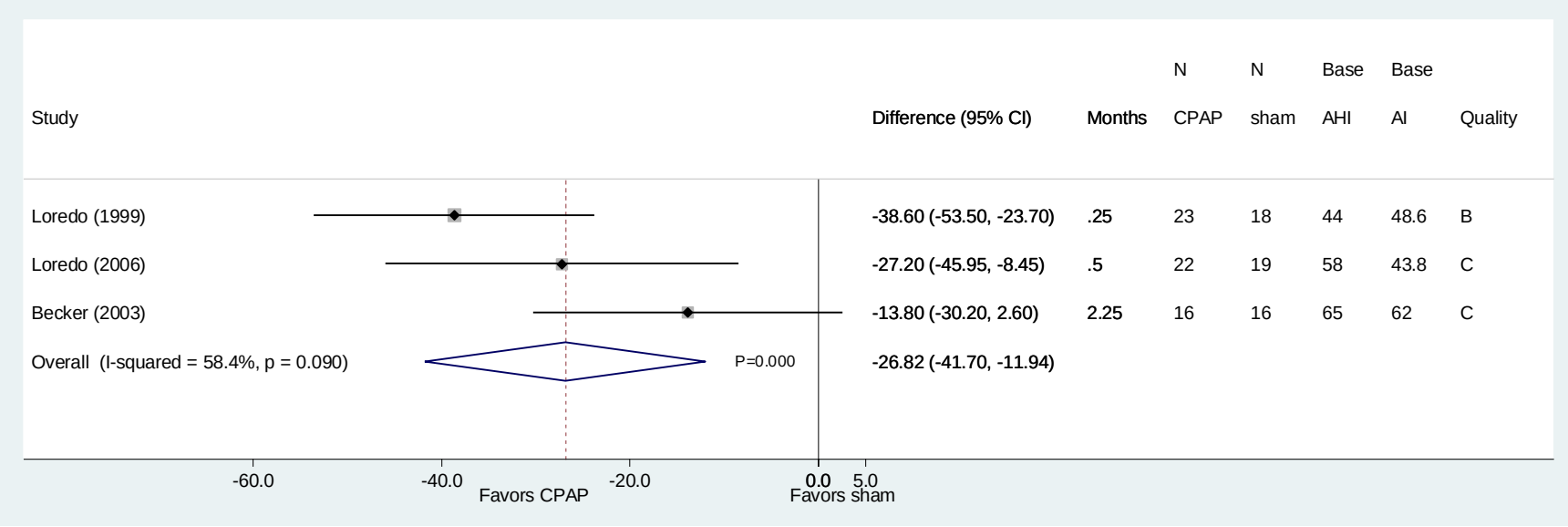
AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure.

Figure 12. Meta-analysis of ESS in randomized controlled trials of CPAP vs. sham CPAP, by type of CPAP



AHI = apnea-hypopnea index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale.

Figure 13. Meta-analysis of arousal index (events/hr) in randomized controlled trials of CPAP vs. sham CPAP



AHI = apnea-hypopnea index, AI = arousal index, CI = confidence interval, CPAP = continuous positive airway pressure.

Comparison of Oral and Nasal CPAP

One crossover trial[171] and one parallel trial[173] compared oral with nasal CPAP; one crossover trial[172] compared a face mask (covering both nose and mouth) with a nasal mask (Appendix D Table 5.3.1). Mean baseline AHI or respiratory disturbance index (RDI) in the studies were 35, 61, and 85 events/hr. Most included patients were obese; the mean body mass index (BMI) across studies ranged from 32 to 43 kg/m^2. None of the studies selectively focused on patients with other comorbidities. Study sample sizes ranged from 20 to 42 (total = 87 across studies).The duration of intervention was 1 month in two studies and 2 months in one study. One study was rated quality B and two were rated quality C. Small sample sizes and incomplete reporting were the main methodological concerns. These studies are applicable mainly to patients with AHI more than 30 events/hr and BMI more than 30 kg/m^2.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance (Appendix D Table 5.3.2)

All three trials provided data on compliance. Mortimore 1998 reported a significant difference in compliance (hours of use per night) favoring nasal CPAP over face mask (nose and mouth) CPAP at 1 month (mean difference 1 hr/night; 95 percent CI 0.3, 1.8; P=0.01).[172] The other two studies did not find a significant difference in the number of hours of use with oral or nasal CPAP.

Epworth Sleepiness Scale (Appendix D Table 5.3.3)

Two trials provided data on daytime sleepiness as assessed using ESS.[171,172] Anderson 2003 reported that both oral and nasal CPAP decreased daytime sleepiness, but that the difference between the two was not significant.[171] Mortimore 1998 did not provide baseline ESS data, but reported that patients in the face mask group had scored significantly higher on the ESS than those in the nasal group at followup (9.8 versus 8.2; P<0.01).

Other Outcomes

Anderson 2003 also provided outcomes on AHI, minimum oxygen saturation, arousal index, REM sleep, and sleep efficiency. The difference between oral and nasal CPAP was not statistically significant for any of these measures. Changes after 1 month within the two arms (oral versus nasal CPAP) were: -69 versus -74 events/hr for AHI; 16 versus 17 percent minimum for oxygen saturation; -54 versus -57 events/hr for arousal index; 16 versus 12 percent of total sleep time for REM sleep; and 11 versus 10 percent of total sleep time for sleep efficiency.

Study Variability

No study reported subgroup analyses with respect to the comparative effect of oral versus nasal CPAP for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway) or severity of OSA. The two studies that described minimum AHI or RDI enrollment criteria did not examine the same efficacy outcomes.[171,173] No conclusions could be drawn regarding indirect comparisons across studies on different patient characteristics or minimum AHI or RDI enrollment criteria.

Summary

Three small trials with inconsistent results preclude any substantive conclusions concerning the efficacy of oral versus nasal CPAP in improving compliance in patients with OSA. Largely due to small sample size, the reported effect estimates in the studies reviewed were generally imprecise. Thus, overall, the strength of evidence is insufficient regarding differences in compliance or other outcomes between oral and nasal CPAP.

Comparison of Autotitrating CPAP and Fixed CPAP

We found 21 RCTs that compared autoCPAP with fixed CPAP treatment in patients with OSA (Appendix D Table 5.4.1).[174-194] Fourteen used a crossover design and seven a parallel design. Across studies, patients' mean AHI ranged from 15 to 55 events/hr. All the studies reviewed included patients who were either overweight or obese (body mass index [BMI] ranged from 29.9 to 42 kg/m^2). None of the studies selectively focused on patients with other comorbidities. Study sample sizes ranged from 10 to 181 (total = 844 across studies). Study durations ranged from 0.75 to 9 months, the majority no longer than 3 months. One was rated quality A, 10 were rated quality B, and 10 quality C. Small sample sizes and incomplete data reporting were the main methodological concerns. These studies are applicable mainly to patients with AHI more than 15 events/hr and BMI more than 30 kg/m^2.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance (Appendix D Table 5.4.2; Figure 14)

All 21 studies provided data on compliance. Seventeen studies did not find statistically significant differences in device usage (hours used per night) between autoCPAP and CPAP; four studies reported a significant increase in the use of autoCPAP compared with CPAP.[181,182,186,194] Meta-analysis revealed a statistically significant, but clinically marginal difference of 11 minutes per night favoring autoCPAP (difference = 0.19 hr; 95 percent CI 0.06, 0.33; P=0.006), without statistical heterogeneity.

Apnea-Hypopnea Index (Appendix D Table 5.4.3; Figure 15)

Fourteen studies provided sufficient data on AHI after treatment.[174-180,184,186,188-190,192,193] Meta-analysis across all studies indicated a difference between autoCPAP and CPAP of 0.23 events/hr (95 percent CI -0.18, 0.64; P=0.27). The crossover and parallel design studies found similar results via meta-analysis (no significant difference by t test). No statistically significant heterogeneity was observed across studies, despite a broad range in the severity of OSA.

Epworth Sleepiness Scale (Appendix D Table 5.4.4; Figure 16)

Seventeen studies provided sufficient ESS data for meta-analysis.[174,176-179,181,182,184-191,193,194] Meta-analysis across all studies yielded a difference between autoCPAP and CPAP of -0.48 (95 percent CI -0.86, -0.11; P=0.012), favoring autoCPAP. No significant difference between the study designs was shown by t- test. Despite the broad range of severity of OSA across studies, there was no statistically significant heterogeneity within the overall meta-analysis.

Arousal Index (Appendix D Table 5.4.5; Figure 17)

Seven studies provided sufficient data on arousal index after treatment.[174,176,178,184,188,190,193] Meta-analysis showed a difference of -1.09 events/hr (95 percent CI -2.4, 0.2; P=0.10), favoring autoCPAP. The summary estimates for the subgroups of studies with crossover or parallel designs were different, but neither found a statistically significant difference. Due to the large confidence intervals, no significant difference between the crossover and parallel design trials was shown (t-test, P=0.38). There was also no statistically significant heterogeneity within the overall meta-analysis as well as the subanalyses.

Minimum Oxygen Saturation (Appendix D Table 5.4.6; Figure 18)

Seven studies provided sufficient data on minimum oxygen saturation after treatment.[176-178,180,184,188,190] Meta-analysis of these trials resulted in a difference between autoCPAP and CPAP of -1.3 percent total sleep time (95 percent CI -2.2, -0.5; P=0.03), favoring CPAP. The crossover and parallel design trials had similar results. There was no statistically significant heterogeneity within the overall meta-analysis.

Sleep Efficiency (Appendix D Table 5.4.7)

Two studies provided data on sleep efficiency.[178,188] Both found no statistically significant difference between autoCPAP and CPAP for the improvement of sleep efficiency.

REM Sleep (Appendix D Table 5.4.8)

Seven studies provided data on REM sleep.[177,178,184,188,190,191,193] All but one study found no statistically significant difference between autoCPAP and CPAP for REM sleep. Only Nolan 2007 reported a greater reduction in REM sleep in patients treated with autoCPAP compared with those treated with CPAP (-0.5 versus +2 percent total sleep time; P=0.06).

Stage 3 or 4 sleep (Appendix D Table 5.4.9)

Six studies provided data on slow wave sleep (stage 3 or 4).[177,178,184,188,190,191] All reported no statistically significant difference between autoCPAP and CPAP for Stage 3 or 4 sleep.

Quality of Life (Appendix D Table 5.4.10)

Eight studies provided data on quality of life.[175,177,179,181,183,186,189,194] Seven used SF-36; one used the Sleep Apnea Quality of Life Index (SAQLI);[181] and two also added a modified Osler test.[189,194] Massie 2003 found a significant difference in the mental health (net difference 5; 95 percent CI 0.16, 9.8; P<0.05) and vitality (net difference 7; 95 percent CI 0.6, 13.4; P<0.05) components of SF-36, favoring those who had autoCPAP.[186] No other significant differences in quality of life measures between autoCPAP and CPAP were reported in the reviewed studies.

Blood Pressure (Appendix D Table 5.4.11)

Two studies reported changes in blood pressure.[178,180] Patruno 2007 reported significant reductions between baseline and followup in systolic and diastolic blood pressure in patients on CPAP, but not in those on autoCPAP; however, the study did not report a statistical analysis of the difference between the two interventions. Our estimates, based on the reported data, suggest a nonsignificant greater reduction in systolic blood pressure (net difference = 6 mm Hg; 95 percent CI -0.9, 12.9; P=0.09) and a significant greater reduction in diastolic blood pressure (net difference = 7.5 mm Hg; 95 percent CI 4.2, 10.8; P<0.001) with CPAP as compared to

autoCPAP. Nolan 2007 reported no significant differences in systolic and diastolic blood pressure changes between autoCPAP and CPAP; however, no quantitative data were provided.

Study Variability

No study reported subgroup analyses with respect to the comparative effect of autoCPAP versus CPAP for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway characteristics) or severity of OSA. Only one study explicitly defined OSA.[185] Most other studies, though, provided explicit study enrollment criteria based on a minimum AHI threshold.

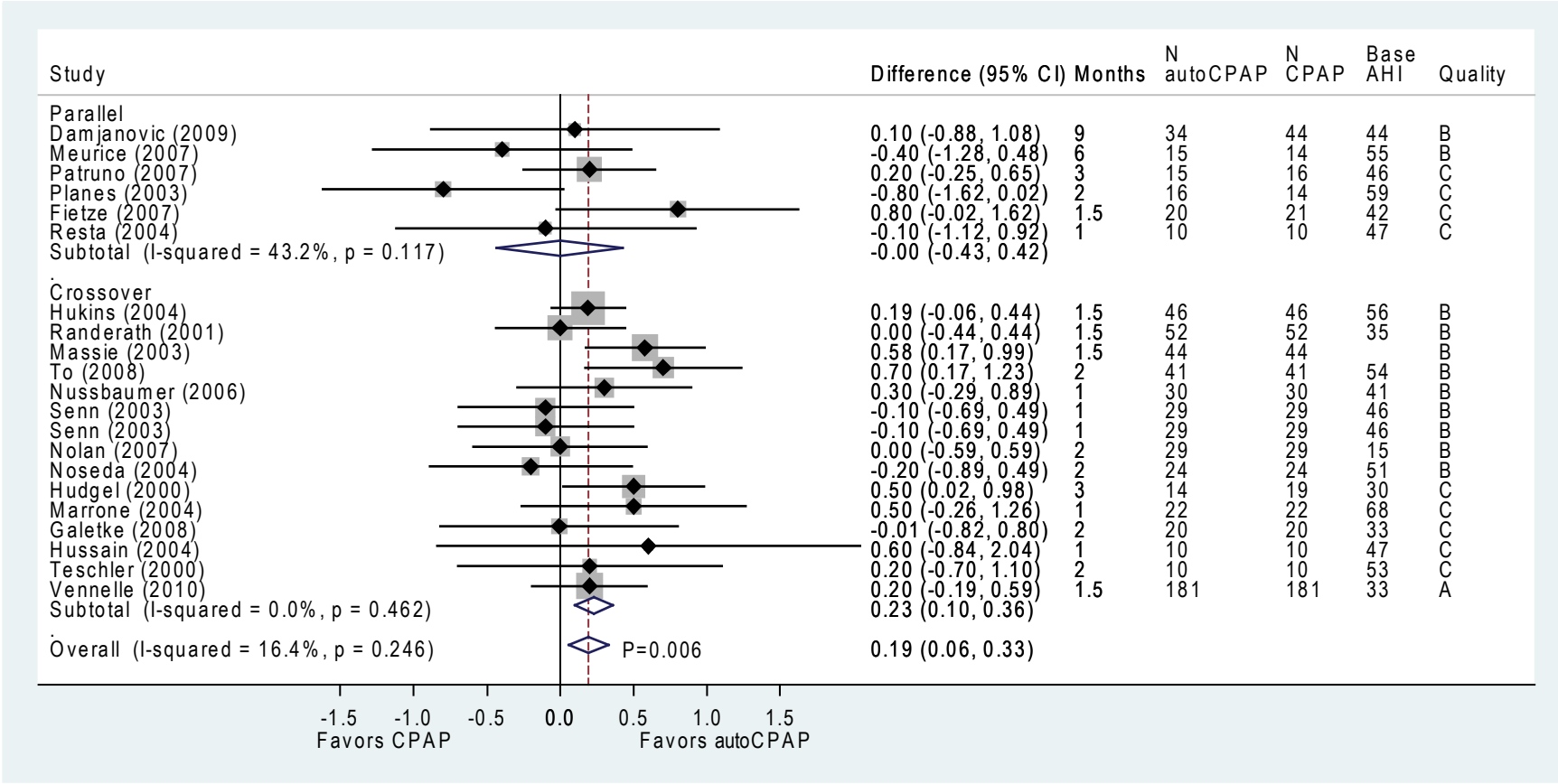
We performed subgroup meta-analyses stratified by different minimum AHI threshold for the AHI and ESS outcomes. No apparent difference in AHI outcomes was observed between autoCPAP and CPAP within any of the AHI subgroups (5, 10, 15, 20, or 30 events/hr). For the ESS, there were significant differences in favor of autoCPAP for the AHI subgroups of 20 and 30 events/hr, but not for the subgroups of studies that included patients with a lower AHI.

Summary

Twenty-one studies (mostly quality B or C) comprising an experimental population of over 800 patients provided evidence that autoCPAP reduces sleepiness as measured by ESS by approximately 0.5 points more than fixed CPAP. The two devices were found to result in clinically similar levels of compliance (hours used per night) and changes in AHI from baseline, quality of life, and most other sleep study measures. However, there is also evidence that minimum oxygen saturation improves more with CPAP than with autoCPAP, although by only about 1 percent. Evidence is limited regarding the relative effect of CPAP and autoCPAP on blood pressure.

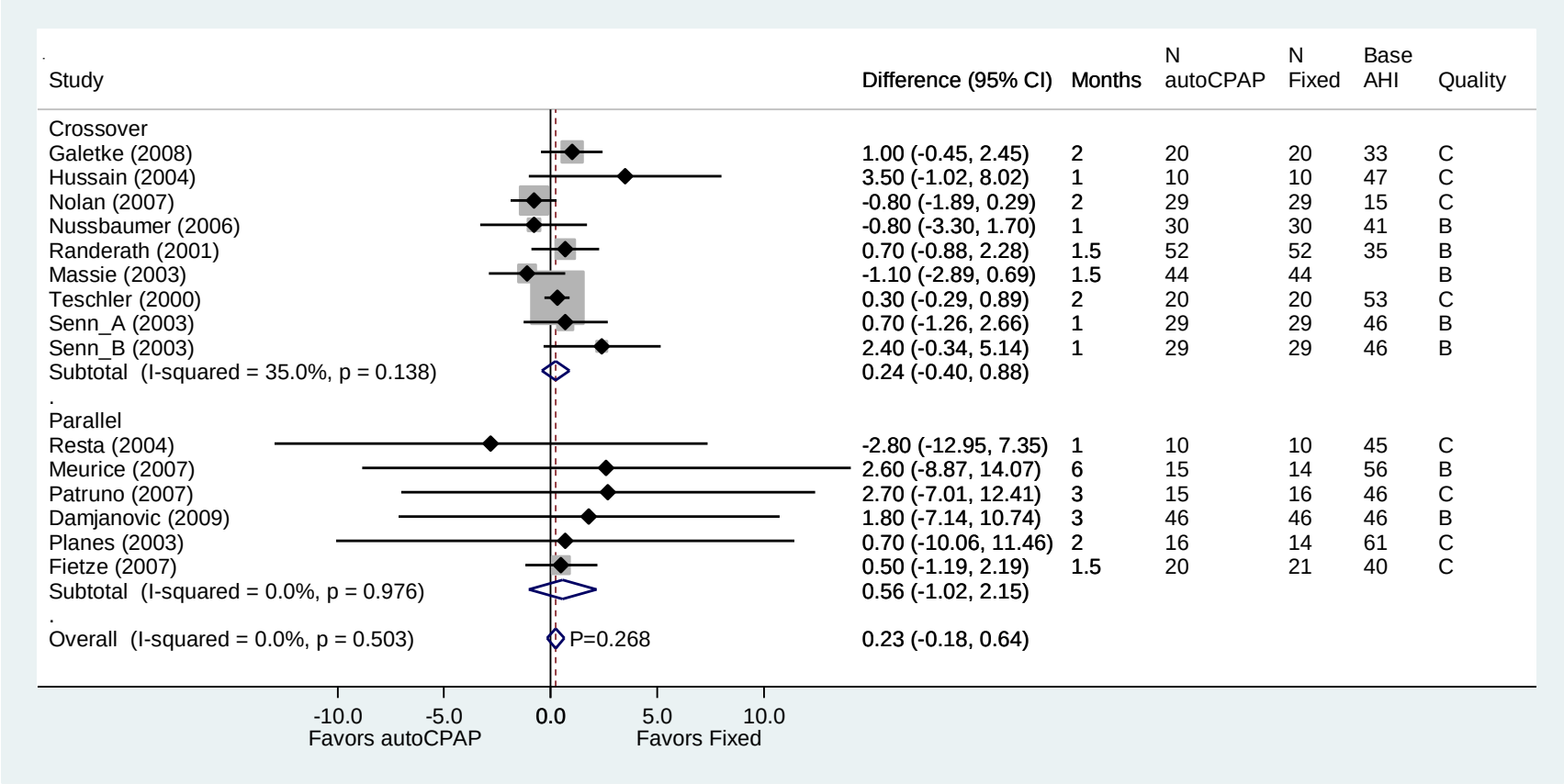
Overall, despite no or weak evidence on clinical outcomes, overall the strength of evidence is moderate that autoCPAP and fixed CPAP result in similar compliance and treatment effects for patients with OSA.

Figure 14. Meta-analysis of CPAP compliance (hr/night) in randomized controlled trials of autoCPAP vs. CPAP, by study design



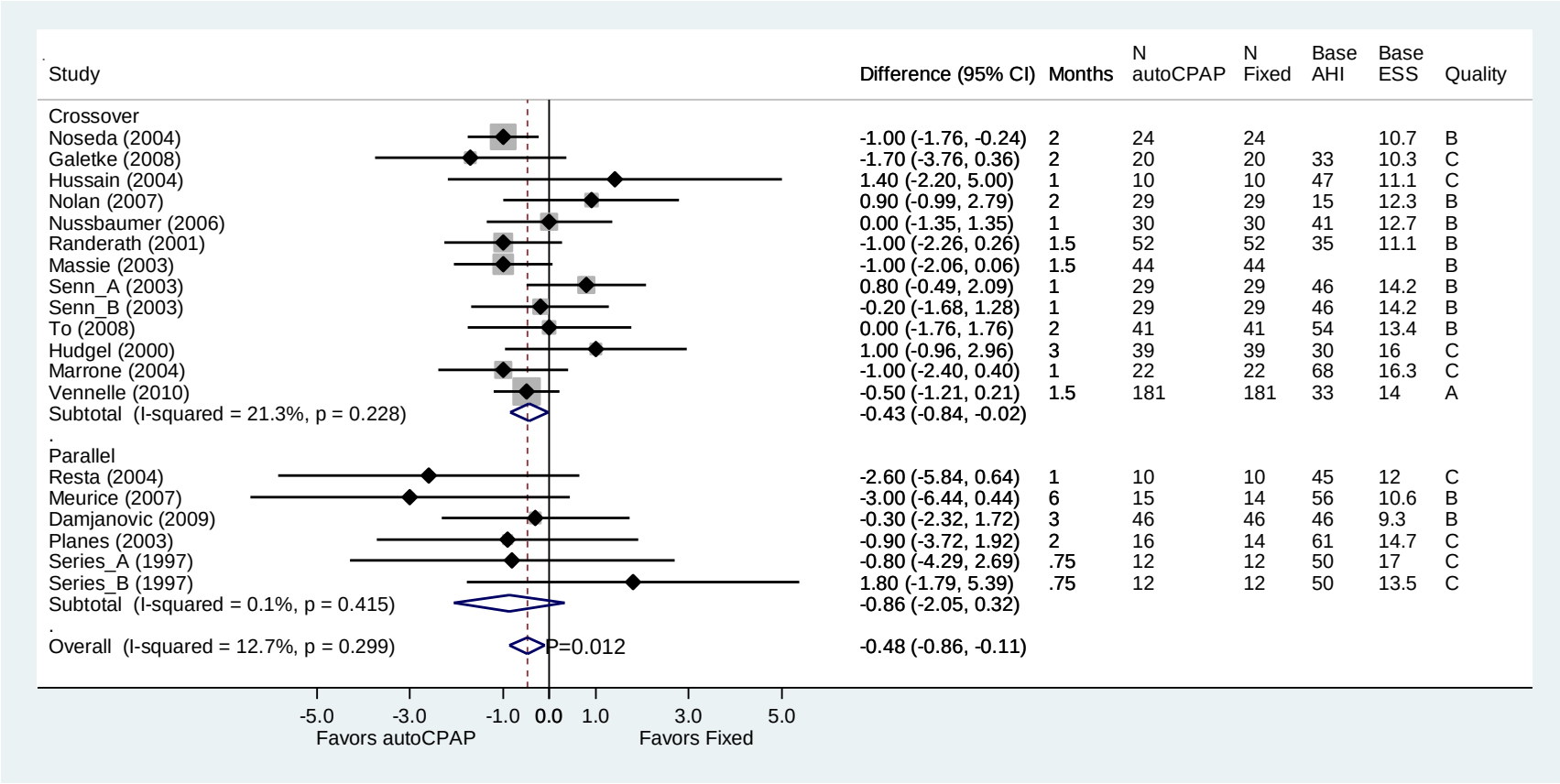
AHI = apnea-hypopnea index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure.

Figure 15. Meta-analysis of AHI (events/hr) in randomized controlled trials of autoCPAP vs. CPAP, by study design



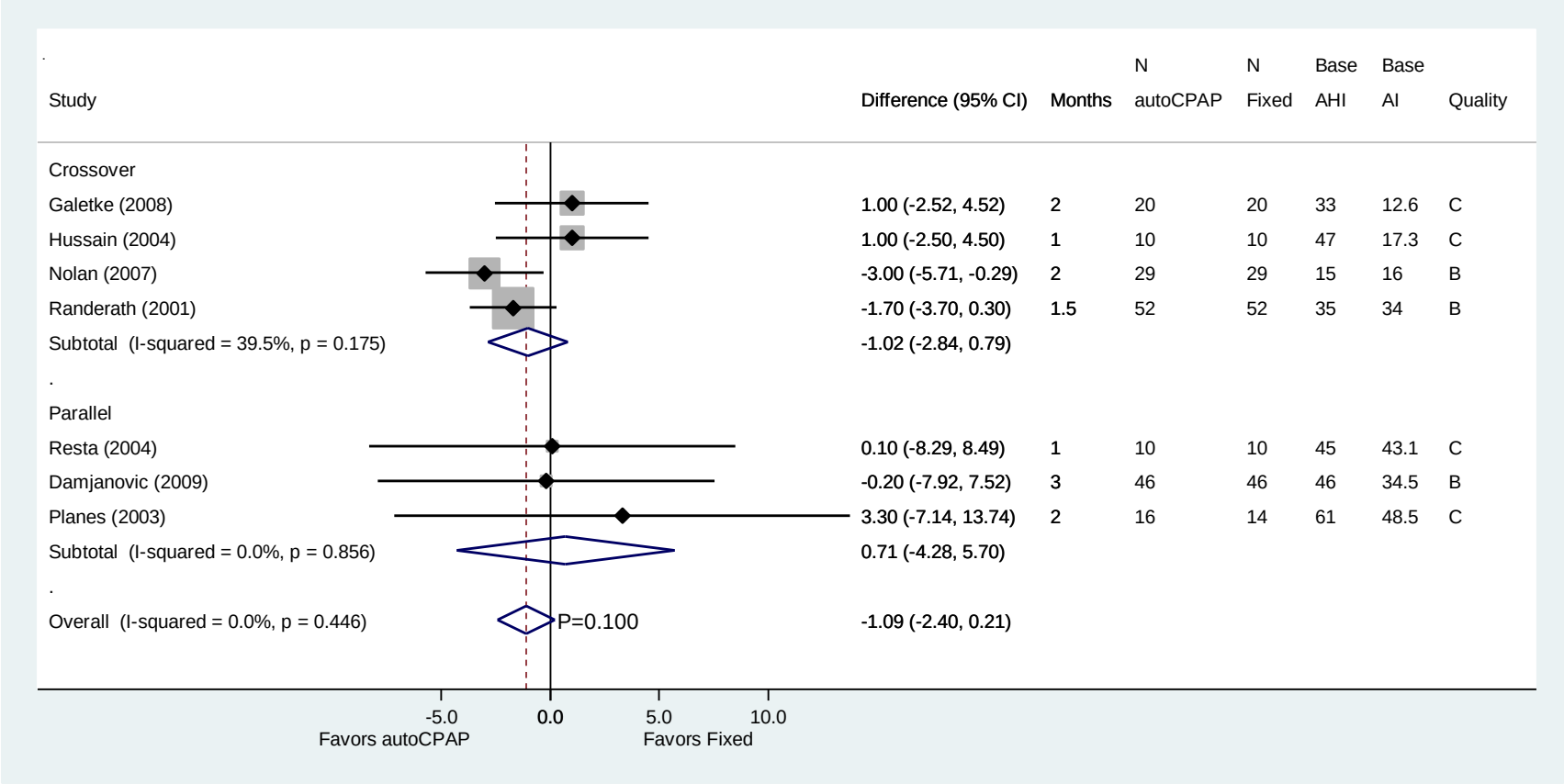
AHI = apnea-hypopnea index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, Fixed = fixed pressure CPAP.

Figure 16. Meta-analysis of ESS in randomized controlled trials of autoCPAP vs. CPAP, by study design



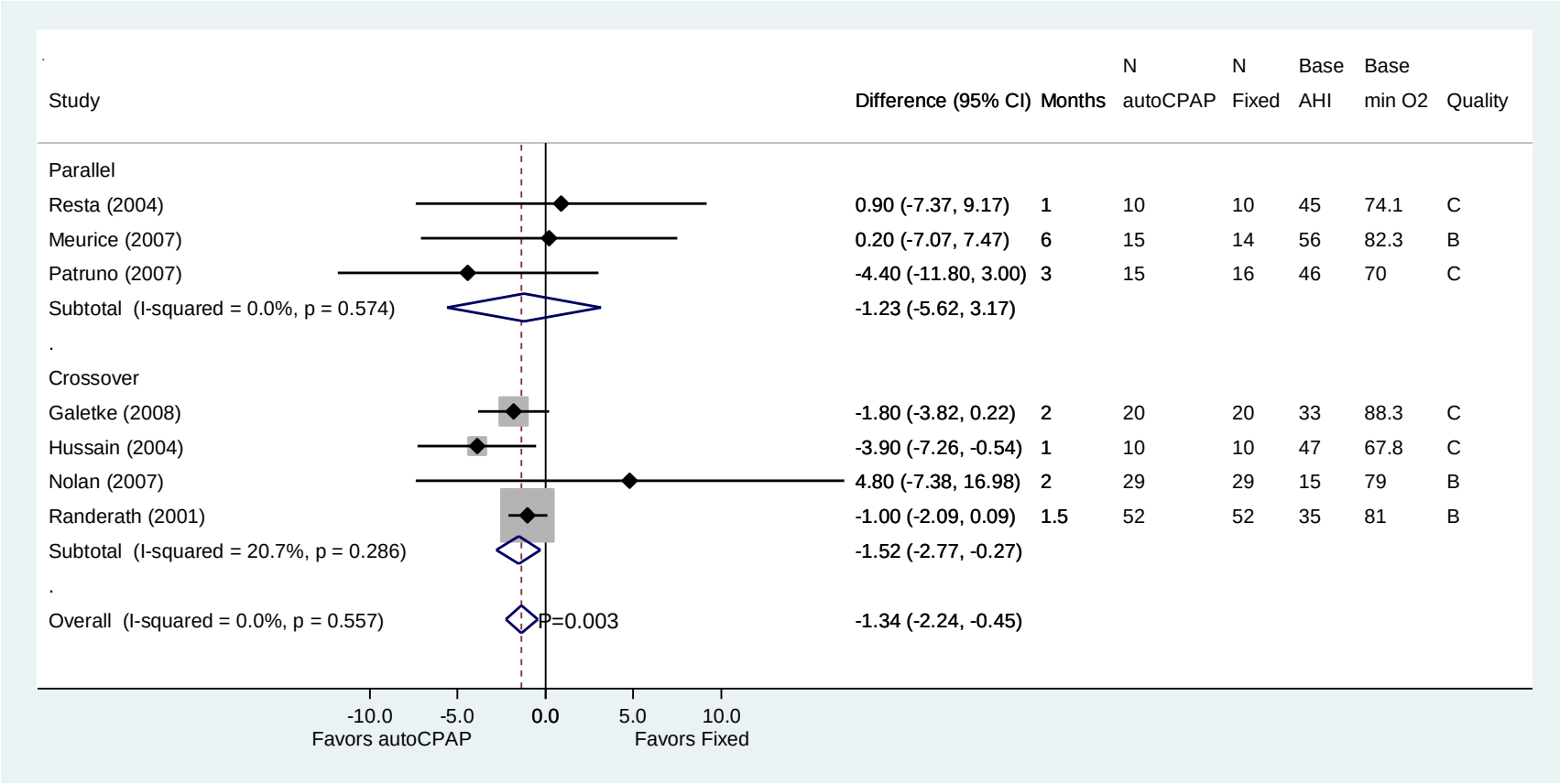
AHI = apnea-hypopnea index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, Fixed = fixed pressure CPAP.

Figure 17. Meta-analysis of arousal index (events/hr) in randomized controlled trials of autoCPAP vs. CPAP, by study design



AHI = apnea-hypopnea index, AI = arousal index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, Fixed = fixed pressure CPAP.

Figure 18. Meta-analysis of minimum oxygen saturation (%) in randomized controlled trials of autoCPAP vs. CPAP, by study design



AHI = apnea-hypopnea index, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, Fixed = fixed pressure CPAP, min O2 = minimum oxygen saturation.

Comparison of Bilevel CPAP and Fixed CPAP

Four parallel trials compared bilevel CPAP with fixed CPAP[195-198] and one crossover trial compared bilevel CPAP with autoCPAP, in patients with OSA (Appendix D Table 5.5.1).[199] Baseline AHI in the four studies with reported data ranged from 32 to 52 events/hr. Piper 2008 included patients with concomitant morbid obesity (mean BMI = 53 kg/m^2) and obesity hypoventilation syndrome. Khayat 2008 included patients with concomitant heart failure (American Heart Association class II or III). Gay 2003 enrolled patients without comorbidities. About 10 percent of the patients in Reeves-Hoche 1995 had restrictive lung pattern on pulmonary function tests secondary to obesity. In the bilevel CPAP versus autoCPAP study, Randerath 2003 specifically enrolled patients who did not tolerate conventional CPAP. Study sample sizes ranged from 24 to 83 (total = 197 across studies). Study durations ranged from 1 to 12 months. One study was rated quality B[197] and the remaining four were rated quality C.[195,196,198,199] Small sample sizes and possible selection bias were the main methodological concerns. These studies are applicable mainly to patients with AHI more than 30 events/hr. Individual studies are applicable to patients with morbid obesity, heart failure, or no comorbidities. Only one study was restricted to patients who did not tolerate fixed CPAP.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance (Appendix D Table 5.5.2)

All five trials provided data on compliance. None of them found a statistically significant difference in usage of the machine (hours used per night or percent days used) between bilevel CPAP and CPAP, or bilevel CPAP and autoCPAP, at followup. Piper 2008 and Gay 2003 reported that patients used the devices for about 6 hours a night, on average, Reeves-Hoche 1995 about 5 hours a night, and Khayat 2008 about 4 hours a night. Randerath 2003 reported that the patients used the machines about 90 percent of the time.

Apnea-Hypopnea Index

Two trials provided data on AHI outcome.[196,199] Khayat 2008 reported that both bilevel CPAP and CPAP decreased AHI after 3 months (-34 versus -26 events/hr, respectively). Randerath 2003 reported that both bilevel CPAP and autoCPAP decreased AHI after 1.5 months (-39 versus -35 events/hr, respectively). The difference between bilevel CPAP and CPAP or autoCPAP was not statistically significant in either trial.

Epworth Sleepiness Scale (Appendix D Table 5.5.3)

Four trials provided data on changes in daytime sleepiness as assessed using ESS.[195-197,199] Each reported that both bilevel CPAP and CPAP decreased daytime sleepiness. The difference between bilevel CPAP and CPAP was not statistically significant in any trial.

Other Sleep Study Measures

Randerath 2003 also provided outcomes on minimum oxygen saturation, arousals, and sleep stages.[199] The difference between bilevel CPAP and autoCPAP was not statistically significant in any of these measures. Changes after 1.5 months within the two arms (bilevel CPAP versus autoCPAP) were 7.4 versus 9.4 percent for minimum oxygen saturation, -25.3 versus -22.5

events/hr for arousal index, -1 versus 0 percent of total sleep time for REM sleep, and 7.8 versus 4.7 percent of total sleep time for stages 3 or 4 sleep, respectively.

Quality of Life and Other Functional Outcomes (Appendix D Table 5.5.4)

Three trials provided data on quality of life outcomes.[195-197] Each study used a different instrument for assessment: the Minnesota Questionnaire for heart failure,[196] the Functional Outcomes of Sleep Questionnaire (FOSQ),[195] and the SF-36.[197] None of the trials found significant differences between bilevel CPAP and CPAP in any quality of life measure.

Neurocognitive and Psychological Tests

One trial reported on neurocognitive outcomes.[197] Piper 2008 found a significant difference in the "mean of slowest 10 percent reaction" subtest of the Psychomotor Vigilance Test, favoring those patients who used bilevel CPAP (change from baseline: 0.32 versus 0.07 (unclear unit); P=0.03). No statistically significant difference was found in the other two subtests.

Blood Pressure

Khayat 2008, which included OSA patients with heart failure, was the only trial to report changes in blood pressure.[196] No significant differences were found between the two treatments; both bilevel CPAP and CPAP decreased systolic (6.3 versus 1.4 mm Hg, respectively; P=0.53) and diastolic blood pressure (7.5 versus 2.3 mm Hg, respectively; P=0.31).

Study Variability

No study reported subgroup analyses with respect to the comparative effect of bilevel CPAP versus CPAP for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway characteristics) or severity of OSA. All studies that reported a minimum AHI for inclusion eligibility used a threshold of 10 events/hr, thus no analysis of comparative effects across studies based on different AHI enrollment criteria was possible.

Summary

Five small trials with largely null findings did not support any substantive differences in the efficacy of bilevel CPAP versus CPAP in the treatment of patients with OSA. The studies were mostly of quality C but reported generally consistent results across outcomes. The studies were highly clinically heterogeneous in their populations, mostly with substantial comorbidities. Thus the studies, overall, have limited directness to the general OSA population. Largely due to small sample sizes, the studies mostly had imprecise estimates of the comparative effects. Due to the clinical heterogeneity and the imprecision, the overall strength of evidence was graded insufficient regarding any difference in compliance or other outcomes between bilevel CPAP and CPAP.

Comparison of Flexible Bilevel CPAP and Fixed CPAP

Only Ballard 2007, a quality B, parallel design RCT, compared flexible bilevel CPAP with fixed CPAP. The study enrolled 104 patients with OSA (mean AHI of 42 events/hr; mean BMI 34.2 kg/m^2) and self-estimated nightly use of CPAP of less than 4 hours.[200] After 3 months, significantly more patients had used flexible bilevel CPAP for more than 4 hours a night compared with CPAP (49 versus 28 percent, respectively; P=0.03). Mean hours used per night

were similarly higher in the flexible bilevel CPAP group than the CPAP group (3.7 versus 2.9 hr/night, respectively; P<0.05) The study also reported that the patients treated with flexible bilevel CPAP displayed a significant increase in mean FOSQ total score of 1.45 (P=0.004); the increase (0.45) in the CPAP group was not significant. Statistical comparison between groups on FOSQ was not reported. By our calculation (based on the reported data) the difference between the two treatments was not statistically significant. The study did not evaluate objective clinical outcomes. This study is applicable mainly to patients with AHI more than 30 events/hr and BMI more than 30 kg/m^2 who were poorly compliant with fixed CPAP.

In conclusion, while a single study found that flexible bilevel CPAP may yield increased compliance compared with fixed CPAP, overall the strength of evidence is insufficient regarding the relative effect of the two interventions.

Comparison of C-Flex™ and Fixed CPAP

Three parallel trials[201-203] and one crossover[204] trial compared C-Flex™ with fixed CPAP in patients with OSA (Appendix D Table 5.7.1). C-Flex is a proprietary CPAP technology that reduces the pressure slightly at the beginning of exhalation. Mean baseline AHI in these studies ranged from 35.4 to 53.3 events/hr. No comorbidities, with the exception of increased BMI (ranged from 31 to 34.9 kg/m^2), were reported. Study sample sizes ranged from 30 to 184 (total = 430 across studies). Study durations ranged from 1.5 to 6 months. Two studies were rated quality B and two were rated quality C. Incomplete and unclear reporting were the main methodological concerns. These studies are applicable mainly to patients with AHI more than 30 events/hr and BMI more than 30 kg/m^2.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance (Appendix D Table 5.7.2)

All four trials provided data on compliance. One study prescreened patients for compliance before acceptance into the study; only those with 4 or more mean hours of nightly CPAP use during a one week screening were admitted.[201] None of the four trials found a statistically significant difference in the relative usage of the machines (hours used per night) at followup. Pepin 2009[203] and Nilius 2006[202] reported that patients used the machines for about 5 hours a night, on average. Dolan 2009[201] and Leidag 2008[204] reported a compliance of about 6 hours a night.

Epworth Sleepiness Scale (Appendix D Table 5.7.3)

Three trials provided data on changes in daytime sleepiness as assessed using ESS.[201-203] Each reported that both C-Flex and CPAP decreased daytime sleepiness. The difference between C-Flex and CPAP was not statistically significant in any trial. Meta-analysis of ESS difference between C-Flex and CPAP in these three studies resulted in a difference of -0.23 (95 percent CI -0.74, 0.27; P=0.36). No statistically significant heterogeneity was observed within the meta-analysis.

Other Sleep Study Measures

Leidag 2008 also provided outcomes on AHI, minimum oxygen saturation, arousals, and sleep stages.[204] Final values at 1.5 months between C-Flex and CPAP were not statistically

significant in any of these measures: 6.2 versus 5.4 events/hr for AHI, 87.7 versus 88 percent for minimum oxygen saturation, 9.3 versus 8.9 events/hr for arousal, 19.5 versus 21.7 percent for REM sleep, and 9 versus 10.2 percent for stage 4 sleep.

Quality of Life

Pepin 2009 also provided data on quality of life outcomes.[203] With the exception of physical functioning and bodily pain in SF-36, both C-Flex and CPAP improved all domains in SF-36 and in the Grenoble Sleep Apnea Quality of Life questionnaire. No significant differences between C-Flex and CPAP were shown in these assessments.

Study Variability

No study reported subgroup analyses with respect to the comparative effect of C-Flex versus CPAP for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway) or severity of OSA.

All the studies used AHI as either part of the definition of OSA or as a minimum study enrollment criterion. The AHI cutoffs used were 5,[204] 10,[201] 15,[203] or 20[202] events/hr. No apparent difference in ESS was noted between C-Flex and CPAP based on different minimum AHI enrollment criteria or OSA definitions across the three studies that provided these data.[201-203]

Summary

Four trials with largely null findings did not support any substantive differences in the efficacy of C-Flex versus fixed CPAP in improving compliance (hours used per night) in patients with OSA. Overall the studies were of quality B and C, but reported generally consistent results across outcomes and had no substantive issues regarding directness to the OSA population. No statistically significant differences in compliance or other outcomes were found between C-Flex and fixed CPAP. The strength of evidence for this finding is rated low because of the mixed quality (Bs and Cs) of the primary studies.

Comparison of Humidification in CPAP

Three parallel trials[205-207] and two crossover trials[208,209] compared different aspects of humidification in fixed CPAP or autoCPAP (Appendix D Table 5.8.1). Three trials compared heated humidified CPAP with dry CPAP.[205,208,209] One trial provided additional data on cold passover humidified CPAP compared with dry CPAP.[209] One trial compared heated-humidified autoCPAP with dry autoCPAP.[207] One trial compared "always on" with "as needed" heated-humidified CPAP.[206] Mean baseline AHI in these studies ranged from 29 to 54 events/hr. No comorbidities, with the exception of increased BMI (ranging from 34.4 to 37.6 kg/m^2), were reported in these studies. Study sample sizes ranged from 42 to 123 (total = 360 across studies). Study durations ranged from 0.75 to 12 months. Three studies were rated quality B and two were rated quality C. Incomplete reporting and unclear analysis were some of the methodological concerns. These studies are applicable mainly to patients with AHI more than 30 events/hr and BMI more than 30 kg/m^2.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance (Appendix D Table 5.8.2)

All five trials provided data on compliance (hours used per night). Two trials reported that patients who used heated-humidified CPAP had increased compliance compared with those who did not (5.7 versus 5.3 hr/night, P=0.03 in Neill 2003; 5.52 versus 4.93 hr/night, P=0.008 in Massie 1999). Ryan 2009 did not find a statistically significant difference in compliance between heated-humidified and dry CPAP. Mador 2005 did not find a statistically significant difference in compliance between ―always on" and ―as needed" heated-humidified CPAP. Massie 1999 did not find a statistically significant difference in compliance between cold passover CPAP and heated-humidified or dry CPAP. Salgado 2008 did not find a statistically significant difference in compliance between heated-humidified and dry autoCPAP. No consistent effect of humidification on compliance was observed across these studies.

Apnea-Hypopnea Index

Only Salgado 2008 provided outcomes on AHI.[207] Both heated-humidified and dry autoCPAP were effective in reducing AHI; there was no statistically significant difference between them (-23.5 versus -24.1 events/hr, respectively).

Epworth Sleepiness Scale (Appendix D Table 5.8.3)

All five trials provided data on changes in daytime sleepiness as assessed using ESS. The difference between the two intervention arms in each of the trials was not statistically significant. Both intervention arms in each trial reported decreased daytime sleepiness. Three trials were sufficiently similar and provided appropriate data to allow meta-analysis.[205,207,208] A meta-analysis showed the difference in ESS between CPAP with and without humidification in these 3 trials to be -0.31 (95 percent CI -1.16, 0.54; P=0.47). No statistically significant heterogeneity was observed within the meta-analysis.

Quality of Life

Two trials provided data on quality of life outcomes.[205,206] Ryan 2009 did not find any statistically significant difference in SF-36 between patients who had heated-humidified CPAP and those who had dry CPAP.[205] However, nasal symptoms were more common in the dry CPAP group compared with the heated humidified group (70 versus 28 percent, P=0.002). Mador 2005 did not find any statistically significant difference in Calgary Sleep Apnea Quality of Life Index between patients who had ―always on" and those who had ―as needed" heated-humidified CPAP.[206]

Study Variability

No study reported subgroup analyses with respect to the comparative effect of humidified versus dry autoCPAP or CPAP for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway characteristics) or severity of OSA.

For variability in minimum AHI or RDI enrollment criteria, three studies used 10 events/hr and two studies did not specify a minimum value. No cross study comparisons based on minimum AHI or RDI criteria were possible.

Summary

Five trials examined different aspects of humidified positive airway pressure treatment for patients with OSA. While some studies reported a benefit of added humidity in positive airway

pressure treatment in improving patient compliance, this effect was not consistent across all the studies. Overall the studies were clinically heterogeneous, small, and not of quality A. Thus, the strength of evidence is insufficient to determine whether there is a difference in compliance or other outcomes between positive airway pressure treatment with and without humidification.

Comparison of Mandibular Advancement Devices and No Treatment

Five trials compared mandibular advancement devices (MAD) with different controls (Appendix D Table 5.9.1). Three were crossover trials[140,210,211] and two had a parallel design.[129,212] All devices were designed to advance the mandible or otherwise mechanically splint the oropharynx during sleep.

Bloch 2000 compared a one-piece MAD or a two-piece MAD with no treatment.[210] Barnes 2004 compared MAD with a placebo tablet.[140] Kato 2000 compared oral appliances of 2 mm, 4 mm, or 6 mm with no treatment.[211] Lam 2007 compared MAD plus conservative management to conservative management alone,[129] and Petri 2008 compared MAD to no treatment.[212]

The mean AHI at baseline ranged from 19 to 34 events/hr. Common exclusion criteria included significant coexisting diseases such as heart disease and diabetes, an unsafe level of sleepiness, and other upper airway or jaw problems. Study sample sizes ranged from 24 to 80, with a total of 301 patients across studies. Kato 2000 did not provide clear outcome reporting, and was rated quality C; all other studies were rated quality B. The main methodological concerns were small sample sizes and lack of blinding in outcome assessors. The studies are generally applicable to patients with AHI ≥15 events/hr, though less so to patients with comorbidities or excessive sleepiness.

While acknowledging the large clinical heterogeneity due to the different devices being tested, data were examined via meta-analyses. Note that the meta-analysis figures include comparisons of MAD with both no treatment and sham MAD (discussed in the next section).

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Apnea-Hypopnea Index (Appendix D Table 5.9.2) and Oxygen Desaturation Index (Figure 19)

Four trials with five device comparisons provided data on AHI as an outcome,[129,140,210,212] while one provided data on ODI.[211] All four trials reporting on AHI reported that AHI decreased significantly more in patients using a MAD compared with controls, with net differences ranging from -6.3 to -14.7 events/hr. Kato 2000 found that ODI decreased significantly in the MAD groups compared with control, with net differences of -8.7 for the 2 mm group, -11.3 for the 4 mm group, and -15.2 for the 6 mm group ($P<0.05$ for each comparison). Meta-analysis of AHI yielded a statistically significant effect (difference = -11 events/hr; 95 percent CI -15, -8), though with some statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices combined yielded similar results (though without statistical heterogeneity).

Epworth Sleepiness Scale (Appendix D Table 5.9.3; Figure 20)

Four trials with five device comparisons provided data on ESS as an outcome.[129,140,210,212] All four trials reported that ESS was significantly improved in patients using a MAD compared to

controls, with differences ranging from -1 to -4.5. Meta-analysis of ESS yielded a statistically significant effect (difference = -1.2; 95 percent CI -1.7, -0.6), without statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results.

Other Sleep Study Measures (Appendix D Table 5.9.4a-e; Figures 21 & 22)

Three trials reported on minimum oxygen saturation.[129,140,211] Kato 2000 and Barnes 2004 found a significantly higher minimum oxygen saturation in the MAD group, while Lam 2007 did not find a significant difference between any of the three MADs examined and the control group. Kato 2000 found that minimum oxygen saturation increased significantly in the MAD groups compared with control, with net differences of 2.0 percent for the 2 mm group, 2.3 percent for the 4 mm group, and 2.4 percent for the 6 mm group ($P<0.05$ for each comparison). Barnes 2004 found a difference of 2.4 percent (95 percent CI 1.4, 3.4; $P=0.001$). Meta-analysis of minimum oxygen saturation yielded a statistically significant effect (difference = 3.0 percent; 95 percent CI 0.4, 5.5), without statistical heterogeneity (Appendix D Table 5.9.4a). Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results (Figure 21).

Three trials reported on arousal index (Appendix D Table 5.9.4b). Barnes 2004 found no significant difference between MAD and control; Lam 2007 found a lower arousal index in MAD compared with control (difference = -8.2; 95 percent CI -9.3, 7.1; $P<0.05$). Bloch 2000 found a lower arousal index for patients using a one-piece MAD compared with control (difference = -14.5; 95 percent CI -22.6, -6.4; $P<0.05$), but no significant difference between patients using a two-piece MAD compared with control (difference = -10.1; 95 percent CI -17.9, 2.3; NS). Bloch 2000 and Barnes 2004 reported on sleep efficiency, and found no significant difference between groups (Appendix D Table 5.9.4c) Meta-analysis of arousal index yielded a statistically significant effect (difference = -7.9 events/hr; 95 percent CI -14, -1.3), though with some statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results (Figure 22).

Bloch 2000 and Barnes 2004 both reported on slow wave sleep. Barnes 2000 found no significant difference between MAD and control. Bloch 2000 found no difference between groups when comparing 2-piece MAD with control, but found a higher percentage of slow wave sleep in the 1-piece MAD group compared with control ($P<0.05$). Three studies reported on REM sleep; no significant difference among groups was reported (Appendix D Table 5.9.4e).[140,210,212]

Quality of Life (Appendix D Table 5.9.5)

Barnes 2004 reported on SF-36, finding no significant difference between MAD and control in SF-36 mean score, physical component summary, or mental component summary. Lam 2007 found no difference in any SF-36 domain between MAD and control. Barnes 2004 also reported no significant difference between groups in Beck Depression Inventory score or Functional Outcomes of Sleep Questionnaire social domain score. Lam 2007 did not find a difference in Sleep Apnea Quality of Life Index (SAQLI) social interactions or treatment-related symptoms scores, but did find an improved overall SAQLI score in the MAD group compared with the control group (difference = 0.7; 95 percent CI 0.6, 0.8; $P<0.001$).

Neurocognitive Tests

Jokic 1999 did not find a significant difference between CPAP and positional therapy in the Wechsler Memory Scale, Purdue Pegboard, Trail-Making Test, Symbol Digit Modalities, Consonant Trigram, or Concentration Endurance Test scores.

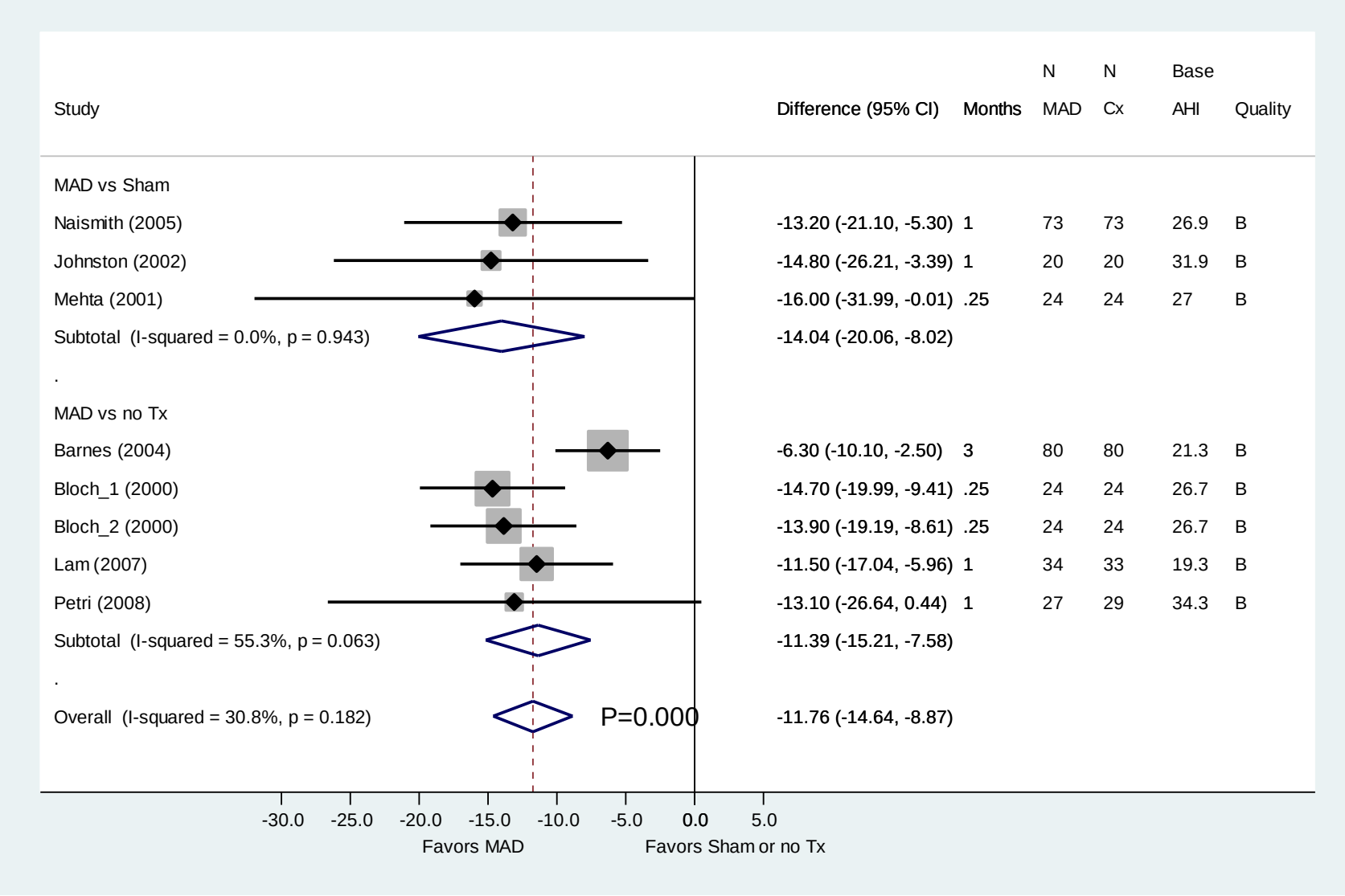
Study Variability

No studies reported subgroup analyses. Control treatments varied by study; Bloch 2000, Kato 2000, and Petri 2008 used no treatment as a control, whereas Barnes 2004 used a placebo tablet, and Lam 2007 used conservative management. Studies were mostly consistent in their findings.

Summary

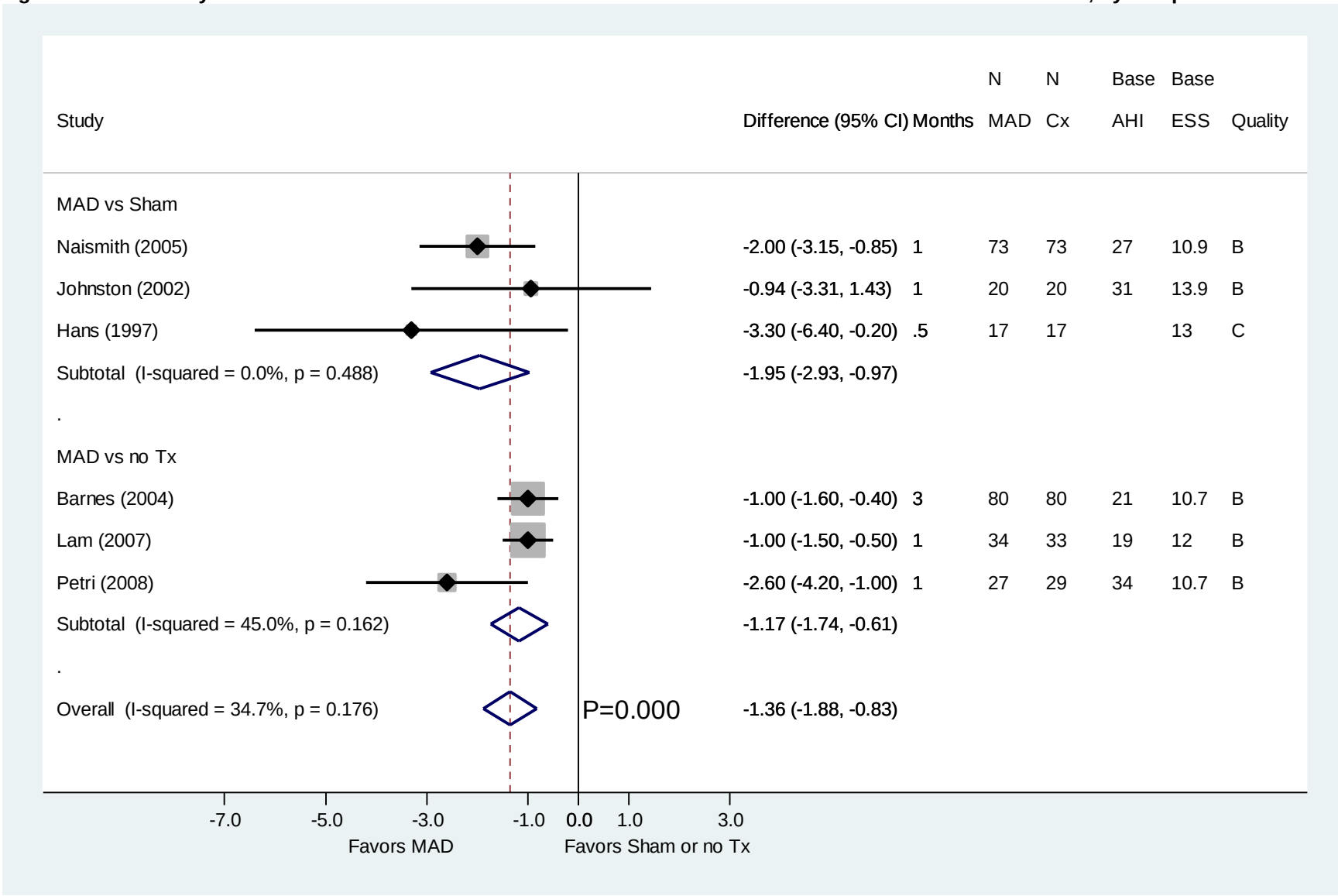
Four quality B trials and one quality C trial compared MAD to no treatment, using a variety of different types of MAD. Individually and by meta-analysis, studies found significant improvements with MAD in AHI, ESS, and other sleep study measures. No trial evaluated long-term objective clinical outcomes. The results of quality of life measures, and neurocognitive tests were equivocal between groups. Overall, despite no or weak evidence on clinical outcomes, overall, the strength of evidence is moderate to show that the use of MAD improves sleep apnea signs and symptoms.

Figure 19. Meta-analysis of AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. control, by comparator



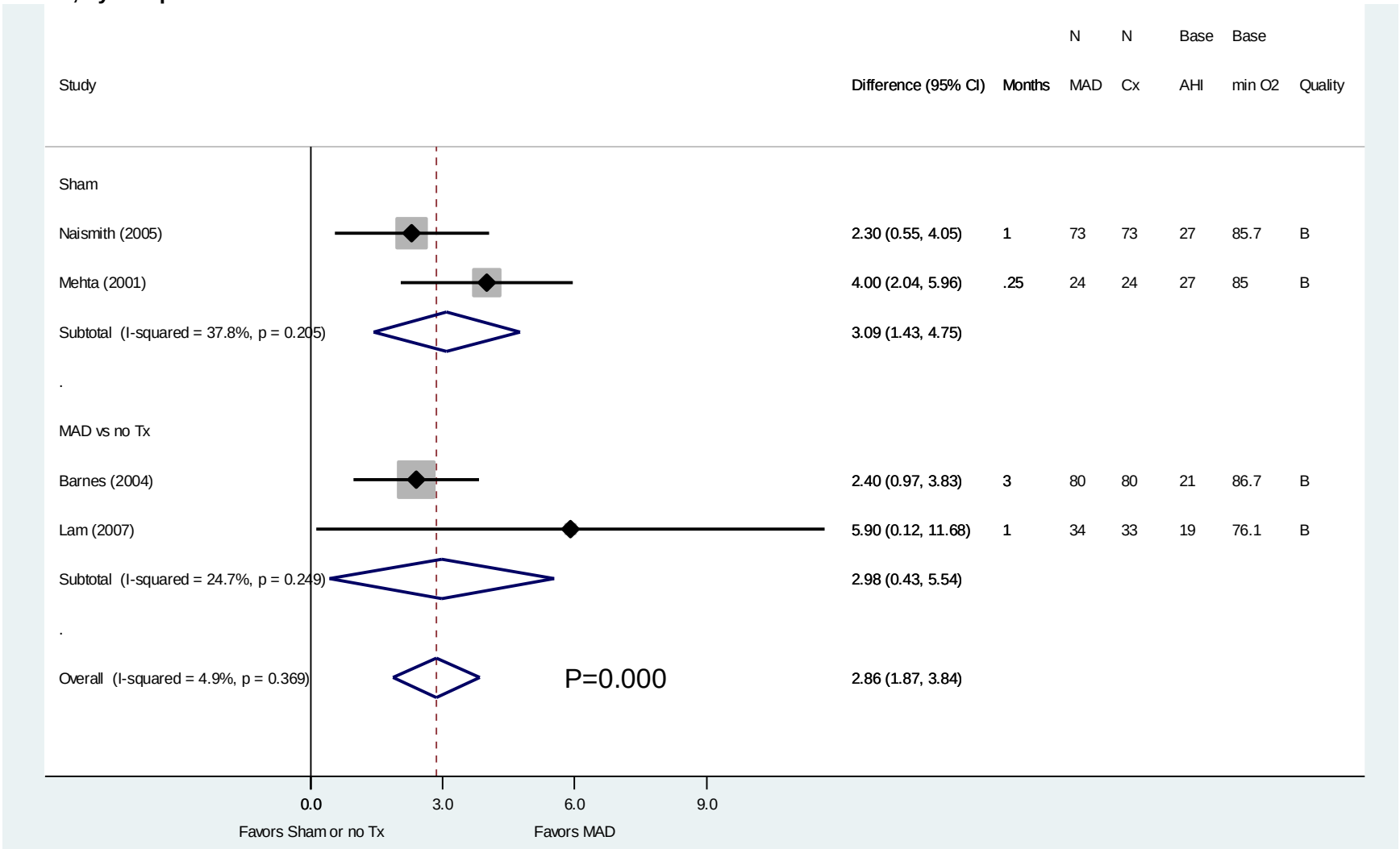
AHI = apnea-hypopnea index, CI = confidence interval, Cx = control, MAD = mandibular advancement device, Tx = treatment.

Figure 20. Meta-analysis of ESS in randomized controlled trials of mandibular advancement devices vs. control, by comparator



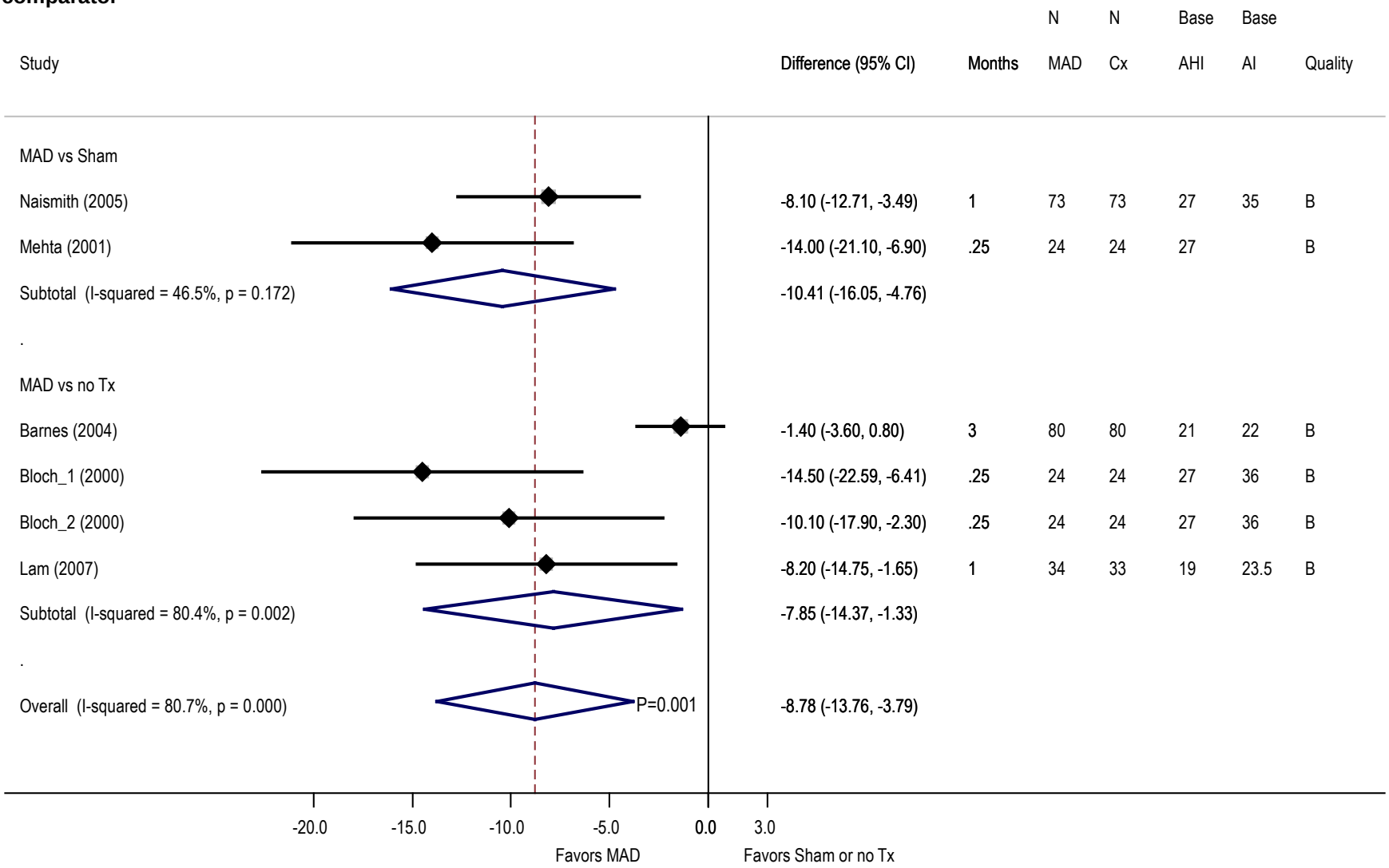
AHI = apnea-hypopnea index, CI = confidence interval, Cx = control, ESS = Epworth Sleepiness Scale, MAD = mandibular advancement device, Tx = treatment.

Figure 21. Meta-analysis of minimum oxygen saturation (%) in randomized controlled trials of mandibular advancement devices vs. control, by comparator



AHI = apnea-hypopnea index, CI = confidence interval, Cx = control, MAD = mandibular advancement device, min O2 = minimum oxygen saturation, Tx = treatment.

Figure 22. Meta-analysis of arousal index (events/hr) in randomized controlled trials of mandibular advancement devices vs. control, by comparator



AHI = apnea-hypopnea index, AI = arousal index, CI = confidence interval, Cx = control, MAD = mandibular advancement device, Tx = treatment.

Comparison of Mandibular Advancement Devices and Inactive (Sham) Oral Devices

One parallel design RCT[212] and four crossover trials compared the effects of MADs to inactive oral devices with no mandibular advancement across six publications (Appendix D Table 5.10.1).[213-218] The baseline AHI (or RDI) ranged from 25 to 36 events/hr. All studies included patients with no other significant comorbidities. Study sample sizes ranged from 17 to 73 (total = 186 patients). Study durations ranged from 8 days to 6 weeks. Hans 1997 was rated quality C due to a 30 percent dropout rate and the lack of a power analysis. The other studies were rated quality B. These studies are applicable primarily to patients with AHI of more than about 25 events/hr who do not have other significant comorbidities. All studies excluded edentulous patients or those with periodontal diseases.

While acknowledging the large clinical heterogeneity due to the different devices being tested, data were examined via meta-analyses.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Apnea-Hypopnea Index and Respiratory Disturbance Index (Appendix D Table 5.10.2; Figure 19)

Five studies provided data on AHI or RDI.[212-218] All found significant improvement in AHI or RDI with MAD compared with sham devices. Net changes in AHI or RDI ranged from -13 to -25 events/hr. Meta-analysis of AHI yielded a statistically significant effect (difference = -14 events/hr; 95 percent CI -20, -8), without statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices combined yielded similar results (see *Comparison of Mandibular Advancement Devices and No Treatment*, above).

Epworth Sleepiness Scale (Appendix D Table 5.10.3; Figure 20)

Four trials in six publications provided data on changes in daytime sleepiness assessed using ESS.[212-217] Gotsopoulos 2002, in a 4 week crossover trial with 73 patients (mean age = 48 yr, 80 percent male) compared a custom-made MAD to an inactive oral device (single upper plate). It found a statistically significant reduction in daytime sleepiness with MAD compared with the inactive oral device (net change in ESS -2; $P<0.001$). The other studies did not find statistically significant differences between MAD and inactive oral devices. Meta-analysis of ESS yielded a statistically significant effect (difference = -1.9; 95 percent CI -2.9, -1.0), without statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results (see *Comparison of Mandibular Advancement Devices and No Treatment*, above).

Other Sleep Study Measures (Appendix D Tables 5.10.4-5.10.7; Figures 21 & 22)

Two trials in four publications reported changes in minimum oxygen saturation (Appendix D Table 5.10.4).[214,215,217,218] Gotsopoulos 2002 (and associated articles) and Mehta 2001 compared MAD with inactive oral devices (single upper plate and lower dental plate) and found statistically significant improvements in minimum oxygen saturation with MAD compared with

the inactive oral devices (differences of 6 and 2 percent, respectively; P<0.0001). Meta-analysis of minimum oxygen saturation yielded a statistically significant effect (difference = 3.1 percent; 95 percent CI 1.4, 4.8), without statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results (see Figure 21 and *Comparison of Mandibular Advancement Devices and No Treatment*, above).

The same trials also reported changes in the number of arousals (Appendix D Table 5.10.5).[214,215,217,218] Naismith 2005 found a significant decrease in the number of arousals in MAD compared with single plate devices (P<0.001). Meta-analysis of arousal index yielded a statistically significant effect (difference = -10 events/hr; 95 percent CI -16, -5; P=0.001), without statistical heterogeneity. Meta-analysis of MAD versus no treatment or inactive devices treatment combined yielded similar results (see Figure 22 and *Comparison of Mandibular Advancement Devices and No Treatment*, above).

Two trials in four publications reported sleep efficiency (Appendix D Table 5.10.6).[214,215,217,218] Neither trial found statistically significant differences in sleep efficiency between MAD and sham devices.

Two trials evaluated changes in sleep stages with MAD compared with sham devices.[212,218] The outcome of interest was the percentage of total sleep time spent in REM, stage 3 and stage 4 sleep. Mehta 2001 found a significant improvement in REM sleep with MAD compared with lower dental plate (P<0.005). Petri 2008 provided sufficient data for comparative calculations between MAD versus an appliance with no mandibular advancement. Our calculations showed a significant increase in percentage of total sleep time spent in stage 3 sleep with MAD compared with nonadvancement (sham) MAD (net difference 2.9 percent; P=0.045). However there was no significant difference in time spent in REM or stage 4 sleep between groups (Appendix D Table 5.10.7).

Quality of Life (Appendix D Table 5.10.9)

Petri 2008 reported quality of life outcomes measured using SF-36.[212] The study found significant improvement in the vitality dimension with MAD compared with sham MAD (P<0.001). There were no statistically significance differences between groups in other domains of SF-36.

Neurocognitive Tests (Appendix D Table 5.10.8)

Gotsopoulos 2002 (and related articles), which compared MAD with an inactive oral appliance (single upper plate) with no mandibular advancement, found significant improvements in the Multiple Sleep Latency Test (P=0.01) with MAD as compared with single upper plate. In addition, the study found significant improvements in somatic items on the Beck Depression Inventory scale (P<0.05) and the choice reaction time task (a speed & vigilance test) on the neuropsychological test (P<0.001) in MAD compared with single upper plate. There were no statistically significant differences between groups in other domains of Beck Depression Inventory or other subtests of the neuropsychological tests.

Neurocognitive Tests (Appendix D Table 5.10.8)

Gotsopoulos 2002 (and related articles) also found significant reductions in 24-hour systolic (P<0.05) and diastolic (P<0.001) blood pressures with MAD as compared with single upper plate.

Study Variability

None of these studies reported subgroup analyses. The studies were generally consistent in their findings and there were no clear differences in effect based on patient characteristics, severity of sleep apnea, other symptoms, or apparent differences in OSA definitions.

Summary

Five trials, most rated quality B, compared the effects of MAD with inactive devices. The studies individually and via meta-analysis showed sufficient evidence that most sleep study measures (AHI, minimum oxygen saturation, arousal index) and ESS were improved with MAD as compared with devices without mandibular advancement. No trials evaluated objective clinical outcomes. The strength of evidence is insufficient concerning other evaluated outcomes due to inconsistent results or a limited number of studies per outcome. Overall, despite no or weak evidence on clinical outcomes, overall the strength of evidence is moderate to show that the use of MAD improves sleep apnea signs and symptoms.

Comparisons of Different Oral Devices

Two parallel design RCTs[219,220] and one crossover trial[221] compared the effects of different types of oral MAD in patients with OSA (Appendix D Table 5.11.1). A fourth study compared MAD with a novel tongue-stabilizing device[222] and a fifth study compared two types of tongue-retaining devices.[223] This study was rated quality C due to inadequate methodology and poor statistical analysis reporting. The other studies were rated quality B. These studies are applicable mostly to patients with AHI of 15 to 30 events/hr and BMI less than 30 kg/m^2. However, one study included mainly obese patients (BMI >30 kg/m^2). All studies were restricted to patients with sufficient number of teeth to anchor the mandibular devices in place.

Each study examined a unique comparison, and, as such, is presented separately.

Different Degrees of Mandibular Advancement (Appendix D Tables 5.11.1, 5.11.2, 5.11.4)

Walker-Engstrom 2003 compared the same MAD at different degrees of mandibular advancement: 75 percent (mean mandibular advancement 7.2 mm) versus 50 percent (mean of 5.0 mm). The trial enrolled 84 male patients, mostly obese (BMI >30 kg/m^2), with severe OSA (AHI ≥20 events/hr). The mean age was 50 years, mean baseline AHI was 50 events/hr, and mean ESS score was 11.5. After 6 months, AHI normalization (AHI<10 events/hr) was achieved by 52 percent of patients who had 75 percent mandibular advancement and 31 percent of patients with 50 percent advancement (P<0.04). However, the trial found no difference in mean AHI or ESS score between groups.

Self-Adjustment Versus Objective Adjustment of Devices (Appendix D Tables 5.11.1-5.11.5)

Campbell 2009 compared two methods of adjustment of the same MAD. One group of patients used self-adjustment of the MAD during the entire study duration. The other had an ~~-o~~bjective adjustment" at 3 weeks following PSG-based feedback. The trial included 28, predominately male patients who had a BMI ≤35 kg/m^2. The mean age was 48 years, mean baseline AHI was 25 events/hr, and baseline ESS score was 11.6. At 6 weeks, the trial found no statistically significant difference between the two groups in the sleep study measures evaluated

(AHI and minimum oxygen saturation) and no statistically significant difference in subjective sleepiness.

Custom-Made Versus Thermoplastic Devices (Appendix D Tables 5.11.1, 5.11.2, 5.11.4, 5.11.5)

Vanderveken 2008 compared custom-made MAD with a premolded thermoplastic MAD. Twenty-three, predominately male patients were evaluated in a crossover study with a 1 month washout period. The mean age was 49 years, mean baseline AHI was 13 events/hr, and baseline ESS score was 8. No statistically significant differences between treatment groups in AHI, sleep efficiency, ESS, or minimum oxygen saturation were found.

Mandibular Advancement Devices Versus Tongue-Stabilizing Device (Appendix D Tables 5.11.1 & 5.11.6)

Deane 2009 reported a 1 week crossover trial that compared the effects of a MAD with a novel tongue-stabilizing device.[222] The MAD produced 75 percent of maximal mandibular protrusion with a 4 mm vertical interincisal opening. The tongue-stabilizing device was a nonadjustable tongue-suction device made of silicone with no mandibular advancement. This study included 22 patients (73 percent male) with an AHI ≥10 events/hr (AHI mean 27 events/hr) and no other comorbid states. The mean age of patients was 49 yr and the mean BMI was 29 kg/m^2. The study reported that 91 percent of the subjects using MAD had a decrease in AHI compared with 77 percent of patients using a tongue-stabilizing device. Our calculations based on the reported data show no significant differences in mean AHI, minimum oxygen saturation, arousal index, or sleep efficiency between groups.

Tongue-Retaining Device With Versus Without Suction (Appendix D Tables 5.11.1 & 5.11.7)

Dort 2008 reported a crossover trial that compared the effects of a tongue-retaining device with or without suction in 32 patients (69 percent male) with primary snoring (RDI <5 events/hr) or mild to moderate OSA (RDI <30 events/hr).[223] The active suction device was designed to allow suction formation on the tip of the tongue when placed in the mouth. After 1 week with each device (and a 1 week washout period), a significant improvement in RDI was observed with the suction tongue-retaining device as compared with the nonsuction device (difference = -4.9 events/hr; 95 percent CI -8.9, -0.85; P=0.019). However, there were no significant differences in ESS score, SAQLI, and compliance (mean hours of use per night) between groups.

Study Variability

A subgroup analysis comparing males and females in Deane 2009 showed no difference between MAD and a tongue-stabilizing device. As there is only one study per comparison, we were unable to assess potential differences due to factors of interest, such as patient characteristics and severity of OSA.

Summary

Five studies with unique comparisons found little to no differences between different types and methods of use of MAD or other oral devices in sleep study or sleepiness measures. No study evaluated objective clinical outcomes. Only one study evaluated compliance; no significant differences were observed. One trial found that a greater degree of mandibular advancement

resulted in an increased number of patients achieving an AHI <10 events/hr; however, the mean AHI was similar between groups.

As the reviewed studies were generally small, and each concerned with a unique comparison, the strength of evidence is insufficient to draw conclusions with regards to the relative efficacy of different types of oral MAD in patients with OSA.

Comparison of Mandibular Advancement Devices and CPAP

Ten trials (11 articles) compared different MAD with CPAP (Appendix D Table 5.12.1). Seven were crossover trials[140,224-229] and three had a parallel design.[129,230-232] All devices were designed to advance the mandible or otherwise mechanically splint the oropharynx during sleep.

Five trials tested branded oral devices, four used custom-made oral devices, and one (Skinner 2004) used a cervicomandibular support collar, which was worn around the neck and shoulders. This latter device was compared with autoCPAP; all other devices were compared with fixed (or undefined) CPAP.

Mean baseline AHI in the reviewed trials ranged from 18 to 40 events/hr; four trials included patients with an AHI ≥5, three with an AHI ≥10, one with an AHI ≥15 events/hr, and two did not report a lower AHI threshold. Four trials included only patients with relatively less severe OSA, with an AHI <30-50 events/hr. Most trials had otherwise unrestricted eligibility criteria with the exception of Barnes 2004, which excluded patients with diabetes, and Tan 2002, which excluded patients with recent cardiovascular disease. The sample size of the studies ranged from 10 to 94 (total = 384 across studies). The smallest study, Skinner 2004, was stopped early after analyzing half the planned participants because of significant results favoring the control (autoCPAP). This study was rated quality C; the remaining studies were all rated quality B. Small sample sizes, lack of outcome assessor blinding, and incomplete reporting were the main methodological concerns. The studies are generally applicable to patients with AHI >5-10 events/hr.

While acknowledging the large clinical heterogeneity due to the different devices being tested, data were examined via meta-analyses.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance

Only Gagnadoux 2009, in a crossover trial of 28 patients, assessed compliance. Patients reported statistically significantly more hours of use per night (7.0 versus 6.0 hr/night; P<0.01) and more nights of use (98 versus 90 percent of nights; P>0.01) with MAD as compared with CPAP.

Treatment Response (Appendix D Table 5.12.2)

Two studies measured treatment response (as a dichotomous outcome). In a 2 month crossover study of 28 patients, Gagnadoux 2009 found that significantly more patients on CPAP, as compared with MAD, had a complete response, defined as a ≥50 percent reduction in AHI to <5 events/hr (risk difference = -29 percent; 95 percent CI -53, -4; P=0.02). However, the large majority of the remaining patients experienced a partial response (≥50 percent reduction in AHI to >5 events/hr) and thus no significant difference in combined or partial response was observed.

Hoekema 2008 evaluated several related outcomes in a 2-3 month parallel trial of 103 patients comparing CPAP with oral appliance. "Effective treatment", defined as a final AHI <5

events/hr or a >50 percent reduction to an AHI<20 events/hr without symptoms, was similar in both groups and in the subgroups of patients with baseline AHI below and above 30 events/hr. However, CPAP was more effective than oral appliance at achieving an AHI of <5 events/hr in all patients (risk difference= -20 percent; 95 percent CI -37, -2; P=0.02).

In the subgroup analyses, a larger, significant effect was found in patients with a baseline AHI >30 events/hr; no difference was observed in those with less severe OSA. The study also did not find a difference in this subgroup in achieving an AHI <10 events/hr.

Apnea-Hypopnea Index (Appendix D Table 5.12.3; Figure 23)

Nine trials provided data on AHI outcomes.[129,140,224,226-232] All trials reported that AHI was lower in patients on CPAP than when using MADs. The results were statistically significant in seven of the trials. Meta-analysis of the eight trials with adequate data found that the difference in AHI between MAD and CPAP was statistically significant, favoring CPAP (difference = 7.7 events/hr; 95 percent CI 5.3, 10.1; P<0.001). Analysis of the net difference assessed in the two parallel trials and of the difference of final values in the six crossover trials yielded similar findings. However, the trial results were statistically heterogeneous.

Epworth Sleepiness Scale (Appendix D Table 5.12.4; Figure 24)

Seven trials provided data on ESS outcomes.[129,140,225,227,229,230,232] Four trials found no significant difference in ESS between the two interventions, while three found a significantly lower ESS in patients on CPAP (net difference 2 and 6 units). However, only Gagnadoux 2009 found a statistically significant lower ESS (-0.5 units) while patients were using MAD. Meta-analysis revealed no significant difference between the two interventions but indicated a trend somewhat favoring CPAP (difference = 1.3; 95 percent CI -0.2, 2.8; P=0.098). A large degree of the statistical heterogeneity across studies was due to Engleman 2002, which found a considerably larger difference favoring CPAP (net difference = 6; estimated 95 percent CI 4.2, 7.8; P<0.001). It is unclear why this study found a different magnitude effect; the study shared features with several other studies that had reported smaller effects. Excluding this one study, meta-analysis indicated no difference between the interventions, though statistical heterogeneity remained (difference = 0.4, 95 percent CI -0.6, 1.3).

Other Sleep Study Measures (Appendix D Table 5.12.5a-c; Figures 25 & 26)

Five studies evaluated arousal index (Figure 25). Meta-analysis revealed that arousals were significantly more common while using MAD than CPAP (difference = 3.5 events/hr; 95 percent CI 1.5, 5.5; P=0.001). All studies reported a higher arousal index on MAD than CPAP, though only Barnes 2004 found a statistically significant difference (and Skinner 2004, discontinued early, which found a large, but marginally nonsignificant difference between the cervicomandibular support collar and autoCPAP) (Appendix D Table 5.12.5a).

Seven studies evaluated minimum oxygen saturation (Figure 26). Meta-analysis revealed that the studies were homogeneous and indicated a statistically significant lower oxygen saturation while using MAD than CPAP (difference = -3.5 percent; 95 percent CI -4.6, -2.4; P<0.001). All studies found a consistent effect, though only two trials were statistically significant (Appendix D Table 5.12.5b).

Six studies found no significant difference in sleep efficiency (range of effects -2.9 percent, 0.4 percent total sleep time) (Appendix D Table 5.12.5c). Five of these studies found a consistent

(though nonsignificant) trend toward less time in slow wave sleep with MAD (range of effects -3.9 percent, -0.6 percent total sleep time) (Appendix D Table 5.12.5d).

Seven studies evaluated REM sleep (Appendix D Table 5.12.5e). No statistically significant difference in percentage of time spent in REM sleep was reported, although the range of differences between the two interventions was large (-4.7 to 6.1). There was no clear explanation for the different results across studies.

Objective Sleepiness and Wakefulness Tests (Appendix D Table 5.12.6)

Two studies evaluated wakefulness tests. Engleman 2002 found no difference in the Maintenance of Wakefulness Test sleep onset latency. Gagnadoux 2009 found no difference in the Oxford Sleep Resistance test sleep latency.

Quality of Life (Appendix D Table 5.12.7a-b; Figure 27)

Three studies measured FOSQ (Appendix D Table 5.12.7a) with inconsistent findings. Hoekema 2008 (in a trial of an oral MAD versus CPAP) and Skinner 2004 (in an aborted trial of a cervicomandibular support collar versus autoCPAP) found no difference in quality of life as measured by FOSQ. In contrast, Engleman 2002 (in a trial of oral MAD versus CPAP) found that quality of life improved significantly less while patients were using MAD than while using CPAP. Meta-analysis revealed no significant effect on FOSQ (difference = -0.86; 95 percent CI -2.5, 0.8).

Seven studies measured various quality of life tests (Appendix D Table 5.12.7b); five used SF-36, two used the Hospital Anxiety and Depression Scale, and one study each used the Beck Depression Index, the Calgary Sleep Apnea Quality of Life Index (SAQLI), the Nottingham Health Profile, a "General Health" measure, and the Scottish National Sleep Laboratory symptom questionnaire. Five of the studies found no significant difference in quality of life among patients using MAD or CPAP. The remaining two studies found differences in components of SF-36 favoring CPAP: Engleman 2002 found significant differences in various components of SF-36, and Lam 2007 found a large net difference in only the Bodily Pain component (-16 points). Lam 2007 also found differences in SAQLI, which separately measures the effect of treatment on quality of life and any treatment-related symptoms (adverse effects). The study found that, overall, CPAP was better at improving quality of life, but that patients treated with CPAP had more treatment-related symptoms. Combining quality of life findings and treatment-related symptoms (the analysis SAQLI A-E), neither intervention was superior.

Neurocognitive Tests (Appendix D Table 5.12.8)

Two studies evaluated neurocognitive tests. Neither Engleman 2002 nor Gagnadoux 2009 found any significant differences in a range of tests of cognitive performance (IQ), executive function (Trailmaking), processing speed (Paced Auditory Serial Addition Test), error making (Oxford sleep resistance), or driving skills (SteerClear).

Study Variability

Only one study reported subgroup analyses. As discussed above, Hoekema 2008 found no difference in the effective treatment rate between interventions in either those with more or less severe OSA (at an AHI threshold of 30 events/hr) after 2 to 3 months. However, those patients with a baseline AHI >30 events/hr were more likely to achieve an AHI of <5 events/hr with

CPAP than MAD, as compared with those with a lower baseline AHI. An evaluation using a final AHI of <10 events/hr did not confirm this difference. This trial was a parallel design RCT, enrolling 103 patients with a minimum AHI of 5 events/hr but a relatively high mean AHI of 40 events/hr and with relatively severe sleepiness (mean ESS = 14.2).

For most evaluated outcomes, the reviewed studies were generally consistent in their findings. Where there were outliers, no clear differences in effect based on patient characteristics, severity of sleep apnea, other symptoms, or apparent differences in OSA definitions (particularly minimum AHI threshold) were observed.

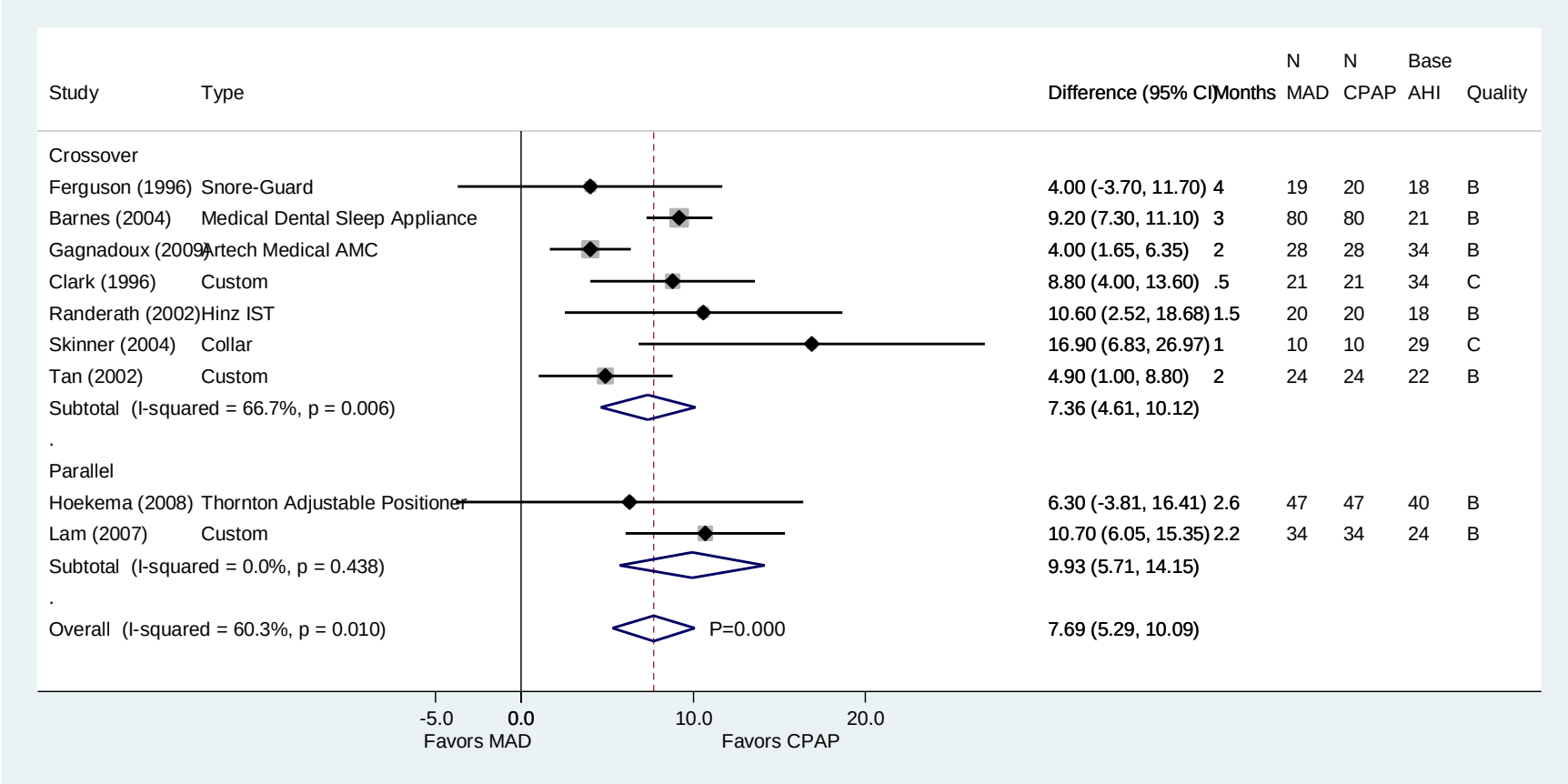
The only consistent difference across studies and outcomes reported was that of the aborted study comparing a cervicomandibular support collar with autoCPAP. This study reported differences in effects (which favored autoCPAP) that were generally larger than the differences for the intraoral MADs compared with CPAP. This, apparently, was the reason that the study was prematurely terminated.

Summary

Ten trials (most quality B) compared MAD with CPAP; nine compared intraoral devices with CPAP and one compared an extraoral device with autoCPAP. The reviewed studies generally found that CPAP was superior in reducing AHI, reducing arousal index, raising minimum oxygen saturation. The evidence regarding relative effects on ESS is unclear due to heterogeneity of results across studies. These findings were confirmed by meta-analysis. No difference in effect was found for other sleep measures. Most studies found no significant difference in effects on quality of life or neurocognitive function, although one study found that the benefits of CPAP over MAD, as measured by SAQLI, were counterbalanced by an increase in perceived treatment-related symptoms under CPAP. Only one of two studies found a difference (favoring CPAP) in treatment response. Only one study evaluated compliance, finding that patients were more compliant with MAD than CPAP. No consistent or substantive differences in effects were found based on patient characteristics, disease severity, or other baseline symptoms.

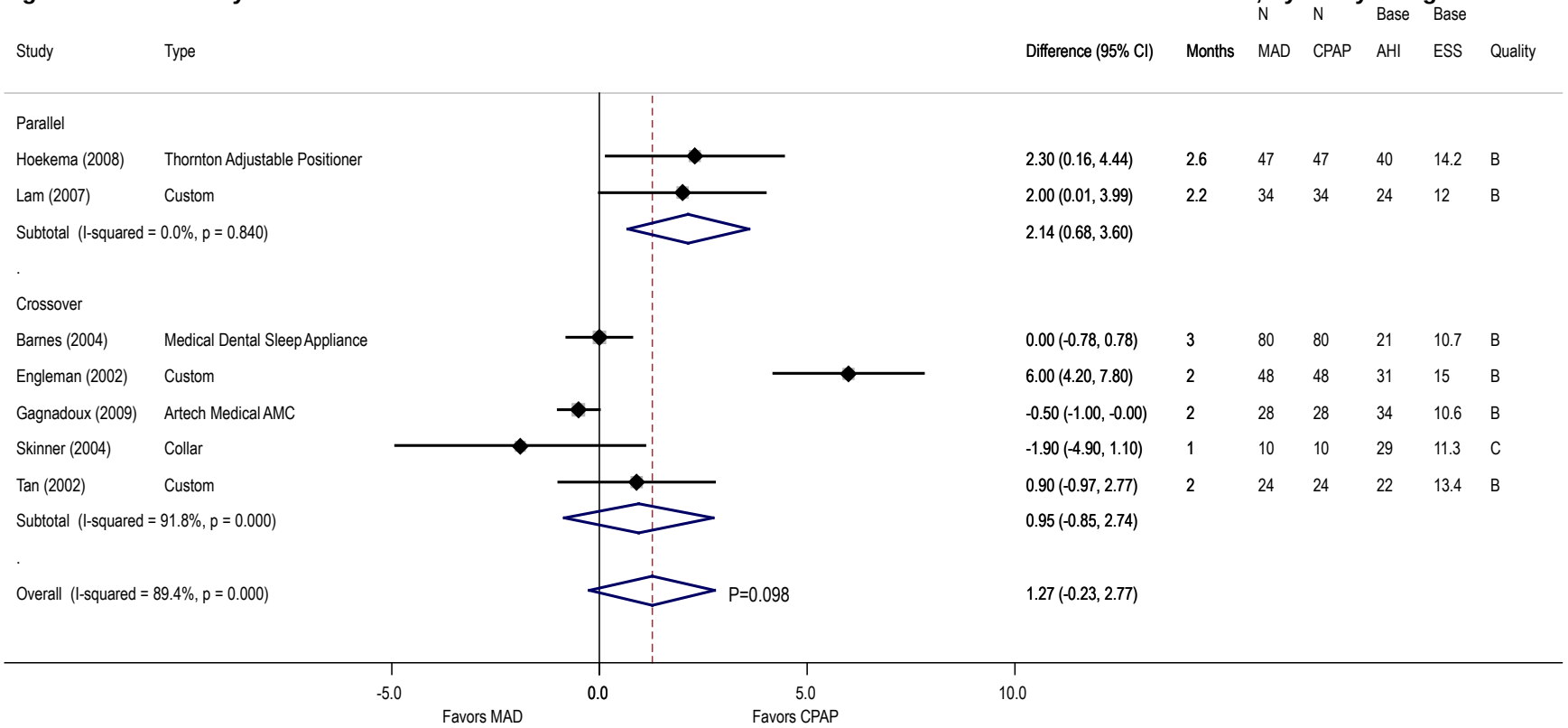
There was sufficient evidence supporting greater improvements in sleep measures with CPAP as compared to MAD, but only weak evidence indicating no or only small differences favoring CPAP for improving compliance, treatment response, quality of life, or neurocognitive measures. There were no data on objective clinical outcomes. Nevertheless, overall there remains a moderate strength of evidence that CPAP is superior to MAD to improve sleep study measures. However, the strength of evidence is insufficient to address which patients might benefit most from either treatment.

Figure 23. Meta-analysis of AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. CPAP, by study design



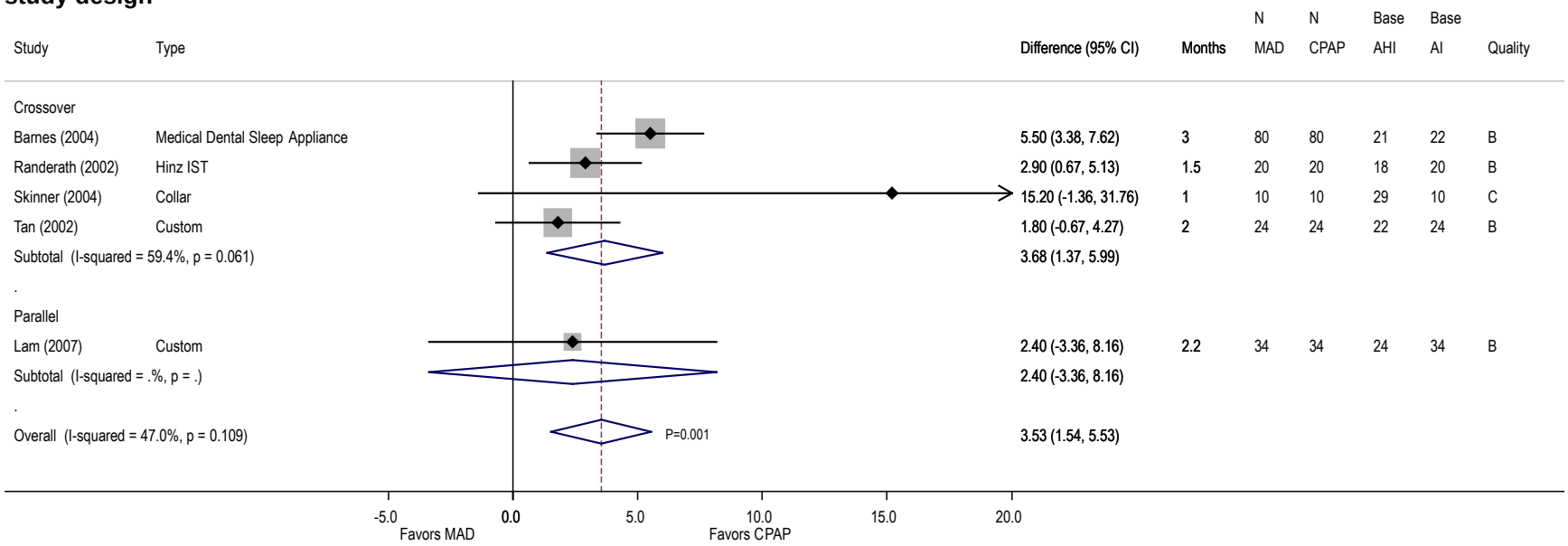
AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure, MAD = mandibular advancement device.

Figure 24. Meta-analysis of ESS in randomized controlled trials of mandibular advancement devices vs. CPAP, by study design



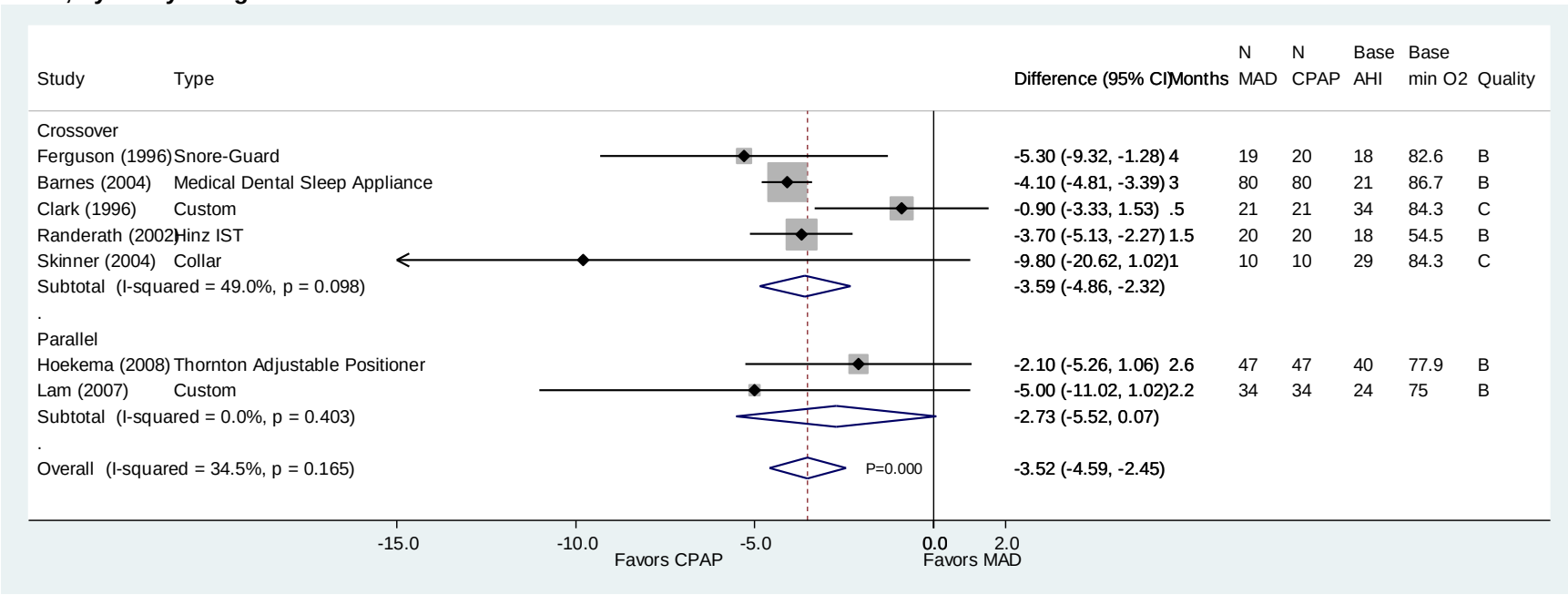
AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, MAD = mandibular advancement device.

Figure 25. Meta-analysis of arousal index (events/hr) in randomized controlled trials of mandibular advancement devices vs. CPAP, by study design



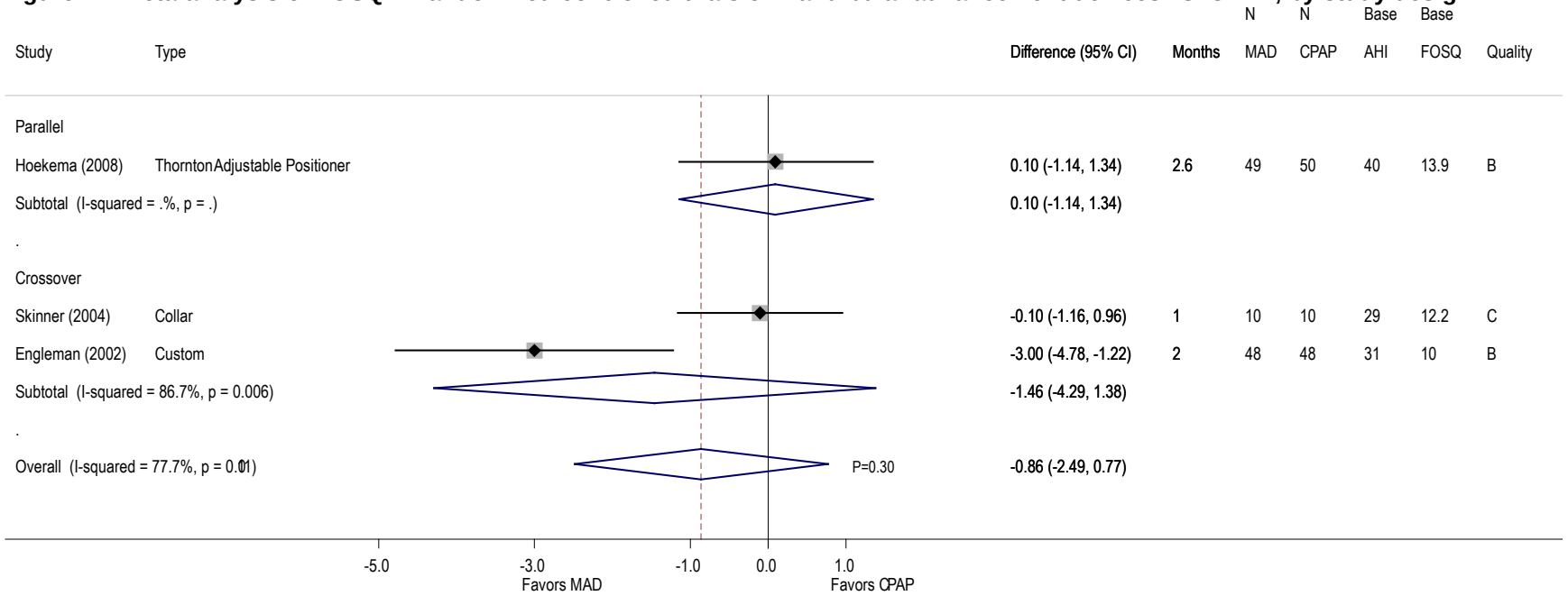
AHI = apnea-hypopnea index, AI = arousal index, CI = confidence interval, CPAP = continuous positive airway pressure, MAD = mandibular advancement device.

Figure 26. Meta-analysis of minimum oxygen saturation (%) in randomized controlled trials of mandibular advancement devices vs. CPAP, by study design



AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure, MAD = mandibular advancement device, min O2 = minimum oxygen saturation.

Figure 27. Meta-analysis of FOSQ in randomized controlled trials of mandibular advancement devices vs. CPAP, by study design



AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure, FOSQ = Functional Outcomes Sleep Questionnaire, MAD = mandibular advancement device.

Comparison of Positional Therapy and CPAP

Three crossover trials compared three different positional devices with CPAP. One trial compared a shoulder head elevation pillow with autoCPAP,[233] and two compared devices worn on the back to prevent sleeping supine with either autoCPAP[234] or CPAP[235] (Appendix D Table 5.16.1). Across studies, mean baseline AHI ranged from 18 to 27 events/hr. Skinner 2004 included patients with an AHI ≥10 events/hr, Skinner 2008 included patients with AHI ≥5, and Jokic 1999 included only patients who were shown to have an AHI <15 events/hr while in the lateral position. All patients had positional OSA; none were patients for whom positional therapy might be contraindicated due to conditions such as chronic musculoskeletal pain or other conditions affecting sleep. Study sample sizes ranged from 13 to 20 patients (total = 47 across studies). All studies were rated quality B. Small sample sizes and lack of patient and outcome assessor blinding were the main methodological quality concerns. These studies are applicable mainly to patients with AHI less than 30 events/hr who have positional OSA, and for whom positional therapy would not be contraindicated due to comorbid conditions.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Compliance

No study evaluated compliance.

Apnea-Hypopnea Index (Appendix D Table 5.16.2a-b)

All three trials provided data on AHI as an outcome. Each trial reported that AHI decreased significantly more in patients on CPAP as compared with those on positional therapy. Jokic 1999 found a difference of 6.1 events/hr (95 percent CI 2.0, 10; P=0.007), Skinner 2004 found a difference of 16 events/hr (95 percent CI 4.2, 28; P=0.008), and Skinner 2008 found a difference of 7.1 (95 percent CI 1.1, 13; P=0.02). Skinner 2008 also reported statistically significantly more patients achieved an AHI of ≤10 events/hr with CPAP (89 percent) than with a Thoracic anti-supine band (72 percent; P=0.004, by Wilcoxin sign-rank test), though the relative risk of achieving a low AHI was nonsignificant (0.81; 95 percent CI 0.58, 1.13).

Epworth Sleepiness Scale (Appendix D Table 5.16.3)

All three trials provided data on ESS as an outcome. Each trial reported that ESS scores were higher in patients on positional therapy than those on CPAP (differences ranged from 0.7 to 1.5), although none of these findings were statistically significant.

Other Sleep Measures (Appendix D Table 5.16.4)

Jokic 1999 reported a nonsignificantly larger drop in arousal index in patients on CPAP as compared with those on positional therapy. No significant differences in maintenance of wakefulness testing, sleep latency, sleep efficiency, percentage of time spent in stage 3-4 sleep, and percentage of time spent in REM sleep were observed. Arousal index was nonsignificantly higher in patients on positional therapy (difference = 4.5 events/hr; 95 percent CI -0.7, 9.4; P=0.08).

Quality of Life (Appendix D Tables 5.16.5 & 5.16.6)

Skinner 2004 and Skinner 2008 both reported no significant difference in SF-36 mental component and physical component summaries for patients in the CPAP group compared with those in the positional therapy group (Appendix D Table 5.16.5a-b). Skinner 2004 also found no significant difference in FOSQ score between the two groups (Appendix D Table 5.16.6).

Jokic 1999 found a lower score in the Nottingham Health Profile energy subscale in the positional therapy group (difference = -1; P=0.04; Appendix D Appendix D Table 5.16.7a) , but no difference between treatments in the Hospital Anxiety and Depression Scale (Appendix D Table 5.16.7b), University of Wales Institute of Science and Technology (UWIST) mood adjective checklist (Appendix D Table 5.16.7c), or General Health Questionnaire (Appendix D Table 5.16.7d).

Neurocognitive Tests (Appendix D Table 5.16.7)

Jokic 1999 found no significant difference between CPAP and positional therapy in the Wechsler Memory Scale, Purdue Pegboard, Trail-Making Test, Symbol Digit Modalities, Consonant Trigram, or Concentration Endurance Test scores.

Study Variability

No studies performed subgroup analyses. As study treatments were heterogeneous, we were unable to examine differences in outcomes based on patient characteristics.

Summary

Three small quality B crossover trials compared different positional treatments with CPAP. AHI was found to be lower in patients using CPAP than in those on positional therapy. ESS scores were not significantly different between groups. Additionally, quality of life measurements and neurocognitive tests showed no difference between positional therapy and CPAP.

Because of the small number of studies and because each study evaluated a different device, the strength of evidence is insufficient to determine the relative merit of positional therapy compared with CPAP in the treatment of OSA.

Comparison of Weight Loss Interventions and Control Interventions

Three parallel trials compared weight loss interventions with control interventions (Appendix D Table 5.17.1).[236-238] Foster 2009 enrolled patients with type 2 diabetes and randomized them to an intensive lifestyle intervention (a behavioral weight loss program involving portion-controlled diets and physical activity prescription) or a diabetes support and education program (three educational sessions on diabetes management over a 1 year period on diet, physical activity, and social support). Johannson 2009 randomized patients to a group following a 9 week low energy diet or a group that was instructed to adhere to their usual diet. Tuomilehto 2009 enrolled obese patients and randomized them to a group following a very low calorie diet complemented with lifestyle changes or a group subject to general counseling on diet and exercise only. Mean baseline AHI in these studies ranged from 9 to 37 events/hr. Study sample sizes ranged from 63 to 264 (total = 345 across studies). Study durations ranged from 2.3 to 12 months. Johansson 2009 was rated quality A, while the other two were rated quality B. The main methodological

concerns were the lack of clarity on whether the outcome data included all initial participants and unclear reporting of outcomes. The inclusion criteria used in these studies varied considerably in terms of baseline OSA severity, presence of comorbidities, and severity of obesity. The studies are generally applicable to people with BMI >30 kg/m^2.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Treatment Response (Appendix D Table 5.17.2)

Tuomilehto 2009 examined cure from OSA as a dichotomous outcome. OSA was considered objectively cured when the AHI was <5 events/hr at 1 year. Treatment with a very low calorie diet was associated with a 4-fold increase in the odds of being cured from OSA at 1 year compared with the control intervention (adjusted odds ratio 4.2; 95 percent CI 1.4, 12; P=0.011).

Apnea-Hypopnea Index (Appendix D Table 5.17.3)

All three studies examined AHI and demonstrated statistically significant reductions in AHI for the arms randomized to weight loss interventions. The reductions ranged from -4 to -23 events/hr. Johansson 2009 showed the largest net reduction in AHI. This study enrolled patients with no comorbidities but with more severe OSA (baseline AHI = 37) as compared to the other two studies; it also involved a much shorter duration of followup (9 weeks).

Epworth Sleepiness Scale (Appendix D Table 5.17.4)

Two trials provided data on changes in daytime sleepiness as assessed using the ESS. Johansson 2009 reported a statistically significant reduction in ESS scores for the low energy diet group, while Tuomilehto 2009 found no significant difference.

Minimum Oxygen Saturation (Appendix D Table 5.17.5)

Only Johansson 2009 reported changes in minimum oxygen saturation; the lower energy diet was associated with a statistically significant net increase in the minimum oxygen saturation as compared to usual diet (5 percent; 95 percent CI 2, 7; P=0.002).

Other Outcomes (Appendix D Tables 5.17.6-5.17.8)

Tuomilehto 2009 examined the impact of a weight loss intervention on blood pressure measurements (Appendix D Table 5.17.6). No statistically significant changes were detected for systolic or diastolic blood pressure. Foster 2009, which was conducted exclusively in diabetic patients, examined the impact of an intensive lifestyle intervention on hemoglobin A1c concentration (Appendix D Table 5.17.7) and reported a statistically significant net difference (-0.5 percent; P<0.001) at 1 year followup.

In all three studies, the weight loss program resulted in large reductions in weight (Appendix D Table 5.17.8) of -10.7, -10.8, and -18.7 kg; the control interventions resulted in near stable weight (changes ranging from -2.4 to +1.1 kg). These differences were all highly statistically significant (P<0.001).

Study Variability

No study reported subgroup analyses with respect to the comparative effect of weight loss interventions versus control interventions for OSA in terms of patient characteristics (age, sex, race, weight, bed partner, and airway) or severity of OSA.

Given the small number of studies and the variability of interventions, no conclusions could be reached regarding whether effects of weight loss interventions varied for different subgroups of patients.

Summary

Findings from three parallel RCTs supported a benefit of intensive weight loss interventions in reducing AHI. The reviewed studies were quality A or B and reported consistent results supporting the improvement of AHI with weight loss interventions, either as a continuous outcome (three studies) or as a dichotomous outcome for cure based on an AHI of less than 5 events/hr (one study). It should be noted, however, that the study that showed the largest benefit had relatively few participants. Conclusive statements cannot be made about other outcomes evaluated due to inconsistent results or a limited number of studies per outcome. No data on objective clinical outcomes were reported. Overall, there is a low strength of evidence to show that some intensive weight loss programs may be effective in relieving the signs and symptoms of sleep apnea in obese patients with OSA.

Comparison of Oropharyngeal Exercise and Control

Three trials compared different methods of oropharyngeal exercise with CPAP (Appendix D Table 5.18.1).[239-241] All three had a parallel design, and tested methods intended to train aspects of the upper airway and reduce symptoms of OSA. These methods included didgeridoo training, oropharyngeal exercise, and tongue training.

Mean baseline AHI ranged from 20 to 27 events/hr. Study sample sizes ranged from 25 to 57 patients. Both Puhan 2005 and Randerath 2004 were rated quality A, while Guimaraes 2009 was rated quality B due to a small sample size and unclear reporting. The studies are generally applicable to patients with AHI ≥15 events/hr.

Study Results (Appendix D Tables 5.18.2-5.18.10)

As the devices compared varied considerably and each study examined different outcomes, trials are described separately below. No study evaluated objective clinical outcomes.

Guimaraes 2009[240] compared oropharyngeal exercise (consisting of exercise of the soft palate, tongue, and facial muscles plus stomatognathic function exercises) to sham therapy (consisting of deep breathing, nasal lavage, and recommendations for bilateral chewing). The sample consisted of 31 patients with moderate OSA (AHI 15-30 events/hr). Patients were excluded if they had a BMI >40 kg/m^2 or major comorbidities. Patients in the oropharyngeal exercise group were 64 percent male and had a mean age of 52 years. Those in the control group were 73 percent male and had a mean age of 48 years. The study found that oropharyngeal exercise resulted in a significantly lower AHI (difference = -12 events/hr, 95 percent CI -19, -5; P<0.001) (Appendix D Table 5.18.2), as well as lower ESS scores (difference = -4.0; 95 percent CI -8, -0.02; P<0.05) (Appendix D Table 5.18.3). No significant differences between groups were observed in minimum oxygen saturation (Appendix D Table 5.18.4) or sleep efficiency (Appendix D Table 5.18.5). The oropharyngeal exercise group had a significantly lower Pittsburgh Quality of Sleep Index score (difference = -3.4; P<0.01) (Appendix D Table 5.18.9).

Randerath 2004[241] compared tongue training (using a muscle stimulator placed under the tongue and chin) to sham training (using the same device but without electrical stimulation). The study consisted of 57 newly diagnosed OSA patients with an AHI of 10-40 events/hr. Patients had no other significant comorbidities. Patients in the tongue training group were 57 percent male and had a mean age of 51 years. Those in the control group were 73 percent male and had a mean age of 53 years. The study found no significant difference between groups in AHI, ESS, minimum oxygen saturation (Appendix D Tables 5.18.2-5.18.4), slow-wave or REM sleep (Appendix D Table 5.18.6), arousal index (Appendix D Table 5.18.6), FOSQ score (Appendix D Table 5.18.8), or Attention Test score (Appendix D Table 5.18.10).

Puhan 2005[239] compared didgeridoo training to no treatment. The study consisted of 25 mostly male patients (mean age: 49 years) with an AHI range of 15-30 events/hr and a mean BMI $\leq$30 kg/m^2. All patients complained of snoring. Training consisted of instruction on the didgeridoo, which involves learning a breathing technique called circular breathing. Patients practiced for 30 minutes daily, 6 days a week. After 4 months, the didgeridoo group had a significantly lower AHI (difference = -6.2 events/hr; 95 percent CI -12.3, -0.1; P=0.05; Appendix D Table 5.18.2) and ESS score (difference = -2.8; 95 percent CI -5.7, -0.3; P=0.04; Appendix D Table 5.18.3). No differences between groups were observed in any domain of SF-36 or in the Pittsburgh Quality of Sleep Index (Appendix D Table 5.18.9).

Study Variability

None of the studies reviewed performed subgroup analyses. No comparisons could be made across studies.

Summary

Three trials with unique comparisons compared oropharyngeal exercise to control for treatment of patients with OSA. One study on a specific form of oropharyngeal exercise and one study on didgeridoo training reported improved sleep study measures. A third study found tongue training to not be beneficial in relieving the symptoms of OSA. Overall, due to the limited number of studies, the strength of evidence is insufficient to determine a definitive benefit of oropharyngeal exercise in the treatment of OSA.

Comparison of Palatal Implant and Placebo Implant

Two RCTs compared palatal implants and placebo implants in patients with OSA (Appendix D Table 5.19.1).[242,243] Both studies included only patients with mild to moderate sleep apnea and no other significant comorbidities. Mean baseline AHI was 20 events/hr in Friedman 2008 and 16 events/hr in Steward 2008; mean ESS values were 11.7 and 10.6, respectively. While Friedman 2008 had an equal sex distribution, Steward 2008 included a majority (79 percent) of men most of whom had retropalatal pharyngeal obstruction. The mean ages of patients in the studies were 39 years (Friedman 2008) and 49 years (Steward 2008). Friedman 2008, a quality A study, enrolled 62 patients and Steward 2008, a quality B study, enrolled 100 patients. Both studies were double-blinded and had a 3 month followup (Appendix D Table 5.19.1). Neither study evaluated objective clinical outcomes. These studies are applicable to patients with AHI of 5 to 40 events/hr and BMI less than 30 kg/m^2.

Study Results (Appendix D Tables 5.19.2-5.19.6)

Friedman 2008 found significant improvements in AHI (P<0.0001; Appendix D Table 5.19.2a), ESS values (P=0.0002; Appendix D Table 5.19.3), and SF-36 total score (P<0.0001) with palatal implants as compared to placebo. The study did not find significant differences in minimum oxygen saturation (Appendix D Table 5.19.4) or REM sleep as a percentage of total sleep time (Appendix D Table 5.19.5) between groups. This study was rated quality A.

In contrast, Steward 2008 did not find statistically significant differences in mean AHI (Appendix D Table 5.19.2a) or ESS values (Appendix D Table 5.19.3) between palatal implants and placebo. However, the study did find that a clinically meaningful reduction in AHI (≥50 percent reduction to <20 events/hr) was more common in the palatal implant group as compared to placebo (26 versus 10 percent, P=0.04; Appendix D Table 5.19.2b). The study also reported significant improvements in minimum oxygen saturation (P=0.007; Appendix D Table 5.19.4) and FOSQ (P<0.05; Appendix D Table 5.19.6) with palatal implants as compared to placebo. This study was rated quality B.

Study Variability

Neither study performed subanalyses. Due to the limited number of studies, we were unable to assess potential differences with regards to factors of interest such as patient characteristics and severity of obstructive sleep apnea.

Summary

Two studies in patients with mild to moderate OSA compared treatment effects of palatal implants to placebo implants. Both studies found significantly greater improvements in sleep study measures and quality of life with palatal implants; however, the studies disagreed as to which specific outcomes palatal implants significantly improved. Overall, due to the limited number of studies reviewed, the strength of evidence is insufficient to determine the relative efficacy of palatal implants versus sham implants in patients with mild to moderate OSA.

Comparison of Surgery and Control Treatments

Six trials in seven publications and one prospective nonrandomized comparative study investigated the effects of several surgical interventions compared to control (Appendix D Table 5.20.1).[124,125,244-249] Each study used a different intervention: uvulopalatopharyngoplasty (UPPP), laser-assisted uvulopalatoplasty (LAUP), radiofrequency ablation (RFA), and combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty, radiofrequency ablation of the inferior nasal turbinates, or combination nasal surgery. The control treatments were sham surgery, conservative therapy, or no treatment.

Patients included in the surgery comparisons were reported to have prior treatment failures with nonsurgical techniques or declined their usage. The mean baseline AHI ranged from 5 to 40 events/hr; three trials included patients with an AHI ≥5, one with an AHI ≥10, and one did not report an AHI threshold. One trial reported ODI (mean at baseline 21- 72 events/hr). All included only patients with relatively less severe OSA (AHI <30-50). Study sample sizes ranged from 26 to 52 (total = 223 across studies). Three studies were rated quality A, one quality B, and two quality C. Guilleminault 2008 was reported as a crossover study comparing several surgical combinations to cognitive behavioral therapy. This study was rated quality C due to an inappropriate study design as the effects of surgery could not be reversed. These studies are applicable mostly to patients with a range of baseline AHI and BMI less than 35 kg/m^2.

Study Results (Appendix D Tables 5.20.2-5.20.7)

As each study evaluated a different surgical technique, each study is described individually. No studies evaluated objective clinical outcomes.

Back 2009 compared a single session of RFA surgery of the soft palate to sham surgery (simulated surgery with no energy administered). The study included 32 male patients with mild sleep apnea (AHI 5-15 events/hr) and habitual snoring following a failed trial of conservative treatment (weight loss, positional therapy, restriction of alcohol and sedatives). Patients were between the ages of 30 and 65 years. At 4 month followup, no statistically significant difference between groups in AHI (Appendix D Table 5.20.2), ESS (Appendix D Table 5.20.3), minimum oxygen saturation (Appendix D Table 5.20.4), and quality of life (as measured by SF-36; Appendix D Table 5.20.7) were found. This study was rated quality A.

Koutsourelakis 2008 randomized patients to either nasal surgery (submucous resection of the deviated septum and bilateral resection of inferior turbinates) or sham surgery (simulated nasal surgery under anesthesia). In addition to OSA (defined as AHI ≥5 events/hr), all patients had fixed nasal obstruction due to deviated nasal septum. The study was conducted on 49, predominately male patients with a mean baseline AHI of 31 events/hr. After 4 months followup, the study found no statistically significant difference between groups in AHI (Appendix D Table 5.20.2) or on ESS (Appendix D Table 5.20.3). This study was rated quality A.

Woodson 2003 conducted a three-arm RCT that included a comparison of multilevel temperature controlled RFA of the soft palate with sham surgery (simulated RFA with no energy delivered). The study was conducted in 51, predominately male patients. Notably, the age of participants between groups was significantly different at baseline. (49 years (RFA) versus 51 years (sham), P=0.04). The mean baseline AHI also differed among groups (21 (RFA) versus 15 (sham) events/hr; P=0.06, including the CPAP study group). After 8 weeks followup, the study found a significantly greater improvement in sleep quality as measured by FOSQ with RFA as compared to sham surgery (P=0.04; Appendix D Table 5.20.6), but no statistically significant difference in AHI (Appendix D Table 5.20.2), ESS (Appendix D Table 5.20.3), minimum oxygen saturation (Appendix D Table 5.20.4), or quality of life as measured by SF-36 (Appendix D Table 5.20.7). This study was rated quality A.

Ferguson 2003 randomized patients to either LAUP or no treatment. In LAUP, the uvula and a specified portion of the palate is vaporized under local anesthesia in an outpatient setting. The goal is to relieve obstruction in patients with mild OSA or snoring. The study included 44 mostly male patients with mild OSA (AHI 10-27 events/hr) and snoring. The patients had a mean age of 45 years and a mean BMI of 31.6 kg/m^2. This study reported disparate followup durations of 15 months in the LAUP group and 8 months in the control group. A statistically significant improvement in AHI was observed following LAUP as compared with no treatment (net change -10.5 events/hr; P=0.04; Appendix D Table 5.20.2). However, there was no statistically significant difference between groups on the ESS (Appendix D Table 5.20.3) or in quality of life as measured by SAQLI (Appendix D Table 5.20.7). This study was rated quality B.

Guilleminault 2008 was reported as a crossover study comparing several surgical combinations to cognitive behavioral therapy in 30 patients with insomnia and mild OSA (mean AHI 10 events/hr). Based on anatomy, disease severity, and comorbidity, patients received combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty, and RFA of the inferior nasal turbinates. Since the surgery could not be undone during the second phase of the study, we evaluated only the first phase as a parallel trial. Results showed that surgery led to improvements in AHI (-6.2 events/hr; P=0.0001; Appendix D Table

5.20.2), ESS (-1.1; P=0.002; Appendix D Table 5.20.3), minimum oxygen saturation (4.4 percent; P=0.0001; Appendix D Table 5.20.4), REM (2.9 percent of total sleep time; P=0.0001; Appendix D Table 5.20.5), and slow wave sleep (3.5 percent of total sleep time; P=0.0001; Appendix D Table 5.20.5) as compared to cognitive behavioral therapy. This study was rated quality C due to the design issues described above.

Lojander 1996 & 1999 compared UPPP with or without mandibular osteotomy to conservative treatment (weight loss, positional therapy, and avoidance of tranquilizers and alcohol at bedtime). The study included 32, predominately male patients with a mean age of 47 years and a mean baseline BMI of 31 kg/m^2. Baseline ODI ranged from 10 to 72 events/hr. A significant improvement in daytime somnolence (net difference -25 on a visual analogue scale ranging from 0 (no somnolence) to 100 (worst); P<0.05) was observed after 12 months; no statistically significant difference was found between groups in cognitive function (Wechsler test; Appendix D Table 5.20.7). This study was rated quality C due to problems with the power calculation, a small sample size, and a possible selection bias stemming from the use of an expert panel to determine which patients would be most suitable for UPPP.

Li 2009, in a nonrandomized prospective study (quality C), compared correction of nasal septum and volume reduction of the inferior turbinates to conservative nasal treatments in patients with snoring, nasal obstruction, and OSA. The study included 66 patients, 44 of whom had surgery. The patients were almost all male, with a mean age of 38 years and a mean BMI of 26.2 kg/m^2. Baseline AHI was 38 events/hr in the surgically treated group and 26 in the conservative treatment group (no significant difference), and baseline ESS was 10.6. The article did not report at what timepoint followup data were collected. The study found a statistically significant difference in ESS, favoring surgery (net difference -3.6; 95 percent CI -6.1, -1.1; P=0.02; Appendix D Table 5.20.3). The study found no difference in AHI, minimum oxygen saturation, slow wave sleep, or REM sleep (Appendix D Tables 5.20.2, 5.20.4, 5.20.5) However, seven of 44 patients receiving surgery had success by the Sher criteria (followup AHI <30 events/hr and reduction in AHI of at least 50 percent) and none of the 22 patients on conservative treatment (P=0.048 per the article). The study did note that six of the seven patients with surgical success had, at baseline, low ESS (<10.5), a low Friedman tongue position (grade II or III), and a low BMI (<25.8 kg/m^2).

Study Variability

None of the studies performed subgroup analyses. As there is only one study per comparison, we were unable to assess potential differences with regards to factors of interest such as patient characteristics and severity of OSA

Summary

Seven studies with unique interventions compared surgery with control treatment for the management of patients with OSA. Due to the heterogeneity of the studies reviewed and inconsistency as to which outcomes were improved with surgery as compared to no or sham surgery, the strength of evidence is insufficient to evaluate the relative efficacy of surgical interventions for the treatment of OSA.

Comparison of Surgery and CPAP Treatments

Two parallel RCTs,[247,250] four prospective studies,[251-254] and six retrospective studies[255-260] investigated the effects of several surgical interventions compared with CPAP in adults with

OSA (Appendix D Table 5.21.1). The surgery modalities compared include temperature-controlled radiofrequency tissue volume reduction of the soft palate, UPPP, maxillomandibular advancement osteotomy, and radiofrequency ablation (RFA). Only one trial (Woodson 2003) included patients who had neither prior surgery nor prior CPAP. The other trial (Vicini 2010) excluded patients with prior surgery but did not report on prior CPAP use. The remaining studies either explicitly or implicitly were biased in that the patients receiving surgery had already failed or refused CPAP or other nonsurgical interventions, in contrast with the patients who were being treated with CPAP.

Mean baseline AHI ranged from 5 to 80 events/hr across the studies. Most studies had a mean age above 45 years and a mean BMI ≤35 kg/m^2. The studies enrolled predominately male subjects (≥70 percent). Although Conradt 1998 included patients with craniofacial abnormalities, all other studies included patients with no important comorbidity. Study sample sizes ranged from 25 to 22,898 patients (total = 24,215 across studies). One study was rated quality A and the remainder rated quality C due to inadequate reporting of eligibility criteria, inconsistent reporting, small sample sizes, and discrepancies between followup periods. Studies included patients with a wide range of baseline AHI, but were heterogeneous in the severity of OSA within each study, thus limiting the applicability of most studies. Studies mostly included patients with BMI ≤35 kg/m$^{2.}$

Mortality (Appendix D Tables 5.21.2 & 5.21.3)

Two retrospective studies evaluated the effects of UPPP compared with CPAP on long-term survival.[257,260] No studies evaluated any other objective clinical outcomes.

Weaver 2004 compared 20,826 patients using CPAP to 2072 patients who had UPPP. All patients were followed for at least 6 years in a database at Veterans Affairs medical facilities. In addition to UPPP, about one-quarter to one-third of patients also received tonsillectomy, septoplasty, or, turbinate procedures, and about 2 percent of patients had tracheotomy or tongue procedures, each. After adjusting for age, sex, race, date of initial treatment, and comorbidities, the study found a higher mortality in the CPAP than in the UPPP group at all time periods throughout the study. The adjusted hazard ratio of death for CPAP versus UPPP was 1.31 (95 percent CI 1.03, 1.67; P=0.03).

Keenan 1994 found no difference in age-adjusted 5 year survival between the cohorts of 275 patients who had received UPPP or CPAP. Compared with those who used CPAP, patients who received UPPP had a significantly lower BMI (30 versus 36 kg/m^2; P<0.001) and a higher arousal index at baseline (25 versus 20 events/hr; P<0.01). However, the results are difficult to interpret as the followup for UPPP patients was significantly longer than that of patients receiving CPAP (43 versus 28 months; P<0.001).

Apnea-Hypopnea Index or Respiratory Disturbance Index (Appendix D Table 5.21.4)

One RCT[250] and four prospective studies reported outcomes on AHI, RDI, or a combination of AHI and RDI.[251,254,256,258] Vicini 2010 randomly assigned 50 patients to either maxillomandibular advancement or autoCPAP therapy and compared treatment effects at the end of 12 months. They found no statistically significant difference in AHI between groups (-48.7 versus -44 events/hr; P=0.21).Ceylan 2009, a prospective, nonrandomized comparative study, reported AHI. This study compared single-stage, multilevel temperature-controlled radiofrequency tissue volume reduction of the soft palate and base of the tongue to CPAP and

found no significant difference in changes in AHI between the two groups after 12 months followup. The other studies reported RDI. As each study evaluated a different surgical technique, each study result is described separately.

After 3 months followup, Conradt 1998 found essentially the same large declines in RDI (-54 events/hr) after maxillomandibular advancement osteotomy and CPAP in prospectively followed cohorts of patients. Lin 2006, in a retrospective analysis comparing extended uvulopalatoplasty (UPP) found a significantly larger improvement in RDI in patients on CPAP as compared to surgery (-63 versus -32 events/hr; P<0.001). However this study also had significant differences between groups in several baseline characteristics including age (51 yr versus 45 yr; P=0.005), BMI (28.1 versus 26.4 kg/m^2; P=0.025), RDI (65.3 versus 43.6 events/hr; P<0.001), and ESS (14.1 versus 11.8; P=0.005).

Katsantonis 1988, using retrospective data, compared patients who had UPPP with those who were treated with CPAP (other reported interventions are not included from this retrospective study). They analyzed 98 mostly male patients with moderate to severe OSA who had UPPP and a sample of 44 of 138 patients who received CPAP. Patients were categorized as good responders (>50 percent improvement in AHI and 85 percent improvement in severity index [number of abnormal breathing events/hr with <85 percent oxygen saturation]), poor responders (<50 percent decrease in AHI and severity index), and moderate responders (those in between). After 18 months followup, the study reported 100 percent of patients using CPAP were good responders. In contrast, of those who received UPPP , 38 percent were good responders, 34 percent moderate responders, and 28 percent poor responders. The study was rated quality C due to poor reporting and a lack of reported eligibility criteria.

Epworth Sleepiness Scale (Appendix D Table 5.21.5)

Two RCTs,[247,250] one prospective nonrandomized study,[252] and three retrospective studies[254,258,259] compared various surgical techniques with CPAP for the treatment of OSA. None of the studies found statistically significant differences in ESS values between surgery and CPAP.

Objective Sleepiness and Wakefulness Tests (Appendix D Tables 5.21.2 & 5.21.6)

Two studies reported objective sleepiness using the Multiple Sleep Latency Test.[253,255] Zorick 1990 compared UPPP with CPAP and found no statistically significant improvement in excessive daytime sleepiness (net difference -4.5; P<0.05). Anand 1991 found that 30 percent of UPPP patients and 41 percent of CPAP patients increased their Multiple Sleep Latency Test score by at least 3 minutes. No statistical analysis was reported.

Other Sleep Study measures (Appendix D Tables 5.21.6 & 5.21.7)

Two studies reported REM and stage 3 and 4 sleep as a percentage of total sleep time,[251,253] one study reported arousal index,[251] and one study reported minimum oxygen saturation.[254] Zorick 1990 found that after 6 weeks of followup there was a statistically significant relative increase in REM and stage 3 or 4 sleep in the CPAP as compared to the UPPP group. Conradt 1998 found no difference in arousal index, sleep efficiency, REM sleep, or stage 3 and 4 sleep 3 months after maxillomandibular advancement osteotomy or CPAP. Ceylan 2009 found a nonsignificant difference of 2.7 percent between temperature-controlled radiofrequency tissue volume reduction of the soft palate and CPAP.

Quality of Life (Appendix D Tables 5.21.6 & 5.21.8)

Three studies, two of which compared temperature-controlled radiofrequency tissue volume reduction of the soft palate and base of the tongue to CPAP and one which compared extended uvulopalatoplasty to CPAP, found no difference between groups in all domains of SF-36.[247,252,258] Both Woodson 2001 and Woodson 2003 found no difference in FOSQ after 2 to 3 months of follow up.[247,252]

Study Variability

One study reported a subgroup analysis. Keenan 1994 retrospectively analyzed data from 208 patients with OSA over a 6 year period. Patients were stratified by apnea index. For patients with an apnea index >20 events/hr, the study found no significant differences in cumulative survival between UPPP and CPAP. No data were reported separately for those patients with apnea index ≤20 events/hr.

Summary

Of 12 studies comparing surgical modalities with CPAP, two were RCTs. The quality A trial was the only unbiased comparison of surgery and CPAP (patients had previously received neither treatment) did not find statistically significant differences in ESS and quality of life measures between patients with mild to moderate OSA (AHI 10 to 30 events/hr) who had temperature-controlled radiofrequency tissue volume reduction of the soft palate and those who had CPAP at 2 months followup. Similarly, the other trial found nonstatistically significant differences in AHI and ESS in patients with severe OSA (AHI ≥30 events/hr) between maxillomandibular advancement osteotomy and CPAP.

For the nonrandomized studies, comparisons between surgery and CPAP are difficult to interpret since baseline patient characteristics (including sleep apnea severity) differed significantly between groups (and not always in a consistent manner, i.e., the surgical group could have a higher AHI than the CPAP group in one study and vice versa in another study). The reported findings on sleep study and quality of life measures were heterogeneous across studies.

Due to the heterogeneity of interventions and outcomes examined, the variability of findings across studies, and the inherent bias of all but one study regarding which patients received surgery, it is not possible to draw useful conclusions comparing surgical interventions with CPAP in the treatment of patients with OSA at this time. Therefore the strength of evidence is insufficient to determine the relative merits of surgical treatments versus CPAP.

Comparison of Surgery and Mandibular Advancement Devices

One parallel design RCT across three publications compared the effects of a MAD with uvulopalatopharyngoplasty (UPPP) in patients with mild to moderate OSA and no other significant comorbidities.[261-263] Subjects were 95 men with a mean age of 50 years and a mean BMI of 27 kg/m^2. Mean baseline AHI was 19 events/hr. Patients were followed for up to 4 years. Results at 12 months showed that 80 percent of patients using MAD achieved a decrease in AHI of ≥50 percent compared to 60 percent who had UPPP ($P<0.05$). A statistically significant reduction in AHI was also observed in the MAD group as compared to the UPPP group at 4 years (-11 versus -6 events/hr; net difference -5 events/hr; 95 percent CI [estimated] -9, -1; $P<0.001$ [P analyzed for final values, not net difference]). Objective clinical outcomes were not evaluated. This study was rated quality B. This study is applicable mainly to patients with apnea index scores between 5 and 25 events/hr. It was restricted to patients with sufficient number of

teeth to anchor the mandibular devices in place. With only one study that evaluated only AHI, the strength of evidence is insufficient regarding the relative merit of MAD versus surgery in the treatment of OSA.

Comparison of Drug Therapy and Control

Seven RCTs compared different drug treatments with controls (Appendix D Table 5.23.1).[205,264,265,265-268] All but Ryan 2009 were crossover trials. The studied drugs included mirtazapine, xylometazoline, fluticasone, paroxetine, pantoprazole, steroid plus CPAP (versus CPAP alone), acetazolamide, and protriptyline (Appendix D Table 5.23.1). All trials used placebo controls except for Ryan 2009, which used CPAP without steroid as a control.

Mean baseline AHI ranged from 10 to 36 events/hr. Study sample sizes ranged from 10 to 81, with a total of 231 across the studies. One study was rated quality A, five were rated quality B, and one was rated quality C. Whyte 1988 was rated quality C because of its lack of exclusion criteria and a washout period.

Study Results (Appendix D Tables 5.23.2-5.23.9)

As each study evaluated a different drug therapy, each study is described individually. No study evaluated objective clinical outcomes.

Carley 2007[264] compared two mirtazapine doses (4.5 mg and 15 mg) to control. Both groups on mirtazapine had a significantly lower AHI than the control group (P=0.004). The 15 mg mirtazapine group had a significantly lower arousal index (P=0.02), higher sleep efficiency (P=0.05), and lower REM sleep percentage (P=0.04) than the controls; however, the 4.5 mg group did not differ from the control group in these outcomes. Neither drug group differed from controls in slow wave sleep, minimum oxygen saturation, or Stanford Sleepiness Scale score.

Clarenbach 2008[269] did not find a difference in AHI, ESS, arousal index, sleep efficiency, slow wave sleep, or REM sleep between the xylometazoline group and control.

Kiely 2004[265] found a significantly lower AHI in the fluticasone group as compared to the placebo group, both in patients with an AHI ≥10 events/hr (median difference = -6.5 events/hr; P<0.05) and in patients with an AHI ≥5 events/hr (median difference = -5.6 events/hr; P=0.01). The drug group did no differ from controls in REM sleep or minimum oxygen saturation.

Kraiczi 1999[266] found a lower AHI in the paroxetine group than in the control group (95 percent CI -17.9, 0.6; P=0.021[i]). The drug group did not differ from the control group in sleep efficiency, slow wave sleep, REM sleep, or Comprehensive Psychopathological Rating Scale (CPRS) score.

Whyte 1988 did not find a significant difference in AHI, arousal index, sleep efficiency, slow wave sleep, REM sleep, or minimum oxygen saturation between acetazolamide and control, or between protriptyline and control.

Suurna 2008 found a lower ESS score in the pantoprazole group as compared to control (difference = -0.5; 95 percent CI -0.98,-0.02; P=0.04), but no significant difference in FOSQ score (difference = 0.06; 95 percent CI -5.3, 0.1; P=0.06).

Ryan 2009 did not find a statistically significant difference in ESS, SF-36 score, or Mini Rhinoconjunctivitis Quality of Life Questionnaire score between the steroid plus CPAP and dry CPAP groups.

Study Variability

None of the studies reviewed performed subgroup analyses. As the drugs used were different in each study, we were not able to examine differences with regard to patient characteristics across studies.

Summary

Seven trials compared different drugs with control for the treatment of patients with OSA. Due to the heterogeneous nature of the drugs examined and the different findings reported, it is not possible to draw any general conclusions about the effects of drugs on the treatment of OSA at this time. As only one study examined each drug, the strength of evidence is insufficient to evaluate the effectiveness of any individual drug for the treatment of OSA.

Comparison of Atrial Overdrive Pacing and Control or CPAP

Two crossover trials examined atrial overdrive pacing in the treatment of OSA (Appendix D Table 5.24.1).[270,271] Both trials evaluated patients who had pacemakers that had been implanted for an underlying arrhythmia. The pacemakers were capable of specific scheduling for overnight atrial overdrive pacing. Melzer 2006 compared atrial overdrive pacing of 75 beats per minute with sham pacing of 45 beats per minute in 20 patients.[270] Simantirakis 2009 compared atrial overdrive pacing (pacing at 14 beats per minute greater than spontaneous mean nocturnal heart rate) with CPAP (and no atrial overdrive pacing) in 16 patients.[271] The mean baseline AHI in the trials were 27[270] and 49 events/hr.[271] Melzer 2006 excluded patients with other ventilatory OSA interventions. This study was rated quality A. Simantirakis 2009 excluded those with left ventricular dysfunction or heart failure. This study was rated quality B, as it did not provide a description of how CPAP pressure was titrated and had a small sample size. The studies are applicable to patients who already have implanted pacemakers without cardiac dysfunction.

Objective Clinical Outcomes

No study evaluated objective clinical outcomes.

Apnea-Hypopnea Index (Appendix D Table 5.24.2)

Both trials provided data on AHI outcomes. Melzer 2006 did not find a statistically significant difference between atrial overdrive pacing and control. Simantirakis 2009 did not find a statistically significant difference between atrial overdrive pacing and CPAP.

Epworth Sleepiness Scale (Appendix D Table 5.24.3)

Simantirakis 2009 did not find a statistically significant difference between atrial overdrive pacing and CPAP in ESS score.

Other Sleep Measures (Appendix D Table 5.24.4)

Melzer 2006 did not find a statistically significant difference between atrial overdrive pacing and CPAP in slow wave sleep or REM sleep.

Study Variability

No study reported subgroup analyses with respect to the comparative effect of atrial overdrive pacing versus no pacing in terms of patient characteristics (age, sex, race, weight, bed partner, and airway) or severity of OSA.

Summary

Two trials examined atrial overdrive pacing in the treatment of OSA. Each trial used a different control comparator (sham pacing or CPAP). Neither trial reported a benefit in sleep study measures with atrial overdrive pacing as compared to the control. As each comparison was unique and the respective sample sizes small, the strength of evidence is insufficient to determine the effect of atrial overdrive pacing on sleep apnea signs and symptoms.

Comparison of Other Interventions and Controls

Five trials, each a parallel design, compared a variety of miscellaneous interventions with different controls.[272-276] Freire 2006 compared acupuncture to sham acupuncture. Wang 2009 compared auricular plaster to vitamin C. Cartwright 1991 compared a tongue-retaining device, a posture alarm, or a combination of the two with no intervention. Krakow 2006 compared nasal dilator strip therapy to no treatment. Grunstein 2007 compared bariatric surgery to another weight loss protocol.

As each study evaluated different, unrelated interventions, each study is described individually. No study evaluated objective clinical outcomes. Each study's applicability is suggested by its eligibility criteria.

Tongue-Retaining Device, Posture Alarm, or Combination Versus No Treatment

Cartwright 1991 compared a tongue-retaining device, posture alarm, or a combination of these therapies against no intervention in an RCT.[273] The study consisted of 60 male patients with positional sleep apnea and an AHI >12.5 events/hr. Neither of the devices nor their combination resulted in significantly different changes in AHI compared to control. From reported data, the odds ratio for achieving an AHI <5.5 events/hr was nonsignificant for each intervention.

The study was rated quality C due to unclear reporting, the lack of an appropriate statistical analysis, and an inadequate description of the interventions.

Bariatric Surgery Versus Routine Management

The Grunstein 2007 study was a nonrandomized comparison of bariatric surgery (gastric bypass, vertical banded gastroplasty, or gastric banding) and routine obesity management (consisting of diet and exercise advice and behavior modification).[272] Patients were included if they had a BMI $\geq$38 kg/m^2, and were excluded if they had undergone previous bariatric surgery. Patients had previously responded to a baseline questionnaire that they had frequent apneas. There were 694 total patients, with 382 patients in the bariatric surgery group and 312 in the control group. Patients were able to choose which treatment they would receive, and were computer-matched to patients in the other treatment group. No baseline data were collected on OSA severity.

After 2 years of followup, patients who had bariatric surgery experienced significantly less persistence of sleep apnea, as defined by fewer symptoms noted on a followup questionnaire (OR = 0.16; 95 percent CI 0.10, 0.23; P<0.001).

The study was rated quality C due to a lack of randomization, a high dropout rate, and dissimilar baseline characteristics between groups.

Nasal Dilator Strip Versus No Treatment

Krakow 2006 compared nasal dilator strip therapy with no treatment in an RCT.[275] Enrolled were 80 patients with nonsevere OSA. The nasal dilator strip group had a significantly better Pittsburgh Sleep Quality Index score (difference = 2.7; P<0.001), better Quality of Life Enjoyment and Satisfaction Questionnaire score (difference = 0.46; P=0.01), improved Insomnia Severity Index score (difference = -0.78; P<0.001), and better FOSQ score (difference = 1.3; P<0.02) than the no treatment group. The study was rated quality C due to the lack of an objective measurement of sleep apnea and unclear reporting.

Acupuncture Versus Control

Freire 2006 compared acupuncture (10 weekly sessions including needle manipulation) to sham acupuncture (10 weekly sessions with needles, but not at acupuncture sites, and no manipulation) or no treatment.[274] Patients (N=26) were included if they had not received acupuncture before and had an AHI of 15-30 events/hr, and were excluded if they had a history of CPAP or oral device use. The mean baseline AHI was 19 events/hr.

Treatment with acupuncture resulted in statistically significant net differences in AHI compared with both sham acupuncture (net difference = -13 events/hr; 95 percent CI -21, -5; P<0.05) and no treatment (net difference = -18 events/hr; 95 percent CI -29, -6; P=0.002). The acupuncture group had no significant difference in ESS scores as compared to sham acupuncture, but a significant net reduction in ESS compared with no treatment (net difference = -5.9 events/hr; 95 percent CI -11.1, -0.7; P<0.05). Patients in the acupuncture group did not differ in sleep efficiency, REM sleep, or SF-36 total score as compared to the other groups.

The study was rated quality C due to a small sample size, an unequal number of dropouts per group, and lower quality of life measurements in the controls at baseline compared with the active treatment group.

Auricular Plaster Therapy

Wang 2009 compared auricular plaster therapy with vitamin C in 45 males with OSA.[276] After 10 days of followup, the group randomized to auricular plaster group was found to have a lower AHI than the vitamin C group (net difference = -13 events/hr; 95 percent CI -18, -8). The study was rated quality B due to incomplete reporting.

Summary

Five studies examined miscellaneous interventions compared with controls in the treatment of OSA. Four of these studies were rated quality C and one was rated quality B. No consistent effects on sleep study measures were reported across different interventions as compared to inactive controls or routine treatments. As each intervention was studied only once, the strength of evidence is insufficient to determine the benefit of each intervention compared with control in the treatment of patients with OSA.

Adverse Events

Across all studies and interventions, the reporting of adverse events (or side effects) was sparse. Almost no RCT was sufficiently large to adequately compare rates of adverse events between different interventions, particularly if analysis is focused on RCTs of actual treatments (as opposed to RCTs with placebo or sham treatment groups). Furthermore, as will be described,

the types of adverse events related to different categories of treatments vary considerably, further hampering direct comparisons.

Adverse events are, therefore, evaluated here based on the cohorts of patients who received specific treatments within RCTs (e.g., CPAP), rather than by the RCT comparisons (e.g., CPAP versus surgery). In addition, based on discussions with the Technical Expert Panel about the likely dearth of RCTs and other comparative studies of surgical treatments, it was also decided that adverse events data would be collected from prospective or retrospective cohort studies of surgical treatments for OSA with at least 100 patients. It should also be noted that the summary tables include adverse event rate data for only those findings study authors reported to be (or we determined to be) clinically important and/or severe outcomes. Less clinically significant adverse events were listed for each intervention in table footnotes. In addition, data concerning a lack of adverse events (e.g., no perioperative deaths) or general results (e.g., "major adverse events") were extracted only from studies with at least 100 patients. We did not collect data on adverse events from control, placebo, or sham treatments.

Of the 143 otherwise eligible comparative studies of two or more interventions for OSA and 13 surgical cohort studies with at least 100 treated patients, 19 comparative studies, and 12 surgical cohort studies reported adverse event data.

Positive Airway Pressure Devices (Appendix D Table 5.25.1)

Only six trials of CPAP reported adverse event (or side effect) data.[171,173,179,183,207,259] Trials enrolled between 21 and 73 patients using CPAP. Four of the trials compared different CPAP devices to each other; the remaining two compared CPAP to other interventions. Four studies evaluated CPAP (two compared nasal to oral CPAP) and three evaluated autoCPAP (one compared humidified to nonhumidified autoCPAP). No study of other types of CPAP reported adverse event data.

The most commonly reported adverse event was claustrophobia. In four studies with 1 to 4 month followups, claustrophobia was reported by one to three patients, representing 1.4 to 23 percent of patients. Epistaxis was reported among patients in two studies: two of 22 patients (9 percent) using nonhumidified autoCPAP, but none of the patients using humidified autoCPAP, and two of 17 patients (12 percent) using nasal CPAP (but implied no patients using oral CPAP). Excessive pressure or pressure intolerance was reported in two studies: five of 55 patients (9 percent) on CPAP in one study and 2 (4 percent) on autoCPAP in the other. Major or excessive oral dryness was reported in two studies of oral CPAP, with one study noting 11 patients (52 percent) and the other 3 (14 percent), complaining of excessive oral dryness. Only one trial reported excessive nasal dryness, with 2 (12 percent) patients noting the complaint. Severe gum pain was also reported in one study of oral CPAP in 3 of 21 (14 percent) patients. A major excess of salivation and sore gums or lips were reported in one trial of oral CPAP in 1 (5 percent) and 2 (10 percent) patients, respectively. Other more minor adverse events reported included skin irritation, nasal irritation or obstruction, dry nose or mouth, excess salivation, minor or moderate sore gums or lips, minor aerophagia, abdominal distension, minor chest wall discomfort, pressure discomfort, and transient or minor epistaxis.

Generally, about 5 to 15 percent of patients reported specific adverse events they considered to be a major problem while using CPAP. However, no study reported a severe adverse event that would not resolve quickly upon discontinuing CPAP or that may be amenable to alleviation with ancillary treatments (such as humidification).

Mandibular Advancement Devices (Appendix D Table 5.25.2)

Only five RCTs of MAD reported adverse event data.[212,216,225,226,262] The trials included between 19 and 48 patients using these devices. Four studies evaluated custom-made devices, with ranges of maximal mandibular advancement from 50 to 100 percent and 2-5 mm interdental clearance, and one study evaluated the Snore-Guard™ (mandible set at 3 mm posterior to maximal acceptable advance with a 7 mm opening). Four studies lasted 1 to 4 months, while one study followed patients for 4 years. All major adverse events were related to tooth, mouth, or jaw pain or damage. In one study with a device with 80 percent mandibular advancement, 3 of 48 patients (6 percent) had a dental crown damaged. One of 31 patients using a maximal advancement device had loosening of teeth. Temporomandibular joint (TMJ) or jaw pain was reported in one patient each of four studies (between 2.2 and 5.2 percent of patients). An aphthous ulcer due to acrylic polymer allergy was also reported by one patient (2.2 percent) in one study. Other more minor adverse events included a sensation of pressure in the mouth, transient morning mouth and TMJ discomfort or sounds, minor sore teeth or jaw, transient mild mucosal erosions, minor excessive salivation, tooth grinding, and sleep disruption.

Overall, about 2 to 4 percent of patients complained of jaw or temporomandibular joint pain with MAD. There were an insufficient number of patients evaluated to determine whether the likelihood of jaw pain might be related to the degree of jaw opening. More permanent damage, namely dental crown damage, occurred in 6 percent of patients in one study, but was not reported in other studies. One patient had an allergic reaction to acrylic polymer.

Airway Surgery Interventions

Ten eligible studies of UPPP (and related surgeries), two studies of RFA, six studies of combinations or other surgeries, and one study of palatal implants alone reported adverse events (or complications).

Uvulopalatopharyngoplasty (Appendix D Table 5.25.3)

Ten eligible studies reported adverse events related to UPPP.[124,245,255,262,277-282] The largest cohort study analyzed 3,130 patients who received UPPP with or without tonsil, nasal, or turbinate surgery. The remaining nine studies ranged in sample size from 18 to 158 patients and generally included similar surgeries, or tracheostomy, or, in one study, osteotomy; one study performed laser assistant uvulopalatoplasty.

Perioperative death (up to 30 days of surgery) was reported by five studies and ranged from 0/158 to 2/132 (1.5 percent) of patients. The largest cohort (Kezirian 2004) reported 7/3,130 (0.2 percent) perioperative mortality. This study reported serious complications (including death) in 51/3,130 (1.6 percent) of patients. These complications included reintubation (17 patients), pneumonia (11), hemorrhage (9), cardiovascular complication (8), emergency tracheotomy (7), and mechanical ventilation for >48 hr (6). No patients suffered deep vein thromboses or kidney failure.

Across studies, reintubation was reported in 0.5 to 5.2 percent of patients (three studies, with no long-term sequelae in one study), pneumonia in 0.4 and 1.5 percent of patients (two studies), major hemorrhage in 0.3 to 5.5 percent of patients (eight studies), and tracheotomy in 0.2 to 5.6 percent of patients (four studies). Other major perioperative adverse events reported across studies included respiratory events (six patients), substantial laryngeal edema (two patients), pulmonary edema (one patient), and postextubation asystole (one patient). Individual studies

reported no perioperative airway complications, abscesses requiring surgical interventions, or rehospitalizations (in 134 patients), or infections or arrhythmias (in 101 patients).

Adverse events reported over the long term (3 months to 1, 4, or 7.25 years) included difficulty with speech or change in voice (0.6 to 15 percent; three studies); velopharyngeal incompetence (11 and 12 percent; two studies); infection requiring surgical intervention (0 and 11 percent; two studies); difficulty swallowing (5 to 10 percent; three studies); pronounced nasal regurgitation of fluids (8 percent; one study); and breathing difficulties, nasal synechiae, loss of taste, and tracheal stenosis in 5 percent of patients or fewer. One study with 158 patients reported no long-term sequelae from complications were reported.

Other adverse events (or side effects or harms) reported by studies included: unplanned medications, mild transient pain and swallowing difficulty, postoperative (minor) hematomas or ulcerations, mild bleeding, mild and transient tongue deviation, transient swelling sensation, pharyngeal dryness, nasal regurgitation (transient), increased mucus secretion, gagging, cough, infection (self-limited), antibiotic-related diarrhea, burning sensation, anosmia, temporary vocal quality change, and difficulty singing, playing saxophone, etc.

Radiofrequency Ablation (Appendix D Table 5.25.4)

Two studies reported adverse events following radiofrequency ablation of the tongue base (or other sites in one study) in 497 and 73 patients, respectively.[252,283] The larger cohort experienced no long-term complications (after 8 days) and the following short-term adverse events: dysphagia requiring hospitalization (4 patients; 0.8 percent), tongue base ulceration requiring surgical intervention (3 patients; 0.6 percent), and in one patient each (0.2 percent) soft palate mucosa ulceration requiring surgical intervention, temporary hypoglossal nerve palsy, and tongue base abscess requiring surgical intervention. The smaller study reported that seven patients (10 percent) had an infection or cellulitis during 6 weeks of followup, four patients (5.5 percent) had severe, suppurative tongue base infections (two of which required surgical intervention), and one patient (1.4 percent) had a tongue abscess.

Other adverse events (or side effects or harms) reported by studies included: unplanned medications, mild transient pain and swallowing difficulty, postoperative (minor) hematomas or ulcerations, mild and transient tongue deviation, transient swelling sensation, and asymptomatic fibrotic narrowing.

Combination or Various Surgeries (Appendix D Table 5.25.5)

Six studies reported adverse events in patients who received a variety of other surgeries.[280,284-287] These included combinations of UPPP and geniotubercle advancement, hyoid suspension, maxillary and/or mandibular osteotomy, and tongue RFA, and multilevel surgeries without UPPP, or stepwise multilevel surgeries.

The studies analyzed between 64 and 233 patients. Only one study specifically reported on perioperative death, noting that no deaths occurred. Two studies reported no major complications, though one also reported five patients (4 percent) with Pillar implant extrusion requiring removal and replacement, two patients (1.6 percent) with turbinate bone exposure, and one patient (0.8 percent) with nasal septum perforation, tongue mucosal ulceration, and hypoglossal nerve weakness lasting less than 1 month. With the exception of the smallest study, all other adverse events were reported in <2 percent of patients, including undescribed bleeding (1.9 percent), new onset atrial fibrillation (1.9 percent), transient nerve paralysis (1.4 percent), bleeding requiring anesthesia (1.3 percent), hypoglossal nerve paralysis (0.7 percent), and new

unstable angina (0.5 percent). The largest study reported no long-term speech or swallowing problems and another study reported no airway complications, abscesses requiring surgical interventions, or rehospitalizations. The smallest study, examining stepwise surgery in 64 patients, had the highest reported complication rates, including paresthesia (not described; 17 percent), dysphagia (not described; 11 percent), voice change (3 percent), infection (not described; 3 percent), taste alteration (1.6 percent), wound dehiscence (1.6 percent), and transient palatal fistula (1.6 percent).

Other adverse events (or side effects or harms) reported by studies included: aspiration, neck seroma, transient dysphagia, transient tongue base ulceration, suture removal for foreign body reaction, and transient facial anesthesia.

Palatal Implants Alone (Appendix D Table 5.25.6)

One study reported adverse events following insertion of Pillar palatal implants in 50 patients.[243] During 1 week of followup, one patient had an undefined infection and two had extrusion of their implants. Other reported adverse events included sore throat and foreign body sensation.

Bariatric surgery (Appendix D Table 5.25.7)

One large study of 1,592 patients reported adverse events following bariatric surgery performed in patients with OSA.[272] Perioperative mortality was 0.21 percent, and 13 percent had bleeding, embolus and/or thrombosis, wound complications, deep infections, pulmonary, and/or other complications.

Weight Loss Diet (Appendix D Table 5.25.8)

One study evaluated a liquid, very low energy diet for 30 patients with OSA.[237] After 9 weeks, one patient had transient gout and two had transient elevated liver enzymes. Other reported adverse events included dizziness, dry lips, and constipation.

Drugs (Appendix D Table 5.25.9)

Three studies evaluating four drugs used for OSA treatment reported adverse events.[266,267,288] Acetazolamide resulted in the largest number of reported adverse events: any paresthesia in 8/10 patients and intolerable paresthesia in one patient. Protriptyline caused severe dry mouth requiring drug discontinuation in 2/10 patients and ―visual upset," urinary symptoms, and altered sexual potency with testicular discomfort in one patient each. Paroxetine use was associated with ejaculation disturbance (15 percent), decreased libido (10 percent), headache (10 percent), and constipation (10 percent). (Other reported adverse events included fatigue, mouth dryness, somnolence, and dizziness with both paroxetine and placebo, and sweating, nervousness, infectious pneumonia and Lyme disease during paroxetine treatment.) During zolpidem use, 1/72 patients (1.4 percent) experienced episodes of sleep walking.

Summary

Each type of OSA treatment carries its own set of potential adverse events. Based on the evidence reported among the eligible (mostly comparative) studies, with only a few exceptions, the only truly serious long-term adverse consequences from OSA treatments occurred among patients having oronasopharyngeal or bariatric surgery. These included perioperative death in up to 1.5 and 1.6 percent of patients undergoing UPPP in two studies. Most studies, however,

reported no deaths. Other major postsurgical complications also included infections, hemorrhage, nerve palsies, emergency surgical treatments, cardiovascular events, respiratory failure, and rehospitalizations. Long-term adverse events included speech or voice changes, difficulties swallowing, airway stenosis, and others. In smaller studies, these events were found to occur in about 2 to 15 percent of patients (when reported). The largest studies (Kezirian 2004 with 3,130 UPPP surgeries and Stuck 2003 with 422 RFA surgeries) reported no long-term complications (not including perioperative death or cardiovascular complications).

All adverse events related to CPAP treatment were potentially transient and could be alleviated with either cessation of treatment or with adjunct interventions. Approximately 5 to 15 percent of patients reported specific adverse events they considered to be a major problem while using CPAP. These included claustrophobia, oral or nasal dryness, epistaxis, irritation, pain, or excess salivation. No adverse event with potentially long-term consequences was reported in patients receiving CPAP.

Among studies of MAD, four patients in two studies (with 79 patients total) incurred dental crown damage or loosening of teeth. TMJ or jaw pain was reported in about 2 to 4 percent of patients, although no study reported on the long-term consequences of these symptoms. It was also not clear whether the severity or frequency of TMJ symptoms was related to the degree of mandibular advancement or jaw opening.

Adverse events related to a very low energy weight loss diet or to various drugs were treatment specific. None appeared to be an adverse event with long-term consequences.

Key Question 6. In OSA patients prescribed nonsurgical treatments, what are the associations of pretreatment patient-level characteristics with treatment compliance?

To address this question, our literature search was restricted to longitudinal studies of at least 100 participants all of whom were prescribed nonsurgical OSA treatments and followed for at least 3 months. Only multivariable analyses of continuous positive airway pressure (CPAP) compliance were included. Because of the small number of potentially eligible mandibular advancement device (MAD) studies, all were included for review. Six studies met criteria. Five evaluated compliance with CPAP,[203,289-292] one compliance with MAD.[293]

Compliance with CPAP

Four of the five eligible studies were prospective cohort studies and one was a randomized control trial (RCT) of C-Flex™ versus fixed CPAP (Appendix D Table 6.1a-b).[203] The patients in the cohort studies were treated with either fixed CPAP, a variety of CPAP devices, or, in one study,[292] autotitrating CPAP (autoCPAP). The number of patients in the studies ranged from 112 to 1,103, and followup ranged from 3 months to 4 years. The studies were conducted mostly from the mid 1980s through the 1990s (or possibly later based on publication dates in two studies). All patients were enrolled at the beginning of their CPAP therapy. The demographics of the five studies were generally similar: a large majority of men, mean age around 50 years, mean BMI about 30 kg/m^2, and, in four of the studies, a mean AHI between 44 and 50 events/hr (Krieger 1996 apparently included patients with more severe OSA, as their mean AHI was 70 events/hr). Three of the studies (McArdle 1999, Krieger 1996, and Wild 2004) described an active followup program to improve CPAP usage. Hui 2001 described only an initial training session. The lone RCT (Pepin 2009) did not describe the initial ancillary care for CPAP usage

(Appendix D Table 6.1a). In general, the studies are applicable to patients initiating CPAP whose AHI is greater than 30 events/hr.

Each study defined compliance differently. Three studies used thresholds of 1, 2, or 3 hours of use per night (or voluntary discontinuation). The RCT used "objective compliance," which was measured by the device, but was not defined. The smallest study evaluated hours of use per night as a continuous variable.

McArdle 1999, the largest study, provided a well documented, complete, and appropriate analysis, with no obvious selection or ascertainment biases; it was rated quality A. Wild 2004 suffered from some incomplete reporting and was rated quality B. The remaining three studies did not adequately define predictors, outcomes, or statistical analyses used, and were rated quality C (Appendix D Table 6.1b).

In McArdle 1999, 16 percent of patients discontinued CPAP at 1 year and 32 percent at 4 years. Krieger 1996 had somewhat better compliance; 14 percent withdrew from CPAP at a mean of 3.2 years. Pepin 2009 and Hui 2001 both found mean CPAP usage of about 5 hr/night at 3 months. Wild 2004 did not report compliance rates.

The four studies that evaluated baseline AHI as a predictor of compliance with CPAP all found a significant association such that a higher baseline AHI was associated with greater compliance. Krieger 1996 and McArdle 1999 found significant associations between an AHI>15 events/hr and greater compliance at 1-4 years (though the latter study found no significant association with an AHI threshold of 30 events/hr). The other two studies reported that a higher AHI (analyzed as a continuous variable) was associated with greater adherence or more hours of use per night at 1 and 3 months. In a secondary analysis, McArdle 1999 also found that AHI, analyzed as a continuous variable, was significantly associated with compliance across the range of AHI.

Three studies evaluated baseline ESS as a predictor of compliance. McArdle 1999, the quality A and largest study with the longest followup duration (4 yr), found that an ESS score >10 (and as a continuous variable) was associated with greater compliance. Wild 2004 found the same significant association, but Krieger 1996 did not find ESS to be an independent predictor, after adjusting for AHI and age. Only Krieger 1996 found that younger age (as a continuous variable) was associated with greater compliance. McArdle 1999 and Pepin 2009 did not find age to be an independent predictor.

Several potential predictors were evaluated by two studies each. In all cases the studies disagreed as to whether the factors were independent predictors of compliance. Snoring was a predictor in McArdle 1999, but not Hui 2001; lower CPAP pressure a predictor in Wild 2004, but not McArdle 1999; and higher BMI a predictor in Wild 2005, but not McArdle 1999.

Pepin 2009 focused primarily on a sleep apnea-specific quality of life scale, and did not report on potential predictors evaluated by the other studies (except age). This study found that at 3 months, higher baseline mean oxygen saturation and greater sleepiness as measured by the Grenoble Sleep Apnea Quality of Life test were associated with greater compliance.

Summary

Across studies, there is a moderate strength of evidence that more severe OSA as measured by higher AHI is associated with greater compliance with CPAP use. There is a moderate strength of evidence that a higher ESS score is also associated with improved compliance. There are low strengths of evidence that younger age, snoring, lower CPAP pressure, higher BMI,

higher mean oxygen saturation, and the sleepiness domain on the Grenoble Sleep Apnea Quality of Life test are each possible independent predictors of compliance.

It is important to note, however, that selective reporting, particularly nonreporting of nonsignificant associations, cannot be ruled out. The heterogeneity of analyzed and reported potential predictors greatly limits these conclusions. Differences across studies as to which variables were independent predictors may be due to the adjustment for different variables, in addition to differences in populations, outcomes, CPAP machines, and CPAP training and followup.

Compliance with Mandibular Advancement Devices

Only one retrospective cohort with 144 patients met criteria for studies evaluating predictors of compliance with MAD (Appendix D Table 6.2a-b).[293] All patients received a custom-made MAD and received "standard" education concerning its use, including adjustment of the device until it was workable. Patients were predominately male with a mean age of 51 years and a mean baseline AHI of 23 events/hr. Notably, 8 percent of the patients were nonapneic snorers with an AHI <5 events/hr. The study was rated quality C as only univariable analyses were reported, predictors were poorly defined, and results were not clearly reported (Appendix D Table 6.2a). No explicit definition of compliance was provided. The study is generally applicable to patients initiating use of custom-made MAD.

The study failed to identify potential predictors that were significantly associated with MAD compliance. Variables that were analyzed included age, sex, occupation, "marital situation," snoring, feeling refreshed after sleep, daytime somnolence, driving problems, ESS, AHI, and CPAP failure or refusal (Appendix D Table 6.2b).

Key Question 7. What is the effect of interventions to improve compliance with device (positive airway pressure, oral appliances, positional therapy) use on clinical and intermediate outcomes?

To address this question, we included only prospective comparative studies that enrolled more than 10 subjects per intervention arm and with 2 weeks or more of followup. We accepted any measure of compliance with a device, whether categorical (compliance versus no compliance) or continuous (time spent using device). We restricted the analysis to those interventions whose primary purpose was to improve compliance with treatment. We also included three studies that evaluated different care models (nurse led care versus others) for patients who had continuous positive airway pressure (CPAP) treatments that also reported compliance outcomes.

Eighteen studies met inclusion criteria (Appendix D Table 7.1).[174,288,294-309] All studies were RCTs, of parallel or crossover design, that evaluated outcomes of compliance with CPAP use. No trials evaluated measures to improve compliance with oral appliances or positional therapy. Fifteen studies examined a wide variety of interventions whose primary purpose was to improve compliance. For the purpose of this report, we categorized these interventions into four broad groups: 1) nine studies on extra support or education;[174,294,296-301,303] 2) three studies on telemonitoring care;[295,304,305] 3) one study on a behavioral intervention;[302] and 4) two studies on miscellaneous interventions.[288,306] The remaining three studies evaluated different care models (nurse led care versus others) for patients who had CPAP treatments.[307-309] These are reviewed separately.

Interventions To Improve Compliance With CPAP Use

Extra Support or Education

Nine studies evaluated the effects of extra support or education on the outcomes of compliance with CPAP use (Appendix D Tables 7.2 & 7.3).[174,294,296-301,303] The patients in these studies were treated with either fixed CPAP or autotitrating CPAP (autoCPAP). Eight studies enrolled new CPAP users or patients who were newly diagnosed with OSA. The remaining study (Chervin 2007) enrolled mostly (69 percent) people who, at study baseline, were already regular CPAP users. The studies were generally small with sample sizes ranging from 10 to 112 patients followed for 3 weeks to 1 year. Seven studies enrolled patients with similar demographics: mostly men, mean age between 45 and 63 years, mean BMI between 30 and 38 kg/m^2, and mean AHI between 42 and 58 events/hr. Wiese 2005 enrolled a nearly equal mix of men and women with mild OSA (mean AHI 9.3 events/hr). Therefore, these studies are applicable mainly to patients initiating CPAP with an AHI above about 30 events/hr and BMI greater than 30 kg/m^2. Of the nine studies, one was rated quality A, four quality B, and the remaining four quality C. Common quality issues in quality C studies included large dropout rates, different dropout rates between compared groups, and a more complete followup in the active intervention arm than the usual care arm.

Seven studies evaluated compliance as a continuous outcome (hours of use per night). These studies compared a variety of extra support protocols (e.g., telephone calls, videotape, literature) or education programs to usual support/care. Findings were generally inconsistent. Three studies showed that intensive support or literature (designed for patient education) significantly increased hours of CPAP use per night (by an average of 1.1 to 2.7 additional hours) compared with usual care.[174,294,297] However, the other four studies found no significant differences in hours of CPAP use per night between the intervention and control groups.[296,298,300,301]

Three studies reported categorical compliance outcomes using different definitions. Hui 2000 defined compliance with CPAP as at least 4 hours of use per night for more than 70 percent of the nights per week. The study found no significant difference in compliance rates between the augmented support and basic support groups. Smith 2009 defined compliance with CPAP use as 4 or more hours per night on at least 9 of each 14 nights (or at least an 80 percent use rate). This study found that the audio-based intervention packet significantly decreased the rate of short-term (1 month) noncompliance compared with placebo intervention (11 versus 45 percent, respectively; $P<0.01$). However, there was no significant difference in noncompliance rates between groups at 6 month followup. It should be noted that all dropouts without CPAP use data were counted as nonadherent patients. Wiese 2005 analyzed return to clinic for 1 month followup as a measure of compliance among patients with mild OSA, and found that significantly more patients in the control group did not return to clinic for followup than patients in the group that received an educational videotape about CPAP use (51 versus 27 percent, $P=0.02$). The authors noted that the CPAP usage data from the device were available only for patients who returned to clinic for the followup, thus the usefulness of these data is limited.

Telemonitoring Care

Three studies evaluated the effects of telemonitoring care on the outcomes of compliance with CPAP use.[295,304,305] Telemonitoring care is a computer-based telecommunications system that functions as an at-home monitor, educator, and counselor to improve health-related behaviors. All studies enrolled new CPAP users or patients who were newly diagnosed with

OSA. Studies were generally small with sample sizes ranging from 30 to 93 patients who were followed for 30 days to 2 months. All three studies enrolled patients with similar demographics: mostly men, mean age between 45 and 59 years, mean BMI between 32 and 38 kg/m^2, and mean AHI 42 events/hr. Of the three studies, one was rated quality B and two were rated quality C.

All three studies compared telemonitoring care to usual care, and reported continuous compliance outcome as hours of CPAP use per night. Two studies found that telemonitoring increased hours of CPAP use per night (average 1.3 and 1.5 additional hours; P=0.07 and 0.08, respectively) compared with usual care at 2 month followup.[295,304] The third study did not find a significant difference in hours of CPAP use per night at 30 days between patients who received telemonitoring support and those who received usual care.[305] It should be noted, however, that patients in this study who had difficulties in using telemonitoring support were excluded from the analyses.

Behavioral Interventions

Only Richards 2007 (quality A) evaluated the effect of cognitive behavioral therapy (given to patients and their partners) on compliance outcomes in 96 patients (mean age 58 years old; mean AHI 26 events/hr) who were treated with CPAP.[302] This study found that cognitive behavioral therapy significantly increased hours of CPAP use per night compared with usual care (difference = 2.8 hours; 95 percent CI 1.8, 3.9; P<0.0001). This study also performed logistic regression modeling to explore predictors of CPAP compliance at 28 days, and found that psychological factors were not independent predictors of compliance. In addition, patients in the cognitive behavioral therapy group were 6.9 times more likely to comply with CPAP use (at least 4 hours per night) than the usual care group (95 percent CI 2.8, 18.2).

Miscellaneous Interventions

Bradshaw 2006, in a quality B study, compared the effects of an oral hypnotic agent (zolpidem 10 mg) to placebo or standard care (without a pill) in 72 patients newly using CPAP (mean age 38 years; mean AHI 43 events/hr). The hypnotic was prescribed with the purpose of improving CPAP compliance. The study found no significant differences in hours of CPAP use or categorical CPAP compliance outcomes (using three different definitions) between groups. In a quality B crossover trial, Massie 2003 compared CPAP with nasal pillows (designed to improve the comfort of the CPAP device) to CPAP with a regular nasal mask in 39 patients newly using CPAP (mean age 49 years; mean AHI 47 events/hr). The results showed that there was no significant difference in hours of CPAP use between the two different CPAP nasal appliances.

Summary

Fifteen RCTs examined a wide variety of interventions to improve compliance among mostly new CPAP users. Studies generally had small sample sizes with less than 1 year of followup. Results from these 15 studies were mixed. Compared to usual care, several interventions were shown to significantly increase hours of CPAP use per night in some studies. These included intensive support or literature (designed for patient education), cognitive behavioral therapy (given to patients and their partners), telemonitoring, and a habit-promoting audio-based intervention. However, the majority of studies did not find a significant difference in CPAP compliance between patients who received interventions to promote compliance with device use and those who received usual care. Overall, there is a low strength of evidence that some specific

adjunct interventions may improve CPAP compliance, but studies are heterogeneous and no general type of intervention (e.g., education) was more promising than others. In addition, no intervention has had its effect on compliance verified.

Studies That Evaluated Different Care Models for Patients Who Had CPAP Treatments

Three RCTs that evaluated different care models (nurse led care versus others) for patients who had CPAP treatments also reported compliance outcomes (Appendix D Tables 7.2 & 7.3).[307-309] Although all three studies compared a nurse-led model of care to usual care (by clinician), the components of both interventions and usual care differed across the studies. These interventions were not designed specifically to improve CPAP compliance and are thus evaluated separately.

A total of 467 patients were analyzed in these studies, which lasted from 3 months to 2 years. Of the three studies, one was rated quality B and two were rated quality C. Common quality issues in quality C studies include differential dropout rates between comparative groups and poor reporting of patient characteristics.

All three studies found no significant differences in CPAP compliance comparing nurse-led models of care to usual care.[307-309]

Summary

Three RCTs did not find improvements in patient compliance with CPAP with nurse-led care compared with usual care models. However, it should be noted that improved CPAP compliance was not a primary goal of the intervention but rather to evaluate whether nurse-led model of care would produce similar health outcomes compared to the usual care models. There is a low strength of evidence that nurse-led care does not improve CPAP compliance.

Summary and Discussion

The following table summarizes the main findings that address the seven Key Questions in this systematic review. Of note, where interventions are not discussed (either diagnostic tests or treatments), this does not imply that the interventions were excluded from analysis (unless explicitly stated); instead, no studies of these interventions met eligibility criteria Discussion regarding the report and recommendations for future research follow.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 1: Diagnosis Portable monitors vs. PSG	Low (Type II monitors); Moderate (Types III & IV monitors)	• No recent studies have compared Type II portable monitors to PSG. [7] A prior systematic review concluded that "based on [3 quality B studies], Type II monitors [used at home] may identify AHI suggestive of OSA with high positive likelihood ratios and low negative likelihood ratios," though "substantial differences in the [measurement of] AHI may be encountered between Type II monitors and facility-based PSG." • There were 29 studies that compared Type III portable monitors [8] with PSG. 7 of these are new since a previous report. 18 Type III monitors have been evaluated. • There were 70 studies that compared Type IV portable monitors [9] to PSG. 24 of these are new since a previous report. 23 Type IV monitors have been evaluated. • Overall, 15 studies were graded quality A, 45 quality B, and 39 quality C. The studies were applicable to the general population of patients being referred to specialized sleep centers or hospitals for evaluation of suspected sleep apnea. It is unclear if the studies are applicable to patients with comorbidities or who may have central sleep apnea. Most of the studies were conducted either in the sleep laboratory setting or at home. • Studies measured either concordance (comparisons of estimates of AHI), test sensitivity and specificity (to diagnose OSA as defined by PSG), or both. • Type III monitors had a wide range of mean biases (difference in AHI estimate from PSG), from -10 to +24 events/hr, with wide limits of agreements within studies. • Type IV monitors had a wide range of mean biases, from -17 to +12 events/hr, with wide limits of agreements within studies. • To diagnose OSA defined as a PSG AHI ≥5 events/hr, Type III monitors had sensitivities of 83–97% and specificities of 48–100%. Type III monitors commonly less accurately diagnosed OSA with AHI ≥15 events/hr, with sensitivities 64–100% and specificities 41–100%. • Evaluation of positive and negative likelihood ratios, and available ROC curves, suggest that Type III monitors are generally accurate in diagnosing OSA (as measured by PSG), with high positive likelihood ratios, low negative likelihood ratios, and high AUC. • To diagnose OSA, Type IV monitors had a very wide range of sensitivities and specificities. • Across studies (by indirect comparison), the range of sensitivities and specificities of both Type III and Type IV monitors largely overlapped, thus not demonstrating greater accuracy with either type of monitor. • **Conclusion**: The strength of evidence is low that Type II monitors are accurate to diagnose OSA (as defined by PSG), but have a wide and variable bias in estimating the actual AHI. • **Conclusion**: The strength of evidence is moderate that Type III and IV monitors are generally accurate to diagnose OSA (as defined by PSG), but have a wide and variable bias in estimating the actual AHI. The evidence is insufficient to adequately compare specific monitors to each other.

[7] Type II monitors are portable devices that record all the same information as PSG (Type I monitors).

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 1: Diagnosis Questionnaires vs. PSG	Low / Insufficient	• There were 6 studies that compared 6 questionnaires with PSG diagnosis of OSA. Overall, these studies are applicable to patients visiting preoperative clinics, sleep laboratories, and primary care centers for evaluation of sleep apnea. • There were 1 quality A and 3 quality C studies that evaluated the Berlin Questionnaire (based on snoring, tiredness, and blood pressure), with OSA defined as AHI ≥5 events/hr; sensitivity ranged from 69–93%, specificity ranged from 56–95%. With an AHI ≥15 events/hr definition, sensitivity was somewhat lower and specificity was similar. To predict severe OSA (AHI ≥30 events/hr), sensitivity and specificity were generally lower. • Each of the following 4 questionnaires was evaluated in a single study (1 quality B, 2 quality C): STOP, STOP-Bang, ASA checklist, Hawaii Sleep Questionnaire), which all had relatively low specificity for OSA (AHI thresholds of 5, 10, or 30 events/hr), ranging from 37–67%. STOP, ESS, and the Hawaii Questionnaire had sensitivities <80%. STOP-Bang had high sensitivity to predict diagnosis of OSA, particularly those with AHI ≥15 or ≥30 events/hr (93 and 100%, respectively). The American Society of Anesthesiologists Checklist had a sensitivity of 87% to predict severe OSA, but lower sensitivity to predict those with lower AHI. In 1 quality A study, ESS had a low sensitivity (49%) and higher specificity (80%) to predict OSA with AHI ≥5. • **Conclusion**: The strength of evidence is low that the Berlin Questionnaire is moderately accurate (sensitivity and specificity generally <90%) to screen for OSA. The strength of evidence is insufficient to evaluate other questionnaires, but 1 study found that STOP-Bang may have high enough sensitivity to accurately screen for OSA.
Key Question 1: Diagnosis Clinical Prediction, Rules vs. PSG	Low	• There were 7 studies that compared 10 validated clinical prediction rules with PSG (3 quality A, 3 quality B, 1 quality C). Only 1 model has been externally validated (by independent researchers); thus the applicability of the studies to the general population is unclear. Of the models, 8 include variables obtainable through routine clinical history and examination. • A single morphometric model and a model that included pulmonary function test data had near perfect discrimination (AUC=0.996) or sensitivity (100%), but neither was independently validated. The other clinical prediction rules had variable accuracy for predicting OSA (AHI ≥5, 10, or 15 events/hr) or severe OSA (AHI ≥30 events/hr). • **Conclusion**: Thestrength of evidence is low that some clinical prediction rules may be useful in the prediction of a diagnosis of OSA.
Key Question 2: Diagnosis Phased testing	Insufficient	• A single quality C study partially addressed the value of phased testing, but had substantial verification bias due to implementation of the phased testing. • **Conclusion**: The strength of evidence is insufficient to determine the utility of phased testing.
Key Question 3: Diagnosis Preoperative screening	Insufficient	• There were 2 quality C studies that assessed the effect of preoperative screening for OSA on surgical outcomes, though only 1 of these was designed to address the question. • The retrospective study that compared mandatory prebariatric-surgery PSG with PSG performed based on clinical parameters (performed during different time periods) did not find significant differences in outcomes. The other study found only that those patients who volunteered for preoperative PSG were more likely to suffer cardiopulmonary perioperative complications than patients who refused PSG. • **Conclusion**: The strength of evidence is insufficient to determine the utility of preoperative sleep apnea screening.

[8] Type III monitors are portable devices that contain at least two airflow channels or one airflow and one effort channel.
[9] Type IV monitors comprise all other devices that fail to fulfill criteria for Type III monitors. They include monitors that record more than two physiological measures as well as single channel monitors.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 4: Predictors AHI as a predictor of long-term clinical outcomes	Variable (High for all-cause mortality; Low for diabetes; Insufficient for other long-term clinical outcomes)	• There were 11 studies (of 8 large cohorts) that performed multivariable analyses of AHI as an independent predictor of long-term clinical outcomes. • There were 4 studies (3 quality A, 1 quality B) that evaluated all-cause mortality. All found that AHI was a statistically significant independent predictor of death during 2–14 years of followup. The association was strongest among people with an AHI >30 events/hr. There was 1 study, however, that found an interaction with sex and age such that AHI was associated with death only in men ≤70 years of age. The evidence on mortality is applicable to the general population, with and without OSA, and also more specifically to men with OSA symptoms or evidence of OSA. • There were 2 quality A studies that evaluated cardiovascular mortality. There was 1 study that found that only AHI >30 events/hr predicted cardiovascular death; the other study found no association. • A single quality A study evaluated nonfatal cardiovascular disease and similarly found that only AHI >30 events/hr was an independent predictor. • A single quality B study suggested that the association between AHI and stroke may be confounded by obesity. • There were 2 studies (1 quality A, 1 quality B) that came to uncertain conclusions regarding the possible association between AHI and incident hypertension. • There were 2 studies (1 quality A, 1 quality B) that suggested an association between AHI and incident type 2 diabetes, though 1 study found that the association was confounded by obesity. • A single quality A study found no significant association between AHI and future quality of life (SF-36 after 5 years). This conclusion appears to be applicable for both the general population and specifically for patients diagnosed with sleep disordered breathing. • **Conclusion**: The strength of evidence is high that an AHI >30 events/hr is an independent predictor of all-cause mortality; although one study found that this was true only in men under age 70. The strength of evidence is low that a higher AHI is associated with incident diabetes, though possibly confounded with obesity. The strength of evidence is insufficient to determine the association between AHI and other clinical outcomes.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments CPAP vs. control	Moderate	• There were 43 trials that compared CPAP devices with either no treatment or sham CPAP. All but 2 evaluated fixed CPAP. Of the 43 trials, 4 were rated quality A, 22 quality B, and 17 quality C. Overall, the studies are applicable to a broad range of patients with OSA. • Only 1 study evaluated a clinical outcome, namely heart failure symptomatology, and found no significant effect after 3 months. • By meta-analysis, CPAP results in a statistically significant large reduction in AHI (-20 events/hr compared with no treatment and -46 events/hr compared with sham CPAP). All studies found statistically significant effects, though there was statistical heterogeneity across studies that could not be fully explained. There were no clear, consistent relationships across studies between definition of OSA (by minimum threshold AHI) or other clinical features and effect size. • By meta-analysis, CPAP results in a statistically and clinically significant improvement in sleepiness as measured by ESS (-2.6 compared with no treatment and -2.7 compared with sham CPAP). The studies were statistically significant and most, but not all, found significant improvements in ESS. No factors clearly explained the heterogeneity. • CPAP also generally resulted in improvements in other sleep study measures, but had inconsistent effects on other sleepiness tests, quality of life tests, neurocognitive tests, and blood pressure. • All adverse events related to CPAP treatment were potentially transient and could be alleviated with either stopping treatment or with ancillary interventions. Generally about 5-15% of patients in trials had specific adverse events they considered to be a major problem while using CPAP. These included claustrophobia, oral or nasal dryness, epistaxis, irritation, pain, and excess salivation. No adverse event with potentially long-term consequences was reported. • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS, and other sleep study measures, the strength of evidence is moderate that CPAP is an effective treatment for OSA. However, the strength of evidence is insufficient to determine which patients might benefit most from treatment.
Key Question 5: Treatment OSA treatments Different CPAP devices vs. each other	Variable (Moderate for autoCPAP vs. CPAP; Low for C-Flex™ vs. CPAP; Insufficient for others)	• No study evaluated clinical outcomes. • There were 21 trials that compared autoCPAP with fixed CPAP. Of these, 1 trial was rated quality A; 10 trials each were rated quality B or C. These studies are applicable mainly to patients with AHI more than 15 events/hr and BMI more than 30 kg/m^2. By meta-analysis there was statistically significant, but clinically nonsignificant better improvement in ESS (-0.5), minimum oxygen saturation (1%), and compliance (11 minutes) with autoCPAP than fixed CPAP, and no statistically significant differences in AHI or arousal index. • There were 4 trials comparing C-Flex™ to fixed CPAP. No statistically significant differences were found for compliance, sleep study measures, or other tested outcomes. • There were 14 trials comparing bilevel or flexible bilevel CPAP with fixed CPAP, humidification with no humidification (with fixed CPAP), or oral with nasal fixed CPAP. The studies had either inconsistent results, were sparse, or had imprecise results. • **Conclusion**: Despite no or weak evidence on clinical outcomes, overall, there is moderate strength of evidence that autoCPAP and fixed CPAP result in similar compliance and treatment effects for patients with OSA. • **Conclusion**: The strength of evidence is low of no substantial difference in compliance or other outcomes between C-Flex and CPAP. • **Conclusion**: The strength of evidence is insufficient regarding comparisons of different CPAP devices (or modifications).

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments MAD vs. control	Moderate	• There were 10 trials comparing various MADs with either no treatment or with sham devices (without mandibular advancement). No studies were rated quality A, 8 quality B, 2 quality C. The studies are generally applicable to patients with AHI ≥15 events/hr, though less so to patients with comorbidities or excessive sleepiness. All studies excluded edentulous patients or those with periodontal diseases. • No study evaluated clinical outcomes. • By meta-analysis, MAD results in a statistically significant reduction in AHI (-12 events/hr). All studies found statistically significant improvements in AHI, ranging from -6 to -25 events/hr, without statistical heterogeneity. • By meta-analysis, MAD results in a statistically and clinically significant improvement in sleepiness as measured by ESS (-1.4). Of 8 studies, 5 found statistically and clinically significant improvements in ESS, ranging from -1 to -4.5, without statistical heterogeneity. • MAD also generally resulted in improvements in other sleep study measures, but had inconsistent effects on or inadequate evidence for other outcomes of interest. • There was insufficient evidence to address whether study heterogeneity could be explained by different definitions of OSA or other clinical factors, particularly in light of the clinical heterogeneity across studies due to the difference in MADs. • In 2 studies about 5% of patients had tooth damage (or loosening). Substantial jaw pain was reported in about 2–4% of patients, but no study reported on the long-term consequences of any adverse events. • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS, and other sleep study measures, overall, the strength of evidence is moderate that MAD is an effective treatment for OSA in patients without comorbidities (including periodontal disease) or excessive sleepiness. However, the strength of evidence is insufficient to address which patients might benefit most from treatment.
Key Question 5: Treatment OSA treatments Oral devices vs. each other	Insufficient	• There were 5 trials comparing different oral devices; 3 compared different MADs; 2 compared different tongue devices. Of these 5 trials, 4 were rated quality B and 1 quality C. These studies are applicable mostly to patients with AHI of15 to 30 events/hr and BMI less than 30 kg/m^2. All studies were restricted to patients with a sufficient number of teeth to anchor the mandibular devices in place. • No study evaluated clinical outcomes. In general, the studies found no differences among devices in sleep study or other measures. Only 1 study (comparing 2 tongue-retaining devices) evaluated compliance and found no difference. • **Conclusion**: The strength of evidence is insufficient regarding comparisons of different oral devices.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments CPAP vs. MAD	Moderate	• There were 10 trials comparing different MADs with CPAP. A single study of an extraoral device vs. autoCPAP was rated quality C; 9 studies of oral MAD vs. fixed CPAP were rated quality B. The studies are generally applicable to patients with AHI >5-10 events/hr. • No study evaluated clinical outcomes. • A single study compared compliance rates, finding that patients used MAD significantly more hours per night and nights per week than CPAP. • There were 2 studies that found that CPAP was significantly more likely to result in 50% reductions in AHI and achieved AHI <5 events/hr, but 1 study found no difference in achieving <10 events/hr. By meta-analysis, CPAP resulted in significantly greater reductions in AHI (-8 events/hr); 7 of 9 studies found statistically significant differences. By meta-analysis, CPAP results in a statistically significant greater improvement in AHI than MAD (-8 events/hr). • The studies had inconsistent findings regarding the relative effects of MAD and CPAP on ESS. • The studies generally found superior effects of CPAP over MAD for other sleep study measures, but no differences in quality of life or neurocognitive function. • A single study found no differences with either device in achieving an AHI of either <5 or <10 events/hr based on baseline severity of OSA (at an AHI threshold of 30 events/hr). • **Conclusion**: Despite no evidence or weak evidence on clinical outcomes, overall the strength of evidence is moderate that the use of CPAP is superior to MAD. However, the strength of evidence is insufficient to address which patients might benefit most from either treatment.
Key Question 5: Treatment OSA treatments Surgery vs. control	Insufficient	• There were 7 studies comparing 7 different surgical interventions to sham surgery, conservative therapy, or no treatment. Of these, 3 studies were rated quality A, 1 quality B, and 3 quality C. • No study evaluated clinical outcomes. • Of these 7 studies, 4 found statistically significant improvements in AHI, other sleep study measures, and/or sleepiness measures. The remaining studies found no differences in these outcomes or quality of life or neurocognitive function. • Adverse events from surgery (also evaluated from large surgical cohort studies) were generally due to perioperative complications, including perioperative death in about 1.5% in two studies of UPPP – though most studies reported no deaths, hemorrhage, nerve palsies, emergency surgical treatments, cardiovascular events, respiratory failure, and rehospitalizations. Long-term adverse events included speech or voice changes, difficulties swallowing, airway stenosis, and others. In smaller studies, when these adverse events were reported they occurred in about 2–15% of patients. However the largest 2 studies (of 3,130 UPPP surgeries and 422 RFA surgeries) reported no long-term complications (not including perioperative death or cardiovascular complications). • **Conclusion**: Overall, the strength of evidence is insufficient to evaluate the relative efficacy of surgical interventions for the treatment of OSA.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 5: Treatment OSA treatments Surgery vs. CPAP	Insufficient	• Of 12 eligible studies comparing surgery with CPAP (1 quality A, 11 quality C), only 2 were RCTs. • There were 2 retrospective studies that evaluated mortality in UPPP vs. CPAP. Of these, 1 study found higher mortality over 6 years among patients using CPAP (HR = 1.31; 95% CI 1.03, 1.67) and 1 study found no difference in 5-year survival. • Both trials found no difference in outcomes either between RFA and CPAP after 2 months or between maxillomandibular advancement osteotomy and CPAP at after 12 months. The remaining studies were heterogeneous in their conclusions. • **Conclusion**: The strength of evidence is insufficient to determine the relative merits of surgical treatments versus CPAP.
Key Question 5: Treatment OSA treatments Surgery vs. MAD	Insufficient	• A single trial (quality B) compared UPPP and MAD treatment. • The trial did not evaluate clinical outcomes. The study found that significantly more patients using MAD achieved 50% reductions in AHI at 1 year and significantly lower AHI at 4 years. • **Conclusion**: The strength of evidence is insufficient to determine the relative merits of surgical treatments versus MAD.
Key Question 5: Treatment OSA treatments/ Other treatments	Variable (Low for weight loss vs. control; Insufficient for others)	• There were 3 trials (1 quality A, 2 quality B) comparing weight loss interventions with control interventions. The studies were heterogeneous in terms of baseline OSA severity, presence of comorbidities, and severity of obesity. The studies are generally applicable to people with BMI >30 kg/m^2. • No study evaluated clinical outcomes. • A single study found increased odds of achieving an AHI <5 events/hr after 1 year of a very low calorie diet compared with no treatment (OR=4.2, 95% CI 1.4, 12). All 3 trials found significant relative reductions in AHI with diet, from -4 to -23 events/hr. Other outcome data are inconsistent or sparse. • A total of 19 studies evaluated 21 other interventions including atrial overdrive pacing, 8 different drugs, palatal implants, oropharyngeal exercises, a tongue-retaining device, a positional alarm, combination tongue-retaining device and positional alarm, bariatric surgery, nasal dilator strips, acupuncture, and auricular plaster. All of these interventions were evaluated by 1 or 2 studies only. No study evaluated clinical outcomes. • **Conclusion**: The strength of evidence is low to show that some intensive weight loss programs are effective treatment for OSA in obese patients. • **Conclusion**: The strength of evidence is insufficient to determine the effects of other potential treatments for OSA.
Key Question 6: Predictors Predictors of treatment compliance	Variable (see Conclusions)	• There were 5 large cohort studies that conducted multivariable analyses of potential predictors of compliance with CPAP treatment. Of these, 1 study was rated quality A, 1 quality B, and 3 quality C. In general, the studies are applicable to patients initiating CPAP whose AHI is greater than 30 events/hr. • Of these 5 cohort studies, 4 studies all found that higher baseline AHI was associated with greater compliance. Also, 2 of 3 studies found that higher baseline ESS was a predictor of greater compliance. And 2 of 3 studies found that age was not a predictor of compliance. Only 1 or 2 studies evaluated other potential predictors, with no consistent findings. • A single quality C cohort study evaluated potential predictors of compliance with newly initiated MAD. The study did not identify any statistically significant predictors. • **Conclusion**: The strength of evidence is moderate that more severe OSA as measured by higher AHI is associated with greater compliance with CPAP use. The strength of evidence is moderate that higher ESS is also associated with improved compliance. • **Conclusion**: The strength of evidence is insufficient regarding potential predictors of compliance with MAD.

Table 4. Summary of findings of studies addressing key questions on obstructive sleep apnea (continued)

Key Question	Strength of Evidence	Summary/Conclusions/Comments
Key Question 7: Treatment Treatments to improve compliance	Low	• There were 18 trials evaluating interventions to improve CPAP compliance. Of these, 2 were rated quality A, 8 quality B, and 8 quality C. These studies are mostly applicable to patients initiating CPAP with AHI >30 events/hr and BMI greater than 30 kg/m^2. No study evaluated interventions to improve compliance with other devices. • There were 9 studies evaluating extra support or education. These studies had inconsistent findings regarding the effect of the interventions on compliance. Only 3 of 7 studies found increased number of hours of CPAP use; only 1 of 3 studies found persistent improved compliance (and that was of compliance with followup visits). • There were 3 studies evaluating telemonitoring. No study found a statistically significant increase in CPAP usage (hours per night). • A single study evaluated the effect of cognitive behavioral therapy, and showed that the behavioral intervention significantly increased hours of CPAP use per night compared with usual care (difference = 2.8 hours; 95% CI 1.8, 3.9; P<0.0001). • There were 2 studies evaluating 2 other interventions: the hypnotic zolpidem and nasal pillows. No intervention was found to be effective to improve compliance. • There were 3 studies evaluating nursing care models. None improved compliance. • **Conclusion**: The strength of evidence is low that some specific adjunct interventions may improve CPAP compliance among overweight patients with more severe OSA who are initiating CPAP treatment. However, studies are heterogeneous and no general type of intervention (e.g., education) was more promising than others.

AHI = apnea-hypopnea index, AUC = area under the ROC curve, autoCPAP = autotitrating CPAP, CI = confidence interval, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, HR = hazard ratio, MAD = mandibular advancement device, OSA = obstructive sleep apnea, PSG = polysomnography (sleep-laboratory based), RFA = radiofrequency ablation, ROC = receiver operating characteristics, SF-36 = Short Form Health Survey 36, UPPP = uvulopalatopharyngoplasty.

General Discussion

In theory, obstructive sleep apnea (OSA) should be relatively simple to diagnose and treat. Diagnosis involves determining whether the number of apnea and hypopnea events caused by upper airway obstruction during sleep exceed a given threshold, and continuous positive airway pressure (CPAP) is an effective treatment t o minimize the apnea-hypopnea index (AHI) and improve symptoms.

Screening and Diagnostic Tests

Polysomnography (PSG), the standard test to diagnose OSA, requires one or more full night stays in a sleep laboratory. This can prove to be a difficult, inconvenient, and resource-intensive procedure requiring separate facilities and a full-time overnight skilled sleep technician. For many patients PSG may not be representative of a typical night's sleep given the foreign setting, lack of nighttime routine, attached equipment, and being under observation. This may be particularly true the first night the test is given. Further complicating diagnosis, definitions of OSA vary widely, employing thresholds of AHI ranging from 5 to 15 events/hr. The American Academy of Sleep Medicine uses a threshold of 15 events/hr (with or without OSA symptoms) or 5 events/hr with OSA symptoms (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).[31,32] Variations in how PSG results are read and interpreted are also inevitable, possibly leading to inconsistent diagnosis of OSA across different sleep laboratories. In fact, as discussed in the Introduction, in-laboratory PSG has never been validated, and its true sensitivity and specificity in diagnosing OSA are not well documented.[26] Moreover, the AHI, which is used as the single metric to define OSA for insurance companies and in clinical settings, can vary from night-to-night and does not take into account symptoms, comorbidities, or response to treatment.[30]

Two approaches have been taken to reduce the resources involved in diagnosing (or ruling out) OSA: tests to screen for the likelihood of OSA and portable monitors instead of sleep-laboratory PSG. Questionnaires and clinical prediction rules have been developed to screen patients with complaints suggestive of OSA to determine whether full testing is warranted. As addressed by Key Question 1, five questionnaires and 10 validated clinical prediction rules have been compared with PSG to test their accuracy to predict diagnosis with OSA (or severity of OSA). However, very few of the screening tests have been evaluated by more than one set of researchers and few have been directly compared with each other. The Berlin questionnaire's accuracy to screen for OSA (based on snoring, tiredness, and blood pressure), the only questionnaire that has been compared with PSG by two sets of investigators is supported by only a low strength of evidence. All other tests, including the commonly used STOP and STOP-Bang questionnaires, have not been adequately tested. To be of clinical value, such tests would need a very high sensitivity (to avoid failures to diagnose) and a sufficiently high specificity to minimize unnecessary testing of patients without OSA. Furthermore, the most clinically useful tests would be those that can be easily performed based on symptoms and signs easily obtainable during a physical examination. Screening tests that require specialized testing, such as pulmonary function tests, are likely of limited clinical value.

The second approach to reduce the resources involved in diagnosing OSA is the use of portable monitors developed for home or outside the laboratory. However, these monitors suffer similar deficiencies in validation. The addition of more recent studies has not substantially changed the conclusions from our Evidence-based Practice Center's 2007 Technology Assessment on *Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*.[26] Numerous monitors have been evaluated across 93 eligible studies. Most of the tested portable monitors fairly accurately predict OSA, with high positive likelihood ratios and low negative likelihood ratios for various AHI cutoffs in laboratory-based PSG; however, it is unclear whether any of the portable monitors are sufficiently accurate to replace laboratory-based PSG. In general, portable monitors use many fewer "channels" (specific physiologic measures) than typical 16-channel PSG. Different portable monitors use different numbers of channels and different specific channels. In general, across studies, monitors with more channels perform better than monitors with fewer channels. However, a lack of direct comparisons between portable monitors in their performance compared with PSG, and the large number and variety of monitors precludes a clear conclusion regarding which monitors perform best. None of the studies explicitly evaluated the monitors in patients with important comorbidities such as chronic lung disease, congestive heart failure, or with neurological disorders.The applicability of the evidence is unclear for these populations and for patients in whom there is a concern about central sleep apnea. Nevertheless, the evidence does suggest that the measured AHI (or similar measures) from portable monitors are likely to be biased and variable compared with PSG-derived AHI. Though, it is unclear to what degree this is due to the inaccuracies of the portable monitors, where the data loss ranged from 0-23 percent (not including the outlier study with a 78 percent data loss) and to what degree

it is due to normal variation in AHI from night-to-night or differences related to sleeping in different settings (home versus a sleep laboratory). Night-to-night variability may be addressed by repeated measurement over several nights, which may be better addressed by the portable monitors than the PSG due to the increased cost of repeated testing. The studies did not allow us to adequately assess any issues related to night-to-night variation. Additionally, among studies that evaluated a portable device in the sleep lab (simultaneous recording of signals by device and PSG) as well as home (nonsimultaneous recording of signals by device and PSG), the range of mean bias, sensitivity and specificity reported were not different for the two settings. More to the point, however, the only truly clinically valuable assessments of portable monitors would be tests of their predictive ability for clinical outcomes or response to treatment. No such studies have been conducted.

With the assumption that screening tests and/or portable monitors are of clinical value to triage patients for the treatment of OSA, further testing for OSA, or further testing for other conditions, the question arises as to what the algorithm for diagnosing these patients should be. Ideally, any proposed algorithms of phased testing should be compared to alternative algorithms, including full testing of all patients with symptoms suggestive of OSA. However, to date, no such studies have been conducted.

An important caveat to the evidence on the diagnostic and screening tests is that almost all the studies were peformed at academic or research centers. It is not clear how the results generated in these settings, under research conditions, should be generalized to acceptance, use, and accuracy when used among the general population.

A related topic of interest to is the value of preoperative screening for OSA. As discussed in the Introduction, patients with OSA are at an increased risk of perioperative pulmonary and cardiovascular complications, but a large proportion of patients with OSA remain undiagnosed. Therefore, it has been suggested that all (or selected) patients undergoing anesthesia or surgery should routinely be screened or tested for OSA; however, the strength of evidence addressing this question is insufficient. One retrospective study of patients undergoing bariatric surgery found that a cohort of patients who had routine PSG had better perioperative outcomes than a cohort of patients who had PSG only if they were considered to be at an increased risk for OSA. There are also no adequate studies that compared phased testing (simple tests followed by more intensive tests in selected patients) to full evaluation (PSG).

Apnea-Hypopnea Index as a Predictor of Clinical Outcomes

As described under Key Question 4, there is a high strength of evidence that higher baseline AHI is a strong and independent predictor of all-cause mortality over several years of followup. The association was strongest among people with severe OSA (AHI over 30 events/hr). The strength of evidence for the association between baseline AHI and other long-term clinical outcomes is either low (for incident diabetes mellitus) or insufficient (for other examined outcomes). These findings would seem to imply that individuals with OSA (and particularly severe OSA) should be treated aggressively to reduce their AHI. Unfortunately, as discussed below, there are almost no trial data to support that treatment of OSA and reduction of AHI improves clinical outcomes. Thus, the clinical value of these associations remains theoretical.

Treatment of Obstructive Sleep Apnea

As previously noted, there is a moderate strength of evidence that fixed CPAP is an effective treatment to minimize AHI and improve sleepiness symptoms. While the relevant trials are

conclusive regarding the effects of CPAP on AHI and sleepiness measures, among over 40 trials of patients treated with CPAP or no treatment, none have reported long-term clinical outcomes. However, compliance with CPAP treatment is poor. Among the large cohort studies (with multivariable analyses for predictors of noncompliance), one reported 16 and 32 percent of patients discontinued CPAP at 1 and 4 years, respectively;[289] 14 percent of patients had CPAP withdrawn for noncompliance at a mean of 3.2 years in a second study;[290] and patients used CPAP for an average of only about 5 hours per night at 3 months in two studies.[203,292] Higher baseline AHI and increased sleepiness as measured by the Epworth Sleepiness Scale are both predictors of improved compliance with CPAP (high strength and moderate strength of evidence, respectively). There are numerous reasons why patients do not tolerate CPAP, including the difficulty of dealing with the equipment and its noisiness, mask discomfort, claustrophobia, oral and nasal irritation and dryness, and others. Among reviewed studies, up to 15 percent of patients described adverse events they considered to be major (though essentially none of the adverse events resulted in long-term consequences).

Because patients frequently do not tolerate fixed CPAP, many alternative treatments have been proposed and used, including alternative CPAP devices, devices to splint the oropharynx open during sleep, surgeries to minimize airway obstructions, and numerous other less commonly used or researched interventions. As discussed in the Introduction, several alternative CPAP devices have been designed to vary the pressure during the patient's inspiratory cycle or to titrate the pressure to a minimum level necessary to maintain airway patency. Other modifications include alternate masks, nasal pads, and humidification. The primary goal of these modifications is to improve comfort and thereby increase compliance with the treatment.

The large majority of the trials that have compared different CPAP machines have compared autotitrating CPAP (autoCPAP) with fixed CPAP. There is a moderate strength of evidence that there are no clinical differences between autoCPAP and fixed CPAP, though, again, none of these trials evaluated clinical outcomes. Meta-analysis revealed patients using autoCPAP used the machines only 11 minutes longer on average than patients using fixed CPAP. A low strength of evidence suggests no statistically significant differences between the proprietary C-Flex™ and fixed CPAP. The strength of evidence is insufficient for other comparisons. Overall, the evidence does not support the use of one device for all patients. The decision as to which CPAP device to use may depend on numerous factors such as patient preference, specific reasons for noncompliance, cost, and others.

For patients who do not tolerate CPAP, or who refuse CPAP, or for whom CPAP is determined to be inappropriate, an alternative is the use of oral devices. A wide range of these devices have been designed with the goal of splinting open the oropharynx to prevent obstruction during sleep. The most common are mandibular advancement devices (MAD), which are generally worn intraorally and force the mandible to protrude forward several millimeters. Ten trials provide a moderate strength of evidence that MAD use is an effective treatment for OSA and results in a significant reduction in AHI and a clinical improvement in ESS score (though there is no trial evidence on clinical outcomes). By indirect comparison across trials, CPAP is more effective than MAD (e.g., meta-analysis summary net AHI reduction with CPAP is -33 events/hr; with MAD -12 events/hr). This was confirmed by trials that directly compared the two types of devices (CPAP versus MAD, net AHI reduction -8 events/hr). There is a moderate strength of evidence that CPAP is superior to MAD in the relief of sleep apnea signs and symptoms. However, given the issues with CPAP compliance, the decision as to whether to use CPAP or MAD will likely depend on patient preference. The adverse events associated with

MAD are different than CPAP and stem from wearing an intraoral device. Most are self-limited, though tooth damage has been reported. Given the wide range of specific oral devices and the small number of trials that have made comparisons among them, the strength of evidence regarding their relative merit remains insufficient.

The third major alternative for OSA treatment includes surgical interventions to alleviate airway obstruction. The Key Questions addressed and the studies reviewed for the present report do not address what the indications for surgery may be, nor which surgery may be the most appropriate. As is often the case for surgical interventions, very few randomized trials have been conducted on surgical treatments for OSA. It is reasonable to assume that patients who choose surgery are fundamentally different from those who are either not offered surgery or who choose a different (or no) treatment. These differences are borne out by the differences in baseline characteristics (including mean AHI and ESS, age, obesity, and others) found in the nonrandomized comparative studies reviewed herein that compare surgery to other treatments. Thus, indirect comparisons of surgical studies and CPAP or MAD studies are inappropriate and even though it was agreed upon to include retrospective comparisons of surgery and CPAP or MAD in this report, the value of these studies is highly suspect. Given these issues, the strength of evidence to determine the relative value of surgery as compared with no treatment, to CPAP, to MAD, or to alternative types of surgery remains insufficient.

Other interventions that have been tested in randomized trials (that met eligibility criteria for this review) include: weight loss programs, atrial overdrive pacing, eight different drugs, palatal implants, oropharyngeal exercises, a tongue-retaining device, a positional alarm, combination tongue-retaining device and positional alarm, bariatric surgery, nasal dilator strips, acupuncture, and auricular plaster. There is a low strength of evidence (from three trials) that some intensive weight loss programs may be an effective treatment for OSA in obese patients; however, the strength of evidence is insufficient to determine the effects of any other of these alternative potential treatments for OSA.

Notably, little evidence exists across interventions supporting any OSA treatment as improving quality of life or neurocognitive function. Although trials did report improvements in these outcomes for CPAP, MAD, and surgical intervention, overall findings were inconsistent. Too few studies evaluated functional outcomes (such as driving skills) to formulate a conclusion.

Potential Different Treatment Effects in Different Patient Subgroups

For all the treatment comparisons, it is of particular interest which subgroups of patients may benefit most from which specific treatments. Unfortunately, the trials reviewed are almost completely silent on this issue. Very few trials reported subgroup analyses based on baseline or patient factors, such as OSA severity or demographics. For most comparisons, there were too few studies or the interventions examined were too heterogeneous (e.g., different types of MAD) to analyze potential differences across studies based on patient characteristics.

There were, however, a large number of trials of CPAP versus control (no treatment, placebo treatment, or sham CPAP). Subgroup meta-analysis of the trials based on their implied definitions of OSA (study eligibility criteria using different minimum AHI thresholds) failed to demonstrate any clear or consistent relationships between strictness of OSA definition and effectiveness of CPAP (to reduce AHI or ESS). Though statistical heterogeneity existed across trials, we were unable to find any patient- or intervention-level factors to explain the heterogeneity. Differences also existed based on whether the study design was parallel or crossover, and whether the control was no treatment or sham CPAP; however, there are no

clinical implications of these findings. A large number of trials, conducted in a wide variety of settings, with a wide range of eligibility criteria, all found statistically and clinically significant improvements in AHI with CPAP. Based on this consistency (despite statistical heterogeneity), it is our conclusion that CPAP is effective (to minimize AHI) in all patients with OSA. The relative effectiveness in different populations may then be a moot point. The one exception might be patients with mild OSA (with AHI <15 events/hr). By definition, people with a low AHI cannot have as large an improvement in their AHI as people with severe OSA. A trial examining long-term clinical outcomes is necessary to make a definitive evaluation in this population.

The other intervention comparison for which cross-study evaluation of effectiveness in different populations may be possible is autoCPAP versus fixed CPAP, for which 21 trials qualified for review. No differences could be discerned based on patient characteristics except that the relative improvement in ESS conferred by autoCPAP was larger in studies restricted to patients with AHI >20 or >30 events/hr, compared with those that included patients with less severe disease (or did not define a minimum AHI threshold).

Interventions to Improve Treatment Compliance

Given the difficulties with treatment compliance, an important question remains on how to improve usage of the interventions. Trials addressing this issue have investigated only interventions to improve CPAP compliance. Eighteen trials have each investigated unique interventions. These can be categorized as intensive education, telemonitoring, nursing care models, cognitive behavioral therapy, and miscellaneous interventions. Although, overall there is a low strength of evidence that some specific adjunct interventions may improve CPAP compliance, the strength of evidence is insufficient regarding any specific intervention. No trials have investigated interventions to improve compliance with any other devices.

Limitations

The present systematic review is subject to several important limitations. The most critical is the failure of the extant research to evaluate long-term clinical outcomes. Secondly, and in a similar vein, is the meagerness of evidence with respect to several Key Questions. Almost no study of diagnostic tests or treatments attempted to assess how results may vary in different subgroups of patients.

In general, intervention trials were of quality B or C, with few quality A studies. Followup durations tended to be very short, on the order of weeks to a few months, and are clearly insufficient for the appraisal of the treatment of a life-long disease whose clinical sequelae may take decades to develop. Study dropout rates were also frequently very high, particularly given the short duration of followup. In some studies, up to 40 percent of participants were lost to followup within weeks. The ability to meaningfully interpret the findings from these studies is clearly diminished. Other frequent methodological problems with studies included incomplete reporting and/or inadequate analyses. In particular, relatively few studies provided the net differences between interventions (in parallel design studies) or the difference between final values with appropriate adjustments for correlation (in crossover studies) with their confidence intervals and P values. Thus, for the large majority of studies we had to estimate the confidence intervals of the differences between interventions. Due to incomplete reporting or analyses, we also frequently had to estimate whether there was a statistically significant difference between interventions.

Patient compliance is an important outcome within this review, being a major outcome for treatment studies (particularly those that compare different devices) and the focus of two additional Key Questions. However, many studies measured self-reported compliance (either hours of use per night or nights of use per week). This raises the concern of inaccurate reporting, although there is no obvious reason to suspect biased reporting in favor of any specific device. In addition, a variety of definitions of compliance were used, complicating interpretation of results across studies.

Publication is a possible major concern for the validity of this review. The large majority of intervention studies (particularly those of diagnostic monitors and of mechanical treatment devices) were sponsored directly or indirectly by the manufacturers of the devices. Unfortunately, due to the magnitude of this review and limited time and resources to perform the review, we were not able to attempt a grey literature search to seek unpublished studies.

Nevertheless, this concern is tempered by a number of factors. Most of our conclusions were that the strength of evidence is either low or inadequate for interventions (minimizing the concern about publication bias among the current literature). The effects of CPAP and MAD on sleep measures were generally large enough that conclusions about the effectiveness of these devices would be unlikely to change with the addition of unpublished trials. However, the reliance of the field on industry funding may partially explain the general lack of long-term trials with clinical outcomes, since these studies are not required by the Food and Drug Administration for device marketing.

Future Research

General Recommendation

- High dropout rates (as high as 40 percent in a matter of weeks) and relatively short followup are recurrent problems with the studies evaluated in the present review. In particular, the issue of high dropout rates bears further investigation. Is this a problem peculiar to this field? Are patients' sleep apnea symptoms interfering with their desire to serve as research participants? Are patients with sleep apnea not sufficiently well-informed about the serious consequences of sleep apnea and therefore less motivated to find out which therapies or methods could effectively help relieve their symptoms? Are treatments so onerous that patients are refusing to continue with them? Although we recommend additional trials that delve more deeply into sleep apnea diagnoses and treatments (see below), they are likely to be of little value if these questions remain unaddressed and high dropout rates and short followup durations continue to be the standard.

Diagnostic Tests

- The most clinically useful evaluation of prediction rules and questionnaires (to screen for or diagnose OSA) would be trials examining whether use of the tests result in improved clinical outcomes, as opposed to simple studies of test accuracy.
- A meta-analysis of individual patient measurements with various portable monitors as compared with facility-based PSG may be the best opportunity to gain insights on the relative contribution of different neurophysiologic signals used by portable monitors. Such a meta-analysis would not provide direct insight on the effects of testing on patients; however, it would provide valuable information for medical device developers and sleep physicians.
- Future studies of the accuracy or bias of diagnostic tests should focus more on head-to-head comparisons of portable monitors, questionnaires, and prediction rules to determine the optimal tool for use in a primary care setting to maximize initial evaluation of OSA and triage high-risk patients for prompt PSG. It is our conclusion that the field would be better served by comparing the existing array of diagnostic tools with each other to try to determine which is most useful for screening or diagnosing, rather than evaluating new devices, questionnaires, or models. It is unlikely that new tests will be sufficiently more accurate or less biased to warrant the expended resources or effort.
- The concept of phased testing, with the goals of maximizing efficiency to OSA diagnosis while minimizing overtesting, is appealing, but has not been properly evaluated by any study. Randomized trials comparing potential phased testing strategies with direct PSG (or portable) testing are needed. Similarly, it would greatly inform decisionmaking to have studies that evaluate which tests would be most appropriate to use for which patients based on the type and severity of their symptoms.
- In comparing different OSA diagnostic devices, it is important that the findings from all participants – regardless of whether the results were above or below the particular device's diagnostic threshold – be verified against an accepted reference standard such as laboratory PSG. Diagnostic test studies that systematically fail to fully test all participants

are generally impossible to meaningfully interpret and have little scientific or clinical value.
- No trials have addressed the value of routine (or selected) preoperative screening for OSA. Well-conducted trials are needed.

Treatments

- Of the 172 studies of treatments covered in this report, only three studies reported clinical outcomes (not including adverse events): one on heart failure with CPAP[126] and two on mortality (surgery versus CPAP).[257,260] We need comparative studies focusing on clinical outcomes like mortality, cardiovascular disease, hypertension, and type 2 diabetes. To be of value, studies must have long-term followup durations (measured in years) and must be adequately powered to detect statistically significant differences.
- Primary studies on the modifying effects of different patient characteristics, baseline disease severity, and other relevant parameters on various treatment outcomes should be undertaken so that treatment options can be optimized for or can be focused on patients with specific profiles, thus maximizing treatment benefits. Studies should be large enough, of sufficient duration, and bear minimal loss-to-followup rates to allow meaningful subgroup or regression analyses.
- Fixed CPAP is clearly an effective treatment to minimize AHI and to improve sleepiness symptoms. With the exception of the evaluation of long-term clinical outcomes, no further trials are needed to compare fixed CPAP with no treatment or with sham CPAP. Given the large effects of CPAP on AHI across all trials, it does not appear to be necessary to determine which subgroups of patients may have relatively larger or smaller benefits from CPAP. Again, the major exception would be for major clinical outcomes. Trials are needed to assess which groups of patients would experience the most long-term clinical benefits from likely life-long CPAP treatment. Probably, the most important subgroups to examine are those based on severity of OSA (as measured by AHI) and those patients with comorbidities.
- Given the effectiveness of fixed CPAP, all other interventions should either be
  - Directly compared with fixed CPAP, among patients naïve to CPAP, or
  - Compared with no treatment or alternative treatment, among patients who have failed to comply with CPAP treatment.
- Mandibular advancement devices also improve AHI and sleepiness symptoms, though their effects on long-term clinical outcomes are unknown (from trial data). While future trials on new variations of these devices are inevitable, they are of secondary interest.
- More trials are needed to determine if different degrees of mandibular advancement would offer corresponding degrees of sleep apnea symptom improvement.
- Studies of interventions other than fixed CPAP should restrict their analyses to groups of patients who are either naïve to CPAP treatment or who have failed (or refused) CPAP treatment. Alternatively, trials should perform sufficiently powered subgroup analyses based on these groups of patients. It is reasonable to assume that patients who have not used CPAP will respond differently to treatments than patients who have tried but stopped using CPAP. Thus trials performed in one group might not be applicable to patients in the other group.

- To understand better treatment options for patients who do not tolerate fixed CPAP, head-to-head comparisons of alternative treatments, including simple adjunctive treatment (like humidification or nasal spray), nonfixed CPAP, MAD, surgery, as well as others, are needed to identify those that are most likely to benefit from these alternative treatments.
- Rigorously conducted head-to-head comparisons of surgical interventions and CPAP are necessary to determine the relative merits of these two forms of treatments as almost all the existing data are from cohort studies, often retrospective, with all their attendant limitations. The trials should clearly identify the criteria used to consider patients for surgery and then investigate surgery versus CPAP in those patients. Trials should not mix in patients who are not seriously considering surgical treatment.
- Many interventions (including drugs, specific oropharyngeal exercises, etc.) have been evaluated by only one or two small studies. Further, more well-conducted studies are needed per intervention to accurately determine the effects of these therapies on sleep apnea symptoms and clinical outcomes.
    - The incremental benefit of weight loss programs in addition to accepted treatments for OSA (e.g., CPAP) should be examined.
    - Suction tongue-retaining devices may be associated with better outcomes than nonsuction tongue-retaining devices, although more studies are needed to confirm this finding.
- Future trials are needed to find effective treatments to improve compliance with both CPAP and MAD. Some specific forms of intensive patient education, cognitive behavioral therapy, telemonitoring, and habit-promoting audio-based interventions hold promise but need further investigation. Ideally, these (and other, superior interventions) should be tested against each other to enable determination of which are the most effective and should be further pursued.

Predictors of Clinical Outcomes and Compliance

- Regarding the question of whether OSA severity (as measured by AHI) is associated with long-term outcomes, it may be of interest to perform patient-level meta-analyses of the Sleep Heart Health Study, the Wisconsin Sleep Cohort Study, and other cohorts of individuals who had sleep testing. All long-term clinical outcomes except all-cause mortality, have yet to be adequately evaluated.
- Studies are needed to assess whether and when patients should be treated with CPAP, MAD, or surgery. This additional research should involve an assessment of how well patients tolerate each of these three treatment modalities. Further high quality studies are also necessary to determine which factors predict compliance with CPAP and MAD, and which predict successful outcomes following surgery.

References

1. Young T, Finn L, Peppard PE et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep* 2008;31:1071-1078.
2. Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Medicine/Public Library of Science* 2009;6:e1000132.
3. Hiestand DM, Britz P, Goldman M, et al. Prevalence of symptoms and risk of sleep apnea in the US population: Results from the national sleep foundation sleep in America 2005 poll. *Chest* 2006;130:780-786.
4. Practice parameters for the indications for polysomnography and related procedures. Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. *Sleep* 1997;20:406-422.
5. Victor LD. Obstructive sleep apnea. *Am Fam Physician* 1999;60:2279-2286.
6. Marin JM, Carrizo SJ, Vicente E, et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lance.* 2005;365:1046-1053.
7. Punjabi NM. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc* 2008;5:136-143.
8. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001;163:19-25.
9. Yaggi HK, Concato J, Kernan WN, et al. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353:2034-2041.
10. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. *JAMA* 2000;283:1829-1836.
11. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. *New Engl J Med* 2000;342:1378-1384.
12. Young T, Peppard P, Palta M, et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. *Arch Intern Med* 1997;157:1746-1752.
13. Babu AR, Herdegen J, Fogelfeld L, et al. Type 2 diabetes, glycemic control, and continuous positive airway pressure in obstructive sleep apnea. *Arch Intern Med* 2005;165:447-452.
14. Caples SM, Gami AS, Somers VK. Obstructive sleep apnea. *Ann Intern Med* 2005;142:187-197.
15. Gruber A, Horwood F, Sithole J, et al. Obstructive sleep apnoea is independently associated with the metabolic syndrome but not insulin resistance state. *Cardiovasc Diabetol* 2006;5:22.
16. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217-1239.
17. Howard ME, Desai AV, Grunstein RR, et al. Sleepiness, sleep-disordered breathing, and accident risk factors in commercial vehicle drivers. *Am J Respir Crit Care Med* 2004;170:1014-1021.
18. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. *N Engl J Med* 1999;340:847-851.
19. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-1235.
20. Young T, Shahar E, Nieto FJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med* 2002;162:893-900.
21. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. *J Appl Physiol* 2005;99:1592-1599.

22. Ancoli-Israel S, Kripke DF, Klauber MR, et al. Sleep-disordered breathing in community-dwelling elderly. *Sleep* 1991;14:486-495.

23. Bixler EO, Vgontzas AN, Ten HT, et al. Effects of age on sleep apnea in men: I. Prevalence and severity. *Am J Respir Crit Care Med* 1998;157:144-148.

24. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 2001;163:608-613.

25. Duran J, Esnaola S, Rubio R, et al. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. *Am J Respir Crit Care Med* 2001;163:685-689.

26. Tufts-New England Medical Center EPC. Home diagnosis of obstructive sleep apnea-hypopnea syndrome. Health Technology Assessment Database. Available at: http://www.cms.gov/determinationprocess/downloads/id48TA pdf. Accessed 2010.

27. Pagel JF. Obstructive sleep apnea (OSA) in primary care: evidence-based practice. *J Am Board Fam Med* 2007;20:392-398.

28. Vakulin A, Baulk SD, Catcheside PG, et al. Effects of alcohol and sleep restriction on simulated driving performance in untreated patients with obstructive sleep apnea. *Ann Intern Med* 2009;151:447-455.

29. Katz ES, D'Ambrosio CM. Pediatric obstructive sleep apnea syndrome. *Clin Chest Med* 2010;31:221-234.

30. Institute of Medicine (US) Committee on Sleep Medicine and Research, Colten HR ABe. Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. *The National Academies Collection: Reports funded by National Institutes of Health.* 2006.

31. American Academy of Sleep Medicine. The International Classification of Sleep Disorders, 2nd Edition: Diagnostic and Coding Manual. 2005. Westchester, IL, American Academy of Sleep Medicine. Ref Type: Report

32. Epstein LJ, Kristo D, Strollo Jr PJ, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of Clinical Sleep Medicine* 2009;5:263-276.

33. Flemons WW, Littner MR, Rowley JA, et al. Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review cosponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. *Chest* 2003;124:1543-1579.

34. Ferber R, Millman R, Coppola M, et al. Portable recording in the assessment of obstructive sleep apnea. ASDA standards of practice. *Sleep* 1994;17:378-392.

35. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540-545.

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

37. Chung SA, Yuan H, Chung F. A systemic review of obstructive sleep apnea and its implications for anesthesiologists. *Anesth Analg* 2008;107:1543-1563.

38. Finkel KJ, Searleman AC, Tymkew H, et al. Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Med* 2009;10:753-758.

39. Gupta RM, Parvizi J, Hanssen AD, et al. Postoperative complications in patients with obstructive sleep apnea syndrome undergoing hip or knee replacement: a case-control study. *Mayo Clin Proc* 2001;76:897-905.

40. Loube DI, Gay PC, Strohl KP, et al. Indications for positive airway pressure treatment of adult obstructive sleep apnea patients: a consensus statement. *Chest* 1999;115:863-866.

41. Veasey SC, Guilleminault C, Strohl KP, et al. Medical therapy for obstructive sleep apnea: a review by the Medical Therapy for Obstructive Sleep Apnea Task Force of the Standards of Practice Committee of the American Academy of Sleep Medicine. *Sleep* 2006;29:1036-1044.

42. Parthasarathy S, Haynes PL, Budhiraja R, et al. A national survey of the effect of sleep medicine specialists and American Academy of Sleep Medicine Accreditation on management of obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 2006;2:133-142.

43. Chasens ER, Pack AI, Maislin G, et al. Claustrophobia and adherence to CPAP treatment. *Western Journal of Nursing Research* 2005;27:307-321.

44. Kushida CA, Littner MR, Hirshkowitz M, et al. Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. *Sleep* 2006;29:375-380.

45. Kushida CA, Chediak A, Berry RB, et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 2008;4:157-171.

46. Sanders MH, Kern NB, Costantino JP, et al. Adequacy of prescribing positive airway pressure therapy by mask for sleep apnea on the basis of a partial-night trial. *American Review of Respiratory Disease* 1993;147:1169-1174.

47. Freedman N. Treatment of obstructive sleep apnea syndrome. *Clin Chest Med* 2010;31:187-201.

48. Masa JF, Jimenez A, Duran J, et al. Alternative methods of titrating continuous positive airway pressure: a large multicenter study. *American Journal of Respiratory & Critical Care Medicine* 2004;170:1218-1224.

49. West SD, Jones DR, Stradling JR. Comparison of three ways to determine and deliver pressure during nasal CPAP therapy for obstructive sleep apnoea. *Thorax* 2006;61:226-231.

50. Ferguson KA, Cartwright R, Rogers R, et al. Oral appliances for snoring and obstructive sleep apnea: a review. *Sleep* 2006;29:244-262.

51. Kushida CA, Morgenthaler TI, Littner MR, et al. Practice parameters for the treatment of snoring and Obstructive Sleep Apnea with oral appliances: an update for 2005. *Sleep* 2006;29:240-243.

52. Garrigue S, Barold SS, Cazeau S, et al. Prevention of atrial arrhythmias during DDD pacing by atrial overdrive. *Pacing Clin Electrophysiol* 1998;21:1751-1759.

53. Garrigue S, Bordier P, Jais P, et al. Benefit of atrial pacing in sleep apnea syndrome. *N Engl J Med* 2002;346:404-412.

54. Benumof JL. Obstructive sleep apnea in the adult obese patient: implications for airway management. *Anesthesiol Clin North America* 2002;20:789-811.

55. Agency for Healthcare Research and Quality. Methods Reference Guide for Effectiveness and Comparative Effectiveness Reviews, Version 1.0. 2010. Ref Type: Generic

56. Wallace BC, Trikalinos TA, Lau J, et al. Semi-automated screening of biomedical citations for systematic reviews. *BMC Bioinformatics* 2010;11:55.

57. Johns M, Hocking B. Daytime sleepiness and sleep habits of Australian workers. *Sleep* 1997;20:844-849.

58. Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and the epworth sleepiness scale: failure of the MSLT as a gold standard. *Journal of Sleep Research* 2000;9:5-11.

59. Richardson GS, Carskadon MA, Flagg W, et al. Excessive daytime sleepiness in man: multiple sleep latency measurement in narcoleptic and control subjects. *Electroencephalography & Clinical Neurophysiology* 1978;45:621-627.

60. Mitler MM, Gujavarty KS, Browman CP. Maintenance of wakefulness test: a polysomnographic technique for evaluation treatment efficacy in patients with excessive somnolence. *Electroencephalography & Clinical Neurophysiology* 1982;53:658-661.

61. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307-310.

62. Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. *Lancet* 1995;346:1085-1087.

63. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. *JAMA* 1994;271:703-707.

64. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-188.

65. Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions—agency for healthcare research and quality and the effective health-care program. *Journal of Clinical Epidemiology* 2010;63:513-523.

66. Garcia-Diaz E, Quintana-Gallego E, Ruiz A, et al. Respiratory polygraphy with actigraphy in the diagnosis of sleep apnea-hypopnea syndrome. *Chest* 2007;131:725-732.

67. 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;32:629-636.

68. To KW, Chan WC, Chan TO, et al. Validation study of a portable monitoring device for identifying OSA in a symptomatic patient population. *Respirology* 2009;14:270-275.

69. Tonelli de Oliveira AC, Martinez D, Vasconcelos LF, et al. Diagnosis of obstructive sleep apnea syndrome and its outcomes with home portable monitoring. *Chest* 2009;135:330-336.

70. Amir O, Barak-Shinar D, Amos Y, et al. An automated sleep-analysis system operated through a standard hospital monitor. *Journal of Clinical Sleep Medicine* 2010;6:59-63.

71. Ng SS, Chan TO, To KW, et al. Validation of Embletta portable diagnostic system for identifying patients with suspected obstructive sleep apnoea syndrome (OSAS). *Respirology* 2010;15:336-342.

72. Planes C, Leroy M, Bouach KN, et al. Home diagnosis of obstructive sleep apnoea in coronary patients: validity of a simplified device automated analysis. *Sleep & Breathing.* 2010;14:25-32.

73. Ayappa I, Norman RG, Seelall V, et al. Validation of a self-applied unattended monitor for sleep disordered breathing. *Journal of Clinical Sleep Medicine* 2008;4:26-37.

74. Abraham WT, Trupp RJ, Phillilps B, et al. Validation and clinical utility of a simple in-home testing tool for sleep-disordered breathing and arrhythmias in heart failure: results of the Sleep Events, Arrhythmias, and Respiratory Analysis in Congestive Heart Failure (SEARCH) study. *Congestive Heart Failure* 2006;12:241-247.

75. Chen H, Lowe AA, Bai Y, et al. Evaluation of a portable recording device (ApneaLink) for case selection of obstructive sleep apnea. *Sleep & Breathing* 2009;13:213-219.

76. Clark AL, Crabbe S, Aziz A, et al. Use of a screening tool for detection of sleep-disordered breathing. *Journal of Laryngology & Otology* 2009;123:746-749.

77. de Almeida FR, Ayas NT, Otsuka R, et al. Nasal pressure recordings to detect obstructive sleep apnea. *Sleep & Breathing* 2006;10:62-69.

78. Erman MK, Stewart D, Einhorn D, et al. Validation of the ApneaLink for the screening of sleep apnea: a novel and simple single-channel recording device. *Journal of Clinical Sleep Medicine* 2007;3:387-392.

79. Goodrich S, Orr WC. An investigation of the validity of the Lifeshirt in comparison to standard polysomnography in the detection of obstructive sleep apnea. *Sleep Medicine* 2009;10:118-122.

80. Heneghan C, de CP, Ryan S, et al. Electrocardiogram recording as a screening tool for sleep disordered breathing. *Journal of Clinical Sleep Medicine* 2008;4:223-228.

81. Heneghan C, Chua CP, Garvey JF, et al. A portable automated assessment tool for sleep apnea using a combined Holter-oximeter. *Sleep* 2008;31:1432-1439.

82. Nakano H, Tanigawa T, Ohnishi Y, et al. Validation of a single-channel airflow monitor for screening of sleep-disordered breathing. *European Respiratory Journal* 2008;32:1060-1067.

83. Nigro CA, Aimaretti S, Gonzalez S, et al. Validation of the WristOx 3100 oximeter for the diagnosis of sleep apnea/hypopnea syndrome. *Sleep & Breathing* 2009;13:127-136.

84. Pang KP, Gourin CG, Terris DJ. A comparison of polysomnography and the WatchPAT in the diagnosis of obstructive sleep apnea. *Otolaryngology - Head & Neck Surgery* 2007;137:665-668.

85. Pepin JL, Defaye P, Vincent E, et al. Sleep apnea diagnosis using an ECG Holter device including a nasal pressure (NP) recording: validation of visual and automatic analysis of nasal pressure versus full polysomnography. *Sleep Medicine* 2009;10:651-656.

86. Reda M, Gibson GJ, Wilson JA. Pharyngoesophageal pressure monitoring in sleep apnea syndrome. *Otolaryngology - Head & Neck Surgery* 2001;125:324-331.

87. Schafer H, Ewig S, Hasper E, et al. Predictive diagnostic value of clinical assessment and nonlaboratory monitoring system recordings in patients with symptoms suggestive of obstructive sleep apnea syndrome. *Respiration* 1997;64:194-199.

88. Smith LA, Chong DW, Vennelle M, et al. Diagnosis of sleep-disordered breathing in patients with chronic heart failure: evaluation of a portable limited sleep study system. *Journal of Sleep Research* 2007;16:428-435.

89. Szyszko A, Franceschini C, Gonzalez-Zuelgaray J. Reliability of a Holter-based methodology for evaluation of sleep apnoea syndrome. *Europace* 2009;11:94-99.

90. Watkins MR, Talmage JB, Thiese MS, et al. Correlation between screening for obstructive sleep apnea using a portable device versus polysomnography testing in a commercial driving population. *Journal of Occupational & Environmental Medicine* 2009;51:1145-1150.

91. White JE, Smithson AJ, Close PR, et al. The use of sound recording and oxygen saturation in screening snorers for obstructive sleep apnoea. *Clinical Otolaryngology & Allied Sciences* 1994;19:218-221.

92. Wong KK, Jankelson D, Reid A, et al. Diagnostic test evaluation of a nasal flow monitor for obstructive sleep apnea detection in sleep apnea research. *Behavior Research Methods* 2008;40:360-366.

93. Yagi H, Nakata S, Tsuge H, et al. Significance of a screening device (Apnomonitor 5) for sleep apnea syndrome. *Auris, Nasus, Larynx* 2009;36:176-180.

94. Agatsuma T, Fujimoto K, Komatsu Y, et al. A novel device (SD-101) with high accuracy for screening sleep apnoea-hypopnoea syndrome. *Respirology* 2009;14:1143-1150.

95. Ragette R, Wang Y, Weinreich G, et al. Diagnostic performance of single airflow channel recording (ApneaLink) in home diagnosis of sleep apnea. *Sleep Breath* 2010;14:109-114.

96. Ng SS, Chan TO, To KW, et al. Validation of a portable recording device (ApneaLink) for identifying patients with suspected obstructive sleep apnoea syndrome. *Internal Medicine Journal* 2009;39:757-762.

97. Chung F, Yegneswaran B, Liao P, et al. Validation of the Berlin questionnaire and American Society of Anesthesiologists checklist as screening tools for obstructive sleep apnea in surgical patients. *Anesthesiology* 2008;108:822-830.

98. Kapuniai LE, Andrew DJ, Crowell DH, et al. Identifying sleep apnea from self-reports. *Sleep* 1988;11:430-436.

99. Netzer NC, Stoohs RA, Netzer CM, et al. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Annals of Internal Medicine* 1999;131:485-491.

100. Sharma SK, Vasudev C, Sinha S, et al. Validation of the modified Berlin questionnaire to identify patients at risk for the obstructive sleep apnoea syndrome. *Indian Journal of Medical Research* 2006;124:281-290.

101. Drager LF, Genta PR, Pedrosa RP, et al. Characteristics and predictors of obstructive sleep apnea in patients with systemic hypertension. *American Journal of Cardiology* 2010;105:1135-1139.

102. Crocker BD, Olson LG, Saunders NA, et al. Estimation of the probability of disturbed breathing during sleep before a sleep study. *American Review of Respiratory Disease* 1990;142:14-18.

103. Gurubhagavatula I, Maislin G, Pack AI. An algorithm to stratify sleep apnea risk in a sleep disorders clinic population. *American Journal of Respiratory & Critical Care Medicine* 2001;164:t-9.

104. Kushida CA, Efron B, Guilleminault C. A predictive morphometric model for the obstructive sleep apnea syndrome. *Annals of Internal Medicine* 1997;127:t-7.

105. Onen SH, Dubray C, Decullier E, et al. Observation-based nocturnal sleep inventory: screening tool for sleep apnea in elderly people. *Journal of the American Geriatrics Society* 2008;56:1920-1925.

106. Rodsutti J, Hensley M, Thakkinstian A, et al. A clinical decision rule to prioritize polysomnography in patients with suspected sleep apnea. *Sleep* 2004;27:694-699.

107. Rowley JA, Aboussouan LS, Badr MS. The use of clinical prediction formulas in the evaluation of obstructive sleep apnea. *Sleep* 2000;23:929-938.

108. Zerah-Lancner F, Lofaso F, d'Ortho MP, et al. Predictive value of pulmonary function parameters for sleep apnea syndrome. *American Journal of Respiratory & Critical Care Medicine* 2000;162:2208-2212.

109. Gurubhagavatula I, Maislin G, Nkwuo JE, et al. Occupational screening for obstructive sleep apnea in commercial drivers. *American Journal of Respiratory & Critical Care Medicine* 2004;170:371-376.

110. Hallowell PT, Stellato TA, Petrozzi MC, et al. Eliminating respiratory intensive care unit stay after gastric bypass surgery[erratum appears in *Surgery* 2008 Feb;143(2):301]. *Surgery* 2007;142:608-612.

111. Lavie P, Lavie L, Herer P. All-cause mortality in males with sleep apnoea syndrome: declining mortality rates with age. *European Respiratory Journal* 2005;25:514-520.

112. Lavie P, Here P, Peled R, et al. Mortality in sleep apnea patients: a multivariate analysis of risk factors. *Sleep* 1995;18:149-157.

113. Arzt M, Young T, Finn L, et al. Association of sleep-disordered breathing and the occurrence of stroke. *American Journal of Respiratory & Critical Care Medicine* 2005;172:1447-1451.

114. O'Connor GT, Caffo B, Newman AB, et al. Prospective study of sleep-disordered breathing and hypertension: the Sleep Heart Health Study. *American Journal of Respiratory & Critical Care Medicine* 2009;179:1159-1164.

115 Reichmuth KJ, Austin D, Skatrud JB, et al. Association of sleep apnea and type II diabetes: a population-based study. *American Journal of Respiratory & Critical Care Medicine* 2005;172:1590-1595.

116. Botros N, Concato J, Mohsenin V, et al. Obstructive sleep apnea as a risk factor for type 2 diabetes. *American Journal of Medicine* 2009;122:1122-1127.

117. Silva GE, An MW, Goodwin JL, et al. Longitudinal evaluation of sleep-disordered breathing and sleep symptoms with change in quality of life: the Sleep Heart Health Study (SHHS). *Sleep* 2009;32:1049-1057.

118. Ballester E, Badia JR, Hernandez L, et al. Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome [erratum appears in *Am J Respir Crit Care Med* 1999 May;159(5 Pt 1):1688]. *Am J Respir Crit Care Med* 1999;159:495-501.

119. Chakravorty I, Cayton RM, Szczepura A. Health utilities in evaluating intervention in the sleep apnoea/hypopnoea syndrome. *European Respiratory Journal* 2002;20:1233-1238.

120. Drager LF, Bortolotto LA, Figueiredo AC, et al. Effects of continuous positive airway pressure on early signs of atherosclerosis in obstructive sleep apnea. *Am J Respir Crit Care Med* 2007;176:706-712.

121. Ip MS, Tse HF, Lam B, et al. Endothelial function in obstructive sleep apnea and response to treatment. *Am J Respir Crit Care Med* 2004;169:348-353.

122. Kajaste S, Brander PE, Telakivi T, et al. A cognitive-behavioral weight reduction program in the treatment of obstructive sleep apnea syndrome with or without initial nasal CPAP: a randomized study. *Sleep Medicine* 2004;5:125-131.

123. Kaneko Y, Floras JS, Usui K, et al. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. *New Engl J Med* 2003;348:1233-1241.

124. Lojander J, Maasilta P, Partinen M, et al. Nasal-CPAP, surgery, and conservative management for treatment of obstructive sleep apnea syndrome. A randomized study. *Chest* 1996;110:114-119.

125. Lojander J, Kajaste S, Maasilta P, et al. Cognitive function and treatment of obstructive sleep apnea syndrome. *Journal of Sleep Research* 1999;8:71-76.

126. Mansfield DR, Gollogly NC, Kaye DM, et al. Controlled trial of continuous positive airway pressure in obstructive sleep apnea and heart failure. *Am J Respir Crit Care Med* 2004;169:361-366.

127. Monasterio C, Vidal S, Duran J, et al. Effectiveness of continuous positive airway pressure in mild sleep apnea-hypopnea syndrome. *Am J Respir Crit Care Med* 2001;164:939-943.

128. Redline S, Adams N, Strauss ME, et al. Improvement of mild sleep-disordered breathing with CPAP compared with conservative therapy. *Am J Respir Crit Care Med* 1998;157:t-65.

129. Lam B, Sam K, Mok WY, et al. Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnoea. *Thorax* 2007;62:354-359.

130. Barbe F, Duran-Cantolla J, Capote F, et al. Long-term effect of continuous positive airway pressure in hypertensive patients with sleep apnea. *Am J Respir Crit Care Med* 2010;181:718-726.

131. Barnes M, Houston D, Worsnop CJ, et al. A randomized controlled trial of continuous positive airway pressure in mild obstructive sleep apnea. *Am J Respir Crit Care Med.* 2002;165:773-780.

132. Comondore VR, Cheema R, Fox J, et al. The impact of CPAP on cardiovascular biomarkers in minimally symptomatic patients with obstructive sleep apnea: a pilot feasibility randomized crossover trial. *Lung* 2009;187:17-22.

133. Engleman HM, Martin SE, Deary IJ, et al. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. *Lancet* 1994;343:572-575.

134. Engleman HM, Gough K, Martin SE, et al. Ambulatory blood pressure on and off continuous positive airway pressure therapy for the sleep apnea/hypopnea syndrome: effects in "non-dippers". *Sleep* 1996;19:378-381.

135. Engleman HM, Martin SE, Deary IJ, et al. Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. *Thorax* 1997;52:114-119.

136. Engleman HM, Martin SE, Kingshott RN, et al. Randomised placebo controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. *Thorax* 1998;53:341-345.

137. Engleman HM, Kingshott RN, Wraith PK, et al. Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep Apnea/Hypopnea syndrome. *Am J Respir Crit Care Med* 1999;159:461-467.

138. Faccenda JF, Mackay TW, Boon NA, et al. Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *Am J Respir Crit Care Med* 2001;163:344-348.

139. McArdle N, Douglas NJ. Effect of continuous positive airway pressure on sleep architecture in the sleep apnea-hypopnea syndrome: a randomized controlled trial. *Am J Respir Crit Care Med* 2001;164:t-63.

140. Barnes M, McEvoy RD, Banks S, et al. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *Am J Resp Crit Care Med* 2004;170:656-664.

141. Arias MA, Garcia-Rio F, Alonso-Fernandez A, et al. Obstructive sleep apnea syndrome affects left ventricular diastolic function: effects of nasal continuous positive airway pressure in men. *Circulation* 2005;112:375-383.

142. Barbe F, Mayoralas LR, Duran J, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. a randomized, controlled trial. *Annals of Internal Medicine* 2001;134:1015-1023.

143. Becker HF, Jerrentrup A, Ploch T, et al. Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. *Circulation* 2003;107:68-73.

144. Campos-Rodriguez F, Grilo-Reina A, Perez-Ronchel J, et al. Effect of continuous positive airway pressure on ambulatory BP in patients with sleep apnea and hypertension: a placebo-controlled trial. *Chest* 2006;129:1459-1467.

145. Coughlin SR, Mawdsley L, Mugarza JA, et al. Cardiovascular and metabolic effects of CPAP in obese males with OSA. *European Respiratory Journal* 2007;29:720-727.

146. Cross MD, Mills NL, Al-Abri M, et al. Continuous positive airway pressure improves vascular function in obstructive sleep apnoea/hypopnoea syndrome: a randomised controlled trial. *Thorax* 2008;63:578-583.

147. Egea CJ, Aizpuru F, Pinto JA, et al. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. *Sleep Medicine* 2008;9:660-666.

148. Haensel A, Norman D, Natarajan L, et al. Effect of a 2 week CPAP treatment on mood states in patients with obstructive sleep apnea: a double-blind trial. *Sleep & Breathing* 2007;11:239-244.

149. Henke KG, Grady JJ, Kuna ST. Effect of nasal continuous positive airway pressure on neuropsychological function in sleep apnea-hypopnea syndrome. A randomized, placebo-controlled trial. *Am J Respir Crit Care Med* 2001;163:911-917.

150. Hui DS, To KW, Ko FW, et al. Nasal CPAP reduces systemic blood pressure in patients with obstructive sleep apnoea and mild sleepiness. *Thorax* 2006;61:1083-1090.

151. Jenkinson C, Davies RJ, Mullins R, et al. Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet* 1999;353:2100-2105.

152. Hack M, Davies RJ, Mullins R, et al. Randomised prospective parallel trial of therapeutic versus subtherapeutic nasal continuous positive airway pressure on simulated steering performance in patients with obstructive sleep apnoea. *Thorax* 2000;55:224-231.

153. Loredo JS, Ancoli-Israel S, Dimsdale JE. Effect of continuous positive airway pressure vs placebo continuous positive airway pressure on sleep quality in obstructive sleep apnea. *Chest* 1999;116:1545-1549.

154. Yu BH, Ancoli-Israel S, Dimsdale JE. Effect of CPAP treatment on mood states in patients with sleep apnea. *Journal of Psychiatric Research* 1999;33:427-432.

155. Bardwell WA, Ancoli-Israel S, Berry CC, et al. Neuropsychological effects of one-week continuous positive airway pressure treatment in patients with obstructive sleep apnea: a placebo-controlled study. *Psychosomatic Medicine* 2001;63:579-584.

156. Profant J, Ancoli-Israel S, Dimsdale JE. A randomized, controlled trial of 1 week of continuous positive airway pressure treatment on quality of life. *Heart & Lung* 2003;32:52-58.

157. Loredo JS, Ancoli-Israel S, Kim EJ, et al. Effect of continuous positive airway pressure versus supplemental oxygen on sleep quality in obstructive sleep apnea: a placebo-CPAP-controlled study. *Sleep* 2006;29:564-571.

158. Bardwell WA, Norman D, Ancoli-Israel S, et al. Effects of 2-week nocturnal oxygen supplementation and continuous positive airway pressure treatment on psychological symptoms in patients with obstructive sleep apnea: a randomized placebo-controlled study. *Behavioral Sleep Medicine* 2007;5:21-38.

159. Marshall NS, Neill AM, Campbell AJ, et al. Randomised controlled crossover trial of humidified continuous positive airway pressure in mild obstructive sleep apnoea. *Thorax* 2005;60:427-432.

160. Mills PJ, Kennedy BP, Loredo JS, et al. Effects of nasal continuous positive airway pressure and oxygen supplementation on norepinephrine kinetics and cardiovascular responses in obstructive sleep apnea. *Journal of Applied Physiology* 2006;100:343-348.

161. Lim W, Bardwell WA, Loredo JS, et al. Neuropsychological effects of 2-week continuous positive airway pressure treatment and supplemental oxygen in patients with obstructive sleep apnea: a randomized placebo-controlled study. *Journal of Clinical Sleep Medicine* 2007;3:380-386.

162. Montserrat JM, Ferrer M, Hernandez L, et al. Effectiveness of CPAP treatment in daytime function in sleep apnea syndrome: a randomized controlled study with an optimized placebo. *Am J Respir Crit Care Med* 2001;164:608-613.

163. Norman D, Loredo JS, Nelesen RA, et al. Effects of continuous positive airway pressure versus supplemental oxygen on 24-hour ambulatory blood pressure. *Hypertension* 2006;47:840-845.

164. Robinson GV, Smith DM, Langford BA, et al. Continuous positive airway pressure does not reduce blood pressure in nonsleepy hypertensive OSA patients. *European Respiratory Journal* 2006;27:1229-1235.

165. Siccoli MM, Pepperell JC, Kohler M, et al. Effects of continuous positive airway pressure on quality of life in patients with moderate to severe obstructive sleep apnea: data from a randomized controlled trial. *Sleep* 2008;31:1551-1558.

166. Smith LA, Vennelle M, Gardner RS, et al. Auto-titrating continuous positive airway pressure therapy in patients with chronic heart failure and obstructive sleep apnoea: a randomized placebo-controlled trial. *European Heart Journal* 2007;28:1221-1227.

167. Spicuzza L, Bernardi L, Balsamo R, et al. Effect of treatment with nasal continuous positive airway pressure on ventilatory response to hypoxia and hypercapnia in patients with sleep apnea syndrome. *Chest* 2006;130:774-779.

168. West SD, Nicoll DJ, Wallace TM, et al. Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. *Thorax* 2007;62:969-974.

169. Lam JC, Lam B, Yao TJ, et al. A randomised controlled trial of nasal continuous positive airway pressure on insulin sensitivity in obstructive sleep apnoea. *European Respiratory Journal* 2010;35:138-145.

170. West SD, Kohler M, Nicoll DJ, et al. The effect of continuous positive airway pressure treatment on physical activity in patients with obstructive sleep apnoea: A randomised controlled trial. *Sleep Medicine* 2009;10:1056-1058.

171. Anderson FE, Kingshott RN, Taylor DR, et al. A randomized crossover efficacy trial of oral CPAP (Oracle) compared with nasal CPAP in the management of obstructive sleep apnea. *Sleep* 2003;26:721-726.

172. Mortimore IL, Whittle AT, Douglas NJ. Comparison of nose and face mask CPAP therapy for sleep apnoea. *Thorax* 1998;53:290-292.

173. Khanna R, Kline LR. A prospective 8 week trial of nasal interfaces vs. a novel oral interface (Oracle) for treatment of obstructive sleep apnea hypopnea syndrome. *Sleep Medicine* 2003;4:333-338.

174. Damjanovic D, Fluck A, Bremer H, et al. Compliance in sleep apnoea therapy: influence of home care support and pressure mode. *European Respiratory Journal* 2009;33:804-811.

175. Fietze I, Glos M, Moebus I, et al. Automatic pressure titration with APAP is as effective as manual titration with CPAP in patients with obstructive sleep apnea. *Respiration* 2007;74:279-286.

176. Galetke W, Anduleit N, Richter K, et al. Comparison of automatic and continuous positive airway pressure in a night-by-night analysis: a randomized, crossover study. *Respiration* 2008;75:163-169.

177. Meurice JC, Cornette A, Philip-Joet F, et al. Evaluation of autoCPAP devices in home treatment of sleep apnea/hypopnea syndrome. *Sleep Medicine* 2007;8:695-703.

178. Nolan GM, Doherty LS, Mc Nicholas WT. Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. *Sleep* 2007;30:189-194.

179. Nussbaumer Y, Bloch KE, Genser T, et al. Equivalence of autoadjusted and constant continuous positive airway pressure in home treatment of sleep apnea. *Chest* 2006;129:638-643.

180. Patruno V, Aiolfi S, Costantino G, et al. Fixed and autoadjusting continuous positive airway pressure treatments are not similar in reducing cardiovascular risk factors in patients with obstructive sleep apnea. *Chest* 2007;131:1393-1399.

181. To KW, Chan WC, Choo KL, et al. A randomized cross-over study of auto-continuous positive airway pressure versus fixed-continuous positive airway pressure in patients with obstructive sleep apnoea. *Respirology* 2008;13:79-86.

182. Hudgel DW, Fung C. A long-term randomized, cross-over comparison of auto-titrating and standard nasal continuous airway pressure. *Sleep* 2000;23:645-648.

183. Hukins C. Comparative study of autotitrating and fixed-pressure CPAP in the home: a randomized, single-blind crossover trial. *Sleep* 2004;27:1512-1517.

184. Hussain SF, Love L, Burt H, et al. A randomized trial of auto-titrating CPAP and fixed CPAP in the treatment of obstructive sleep apnea-hypopnea. *Respiratory Medicine* 2004;98:330-333.

185. Marrone O, Resta O, Salvaggio A, et al. Preference for fixed or automatic CPAP in patients with obstructive sleep apnea syndrome. *Sleep Medicine* 2004;5:247-251.

186. Massie CA, McArdle N, Hart RW, et al. Comparison between automatic and fixed positive airway pressure therapy in the home. *Am J Respir Crit Care Med* 2003;167:20-23.

187. Noseda A, Kempenaers C, Kerkhofs M, et al. Constant vs auto-continuous positive airway pressure in patients with sleep apnea hypopnea syndrome and a high variability in pressure requirement. *Chest* 2004;126:31-37.

188. Resta O, Carratu P, Depalo A, et al. Effects of fixed compared to automatic CPAP on sleep in Obstructive Sleep Apnoea Syndrome. *Monaldi Archives for Chest Disease* 2004;61:153-156.

189. Senn O, Brack T, Matthews F, et al. Randomized short-term trial of two autoCPAP devices versus fixed continuous positive airway pressure for the treatment of sleep apnea. *Am J Respir Crit Care Med* 2003;168:1506-1511.

190. Randerath WJ, Schraeder O, Galetke W, et al. Autoadjusting CPAP therapy based on impedance efficacy, compliance and acceptance. *Am J Respir Crit Care Med* 2001;163:t-7.

191. Series F, Marc I. Efficacy of automatic continuous positive airway pressure therapy that uses an estimated required pressure in the treatment of the obstructive sleep apnea syndrome. *Annals of Internal Medicine.* 1997;127:t-95.

192. Teschler H, Wessendorf TE, Farhat AA, et al. Two months auto-adjusting versus conventional nCPAP for obstructive sleep apnoea syndrome. *European Respiratory Journal* 2000;15:990-995.

193. Planes C, d'Ortho MP, Foucher A, et al. Efficacy and cost of home-initiated auto-nCPAP versus conventional nCPAP. *Sleep* 2003;26:156-160.

194. Vennelle M, White S, Riha RL, et al. Randomized controlled trial of variable-pressure versus fixed-pressure continuous positive airway pressure (CPAP) treatment for patients with obstructive sleep apnea/hypopnea syndrome (OSAHS). *Sleep* 2010;33:267-271.

195. Gay PC, Herold DL, Olson EJ. A randomized, double-blind clinical trial comparing continuous positive airway pressure with a novel bilevel pressure system for treatment of obstructive sleep apnea syndrome. *Sleep* 2003;26:864-869.

196. Khayat RN, Abraham WT, Patt B, et al. Cardiac effects of continuous and bilevel positive airway pressure for patients with heart failure and obstructive sleep apnea: a pilot study. *Chest* 2008;134:1162-1168.

197. Piper AJ, Wang D, Yee BJ, et al. Randomised trial of CPAP vs bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation. *Thorax* 2008;63:395-401.

198. Reeves-Hoche MK, Hudgel DW, Meck R, et al. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. *Am J Respir Crit Care Med* 1995;151:t-9.

199. Randerath WJ, Galetke W, Ruhle KH. Auto-adjusting CPAP based on impedance versus bilevel pressure in difficult-to-treat sleep apnea syndrome: a prospective randomized crossover study. *Medical Science Monitor* 2003;9:CR353-CR358.

200. Ballard RD, Gay PC, Strollo PJ. Interventions to improve compliance in sleep apnea patients previously non-compliant with continuous positive airway pressure. *Journal of Clinical Sleep Medicine* 2007;3:706-712.

201. Dolan DC, Okonkwo R, Gfullner F, et al. Longitudinal comparison study of pressure relief (C-Flex) vs. CPAP in OSA patients. *Sleep & Breathing* 2009;13:73-77.

202. Nilius G, Happel A, Domanski U, et al. Pressure-relief continuous positive airway pressure vs constant continuous positive airway pressure: a comparison of efficacy and compliance. *Chest* 2006;130:1018-1024.

203. Pepin JL, Muir JF, Gentina T, et al. Pressure reduction during exhalation in sleep apnea patients treated by continuous positive airway pressure. *Chest* 2009;136:490-497.

204. Leidag M, Hader C, Keller T, et al. Mask leakage in continuous positive airway pressure and C-Flex. *Journal of Physiology & Pharmacology* 2008;59:Suppl-6.

205. Ryan S, Doherty LS, Nolan GM, et al. Effects of heated humidification and topical steroids on compliance, nasal symptoms, and quality of life in patients with obstructive sleep apnea syndrome using nasal continuous positive airway pressure. *Journal of Clinical Sleep Medicine* 2009;5:422-427.

206. Mador MJ, Krauza M, Pervez A, et al. Effect of heated humidification on compliance and quality of life in patients with sleep apnea using nasal continuous positive airway pressure. *Chest* 2005;128:2151-2158.

207. Salgado SM, Boleo-Tome JP, Canhao CM, et al. Impact of heated humidification with automatic positive airway pressure in obstructive sleep apnea therapy. *Jornal Brasileiro De Pneumologia: Publicacao Oficial Da Sociedade Brasileira De Pneumologia E Tisilogia* 2008;34:690-694.

208. Neill AM, Wai HS, Bannan SP, et al. Humidified nasal continuous positive airway pressure in obstructive sleep apnoea. *European Respiratory Journal* 2003;22:258-262.

209. Massie CA, Hart RW, Peralez K, et al. Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure. *Chest* 1999;116:403-408.

210. Bloch KE, Iseli A, Zhang JN, et al. A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. *Am J Respir Crit Care Med* 2000;162:246-251.

211. Kato J, Isono S, Tanaka A, et al. Dose-dependent effects of mandibular advancement on pharyngeal mechanics and nocturnal oxygenation in patients with sleep-disordered breathing. *Chest* 2000;117:1065-1072.

212. Petri N, Svanholt P, Solow B, et al. Mandibular advancement appliance for obstructive sleep apnoea: results of a randomised placebo controlled trial using parallel group design. *Journal of Sleep Research* 2008;17:221-229.

213. Hans MG, Nelson S, Luks VG, et al. Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). *American Journal of Orthodontics & Dentofacial Orthopedics* 1997;111:562-570.

214. Gotsopoulos H, Chen C, Qian J, et al. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. *Am J Respir Crit Care Med* 2002;166:743-748.

215. Gotsopoulos H, Kelly JJ, Cistulli PA. Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. *Sleep* 2004;27:934-941.

216. Johnston CD, Gleadhill IC, Cinnamond MJ, et al. Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. *European Journal of Orthodontics* 2002;24:251-262.

217. Naismith SL, Winter VR, Hickie IB, et al. Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. *Journal of Clinical Sleep Medicine* 2005;1:374-380.

218. Mehta A, Qian J, Petocz P, et al. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. *Am J Respir Crit Care Med* 2001;163:1457-1461.

219. Campbell AJ, Reynolds G, Trengrove H, et al. Mandibular advancement splint titration in obstructive sleep apnoea. *Sleep & Breathing* 2009;13:157-162.

220. Walker-Engstrom ML, Ringqvist I, Vestling O, et al. A prospective randomized study comparing two different degrees of mandibular advancement with a dental appliance in treatment of severe obstructive sleep apnea. *Sleep & Breathing* 2003;7:119-130.

221. Vanderveken OM, Devolder A, Marklund M, et al. Comparison of a custom-made and a thermoplastic oral appliance for the treatment of mild sleep apnea. *Am J Respir Crit Care Med* 2008;178:197-202.

222. Deane SA, Cistulli PA, Ng AT, et al. Comparison of mandibular advancement splint and tongue stabilizing device in obstructive sleep apnea: a randomized controlled trial. *Sleep* 2009;32:648-653.

223. Dort L, Brant R. A randomized, controlled, crossover study of a noncustomized tongue retaining device for sleep disordered breathing. *Sleep & Breathing* 2008;12:369-373.

224. Clark GT, Blumenfeld I, Yoffe N, et al. A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. *Chest* 1996;109:1477-1483.

225. Engleman HM, McDonald JP, Graham D, et al. Randomized crossover trial of two treatments for sleep apnea/hypopnea syndrome: continuous positive airway pressure and mandibular repositioning splint. *Am J Respir Crit Care Med* 2002;166:855-859.

226. Ferguson KA, Ono T, Lowe AA, et al. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest* 1996;109:1269-1275.

227. Gagnadoux F, Fleury B, Vielle B, et al. Titrated mandibular advancement versus positive airway pressure for sleep apnoea. *European Respiratory Journal* 2009;34:914-920.

228. Randerath WJ, Heise M, Hinz R, et al. An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest* 2002;122:569-575.

229. Tan YK, L'Estrange PR, Luo YM, et al. Mandibular advancement splints and continuous positive airway pressure in patients with obstructive sleep apnoea: a randomized cross-over trial. *European Journal of Orthodontics* 2002;24:239-249.

230. Hoekema A, Stegenga B, Wijkstra PJ, et al. Obstructive sleep apnea therapy. *Journal of Dental Research* 2008;87:882-887.

231. Hoekema A, Stel AL, Stegenga B, et al. Sexual function and obstructive sleep apnea-hypopnea: a randomized clinical trial evaluating the effects of oral-appliance and continuous positive airway pressure therapy. *Journal of Sexual Medicine* 2007;4:t-62.

232. Skinner MA, Kingshott RN, Jones DR, et al. Lack of efficacy for a cervicomandibular support collar in the management of obstructive sleep apnea. *Chest* 2004;125:118-126.

233. Skinner MA, Kingshott RN, Jones DR, et al. Elevated posture for the management of obstructive sleep apnea. *Sleep & Breathing* 2004;8:193-200.

234. Skinner MA, Kingshott RN, Filsell S, et al. Efficacy of the 'tennis ball technique' versus nCPAP in the management of position-dependent obstructive sleep apnoea syndrome. *Respirology* 2008;13:708-715.

235. Jokic R, Klimaszewski A, Crossley M, et al. Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea syndrome. *Chest* 1999;115:771-781.

236. Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Archives of Internal Medicine* 2009;169:1619-1626.

237. Johansson K, Neovius M, Lagerros YT, et al. Effect of a very low energy diet on moderate and severe obstructive sleep apnoea in obese men: a randomised controlled trial. *BMJ* 2009;339:b4609.

238. Tuomilehto HP, Seppa JM, Partinen MM, et al. Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. *Am J Respir Crit Care Med* 2009;179:320-327.

239. Puhan MA, Suarez A, Lo CC, et al. Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. *BMJ* 2006;332:266-270.

240. Guimaraes KC, Drager LF, Genta PR, et al. Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2009;179:962-966.

241. Randerath WJ, Galetke W, Domanski U, et al. Tongue-muscle training by intraoral electrical neurostimulation in patients with obstructive sleep apnea. *Sleep* 2004;27:254-259.

242. Friedman M, Schalch P, Lin HC, et al. Palatal implants for the treatment of snoring and obstructive sleep apnea/hypopnea syndrome. *Otolaryngology - Head & Neck Surgery* 2008;138:209-216.

243. Steward DL, Huntley TC, Woodson BT, et al. Palate implants for obstructive sleep apnea: multi-institution, randomized, placebo-controlled study. *Otolaryngology - Head & Neck Surgery* 2008;139:506-510.

244. Back LJ, Liukko T, Rantanen I, et al. Radiofrequency surgery of the soft palate in the treatment of mild obstructive sleep apnea is not effective as a single-stage procedure: A randomized single-blinded placebo-controlled trial. *Laryngoscope* 2009;119:1621-1627.

245. Ferguson KA, Heighway K, Ruby RR. A randomized trial of laser-assisted uvulopalatoplasty in the treatment of mild obstructive sleep apnea. *Am J Respir Crit Care Med* 2003;167:15-19.

246. Koutsourelakis I, Georgoulopoulos G, Perraki E, et al. Randomised trial of nasal surgery for fixed nasal obstruction in obstructive sleep apnoea. *European Respiratory Journal* 2008;31:110-117.

247. Woodson BT, Steward DL, Weaver EM, et al. A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. *Otolaryngology-Head & Neck Surgery* 2003;128:848-861.

248. Guilleminault C, Davis K, Huynh NT. Prospective randomized study of patients with insomnia and mild sleep disordered breathing. *Sleep* 2008;31:1527-1533.

249. Li HY, Lee LA, Wang PC, et al. Can nasal surgery improve obstructive sleep apnea: subjective or objective? *American Journal of Rhinology & Allergy* 2009;23:e51-e55.

250. Vicini C, Dallan I, Campanini A, et al. Surgery vs ventilation in adult severe obstructive sleep apnea syndrome. *American Journal of Otolaryngology* 2010;31:14-20.

251. Conradt R, Hochban W, Heitmann J, et al. Sleep fragmentation and daytime vigilance in patients with OSA treated by surgical maxillomandibular advancement compared to CPAP therapy. *Journal of Sleep Research.* 1998;7:217-223.

252. Woodson BT, Nelson L, Mickelson S, et al. A multi-institutional study of radiofrequency volumetric tissue reduction for OSAS. *Otolaryngology - Head & Neck Surgery* 2001;125:303-311.

253. Zorick FJ, Roehrs T, Conway W, et al. Response to CPAP and UPPP in apnea. *Henry Ford Hospital Medical Journal* 1990;38:223-226.

254. Ceylan K, Emir H, Kizilkaya Z, et al. First-choice treatment in mild to moderate obstructive sleep apnea: single-stage, multilevel, temperature-controlled radiofrequency tissue volume reduction or nasal continuous positive airway pressure. *Archives of Otolaryngology -- Head & Neck Surgery* 2009;135:915-919.

255. Anand VK, Ferguson PW, Schoen LS. Obstructive sleep apnea: a comparison of continuous positive airway pressure and surgical treatment. *Otolaryngology - Head & Neck Surgery* 1991;105:382-390.

256. Katsantonis GP, Schweitzer PK, Branham GH, et al. Management of obstructive sleep apnea: comparison of various treatment modalities. *Laryngoscope* 1988;98:304-309.

257. Keenan SP, Burt H, Ryan CF, et al. Long-term survival of patients with obstructive sleep apnea treated by uvulopalatopharyngoplasty or nasal CPAP. *Chest* 1994;105:155-159.

258. Lin SW, Chen NH, Li HY, et al. A comparison of the long-term outcome and effects of surgery or continuous positive airway pressure on patients with obstructive sleep apnea syndrome. *Laryngoscope* 2006;116:1012-1016.

259. Robinson S, Chia M, Carney AS, et al. Upper airway reconstructive surgery long-term quality-of-life outcomes compared with CPAP for adult obstructive sleep apnea. *Otolaryngology - Head & Neck Surgery* 2009;141:257-263.

260. Weaver EM, Maynard C, Yueh B. Survival of veterans with sleep apnea: continuous positive airway pressure versus surgery [erratum appears in Otolaryngol Head Neck Surg. 2004 Jul;131(1):144]. *Otolaryngology - Head & Neck Surgery* 2004;130:659-665.

261. Wilhelmsson B, Tegelberg A, Walker-Engstrom ML, et al. A prospective randomized study of a dental appliance compared with uvulopalatopharyngoplasty in the treatment of obstructive sleep apnoea. *Acta Oto-Laryngologica* 1999;119:503-509.

262. Walker-Engstrom ML, Tegelberg A, Wilhelmsson B, et al. 4-year follow-up of treatment with dental appliance or uvulopalatopharyngoplasty in patients with obstructive sleep apnea: a randomized study. *Chest* 2002;121:739-746.

263. Walker-Engstrom ML, Wilhelmsson B, Tegelberg A, et al. Quality of life assessment of treatment with dental appliance or UPPP in patients with mild to moderate obstructive sleep apnoea. A prospective randomized 1-year follow-up study. *Journal of Sleep Research* 2000;9:303-308.

264. Carley DW, Olopade C, Ruigt GS, et al. Efficacy of mirtazapine in obstructive sleep apnea syndrome. *Sleep* 2007;30:35-41.

265. Kiely JL, Nolan P, McNicholas WT. Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. *Thorax* 2004;59:50-55.

266. Kraiczi H, Hedner J, Dahlof P, et al. Effect of serotonin uptake inhibition on breathing during sleep and daytime symptoms in obstructive sleep apnea. *Sleep* 1999;22:61-67.

267. Whyte KF, Gould GA, Airlie MA, et al. Role of protriptyline and acetazolamide in the sleep apnea/hypopnea syndrome. *Sleep* 1988;11:463-472.

268. Suurna MV, Welge J, Surdulescu V, et al. Randomized placebo-controlled trial of pantoprazole for daytime sleepiness in GERD and obstructive sleep disordered breathing. *Otolaryngology - Head & Neck Surgery* 2008;139:286-290.

269. Clarenbach CF, Kohler M, Senn O, et al. Does nasal decongestion improve obstructive sleep apnea? *Journal of Sleep Research* 2008;17:444-449.

270. Melzer C, Fietze I, Duru F, et al. Nocturnal overdrive pacing for the treatment of sleep apnea syndrome. *Sleep* 2006;29:1197-1202.

271. Simantirakis EN, Schiza SE, Chrysostomakis SI, et al. Atrial overdrive pacing for the obstructive sleep apnea-hypopnea syndrome. *New Engl J Med* 2005;353:2568-2577.

272. Grunstein RR, Stenlof K, Hedner JA, et al. Two year reduction in sleep apnea symptoms and associated diabetes incidence after weight loss in severe obesity. *Sleep* 2007;30:703-710.

273. Cartwright R, Ristanovic R, Diaz F, et al. A comparative study of treatments for positional sleep apnea. *Sleep* 1991;14:546-552.

274. Freire AO, Sugai GC, Chrispin FS, et al. Treatment of moderate obstructive sleep apnea syndrome with acupuncture: a randomised, placebo-controlled pilot trial. *Sleep Medicine* 2007;8:43-50.

275. Krakow B, Melendrez D, Sisley B, et al. Nasal dilator strip therapy for chronic sleep-maintenance insomnia and symptoms of sleep-disordered breathing: a randomized controlled trial. *Sleep & Breathing* 2006;10:16-28.

276. Wang XH, Xiao LY, Wang BF, et al. Influence of auricular plaster therapy on sleeping structure in OSAS patients. *Journal of Traditional Chinese Medicine* 2009;29:3-5.

277. Kezirian EJ, Weaver EM, Yueh B, et al. Incidence of serious complications after uvulopalatopharyngoplasty. *Laryngoscope* 2004;114:450-453.

278. Lundkvist K, Januszkiewicz A, Friberg D. Uvulopalatopharyngoplasty in 158 OSAS patients failing non-surgical treatment. *Acta Oto-Laryngologica* 2009;129:1280-1286.

279. Esclamado RM, Glenn MG, McCulloch TM, et al. Perioperative complications and risk factors in the surgical treatment of obstructive sleep apnea syndrome. *Laryngoscope* 1989;99:1125-1129.

280. Friedman M, Ibrahim H, Joseph NJ. Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. *Laryngoscope* 2004;114:454-459.

281. Harmon JD, Morgan W, Chaudhary B. Sleep apnea: morbidity and mortality of surgical treatment. *Southern Medical Journal* 1989;82:161-164.

282. Haavisto L, Suonpaa J. Complications of uvulopalatopharyngoplasty. *Clinical Otolaryngology & Allied Sciences* 1994;19:243-247.

283. Stuck BA, Starzak K, Verse T, et al. Complications of temperature-controlled radiofrequency volumetric tissue reduction for sleep-disordered breathing. *Acta Oto-Laryngologica* 2003;123:532-535.

284. Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. *Otolaryngology - Head & Neck Surgery* 1993;108:117-125.

285. Riley RW, Powell NB, Guilleminault C, et al. Obstructive sleep apnea surgery: risk management and complications. *Otolaryngology - Head & Neck Surgery* 1997;117:648-652.

286. Friedman M, Lin HC, Gurpinar B, et al. Minimally invasive single-stage multilevel treatment for obstructive sleep apnea/hypopnea syndrome. *Laryngoscope* 2007;117:1859-1863.

287. Benazzo M, Pagella F, Matti E, et al. Hyoidthyroidpexia as a treatment in multilevel surgery for obstructive sleep apnea. *Acta Oto-Laryngologica* 2008;128:680-684.

288. Bradshaw DA, Ruff GA, Murphy DP. An oral hypnotic medication does not improve continuous positive airway pressure compliance in men with obstructive sleep apnea. *Chest* 2006;130:1369-1376.

289. McArdle N, Devereux G, Heidarnejad H, et al. Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 1999;159:t-14.

290. Krieger J, Kurtz D, Petiau C, et al. Long-term compliance with CPAP therapy in obstructive sleep apnea patients and in snorers. *Sleep* 1996;19:Suppl-43.

291. Wild MR, Engleman HM, Douglas NJ, et al. Can psychological factors help us to determine adherence to CPAP? A prospective study. *European Respiratory Journal* 2004;24:461-465.

292. Hui DS, Choy DK, Li TS, et al. Determinants of continuous positive airway pressure compliance in a group of Chinese patients with obstructive sleep apnea. *Chest* 2001;120:170-176.

293. Izci B, McDonald JP, Coleman EL, et al. Clinical audit of subjects with snoring & sleep apnoea/hypopnoea syndrome fitted with mandibular repositioning splint. *Respiratory Medicine* 2005;99:337-346.

294. Chervin RD, Theut S, Bassetti C, et al. Compliance with nasal CPAP can be improved by simple interventions. *Sleep* 1997;20:284-289.

295. DeMolles DA, Sparrow D, Gottlieb DJ, et al. A pilot trial of a telecommunications system in sleep apnea management. *Medical Care* 2004;42:764-769.

296. Fletcher EC, Luckett RA. The effect of positive reinforcement on hourly compliance in nasal continuous positive airway pressure users with obstructive sleep apnea. *American Review of Respiratory Disease* 1991;143:t-41.

297. Hoy CJ, Vennelle M, Kingshott RN, et al. Can intensive support improve continuous positive airway pressure use in patients with the sleep apnea/hypopnea syndrome? *Am J Respir Crit Care Med* 1999;159:t-100.

298. Hui DS, Chan JK, Choy DK, et al. Effects of augmented continuous positive airway pressure education and support on compliance and outcome in a Chinese population. *Chest* 2000;117:1410-1416.

299. Jean WH, Boethel C, Phillips B, et al. CPAP compliance: video education may help! *Sleep Medicine* 2005;6:171-174.

300. Lewis KE, Bartle IE, Watkins AJ, et al. Simple interventions improve re-attendance when treating the sleep apnoea syndrome. *Sleep Medicine* 2006;7:241-247.

301. Meurice JC, Ingrand P, Portier F, et al. A multicentre trial of education strategies at CPAP induction in the treatment of severe sleep apnoea-hypopnoea syndrome. *Sleep Medicine* 2007;8:37-42.

302. Richards D, Bartlett DJ, Wong K, et al. Increased adherence to CPAP with a group cognitive behavioral treatment intervention: a randomized trial. *Sleep* 2007;30:635-640.

303. Smith CE, Dauz E, Clements F, et al. Patient education combined in a music and habit-forming intervention for adherence to continuous positive airway (CPAP) prescribed for sleep apnea. *Patient Education & Counseling* 2009;74:184-190.

304. Stepnowsky CJ, Palau JJ, Marler MR, et al. Pilot randomized trial of the effect of wireless telemonitoring on compliance and treatment efficacy in obstructive sleep apnea. *Journal of Medical Internet Research.* 2007;9:e14.

305. Taylor Y, Eliasson A, Andrada T, et al. The role of telemedicine in CPAP compliance for patients with obstructive sleep apnea syndrome. *Sleep & Breathing* 2006;10:132-138.

306. Massie CA, Hart RW. Clinical outcomes related to interface type in patients with obstructive sleep apnea/hypopnea syndrome who are using continuous positive airway pressure. *Chest* 2003;123:1112-1118.

307. Antic NA, Buchan C, Esterman A, et al. A randomized controlled trial of nurse-led care for symptomatic moderate-severe obstructive sleep apnea. *Am J Respir Crit Care Med* 2009;179:501-508.

308. Holmdahl C, Schollin IL, Alton M, et al. CPAP treatment in obstructive sleep apnoea: a randomised, controlled trial of follow-up with a focus on patient satisfaction. *Sleep Medicine* 2009;10:869-874.

309. Palmer S, Selvaraj S, Dunn C, et al. Annual review of patients with sleep apnea/hypopnea syndrome—a pragmatic randomised trial of nurse home visit versus consultant clinic review. *Sleep Medicine* 2004;5:61-65.

Acronyms and Abbreviations

ACP	American College of Physicians
AHI	apnea-hypopnea index
ASA	American Society of Anesthesiologists
AUC	area under the receiver operating characteristics curve
AutoCPAP	autotitrating continuous positive airway pressure
BMI	body mass index
CER	Comparative Effectiveness Review
CI	confidence interval
CPAP	continuous positive airway pressure
ECG	electrocardiography
ESS	Epworth Sleepiness Scale
FOSQ	Functional Outcomes Sleep Questionnaire
ICU	intensive care unit
LAUP	laser-assisted uvulopalatoplasty
MAD	mandibular advancement device
MED	Medicaid Evidence-based Decisions project
MSLT	Multiple sleep latency test
ODI	Oxygen desaturation index
OSA	obstructive sleep apnea
PICOD	population, interventions, comparators, outcomes, and study designs
PSG	polysomnography
RCT	randomized controlled trial
RDI	respiratory disturbance index
REM	rapid eye movement
RFA	radiofrequency ablation
ROC	receiver operating characteristics
SAQLI	Sleep Apnea Quality of Life Index
SF-36	Short Form (36) Health Survey
SHHS	Sleep Heart Health Study
STOP	snoring, tiredness during daytime, observed apnea, and high blood pressure
STOP-Bang	STOP with BMI, age, neck circumference, and sex variables
TEP	technical expert panel
TMJ	temporomandibular joint
TOO	task order officer
UPPP	uvulopalatopharyngoplasty

Appendix A. Literature Search Strategy

Databases: Ovid MEDLINE, MEDLINE(R) In-Process, Cochrane Controlled Trials Register (CCTR)
Last run 2/17/2010

#	Searches	Results	
1	exp Sleep Apnea Syndromes/ or exp Sleep Apnea, Obstructive/	19267	Sleep Apnea
2	exp Airway Resistance/	13219	
3	exp snoring/	2922	
4	Upper airway resistance syndrome.mp.	229	
5	Respiratory disturbance.mp.	1151	
6	obstructive sleep apn?ea.mp.	11746	
7	or/1-6	35183	
8	randomized controlled trial.pt.	561439	Comparative Studies
9	controlled clinical trial.pt.	161324	
10	randomized controlled trials/	67116	
11	Random Allocation/	88433	
12	Double-blind Method/	194574	
13	Single-Blind Method/	22535	
14	clinical trial.pt.	748992	
15	Clinical Trials.mp. or exp Clinical Trials/	282752	
16	(clinic$ adj25 trial$).tw.	234940	
17	((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw.	223366	
18	Placebos/	48648	
19	placebo$.tw.	236373	
20	random$.tw.	781376	
21	trial$.tw.	607720	
22	(randomized control trial or clinical control trial).sd.	227662	
23	(latin adj square).tw.	3635	
24	Comparative Study.tw. or Comparative Study.pt.	1644250	
25	exp Evaluation studies/	149831	
26	Follow-Up Studies/	437652	
27	Prospective Studies/	331595	
28	(control$ or prospectiv$ or volunteer$).tw.	2591469	
29	Cross-Over Studies/	45716	
30	Or/8-29	5078479	
31	exp Positive-Pressure Respiration/ or exp Continuous Positive Airway Pressure/	18518	Treatments
32	exp Intermittent Positive-Pressure Ventilation/ or exp Ventilators, Mechanical/ or exp Masks/	16688	
33	general surgery/ or neurosurgery/ or otolaryngology/ or surgery, plastic/ or thoracic surgery/	80977	
34	Surgical Procedures, Operative/	46806	
35	oral appliances.mp.	286	
36	exp Physical Therapy Modalities/ or exp Exercise Therapy/	107007	
37	positional therapy.mp.	41	
38	exp Weight Loss/	22268	
39	exp Exercise/ or exp Exercise Therapy/	78677	
40	exp Therapeutics/	2836406	
41	exp Anesthesia/ or Pre-operative screening/ or Anesthetic agents/	164281	
42	Sleep Apnea, Obstructive/th	2408	
43	*tonsillectomy/	4707	
44	or/31-43	3119682	

#	Searches	Results	
45	exp Polysomnography/	11867	Sleep Apnea Diagnostic Terms
46	exp Oximetry/	10559	
47	exp Monitoring, Physiologic/	110172	
48	pulse transit time.mp.	246	
49	exp Monitoring, Ambulatory/	18720	
50	peripheral Arterial Tonometry.mp.	62	
51	exp Questionnaires/	224876	
52	exp Diagnostic Tests, Routine/	5348	
53	exp "Laboratory Techniques and Procedures"/	1586381	
54	(Epworth or Stanford or Berlin or Pittsburgh or scale).af.	470093	
55	(friedman or surgical or staging).mp.	887171	
56	STOP-Bang.af.	2	
57	Sleep Apnea, Obstructive/di	2379	
58	or/45-57	3098114	
59	exp "sensitivity and specificity"/	320624	General Diagnostic Tests
60	exp Predictive Value of Tests/	104513	
61	exp ROC CURVE/	17069	
62	exp Mass Screening/	102939	
63	exp diagnosis/	5190511	
64	exp REPRODUCIBILITY OF RESULTS/	203415	
65	exp false negative reactions/ or false positive reactions/	30462	
66	predictive value.tw.	44461	
67	(sensitivity or specificity).tw.	582712	
68	accuracy.tw.	162713	
69	screen$.tw.	350059	
70	diagno$.tw.	1333212	
71	roc.tw.	12925	
72	reproducib$.tw.	90416	
73	(false positive or false negative).tw.	39967	
74	likelihood ratio.tw.	4450	
75	accuracy.tw.	162713	
76	di.fs.	1684695	
77	or/59-76	6907870	
78	7 and 30 and 44	6008	Group 1: Comparative studies OSA & treatment
79	limit 78 to english language [Limit not valid in CCTR; records were retained]	5354	
80	limit 79 to humans [Limit not valid in CCTR; records were retained]	4883	
81	79 and humans.sh.	4876	
82	80 or 81	4883	
83	remove duplicates from 82	**3751**	
84	7 and 44	11488	Group 2: All but comparative studies on OSA & treatment (not some study designs)
85	84 not 83	7737	
86	limit 85 to english language [Limit not valid in CCTR; records were retained]	5933	
87	limit 86 to humans [Limit not valid in CCTR; records were retained]	4943	
88	86 and humans.sh.	4942	
89	87 or 88	4943	
90	remove duplicates from 89	4596	
91	limit 90 to (addresses or bibliography or biography or case reports or comment or congresses or consensus development conference or dictionary or directory or festschrift or in vitro or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or "scientific integrity review" or twin study)	913	
92	90 not 91	**3683**	

#	Searches	Results	
93	7 and 30 and 58	6424	Group 3: Comparative studies specific to OSA diagnosis
94	limit 93 to english language [Limit not valid in CCTR; records were retained]	5775	
95	limit 94 to humans [Limit not valid in CCTR; records were retained]	5492	
96	94 and humans.sh.	5453	
97	95 or 96	5492	
98	remove duplicates from 97	4295	
99	98 not (83 or 92)	**2477**	
100	7 and 58 and 77	11451	**Group 4: Other OSA diagnosis**
101	limit 100 to english language [Limit not valid in CCTR; records were retained]	9709	
102	limit 101 to humans [Limit not valid in CCTR; records were retained]	9209	
103	101 and humans.sh.	9199	
104	102 or 103	9209	
105	104 not (83 or 92 or 99)	3623	
106	remove duplicates from 105	**3296**	
107	limit 7 to (guideline or meta analysis or practice guideline)	151	**Group 5: Systematic Reviews and Practice Guidelines on OSA**
108	7 and Cochrane Database of Systematic Reviews.jn.	25	
109	107 or 108	170	
110	remove duplicates from 109	129	
111	110 not (83 or 92 or 99 or 106)	**41**	
112	83 or 92 or 99 or 106 or 111	***13248 (+188, from 2/17/10, below)***	

	113-120 run on 2/17/2010		
113	7 and 30	12165	**Group 6: Cohort studies for KQ 2 & 6**
114	113 not 112	5912	
115	(ep or co or mo).fs.	2293973	
116	(incidence or longitudinal studies or prospective studies or survival analysis or follow-up studies or logistic models or Proportional Hazards Models or Linear Models or Regression Analysis).sh.	967098	
117	exp patient compliance/ or exp medication adherence/ or exp treatment refusal/	47071	
118	or/115-117	2893257	
119	114 and 118	1771	
120	limit 119 to (english language and humans)	**1088**	
121	112 or 120	*14524*	
122	exp Orthodontic Appliances, Removable/	3929	**Group 1a: Additional interventions**
123	Palate, Soft/su or Pharynx/su or Uvula/su or Sleep Apnea Syndromes/su	3669	
124	Sleep Apnea Syndromes/pc	188	
125	or/122-124	7766	
126	7 and 30 and 125	755	
127	126 not (112 or 119)	77	
128	limit 127 to (english language and humans)	**32**	
	Update run on 9/30/2010		
129	Medline search (all above) limited to 201001$.ed to 201009$.ed	631	
130	Cochrane searches (all above) limited to year = 2010	10	
131	Duplicates removed	**604**	

Appendix B. Excluded Studies

Studies are listed in alphabetical order by author. The reason for rejection for each study is indicated after the study.

Aboussouan LS, Golish JA, Wood BG, Mehta AC, Wood DE, Dinner DS. Dynamic pharyngoscopy in predicting outcome of uvulopalatopharyngoplasty for moderate and severe obstructive sleep apnea. Chest. 1995;107:946-951.
PMID 7705159
Surgical cohort <100/intervention

Acebo C, Watson RK, Bakos L, Thoman EB. Sleep and apnea in the elderly: reliability and validity of 24-hour recordings in the home. Sleep. 1991;14:56-64.
PMID 1811321
No intervention of interest

Akkina NC, Kumar S, Fulambaker A, Cohen M, Farooki B, Copur AS. Role of empiric treatment with autotitrating-cpap in patients suspected of having obstructive sleep apnea. Chest. 2007;132:503b-5504.
Cochrane CN-00642825
Not peer reviewed

Al-Jawder S, Bahammam A. Acceptance of C-FLEX therapy in patients with obstructive sleep apnea who refused auto-continuous positive airway pressure. Saudi Medical Journal. 2008;29:144-145.
PMID 18176692
N<10/intervention

Aloia MS, Di DL, Ilniczky N, Perlis ML, Greenblatt DW, Giles DE. Improving compliance with nasal CPAP and vigilance in older adults with OAHS. Sleep & Breathing. 2001;5:13-21.
PMID 11868136
N<10/intervention

Aloia MS, Stanchina M, Arnedt JT, Malhotra A, Millman RP. Treatment adherence and outcomes in flexible vs standard continuous positive airway pressure therapy. Chest. 2005;127:2085-2093.
PMID 15947324
Not randomized

Alonso-Fernandez A, Garcia-Rio F, Arias MA et al. Effects of CPAP on oxidative stress and nitrate efficiency in sleep apnoea: a randomised trial. Thorax. 2009;64:581-586.
PMID 19074930
No outcomes of interest

Alonso-Fernandez A, Garcia-Rio F, Arias MA et al. Obstructive sleep apnoea-hypoapnoea syndrome reversibly depresses cardiac response to exercise. European Heart Journal. 2006;27:207-215.
PMID 16267074
No outcomes of interest

Altman JS, Halpert RD, Mickelson SA, Senior BA. Effect of uvulopalatopharyngoplasty and genial and hyoid advancement on swallowing in patients with obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 1999;120:454-457.
PMID 10187932
Surgical cohort <100/intervention

Alvarez D, Hornero R, Abasolo D, del CF, Zamarron C. Nonlinear characteristics of blood oxygen saturation from nocturnal oximetry for obstructive sleep apnoea detection. Physiological Measurement. 2006;27:399-412.
PMID 16537981
In 2007 EPC Report

Alvarez D, Hornero R, Garcia M, del CF, Zamarron C. Improving diagnostic ability of blood oxygen saturation from overnight pulse oximetry in obstructive sleep apnea detection by means of central tendency measure. Artificial Intelligence in Medicine. 2007;41:13-24.
PMID 17643971
Duplicate of previous study (Previous report)

Amfilochiou A, Tsara V, Kolilekas L et al. Determinants of continuous positive airway pressure compliance in a group of Greek patients with obstructive sleep apnea. European Journal of Internal Medicine. 2009;20:645-650.
PMID 19782930
N<100 (KQ 6)

Ancoli-Israel S, Mason W, Coy TV, Stepnowsky C, Clausen JL, Dimsdale J. Evaluation of sleep disordered breathing with unattended recording: the Nightwatch System. Journal of Medical Engineering & Technology. 1997;21:10-14.
PMID 9080356
In 2007 EPC Report

Ancoli-Israel S, Palmer BW, Cooke JR et al. Cognitive effects of treating obstructive sleep apnea in Alzheimer's disease: a randomized controlled study. Journal of the American Geriatrics Society. 2008;56:2076-2081.
PMID 18795985
Population: Alzheimers

Anttalainen U, Saaresranta T, Kalleinen N, Aittokallio J, Vahlberg T, Polo O. CPAP adherence and partial upper airway obstruction during sleep. Sleep & Breathing. 2007;11:171-176.
PMID 17287956
KQ 6 Retrospective

Argekar P, Griffin V, Litaker D, Rahman M. Sleep apnea in hemodialysis patients: risk factors and effect on survival. Hemodialysis International. 2007;11:435-441.
PMID 17922741
N<500 (KQ 2)

Arias MA, Garcia-Rio F, Alonso-Fernandez A et al. CPAP decreases plasma levels of soluble tumour necrosis factor-alpha receptor 1 in obstructive sleep apnoea. European Respiratory Journal. 2008;32:1009-1015.
PMID 18508832
No outcomes of interest

Arias MA, Garcia-Rio F, Alonso-Fernandez A, Martinez I, Villamor J. Pulmonary hypertension in obstructive sleep apnoea: effects of continuous positive airway pressure: a randomized, controlled cross-over study. European Heart Journal. 2006;27:1106-1113.
PMID 16497687
Superceded by other article

Atef A, Mosleh M, Hesham M, Fathi A, Hassan M, Fawzy M. Radiofrequency vs laser in the management of mild to moderate obstructive sleep apnoea: does the number of treatment sessions matter? Journal of Laryngology & Otology. 2005;119:888-893.
PMID 16354341
Surgical cohort <100/intervention

Ayalon L, Ancoli-Israel S, Stepnowsky C et al. Adherence to continuous positive airway pressure treatment in patients with Alzheimer's disease and obstructive sleep apnea. American Journal of Geriatric Psychiatry. 2006;14:176-180.
PMID 16473983
Population: Alzheimers

Ayappa I, Norman RG, Suryadevara M, Rapoport DM. Comparison of limited monitoring using a nasal-cannula flow signal to full polysomnography in sleep-disordered breathing. Sleep. 2004;27:1171-1179.
PMID 15532212
In 2007 EPC Report

Ayas NT, Pittman S, MacDonald M, White DP. Assessment of a wrist-worn device in the detection of obstructive sleep apnea. Sleep Medicine. 2003;4:435-442.
PMID 14592285
In 2007 EPC Report

Bachour A, Virkkala JT, Maasilta PK. AutoCPAP initiation at home: optimal trial duration and cost-effectiveness. Sleep Medicine. 2007;8:704-710.
PMID 17531533
No predictors of compliance

Back L, Palomaki M, Piilonen A, Ylikoski J. Sleep-disordered breathing: radiofrequency thermal ablation is a promising new treatment possibility. Laryngoscope. 2001;111:464-471.
PMID 11224777
Surgical cohort <100/intervention

Back LJ, Liukko T, Rantanen I et al. Hypertonic saline injections to enhance the radiofrequency thermal ablation effect in the treatment of base of tongue in obstructive sleep apnoea patients: a pilot study. Acta Oto-Laryngologica. 2009;129:302-310.
PMID 18615334
Surgical cohort <100/intervention

Bagnato MC, Nery LE, Moura SM, Bittencourt LR, Tufik S. Comparison of AutoSet and polysomnography for the detection of apnea-hypopnea events. Brazilian Journal of Medical & Biological Research. 2000;33:515-519.
PMID 10775882
In 2007 EPC Report

Baisch A, Maurer JT, Hormann K. The effect of hyoid suspension in a multilevel surgery concept for obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2006;134:856-861.
PMID 16647548
Surgical cohort <100/intervention

Baldwin CM, Griffith KA, Nieto FJ, O'Connor GT, Walsleben JA, Redline S. The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. Sleep. 2001;24:96-105.
PMID 11204058
Cross-sectional

Ballester E, Solans M, Vila X et al. Evaluation of a portable respiratory recording device for detecting apnoeas and hypopnoeas in subjects from a general population. European Respiratory Journal. 2000;16:123-127.
PMID 10933097
In 2007 EPC Report

Ballon JS, Feifel D. A systematic review of modafinil: Potential clinical uses and mechanisms of action. Journal of Clinical Psychiatry. 2006;67:554-566.
PMID 16669720
Not drug of interest

Baltzan MA, Elkholi O, Wolkove N. Evidence of interrelated side effects with reduced compliance in patients treated with nasal continuous positive airway pressure. Sleep Medicine. 2009;10:198-205.
PMID 18314388
Not patient level factors (KQ 6)

Baltzan MA, Verschelden P, Al-Jahdali H, Olha AE, Kimoff RJ. Accuracy of oximetry with thermistor (OxiFlow) for diagnosis of obstructive sleep apnea and hypopnea. Sleep. 2000;23:61-69.
PMID 10678466
In 2007 EPC Report

Bao X, Nelesen RA, Loredo JS, Dimsdale JE, Ziegler MG. Blood pressure variability in obstructive sleep apnea: role of sympathetic nervous activity and effect of continuous positive airway pressure. Blood Pressure Monitoring. 2002;7:301-307.
PMID 12488649
No outcomes of interest

Bar A, Pillar G, Dvir I, Sheffy J, Schnall RP, Lavie P. Evaluation of a portable device based on peripheral arterial tone for unattended home sleep studies. Chest. 2003;123:695-703.
PMID 12628865
In 2007 EPC Report

Barakate M, Havas T. Lingual tonsillectomy: a review of 5 years experience and evolution of surgical technique. Otolaryngology - Head & Neck Surgery. 2008;139:222-227.
PMID 18656719
Surgical cohort <100/intervention

Bassiouny A, El SA, Abd El-Tawab M, Atef A. Bipolar radiofrequency treatment for snoring with mild to moderate sleep apnea: a comparative study between the radiofrequency assisted uvulopalatoplasty technique and the channeling technique. European Archives of Oto-Rhino-Laryngology. 2007;264:659-667.
PMID 17294208
Surgical cohort <100/intervention

Behbehani K, Yen FC, Lucas EA, Burk JR. A sleep laboratory evaluation of an automatic positive airway pressure system for treatment of obstructive sleep apnea. Sleep. 1998;21:485-491.
PMID 9703588
In-lab study

Bennett LS, Davies RJ, Stradling JR. Oral appliances for the management of snoring and obstructive sleep apnoea. Thorax. 1998;53:Suppl-64.
PMID 10193350
Superceded by other article

Berger G, Finkelstein Y, Stein G, Ophir D. Laser-assisted uvulopalatoplasty for snoring: medium- to long-term subjective and objective analysis. Archives of Otolaryngology -- Head & Neck Surgery. 2001;127:412-417.
PMID 11296050
Surgical cohort <100/intervention

Berger G, Stein G, Ophir D, Finkelstein Y. Is there a better way to do laser-assisted uvulopalatoplasty? Archives of Otolaryngology -- Head & Neck Surgery. 2003;129:447-453.
PMID 12707193
Surgical cohort <100/intervention

Berry RB, Hill G, Thompson L, McLaurin V. Portable monitoring and autotitration versus polysomnography for the diagnosis and treatment of sleep apnea. Sleep. 2008;31:1423-1431.
PMID 18853940
No analyses of interest

Bertolazi AN, Fagondes SC, Hoff LS, Pedro VD, Menna Barreto SS, Johns MW. Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. Jornal Brasileiro De Pneumologia: Publicacao Oficial Da Sociedade Brasileira De Pneumologia E Tisilogia. 2009;35:877-883.
PMID 19820814
No validation set analysis

Bettega G, Pepin JL, Veale D, Deschaux C, Raphael B, Levy P. Obstructive sleep apnea syndrome. fifty-one consecutive patients treated by maxillofacial surgery. American Journal of Respiratory & Critical Care Medicine. 2000;162:t-9.
PMID 10934100
Surgical cohort <100/intervention

Bittencourt LR, Lucchesi LM, Rueda AD et al. Placebo and modafinil effect on sleepiness in obstructive sleep apnea. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2008;32:552-559.
PMID 18053628
Not drug of interest

Black JE, Hirshkowitz M. Modafinil for treatment of residual excessive sleepiness in nasal continuous positive airway pressure-treated obstructive sleep apnea/hypopnea syndrome. Sleep. 2005;28:464-471.
PMID 16171291
Not drug of interest

Blanco J, Zamarron C, Abeleira Pazos MT, Lamela C, Suarez QD. Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome. Sleep & Breathing. 2005;9:20-25.
PMID 15785917
N<10/intervention

Blumen MB, Coquille F, Rocchicioli C, Mellot F, Chabolle F. Radiofrequency tongue reduction through a cervical approach: a pilot study. Laryngoscope. 2006;116:1887-1893.
PMID 17003707
Surgical cohort <100/intervention

Blumen MB, Dahan S, Fleury B, Hausser-Hauw C, Chabolle F. Radiofrequency ablation for the treatment of mild to moderate obstructive sleep apnea. Laryngoscope. 2002;112:2086-2092.
PMID 12439186
Surgical cohort <100/intervention

Boland LL, Shahar E, Iber C et al. Measures of cognitive function in persons with varying degrees of sleep-disordered breathing: the Sleep Heart Health Study. Journal of Sleep Research. 2002;11:265-272.
PMID 12220323
<1 y f/up (KQ 2)

Bolitschek J, Rieder A, Broinger G, Rosenberger A, Kunze M, Aigner K. N-CPAP rejecters--a specific group of noncompliant patients with obstructive sleep apnea syndrome. Wiener Klinische Wochenschrift. 2001;113:245-248.
PMID 11383384
Not RCT (CPAP vs control)

Bonsignore G, Marrone O, Macaluso C, Salvaggio A, Stallone A, Bellia V. Validation of oximetry as a screening test for obstructive sleep apnoea syndrome. European Respiratory Journal - Supplement. 1990;11:542s-544s.
PMID 2278624
In 2007 EPC Report

Boot H, Poublon RM, Van WR et al. Uvulopalatopharyngoplasty for the obstructive sleep apnoea syndrome: value of polysomnography, Mueller manoeuvre and cephalometry in predicting surgical outcome. Clinical Otolaryngology & Allied Sciences. 1997;22:504-510.
PMID 9466058
Surgical cohort <100/intervention

Boot H, Van WR, Poublon RM, Bogaard JM, Schmitz PI, Van der Meche FG. Long-term results of uvulopalatopharyngoplasty for obstructive sleep apnea syndrome. Laryngoscope. 2000;110:t-75.
PMID 10718440
Surgical cohort <100/intervention

Borgel J, Sanner BM, Bittlinsky A et al. Obstructive sleep apnoea and its therapy influence high-density lipoprotein cholesterol serum levels. European Respiratory Journal. 2006;27:121-127.
PMID 16387944
No outcomes of interest

Borgel J, Sanner BM, Keskin F et al. Obstructive sleep apnea and blood pressure. Interaction between the blood pressure-lowering effects of positive airway pressure therapy and antihypertensive drugs. American Journal of Hypertension. 2004;17:t-7.
PMID 15607612
N<500 (KQ 2)

Boudewyns A, De CW, Willemen M, Wagemans M, De BW, Van de Heyning PH. Influence of uvulopalatopharyngoplasty on alpha-EEG arousals in nonapnoeic snorers. European Respiratory Journal. 1997;10:129-132.
PMID 9032504
Surgical cohort <100/intervention

Bowden MT, Kezirian EJ, Utley D, Goode RL. Outcomes of hyoid suspension for the treatment of obstructive sleep apnea. Archives of Otolaryngology -- Head & Neck Surgery. 2005;131:440-445.
PMID 15897424
Surgical cohort <100/intervention

Bradley PA, Mortimore IL, Douglas NJ. Comparison of polysomnography with ResCare Autoset in the diagnosis of the sleep apnoea/hypopnoea syndrome. Thorax. 1995;50:1201-1203.
PMID 8553279
In 2007 EPC Report

Brin YS, Reuveni H, Greenberg S, Tal A, Tarasiuk A. Determinants affecting initiation of continuous positive airway pressure treatment. Israel Medical Association Journal: Imaj. 2005;7:13-18.
PMID 15658139
<1 mo (KQ 6)

Brostrom A, Stromberg A, Martensson J, Ulander M, Harder L, Svanborg E. Association of Type D personality to perceived side effects and adherence in CPAP-treated patients with OSAS. Journal of Sleep Research. 2007;16:439-447.
PMID 18036091
KQ 6 Retrospective

Brown DJ, Kerr P, Kryger M. Radiofrequency tissue reduction of the palate in patients with moderate sleep-disordered breathing. Journal of Otolaryngology. 2001;30:193-198.
PMID 11771028
Surgical cohort <100/intervention

Brownell LG, Perez-Padilla R, West P, Kryger MH. The role of protriptyline in obstructive sleep apnea. Bulletin europeen de physiopathologie respiratoire. 1983;19:621-624.
PMID 6360257
N<10/intervention

Brownell LG, West P, Sweatman P, Acres JC, Kryger MH. Protriptyline in obstructive sleep apnea: a double-blind trial. New England Journal of Medicine. 1982;307:1037-1042.
PMID 6750396
N<10/intervention

Bruckert E, Duchene E, Bonnefont-Rousselot D et al. Proof of concept study: does fenofibrate have a role in sleep apnoea syndrome? Current Medical Research & Opinion. 2010;26:1185-1192.
PMID 20297950
No intervention of interest

Buchner NJ, Sanner BM, Borgel J, Rump LC. Continuous positive airway pressure treatment of mild to moderate obstructive sleep apnea reduces cardiovascular risk. American Journal of Respiratory & Critical Care Medicine. 2007;176:1274-1280.
PMID 17673692
Not randomized

Budhiraja R, Parthasarathy S, Drake CL et al. Early CPAP use identifies subsequent adherence to CPAP therapy. Sleep. 2007;30:320-324.
PMID 17425228
Not multivariate (KQ 6, CPAP)

Busaba NY. Same-stage nasal and palatopharyngeal surgery for obstructive sleep apnea: is it safe? Otolaryngology - Head & Neck Surgery. 2002;126:399-403.
PMID 11997780
Surgical cohort <100/intervention

Cahali MB. Lateral pharyngoplasty: a new treatment for obstructive sleep apnea hypopnea syndrome. Laryngoscope. 2003;113:1961-1968.
PMID 14603056
Surgical cohort <100/intervention

Cahali MB, Formigoni GG, Gebrim EM, Miziara ID. Lateral pharyngoplasty versus uvulopalatopharyngoplasty: a clinical, polysomnographic and computed tomography measurement comparison. Sleep. 2004;27:942-950.
PMID 15453553
Surgical cohort <100/intervention

Caldarelli DD, Cartwright R, Lilie JK. Severity of sleep apnea as a predictor of successful treatment by palatopharyngoplasty. Laryngoscope. 1986;96:t-7.
PMID 3747695
Surgical cohort <100/intervention

Caldarelli DD, Cartwright RD, Lilie JK. Obstructive sleep apnea: variations in surgical management. Laryngoscope. 1985;95:t-3.
PMID 4033329
Surgical cohort <100/intervention

Calleja JM, Esnaola S, Rubio R, Duran J. Comparison of a cardiorespiratory device versus polysomnography for diagnosis of sleep apnoea. European Respiratory Journal. 2002;20:1505-1510.
PMID 12503711
In 2007 EPC Report

Canisius S, Kesper K, Jerrentrup L et al. C-Flex technology: effects on breathing parameters and inspiratory flow limitation. Respiration. 2009;78:168-176.
PMID 19122451
In-lab study

Carmona BC, Capote GF, Botebol BG, Garcia LP, Sanchez AA, Castillo GJ. Assessment of excessive day-time sleepiness in professional drivers with suspected obstructive sleep apnea syndrome. Archivos de bronconeumologia. 2000;36:436-440.
Cochrane CN-00361710
No analyses of interest

Carrasco O, Montserrat JM, Lloberes P et al. Visual and different automatic scoring profiles of respiratory variables in the diagnosis of sleep apnoea-hypopnoea syndrome. European Respiratory Journal. 1996;9:125-130.
PMID 8834345
In 2007 EPC Report

Carratu P, Karageorgiou G, Bonfitto P et al. Long-term evaluation of mental fatigue by Maastricht Questionnaire in patients with OSAS treated with CPAP. Monaldi Archives for Chest Disease. 2007;67:6-9.
PMID 17564278
Not RCT (CPAP vs control)

Casale M, Rinaldi V, Bressi F et al. A suitable test for identifying high risk adult patients of moderate-severe obstructive sleep apnea syndrome. European Review for Medical & Pharmacological Sciences. 2008;12:275-280.
PMID 18727462
No validation set analysis

Chabolle F, Wagner I, Blumen MB, Sequert C, Fleury B, De DT. Tongue base reduction with hyoepiglottoplasty: a treatment for severe obstructive sleep apnea. Laryngoscope. 1999;109:1273-1280.
PMID 10443833
Surgical cohort <100/intervention

Chasens ER, Pack AI, Maislin G, Dinges DF, Weaver TE. Claustrophobia and adherence to CPAP treatment. Western Journal of Nursing Research. 2005;27:307-321.
PMID 15781905
Not multivariate (KQ 6, CPAP)

Chiner E, Signes-Costa J, Arriero JM, Marco J, Fuentes I, Sergado A. Nocturnal oximetry for the diagnosis of the sleep apnoea hypopnoea syndrome: a method to reduce the number of polysomnographies? Thorax. 1999;54:968-971.
PMID 10525553
In 2007 EPC Report

Chisholm E, Kotecha B. Oropharyngeal surgery for obstructive sleep apnoea in CPAP failures. European Archives of Oto-Rhino-Laryngology. 2007;264:51-55.
PMID 16944237
Surgical cohort <100/intervention

Choi JH, Kim EJ, Choi J et al. The effect of adenotonsillectomy on changes of position during sleep in pediatric obstructive sleep apnea syndrome. American Journal of Rhinology & Allergy. 2009;23:e56-e58.
PMID 19793418
Pediatric

Choi S, Bennett LS, Mullins R, Davies RJ, Stradling JR. Which derivative from overnight oximetry best predicts symptomatic response to nasal continuous positive airway pressure in patients with obstructive sleep apnoea? Respiratory Medicine. 2000;94:895-899.
PMID 11001083
Not RCT

Choi S, Mullins R, Crosby JH, Davies RJO, Stradling JR. Is (re)titration of nasal continuous positive airway pressure for obstructive sleep apnoea necessary? Sleep Medicine. 2001;2:431-435.
Cochrane CN-00425066
Superceded by other article

Chong MS, Ayalon L, Marler M et al. Continuous positive airway pressure reduces subjective daytime sleepiness in patients with mild to moderate Alzheimer's disease with sleep disordered breathing. Journal of the American Geriatrics Society. 2006;54:777-781.
PMID 16696743
Population: Alzheimers

Cillo JE, Jr., Finn R, Dasheiff RM. Combined open rhinoplasty with spreader grafts and laser-assisted uvuloplasty for sleep-disordered breathing: long-term subjective outcomes. Journal of Oral & Maxillofacial Surgery. 2006;64:1241-1247.
PMID 16860217
Surgical cohort <100/intervention

Cincik H, Cekin E, Cetin B, Gungor A, Poyrazoglu E. Comparison of uvulopalatopharyngoplasty, laser-assisted uvulopalatoplasty and cautery-assisted uvulopalatoplasty in the treatment of primary snoring. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 2006;68:149-155.
PMID 16462150
Surgical cohort <100/intervention

Cistulli PA, Palmisano RG, Poole MD. Treatment of obstructive sleep apnea syndrome by rapid maxillary expansion. Sleep. 1998;21:831-835.
PMID 9871945
Surgical cohort <100/intervention

Clark GT, Arand D, Chung E, Tong D. Effect of anterior mandibular positioning on obstructive sleep apnea. American Review of Respiratory Disease. 1993;147:624-629.
PMID 8442597
Not comparative

Coleman JA, Jr. Laser-assisted uvulopalatoplasty: long-term results with a treatment for snoring. Ear, Nose, & Throat Journal. 1998;77:22-24.
PMID 9473829
Surgical cohort <100/intervention

Collen J, Lettieri C, Kelly W, Roop S. Clinical and polysomnographic predictors of short-term continuous positive airway pressure compliance. Chest. 2009;135:704-709.
PMID 19017888
KQ 6 Retrospective

Collop NA. Home sleep testing: it is not about the test. Chest. 2010;138:245-246.
PMID 20682524
Not original study

Conradt R, Hochban W, Brandenburg U, Heitmann J, Peter JH. Long-term follow-up after surgical treatment of obstructive sleep apnoea by maxillomandibular advancement. European Respiratory Journal. 1997;10:123-128.
PMID 9032503
Surgical cohort <100/intervention

Conway W, Fujita S, Zorick F et al. Uvulopalatopharyngoplasty. One-year followup. Chest. 1985;88:385-387.
PMID 4028849
Surgical cohort <100/intervention

Craig S, Pepperell JC, Kohler M, Crosthwaite N, Davies RJ, Stradling JR. Continuous positive airway pressure treatment for obstructive sleep apnoea reduces resting heart rate but does not affect dysrhythmias: a randomised controlled trial. Journal of Sleep Research. 2009;18:329-336.
PMID 19549077
No outcomes of interest

Croft CB, Golding-Wood DG. Uses and complications of uvulopalatopharyngoplasty. Journal of Laryngology & Otology. 1990;104:871-875.
PMID 2266310
Surgical cohort <100/intervention

Cross MD, Vennelle M, Engleman HM et al. Comparison of CPAP titration at home or the sleep laboratory in the sleep apnea hypopnea syndrome. Sleep. 2006;29:1451-1455.
PMID 17162992
No intervention of interest

Dattilo DJ, Drooger SA. Outcome assessment of patients undergoing maxillofacial procedures for the treatment of sleep apnea: comparison of subjective and objective results. Journal of Oral & Maxillofacial Surgery. 2004;62:164-168.
PMID 14762748
Surgical cohort <100/intervention

Davis JA, Fine ED, Maniglia AJ. Uvulopalatopharyngoplasty for obstructive sleep apnea in adults: clinical correlation with polysomnographic results. Ear, Nose, & Throat Journal. 1993;72:63-66.
PMID 8444131
Surgical cohort <100/intervention

de Almeida FR, Lowe AA, Tsuiki S et al. Long-term compliance and side effects of oral appliances used for the treatment of snoring and obstructive sleep apnea syndrome. Journal of Clinical Sleep Medicine. 2005;1:143-152.
PMID 17561628
KQ 6 Retrospective

Defaye P, Pepin JL, Poezevara Y et al. Automatic recognition of abnormal respiratory events during sleep by a pacemaker transthoracic impedance sensor. Journal of Cardiovascular Electrophysiology. 2004;15:1034-1040.
PMID 15363076
Not diagnostic test of interest

del Campo F, Hornero R, Zamarron C, Abasolo DE, Alvarez D. Oxygen saturation regularity analysis in the diagnosis of obstructive sleep apnea. Artificial Intelligence in Medicine. 2006;37:111-118.
PMID 16386411
In 2007 EPC Report

Delides A, Viskos A. Fractal quantitative endoscopic evaluation of the upper airway in patients with obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2010;143:85-89.
PMID 20620624
Not diagnostic test of interest

den Herder C, Kox D, van Tinteren H, de Vries N. Bipolar radiofrequency induced thermotherapy of the tongue base: Its complications, acceptance and effectiveness under local anesthesia. European Archives of Oto-Rhino-Laryngology. 2006;263:1031-1040.
PMID 16862445
Surgical cohort <100/intervention

den Herder C, van Tinteren H, de Vries N. Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome.[reprint in Ned Tijdschr Geneeskd. 2006 Jan 28;150(4):198-203; PMID: 16471236]. Laryngoscope. 2005;115:740-745.
PMID 15805891
Surgical cohort <100/intervention

Dickson RI, Mintz DR. One-stage laser-assisted uvulopalatoplasty. Journal of Otolaryngology. 1996;25:155-161.
PMID 8783079
Surgical cohort No complication data

Dimsdale JE, Loredo JS, Profant J. Effect of continuous positive airway pressure on blood pressure : a placebo trial. Hypertension. 2000;35:t-7.
PMID 10642289
No outcomes of interest

Ding J, Nieto FJ, Beauchamp NJ, Jr. et al. Sleep-disordered breathing and white matter disease in the brainstem in older adults. Sleep. 2004;27:474-479.
PMID 15164901
No outcomes of interest

Dinges DF, Weaver TE. Effects of modafinil on sustained attention performance and quality of life in OSA patients with residual sleepiness while being treated with nCPAP. Sleep Medicine. 2003;4:393-402.
PMID 14592280
Not drug of interest

Dingli K, Coleman EL, Vennelle M et al. Evaluation of a portable device for diagnosing the sleep apnoea/hypopnoea syndrome. European Respiratory Journal. 2003;21:253-259.
PMID 12608438
In 2007 EPC Report

Djupesland G, Schrader H, Lyberg T, Refsum H, Lilleas F, Godtlibsen OB. Palatopharyngoglossoplasty in the treatment of patients with obstructive sleep apnea syndrome. Acta Oto-Laryngologica Supplement. 1992;492:50-54.
PMID 1632251
Surgical cohort <100/intervention

Dort LC, Hussein J. Snoring and obstructive sleep apnea: compliance with oral appliance therapy. Journal of Otolaryngology. 2004;33:172-176.
PMID 15841995
N<100 (KQ 6)

d'Ortho MP, Grillier-Lanoir V, Levy P et al. Constant vs. automatic continuous positive airway pressure therapy: home evaluation. Chest. 2000;118:1010-1017.
PMID 11035671
Not RCT (CPAP vs CPAP)

Douglas NJ, Thomas S, Jan MA. Clinical value of polysomnography. Lancet. 1992;339:347-350.
PMID 1346422
In 2007 EPC Report

Drigo R, Fontana M, Coin A, Ferraresso A, Enzo E, Zambotto FM. APAP titration in patients with mild to moderate OSAS and periodic limb movement syndrome. Monaldi Archives for Chest Disease. 2006;65:196-203.
PMID 17393664
In-lab study

Dunlevy TM, Karakla DW. Uvulopalatopharyngoplasty: the Naval Medical Center, Portsmouth, experience. American Journal of Otolaryngology. 1998;19:174-177.
PMID 9617929
Surgical cohort <100/intervention

Elasfour A, Miyazaki S, Itasaka Y, Yamakawa K, Ishikawa K, Togawa K. Evaluation of uvulopalatopharyngoplasty in treatment of obstructive sleep apnea syndrome. Acta Oto-Laryngologica Supplement. 1998;537:52-56.
PMID 9870650
Surgical cohort <100/intervention

Elbaz M, Roue GM, Lofaso F, Quera Salva MA. Utility of actigraphy in the diagnosis of obstructive sleep apnea. Sleep. 2002;25:527-531.
PMID 12150319
Not diagnostic test of interest

Elshaug AG, Moss JR, Southcott AM, Hiller JE. An analysis of the evidence-practice continuum: is surgery for obstructive sleep apnoea contraindicated? Journal of Evaluation in Clinical Practice. 2007;13:3-9.
PMID 17286716
Surgical cohort <100/intervention

el-Solh AA, Mador MJ, Ten-Brock E, Shucard DW, Abul-Khoudoud M, Grant BJ. Validity of neural network in sleep apnea. Sleep. 1999;22:105-111.
PMID 9989371
No validation set analysis

Emsellem HA, Corson WA, Rappaport BA, Hackett S, Smith LG, Hausfeld JN. Verification of sleep apnea using a portable sleep apnea screening device. Southern Medical Journal. 1990;83:748-752.
PMID 2371595
In 2007 EPC Report

Engelke WG, Mendoza M, Repetto G. Preliminary radiographic observations of the tongue-repositioning manoeuvre. European Journal of Orthodontics. 2006;28:618-623.
PMID 17101703
Surgical cohort <100/intervention

Engleman HM, Asgari-Jirhandeh N, McLeod AL, Ramsay CF, Deary IJ, Douglas NJ. Self-reported use of CPAP and benefits of CPAP therapy: a patient survey. Chest. 1996;109:1470-1476.
PMID 8769496
No predictors of compliance

Engleman HM, Cheshire KE, Deary IJ, Douglas NJ. Daytime sleepiness, cognitive performance and mood after continuous positive airway pressure for the sleep apnoea/hypopnoea syndrome. Thorax. 1993;48:911-914.
PMID 8236074
Not randomized

Epstein LJ, Dorlac GR. Cost-effectiveness analysis of nocturnal oximetry as a method of screening for sleep apnea-hypopnea syndrome. Chest. 1998;113:97-103.
PMID 9440575
In 2007 EPC Report

Esnaola S, Duran J, Infante-Rivard C, Rubio R, Fernandez A. Diagnostic accuracy of a portable recording device (MESAM IV) in suspected obstructive sleep apnoea. European Respiratory Journal. 1996;9:2597-2605.
PMID 8980975
In 2007 EPC Report

Eun YG, Kim SW, Kwon KH, Byun JY, Lee KH. Single-session radiofrequency tongue base reduction combined with uvulopalatopharyngoplasty for obstructive sleep apnea syndrome. European Archives of Oto-Rhino-Laryngology. 2008;265:1495-1500.
PMID 18443811
Surgical cohort <100/intervention

Eun YG, Kwon KH, Shin SY, Lee KH, Byun JY, Kim SW. Multilevel surgery in patients with rapid eye movement-related obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2009;140:536-541.
PMID 19328343
Surgical cohort <100/intervention

Eveloff SE, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a Herbst mandibular advancement device in obstructive sleep apnea. American Journal of Respiratory & Critical Care Medicine. 1994;149:t-9.
PMID 8143054
Not comparative

Faber CE, Hilberg O, Grymer L. Flextube reflectometry for level diagnosis in patients with obstructive sleep apnoea and snoring. Rhinology. 2002;40:122-128.
PMID 12357711
No reference standard (overnight PSG)

Farney RJ, Walker LE, Jensen RL, Walker JM. Ear oximetry to detect apnea and differentiate rapid eye movement (REM) and non-REM (NREM) sleep. Screening for the sleep apnea syndrome. Chest. 1986;89:533-539.
PMID 3956278
In 2007 EPC Report

Ferguson KA, Ono T, Lowe AA, al-Majed S, Love LL, Fleetham JA. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. Thorax. 1997;52:362-368.
PMID 9196520
Superceded by other article

Ferland A, Poirier P, Series F. Sibutramine versus continuous positive airway pressure in obese obstructive sleep apnoea patients. European Respiratory Journal. 2009;34:694-701.
PMID 19357147
Not randomized

Fernandez-Julian E, Munoz N, Achiques MT, Garcia-Perez MA, Orts M, Marco J. Randomized study comparing two tongue base surgeries for moderate to severe obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2009;140:917-923.
PMID 19467415
Surgical cohort <100/intervention

Fibbi A, Ameli F, Brocchetti F, Mignosi S, Cabano ME, Semino L. Tongue base suspension and radiofrequency volume reduction: a comparison between 2 techniques for the treatment of sleep-disordered breathing. American Journal of Otolaryngology. 2009;30:401-406.
PMID 19880029
Surgical cohort <100/intervention

Ficker JH, Clarenbach CF, Neukirchner C et al. Auto-CPAP therapy based on the forced oscillation technique. Biomedizinische Technik. 2003;48:68-72.
PMID 12701337
In-lab study

Ficker JH, Fuchs FS, Wiest GH, Asshoff G, Schmelzer AH, Hahn EG. An auto-continuous positive airway pressure device controlled exclusively by the forced oscillation technique. European Respiratory Journal. 2000;16:914-920.
PMID 11153592
In-lab study

Ficker JH, Wiest GH, Lehnert G, Wiest B, Hahn EG. Evaluation of an auto-CPAP device for treatment of obstructive sleep apnoea. Thorax. 1998;53:643-648.
PMID 9828849
In-lab study

Ficker JH, Wiest GH, Wilpert J, Fuchs FS, Hahn EG. Evaluation of a portable recording device (Somnocheck) for use in patients with suspected obstructive sleep apnoea. Respiration. 2001;68:307-312.
PMID 11416253
In 2007 EPC Report

Fietze I, Glos M, Rottig J, Witt C. Automated analysis of data is inferior to visual analysis of ambulatory sleep apnea monitoring. Respiration. 2002;69:235-241.
PMID 12097767
In 2007 EPC Report

Fietze I, Quispe-Bravo S, Hansch T, Rottig J, Baumann G, Witt C. Arousals and sleep stages in patients with obstructive sleep apnoea syndrome: Changes under nCPAP treatment. Journal of Sleep Research. 1997;6:128-133.
PMID 9377532
In-lab study

Findley L, Smith C, Hooper J, Dineen M, Suratt PM. Treatment with nasal CPAP decreases automobile accidents in patients with sleep apnea. American Journal of Respiratory & Critical Care Medicine. 2000;161:t-9.
PMID 10712333
Not RCT (CPAP vs control)

Finkelstein Y, Shapiro-Feinberg M, Stein G, Ophir D. Uvulopalatopharyngoplasty vs laser-assisted uvulopalatoplasty. Anatomical considerations. Archives of Otolaryngology -- Head & Neck Surgery. 1997;123:265-276.
PMID 9076231
Surgical cohort No complication data

Finkelstein Y, Stein G, Ophir D, Berger R, Berger G. Laser-assisted uvulopalatoplasty for the management of obstructive sleep apnea: myths and facts. Archives of Otolaryngology -- Head & Neck Surgery. 2002;128:429-434.
PMID 11926920
Surgical cohort <100/intervention

Fischer Y, Khan M, Mann WJ. Multilevel temperature-controlled radiofrequency therapy of soft palate, base of tongue, and tonsils in adults with obstructive sleep apnea. Laryngoscope. 2003;113:1786-1791.
PMID 14520107
Surgical cohort <100/intervention

Fitzpatrick MF, Alloway CE, Wakeford TM, MacLean AW, Munt PW, Day AG. Can patients with obstructive sleep apnea titrate their own continuous positive airway pressure? American Journal of Respiratory & Critical Care Medicine. 2003;167:716-722.
PMID 12598214
Not comparison of different PAP types

Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. American Journal of Respiratory & Critical Care Medicine. 1994;150:t-85.
PMID 7952553
No validation set analysis

Fleury B, Rakotonanahary D, Hausser-Hauw C, Lebeau B, Guilleminault C. A laboratory validation study of the diagnostic mode of the Autoset system for sleep-related respiratory disorders. [erratum appears in Sleep 1996 Sep;19(7):601]. Sleep. 1996;19:502-505.
PMID 8865509
In 2007 EPC Report

Foltan R, Hoffmannova J, Pretl M, Donev F, Vlk M. Genioglossus advancement and hyoid myotomy in treating obstructive sleep apnoea syndrome - A follow-up study. Journal of Cranio-Maxillo-Facial Surgery. 2007;35:246-251.
PMID 17761431
Surgical cohort <100/intervention

Fong SY, Ho CK, Wing YK. Comparing MSLT and ESS in the measurement of excessive daytime sleepiness in obstructive sleep apnoea syndrome. Journal of Psychosomatic Research. 2005;58:55-60.
PMID 15771871
No analyses of interest

Fransson AM, Isacsson G, Leissner LC, Nasman AB, Alton MK. Treatment of snoring and obstructive sleep apnea with a mandibular protruding device: an open-label study. Sleep & Breathing. 2001;5:23-33.
PMID 11868137
Not RCT (Oral vs Cx)

Freedman RR, Roehrs TA. Sleep disturbance in menopause. Menopause. 2007;14:826-829.
PMID 17486023
Not diagnostic test

Friedman M, Duggal P, Joseph NJ. Revision uvulopalatoplasty by Z-palatoplasty. Otolaryngology - Head & Neck Surgery. 2007;136:638-643.
PMID 17418265
Surgical cohort <100/intervention

Friedman M, Ibrahim H, Bass L. Clinical staging for sleep-disordered breathing. Otolaryngology - Head & Neck Surgery. 2002;127:13-21.
PMID 12161725
Surgical cohort No complication data

Friedman M, Ibrahim H, Joseph NJ. Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope. 2004;114:454-459.
PMID 15091218
Superceded by other article

Friedman M, Ibrahim H, Lowenthal S, Ramakrishnan V, Joseph NJ. Uvulopalatoplasty (UP2): a modified technique for selected patients. Laryngoscope. 2004;114:441-449.
PMID 15091216
Surgical cohort <100/intervention

Friedman M, Ibrahim HZ, Vidyasagar R, Pomeranz J, Joseph NJ. Z-palatoplasty (ZPP): a technique for patients without tonsils. Otolaryngology - Head & Neck Surgery. 2004;131:89-100.
PMID 15243563
Surgical cohort <100/intervention

Friedman M, Schalch P, Joseph NJ. Palatal stiffening after failed uvulopalatopharyngoplasty with the Pillar Implant System. Laryngoscope. 2006;116:1956-1961.
PMID 17075397
Surgical cohort <100/intervention

Friedman M, Soans R, Gurpinar B, Lin HC, Joseph N. Evaluation of submucosal minimally invasive lingual excision technique for treatment of obstructive sleep apnea/hypopnea syndrome. Otolaryngology - Head & Neck Surgery. 2008;139:378-384.
PMID 18722216
Surgical cohort <100/intervention

Friedman M, Soans R, Joseph N, Kakodkar S, Friedman J. The effect of multilevel upper airway surgery on continuous positive airway pressure therapy in obstructive sleep apnea/hypopnea syndrome. Laryngoscope. 2009;119:193-196.
PMID 19117285
Surgical cohort <100/intervention

Friedman M, Tanyeri H, La RM et al. Clinical predictors of obstructive sleep apnea. Laryngoscope. 1999;109:1901-1907.
PMID 10591345
No validation set analysis

Friedman M, Vidyasagar R, Bliznikas D, Joseph N. Does severity of obstructive sleep apnea/hypopnea syndrome predict uvulopalatopharyngoplasty outcome? Laryngoscope. 2005;115:2109-2113.
PMID 16369152
Superceded by other article

Friedman M, Vidyasagar R, Bliznikas D, Joseph NJ. Patient selection and efficacy of pillar implant technique for treatment of snoring and obstructive sleep apnea/hypopnea syndrome. Otolaryngology - Head & Neck Surgery. 2006;134:187-196.
PMID 16455363
Surgical cohort <100/intervention

Fry JM, DiPhillipo MA, Curran K, Goldberg R, Baran AS. Full polysomnography in the home. Sleep. 1998;21:635-642.
PMID 9779523
In 2007 EPC Report

Fujita S, Conway W, Zorick F, Roth T. Surgical correction of anatomic azbnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngology - Head & Neck Surgery. 1981;89:923-934.
PMID 6801592
Surgical cohort <100/intervention

Fujita S, Conway WA, Zorick FJ et al. Evaluation of the effectiveness of uvulopalatopharyngoplasty. Laryngoscope. 1985;95:70-74.
PMID 3965833
Surgical cohort <100/intervention

Fujita S, Woodson BT, Clark JL, Wittig R. Laser midline glossectomy as a treatment for obstructive sleep apnea. Laryngoscope. 1991;101:805-809.
PMID 1865726
Surgical cohort <100/intervention

Furuta H, Kaneda R, Kosaka K, Arai H, Sano J, Koshino Y. Epworth Sleepiness Scale and sleep studies in patients with obstructive sleep apnea syndrome. Psychiatry & Clinical Neurosciences. 1999;53:301-302.
PMID 10459718
No analyses of interest

Gagnadoux F, Pelletier-Fleury N, Philippe C, Rakotonanahary D, Fleury B. Home unattended vs hospital telemonitored polysomnography in suspected obstructive sleep apnea syndrome: a randomized crossover trial. Chest. 2002;121:753-758.
PMID 11888956
In 2007 EPC Report

Galetke W, Randerath WJ, Stieglitz S et al. Comparison of manual titration and automatic titration based on forced oscillation technique, flow and snoring in obstructive sleep apnea. Sleep Medicine. 2009;10:337-343.
PMID 18650127
Not comparison of different PAP types

Gali B, Whalen FX, Schroeder DR, Gay PC, Plevak DJ. Identification of patients at risk for postoperative respiratory complications using a preoperative obstructive sleep apnea screening tool and postanesthesia care assessment. Anesthesiology. 2009;110:869-877.
PMID 19293694
No analyses of interest

Garza CA, Pellikka PA, Somers VK et al. Structural and functional changes in left and right ventricles after major weight loss following bariatric surgery for morbid obesity. American Journal of Cardiology. 2010;105:550-556.
PMID 20152253
No outcomes of interestGauthier L, Laberge L, Beaudry M, Laforte M, Rompre PH, Lavigne GJ. Efficacy of two mandibular advancement appliances in the management of snoring and mild-moderate sleep apnea: a cross-over randomized study. Sleep Medicine. 2009;10:329-336.
PMID 18583187
Not comparison of different MAD types

Ghazal A, Sorichter S, Jonas I, Rose EC. A randomized prospective long-term study of two oral appliances for sleep apnoea treatment. Journal of Sleep Research. 2009;18:321-328.
PMID 19493297
Not comparison of different MAD types

Gilman MP, Floras JS, Usui K, Kaneko Y, Leung RS, Bradley TD. Continuous positive airway pressure increases heart rate variability in heart failure patients with obstructive sleep apnoea. Clinical Science. 2008;114:243-249.
PMID 17824846
N<10/intervention

Gislason T, Lindholm CE, Almqvist M et al. Uvulopalatopharyngoplasty in the sleep apnea syndrome. Predictors of results. Archives of Otolaryngology -- Head & Neck Surgery. 1988;114:45-51.
PMID 3334818
Surgical cohort <100/intervention

Gislason T, Tammivaara R. Airway obstruction, obesity and CO2 ventilatory responsiveness in the sleep apnea syndrome. Upsala Journal of Medical Sciences. 1992;97:141-148.
PMID 1471313
Surgical cohort <100/intervention

Goessler UR, Hein G, Verse T, Stuck BA, Hormann K, Maurer JT. Soft palate implants as a minimally invasive treatment for mild to moderate obstructive sleep apnea. Acta Oto-Laryngologica. 2007;127:527-531.
PMID 17453480
Surgical cohort <100/intervention

Goh YH, Lim KA. Modified maxillomandibular advancement for the treatment of obstructive sleep apnea: a preliminary report. Laryngoscope. 2003;113:1577-1582.
PMID 12972937
Surgical cohort <100/intervention

Goh YH, Mark I, Fee WE, Jr. Quality of life 17 to 20 years after uvulopalatopharyngoplasty. Laryngoscope. 2007;117:503-506.
PMID 17334312
Surgical cohort <100/intervention

Golpe R, Jimenez A, Carpizo R. Home sleep studies in the assessment of sleep apnea/hypopnea syndrome. Chest. 2002;122:1156-1161.
PMID 12377836
In 2007 EPC Report

Golpe R, Jimenez A, Carpizo R, Cifrian JM. Utility of home oximetry as a screening test for patients with moderate to severe symptoms of obstructive sleep apnea. Sleep. 1999;22:932-937.
PMID 10566911
In 2007 EPC Report

Grontved AM, Karup P. Complaints and satisfaction after uvulopalatopharyngoplasty. Acta Oto-Laryngologica Supplement. 2000;543:190-192.
PMID 10909017
Surgical cohort <100/intervention

Gugger M. Comparison of ResMed AutoSet (version 3.03) with polysomnography in the diagnosis of the sleep apnoea/hypopnoea syndrome. European Respiratory Journal. 1997;10:587-591.
PMID 9072989
In 2007 EPC Report

Gugger M, Mathis J, Bassetti C. Accuracy of an intelligent CPAP machine with in-built diagnostic abilities in detecting apnoeas: a comparison with polysomnography. Thorax. 1995;50:1199-1201.
PMID 8553278
In 2007 EPC Report

Guilleminault C, Hayes B. Naloxone, theophylline, bromocriptine, and obstructive sleep apnea. Negative results. Bulletin europeen de physiopathologie respiratoire. 1983;19:632-634.
PMID 6360259
Not drug of interest

Guilleminault C, Hayes B, Smith L, Simmons FB. Palatopharyngoplasty and obstructive sleep apnea syndrome. Bulletin europeen de physiopathologie respiratoire. 1983;19:595-599.
PMID 6652266
Surgical cohort <100/intervention

Gyulay S, Gould D, Sawyer B, Pond D, Mant A, Saunders N. Evaluation of a microprocessor-based portable home monitoring system to measure breathing during sleep. Sleep. 1987;10:130-142.
PMID 3589326
In 2007 EPC Report

Gyulay S, Olson LG, Hensley MJ, King MT, Allen KM, Saunders NA. A comparison of clinical assessment and home oximetry in the diagnosis of obstructive sleep apnea. American Review of Respiratory Disease. 1993;147:50-53.
PMID 8420431
In 2007 EPC Report

Hagert B, Wahren LK, Wikblad K, Odkvist L. Patients' and cohabitants' reports on snoring and daytime sleepiness, 1-8 years after surgical treatment of snoring. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 1999;61:19-24.
PMID 9892865
Surgical cohort No complication data

Han F, Song W, Li J, Zhang L, Dong X, He Q. Influence of UPPP surgery on tolerance to subsequent continuous positive airway pressure in patients with OSAHS. Sleep & Breathing. 2006;10:37-42.
PMID 16432757
Surgical cohort <100/intervention

Hanada T, Furuta S, Tateyama T, Uchizono A, Seki D, Ohyama M. Laser-assisted uvulopalatoplasty with Nd:YAG laser for sleep disorders. Laryngoscope. 1996;106:t-3.
PMID 8948617
Surgical cohort <100/intervention

Haraldsson PO, Bredbacka S. Laser-uvulopalatoplasty (LUPP) under local anesthesia: effective, safe and comfortable. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 1996;58:99-104.
PMID 8736055
Surgical cohort <100/intervention

Haraldsson PO, Carenfelt C, Knutsson E, Persson HE, Rinder J. Preliminary report: validity of symptom analysis and daytime polysomnography in diagnosis of sleep apnea. Sleep. 1992;15:261-263.
PMID 1621028
Not diagnostic test of interest

Haraldsson PO, Carenfelt C, Lysdahl M, Tornros J. Long-term effect of uvulopalatopharyngoplasty on driving performance. Archives of Otolaryngology -- Head & Neck Surgery. 1995;121:90-94.
PMID 7803027
Surgical cohort <100/intervention

Hattori C, Nishimura T, Kawakatsu K, Hayakawa M, Suzuki K. Comparison of surgery and nasal continuous positive airway pressure treatment for obstructive sleep apnea syndrome. Acta Oto-Laryngologica Supplement (550):46-50, 2003. 2003;46-50.
PMID 12737342
Surgical cohort <100/intervention

Hayakawa M, Nishimura T, Suzuki K et al. Comparison of the state of sleep in patients with sleep-disordered breathing before and after surgical treatment. Acta Oto-Laryngologica Supplement (550):51-5, 2003. 2003;51-55.
PMID 12737343
Surgical cohort <100/intervention

He J, Kryger MH, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest. 1988;94:9-14.
PMID 3289839
N<500 (KQ 2)

Hedner J, Kraiczi H, Peker Y, Murphy P. Reduction of sleep-disordered breathing after physostigmine. American Journal of Respiratory & Critical Care Medicine. 2003;168:1246-1251.
PMID 12958052
In-lab study

Hedner J, Pillar G, Pittman SD, Zou D, Grote L, White DP. A novel adaptive wrist actigraphy algorithm for sleep-wake assessment in sleep apnea patients. Sleep. 2004;27:1560-1566.
PMID 15683148
In 2007 EPC Report

Hendler BH, Costello BJ, Silverstein K, Yen D, Goldberg A. A protocol for uvulopalatopharyngoplasty, mortised genioplasty, and maxillomandibular advancement in patients with obstructive sleep apnea: an analysis of 40 cases. Journal of Oral & Maxillofacial Surgery. 2001;59:892-897.
PMID 11474445
Surgical cohort <100/intervention

Herer B, Roche N, Carton M, Roig C, Poujol V, Huchon G. Value of clinical, functional, and oximetric data for the prediction of obstructive sleep apnea in obese patients. Chest. 1999;116:1537-1544.
PMID 10593773
In 2007 EPC Report

Herford AS, Finn R. Single-stage CO2 laser assisted uvuloplasty for treatment of snoring and mild obstructive sleep apnoea. Journal of Cranio-Maxillo-Facial Surgery. 2000;28:213-216.
PMID 11110152
Surgical cohort <100/intervention

Hermida RC, Zamarron C, Ayala DE, Calvo C. Effect of continuous positive airway pressure on ambulatory blood pressure in patients with obstructive sleep apnoea. Blood Pressure Monitoring. 2004;9:193-202.
PMID 15311146
Not RCT (CPAP vs control)

Hertegonne KB, Rombaut B, Houtmeyers P, Van MG, Pevernagie DA. Titration efficacy of two auto-adjustable continuous positive airway pressure devices using different flow limitation-based algorithms. Respiration. 2008;75:48-54.
PMID 17541262
Not comparison of different PAP types

Hertegonne KB, Volna J, Portier S, De PR, Van MG, Pevernagie DA. Titration procedures for nasal CPAP: automatic CPAP or prediction formula? Sleep Medicine. 2008;9:732-738.
PMID 17921064
In-lab study

Hessel NS, de VN. Results of uvulopalatopharyngoplasty after diagnostic workup with polysomnography and sleep endoscopy: a report of 136 snoring patients. European Archives of Oto-Rhino-Laryngology. 2003;260:91-95.
PMID 12582786
Surgical cohort <100/intervention

Hessel NS, Vries N. Increase of the apnoea-hypopnoea index after uvulopalatopharyngoplasty: analysis of failure. Clinical Otolaryngology & Allied Sciences. 2004;29:682-685.
PMID 15533159
Surgical cohort <100/intervention

Hester TO, Phillips B, Archer SM. Surgery for obstructive sleep apnea: effects on sleep, breathing, and oxygenation. Southern Medical Journal. 1995;88:907-910.
PMID 7660205
Surgical cohort <100/intervention

Hira HS. Obstructive sleep apnea syndrome: evaluation of subcritical continuous positive airway pressure. Journal of the Association of Physicians of India. 1998;46:796-797.
PMID 11229251
Not RCT (CPAP vs control)

Hirshkowitz M, Black JE, Wesnes K, Niebler G, Arora S, Roth T. Adjunct armodafinil improves wakefulness and memory in obstructive sleep apnea/hypopnea syndrome. Respiratory Medicine. 2007;101:616-627.
PMID 16908126
Not drug of interest

Hla KM, Young T, Finn L, Peppard PE, Szklo-Coxe M, Stubbs M. Longitudinal association of sleep-disordered breathing and nondipping of nocturnal blood pressure in the Wisconsin Sleep Cohort Study. Sleep. 2008;31:795-800.
PMID 18548823
N<500 (KQ 2)

Hochban W, Brandenburg U, Peter JH. Surgical treatment of obstructive sleep apnea by maxillomandibular advancement. Sleep. 1994;17:624-629.
PMID 7846461
Surgical cohort <100/intervention

Hochban W, Conradt R, Brandenburg U, Heitmann J, Peter JH. Surgical maxillofacial treatment of obstructive sleep apnea. Plastic & Reconstructive Surgery. 627;99:619-626.
PMID 9047179
Surgical cohort <100/intervention

Hoekema A. Efficacy and comorbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: a systematic review and preliminary results of a randomized trial. Sleep & Breathing. 2006;10:102-103.
PMID 16408240
Short communication

Hoekema A, Stegenga B, Bakker M et al. Simulated driving in obstructive sleep apnoea-hypopnoea; effects of oral appliances and continuous positive airway pressure. Sleep & Breathing. 2007;11:129-138.
PMID 17245607
N<10/intervention

Hoekema A, Voors AA, Wijkstra PJ et al. Effects of oral appliances and CPAP on the left ventricle and natriuretic peptides. International Journal of Cardiology. 2008;128:232-239.
PMID 17727981
Duplicate of previous study

Hofer SO, Dhar BK, Robinson PH, Goorhuis-Brouwer SM, Nicolai JP. A 10-year review of perioperative complications in pharyngeal flap surgery. Plastic & Reconstructive Surgery. 1398;110:1393-1397.
PMID 12409754
Not OSA

Hoffstein V, Szalai JP. Predictive value of clinical features in diagnosing obstructive sleep apnea. Sleep. 1993;16:118-122.
PMID 8446830
No validation set analysis

Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. American Review of Respiratory Disease. 1992;145:t-5.
PMID 1554212
N<100 (KQ 6)

Hollandt JH, Mahlerwein M. Nasal breathing and continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA). Sleep & Breathing. 2003;7:87-94.
PMID 12861488
Not multivariate (KQ 6, CPAP)

Hsiao HR, Wang PC, Cheng WN et al. Survey of short-term patient satisfaction after surgery for obstructive sleep apnea. Chang Gung Medical Journal. 2009;32:212-219.
PMID 19403012
Surgical cohort <100/intervention

Hsu CY, Vennelle M, Li HY, Engleman HM, Dennis MS, Douglas NJ. Sleep-disordered breathing after stroke: a randomised controlled trial of continuous positive airway pressure. Journal of Neurology, Neurosurgery & Psychiatry. 2006;77:1143-1149.
PMID 16772358
Population: stroke

Huang TW, Cheng PW. Microdebrider-assisted extended uvulopalatoplasty: an effective and safe technique for selected patients with obstructive sleep apnea syndrome. Archives of Otolaryngology -- Head & Neck Surgery. 2008;134:141-145.
PMID 18283155
Surgical cohort <100/intervention

Hultcrantz E, Johansson K, Bengtson H. The effect of uvulopalatopharyngoplasty without tonsillectomy using local anaesthesia: a prospective long-term follow-up. Journal of Laryngology & Otology. 1999;113:542-547.
PMID 10605585
Surgical cohort <100/intervention

Iber C, Redline S, Kaplan Gilpin AM et al. Polysomnography performed in the unattended home versus the attended laboratory setting--Sleep Heart Health Study methodology. Sleep. 2004;27:536-540.
PMID 15164911
In 2007 EPC Report

Ibrahim LH, Jacono FJ, Patel SR et al. Heritability of abnormalities in cardiopulmonary coupling in sleep apnea: use of an electrocardiogram-based technique. Sleep. 2010;33:643-646.
PMID 20469806
Not diagnostic test of interest

Insalaco G, Romano S, Marrone O, Salvaggio A, Bonsignore G. A new method of negative expiratory pressure test analysis detecting upper airway flow limitation to reveal obstructive sleep apnea. Chest. 2005;128:2159-2165.
PMID 16236869
No analyses of interest

Ip MS, Lam B, Ng MM, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. American Journal of Respiratory & Critical Care Medicine. 2002;165:670-676.
PMID 11874812
N<500 (KQ 2)

Issa FG, Morrison D, Hadjuk E, Iyer A, Feroah T, Remmers JE. Digital monitoring of sleep-disordered breathing using snoring sound and arterial oxygen saturation. American Review of Respiratory Disease. 1993;148:t-9.
PMID 8214920
In 2007 EPC Report

Itasaka Y, Miyazaki S, Tanaka T, Ishikawa K. Uvulopalatopharyngoplasty for obstructive sleep-related breathing disorders: one-year follow up. Psychiatry & Clinical Neurosciences. 2001;55:261-262.
PMID 11422867
Surgical cohort <100/intervention

Jacobowitz O. Palatal and tongue base surgery for surgical treatment of obstructive sleep apnea: a prospective study. Otolaryngology - Head & Neck Surgery. 2006;135:258-264.
PMID 16890079
Surgical cohort <100/intervention

Janson C, Gislason T, Bengtsson H et al. Long-term follow-up of patients with obstructive sleep apnea treated with uvulopalatopharyngoplasty. Archives of Otolaryngology -- Head & Neck Surgery. 1997;123:257-262.
PMID 9076230
Surgical cohort <100/intervention

Jenkinson C, Davies RJ, Mullins R, Stradling JR. Long-term benefits in self-reported health status of nasal continuous positive airway pressure therapy for obstructive sleep apnoea. Qjm. 2001;94:95-99.
PMID 11181985
Not RCT

Jobin V, Mayer P, Bellemare F. Predictive value of automated oxygen saturation analysis for the diagnosis and treatment of obstructive sleep apnoea in a home-based setting. Thorax. 2007;62:422-427.
PMID 17251319
No reference standard (overnight PSG)

Johal A. Health-related quality of life in patients with sleep-disordered breathing: effect of mandibular advancement appliances. Journal of Prosthetic Dentistry. 2006;96:298-302.
PMID 17052475
Not RCT (Oral vs Cx)

Kamami YV. Outpatient treatment of sleep apnea syndrome with CO2 laser: laser-assisted UPPP. Journal of Otolaryngology. 1994;23:395-398.
PMID 7897767
Surgical cohort <100/intervention

Kao YH, Shnayder Y, Lee KC. The efficacy of anatomically based multilevel surgery for obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2003;129:327-335.
PMID 14574285
Surgical cohort <100/intervention

Karason K, Lindroos AK, Stenlof K, Sjostrom L. Relief of cardiorespiratory symptoms and increased physical activity after surgically induced weight loss: results from the Swedish Obese Subjects study. Archives of Internal Medicine. 2000;160:1797-1802.
PMID 10871973
Superceded by later article

Katz I, Zamel N, Slutsky AS, Rebuck AS, Hoffstein V. An evaluation of flow-volume curves as a screening test for obstructive sleep apnea. Chest. 1990;98:337-340.
PMID 2198137
In 2007 EPC Report

Kawakatsu K, Nishimura T. Long-term surgical follow-up of sleep apnea syndrome. Acta Oto-Laryngologica Supplement (550):11-21, 2003. 2003;11-21.
PMID 12737335
Surgical cohort No complication data

Keenan SP, Anderson B, Wiggs B, Ryan CF, Fleetham JA. The predictive accuracy of home oximetry in patients with suspected obstructive sleep apnea. Sleep. 1993;16:Suppl-4.
PMID 8178005
No validation set analysis

Kern RC, Kutler DI, Reid KJ, Conley DB, Herzon GD, Zee P. Laser-assisted uvulopalatoplasty and tonsillectomy for the management of obstructive sleep apnea syndrome. Laryngoscope. 2003;113:1175-1181.
PMID 12838016
Surgical cohort <100/intervention

Khan A, Ramar K, Maddirala S, Friedman O, Pallanch JF, Olson EJ. Uvulopalatopharyngoplasty in the management of obstructive sleep apnea: the mayo clinic experience. Mayo Clinic Proceedings. 2009;84:795-800.
PMID 19720777
Surgical cohort <100/intervention

Khan W, Gleason R, Strome M, Regestein Q. Clinical features as diagnostic guides in obstructive sleep apnea. Comprehensive Psychiatry. 1995;36:46-52.
PMID 7705087
Retrospective

Khayat RN, Abraham WT, Patt B, Pu M, Jarjoura D. In-hospital treatment of obstructive sleep apnea during decompensation of heart failure. Chest. 2009;136:991-997.
PMID 19567491
No outcomes of interest

Kiely JL, Delahunty C, Matthews S, McNicholas WT. Comparison of a limited computerized diagnostic system (ResCare Autoset) with polysomnography in the diagnosis of obstructive sleep apnoea syndrome. European Respiratory Journal. 1996;9:2360-2364.
PMID 8947086
In 2007 EPC Report

Kiely JL, Murphy M, McNicholas WT. Subjective efficacy of nasal CPAP therapy in obstructive sleep apnoea syndrome: a prospective controlled study. European Respiratory Journal. 1999;13:1086-1090.
PMID 10414408
Not RCT (CPAP vs control)

Kim JA, Lee JJ, Jung HH. Predictive factors of immediate postoperative complications after uvulopalatopharyngoplasty. Laryngoscope. 2005;115:1837-1840.
PMID 16222206
Surgical cohort <100/intervention

Kim ST, Choi JH, Jeon HG, Cha HE, Kim DY, Chung YS. Polysomnographic effects of nasal surgery for snoring and obstructive sleep apnea. Acta Oto-Laryngologica. 2004;124:297-300.
PMID 15141758
Surgical cohort <100/intervention

Kingshott RN, Douglas NJ. The effect of in-laboratory polysomnography on sleep and objective daytime sleepiness. Sleep. 2000;23:1109-1113.
PMID 11145325
Not diagnostic test

Kingshott RN, Vennelle M, Coleman EL, Engleman HM, Mackay TW, Douglas NJ. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of residual excessive daytime sleepiness in the sleep apnea/hypopnea syndrome. American Journal of Respiratory & Critical Care Medicine. 2001;163:918-923.
PMID 11282766
Not drug of interest

Kita H, Ohi M, Chin K et al. Effects of nasal continuous positive airway pressure therapy on respiratory parameters of upper airway patency in patients with obstructive sleep apnea syndrome. Chest. 1998;114:691-696.
PMID 9743152
In-lab study

Kohler M, Pepperell JC, Casadei B et al. CPAP and measures of cardiovascular risk in males with OSAS. European Respiratory Journal. 2008;32:1488-1496.
PMID 18653654
Superceded by other article

Konermann M, Sanner BM, Vyleta M et al. Use of conventional and self-adjusting nasal continuous positive airway pressure for treatment of severe obstructive sleep apnea syndrome: a comparative study. Chest. 1998;113:714-718.
PMID 9515848
Not RCT (CPAP vs CPAP)

Koziej M, Cieslicki JK, Gorzelak K, Sliwinski P, Zielinski J. Hand-scoring of MESAM 4 recordings is more accurate than automatic analysis in screening for obstructive sleep apnoea. European Respiratory Journal. 1994;7:1771-1775.
PMID 7828683
In 2007 EPC Report

Krahn AD, Yee R, Erickson MK et al. Physiologic pacing in patients with obstructive sleep apnea: a prospective, randomized crossover trial. Journal of the American College of Cardiology. 2006;47:379-383.
PMID 16412864
In-lab study

Krakow B, Melendrez D, Ferreira E et al. Prevalence of insomnia symptoms in patients with sleep-disordered breathing. Chest. 2001;120:1923-1929.
PMID 11742923
N<500 (KQ 2)

Krekmanov L, Andersson L, Ringqvist M et al. Anterior-inferior mandibular osteotomy in treatment of obstructive sleep apnea syndrome. International Journal of Adult Orthodontics & Orthognathic Surgery. 1998;13:289-298.
PMID 10196816
Surgical cohort <100/intervention

Krieger J. Long-term compliance with nasal continuous positive airway pressure (CPAP) in obstructive sleep apnea patients and nonapneic snorers. Sleep. 1992;15:Suppl-6.
PMID 1470808
Not multivariate (KQ 6, CPAP)

Krieger J, Meslier N, Lebrun T et al. Accidents in obstructive sleep apnea patients treated with nasal continuous positive airway pressure: a prospective study. The Working Group ANTADIR, Paris and CRESGE, Lille, France. Association Nationale de Traitement a Domicile des Insuffisants Respiratoires. Chest. 1997;112:1561-1566.
PMID 9404754
Not multivariate (with AHI, KQ 2)

Krystal AD, Harsh JR, Yang RR, Rippon GA, Lankford DA. A double-blind, placebo-controlled study of armodafinil for excessive sleepiness in patients with treated obstructive sleep apnea and comorbid depression. Journal of Clinical Psychiatry. 2010;71:32-40.
PMID 20051221
No intervention of interest

Kuhnel TS, Schurr C, Wagner B, Geisler P. Morphological changes of the posterior airway space after tongue base suspension. Laryngoscope. 2005;115:475-480.
PMID 15744161
Surgical cohort <100/intervention

Kushida CA, Nichols DA, Quan SF et al. The Apnea Positive Pressure Long-term Efficacy Study (APPLES): rationale, design, methods, and procedures. Journal of Clinical Sleep Medicine. 2006;2:288-300.
PMID 17561541
Not RCT

Langin T, Pepin JL, Pendlebury S et al. Upper airway changes in snorers and mild sleep apnea sufferers after uvulopalatopharyngoplasty (UPPP). Chest. 1998;113:1595-1603.
PMID 9631799
Surgical cohort <100/intervention

Larsson H, Carlsson-Nordlander B, Svanborg E. Long-time follow-up after UPPP for obstructive sleep apnea syndrome. Results of sleep apnea recordings and subjective evaluation 6 months and 2 years after surgery. Acta Oto-Laryngologica. 1991;111:582-590.
PMID 1887784
Surgical cohort <100/intervention

Larsson LH, Carlsson-Nordlander B, Svanborg E. Four-year follow-up after uvulopalatopharyngoplasty in 50 unselected patients with obstructive sleep apnea syndrome. Laryngoscope. 1994;104:t-8.
PMID 7968165
Surgical cohort <100/intervention

Lauretano AM, Khosla RK, Richardson G et al. Efficacy of laser-assisted uvulopalatoplasty. Lasers in Surgery & Medicine. 1997;21:109-116.
PMID 9261787
Surgical cohort No complication data

Lavie P, Lavie L. Unexpected survival advantage in elderly people with moderate sleep apnoea. Journal of Sleep Research. 2009;18:397-403.
PMID 19663998
No intervention of interest

Lawton HM, Battagel JM, Kotecha B. A comparison of the Twin Block and Herbst mandibular advancement splints in the treatment of patients with obstructive sleep apnoea: a prospective study. European Journal of Orthodontics. 2005;27:82-90.
PMID 15743867
Not comparison of different MAD types

Lee CH, Shin HW, Han DH et al. The implication of sleep position in the evaluation of surgical outcomes in obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2009;140:531-535.
PMID 19328342
Surgical cohort <100/intervention

Lee NR, Givens CD, Jr., Wilson J, Robins RB. Staged surgical treatment of obstructive sleep apnea syndrome: a review of 35 patients. Journal of Oral & Maxillofacial Surgery. 1999;57:382-385.
PMID 10199488
Surgical cohort <100/intervention

Leng PH, Mosharraf-Hossain AK, Chan YH, Tan WC. The clinical predictors of hypertension and sleepiness in an Asian population with sleep-disordered breathing. Annals of the Academy of Medicine, Singapore. 2006;35:6-10.
PMID 16470267
N<500 (KQ 2)

Levy P, Pepin JL, Deschaux-Blanc C, Paramelle B, Brambilla C. Accuracy of oximetry for detection of respiratory disturbances in sleep apnea syndrome. Chest. 1996;109:395-399.
PMID 8620711
In 2007 EPC Report

Lewis MR, Ducic Y. Genioglossus muscle advancement with the genioglossus bone advancement technique for base of tongue obstruction. Journal of Otolaryngology. 2003;32:168-173.
PMID 12921135
Surgical cohort <100/intervention

Li HY, Chen NH, Lee LA, Shu YH, Fang TJ, Wang PC. Use of morphological indicators to predict outcomes of palatopharyngeal surgery in patients with obstructive sleep apnea. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 2004;66:119-123.
PMID 15316231
Surgical cohort No complication data

Li HY, Chen NH, Shu YH, Wang PC. Changes in quality of life and respiratory disturbance after extended uvulopalatal flap surgery in patients with obstructive sleep apnea. Archives of Otolaryngology -- Head & Neck Surgery. 2004;130:195-200.
PMID 14967750
Surgical cohort <100/intervention

Li HY, Huang YS, Chen NH, Fang TJ, Liu CY, Wang PC. Mood improvement after surgery for obstructive sleep apnea. Laryngoscope. 2004;114:1098-1102.
PMID 15179220
Surgical cohort <100/intervention

Li HY, Lee LA. Relocation pharyngoplasty for obstructive sleep apnea. Laryngoscope. 2009;119:2472-2477.
PMID 19688851
Surgical cohort <100/intervention

Li HY, Li KK, Chen NH, Wang CJ, Liao YF, Wang PC. Three-dimensional computed tomography and polysomnography findings after extended uvulopalatal flap surgery for obstructive sleep apnea. American Journal of Otolaryngology. 2005;26:7-11.
PMID 15635574
Surgical cohort <100/intervention

Li HY, Li KK, Chen NH, Wang PC. Modified uvulopalatopharyngoplasty: The extended uvulopalatal flap. American Journal of Otolaryngology. 2003;24:311-316.
PMID 13130443
Surgical cohort <100/intervention

Li HY, Lin Y, Chen NH, Lee LA, Fang TJ, Wang PC. Improvement in quality of life after nasal surgery alone for patients with obstructive sleep apnea and nasal obstruction. Archives of Otolaryngology -- Head & Neck Surgery. 2008;134:429-433.
PMID 18427011
Surgical cohort <100/intervention

Li HY, Wang PC, Hsu CY, Chen NH, Lee LA, Fang TJ. Same-stage palatopharyngeal and hypopharyngeal surgery for severe obstructive sleep apnea. Acta Oto-Laryngologica. 2004;124:820-826.
PMID 15370567
Surgical cohort <100/intervention

Li HY, Wang PC, Hsu CY, Lee SW, Chen NH, Liu SA. Combined nasal-palatopharyngeal surgery for obstructive sleep apnea: simultaneous or staged? Acta Oto-Laryngologica. 2005;125:298-303.
PMID 15966701
Surgical cohort <100/intervention

Li HY, Wang PC, Lee LA, Chen NH, Fang TJ. Prediction of uvulopalatopharyngoplasty outcome: anatomy-based staging system versus severity-based staging system. Sleep. 2006;29:1537-1541.
PMID 17252884
Surgical cohort No complication data

Li KK, Guilleminault C, Riley RW, Powell NB. Obstructive sleep apnea and maxillomandibular advancement: an assessment of airway changes using radiographic and nasopharyngoscopic examinations. Journal of Oral & Maxillofacial Surgery. 2002;60:526-530.
PMID 11988930
Surgical cohort <100/intervention

Li KK, Powell NB, Riley RW, Guilleminault C. Temperature-controlled radiofrequency tongue base reduction for sleep-disordered breathing: Long-term outcomes. Otolaryngology - Head & Neck Surgery. 2002;127:230-234.
PMID 12297815
Surgical cohort <100/intervention

Li KK, Powell NB, Riley RW, Zonato A, Gervacio L, Guilleminault C. Morbidly obese patients with severe obstructive sleep apnea: is airway reconstructive surgery a viable treatment option? Laryngoscope. 2000;110:982-987.
PMID 10852518
Surgical cohort <100/intervention

Li KK, Riley RW, Powell NB, Gervacio L, Troell RJ, Guilleminault C. Obstructive sleep apnea surgery: patient perspective and polysomnographic results. Otolaryngology - Head & Neck Surgery. 2000;123:572-575.
PMID 11077343
Surgical cohort <100/intervention

Li KK, Riley RW, Powell NB, Guilleminault C. Maxillomandibular advancement for persistent obstructive sleep apnea after phase I surgery in patients without maxillomandibular deficiency. Laryngoscope. 2000;110:t-8.
PMID 11037825
Surgical cohort <100/intervention

Li KK, Riley RW, Powell NB, Troell RJ. Obstructive sleep apnea surgery: genioglossus advancement revisited. Journal of Oral & Maxillofacial Surgery. 2001;59:1181-1184.
PMID 11573177
Surgical cohort <100/intervention

Liesching TN, Carlisle C, Marte A, Bonitati A, Millman RP. Evaluation of the accuracy of SNAP technology sleep sonography in detecting obstructive sleep apnea in adults compared to standard polysomnography. Chest. 2004;125:886-891.
PMID 15006946
Retrospective

Lin CC, Chang KC, Lee KS. Effects of treatment by laser-assisted uvuloplasty on sleep energy expenditure in obstructive sleep apnea patients. Metabolism: Clinical & Experimental. 2002;51:622-627.
PMID 11979396
Surgical cohort <100/intervention

Lin CC, Chang KC, Lee KS, Wu KM, Chou CS, Lin CK. Effect of treatment by laser-assisted uvulopalatoplasty on cardiopulmonary exercise test in obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2005;133:55-61.
PMID 16025053
Surgical cohort <100/intervention

Lin CC, Lee KS, Chang KC, Wu KM, Chou CS. Effect of laser-assisted uvulopalatoplasty on oral airway resistance during wakefulness in obstructive sleep apnea syndrome. European Archives of Oto-Rhino-Laryngology. 2006;263:241-247.
PMID 16163511
Surgical cohort <100/intervention

Lin CC, Lee KS, Wang YP et al. Effect of uvulopalatopharyngoplasty on work of breathing during wakefulness in obstructive sleep apnea syndrome. Annals of Otology, Rhinology & Laryngology. 2007;116:271-277.
PMID 17491526
Surgical cohort <100/intervention

Lin CL, Yeh C, Yen CW, Hsu WH, Hang LW. Comparison of the indices of oxyhemoglobin saturation by pulse oximetry in obstructive sleep apnea hypopnea syndrome. Chest. 2009;135:86-93.
PMID 18689584
Not Dx'ic study (already diagnosed w/OSA)

Liu SA, Li HY, Tsai WC, Chang KM. Associated factors to predict outcomes of uvulopharyngopalatoplasty plus genioglossal advancement for obstructive sleep apnea. Laryngoscope. 2005;115:2046-2050.
PMID 16319622
Surgical cohort <100/intervention

Lloberes P, Marti S, Sampol G et al. Predictive factors of quality-of-life improvement and continuous positive airway pressure use in patients with sleep apnea-hypopnea syndrome: study at 1 year. Chest. 2004;126:1241-1247.
PMID 15486388
Not multivariate (KQ 6, CPAP)

Lloberes P, Montserrat JM, Ascaso A et al. Comparison of partially attended night time respiratory recordings and full polysomnography in patients with suspected sleep apnoea/hypopnoea syndrome. Thorax. 1996;51:1043-1047.
PMID 8977607
In 2007 EPC Report

Lloberes P, Sampol G, Levy G et al. Influence of setting on unattended respiratory monitoring in the sleep apnoea/hypopnoea syndrome. European Respiratory Journal. 2001;18:530-534.
PMID 11589351
In 2007 EPC Report

Lu SJ, Chang SY, Shiao GM. Comparison between short-term and long-term post-operative evaluation of sleep apnoea after uvulopalatopharyngoplasty. Journal of Laryngology & Otology. 1995;109:308-312.
PMID 7782686
Surgical cohort <100/intervention

Ludwig A. Results of electromyostimulation therapy in obstructive sleep apnea. Artificial Organs. 2008;32:655-658.
PMID 18782139
No outcomes of interest

Lye KW, Waite PD, Meara D, Wang D. Quality of life evaluation of maxillomandibular advancement surgery for treatment of obstructive sleep apnea. Journal of Oral & Maxillofacial Surgery. 2008;66:968-972.
PMID 18423288
Surgical cohort <100/intervention

Lysdahl M, Haraldsson PO. Uvulopalatopharyngoplasty versus laser uvulopalatoplasty: prospective long-term follow-up of self-reported symptoms. Acta Oto-Laryngologica. 2002;122:752-757.
PMID 12484653
Surgical cohort <100/intervention

Macaluso RA, Reams C, Gibson WS, Vrabec DP, Matragrano A. Uvulopalatopharyngoplasty: postoperative management and evaluation of results. Annals of Otology, Rhinology & Laryngology. 1989;98:t-7.
PMID 2751209
Surgical cohort <100/intervention

Magalang UJ, Dmochowski J, Veeramachaneni S et al. Prediction of the apnea-hypopnea index from overnight pulse oximetry. Chest. 2003;124:1694-1701.
PMID 14605037
In 2007 EPC Report

Magnan A, Philip-Joet F, Rey M, Reynaud M, Porri F, Arnaud A. End-tidal CO2 analysis in sleep apnea syndrome. Conditions for use. Chest. 1993;103:129-131.
PMID 8417866
Not diagnostic test of interest

Maisel RH, Antonelli PJ, Iber C et al. Uvulopalatopharyngoplasty for obstructive sleep apnea: a community's experience. Laryngoscope. 1992;102:604-607.
PMID 1602908
Surgical cohort <100/intervention

Maislin G, Pack AI, Kribbs NB et al. A survey screen for prediction of apnea. Sleep. 1995;18:158-166.
PMID 7610311
No validation set analysis

Malbois M, Giusti V, Suter M, Pellaton C, Vodoz JF, Heinzer R. Oximetry alone versus portable polygraphy for sleep apnea screening before bariatric surgery. Obesity Surgery. 2010;20:326-331.
PMID 20052560
Retrospective

Malow BA, Foldvary-Schaefer N, Vaughn BV et al. Treating obstructive sleep apnea in adults with epilepsy: a randomized pilot trial. Neurology. 2008;71:572-577.
PMID 18711110
Population: Epilepsy

Man GC, Kang BV. Validation of a portable sleep apnea monitoring device. Chest. 1995;108:388-393.
PMID 7634872
In 2007 EPC Report

Marcos JV, Hornero R, Alvarez D, del CF, Lopez M. Applying neural network classifiers in the diagnosis of the obstructive sleep apnea syndrome from nocturnal pulse oximetric recordings. Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine & Biology Society. 2007;2007:5174-5177.
PMID 18003173
Duplicate of previous study

Marcos JV, Hornero R, Alvarez D, Nabney IT, del CF, Zamarron C. The classification of oximetry signals using Bayesian neural networks to assist in the detection of obstructive sleep apnoea syndrome. Physiological Measurement. 2010;31:375-394.
PMID 20130342
Not diagnostic test of interest

Marklund M. Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. American Journal of Orthodontics & Dentofacial Orthopedics. 2006;129:214-221.
PMID 16473713
KQ 6 Retrospective

Marklund M, Franklin KA. Long-term effects of mandibular repositioning appliances on symptoms of sleep apnoea. Journal of Sleep Research. 2007;16:414-420.
PMID 18036087
No predictors of compliance

Marklund M, Stenlund H, Franklin KA. Mandibular advancement devices in 630 men and women with obstructive sleep apnea and snoring: tolerability and predictors of treatment success. Chest. 2004;125:1270-1278.
PMID 15078734
No predictors of compliance

Marrone O, Salvaggio A, Insalaco G, Bonsignore MR, Bonsignore G. Evaluation of the POLYMESAM system in the diagnosis of obstructive sleep apnea syndrome. Monaldi Archives for Chest Disease. 2001;56:486-490.
PMID 11980277
In 2007 EPC Report

Marshall NS, Neill AM, Campbell AJ. Randomised trial of compliance with flexible (C-Flex) and standard continuous positive airway pressure for severe obstructive sleep apnea. Sleep & Breathing. 2008;12:393-396.
PMID 18516638
N<10/intervention

Masdeu MJ, Ayappa I, Hwang D, Mooney AM, Rapoport DM. Impact of clinical assessment on use of data from unattended limited monitoring as opposed to full-in lab PSG in sleep disordered breathing. Journal of Clinical Sleep Medicine. 2010;6:51-58.
PMID 20191938
Duplicate of previous study

Martinho FL, Tangerina RP, Moura SM, Gregorio LC, Tufik S, Bittencourt LR. Systematic head and neck physical examination as a predictor of obstructive sleep apnea in class III obese patients. Brazilian Journal of Medical & Biological Research. 2008;41:1093-1097.
PMID 19148371
No analyses of interest

Mayer P, Meurice JC, Philip-Joet F et al. Simultaneous laboratory-based comparison of ResMed Autoset with polysomnography in the diagnosis of sleep apnoea/hypopnoea syndrome. European Respiratory Journal. 1998;12:770-775.
PMID 9817143
In 2007 EPC Report

McArdle N, Kingshott R, Engleman HM, Mackay TW, Douglas NJ. Partners of patients with sleep apnoea/hypopnoea syndrome: effect of CPAP treatment on sleep quality and quality of life. Thorax. 2001;56:513-518.
PMID 11413348
No outcomes of interest

McArdle N, Singh B, Murphy M et al. Continuous positive airway pressure titration for obstructive sleep apnoea: automatic versus manual titration. Thorax. 2010;65:606-611.
PMID 20627917
Titration study

McFadyen TA, Espie CA, McArdle N, Douglas NJ, Engleman HM. Controlled, prospective trial of psychosocial function before and after continuous positive airway pressure therapy. European Respiratory Journal. 2001;18:996-1002.
PMID 11829108
Not randomized

McGuirt WF, Jr., Johnson JT, Sanders MH. Previous tonsillectomy as prognostic indicator for success of uvulopalatopharyngoplasty. Laryngoscope. 1995;105:1253-1255.
PMID 7475885
Surgical cohort <100/intervention

McLean HA, Urton AM, Driver HS et al. Effect of treating severe nasal obstruction on the severity of obstructive sleep apnoea. European Respiratory Journal. 2005;25:521-527.
PMID 15738298
In-lab study

Mehra R, Principe-Rodriguez K, Kirchner HL, Strohl KP. Sleep apnea in acute coronary syndrome: high prevalence but low impact on 6-month outcome. Sleep Medicine. 2006;7:521-528.
PMID 16931151
No predictors of compliance

Mendez MO, Bianchi AM, Matteucci M, Cerutti S, Penzel T. Sleep apnea screening by autoregressive models from a single ECG lead. IEEE Transactions on Biomedical Engineering. 2009;56:2838-2850.
PMID 19709961
Not diagnostic test of interest

Mendez MO, Corthout J, Van HS et al. Automatic screening of obstructive sleep apnea from the ECG based on empirical mode decomposition and wavelet analysis. Physiological Measurement. 2010;31:273-289.
PMID 20086277
Not diagnostic test of interest

Meston N, Davies RJ, Mullins R, Jenkinson C, Wass JA, Stradling JR. Endocrine effects of nasal continuous positive airway pressure in male patients with obstructive sleep apnoea. Journal of Internal Medicine. 2003;254:447-454.
PMID 14535966
No outcomes of interest

Meurice JC, Marc I, Series F. Efficacy of auto-CPAP in the treatment of obstructive sleep apnea/hypopnea syndrome. American Journal of Respiratory & Critical Care Medicine. 1996;153:794-798.
PMID 8564134
N<10/intervention

Michaelson PG, Allan P, Chaney J, Mair EA. Validations of a portable home sleep study with twelve-lead polysomnography: comparisons and insights into a variable gold standard. Annals of Otology, Rhinology & Laryngology. 2006;115:802-809.
PMID 17165661
In 2007 EPC Report

Mickelson SA, Rosenthal L. Midline glossectomy and epiglottidectomy for obstructive sleep apnea syndrome. Laryngoscope. 1997;107:614-619.
PMID 8544614
Surgical cohort <100/intervention

Mickelson SA, Ahuja A. Short-term objective and long-term subjective results of laser-assisted uvulopalatoplasty for obstructive sleep apnea. Laryngoscope. 1999;109:362-367.
PMID 10089958
Surgical cohort <100/intervention

Miles PG, Nimkarn Y. Maxillomandibular advancement surgery in patients with obstructive sleep apnea: mandibular morphology and stability. International Journal of Adult Orthodontics & Orthognathic Surgery. 1995;10:193-200.
PMID 9082007
Surgical cohort <100/intervention

Miljeteig H, Tvinnereim M. Uvulopalatopharyngoglossoplasty (UPPGP) in the treatment of the obstructive sleep apnea syndrome. Acta Oto-Laryngologica Supplement. 1992;492:86-89.
PMID 1632261
Surgical cohort <100/intervention

Milleron O, Pilliere R, Foucher A et al. Benefits of obstructive sleep apnoea treatment in coronary artery disease: a long-term follow-up study. European Heart Journal. 2004;25:728-734.
PMID 15120882
No specific treatment

Millman RP, Carlisle CC, Rosenberg C, Kahn D, McRae R, Kramer NR. Simple predictors of uvulopalatopharyngoplasty outcome in the treatment of obstructive sleep apnea. Chest. 2000;118:1025-1030.
PMID 11035673
Surgical cohort <100/intervention

Millman RP, Kipp GJ, Beadles SC, Braman SS. A home monitoring system for nasal CPAP. Chest. 1988;93:730-733.
PMID 3280258
Not Dx'ic study (already on CPAP)

Millman RP, Rosenberg CL, Carlisle CC, Kramer NR, Kahn DM, Bonitati AE. The efficacy of oral appliances in the treatment of persistent sleep apnea after uvulopalatopharyngoplasty. Chest. 1998;113:992-996.
PMID 9554637
Not comparative

Miyamoto T, Miyamoto M, Iwanami M et al. The REM sleep behavior disorder screening questionnaire: validation study of a Japanese version. Sleep Medicine. 2009;10:1151-1154.
PMID 19604719
No outcomes of interest

Miyata S, Noda A, Nakata S et al. Daytime polysomnography for early diagnosis and treatment of patients with suspected sleep-disordered breathing. Sleep & Breathing. 2007;11:109-115.
PMID 17221275
Not diagnostic test of interest

Miyazaki S, Tanaka T, Itasaka Y, Ishikawa K. A trial study of RhinoSleep for the diagnosis of sleep apnea. Psychiatry & Clinical Neurosciences. 2001;55:249-250.
PMID 11422861
No reference standard (overnight PSG)

Mizuma H, Sonnenschein W, Meier-Ewert K. Diagnostic use of daytime polysomnography versus nocturnal polysomnography in sleep apnea syndrome. Psychiatry & Clinical Neurosciences. 1996;50:211-216.
PMID 9201778
Not diagnostic test of interest

Mooe T, Franklin KA, Holmstrom K, Rabben T, Wiklund U. Sleep-disordered breathing and coronary artery disease: long-term prognosis. American Journal of Respiratory & Critical Care Medicine. 2001;164:t-3.
PMID 11734445
N<500 (KQ 2)

Moraes W, Poyares D, Sukys-Claudino L, Guilleminault C, Tufik S. Donepezil improves obstructive sleep apnea in Alzheimer disease: a double-blind, placebo-controlled study. Chest. 2008;133:677-683.
PMID 18198262
Not drug of interest

Morales Divo C, Selivanova O, Mewes T, Gosepath J, Lippold R, Mann WJ. Polysomnography and ApneaGraph in patients with sleep-related breathing disorders. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 2009;71:27-31.
PMID 18953186
No analyses of interest

Morinaga M, Nakata S, Yasuma F et al. Pharyngeal morphology: a determinant of successful nasal surgery for sleep apnea. Laryngoscope. 2009;119:1011-1016.
PMID 19301414
Surgical cohort <100/intervention

Morris LG, Kleinberger A, Lee KC, Liberatore LA, Burschtin O. Rapid risk stratification for obstructive sleep apnea, based on snoring severity and body mass index. Otolaryngology - Head & Neck Surgery. 2008;139:615-618.
PMID 18984252
No validation set analysis

Morrish E, Shneerson JM, Smith IE. Why does gender influence survival in obstructive sleep apnoea? Respiratory Medicine. 2008;102:1231-1236.
PMID 18617382
N<500 (KQ 2)

Mueller A, Fietze I, Voelker R et al. Screening for sleep-related breathing disorders by transthoracic impedance recording integrated into a Holter ECG system. Journal of Sleep Research. 2006;15:455-462.
PMID 17118103
Not diagnostic test of interest

Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. Annals of Internal Medicine. 2007;146:157-166.
PMID 17283346
In 2007 EPC Report

Mulgrew AT, Lawati NA, Ayas NT et al. Residual sleep apnea on polysomnography after 3 months of CPAP therapy: clinical implications, predictors and patterns. Sleep Medicine. 2010;11:119-125.
PMID 20083429
Titration study

Munoz R, Duran-Cantolla J, Martinez-Vila E et al. Severe sleep apnea and risk of ischemic stroke in the elderly. Stroke. 2006;37:2317-2321.
PMID 16888274
N<500 (KQ 2)

Myatt HM, Croft CB, Kotecha BT, Ruddock J, Mackay IS, Simonds AK. A three-centre prospective pilot study to elucidate the effect of uvulopalatopharyngoplasty on patients with mild obstructive sleep apnoea due to velopharyngeal obstruction. Clinical Otolaryngology & Allied Sciences. 1999;24:95-103.
PMID 10225152
Surgical cohort <100/intervention

Nader NZ, Steinel JA, Auckley DH. Newly identified obstructive sleep apnea in hospitalized patients: analysis of an evaluation and treatment strategy. Journal of Clinical Sleep Medicine. 2006;2:431-437.
PMID 17557473
Not RCT (CPAP vs control)

Nakano H, Hayashi M, Ohshima E, Nishikata N, Shinohara T. Validation of a new system of tracheal sound analysis for the diagnosis of sleep apnea-hypopnea syndrome. Sleep. 2004;27:951-957.
PMID 15453554
In 2007 EPC Report

Nakano H, Ikeda T, Hayashi M et al. Effect of body mass index on overnight oximetry for the diagnosis of sleep apnea. Respiratory Medicine. 2004;98:421-427.
PMID 15139571
In 2007 EPC Report

Nakata S, Miyazaki S, Ohki M et al. Reduced nasal resistance after simple tonsillectomy in patients with obstructive sleep apnea. American Journal of Rhinology. 2007;21:192-195.
PMID 17424878
Surgical cohort <100/intervention

Nakata S, Noda A, Yagi H et al. Nasal resistance for determinant factor of nasal surgery in CPAP failure patients with obstructive sleep apnea syndrome. Rhinology. 2005;43:296-299.
PMID 16405275
Surgical cohort <100/intervention

Nakata S, Noda A, Yanagi E, Suzuki K, Yamamoto H, Nakashima T. Tonsil size and body mass index are important factors for efficacy of simple tonsillectomy in obstructive sleep apnoea syndrome. Clinical Otolaryngology. 2006;31:41-45.
PMID 16441801
Surgical cohort <100/intervention

Nakata S, Noda A, Yasuma F et al. Effects of nasal surgery on sleep quality in obstructive sleep apnea syndrome with nasal obstruction. American Journal of Rhinology. 2008;22:59-63.
PMID 18284861
Surgical cohort <100/intervention

Nelson LM. Combined temperature-controlled radiofrequency tongue reduction and UPPP in apnea surgery. Ear, Nose, & Throat Journal. 2001;80:640-644.
PMID 11579850
Surgical cohort <100/intervention

Neruntarat C. Genioglossus advancement and hyoid myotomy under local anesthesia. Otolaryngology - Head & Neck Surgery. 2003;129:85-91.
PMID 12869922
Surgical cohort <100/intervention

Neruntarat C. Genioglossus advancement and hyoid myotomy: short-term and long-term results. Journal of Laryngology & Otology. 2003;117:482-486.
PMID 12818058
Surgical cohort <100/intervention

Neruntarat C. Hyoid myotomy with suspension under local anesthesia for obstructive sleep apnea syndrome. European Archives of Oto-Rhino-Laryngology. 2003;260:286-290.
PMID 12750922
Surgical cohort <100/intervention

Neruntarat C, Chantapant S. Radiofrequency surgery for the treatment of obstructive sleep apnea: short-term and long-term results. Otolaryngology - Head & Neck Surgery. 2009;141:722-726.
PMID 19932844
Surgical cohort <100/intervention

Nilius G, Domanski U, Franke KJ, Ruhle KH. Impact of a controlled heated breathing tube humidifier on sleep quality during CPAP therapy in a cool sleeping environment. European Respiratory Journal. 2008;31:830-836.
PMID 18184678
Not comparison of different PAP types

Nimkarn Y, Miles PG, Waite PD. Maxillomandibular advancement surgery in obstructive sleep apnea syndrome patients: long-term surgical stability. Journal of Oral & Maxillofacial Surgery. 1995;53:1414-1418.
PMID 7490651
Surgical cohort <100/intervention

Nino-Murcia G, McCann CC, Bliwise DL, Guilleminault C, Dement WC. Compliance and side effects in sleep apnea patients treated with nasal continuous positive airway pressure. Western Journal of Medicine. 1989;150:165-169.
PMID 2658326
Not multivariate (KQ 6, CPAP)

Nordgard S, Hein G, Stene BK, Skjostad KW, Maurer JT. One-year results: palatal implants for the treatment of obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2007;136:818-822.
PMID 17478222
Surgical cohort <100/intervention

Nordgard S, Stene BK, Skjostad KW. Soft palate implants for the treatment of mild to moderate obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2006;134:565-570.
PMID 16564373
Surgical cohort <100/intervention

Noseda A, Jann E, Hoffmann G, Linkowski P, Kerkhofs M. Compliance with nasal continuous positive airway pressure assessed with a pressure monitor: pattern of use and influence of sleep habits. Respiratory Medicine. 2000;94:76-81.
PMID 10714483
Not multivariate (KQ 6, CPAP)

Noseda A, Nouvelle M, Lanquart JR et al. High leg motor activity in sleep apnea hypopnea patients: efficacy of clonazepam combined with nasal CPAP on polysomnographic variables. Respiratory Medicine. 2002;96:693-699.
PMID 12243315
In-lab study

Noseda A, Andre S, Potmans V, Kentos M, de M, V, Hoffmann G. CPAP with algorithm-based versus titrated pressure: A randomized study. Sleep Medicine. 2009;10:988-992.
PMID 19230758
Titration study

Ohayon MM, Guilleminault C, Zulley J, Palombini L, Raab H. Validation of the sleep-EVAL system against clinical assessments of sleep disorders and polysomnographic data. Sleep. 1999;22:925-930.
PMID 10566910
No analyses of interest

Okabayashi K, Kasahara E, Uchiyama H et al. Obstructive sleep apnea-hypopnea syndrome patients with overweight and hypertension in a Japanese workplace. Journal of Occupational Health. 2007;49:117-124.
PMID 17429169
No analyses of interest

Olson LG, Ambrogetti A, Gyulay SG. Prediction of sleep-disordered breathing by unattended overnight oximetry. Journal of Sleep Research. 1999;8:51-55.
PMID 10188136
In 2007 EPC Report

Omur M, Ozturan D, Elez F, Unver C, Derman S. Tongue base suspension combined with UPPP in severe OSA patients. Otolaryngology - Head & Neck Surgery. 2005;133:218-223.
PMID 16087018
Surgical cohort <100/intervention

Orr WC, Eiken T, Pegram V, Jones R, Rundell OH. A laboratory validation study of a portable system for remote recording of sleep-related respiratory disorders. Chest. 1994;105:160-162.
PMID 8275725
In 2007 EPC Report

Osman EZ, Osborne J, Hill PD, Lee BW. The Epworth Sleepiness Scale: can it be used for sleep apnoea screening among snorers? Clinical Otolaryngology & Allied Sciences. 1999;24:239-241.
PMID 10384854
No analyses of interest

Osnes T, Rollheim J, Hartmann E. Effect of UPPP with respect to site of pharyngeal obstruction in sleep apnoea: follow-up at 18 months by overnight recording of airway pressure and flow. Clinical Otolaryngology & Allied Sciences. 2002;27:38-43.
PMID 11903370
Surgical cohort <100/intervention

Overland B, Bruskeland G, Akre H, Skatvedt O. Evaluation of a portable recording device (Reggie) with actimeter and nasopharyngeal/esophagus catheter incorporated. Respiration. 2005;72:600-605.
PMID 15988172
In 2007 EPC Report

Ozegowski S, Wilczynska E, Piorunek T, Szymanowska K, Paluszkiewicz L. Usefulness of ambulatory ECG in the diagnosis of sleep-related breathing disorders. Kardiologia Polska. 2007;65:1321-1328.
PMID 18058583
Non-English

Pack AI, Black JE, Schwartz JR, Matheson JK. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. American Journal of Respiratory & Critical Care Medicine. 2001;164:1675-1681.
PMID 11719309
Not drug of interest

Pang KP. One-stage nasal and multi-level pharyngeal surgery for obstructive sleep apnoea: safety and efficacy. Journal of Laryngology & Otology. 2005;119:272-276.
PMID 15949079
Surgical cohort <100/intervention

Pang KP, Dillard TA, Blanchard AR, Gourin CG, Podolsky R, Terris DJ. A comparison of polysomnography and the SleepStrip in the diagnosis of OSA. Otolaryngology - Head & Neck Surgery. 2006;135:265-268.
PMID 16890080
In 2007 EPC Report

Pang KP, Terris DJ. Modified cautery-assisted palatal stiffening operation: new method for treating snoring and mild obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2007;136:823-826.
PMID 17478223
Surgical cohort <100/intervention

Pang KP, Woodson BT. Expansion sphincter pharyngoplasty: a new technique for the treatment of obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2007;137:110-114.
PMID 17599576
Surgical cohort <100/intervention

Parra O, Garcia-Esclasans N, Montserrat JM et al. Should patients with sleep apnoea/hypopnoea syndrome be diagnosed and managed on the basis of home sleep studies? European Respiratory Journal. 1997;10:1720-1724.
PMID 9272909
In 2007 EPC Report

Partinen M, Guilleminault C. Daytime sleepiness and vascular morbidity at seven-year follow-up in obstructive sleep apnea patients. Chest. 1990;97:27-32.
PMID 2295260
Not randomized

Penzel T, Fricke R, Jerrentrup A, Peter JH, Vogelmeier C. Peripheral arterial tonometry for the diagnosis of obstructive sleep apnea. Biomedizinische Technik. 2002;47:Suppl-7.
PMID 12451851
Not diagnostic test of interest

Penzel T, Kesper K, Pinnow I, Becker HF, Vogelmeier C. Peripheral arterial tonometry, oximetry and actigraphy for ambulatory recording of sleep apnea. Physiological Measurement. 2004;25:1025-1036.
PMID 15382839
In 2007 EPC Report

Pepin JL, Viot-Blanc V, Escourrou P et al. Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: the French multicentre study. European Respiratory Journal. 2009;33:1062-1067.
PMID 19407048
Cross-sectional

Peppard PE, Szklo-Coxe M, Hla KM, Young T. Longitudinal association of sleep-related breathing disorder and depression. Archives of Internal Medicine. 2006;166:1709-1715.
PMID 16983048
Cross-sectional

Pepperell JC, Ramdassingh-Dow S, Crosthwaite N et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. Lancet. 2002;359:204-210.
PMID 11812555
No outcomes of interest

Perez de Llano LA, Golpe R, Piquer MO et al. Clinical heterogeneity among patients with obesity hypoventilation syndrome: therapeutic implications. Respiration. 2008;75:34-39.
PMID 17622772
Not RCT (CPAP vs NIPPV)

Permut I, az-Abad M, Chatila W et al. Comparison of positional therapy to CPAP in patients with positional obstructive sleep apnea. Journal of Clinical Sleep Medicine. 2010;6:238-243.
PMID 20572416
In-lab study

Persson HE, Svanborg E. Sleep deprivation worsens obstructive sleep apnea. Comparison between diurnal and nocturnal polysomnography. Chest. 1996;109:645-650.
PMID 8617071
Not diagnostic test of interest

Petri N, Suadicani P, Wildschiodtz G, Bjorn-Jorgensen J. Predictive value of Muller maneuver, cephalometry and clinical features for the outcome of uvulopalatopharyngoplasty. Evaluation of predictive factors using discriminant analysis in 30 sleep apnea patients. Acta Oto-Laryngologica. 1994;114:565-571.
PMID 7825443
Surgical cohort <100/intervention

Phillips BA, Schmitt FA, Berry DT, Lamb DG, Amin M, Cook YR. Treatment of obstructive sleep apnea. A preliminary report comparing nasal CPAP to nasal oxygen in patients with mild OSA. Chest. 1990;98:325-330.
PMID 2198135
N<10/intervention

Piccirillo JF, Gates GA, White DL, Schectman KB. Obstructive sleep apnea treatment outcomes pilot study. Otolaryngology - Head & Neck Surgery. 1998;118:833-844.
PMID 9627245
No treatment comparison

Pieters T, Collard P, Aubert G, Dury M, Delguste P, Rodenstein DO. Acceptance and long-term compliance with nCPAP in patients with obstructive sleep apnoea syndrome. European Respiratory Journal. 1996;9:939-944.
PMID 8793455
N<100 (KQ 6)

Pillar G, Bar A, Betito M et al. An automatic ambulatory device for detection of AASM defined arousals from sleep: the WP100. Sleep Medicine. 2003;4:207-212.
PMID 14592323
In 2007 EPC Report

Pillar G, Bar A, Shlitner A, Schnall R, Shefy J, Lavie P. Autonomic arousal index: an automated detection based on peripheral arterial tonometry. Sleep. 2002;25:543-549.
PMID 12150321
In 2007 EPC Report

Piper AJ, Laks L, Sullivan CE. Effectiveness of short-term NIPPV in the management of patients with severe OSA and REM hypoventilation. Sleep.16:Suppl-6.
PMID 8177997
Not randomized

Pitsis AJ, Darendeliler MA, Gotsopoulos H, Petocz P, Cistulli PA. Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. American Journal of Respiratory & Critical Care Medicine. 2002;166:860-864.
PMID 12231498
Not comparison of different MAD types

Pittman SD, Ayas NT, MacDonald MM, Malhotra A, Fogel RB, White DP. Using a wrist-worn device based on peripheral arterial tonometry to diagnose obstructive sleep apnea: in-laboratory and ambulatory validation. Sleep. 2004;27:923-933.
PMID 15453551
In 2007 EPC Report

Pittman SD, Pillar G, Berry RB, Malhotra A, MacDonald MM, White DP. Follow-up assessment of CPAP efficacy in patients with obstructive sleep apnea using an ambulatory device based on peripheral arterial tonometry. Sleep & Breathing. 2006;10:123-131.
PMID 16586136
Not Dx'ic study (already on CPAP)

Platt AB, Field SH, Asch DA et al. Neighborhood of residence is associated with daily adherence to CPAP therapy. Sleep. 2009;32:799-806.
PMID 19544757
KQ 6 Retrospective

Platt AB, Kuna ST, Field SH et al. Adherence to sleep apnea therapy and use of lipid-lowering drugs: a study of the healthy-user effect. Chest. 2010;137:102-108.
PMID 19820075
KQ 6 Retrospective

Polo O, Brissaud L, Fraga J, Dejean Y, Billiard M. Partial upper airway obstruction in sleep after uvulopalatopharyngoplasty. Archives of Otolaryngology -- Head & Neck Surgery. 1989;115:1350-1354.
PMID 2803716
Surgical cohort <100/intervention

Popescu G, Latham M, Allgar V, Elliott MW. Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. Thorax. 2001;56:727-733.
PMID 11514695
Multivariate analysis not adequately reported

Portier F, Portmann A, Czernichow P et al. Evaluation of home versus laboratory polysomnography in the diagnosis of sleep apnea syndrome. American Journal of Respiratory & Critical Care Medicine. 2000;162:t-8.
PMID 10988088
In 2007 EPC Report

Poulet C, Veale D, Arnol N, Levy P, Pepin JL, Tyrrell J. Psychological variables as predictors of adherence to treatment by continuous positive airway pressure. Sleep Medicine. 2009;10:993-999.
PMID 19332381
KQ6: <3 mo

Powell N, Riley R, Guilleminault C, Troell R. A reversible uvulopalatal flap for snoring and sleep apnea syndrome. Sleep. 1996;19:593-599.
PMID 8899940
Surgical cohort <100/intervention

Powell NB, Riley RW, Guilleminault C. Radiofrequency tongue base reduction in sleep-disordered breathing: A pilot study. Otolaryngology - Head & Neck Surgery. 1999;120:656-664.
PMID 10229589
Surgical cohort <100/intervention

Powell NB, Riley RW, Troell RJ, Li K, Blumen MB, Guilleminault C. Radiofrequency volumetric tissue reduction of the palate in subjects with sleep-disordered breathing. Chest. 1998;113:1163-1174.
PMID 9596289
Surgical cohort <100/intervention

Powell NB, Zonato AI, Weaver EM et al. Radiofrequency treatment of turbinate hypertrophy in subjects using continuous positive airway pressure: a randomized, double-blind, placebo-controlled clinical pilot trial. Laryngoscope. 2001;111:1783-1790.
PMID 11801946
N<10/intervention

Pradhan PS, Gliklich RE, Winkelman J. Screening for obstructive sleep apnea in patients presenting for snoring surgery.[erratum appears in Laryngoscope 1997 Jan;107(1):149]. Laryngoscope. 1996;106:1393-1397.
PMID 8914907
No validation set analysis

Pribitkin EA, Schutte SL, Keane WM et al. Efficacy of laser-assisted uvulopalatoplasty in obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 1998;119:643-647.
PMID 9852540
Surgical cohort <100/intervention

Prinsell JR. Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. Chest. 1999;116:1519-1529.
PMID 10593771
Surgical cohort <100/intervention

Proctor A, Billings C, Billings C, Moloney ED. Improvement in energy and vitality over a short-term CPAP trial predicts long-term compliance in patients with obstructive sleep apnea. Journal of Sleep Research. 2007;16:448-449.
PMID 18036092
Letter

Punjabi NM, Shahar E, Redline S et al. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. American Journal of Epidemiology. 2004;160:521-530.
PMID 15353412
Cross-sectional

Quintana-Gallego E, Villa-Gil M, Carmona-Bernal C et al. Home respiratory polygraphy for diagnosis of sleep-disordered breathing in heart failure. European Respiratory Journal. 2004;24:443-448.
PMID 15358704
In 2007 EPC Report

Ramirez SG, Loube DI. Inferior sagittal osteotomy with hyoid bone suspension for obese patients with sleep apnea. Archives of Otolaryngology -- Head & Neck Surgery. 1996;122:953-957.
PMID 8797559
Surgical cohort <100/intervention

Randerath W, Parys K, Lehmann D, Sanner B, Feldmeyer F, Ruhle KH. Self-adjusting continuous positive airway pressure therapy based on the measurement of impedance. A comparison of free pressure variation and individually fixed higher minimum pressure. Respiration. 2000;67:272-279.
PMID 10867595
In-lab study

Randerath WJ, Parys K, Feldmeyer F, Sanner B, Ruhle KH. Self-adjusting nasal continuous positive airway pressure therapy based on measurement of impedance: A comparison of two different maximum pressure levels. Chest. 1999;116:991-999.
PMID 10531164
Not comparison of different PAP types

Rauscher H, Formanek D, Popp W, Zwick H. Nasal CPAP and weight loss in hypertensive patients with obstructive sleep apnoea. Thorax. 1993;48:529-533.
PMID 8322241
Not RCT (CPAP vs control)

Rauscher H, Popp W, Zwick H. Quantification of sleep disordered breathing by computerized analysis of oximetry, heart rate and snoring. European Respiratory Journal. 1991;4:655-659.
PMID 1889491
In 2007 EPC Report

Redline S, Tosteson T, Boucher MA, Millman RP. Measurement of sleep-related breathing disturbances in epidemiologic studies. Assessment of the validity and reproducibility of a portable monitoring device. Chest. 1991;100:1281-1286.
PMID 1935282
In 2007 EPC Report

Rees K, Wraith PK, Berthon-Jones M, Douglas NJ. Detection of apnoeas, hypopnoeas and arousals by the AutoSet in the sleep apnoea/hypopnoea syndrome. European Respiratory Journal. 1998;12:764-769.
PMID 9817142
In 2007 EPC Report

Reichert JA, Bloch DA, Cundiff E, Votteri BA. Comparison of the NovaSom QSG, a new sleep apnea home-diagnostic system, and polysomnography. Sleep Medicine. 2003;4:213-218.
PMID 14592324
In 2007 EPC Report

Reimao R, Lemmi H, Akiskal H, Cocke E. Obstructive sleep apnea treated with uvulopalatopharyngoplasty: a systematic follow-up study. Southern Medical Journal. 1986;79:1064-1066.
PMID 3749988
Surgical cohort <100/intervention

Ribeiro Franco CM, Cestaro BJ, Jaguaribe AM, Ataide L, Jr. Study into the use of continuous positive airway pressure in obstructive sleep apnoea-hypopnoea syndrome patients with daytime drowsiness. Revista Portuguesa de Pneumologia. 2009;15:215-226.
PMID 19280070
Not RCT (CPAP vs control)

Richard W, Kox D, den HC, van TH, de VN. One stage multilevel surgery (uvulopalatopharyngoplasty, hyoid suspension, radiofrequent ablation of the tongue base with/without genioglossus advancement), in obstructive sleep apnea syndrome. European Archives of Oto-Rhino-Laryngology. 2007;264:439-444.
PMID 17063353
Surgical cohort <100/intervention

Riley RW, Powell NB, Guilleminault C. Maxillofacial surgery and nasal CPAP. A comparison of treatment for obstructive sleep apnea syndrome. Chest. 1990;98:1421-1425.
PMID 2245683
Not comparative

Riley RW, Powell NB, Guilleminault C. Maxillary, mandibular, and hyoid advancement for treatment of obstructive sleep apnea: a review of 40 patients. Journal of Oral & Maxillofacial Surgery. 1990;48:20-26.
PMID 2294208
Surgical cohort <100/intervention

Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea and the hyoid: a revised surgical procedure. Otolaryngology - Head & Neck Surgery. 1994;111:717-721.
PMID 7991249
Surgical cohort <100/intervention

Riley RW, Powell NB, Guilleminault C. Maxillofacial surgery and obstructive sleep apnea: a review of 80 patients. Otolaryngology - Head & Neck Surgery. 1989;101:353-361.
PMID 2508006
Surgical cohort <100/intervention

Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: a surgical protocol for dynamic upper airway reconstruction. Journal of Oral & Maxillofacial Surgery. 1993;51:742-747.
PMID 8509912
Surgical cohort No complication data

Riley RW, Powell NB, Li KK, Troell RJ, Guilleminault C. Surgery and obstructive sleep apnea: long-term clinical outcomes. Otolaryngology - Head & Neck Surgery. 2000;122:415-421.
PMID 10699820
Surgical cohort <100/intervention

Riley RW, Powell NB, Li KK, Weaver EM, Guilleminault C. An adjunctive method of radiofrequency volumetric tissue reduction of the tongue for OSAS. Otolaryngology - Head & Neck Surgery. 2003;129:37-42.
PMID 12869914
Surgical cohort <100/intervention

Ringqvist M, Walker-Engstrom ML, Tegelberg A, Ringqvist I. Dental and skeletal changes after 4 years of obstructive sleep apnea treatment with a mandibular advancement device: a prospective, randomized study. American Journal of Orthodontics & Dentofacial Orthopedics. 2003;124:53-60.
PMID 12867898
No outcomes of interest

Robbins J, Redline S, Ervin A, Walsleben JA, Ding J, Nieto FJ. Associations of sleep-disordered breathing and cerebral changes on MRI. Journal of Clinical Sleep Medicine. 2005;1:159-165.
PMID 17561631
No outcomes of interest

Robinson GV, Pepperell JC, Segal HC, Davies RJ, Stradling JR. Circulating cardiovascular risk factors in obstructive sleep apnoea: data from randomised controlled trials. Thorax. 2004;59:777-782.
PMID 15333855
No outcomes of interest

Robinson S, Lewis R, Norton A, McPeake S. Ultrasound-guided radiofrequency submucosal tongue-base excision for sleep apnoea: a preliminary report. Clinical Otolaryngology & Allied Sciences. 2003;28:341-345.
PMID 12871249
Surgical cohort <100/intervention

Roche N, Herer B, Roig C, Huchon G. Prospective testing of two models based on clinical and oximetric variables for prediction of obstructive sleep apnea. Chest. 2002;121:747-752.
PMID 11888955
In 2007 EPC Report

Rolfe I, Olson LG, Saunders NA. Long-term acceptance of continuous positive airway pressure in obstructive sleep apnea. American Review of Respiratory Disease. 1991;144:1130-1133.
PMID 1952444
Not multivariate (KQ 6, CPAP)

Roosli C, Schneider S, Hausler R. Long-term results and complications following uvulopalatopharyngoplasty in 116 consecutive patients. European Archives of Oto-Rhino-Laryngology. 2006;263:754-758.
PMID 16715302
Not OSA

Rosenberg R, Roach JM, Scharf M, Amato DA. A pilot study evaluating acute use of eszopiclone in patients with mild to moderate obstructive sleep apnea syndrome. Sleep Medicine. 2007;8:464-470.
PMID 17512799
Not drug of interest

Roth T, White D, Schmidt-Nowara W et al. Effects of armodafinil in the treatment of residual excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome: a 12-week, multicenter, double-blind, randomized, placebo-controlled study in nCPAP-adherent adults. Clinical Therapeutics. 2006;28:689-706.
PMID 16861091
Not drug of interest

Rubin AH, Eliaschar I, Joachim Z, Alroy G, Lavie P. Effects of nasal surgery and tonsillectomy on sleep apnea. Bulletin europeen de physiopathologie respiratoire. 1983;19:612-615.
PMID 6652269
Surgical cohort <100/intervention

Ryan CF, Love LL. Unpredictable results of laser assisted uvulopalatoplasty in the treatment of obstructive sleep apnoea. Thorax. 2000;55:399-404.
PMID 10770822
Surgical cohort <100/intervention

Ryan CM, Usui K, Floras JS, Bradley TD. Effect of continuous positive airway pressure on ventricular ectopy in heart failure patients with obstructive sleep apnoea. Thorax. 2005;60:781-785.
PMID 15994252
N<10/intervention

Ryan PJ, Hilton MF, Boldy DA et al. Validation of British Thoracic Society guidelines for the diagnosis of the sleep apnoea/hypopnoea syndrome: can polysomnography be avoided? Thorax. 1995;50:972-975.
PMID 8539678
In 2007 EPC Report

Saarelainen S, Himanen SL, Hasan J, Virkkala J, Koobi T. Whole-body impedance recording--a practical method for the diagnosis of sleep apnoea. Clinical Physiology & Functional Imaging. 2003;23:110-113.
PMID 12641606
In 2007 EPC Report

Sagaspe P, Leger D, Taillard J, Bayon V, Chaumet G, Philip P. Might the Berlin Sleep Questionnaire applied to bed partners be used to screen sleep apneic patients? Sleep Medicine. 2010;11:479-483.
PMID 20363669
No intervention of interest

Sahlman J, Seppa J, Peltonen M, Pukkila M, Partinen M, Tuomilehto H. Surgical intervention represents a feasible option for patients with mild obstructive sleep apnoea. Acta Oto-Laryngologica. 2009;129:1266-1273.
PMID 19863323
No outcomes of interest

Sakurai S, Nishijima T, Takahashi S, Yamauchi K, Arihara Z, Takahashi K. Clinical significance of daytime plasma orexin-A-like immunoreactivity concentrations in patients with obstructive sleep apnea hypopnea syndrome. Respiration. 2004;71:380-384.
PMID 15316212
No analyses of interest

Saletu A, Anderer P, Parapatics S, Matthai C, Matejka M, Saletu B. Effects of a mandibular repositioning appliance on sleep structure, morning behavior and clinical symptomatology in patients with snoring and sleep-disordered breathing. Neuropsychobiology. 2007;55:184-193.
PMID 17700043
Not RCT (Oral vs Cx)

Saletu B, Oberndorfer S, Anderer P et al. Efficiency of continuous positive airway pressure versus theophylline therapy in sleep apnea: comparative sleep laboratory studies on objective and subjective sleep and awakening quality. Neuropsychobiology. 1999;39:151-159.
PMID 10087460
Not randomized

Salmi T, Telakivi T, Partinen M. Evaluation of automatic analysis of SCSB, airflow and oxygen saturation signals in patients with sleep related apneas. Chest. 1989;96:255-261.
PMID 2752807
No reference standard (overnight PSG)

Sampol G, Rodes G, Romero O, Jurado MJ, Lloberes P. Adherence to nCPAP in patients with coronary disease and sleep apnea without sleepiness. Respiratory Medicine. 2007;101:461-466.
PMID 16919928
Not multivariate (KQ 6, CPAP)

Sandberg O, Franklin KA, Bucht G, Eriksson S, Gustafson Y. Nasal continuous positive airway pressure in stroke patients with sleep apnoea: a randomized treatment study. European Respiratory Journal. 2001;18:630-634.
PMID 11716166
Population: stroke

Santos Junior JF, Abrahao M, Gregorio LC, Zonato AI, Gumieiro EH. Genioplasty for genioglossus muscle advancement in patients with obstructive sleep apnea-hypopnea syndrome and mandibular retrognathia. Revista Brasileira de Otorrinolaringologia. 2007;73:480-486.
PMID 17923918
Surgical cohort <100/intervention

Sato M, Suzuki M, Oshima T et al. Long-term follow-up of obstructive sleep apnea syndrome following surgery in children and adults. Tohoku Journal of Experimental Medicine. 2000;192:165-172.
PMID 11249146
Surgical cohort <100/intervention

Scharf MB, Brannen DE, McDannold MD, Berkowitz DV. Computerized adjustable versus fixed NCPAP treatment of obstructive sleep apnea. Sleep. 1996;19:491-496.
PMID 8865507
In-lab study

Scharf MB, Stover R, McDannold MD, Spinner O, Berkowitz DV, Conrad C. Outcome evaluation of long-term nasal continuous positive airway pressure therapy in obstructive sleep apnea. American Journal of Therapeutics. 1999;6:293-297.
PMID 11329112
N<500 (KQ 2)

Scharf SM, Garshick E, Brown R, Tishler PV, Tosteson T, McCarley R. Screening for subclinical sleep-disordered breathing. Sleep. 1990;13:344-353.
PMID 2267477
No validation set analysis

Seemann RP, DiToppa JC, Holm MA, Hanson J. Does laser-assisted uvulopalatoplasty work? An objective analysis using pre- and postoperative polysomnographic studies. Journal of Otolaryngology. 2001;30:212-215.
PMID 11771032
Surgical cohort <100/intervention

Senior BA, Rosenthal L, Lumley A, Gerhardstein R, Day R. Efficacy of uvulopalatopharyngoplasty in unselected patients with mild obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2000;123:179-182.
PMID 10964287
Surgical cohort <100/intervention

Serafini FM, MacDowell AW, Rosemurgy AS, Strait T, Murr MM. Clinical predictors of sleep apnea in patients undergoing bariatric surgery. Obesity Surgery. 2001;11:28-31.
PMID 11361164
Verification bias

Sergi M, Rizzi M, Greco M et al. Validity of diurnal sleep recording performed by an ambulatory device in the diagnosis of obstructive sleep apnoea. Respiratory Medicine. 1998;92:216-220.
PMID 9616515
Not diagnostic test of interest

Series F, Marc I. Importance of sleep stage- and body position-dependence of sleep apnoea in determining benefits to auto-CPAP therapy. European Respiratory Journal. 2001;18:170-175.
PMID 11510790
Superceded by other article

Series F, Marc I, Cormier Y, La FJ. Utility of nocturnal home oximetry for case finding in patients with suspected sleep apnea hypopnea syndrome. Annals of Internal Medicine. 1993;119:449-453.
PMID 8357109
In 2007 EPC Report

Series F, Plante J, Lacasse Y. Reliability of home CPAP titration with different automatic CPAP devices. Respiratory Research. 2008;9:56.
PMID 18652688
Not comparison of different PAP types

Series F, St PS, Carrier G. Effects of surgical correction of nasal obstruction in the treatment of obstructive sleep apnea. American Review of Respiratory Disease. 1992;146:t-5.
PMID 1443882
Surgical cohort <100/intervention

Series F, St PS, Carrier G. Surgical correction of nasal obstruction in the treatment of mild sleep apnoea: importance of cephalometry in predicting outcome. Thorax. 1993;48:360-363.
PMID 8511733
Surgical cohort <100/intervention

Shalaby A, Atwood C, Hansen C et al. Feasibility of automated detection of advanced sleep disordered breathing utilizing an implantable pacemaker ventilation sensor. Pacing & Clinical Electrophysiology. 2006;29:1036-1043.
PMID 17038134
Not diagnostic test of interest

Shalaby AA, Atwood CW, Hansen C et al. Analysis of interaction of acute atrial overdrive pacing with sleep-related breathing disorder. American Journal of Cardiology. 2007;99:573-578.
PMID 17293206
In-lab study

Sharma S, Wali S, Pouliot Z, Peters M, Neufeld H, Kryger M. Treatment of obstructive sleep apnea with a self-titrating continuous positive airway pressure (CPAP) system. Sleep. 1996;19:497-501.
PMID 8865508
In-lab study

Shibata N, Nishimura T, Hasegawa K, Hattori C, Suzuki K. Influence of sleep respiratory disturbance on nocturnal blood pressure. Acta Oto-Laryngologica Supplement (550):32-5, 2003. 2003;32-35.
PMID 12737339
Surgical cohort <100/intervention

Shin JH, Chee YJ, Jeong DU, Park KS. Nonconstrained sleep monitoring system and algorithms using air-mattress with balancing tube method. IEEE Transactions on Information Technology in Biomedicine. 2010;14:147-156.
PMID 19846378
No intervention of interest

Shin SH, Ye MK, Kim CG. Modified uvulopalatopharyngoplasty for the treatment of obstructive sleep apnea-hypopnea syndrome: resection of the musculus uvulae. Otolaryngology - Head & Neck Surgery. 2009;140:924-929.
PMID 19467416
Surgical cohort <100/intervention

Shine NP, Lewis RH. Transpalatal advancement pharyngoplasty for obstructive sleep apnea syndrome: results and analysis of failures. Archives of Otolaryngology -- Head & Neck Surgery. 2009;135:434-438.
PMID 19451461
Surgical cohort <100/intervention

Shine NP, Lewis RH. The "Propeller" incision for transpalatal advancement pharyngoplasty: a new approach to reduce post-operative oronasal fistulae. Auris, Nasus, Larynx. 2008;35:397-400.
PMID 18029127
Surgical cohort <100/intervention

Simmons FB, Guilleminault C, Miles LE. The palatopharyngoplasty operation for snoring and sleep apnea: an interim report. Otolaryngology - Head & Neck Surgery. 1984;92:375-380.
PMID 6435056
Inadequate results reporting

Simmons FB, Guilleminault C, Silvestri R. Snoring, and some obstructive sleep apnea, can be cured by oropharyngeal surgery. Archives of Otolaryngology. 1983;109:503-507.
PMID 6870641
Surgical cohort <100/intervention

Simon-Tuval T, Reuveni H, Greenberg-Dotan S, Oksenberg A, Tal A, Tarasiuk A. Low socioeconomic status is a risk factor for CPAP acceptance among adult OSAS patients requiring treatment. Sleep. 2009;32:545-552.
PMID 19413149
No predictors of compliance

Sin DD, Mayers I, Man GC, Ghahary A, Pawluk L. Can continuous positive airway pressure therapy improve the general health status of patients with obstructive sleep apnea?: a clinical effectiveness study. Chest. 2002;122:1679-1685.
PMID 12426271
Not AHI prediction analysis

Singh A, Al-Reefy H, Hewitt R, Kotecha B. Evaluation of ApneaGraph in the diagnosis of sleep-related breathing disorders. European Archives of Oto-Rhino-Laryngology. 2008;265:1489-1494.
PMID 18463886
Test not used to diagnose SA

Sinha AM, Bauer A, Skobel EC, et al. Long-term effects of dynamic atrial overdrive pacing on sleep-related breathing disorders in pacemaker or cardioverter defibrillator recipients. Pacing & Clinical Electrophysiology. 2009; 32 Suppl 1:S219-22.
PMID 19250100
N<10/intervention (as analyzed)

Skatvedt O, Akre H, Godtlibsen OB. Nocturnal polysomnography with and without continuous pharyngeal and esophageal pressure measurements. Sleep. 1996;19:485-490.
PMID 8865506
Not portable test

Skatvedt O, Akre H, Godtlibsen OB. Continuous pressure measurements in the evaluation of patients for laser assisted uvulopalatoplasty. European Archives of Oto-Rhino-Laryngology. 1996;253:390-394.
PMID 8891481
Surgical cohort <100/intervention

Skomro RP, Cotton DJ, Gjevre JA et al. An empirical continuous positive airway pressure trial for suspected obstructive sleep apnea. Canadian Respiratory Journal. 2007;14:159-163.
PMID 17464380
KQ 6 Retrospective

Skomro RP, Gjevre J, Reid J et al. Outcomes of home-based diagnosis and treatment of obstructive sleep apnea. Chest. 2010;138:257-263.
PMID 20173052
No intervention of interest

Smatt Y, Ferri J. Retrospective study of 18 patients treated by maxillomandibular advancement with adjunctive procedures for obstructive sleep apnea syndrome. Journal of Craniofacial Surgery. 2005;16:770-777.
PMID 16192855
Surgical cohort <100/intervention

Smith CE, Dauz ER, Clements F et al. Telehealth services to improve nonadherence: A placebo-controlled study. Telemedicine Journal & E-Health. 2006;12:289-296.
PMID 16796496
N<10/intervention

Souter MA, Stevenson S, Sparks B, Drennan C. Upper airway surgery benefits patients with obstructive sleep apnoea who cannot tolerate nasal continuous positive airway pressure. Journal of Laryngology & Otology. 2004;118:270-274.
PMID 15117464
Surgical cohort <100/intervention

Stammnitz A, Jerrentrup A, Penzel T, Peter JH, Vogelmeier C, Becker HF. Automatic CPAP titration with different self-setting devices in patients with obstructive sleep apnoea. European Respiratory Journal. 2004;24:273-278.
PMID 15332397
In-lab study

Stevenson EW, Turner GT, Sutton FD, Doekel RC, Pegram V, Hernandez J. Prognostic significance of age and tonsillectomy in uvulopalatopharyngoplasty. Laryngoscope. 1990;100:820-823.
PMID 2381257
Surgical cohort No complication data

Steward DL. Effectiveness of multilevel (tongue and palate) radiofrequency tissue ablation for patients with obstructive sleep apnea syndrome. Laryngoscope. 2004;114:2073-2084.
PMID 15564825
Surgical cohort <100/intervention

Steward DL, Weaver EM, Woodson BT. Multilevel temperature-controlled radiofrequency for obstructive sleep apnea: extended follow-up. Otolaryngology - Head & Neck Surgery. 2005;132:630-635.
PMID 15806059
Surgical cohort <100/intervention

Steward DL, Weaver EM, Woodson BT. A comparison of radiofrequency treatment schemes for obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2004;130:579-585.
PMID 15138424
Surgical cohort <100/intervention

Stockx EM, Camilleri P, Skuza EM et al. New acoustic method for detecting upper airway obstruction in patients with sleep apnoea. Respirology. 2010;15:326-335.
PMID 20199643
Not diagnostic test

Stoohs R, Guilleminault C. MESAM 4: an ambulatory device for the detection of patients at risk for obstructive sleep apnea syndrome (OSAS). Chest. 1992;101:1221-1227.
PMID 1582275
In 2007 EPC Report

Stoohs R, Guilleminault C. Investigations of an automatic screening device (MESAM) for obstructive sleep apnoea. European Respiratory Journal. 1990;3:823-829.
PMID 2261972
In 2007 EPC Report

Storre JH, Seuthe B, Fiechter R et al. Average volume-assured pressure support in obesity hypoventilation: A randomized crossover trial. Chest. 2006;130:815-821.
PMID 16963680
Not OSA

Stradling JR, Barbour C, Pitson DJ, Davies RJ. Automatic nasal continuous positive airway pressure titration in the laboratory: patient outcomes. Thorax. 1997;52:72-75.
PMID 9039254
Not comparison of different PAP types

Stradling JR, Davies RJ. Is more NCPAP better? Sleep. 2000;23:Suppl-3.
PMID 10893091
Superceded by other article

Stuck BA, Kopke J, Hormann K et al. Volumetric tissue reduction in radiofrequency surgery of the tongue base. Otolaryngology - Head & Neck Surgery. 2005;132:132-135.
PMID 15632924
Surgical cohort <100/intervention

Stuck BA, Maurer JT, Verse T, Hormann K. Tongue base reduction with temperature-controlled radiofrequency volumetric tissue reduction for treatment of obstructive sleep apnea syndrome. Acta Oto-Laryngologica. 2002;122:531-536.
PMID 12206264
Surgical cohort <100/intervention

Stuck BA, Starzak K, Hein G, Verse T, Hormann K, Maurer JT. Combined radiofrequency surgery of the tongue base and soft palate in obstructive sleep apnoea. Acta Oto-Laryngologica. 2004;124:827-832.
PMID 15370568
Surgical cohort <100/intervention

Su S, Baroody FM, Kohrman M, Suskind D. A comparison of polysomnography and a portable home sleep study in the diagnosis of obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2004;131:844-850.
PMID 15577778
In 2007 EPC Report

Sulit L, Storfer-Isser A, Kirchner HL, Redline S. Differences in polysomnography predictors for hypertension and impaired glucose tolerance. Sleep. 2006;29:777-783.
PMID 16796216
N<500 (KQ 2)

Sun X, Yi H, Cao Z, Yin S. Reorganization of sleep architecture after surgery for OSAHS. Acta Oto-Laryngologica. 2008;128:1242-1247.
PMID 18607962
Surgical cohort <100/intervention

Suzuki M, Saigusa H, Kurogi R, Morita S, Ishizuka Y. Postoperative monitoring of esophageal pressure in patients with obstructive sleep apnea-hypopnea syndrome who have undergone tonsillectomy with uvulopalatopharyngoplasty. Annals of Otology, Rhinology & Laryngology. 2008;117:849-853.
PMID 19102132
Recovery room study

Svanborg E, Larsson H, Carlsson-Nordlander B, Pirskanen R. A limited diagnostic investigation for obstructive sleep apnea syndrome. Oximetry and static charge sensitive bed. Chest. 1990;98:1341-1345.
PMID 2245672
In 2007 EPC Report

Taha BH, Dempsey JA, Weber SM et al. Automated detection and classification of sleep-disordered breathing from conventional polysomnography data. Sleep. 1997;20:991-1001.
PMID 9456464
In 2007 EPC Report

Tanaka S, Shima M. Assessment of screening tests for sleep apnea syndrome in the workplace. Journal of Occupational Health. 2010;52:99-105.
PMID 20110621
Cross sectional

Tarasiuk A, Greenberg-Dotan S, Simon T, Tal A, Oksenberg A, Reuveni H. Low socioeconomic status is a risk factor for cardiovascular disease among adult obstructive sleep apnea syndrome patients requiring treatment. Chest. 2006;130:766-773.
PMID 16963673
Cross-sectional

Taskin U, Yigit O, Acioglu E, Aricigil M, Toktas G, Guzelhan Y. Erectile dysfunction in severe sleep apnea patients and response to CPAP. International Journal of Impotence Research. 2010;22:134-139.
PMID 19940853
No outcomes of interest

Tegelberg A, Walker-Engstrom ML, Vestling O, Wilhelmsson B. Two different degrees of mandibular advancement with a dental appliance in treatment of patients with mild to moderate obstructive sleep apnea. Acta Odontologica Scandinavica. 2003;61:356-362.
PMID 14960007
Surgical cohort <100/intervention

Terris DJ, Coker JF, Thomas AJ, Chavoya M. Preliminary findings from a prospective, randomized trial of two palatal operations for sleep-disordered breathing. Otolaryngology - Head & Neck Surgery. 2002;127:315-323.
PMID 12402011
Surgical cohort <100/intervention

Terris DJ, Kunda LD, Gonella MC. Minimally invasive tongue base surgery for obstructive sleep apnoea. Journal of Laryngology & Otology. 2002;116:716-721.
PMID 12437808
Surgical cohort <100/intervention

Thatcher GW, Maisel RH. The long-term evaluation of tracheostomy in the management of severe obstructive sleep apnea. Laryngoscope. 2003;113:201-204.
PMID 12567068
Surgical cohort <100/intervention

Thong JF, Pang KP. Clinical parameters in obstructive sleep apnea: are there any correlations? Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale. 2008;37:894-900.
PMID 19128723
No analyses of interest

Tiihonen P, Hukkanen T, Tuomilehto H, Mervaala E, Toyras J. Evaluation of a novel ambulatory device for screening of sleep apnea. Telemedicine Journal & E-Health. 2009;15:283-289.
PMID 19382867
No outcomes of interest

Tiihonen P, Paakkonen A, Mervaala E, Hukkanen T, Toyras J. Design, construction and evaluation of an ambulatory device for screening of sleep apnea. Medical & Biological Engineering & Computing. 2009;47:59-66.
PMID 18985400
No outcomes of interest

Tryfon S, Stanopoulos I, Dascalopoulou E, Argyropoulou P, Bouros D, Mavrofridis E. Sleep apnea syndrome and diastolic blood pressure elevation during exercise. Respiration. 2004;71:499-504.
PMID 15467328
No analyses of interest

Tsai WH, Remmers JE, Brant R, Flemons WW, Davies J, Macarthur C. A decision rule for diagnostic testing in obstructive sleep apnea. American Journal of Respiratory & Critical Care Medicine. 2003;167:1427-1432.
PMID 12738600
In 2007 EPC Report

Tsara V, Kaimakamis E, Serasli E, Katsarou Z, Christaki P. Health related quality of life in Greek patients with sleep apnea-hypopnea syndrome treated with continuous positive airway pressure. Sleep Medicine. 2009;10:217-225.
PMID 18280789
Not randomized

Tschopp K, Thomaser EG, Staub C. Therapy of snoring and obstructive sleep apnea using the Velumount palatal device. Orl; Journal of Oto-Rhino-Laryngology & its Related Specialties. 2009;71:148-152.
PMID 19420980
Not RCT

Tsuiki S, Lowe AA, Almeida FR, Kawahata N, Fleetham JA. Effects of mandibular advancement on airway curvature and obstructive sleep apnoea severity. European Respiratory Journal. 2004;23:263-268.
PMID 14979501
Not comparative

Tugrul S, Akinci O, Ozcan PE et al. Effects of sustained inflation and postinflation positive end-expiratory pressure in acute respiratory distress syndrome: focusing on pulmonary and extrapulmonary forms. Critical Care Medicine. 2003;31:738-744.
PMID 12626977
Not OSA

Turkington PM, Sircar M, Saralaya D, Elliott MW. Time course of changes in driving simulator performance with and without treatment in patients with sleep apnoea hypopnoea syndrome. Thorax. 2004;59:56-59.
PMID 14694250
Not RCT (CPAP vs control)

Tvinnereim M, Cole P, Haight JS, Hoffstein V. Diagnostic airway pressure recording in sleep apnea syndrome. Acta Oto-Laryngologica. 1995;115:449-454.
PMID 7653270
Not diagnostic test of interest

Tvinnereim M, Mitic S, Hansen RK. Plasma radiofrequency preceded by pressure recording enhances success for treating sleep-related breathing disorders. Laryngoscope. 2007;117:731-736.
PMID 17415146
Surgical cohort <100/intervention

Ueda H, Almeida FR, Chen H, Lowe AA. Effect of 2 jaw exercises on occlusal function in patients with obstructive sleep apnea during oral appliance therapy: a randomized controlled trial. American Journal of Orthodontics & Dentofacial Orthopedics. 2009;135:430-437.
PMID 19361725
No outcomes of interest

Uematsu M. Is right ventricular dysfunction in obstructive sleep apnea a potential screening tool? Circulation Journal. 2010;74:250-251.
PMID 20065607
No outcomes of interest

Unterberg C, Luthje L, Szych J, Vollmann D, Hasenfuss G, Andreas S. Atrial overdrive pacing compared to CPAP in patients with obstructive sleep apnoea syndrome. European Heart Journal. 2005;26:2568-2575.
PMID 16126716
In-lab study

Ueno K, Kasai T, Brewer G et al. Evaluation of the apnea-hypopnea index determined by the S8 auto-CPAP, a continuous positive airway pressure device, in patients with obstructive sleep apnea-hypopnea syndrome. Journal of Clinical Sleep Medicine. 2010;6:146-151.
PMID 20411691
Not diagnostic test of interest

Valham F, Mooe T, Rabben T, Stenlund H, Wiklund U, Franklin KA. Increased risk of stroke in patients with coronary artery disease and sleep apnea: a 10-year follow-up. Circulation. 2008;118:955-960.
PMID 18697817
N<500 (KQ 2)

van den Broek E, Richard W, van TH, de VN. UPPP combined with radiofrequency thermotherapy of the tongue base for the treatment of obstructive sleep apnea syndrome. European Archives of Oto-Rhino-Laryngology. 2008;265:1361-1365.
PMID 18347810
Surgical cohort <100/intervention

Van Meerhaeghe A, Delpire P, Stenuit P, Kerkhofs M. Operating characteristics of the negative expiratory pressure technique in predicting obstructive sleep apnoea syndrome in snoring patients. Thorax. 2004;59:883-888.
PMID 15454655
Not a sleep monitor

Van Surrell C, Lemaigre D, Leroy M, Foucher A, Hagenmuller MP, Raffestin B. Evaluation of an ambulatory device, CID 102, in the diagnosis of obstructive sleep apnoea syndrome. European Respiratory Journal. 1995;8:795-800.
PMID 7656952
In 2007 EPC Report

Vazquez JC, Tsai WH, Flemons WW et al. Automated analysis of digital oximetry in the diagnosis of obstructive sleep apnoea. Thorax. 2000;55:302-307.
PMID 10722770
In 2007 EPC Report

Veale D, Chailleux E, Hoorelbeke-Ramon A et al. Mortality of sleep apnoea patients treated by nasal continuous positive airway pressure registered in the ANTADIR observatory. Association Nationale pour le Traitement A Domicile de l'Insuffisance Respiratoire chronique. European Respiratory Journal. 2000;15:326-331.
PMID 10706500
Sleep measures not tested

Vecchierini MF, Leger D, Laaban JP et al. Efficacy and compliance of mandibular repositioning device in obstructive sleep apnea syndrome under a patient-driven protocol of care. Sleep Medicine. 2008;9:762-769.
PMID 17980654
Not comparative

Ventura C, Oliveira AS, Dias R et al. The role of nocturnal oximetry in obstructive sleep apnoea-hypopnoea syndrome screening. Revista Portuguesa de Pneumologia. 2007;13:525-551.
PMID 17898912
Non-English

Verse T, Baisch A, Maurer JT, Stuck BA, Hormann K. Multilevel surgery for obstructive sleep apnea: short-term results. Otolaryngology - Head & Neck Surgery. 2006;134:571-577.
PMID 16564374
Surgical cohort <100/intervention

Verse T, Kroker BA, Pirsig W, Brosch S. Tonsillectomy as a treatment of obstructive sleep apnea in adults with tonsillar hypertrophy. Laryngoscope. 2000;110:1556-1559.
PMID 10983961
Surgical cohort <100/intervention

Verse T, Pirsig W, Junge-Hulsing B, Kroker B. Validation of the POLY-MESAM seven-channel ambulatory recording unit. Chest. 2000;117:1613-1618.
PMID 10858392
In 2007 EPC Report

Vicente E, Marin JM, Carrizo S, Naya MJ. Tongue-base suspension in conjunction with uvulopalatopharyngoplasty for treatment of severe obstructive sleep apnea: long-term follow-up results. Laryngoscope. 2006;116:1223-1227.
PMID 16826064
Surgical cohort <100/intervention

Vilaseca I, Morello A, Montserrat JM, Santamaria J, Iranzo A. Usefulness of uvulopalatopharyngoplasty with genioglossus and hyoid advancement in the treatment of obstructive sleep apnea. Archives of Otolaryngology -- Head & Neck Surgery. 2002;128:435-440.
PMID 11926921
Surgical cohort <100/intervention

Viner S, Szalai JP, Hoffstein V. Are history and physical examination a good screening test for sleep apnea? Annals of Internal Medicine. 1991;115:356-359.
PMID 1863025
No validation set analysis

Virkkula P, Bachour A, Hytonen M et al. Snoring is not relieved by nasal surgery despite improvement in nasal resistance. Chest. 2006;129:81-87.
PMID 16424416
Surgical cohort <100/intervention

von Kanel R, Loredo JS, Ancoli-Israel S, Dimsdale JE. Association between sleep apnea severity and blood coagulability: Treatment effects of nasal continuous positive airway pressure. Sleep & Breathing. 2006;10:139-146.
PMID 16565866
Superceded by other article

Waite PD, Wooten V, Lachner J, Guyette RF. Maxillomandibular advancement surgery in 23 patients with obstructive sleep apnea syndrome. Journal of Oral & Maxillofacial Surgery. 1989;47:1256-1261.
PMID 2585177
Surgical cohort <100/intervention

Waldhorn RE, Herrick TW, Nguyen MC, O'Donnell AE, Sodero J, Potolicchio SJ. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest. 1990;97:33-38.
PMID 2403899
KQ 6 Retrospective

Walker EB, Frith RW, Harding DA, Cant BR. Uvulopalatopharyngoplasty in severe idiopathic obstructive sleep apnoea syndrome. Thorax. 1989;44:205-208.
PMID 2650012
Surgical cohort <100/intervention

Walker RP, Garrity T, Gopalsami C. Early polysomnographic findings and long-term subjective results in sleep apnea patients treated with laser-assisted uvulopalatoplasty. Laryngoscope. 1999;109:1438-1441.
PMID 10499051
Surgical cohort No complication data

Walker RP, Grigg-Damberger MM, Gopalsami C. Laser-assisted uvulopalatoplasty for the treatment of mild, moderate, and severe obstructive sleep apnea. Laryngoscope. 1999;109:79-85.
PMID 9917045
Surgical cohort <100/intervention

Walker RP, Grigg-Damberger MM, Gopalsami C. Uvulopalatopharyngoplasty versus laser-assisted uvulopalatoplasty for the treatment of obstructive sleep apnea. Laryngoscope. 1997;107:76-82.
PMID 9001269
Surgical cohort <100/intervention

Walker RP, Grigg-Damberger MM, Gopalsami C, Totten MC. Laser-assisted uvulopalatoplasty for snoring and obstructive sleep apnea: results in 170 patients. Laryngoscope. 1995;105:t-43.
PMID 7666729
Surgical cohort <100/intervention

Walker RP, Levine HL, Hopp ML, Greene D, Pang K. Palatal implants: a new approach for the treatment of obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2006;135:549-554.
PMID 17011415
Surgical cohort <100/intervention

Wang X-H, Yuan Y-D, Wang B-F, Xiao L-Y, Pan W-S, Shi Y-Z. Auricular acupoint pressing therapy in the treatment of obstructive sleep apnea syndrome. Chinese Journal of Clinical Rehabilitation. 2006;10:165-167.
Cochrane CN-00641789
Superceded by later article

Wassmuth Z, Mair E, Loube D, Leonard D. Cautery-assisted palatal stiffening operation for the treatment of obstructive sleep apnea syndrome. Otolaryngology - Head & Neck Surgery. 2000;123:t-60.
PMID 10889482
Surgical cohort <100/intervention

Watkins MR, Talmage JB, Thiese MS, Hudson TB, Hegmann KT. Correlation between screening for obstructive sleep apnea using a portable device versus polysomnography testing in a commercial driving population. Journal of Occupational & Environmental Medicine. 2009;51:1145-1150.
PMID 19786903
Duplicate of previous study

Watson RK, Thompson AS. Treatment outcome of sleep apnea. Connecticut Medicine. 1992;56:125-129.
PMID 1582204
KQ 6 Retrospective

Weatherwax KJ, Lin X, Marzec ML, Malow BA. Obstructive sleep apnea in epilepsy patients: the Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ) is a useful screening instrument for obstructive sleep apnea in a disease-specific population. Sleep Medicine. 2003;4:517-521.
PMID 14607345
No validation set analysis

Weaver EM, Kapur V, Yueh B. Polysomnography vs self-reported measures in patients with sleep apnea. Archives of Otolaryngology -- Head & Neck Surgery. 2004;130:453-458.
PMID 15096430
No analyses of interest

Weaver TE, Chasens ER, Arora S. Modafinil improves functional outcomes in patients with residual excessive sleepiness associated with CPAP treatment. Journal of Clinical Sleep Medicine. 2009;5:499-505.
PMID 20465014
Not original study

Westbrook PR, Levendowski DJ, Cvetinovic M et al. Description and validation of the apnea risk evaluation system: a novel method to diagnose sleep apnea-hypopnea in the home. Chest. 2005;128:2166-2175.
PMID 16236870
In 2007 EPC Report

White DP, Gibb TJ, Wall JM, Westbrook PR. Assessment of accuracy and analysis time of a novel device to monitor sleep and breathing in the home. Sleep. 1995;18:115-126.
PMID 7792491
In 2007 EPC Report

Whitelaw WA, Brant RF, Flemons WW. Clinical usefulness of home oximetry compared with polysomnography for assessment of sleep apnea. American Journal of Respiratory & Critical Care Medicine. 2005;171:188-193.
PMID 15486338
In 2007 EPC Report

Whittle AT, Finch SP, Mortimore IL, Mackay TW, Douglas NJ. Use of home sleep studies for diagnosis of the sleep apnoea/hypopnoea syndrome. Thorax. 1997;52:1068-1073.
PMID 9516901
In 2007 EPC Report

Wiest GH, Harsch IA, Fuchs FS et al. Initiation of CPAP therapy for OSA: does prophylactic humidification during CPAP pressure titration improve initial patient acceptance and comfort? Respiration. 2002;69:406-412.
PMID 12232447
In-lab study

Williams AJ, Yu G, Santiago S, Stein M. Screening for sleep apnea using pulse oximetry and a clinical score. Chest. 1991;100:631-635.
PMID 1889245
In 2007 EPC Report

Williams SC, Rogers NL, Marshall NS, Leung S, Starmer GA, Grunstein RR. The effect of modafinil following acute CPAP withdrawal: a preliminary study. Sleep & Breathing. 2008;12:359-364.
PMID 18311493
In-lab study

Williams SC, Marshall NS, Kennerson M, Rogers NL, Liu PY, Grunstein RR. Modafinil effects during acute continuous positive airway pressure withdrawal: a randomized crossover double-blind placebo-controlled trial. American Journal of Respiratory & Critical Care Medicine. 2010;181:825-831.
PMID 20056901
No intervention of interest

Wiltshire N, Kendrick AH, Catterall JR. Home oximetry studies for diagnosis of sleep apnea/hypopnea syndrome: limitation of memory storage capabilities. Chest. 2001;120:384-389.
PMID 11502633
In 2007 EPC Report

Wolfe L, Massie CA, Mutlu GM, Gordon N, Casal E. Comparative efficacy of two expiratory pressure reduction systems in the treatment of obstructive sleep apnea. Chest. 2007;132:665b, 2007.
Cochrane CN-00642710
Not peer reviewed

Woodson BT. A tongue suspension suture for obstructive sleep apnea and snorers. Otolaryngology - Head & Neck Surgery. 2001;124:297-303.
PMID 11240995
Surgical cohort <100/intervention

Woodson BT, Conley SF. Prediction of uvulopalatopharyngoplasty response using cephalometric radiographs. American Journal of Otolaryngology. 1997;18:179-184.
PMID 9164620
Surgical cohort <100/intervention

Woodson BT, Derowe A, Hawke M et al. Pharyngeal suspension suture with repose bone screw for obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 2000;122:395-401.
PMID 10699817
Surgical cohort <100/intervention

Woodson BT, Fujita S. Clinical experience with lingualplasty as part of the treatment of severe obstructive sleep apnea. Otolaryngology - Head & Neck Surgery. 1992;107:40-48.
PMID 1528601
Surgical cohort <100/intervention

Woodson BT, Robinson S, Lim HJ. Transpalatal advancement pharyngoplasty outcomes compared with uvulopalatopharygoplasty. Otolaryngology - Head & Neck Surgery. 2005;133:211-217.
PMID 16087017
Surgical cohort <100/intervention

Yamadera W. Improvement in excessive daytime sleepiness after surgical treatment for obstructive sleep apnea syndrome. Psychiatry & Clinical Neurosciences. 1995;49:213-221.
PMID 9179940
Surgical cohort <100/intervention

Yamashiro Y, Kryger MH. Nocturnal oximetry: is it a screening tool for sleep disorders? Sleep. 1995;18:167-171.
PMID 7610312
In 2007 EPC Report

Yi B, Zhang XE, Zhang ZK, Wang X, Huang XZ. Orthognathic surgery correction of mandibular hypoplasia accompanying obstructive sleep apnea syndrome. Chinese Journal of Dental Research. 1999;2:59-64.
PMID 10863419
Surgical cohort <100/intervention

Yi HL, Yin SK, Zhang YJ et al. Z-palatopharyngoplasty for obstructive sleep apnea/hypopnea syndrome. Otolaryngology - Head & Neck Surgery. 2009;140:640-645.
PMID 19393403
Surgical cohort <100/intervention

Yin M, Miyazaki S, Ishikawa K. Evaluation of type 3 portable monitoring in unattended home setting for suspected sleep apnea: factors that may affect its accuracy. Otolaryngology - Head & Neck Surgery. 2006;134:204-209.
PMID 16455365
In 2007 EPC Report

Yonekura A, Kawakatsu K, Suzuki K, Nishimura T. Laser midline glossectomy and lingual tonsillectomy as treatments for sleep apnea syndrome. Acta Oto-Laryngologica Supplement (550):56-8, 2003. 2003;56-58.
PMID 12737344
Surgical cohort <100/intervention

Young T, Blustein J, Finn L, Palta M. Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. Sleep. 1997;20:608-613.
PMID 9351127
Cross-sectional

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;108:246-249.
PMID 19743755
Review

Zamarron C, Gude F, Barcala J, Rodriguez JR, Romero PV. Utility of oxygen saturation and heart rate spectral analysis obtained from pulse oximetric recordings in the diagnosis of sleep apnea syndrome. Chest. 2003;123:1567-1576.
PMID 12740275
In 2007 EPC Report

Zamarron C, Pichel F, Romero PV. Coherence between oxygen saturation and heart rate obtained from pulse oximetric recordings in obstructive sleep apnoea. Physiological Measurement. 2005;26:799-810.
PMID 16088069
Duplicate of previous study

Zamarron C, Romero PV, Gude F, Amaro A, Rodriguez JR. Screening of obstructive sleep apnoea: heart rate spectral analysis of nocturnal pulse oximetric recording. Respiratory Medicine. 2001;95:759-765.
PMID 11575898
In 2007 EPC Report

Zamarron C, Romero PV, Rodriguez JR, Gude F. Oximetry spectral analysis in the diagnosis of obstructive sleep apnoea. Clinical Science. 1999;97:467-473.
PMID 10491347
In 2007 EPC Report

Zohar Y, Finkelstein Y, Strauss M, Shvilli Y. Surgical treatment of obstructive sleep apnea. Technical variations. Archives of Otolaryngology -- Head & Neck Surgery. 1993;119:1023-1029.
PMID 8357584
Surgical cohort <100/intervention

Zohar Y, Finkelstein Y, Talmi YP, Bar-Ilan Y. Uvulopalatopharyngoplasty: evaluation of postoperative complications, sequelae, and results. Laryngoscope. 1991;101:t-9.
PMID 2062161
Surgical cohort <100/intervention

Zohar Y, Talmi YP, Frenkel H et al. Cardiac function in obstructive sleep apnea patients following uvulopalatopharyngoplasty. Otolaryngology - Head & Neck Surgery. 1992;107:390-394.
PMID 1383911
Surgical cohort <100/intervention

Zonato AI, Bittencourt LR, Martinho FL, Gregorio LC, Tufik S. Upper airway surgery: the effect on nasal continuous positive airway pressure titration on obstructive sleep apnea patients. European Archives of Oto-Rhino-Laryngology. 2006;263:481-486.
PMID 16450157
Surgical cohort <100/intervention

Zorick F, Roehrs T, Conway W, Fujita S, Wittig R, Roth T. Effects of uvulopalatopharyngoplasty on the daytime sleepiness associated with sleep apnea syndrome. Bulletin europeen de physiopathologie respiratoire. 1983;19:600-603.
PMID 6652267
Surgical cohort <100/intervention

Zou D, Grote L, Peker Y, Lindblad U, Hedner J. Validation a portable monitoring device for sleep apnea diagnosis in a population based cohort using synchronized home polysomnography. Sleep. 2006;29:367-374.
PMID 16553023
In 2007 EPC Report

Zou D, Grote L, Eder DN, Radlinski J, Hedner J. A double-blind, crossover study of Doxazosin and Enalapril on peripheral vascular tone and nocturnal blood pressure in sleep apnea patients. Sleep Medicine. 2010;11:325-328.
PMID 20171140
No intervention of interest

Zucconi M, Ferini-Strambi L, Castronovo V, Oldani A, Smirne S. An unattended device for sleep-related breathing disorders: validation study in suspected obstructive sleep apnoea syndrome. European Respiratory Journal. 1996;9:1251-1256.
PMID 8804946
In 2007 EPC Report

Appendix C. Data Extraction Form

A. Source and Extractor

Author, Year				**Reference test**	
PMID		**RefID**		**Index test 1**	
Key Question(s)				**Index test 2**	
Extractor				**Comments**	

B. Study description

Sampling population [A]	**Recruitment method** [B]	**Multicenter?**	**Enrollment Years**	**Country**	**Funding source**	**Index Test Readers BLIND to Reference Test Results?**
Comments						

[A] Patients representative of the general population? Patients referred to a specialized center? [However defined] high-risk patients?
[B] Consecutive patients, random sampling, case series/convenience sample

C. Participant characteristics and baseline "severity/risk"

Study design*	**Prospective vs retrospective (exclude case control studies)**	**Inclusion criteria**	**Exclusion criteria**
Cross-sectional			
Comments			

* Change from Cross-sectional if other design used.

D. Description of facility-based polysomnography and portable device monitoring (whatever is applicable)

D1. PSG

Equipment	**Manufacturer (Location)**	**Setting (eg, Sleep lab)**	**Scoring (manual, automated, automated with manual review)**	**Standard scoring system used? If not, describe criteria used**	**Denominator***
Definition of Apnea:					
Definition of Hypopnea:					
Thresholds used:			**Definitions:**		
Comments:					

* Total sleep time (AHI) versus Total recording time (RDI)

D2. Other Devices

Type	Name (equipment)	Manufacturer (Location)	Channels[A]	Actigraphy (Y/N)	Setting[B]	Timing[C]	Scoring (manual, automated, automated with manual review)	Scoring system, if not identical that for PSG	Denominator [D]	RDI or AHI (only with Type II devices)
			•							
Definition of Apnea:										
Definition of Hypopnea:										
Thresholds used:				**Definitions:**						
Comments:										

A Describe Flow and Effort channels / indicate nd if not described in the study
B Setting: sleep lab/ hospital/community center, etc,
C Timing: Simultaneous with PSG/ Different day; If different, how many days between PSG and device measurement
D Total sleep time (AHI) versus Total recording time (RDI)

D2.1 (Type definitions)

Type	Portability	Indicative Nchannels	Indicative signals	≥2 airflow/ effort channels	Identifies sleep / wake	AHI
I	Facility-based	~14-16	EEG, EOG, EMG, ECG/HR, airflow, effort, SaO2	Yes	Yes	Yes
II	Portable	≥7	(may have EEG), HR*, EOG, chin EMG, ECG/HR, airflow, effort, SaO2	Yes	Yes	Yes
III	Portable	≥4	Airflow and/or effort, ECG/HR, SaO2	Yes	No	No
IV	Portable	~1-3**	[All monitors not qualifying for type III]	No	No***	No

AHI: Apnea-Hypopnea index; ECG: electrocardiogram; EEG: Electroencephalogram; EMG: electromyography; EOG: Electro-oculogram; HR: heart rate; SaO2: arterial O2 saturation; *Heart rate is allowed instead of EEG in type II monitors. Essentially, many type II monitors gather the same signals as type I monitors. **May have more than three channels, provided that criteria for type III are not met; ***May include monitors that measure signals that are in principle able to identify arousals from sleep.

D3. Questionnaire

Description of Test Used	
Name * **Thresholds Used (Cut-Offs included) **** **Comments:**	**Description of Test (only if not on our list)**

* Epworth / STOP-BANG/ Stanford / Berlin/ Pittsburgh Scale/ Friedman surgical or staging
** Use Enter (return carriage) at the end of each threshold definition

E.1 Baseline Characteristics. ***If total not presented, add rows for subgroups evaluated and note significant differences***

N enrolled (analyzed)	Male, %	Age, y	Race	BMI*	HTN, % (how defined?) or BP	AFib/AFlutter, %	CVD †, % (specify)
NIDDM, %	**Smokers, % (define)**	**GERD, %**	**MVA ‡ etc, %**	**Cognitive Function ****	**Depression, %**	**Other Comorbidities, % (specify)**	**Is this a Special Population? (which?)**

* Mean±SD. If median, SE, range, IQR, or other, specify these.
† Including CVD, CAD, IHD, previous MI, previous stroke, etc.
‡ Motor vehicle accident.
** Either score on a test (which test?) or % with cognitive dysfunction

E.2 Baseline Characteristics.

Habitual Snoring *	Bed partner, %	Craniofacial abnormalities/ congenital abnormalities	Epworth	MSLT	Other Clinical symptoms, % (specify)	Other characteristics (specify)

* Mean±SD. If median, SE, range, IQR, or other, specify these.

F. PSG: Polysomnography (facility-based) Results.

Mean AHI (Range)	AHI ≥5 n/N (%)	AHI ≥10 n/N (%)	AHI ≥15 n/N (%)	AHI ≥20 n/N (%)	AHI ≥30 n/N (%)	AHI ≥?* n/N (%)

AHI: Apnea-hypopnea index; RDI: respiratory distress index
* Fill in this column only if any cut-offs other than 5 & 15 are used. Replace "?" with number.

G1. Results: Concordance [agreement between measurements – assume no gold standard]

Comparison		N Enrolled	N Analyzed	Concordance Metric*	Value (95% CI or LOA)**	Other Text Description (eg, of bias)
Index	Ref					

* Bland Altman plot; LOA, Limits of Agreement (±2SD); NOT correlation coefficients and OLS regression
** Delete or correct the incorrect value/item. If change, highlight yellow.

G2. Results: Diagnostic performances (Extract all reported data) [assumes gold standard]

Comparison (Index v Ref)	Index cutoff	Reference standard cutoff	Sn data		Sp data		Sens	(95% CI)	Spec	(95% CI)	ROC AUC (Q*)	Other
			TP	FN	TN	FP						

TP, Index + / Ref +
FN, Index – / Ref +
FP, Index + / Ref –
TN, Index – / Ref –

Comments on Results:	

H. Subgroup Analysis (If present)

If sub-group analysis is presented, copy the relevant tables (6 or 7) for presenting each sub-group separately. Record only those studies that have assessed an interaction test for the groups

I. REASONS FOR TREATMENT DISCONTINUATION or DROPOUT or LACK OF COMPLIANCE or LACK OF ANALYSIS

n/N	% Dropout or analysis failure	Reasons

J. Methodological Quality

Prospective or Retrospective?	
Verification bias? (Yes/No; if yes describe)	
Blinding? (Yes/No)	
Analytic problem? (Yes/No, if yes describe) *	
Adequate description of tests (Yes/No, if no describe)	
Clear description of population studied (Yes/No, if no describe)	
Data loss / not analyzed (%)	
Overall Quality (A/B/C)	

* e.g., improper accounting for multiple measurements in same patient (should do clustered analysis).

Quality: Grade A (good) studies fulfill most commonly held concepts of high quality, including the following: blinding of assessors to results of the other test, blinding to clinical information, enrollment of consecutive patients, random order of measurements or simultaneous measurements with the compared methods, clear description of the evaluated population, setting, and measurement methods; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; not excessive data loss (<20%); and no obvious bias. Grade B (moderate) studies may be susceptible to some bias, but not sufficient to invalidate the results. Such studies do not meet the criteria described in category A. They have some deficiencies but none likely to cause major bias. Study may be missing information making assessment of the limitations and potential problems difficult. Grade C (poor) studies are subject to significant bias that may invalidate the results. Such studies may have serious errors in design, analysis or reporting. These studies may have large amounts of missing information or discrepancies in reporting.

K. OTHER COMMENTS CONCERNING THE STUDY

Comments

A.

Author, Year				**Intervention 1**	
PMID*		**RefID**		**Intervention 2**	
Key Question(s)				**Intervention 3**	
Design †				**Control**	
Extractor				**Comments**	

* or Cochrane number

† RCT; Randomized Cross-over; NRCS, prospective; NRCS, retrospective; Cross-over, nonrandomized; Cohort, prospective; Cohort, retrospective

B. ELIGIBILITY CRITERIA AND OTHER CHARACTERISTICS

Inclusion	Exclusion	AHI Criteria to Dx OSA	Enrollment Years	Multicenter?	Country	Funding source	Power calculation? (specify outcome)	Blinding, patient	Blinding, outcome assessor
If NRCS, details about how was study adjusted (eg, matching, statistical adjustment):									

C. BASELINE CHARACTERISTICS:

Group	N enrolled (analyzed)	Male, %	Age, y	Race	BMI*	HTN, % (how defined?) or BP	AFib/AFlutter, %	CVD †, % (specify)
Tx								
Cx								
Total								
	NIDDM, %	**Smokers, % (define)**	**GERD, %**	**MVA ‡ etc, %**	**Cognitive Function ****	**Depression, %**	**Other Comorbidities, % (specify)**	**Is this a Special Population? (which?)**
Tx								
Cx								
Total								
	Treatments used (prior to trial, including surgery)							
Tx								
Cx								
Total								

* Mean±SD. If median, SE, range, IQR, or other, specify these.

† Including CVD, CAD, IHD, previous MI, previous stroke, etc.

‡ Motor vehicle accident.

** Either score on a test (which test?) or % with cognitive dysfunction

D. OSA "SEVERITY" AT BASELINE

	N analyzed	AHI*	Epworth*	MSLT* †	Habitual Snoring *	Bed partner, %	Time Since Diagnosis	Other (specify)
Treatment:								
Control:								
Total:								
Other Clinical symptoms, % (specify)						**Airway characteristics, % (specify)**		**Other characteristics**

* Mean±SD. If median, SE, range, IQR, or other, specify these.

† Multiple Sleep Latency Test

E. DEFINITION OF OBSTRUCTIVE SLEEP APNEA

Test Used	AHI	ODI	Definition of Apnea	Definition of Hypopnea*	Symptoms	Split night or separate nights †	Other

* Definition used to define AHI (usually 3% or 4% decline in O_2 saturation)
† Was introduction of CPAP done on the same night as diagnosis (split night) or was CPAP titration done on a separate night?

F. INTERVENTIONS*

	Intervention Category †	Specific Intervention ‡	Brand Name or Equivalent	Description
1				
2				
3				
Control				
For CPAP:		**How was the Pressure selected?**		

* If a cointervention (eg, education) is used in all patients, enter info in G, not here.
If an intervention has multiple components (that are all different than in other study arms) enter each on a separate row and renumber the 1st column as needed.
† PAP; Oral appliance; Surgery; Positional therapy; Physical therapy; Bariatric surgery; Weight loss program; Exercise program; No Treatment; Other.
‡ PAP: CPAP (fixed); Auto-titrating CPAP; Bilevel PAP; C-Flex; with/without Humidity (hot or cold)

G. CO-INTERVENTIONS

Co-intervention	Description	
For CPAP:	**Describe the frequency of the initial education follow-up**	

H. OUTCOMES (all outcomes listed should match one-for-one with outcomes in results sections)

	Outcome Category*	Specific Outcome	Time points measured	Definition of Outcome
1				
2				
3				
4				

* QoL; Sleepiness measures; General symptom scales; Psych scale; Cognitive scale; Physical scale; Accidents; Sleep quality; Work days lost; Death; CVD events; NIDDM; Sleep study measures; Compliance; Harms;

I. RESULTS (dichotomized or categorical outcomes) **If a value is calculated by us (not reported), highlight yellow**
Leave an empty row between outcomes data

Author, Year Country PMID	Outcome		Intervention	Follow-up	n Event	N Total	Unadjusted (reported)				Adjusted (reported)			
							Metric*	Result	95% CI	P btw	Result	95% CI	P btw	Adjusted for:
		Tx												
		Cx												

* RR, OR, HR, RD

J. RESULTS (continuous measures) **If a value is calculated by us (not reported), highlight yellow ****

Leave an empty row between outcomes data
A1c, BP, Sleep measures (AHI etc), ESS, MSLT, MWT, Driving tests, Other sleep-related tests?
SF-36 Physical and Mental Component Summaries; FOSQ (summary only), Calgary questionnaire? EuroQol EQ-5D?

Author, Year Country PMID	Outcome	Unit		Intervention	Follow-up	No. Analyzed	Baseline		Final		Change (Final – Baseline)			Net Δ /Difference* (Δ test – Δ control)*		
							Value	SD/SE*	Value	SD/SE*	Value	SD/SE*	P	Value	SD/SE*	P
			Tx													
			Cx													

* Delete or correct the incorrect value/item. If change, highlight yellow.
** If data is presented graphically, please reference the appropriate figure in the primary paper

J.1. RESULTS (summary of continuous measures)

QoL (except as above), Cognitive function, Executive function, Psychological tests, Physical function tests

Author, Year Country PMID	Test/Scale	Subscale	Follow-up	Intervention 1		Intervention 2		Favors**	If Significant Difference				
				Name	N	Name	N		Analysis***	Net Effect	Test Range "Worst"	Test Range "Best"	P

* If more than 2 interventions being tested in study
** Note which intervention statistically significantly favors the patient (net better score on test). If NS, type: 0
*** "Net Difference" or "Final Difference"

K. RESULTS (other reporting)

Author, Year Country PMID	Outcome		Intervention	Follow-up	Results
		Tx			
		Cx			

Comments on Results	

L. REASONS FOR TREATMENT DISCONTINUATION or DROPOUT or LACK OF COMPLIANCE

Intervention	% Dropout	Reasons

SUBGROUPS: Eg, Subgroups = male/female; age group (<50, 50-70, >70); AHI <>15; others

M. SUBGROUP RESULTS (dichotomized or categorical outcomes)

Subgroup	Author, Year Country PMID	Outcome		Intervention	Follow-up	n Event	N Total	Unadjusted (reported)				Adjusted (reported)			
								Metric*	Result	95% CI	P btw	Result	95% CI	P btw	Adjusted for:
			Tx												
			Cx												

* RR, OR, HR, RD

N. SUBGROUP RESULTS (continuous measures)

Subgroup	Author, Year Country PMID	Outcome	Unit		Intervention	Follow-up	No. Analyzed	Baseline		Final		Change			Net Δ /Difference* (Δ test – Δ control)*		
								Value	SD/SE*	Value	SD/SE*	Value	SD/SE*	P	Value	SD/SE*	P
				Tx													
				Cx													

* Delete or correct the incorrect value/item. If change, highlight yellow.
** If data is presented graphically, please reference the appropriate figure in the primary paper

O. SUBGROUP RESULTS (other reporting)

Subgroup	Author, Year Country PMID	Outcome		Intervention	Follow-up	Results
			Tx			
			Cx			

Comments on Subgroup Results	

P. ADVERSE EVENTS (Any)

Author, Year Country UI	Adverse Event	Follow-up	Intervention	Intervention	Intervention	Intervention

Q. QUALITY

RCT (y/n)	Appropriate Randomization Technique (y/n/nd/NA)	Allocation Concealment (y/n/nd/NA)	Dropout Rate <20% (y/n)	Blinded Patient (y/n/nd)	Blinded Outcome Assessment (y/n/nd)	Intention to Treat Analysis (y/n/nd)	Appropriate Statistical Analysis (y/n)	If Multicenter, Was this accounted for in analysis? (y/n/NA)	Were Potential Confounders Properly Accounted For? (y/n/nd/NA)	Clear Reporting with No Discrepancies (y/n)
	Were Eligibility Criteria Clear? (y/n)	Was Selection Bias Likely (if yes, explain below)? (y/n)	Were Interventions Adequately Described? (y/n)	Were the Outcomes Fully Defined? (y/n)	Did the Analyses Account for Compliance? (y/n/NA)	If CPAP Used, Was Pressure Titrated? † (y/n/nd/NA)	If a Crossover study with N<30, was a Power Analysis reported (and was N sufficiently large)?			If a Crossover study, was the Washout period adequate?

Reasons for drop-outs:	
Other Issues:	
Overall Quality (A, B, C)	

*non-randomized cannot be A, retrospective study is always C
N must be ≥30 per intervention in a parallel RCT for quality to be A. For a cross-over study, N≥10, so long as an adequate power analysis was reported.
Dropout must be <20% for quality to be A.
† as opposed to simply selecting a pressure for the patients.

R. SPECIFIC COMMENTS CONCERNING THE STUDY

Comments

A.

Author, Year				**Intervention 1**	
PMID*		**RefID**		**Intervention 2**	
Key Question(s)				**Intervention 3**	
Design †				**Control**	
Extractor				**Comments**	

* or Cochrane number

† RCT; Randomized Cross-over; NRCS, prospective; NRCS, retrospective; Cross-over, nonrandomized; Cohort, prospective; Cohort, retrospective

B. ELIGIBILITY CRITERIA AND OTHER CHARACTERISTICS

Inclusion	Exclusion	AHI Criteria to Dx OSA	Enrollment Years	Multicenter?	Country	Funding source

C. BASELINE CHARACTERISTICS:

Group	N enrolled (analyzed)	Male, %	Age, y	Race	BMI*	HTN, % (how defined?) or BP	Other, % (specify)	Is this a Special Population? (which?)
Tx								
	Treatments used (prior to trial, including surgery)							
Tx								

* Mean±SD. If median, SE, range, IQR, or other, specify these.

† Including CVD, CAD, IHD, previous MI, previous stroke, etc.

‡ Motor vehicle accident.

** Either score on a test (which test?) or % with cognitive dysfunction

D. OSA "SEVERITY" AT BASELINE

	N analyzed	AHI*	Epworth*	MSLT* †	Habitual Snoring *	Bed partner, %	Time Since Diagnosis	Other (specify)
Treatment:								
Other Clinical symptoms, % (specify)						**Airway characteristics, % (specify)**		**Other characteristics**

* Mean±SD. If median, SE, range, IQR, or other, specify these.

† Multiple Sleep Latency Test

F. INTERVENTIONS

	Intervention Category	Specific Intervention	Description
1	Surgery		
2			
3			

G. CO-INTERVENTIONS

Co-intervention	Description	
For CPAP:	**Describe the frequency of the initial education follow-up**	

H. OUTCOMES (all outcomes listed should match one-for-one with outcomes in results sections)

	Outcome Category*	Specific Outcome	Time points measured	Definition of Outcome
1				
2				
3				
4				

* QoL; Sleepiness measures; General symptom scales; Psych scale; Cognitive scale; Physical scale; Accidents; Sleep quality; Work days lost; Death; CVD events; NIDDM; Sleep study measures; Compliance; Harms;

P. ADVERSE EVENTS (Any)

Author, Year Country UI	Adverse Event	Follow-up	Intervention	Intervention	Intervention	Intervention

R. SPECIFIC COMMENTS CONCERNING THE STUDY

Comments

A. Source and Extractor

Author, Year				**Outcomes**	
PMID		**RefID**			
Key Question(s)				**Design †**	
Extractor				**Comments**	

† RCT; Randomized Cross-over; NRCS, prospective; NRCS, retrospective; Cross-over, nonrandomized; Cohort, prospective; Cohort, retrospective

B. ELIGIBILITY CRITERIA AND OTHER CHARACTERISTICS

Inclusion	Exclusion	AHI Criteria to Dx OSA	Study Years	Multicenter?	Prospective vs retrospective	Country	Funding source

C. BASELINE CHARACTERISTICS:

N enrolled (analyzed)	Male, %	Age, y	Race	BMI*	HTN, % (how defined?) or BP	AFib/AFlutter, %	CVD †, % (specify)
NIDDM, %	**Smokers, % (define)**	**GERD, %**	**MVA ‡ etc, %**	**Cognitive Function ****	**Depression, %**	**Other Comorbidities, % (specify)**	**Is this a Special Population? (which?)**

* Mean±SD. If median, SE, range, IQR, or other, specify these.
† Including CVD, CAD, IHD, previous MI, previous stroke, etc.
‡ Motor vehicle accident.
** Either score on a test (which test?) or % with cognitive dysfunction

D. OSA "SEVERITY" & TREATMENT AT BASELINE

All had Sleep Study?	Which?	AHI*	Epworth*	MSLT* †	Habitual Snoring *	Bed partner, %	Time Since Diagnosis	Other (specify)
Other Clinical symptoms, % (specify)						**Airway characteristics, % (specify)**		**Other characteristics**
Timing of Baseline (OSA Dx, Time of survey, Other):								
Treatments Being Used:								

* Mean±SD. If median, SE, range, IQR, or other, specify these.
† Multiple Sleep Latency Test

E. DEFINITION OF OBSTRUCTIVE SLEEP APNEA

Test Used	AHI	ODI	Definition of Apnea	Definition of Hypopnea*	Symptoms	Other

* Definition used to define AHI (usually 3% or 4% decline in O_2 saturation)

F. INTERVENTIONS*

	Intervention Category †	Specific Intervention ‡	Brand Name or Equivalent	Description
1				
2				
3				
Control				
For CPAP:		How was the Pressure selected?		

* If a cointervention (eg, education) is used in all patients, enter info in G, not here.
If an intervention has multiple components (that are all different than in other study arms) enter each on a separate row and renumber the 1st column as needed.
† PAP; Oral appliance; Surgery; Positional therapy; Physical therapy; Bariatric surgery; Weight loss program; Exercise program; No Treatment; Other.
‡ PAP: CPAP (fixed); Auto-titrating CPAP; Bilevel PAP; C-Flex; with/without Humidity (hot or cold)

G. STATISTICAL ANALYSES PERFORMED

	METHOD
Univariate	
Multivariate	

H. PREDICTORS TESTED

	Category	Predictor	Definition	Time Point Measured	Strata	Tested in Univariable Analysis?	Tested in Multivariable Analysis?	Comment
1								
2								
3								
4								
5								
6								
	Criteria Used to Test Predictors in Multivariable Analysis							

I. OUTCOMES (all outcomes listed should match one-for-one with outcomes in results sections)

	Outcome Category*	Specific Outcome	Time points measured	Definition of Outcome	How Ascertained?
1					
2					
3					
4					

* QoL; Sleepiness measures; General symptom scales; Psych scale; Cognitive scale; Physical scale; Accidents; Sleep quality; Work days lost;
Death; CVD events; NIDDM; Sleep study measures; Compliance; Preference; Harms;

J. RESULTS (dichotomized or categorical outcomes) If a value is calculated by us (not reported), highlight yellow

Author, Year Country PMID	Outcome	Predictor				Follow-up	n Event	N Total	Pct	Unadjusted (reported)				Adjusted (reported)				
		Predictor	Unit	Base	Final					Metric*	Result	95% CI	P	Metric*	Result	95% CI	P	Adjusted for:

* RR, OR, HR, RD

K. RESULTS (other reporting)

Author, Year Country PMID	Outcome	Predictor	Follow-up	Results	

Comments on Results	

L. REASONS FOR DROPOUT / POST HOC EXCLUSION FROM ANALYSIS

n/N	% Not Included in Analyses	Reasons

M. QUALITY

Appendix D. Summary Tables

Appendix D Contents

Abbreviations and Acronyms Used in Tables

Abbreviation/Acronym	Definition
AHI	apnea-hypopnea index in events/hour of sleep
AOP	atrial overdrive pacing
ASA	American Society of Anesthesiologists
AUC	area under the curve
Auto	automated scoring
autoCPAP	autotitrating positive airway pressure
BDI	Beck Depression Inventory
Block Design	Block Design and Digit Symbol Substitution
BMI	body mass index
bpm	beats per minute
Calgary	Calgary Sleep Apnea Quality of Life Index
C-flex™	splinted airway pressure
CHF	congestive heart failure
CI	confidence interval
CM	conservative management (sleep hygiene and weight control)
CMS collar	cervicomandibular support collar
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CT	conservative treatment
CVD	cardiovascular disease
DBP	diastolic blood pressure
Diff	difference
DM	diabetes mellitus (Type 2 Diabetes)
ED	emergency department
ESS	Epworth Sleepiness Scale (no units)
FOSQ	Functional Outcomes of Sleep Questionnaire
GA	geniotubercle advancement
GAHM	genioglossus advancement with hyoid myotomy/suspension
GERD	gastroesophageal reflux disease
GHQ-28	general health questionnaire
GrenobleSAQOL	Grenoble Sleep Apnea Quality of Life test
HADS	Hospital Anxiety and Depression Scale
HR	hazard ratio
HS	hyoid suspension (hyothyroidopexy)
HTN	hypertension
IQR	interquartile range
ISI	Insomnia Severity Index
LAUP	laser-assisted uvulopalatoplasty
LOA	limits of agreement
MAD	mandibular advancement device
MCS	Mental Component Summary (SF-36)
MLHFQ	Minnesota Living with Heart Failure questionnaire
MMO	maxillomandibular advancement osteotomy

MMSE	Mini Mental Status Examination
MSLT	Multiple Sleep Latency Test
nd	no data
NHP	Nottingham Health Profile
O2 desat	oxygen desaturation
OR	odds ratio
OSA	obstructive sleep apnea
OSLER	Oxford sleep resistance
P Btw	P value of difference between two interventions
PASAT	Paced Auditory Serial Addition Test
PCS	Physical Component Summary (SF-36)
PL	parallel design
PMID	Pubmed identifier (also known as unique identifier)
PSG	polysomnography; STOP
QLSESQ	Quality of Life Enjoyment and Satisfaction Questionnaire
RCT	randomized controlled trial
ROC	Receiver operating characteristics
RDI	respiratory disturbance index
Resp dz	respiratory disease
RFA	radiofrequency ablation
RFVTR	radiofrequency volumetric tissue reduction
RH	reinforced education by the homecare team
ROC	receiver-operator characteristic curve
RP	reinforced education by the prescriber
RR	relative risk
SACS	sleep apnea clinical score
SAHS	sleep apnea-hypopnea syndrome-related symptoms questionnaire
SAQLI	Sleep Apnea Quality of Life Index
SBP	systolic blood pressure
SD	standard deviation
SDB	sleep disordered breathing
SF-36	Short Form (36) Health Survey
SH	standard education by the homecare network
SHEP	shoulder head elevation pillow
SHHS	Sleep Heart Health Study
SP	standard education by the prescriber
SQ	Scottish National Sleep Laboratory symptom questionnaire
STOP	Snoring, tiredness during daytime, observed apnea, and high blood pressure
STOP-Bang	STOP with BMI, age, neck circumference, and gender variables
TAP	transpalatal advancement pharyngoplasty
TASB	thoracic anti-supine band
TC	total cholesterol
TCA	tricyclic antidepressants
TCRFTVR	temperature controlled radiofrequency tissue volume reduction of the soft palate

Tg	triglycerides
TMJ	temporomandibular joint
TSD	tongue stabilizing device
Tx	treatment
UMACL	University of Wales mood adjective list energetic arousal score
UPP	uvulopalatoplasty
UPPP	uvulopalatopharyngoplasty
VLCD	very low calorie diet
WAIS	Wechsler Adult Intelligence Scale
WHR	waist-hip ratio
WMS	Wechsler Memory Scale
WSCS	Wisconsin Sleep Cohort Study
XO	crossover design

Table 1.1.1. Type III monitors vs. PSG: study characteristics

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Amir, 2010[70] 20191939	Suspected sleep apnea-hypopnea syndrome patients	USA(nd)	53	15.4 [0,106.6]	nd	48	68%	32	Sleep lab	AHI ≥ 15	Total sleep time (AHI)	
Garcia-Diaz, 2007[66] 17356086	Suspected sleep apnea-hypopnea syndrome patients	Spain (nd)	65	30 (33) [nd]	12 (3.7)	54	87%	30.1	Sleep lab & Home	nd	Total recording time (RDI)	No clear population description
Ng, 2010[71] 20199644	Suspected OSA referred to respiratory clinic	China (nd)	80	21.6 (19.1)	9.7 (5.3)	51	79%	27.1	Sleep lab	nd	Total recording time (RDI)	
Planès, 2010[72] 19533191	Pts with coronary artery disease	France (Apr 2004 – July 2007)	45	23.8 (15.3) [2,67]	8 (8.3)	63	98%	26.4	Home	nd	Total recording time (RDI)	Selection bias
Santos-Silva, 2009[67] 19480230	Suspected OSA and healthy subjects	Brazil (nd)	82	23 (34) [nd]	10.4 (5.8)	47	57%	28	Sleep lab & Home	nd	Total recording time	No clear population description – baseline severity by AHI
To, 2009[68] 19210658	Suspected OSA referred to respiratory clinic	China (2005)	184	40	10.4	49	75%	28.7	Sleep lab	AHI > 5	Total recording time	B-A plots are not interpretable; no clear population description
Tonelli de Oliveira, 2009[69] 19201709	Referred for sleep center	Brazil (2004-2006)	157	30 (28)	11 (5.0)	45	73%	29.1	Sleep lab & Home	AHI ≥ 5	Total recording time	Analytical problem – no adjustment for multiple measures on same patient

Respiratory events across all studies were of at least 10 seconds duration. As mentioned in the header row, respiratory events were defined identically in for the portable monitors as with laboratory-based PSG. Studies are ordered by decreasing number of analyzed people.

Table 1.1.2. Complete list of type III and type IV monitors from our previous report[26] as well as in the update

Name of Monitor	Monitor Classification	No. of studies	Studies
ApneaScreen II	III	2	Quintana-Gallego 2004, Garcia-Diaz 2007
ARES Unicorder	III	1	To 2009
Bedbugg	III	1	Claman 2001
CID102L8 Type III system	III	1	Planès 2010
Edent 4700	III	1	Redline 1991
Edentrace	III	3	Parra 1997, Whittle 1997, Emsellem 1990
Embletta	III	2	Dingli 2003, Ng 2010
Merlin	III	2	Calleja 2002, Fietze 2002
Micro Digitraper-S	III	1	Zucconi 1996
Morpheus Hx bedside computer analysis system	III	1	Amir 2010
Nightwatch	III	2	Ancoli-Israel 1997, White 1995
NovaSom QSG	III	1	Reichert 2003
Poly Mesam	III	2	Marrone 2001, Verse 2000
PolyG	III	1	Man 1995
Sibel Home-300	III	1	Ballester 2000
SNAP	III	1	Su 2004
Somno check	III	2	Ficker 2001, Tonelli de Oliveira 2009,
Stardust II	III	2	Yim 2006, Santos-Silva 2009
Unnamed Monitors - Respiratory Monitoring	III	2	Carasco 1996, Llobres 1996
Apnealink	IV	5	Erman 2007, Ng 2009, Ragette 2010, Chen 2009, Clark 2009
Apnomonitor 5	IV	1	Yagi 2009
Apno screen I	IV	1	Golpe 2002
ARES	IV	2	Ayappa 2008, Westbrook 2005
Autoset	IV	8	Bagnato 2000, Bradley 1995, Gugger 1995, Gugger 1997, Kiely 1996, Mayer 1998, Rees 1998, Fleury 1996
CID102	IV	1	vanSurell 1995
ClearPath	IV	1	Abraham 2006
Embletta	IV	1	Smith 2007
FlowWizard	IV	1	Wong 2008
Holter (with and without ECG)	IV	3	Szyszko 2009, Pepin 2009, Heneghan 2008
Lifeshirt	IV	1	Goodrich 2009
MESAM IV	IV	5	Esnaola 1996, Stoohs 1992, Koziej 1994, Schafer 1997, Rauscher 1991
Oxiflow	IV	2	Baltzan 2000, Ayappa 2004

Table 1.1.2. Complete list of type III and type IV monitors from our previous report[26] as well as in the update (continued)

Name of Monitor	Monitor Classification	No. of studies	Studies
Oximeter with or without snoring sound recording, ECG and actigraphy	IV	22	Adachi 2003, Alvarez 2006, Bonsignore 1990, Bradley 1995, Chiner 1999, Cooper 1991, Douglas 1992, Gurubhagavatula 2004, Gyulay 1987, Heneghan 2008, Issa 1993, Levy 1996, Pepin 1991, Rauscher 1993, Ryan 1995, Series 1993, Vazquez 2000, White 1994, Williams 1991, Wiltshire 2001, Zamarron 1999, Zamarron 2003,
Reggie	IV	1	Overland 2005
RUSleeping RTS	IV	1	Watkins 2009
SD-101 (respiratory effort)	IV	1	Agatsuma 2009
Sleep Strip	IV	2	Shochat 2002, Pang 2006
Sleep Check	IV	1	de Almeida 2006
SNAP	IV	1	Michaelson 2006
SOMNIE	IV	1	Nakano 2008
Watch PAT 100	IV	7	Ayas 2003, Bar 2003, Bar 1995 Penzel 2004, Pittman 2004, Pang 2007, Pillar 2003
WristOx 3100	IV	1	Nigro 2009

Table 1.1.3. Type III monitors vs. PSG: study results

Study PMID	Index Test (vs. PSG)	N	Setting	Bland-Altman		ROC Analysis					Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Garcia-Diaz, 2007[66] 17356086	Respiratory Polygraph – Apnoescreen II in Lab (Obs A)	62	Sleep lab (& home)	95% LOA	2.8 (-18, 23)	RDI≥10	AHI≥10	94.6 (87.3,100)	96 (88.3,100)	0.977	A
						RDI≥15	AHI≥15	100	96.7 (90.2,100)	0.998	
						RDI≥30	AHI≥30	95.8 (87.8,100)	94.7 (87.6,100)	0.986	
	Respiratory Polygraph – Apnoescreen II in Lab (Obs B)				1.03 (-19, 21)	RDI≥10	AHI≥10	94.6 (87.3,100)	88 (75.2,100)	0.974	
						RDI≥15	AHI≥15	100	96.7 (90.2,100)	0.997	
						RDI≥30	AHI≥30	95.8 (87.8,100)	94.7 (87.6,100)	0.987	
	Respiratory Polygraph – Apnoescreen II at Home (Obs A)				3.1 (-30, 36)	RDI≥10	AHI≥10	86.4 (75.4,97.5)	100	0.969	
						RDI≥15	AHI≥15	87.5 (76, 98.9)	96.7 (90.2,100)	0.972	
						RDI≥30	AHI≥30	91.7 (80.6,100)	94.7 (87.6,100)	0.986	
	Respiratory Polygraph – Apnoescreen II at Home (Obs B)				1.6 (-31, 34)	RDI≥10	AHI≥10	83.8 (71.9,95.6)	92 (81.3,100)	0.976	
						RDI≥15	AHI≥15	84.4 (71.8, 96.9)	96.7 (90.2,100)	0.977	
						RDI≥30	AHI≥30	95.8 (87.8, 100)	94.7 (87.6,100)	0.985	
Amir, 2010[70] 20191939	Morpheus Hx (bedside computerized analysis system) vs PSG	53	Sleep Lab	95% CI	-0.06 (-14.3, 14.2)	≥ 5	≥ 5	97.2 (nd)	94.1 (nd)		A
						≥ 15	≥ 15	100 (nd)	92.7 (nd)		

Table 1.1.3. Type III monitors vs. PSG: study results (continued)

Study PMID	Index Test (vs. PSG)	N	Setting	Bland-Altman		ROC Analysis					Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Santos-Silva, 2009[67] 19480230	STD at-home vs. PSG in-lab	80	Sleep Lab & Home	95% LOA	-0.7 (-24, 22.6)	≥5	≥5	93 (nd)	59 (nd)	0.90	A
						≥15	≥15	85 (nd)	80 (nd)	0.92	
						≥30	≥30	77 (nd)	93 (nd)	0.95	
	STD in-lab (done with PSG) vs. PSG in-lab				-4.0 (-26.6, 18.6)	≥5	≥5	92 (nd)	48 (nd)	0.91	
						≥15	≥15	94 (nd)	71 (nd)	0.93	
						≥30	≥30	86 (nd)	79 (nd)	0.95	
	STD at-home vs. PSG in-lab (done with STD)				1.6 (-22.2, 25.4)	≥5	≥5	95 (nd)	62 (nd)	0.95	
						≥15	≥15	86 (nd)	78 (nd)	0.95	
						≥30	≥30	74 (nd)	96 (nd)	0.96	
	STD in-lab (done with PSG) vs. PSG in-lab (done with STD)				-1.1 (-24.9, 22.8)	≥5	≥5	98 (nd)	62 (nd)	0.97	
						≥15	≥15	97 (nd)	74 (nd)	0.98	
						≥30	≥30	96 (nd)	92 (nd)	0.98	
Ng, 2010[71] 20199644	Embletta portable diagnostic system vs PSG	80	Sleep lab	95% CI	1.0 (-7, 8.6) **	≥ 5	≥ 5	92.4 (nd)	85.7 (nd)	0.948	B
						≥ 10	≥ 10	90 (nd)	86.7 (nd)	0.975	
						≥ 15	≥ 15	87.8 (nd)	94.9 (nd)	0.985	
						≥ 20	≥ 20	85.3 (nd)	95.7 (nd)	0.984	
Planès, 2010[72] 19533191	Type III device (CID102L8) vs Type II PSG (extended version of CID102L8)	45	Sleep lab	95% CI	-3.4 (-18.4, 11.6) **	≥5	≥5	95 (82, 99)	67 (12, 98)		B
						≥15	≥15	71 (52, 85)	93 (64, 100)		
						≥30	≥30	75 (43, 93)	97 (82, 100)		
To, 2009[68] 19210658	ARES Unicorder vs. PSG	141	Hospital	nd	Data not interpretable from figure	≥5 at 4% O_2 desat	≥ 5	84 (77, 90)	100	0.96	B
						≥5 at 3% O_2 desat	≥5	89 (84, 94)	100	0.97	
						≥5 at 1% O_2 desat	≥5	97 (94, 99)	63 (55, 71)	0.98	

Table 1.1.3. Type III monitors vs. PSG: study results (continued)

Study PMID	Index Test (vs. PSG)	N	Setting	Bland-Altman		ROC Analysis					Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Tonelli de Oliveira, 2009[69] 19201709	Somnocheck-lab vs. PSG	149	Sleep lab & Home	95% LOA	2.6 (-17.7, 22.8)						B
	Somnocheck-Home vs. PSG				3.2 (-28, 34.3)	≥7	AHI≥5	96.15 (92.5, 99.8)	64.7 (42.0, 87.4)	0.96	
						≥9	AHI≥10	90.7 (82.7, 95.2)	82.9 (67.3, 91.9)	0.92	
						≥9	AHI≥15	81.3 (71.1, 88.5)	88.4 (78.8, 94.0)	0.91	
						≥33	AHI≥30	80 (68.3, 91.7)	92.1 (86, 98.2)	0.92	

Table 1.2.1. Type IV monitors (≥3 channels) vs. PSG: study characteristics

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Ayappa, 2008[73] 18350959	Referred to specialized center	US (2005-2006)	80	nd	8.8 (nd)	46	78%	30	Sleep lab & Home	nd	Total sleep time as well as total recording time	Baseline AHI not reported
Goodrich, 2009[79] 18083629	Symptoms suggestive of OSA & GERD	US (nd)	50	[5–105]	nd	44	73%	nd	Sleep lab	nd	Total recording time (RDI)	No data on test reader blinding
Ng, 2009[96] 19220528	Suspected sleep apnea patients	China (nd)	50	nd	10.1 (5.5)	50	88%	27.9	Sleep lab	nd	Total recording time (RDI)	Incomplete reporting of population
Pang, 2007[84] 17903588	Referred to sleep center	US (nd)	37	35 (20) [nd]	13.9	50	32%	34.6	Sleep lab	nd	Total sleep time*	Unclear results reporting; unclear population description
Schafer, 1997[87] 9154670	Suspected sleep-related breathing disorders	Germany (nd)	114	29 (24) [nd]	nd	56	88%	30.8	Sleep lab & Home	RDI ≥10	Total recording time	Nonconsecutive subjects
Smith, 2007[88] 18036089	Chronic heart failure	UK (nd)	20	26 (22) [nd]	8 (4.0)	61	70%	29	Sleep lab & Home	AHI >20	Total recording time	OSA cut-off different for PSG device
Yagi, 2009[93] 18635324	Suspected sleep apnea syndrome	Japan (2005-2006)	22	44 (21) [nd]	nd	53	77%	25.7	Sleep lab	AHI ≥15	Total recording time	Incomplete reporting of population, OSA severity, methods, or analyses

* As described, the device should only be capable of using the total recording time
** Estimated from Figure of plot in the publication, using the Engauge Digitizer software program

Table 1.2.2. Type IV monitors (2 channels) vs. PSG: study characteristics

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Abraham, 2006[74] 17033271	Heart failure	US & UK (nd)	50	[0-92]	10.6 (4.4)	56	68%	32.6	Sleep lab & Home	RDI ≥5	Total sleep time	Significant difference among sites; home test data not presented; unclear criteria for tests
Chen, 2009[75] 19052790	Suspected sleep disordered breathing patients	Canada (nd)	54	30 (26) [1–86]	nd	49	64%	32.2	Sleep lab	OSA: AHI≥ 5	Total sleep time	
Clark, 2009[76] 19222876	Suspected sleep disordered breathing patients	UK (nd)	67	22 (23) [0–87]	13.3 (5.2)	51	76%	35.0	Home	CPAP Tx needed: AHI ≥ 15	Total recording time (RDI)	B-A plots are not interpretable; no clear population description
Heneghan, 2008[81] 18853941	Suspected OSA	Ireland (nd)	63	nd	11.3	51	88%	30.9	Sleep lab	AHI≥15	Total recording time	
Pepin, 2009[85] 19028140	Referred for sleep center	France (nd)	34	20 (19) [nd]	10 (6.0)	47	63%	25.4	Sleep lab	AHI >20	Total recording time	Unclear population description
Ragette, 2010[95] 19714380	Referred for sleep lab	Germany (Jul – Oct 2003)	102	nd	nd	54	76%	29.5	Sleep lab	nd	Total recording time	Unclear population description
Ragette, 2010[95] 19714380	Referred for sleep lab day clinic	Germany (Jan 2005 – Feb 2006)	131	nd	nd	59	73%	28	Home	nd	Total recording time	Unclear population description

Table 1.2.2. Type IV monitors (2 channels) vs. PSG: study characteristics (continued)

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Szyszko, 2009[89] 18971289	Suspected OSA	Argentina (nd)	20	24 (26) [5–119]	10.9 (5.2)	49	50%	41.3	Sleep lab	AHI ≥10	Total recording time	
White, 1994[91] 7923843	Referred for UPPP	UK (nd)	37	nd	nd	37	68%	nd	Sleep lab	AHI ≥10	Total sleep time	Unclear description of population and tests; discrepancy in results reporting

Table 1.2.3. Type IV monitors (1 channel) vs. PSG: study characteristics

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Agatsuma, 2009[94] 19818056	Suspected disordered sleep patients and healthy truck drivers	Japan (Mar 2004 – Aug 2007)	366	19.7 †††	5.8 ‡‡‡	49	87	25.2	Sleep lab & Home	AHI ≥ 15 w/o symptoms or AHI ≥ 5 - < 15 w/ symptoms	Total recording time (RDI)	Data from two dissimilar groups was combined to estimate sens and sp for the device
de Almeida, 2006[77] 16502297	Patients referred to sleep center for suspected sleep-related breathing disorders	Canada (nd)	35	19 (22) [nd]	nd	44	77%	31.1	Sleep lab	AHI >5	Total recording time (RDI)	16% of sample was excluded without reason
Erman, 2007[78] 17694728	Patients with type 2 diabetes mellitus	USA (nd)	68	nd	nd	57	49%	32.6	Sleep lab & Home	nd	Total recording time (RDI)	
Heneghan, 2008[80] 18595434	Suspected OSA and healthy male subjects	Ireland (nd)	98	33 (nd) [nd]	11.9 (nd)	42	100%	33.9	Sleep lab	AHI≥15	Total recording time	Results not interpretable
Nakano, 2008[82] 18480104	Patients referred for sleep disorders	Japan (nd)	100	30 [10-65]	nd	45.3 *	80%	26.9	Sleep lab & Home	nd	Total recording time	

††† weighted mean; suspected disordered sleep gp: 28.6 ± 23.0; healthy truck drivers group: 8.9 ± 14.3
‡‡‡ weighted mean

Table 1.2.3. Type IV monitors (1 channel) vs. PSG: study characteristics (continued)

Study PMID	Participants	Country (enrollment years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Denominator	Quality Issues
Nigro, 2009[83] 18830731	Suspected OSA	Argentina (nd)	166	14 [4-29] †	nd	51	77%	28.3	Sleep lab	AHI ≥5	Total recording time	Unclear description of population
Watkins, 2009[90] 19786903	Commercial motor drivers at high risk for OSA	USA (Sept 2007 – Oct 2008)	159	19 (nd) [1–117]	nd	nd	nd	nd	Sleep lab & Community	AHI ≥ 5	Total recording time	No clear population description; 78% drop outs; no clear description of PSG
Reda, 2001[86] 11593166	Sleep-related breathing disorders	UK (nd)	59	nd	nd	Range: 20-70	nd	nd	Sleep lab	AHI ≥15	Total recording time	Unclear population description; test readers not blinded
White, 1994[91] 7923843	Referred for UPPP	UK (nd)	37	nd	nd	37	68%	nd	Sleep lab	AHI ≥10	Total sleep time	Unclear description of population and tests; discrepancy in results reporting
Wong, 2008[92] 18411561	Referred for sleep center	Australia (nd)	34	32 (27) [0-100]	11.9 (4.7)	42	97%	30.2	Sleep lab & Home	AHI ≥10	Total recording time	Unclear description of population

* Average of the mean values of the two centers of the study
† Median and interquartile range

Table1.3.1. Type IV monitors (≥3 channels) vs. PSG: study results

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis					Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Ayappa 2008[73] 18350959	ARES * in-Lab vs PSG	73	Sleep lab (& home)	95% LOA	0.7 (-1.2, 2.6)	AHI >5 4% O_2 des	AHI >5 4% O_2 des	0.98 (0.88, 1)	0.76 (0.52, 0.91)		A
						AHI >5 4% O_2 des	AHI >10 4% O_2 des	0.97 (0.84, 1)	0.78 (0.6, 0.89)		
						AHI >5 4% O_2 des	AHI >15 4% O_2 des	0.91 (0.75, 0.98)	0.92 (0.78, 0.98)		
	ARES in-Lab vs PSG (RDI)	73			3.3 (0.8, 5.9)	AHI >10 1% O_2 des	RDI >10	0.95 (0.86, 0.99)	0.73 (0.39, 0.93)		
						AHI ≥15 1% O_2 des	RDI≥15	0.94 (0.84, 0.99)	0.89 (0.65, 0.98)		
	ARES at-home vs PSG	67			5.2 (1.0, 9.4)	AHI >5 4% O_2 des	AHI >5 4% O_2 des	0.92 (0.8, 0.97)	0.67 (0.41, 0.86)		
						AHI >5 4% O_2 des	AHI >10 4% O_2 des	0.89 (0.72, 0.96)	0.72 (0.53, 0.86)		
						AHI >5 4% O_2 des	AHI >15 4% O_2 des	0.76 (0.57, 0.88)	0.82 (0.65, 0.93)		
	ARES at-home vs PSG (RDI)	67			10.3 (5.9, 14.6)	AHI >10 1% O_2 des	RDI >10	0.9 (0.78, 0.96)	0.78 (0.4, 0.96)		
						AHI ≥15 1% O_2 des	RDI≥15	0.84 (0.71, 0.93)	0.81 (0.54, 0.95)		
Goodrich 2009[79] 18083629	Lifeshirt	48	Lab	95% LOA	1.02 (-16.4, 16.4)	≥5	≥5	85 (nd)	67 (nd)	0.76	B
						≥10	≥10	92 (nd)	88 (nd)	0.90	
						≥15	≥15	87 (nd)	82 (nd)	0.84	
						≥20	≥20	85 (nd)	94 (nd)	0.90	
						≥25	≥25	100 (nd)	97 (nd)	0.99	
						≥30	≥30	88 (nd)	100 (nd)	0.94	
Ng, 2009[96] 19220528	ApneaLink (AHI) vs PSG	50	Sleep lab	95% CI	2.0 (-6.7, 10.5) **	≥5	≥5	100 (nd)	100 (nd)	1.000	B
						≥10	≥10	97.7 (nd)	100 (nd)	1.000	
						≥15	≥15	94.7 (nd)	100 (nd)	0.998	
						≥20	≥20	96.9 (nd)	100 (nd)	1.000	
	ApneaLink (ODI) vs PSG	50	Sleep Lab	95% CI	10.9 (-8.6, 30) **	≥5	≥5	95.8 (nd)	50 (nd)	0.964	
						≥10	≥10	88.3 (nd)	85.7 (nd)	0.935	
						≥15	≥15	73.7 (nd)	91.7 (nd)	0.931	
						≥20	≥20	75 (nd)	88.9 (nd)	0.922	

Table1.3.1. Type IV monitors (≥3 channels) vs. PSG: study results (continued)

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis				Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Yagi 2009[93] 18635324	Apnomonitor vs PSG	22	Sleep lab			≥15	≥15	95			C
Pang 2007[84] 17903588	WatchPAT	32	Sleep Lab			>5	>5	94 (nd)	80 (nd)		C
						>15	>15	96 (nd)	79 (nd)		
						>35	>35	83 (nd)	72 (nd)		
Smith 2007[88] 18036089	Embletta in-Lab	20	Sleep lab & Home	95% LOA	6 (-11, 24)						B
	Embletta at-home	20	Sleep lab & Home		12 (-25, 49)	AHI≥10	AHI ≥15	87.5 (nd)	58.3		
						AHI≥20	AHI ≥15	75 (nd)	50		
Schafer 1997[87] 9154670	MESAM 4	114	Sleep lab & Home	nd	Data not interpretable from figure	≥5	≥5	96 (nd)	15 (nd)		B
						≥10	≥10	95 (nd)	41 (nd)		
						≥15	≥15	83 (nd)	62 (nd)		
						≥20	≥20	68 (nd)	74 (nd)		
						≥25	≥25	60 (nd)	85 (nd)		

* ARES: Apnea Risk Evaluation System Unicorder
** Estimated from Figure of plot in the publication, using the Engauge Digitizer software program

Table 1.3.2. Type IV monitors (2 channels) vs. PSG: study results

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman Metric	Bland-Altman Result, events/hr	ROC Analysis Threshold, events/hr		ROC Analysis Sensitivity, % (95% CI)	ROC Analysis Specificity, % (95% CI)	AUC	Quality
Pepin 2009[85] 19028140	ECG/nasal pressure holter monitoring visual	19	Sleep lab	95% CI	5.8 (-3.9, 15.5)	>35	>20	57 (nd)	100 (nd)	0.97	B
	ECG/nasal pressure holter monitoring automated	19	Sleep lab		2.3 (-18.9, 23.4)	>35	>20	71 (nd)	100 (nd)	0.85	
Chen 2009[75] 19052790	ApneaLink (AASM criteria *)	50	Sleep lab	95% LOA	-6.3 (-25.5, 12.9)	AHI≥5	AHI≥5	97.7 (nd)	66.7 (nd)	0.964	A
						AHI≥10	AHI≥10	95.0 (nd)	90.0 (nd)	0.978	
						AHI≥15	AHI≥15	87.5 (nd)	88.9 (nd)	0.944	
						AHI≥20	AHI≥20	88.0 (nd)	88.0 (nd)	0.944	
						AHI≥30	AHI≥30	88.2 (nd)	93.9 (nd)	0.954	
	ApneaLink (Sandman setting †)				-0.5 (-17.9, 16.9)	AHI≥5	AHI≥5	93.2 (nd)	83.3 (nd)	0.951	
						AHI≥10	AHI≥10	97.5 (nd)	90.0 (nd)	0.983	
						AHI≥15	AHI≥15	90.6 (nd)	77.8 (nd)	0.944	
						AHI≥20	AHI≥20	92.0 (nd)	84.0 (nd)	0.934	
						AHI≥30	AHI≥30	94.1 (nd)	81.8 (nd)	0.955	
Ragette, 2010[95] 19714380	Apnealink-in Lab vs PSG	102	Sleep lab	95% CI	-0.7 (-14,12) **	≥5	≥5	93.9 (nd)	50 (nd)		B
						≥10	≥10	91.9 (nd)	87.5 (nd)		
						≥15	≥15	92 (nd)	88.5 (nd)		
	Apnealink-at Home vs PSG	131	Home	95% CI	1.2 (-18.8,18.7) **	≥5	≥5	91.8 (nd)	76.5 (nd)		
						≥10	≥10	80 (nd)	85.5 (nd)		
						≥15	≥15	73.1 (nd)	84.7 (nd)		
Clark 2009[76] 19222876	ApneaLink ‡	50	Home	nd	Data not interpretable from figure	AHI≥15	AHI≥15	92 (nd)	96.7 (nd)		B
Abraham 2006[74] 17033271	Home Cardiorespiratory system (ClearPath System Nx-301)	50	Sleep lab			RDI≥5	RDI≥5	92 (nd)	52 (nd)		B
						RDI≥10	RDI≥10	88 (nd)	63 (nd)		
						RDI≥15	RDI≥15	67 (nd)	78 (nd)		
Heneghan 2008[81] 18853941	ECG-Oximetry analysis	59	Sleep lab	95% LOA	-0.9 /hr (-18, 16.2)	≥5	≥5	93.8 (86.9, 100)	100		A
						≥10	≥10	81.6 (69.3, 93.9)	90.5 (77.9, 100)		
						≥15	≥15	74.2 (58.8, 89.6)	96.4 (89.6, 100)		
	Oximetry	59	Sleep lab		1.1 /hr (-16.5, 18.4)						

Table 1.3.2. Type IV monitors (2 channels) vs. PSG: study results (continued)

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis				Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
Heneghan 2008[80] 18595434	Holter ECG analysis algorithm	92	Sleep lab	nd	Data not interpretable from figure	≥15	≥15	92 (nd)	69 (nd)		B
						≥5 - <15	≥5 - <15	60 § (nd)	86 (nd)		
						< 5	< 5	37 (nd)	95 (nd)		
Szyszko 2009[89] 18971289	Holter Monitor	20	Sleep lab	95% LOA	4.7 (-30.1, 39.4)	RDI ≥10	AHI ≥10	78.5 (48.2, 94.2)	83.3 (25.8, 89.7)	0.81	A
White 1994[91] 7923843	O_2 saturation & snoring sound vs PSG	37	Sleep lab			nd	AHI≥10	62	100		C
						nd	AHI≥15	86	78		
						nd	AHI≥20	100	76		

* Apnea: Reduction of inspiratory airflow by 80% to 100% over 10 secs (max 80 ss); Hypopnea: Reduction of tidal breathing of 50% from baseline tidal breathing lasting (Max100 secs)
† Sandman Sleep Diagnostic System setting - Apnea: 85% or more reduction of normal flow that lasts (max 100 s); Hypopnea: 40% reduction of normal flow lasting 10 s (max 120 s)
‡ Using home-based PSG (Embletta)
§ Calculated from data provided
** Estimated CI from Figure of plot in the publication, using the Engauge Digitizer software program

Table 1.3.3. Type IV monitors (1 channel) vs. PSG: study results

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis				Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
Erman 2007[78] 17694728	ApneaLink	58	Lab	95% LOA	~ -2 (-22, 18) *	AHI >5	AHI >5	85.4 (nd)	50.0 (nd)	0.863	A
						AHI >10	AHI >10	82.1 (nd)	83.9 (nd)	0.862	
						AHI >15	AHI >15	90.9 (nd)	94.6 (nd)	0.977	
						AHI >20	AHI >20	83.3 (nd)	92.7 (nd)	0.967	
de Almeida 2006[77] 16502297	Sleep Check	30	Sleep lab	95% LOA	0 (-26.6, 26.6)	>5	>5	86.4	75	0.886	B
						>10	>10	85.7	87.5	0.915	
						>15	>15	83.5	83.5	0.898	
						>20	>20	88.9	81	0.910	
Nakano 2008[82] 18480104	SOMNIE single-channel airflow monitor	100	Home	95% LOA	-9.5 (-30.4,11.4)	>5.3	>5	96 (91,100)	82 (59,100)	0.95	A
						>11.4	>15	91 (84, 98)	82 (70, 95)	0.96	
						>19.6	>30	89 (80, 97)	96 (90,100)	0.98	
			Female			>5.3	>5	88 (nd)	67 (nd)	0.88	
						>11.4	>15	75 (nd)	83 (nd)	0.89	
						>19.6	>30	100	94 (nd)	1.0	
			BMI <25 kg/m^2			>5.3	>5	97 (nd)	71 (nd)	0.94	
						>11.4	>15	78 (nd)	89 (nd)	0.92	
						>19.6	>30	91 (nd)	92 (nd)	0.97	
			AHI <15			>5.3	>5	83 (nd)	82 (nd)	0.81	
Watkins 2009[90] 19786903	RUSleeping RTS vs. PSG	34	Sleep lab & Community			>5	>15	100	42		C
						>10	>15	100	71		
						>15	>15	70	83		
						>20	>15	70	83		
						>30	>15	43	96		

Table 1.3.3. Type IV monitors (1 channel) vs. PSG: study results (continued)

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis					Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
Wong 2008[92] 18411561	FlowWizard in lab vs PSG	31	Sleep lab	95% LOA	1.8 (-32.4, 36.0)	AHI>18	AHI≥10	96	71	0.95	A
	FlowWizard at home (3 night average) vs PSG	31	Sleep lab & Home		7.1 (-14.8, 29.0)	AHI>8	AHI≥10	100	43	0.96	
						AHI>12		96	71		
						AHI>18		92	86		
						AHI>21		88	100		
						AHI>21	AHI≥30	100	50	0.85	
						AHI>28		91	75		
						AHI>45		36	90		
						AHI>59		18	100		
						AHI from first night on FlowWizard	AHI≥30			0.89	
	FlowWizard at home (1 night) vs PSG	31	Sleep lab & Home			AHI from first night on FlowWizard	AHI≥10			0.92	
	MAPI v PSG	31	Sleep lab & Home				AHI≥10			0.68	
	Combined FlowWizard (home, 3 night) & MAPI v PSG	31	Sleep lab & Home				AHI≥10			0.96	

Table 1.3.3. Type IV monitors (1 channel) vs. PSG: study results (continued)

Study PMID	Index Test (vs PSG)	N	Setting	Bland-Altman		ROC Analysis				Quality
				Metric	Result, events/hr	Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
Nigro 2009[83] 18830731	O_2 saturation (WristOx 3100)	154	Sleep lab			ADI2 † >12.2	AHI ≥5	100 (96.4, 100)	57.69 (43.2, 71.3)	0.959	B
						ADI2 >19.3	AHI ≥5	89.22 (81.5, 94.5)	94.23 (84.0, 98.7)		
						ADI5 >4.3	AHI ≥5	92.75 (52.6, 72.1)	100 (93.1, 100)	0.907	
						ADI2 >12.2	AHI ≥10	100 (95.8, 100)	44.12 (32.1, 56.7)	0.957	
						ADI3 >10.5	AHI ≥10	88.37 (79.6, 94.3)	94.12 (85.6, 98.3)	0.965	
						ADI5 >4.3	AHI ≥10	74.42 (63.9, 83.2)	100 (94.7, 100)	0.930	
						ADI3 >4.4	AHI ≥15	100 (95.0, 100)	49.38 (38.1, 60.7)	0.945	
						ADI3 >13.4	AHI ≥15	87.67 (77.9, 94.2)	90.12 (81.5, 95.6)		
						ADI3 >32	AHI ≥15	42.47 (31.0, 54.6)	100 (95.5, 100)		
White 1994[91] 7923843	O_2 saturation vs PSG	37	Sleep lab			nd	AHI≥10	30	100		C
						nd	AHI≥15	71	94		
						nd	AHI≥20	100	94		
Reda 2001[86] 11593166	Pharyngoesophageal monitoring	59	Sleep lab	95% LOA	0.22 (-8.68, 9.02)	<15	<15	100 (nd)	100 (nd)		C
						15-20	15-20	80 (nd)	96 (nd)		
				95% CI	(-0.93, 1.38)	20-40	20-40	90 (nd)	97 (nd)		
						>40	>40	100 (nd)	100 (nd)		
Agatsuma, 2009[94] 19818056 ‡	SD-101 (Resp. effort) vs PSG	366	Sleep Lab and Home	95% CI	-4.7 (-19.7, 10.4)	12.4	≥ 5	87.5 (nd)	88 (nd)	0.96	C
						18.6	≥ 15	89.7 (nd)	90.5 (nd)	0.97	

* Estimated from Figure of plot in the publication, using the Engauge Digitizer software program

† ADI - Adjusted O_2 desaturation index (ADI): mean number of O_2 desaturations per hour of analyzed recording ≥2%, 3%, 5% (ADI2, ADI3, ADI5)

‡ Results from the two separate groups were reported but not presented.

Table 1.4.1. Questionnaires vs. PSG: study characteristics

Study PMID	Participants	Country (years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Quality issues
Chung, 2008[36] 18431116	Preoperative	Canada (nd)	211	20 (6) [nd]	nd	55	50	30	Hospital	AHI>5	Selection bias
Chung, 2008[97] 18431117	Preoperative	Canada (nd)	211	20 (6) [nd]	nd	55	50	30	Hospital	AHI>5	Selection bias
Kapuniai, 1988[98] 3227223	Sleep disorder center	US (nd)	53	nd	nd	46	79	nd	Sleep lab	AI / AHI >5	PSG results not reported
Netzer, 1999[99] 10507956	General population visiting primary care physician	US (nd)	1008	High-risk group: 21 (18) [0, 101] Low-risk group: 5 (7) [0, 37]	nd	49	42	29	Home	RDI ≥5	Probable selection bias
Sharma, 2006[100] 17085831	Attending the medical outpatient department	India (2000-02)	180	nd	nd	40	80	28.2	Sleep lab and hospital	AHI >5	Modified questionnaire not validated, 42% dropout rate
Drager, 2010[101] 20381666	Patiens attending a hypertension clinic of a hoslital	Brazil (2009)	99	7.9 (2.3,29.1)	9 (5)	46	53	28.8 * *	Hospital	AHI > 5	None †

* Median

† No quality issues in reporting. The study was not primarily designed to evaluate the two instruments; the study assessed the association of various clinical factors with the risk for OSA. The sensitivity and specificity for the index tests was reported, along with other anthropometric and clinical indicators.

Table 1.4.2. Questionnaires vs. PSG: study results

Study PMID	Index test	Reference test	N	Setting	Bland-Altman		ROC Analysis				Quality
					Metric[A]	Result	Threshold, events/hr		Sensitivity (95% CI)	Specificity (95% CI)	AUC	
							Index	PSG				
Chung, 2008[36] 18431116	STOP	PSG	177	Sleep lab			High vs. low	>5	65.6 (56.4, 73.9)	60 (45.9, 73.0)	0.703	C
								>15	74.3 (62.4, 84.0)	53.3 (43.4, 63.0)	0.722	
								>30	79.5 (63.5, 90.7)	48.6 (40.0, 63.0)	0.769	
	STOP-Bang						High vs. low	>5	83.6 (75.8, 89.7)	56.4 (42.3, 69.7)	0.806	
								>15	92.9 (84.1, 97.6)	43 (33.5, 52.9)	0.782	
								>30	100 (91.0, 100.0)	37 (28.9, 45.6)	0.822	
Chung, 2008[97] 18431117	Berlin	PSG	211	Sleep lab			High vs. low	>5	68.9 (59.8, 76.9)	56.4 (42.3, 69.7)	0.69	C
								>15	78.6 (67.1, 87.5)	50.5 (40.6, 62.3)	0.672	
								>30	87.2 (72.6, 95.7)	46.4 (37.9, 55.1)	0.668	
	ASA checklist						High vs. low	>5	72.1 (63.3, 79.9)	38.2 (25.4, 52.3)	0.783	
								>15	78.6 (67.1, 87.5)	37.4 (28.2, 47.3)	0.73	
								>30	87.2 (72.6, 95.7)	36.2 (28.2, 44.8)	0.617	
Kapuniai, 1988[98] 3227223	Apnea score derived from the Hawaii Sleep Questionnaire*	PSG	53	Sleep lab			≥3	>5	59 (nd)	69 (nd)		B
							≥2 (no adenoidectomy score)	>5	70 (nd)	65 (nd)		
							≥2 (no adenoidectomy score)	>10	78 (nd)	67 (nd)		
Netzer, 1999[99] 10507956	Berlin	PSG	100	Home			High-risk (high risk in 2/3 categories) vs. low-risk †	≤ 5	77 (nd)	89 (nd)		C
								>5	86 (nd)	77 (nd)		
								>15	54 (nd)	97 (nd)		
								>30	17 (nd)	97 (nd)		
Sharma, 2006[100] 17085831	Berlin Questionnaire, ‡ modified	PSG	104	Sleep lab & Hospital			High risk vs. low risk	>5	86 (nd)	95 (nd)		C
Drager, 2010[101] 20381666	Berlin Questionnaire	PSG	99	Hospital			High risk vs. low risk	≥ 5	93 (82,98)	59 (43,73)		A
	ESS						10	≥ 5	49 (36,63)	80 (64,90)		

* The HSQ includes questions on characteristics in sleep apnea patients: (a) stopping breathing during sleep, (b) loud snoring, and (c) waking from sleep gasping or short of breath. Additional questions on sex, age, height, weight, sleep history and history of tonsillectomy or adenoidectomy. The final model included self-reports of loud snoring, breathing cessation during sleep and adenoidectomy.

† High Risk: classified as "high risk" in 2 of 3 symptom categories - (a) snoring (b) wake time sleepiness and drowsy driving (c) hr/o high blood pressure or BMI >30 kg/m^2; Low Risk: all others.

‡ The Berlin Questionnaire was customized to the Indian setting (re: questions on driving) but the scoring remained the same. The screening questionnaire used was not a validated one.

Table 1.5.1. Clinical prediction rules vs. PSG: study characteristics

Study PMID	Participants	Country (years)	N	Baseline AHI (SD) [range]	Baseline ESS (SD)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Setting	Sleep Apnea Definition	Quality Issues
Crocker, 1990[102] 2368960	Referred for suspected abnormal breathing	Australia (1987-88)	114	nd	nd	51	82	30.4	Sleep lab	AHI >15	Baseline AHI severity not reported
Gurubhagavatula, 2001[103] 11734444	Referred for suspected OSA	US (nd)	421	26 (30) [nd]	nd	47	68	32.4	Sleep lab	RDI ≥5	
Kushida, 1997[104] 9341055	Referred for sleep disorders	US (nd)	423	35 [nd]	10.9	47	75	32	Sleep lab	RDI ≥5	Selection bias; 29% dropout rate
Onen, 2008[105] 18775037	Elderly (≥70 y) referred to a sleep center	France (2005-06)	121	nd	nd	79	50	29.4	Sleep lab & Hospital	AHI ≥15	Incomplete ROC data; other thresholds not reported
Rodsutti, 2004[106] 15283004	Referred for suspected sleep-disordered breathing	Australia (2003)	243	nd	nd	51	63	32.8	Sleep lab	AHI ≥5	
Rowley, 2000[107] 11083602	Referred for sleep-disordered breathing	US (1996-97)	425	19 (7-52) *	nd	Median 47	52	37.1	Sleep lab	AHI ≥10	
Zerah-Lancner, 2000[108] 11112139	Referred for snoring and suspected sleep apnea	France (nd)	101	Group with AHI <15: 6 (4) Group with AHI≥15: 42 (24)	nd	nd	nd	28.8	Sleep lab	AHI ≥15	Unclear description of population

* Median and inter-quartile range

Table 1.5.2. Clinical prediction rules vs. PSG: study results

Study PMID	Index test	Reference test	N	Setting	Subgroup	ROC Analysis					Quality
						Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Crocker, 1990[102] 2368960	Statistical model *	PSG	105	Sleep lab		Probability of OSA >0.15	>15	92 (nd)	51 (nd)		B
Gurubhagavatula, 2001[103] 11734444	Clinical prediction rule, † derived	PSG	359	Sleep lab		Upper bound= 0.58 Lower bound= 0.14 ODI threshold= 5.02	≥5	94.1 (nd)	66.7 (nd)		A
						Upper bound = 0.9 Lower bound = 0.38 ODI threshold = 21	≥30	83.3 (nd)	94.7 (nd)		
Kushida, 1997[104] 9341055	Morphometric model ‡	PSG	300	Sleep lab		≥70	≥5	97.6 (95, 98.9)	100 (92,100)	0.996	C
Onen, 2008[105] 18775037	Observation-based Nocturnal Sleep Inventory (ONSI) §	PSG	115	Hospital		≥2 snoring episodes or ≥1 apnea episode	AHI≥15	89.7 (82, 97)	81.4 (70,93)		B
						≥5 snoring or ≥1 apnea	AHI≥15	56 (44, 68)	100		
						≥3 snoring or ≥1 apnea	AHI≥15	74 (63, 84)	93 (85,100)		
Rodsutti, 2004[106] 15283004	Clinical prediction rule, ** derived	PSG	243	Sleep lab		< 2.5	≥5	0 (nd)	89 (nd)	0.789	A
						2.5 - < 4.2	≥5	44 (nd)	85 (nd)		
						≥4.2	≥5	76 (nd)	60 (nd)		

Table 1.5.2. Clinical prediction rules vs. PSG: study results (continued)

Study PMID	Index test	Reference test	N	Setting	Subgroup	ROC Analysis					Quality
						Threshold, events/hr		Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC	
						Index	PSG				
Rowley, 2000[107] 11083602	Model #1 ††	PSG	370	Sleep lab	All	0.15	≥10	84 (nd)	39 (nd)	0.669	A
						0.95	≥20	33 (nd)	90 (nd)	0.7	
					Men	0.15	≥10			0.761	
					Women	0.15	≥10			0.633	
	Model #2 ‡‡				All	0.20	≥10	96 (nd)	13 (nd)	0.695	
						0.95	≥20	34 (nd)	87 (nd)	0.722	
					Men	0.2	≥10			0.801	
					Women	0.2	≥10			0.626	
	Model #3 §§				All	10	≥10	76 (nd)	54 (nd)	0.696	
						35	≥20	34 (nd)	89 (nd)	0.733	
					Men	10	≥10			0.707	
					Women	10	≥10			0.648	
	Model #4 ***				All	0.5	≥10	87 (nd)	35 (nd)	0.736	
						0.85	≥20	39 (nd)	93 (nd)	0.757	
					Men	0.5	≥10			0.801	
					Women	0.5	≥10			0.611	
Zerah-Lancner, 2000[108] 11112139	Based on Pulmonary function data †††	PSG	101	Sleep Lab		0.5	≥15	100 (nd)	84 (nd)		B

Bland-Altman column omitted. No study reported Bland-Altman data.

* Derived by logistic regression on data from a 24-item questionnaire and clinical features.

† Combination of Multivariable Apnea Prediction (MAP) questionnaire score and oximetry results. MAP score predicts apnea risk using a score between 0 and 1, with 0 representing low risk and 1 representing high risk. Oximetry desaturation index (ODI) using a 3% drop (ODI3) as well as a 4% drop (ODI4) in oxygen saturation. Optimal model parameters obtained by the bootstrapping technique.

‡ Model: P + (Mx - Mn) + 3 X OJ + 3 X [Max (BMI -25, 0)] X (NC / BMI)

P = palatal height (in millimeters); Mx is the maxillary intermolar distance (in millimeters) between the mesial surfaces of the crowns of the maxillary second molars; Mn is the mandibular intermolar distance (in millimeters) between the mesial surfaces of the crowns of the mandibular second molars; OJ is the overjet (in millimeters) or the horizontal overlap of the crowns of the maxillary and mandibular right central incisors; BMI is the body mass index (kg/m2; ideal BMI < 25); Max (BMI -25, 0) refers to the larger of the two quantities: BMI - 25, or zero. If BMI is <= 25, then [Max (BMI - 25, 0)] is zero; if BMI >25, then BMI - 25 is inserted into the formula; NC is neck circumference (in centimeters) measured at the level of the cricothyroid membrane.

§ Nurse observations made in five standardized hourly bedside visits over the course of one night.

** Sum of the individual scores for age, sex, snoring, stops breathing, and BMI; range = 0 -7.3.

†† Clinical prediction model #1: Probability of predicting AHI ≥10 = $1/ (1 + e^{-(-13.9+0.06a+2.98b+0.23c+1.35d)})$ where a = age; b= I if witnessed apneas present, 0 if witnessed apneas absent; c = BMI; d = 1 if patient has hypertension, 0 if hypertension absent.

‡‡ Clinical prediction model #2: Probability of predicting AHI ≥10 = $e^{x}/ (1+e^{x})$ where, x = -10.5132 + 0.9164*sex + 0.0470*age + 0.1869*BMI+1.932*snoring; where sex = 1 for male, 0 for female, snoring = 1 for present, 0 for absent.

§§ Clinical prediction model #3: Probability of predicting AHI $\geq 10 = (10^{(-2.132 + 0.069*NC + 0.31*H + 0.206'*HS + 0.224*PR)} + 1)$ where NC=neck circumference; H=1 if hypertension, 0 if hypertension absent, HS=1 if habitual snorer, 0 if not, PR = 1 if reports nocturnal choking/gasping, 0 if no nocturnal choking/gasping.

*** Clinical prediction model #4: Probability of predicting AHI $\geq 10 = e^x / (1+e^x)$ where, x = -8.160+1.299*Index1+O.163*BMI-0.025*BMI*Index1+0.032*age +1.278*sex where, sex=1 if male, 0 if female, index1 = the mean of non-missing values for frequency of snorting/gasping; loud snoring; breathing stops/chokes.

††† Probability (p) of having a polysomnography positive for SAS: logit (p)= -136 sGrs + 2.5 (100 - SaO_2) + 4.2 where specific respiratory conductance (sGrs) (in $cmH_20^{-1} * s^{-1}$) = respiratory conductance (Grs) / functional reserve capacity (FRC) SaO_2 = daytime arterial oxygen saturation in %. The estimated value of p was derived from logit (p)= $\log_e(p/1-p)$, from 0 to 1 range.

Table 3.1. Comparative studies of preoperative sleep apnea screening prior to surgical intervention: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Hallowell, 2007[110] 17950355	Mandatory PSG PSG based on ESS or clinical suspicion	43	13	51	Patients who have undergone bariatric surgery	US (1998-2005)	Selection bias; discrepancy in reporting of results
Chung, 2008[97] 18431117	PSG No PSG	55	51	30.1	All pre-op patients in general surgery, gynecology, orthopedics, urology, plastic surgery, ophthalmology, or neurosurgery	Canada (nd)	Selection bias in participants who underwent PSG

Table 3.2. Duration of hospital stay (hr) in comparative studies of preoperative PSG testing

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Diff	95% CI	P Btw	Dropout, %	Study Quality
Hallowell, 2007[110] 17950355	nd	nd	Immediate postoperative (retrospective chart review)	Mandatory PSG	318	nd	74.4 (2.4)	-9.6	nd	nd	0	C
				PSG only after clinical indications	576	nd	84.0 (4.8)					
Chung, 2008[97] 18431117	20 (6) [nd]	nd	30 d (prospective case series)	Accepted preoperative PSG	211	nd	Median 44.8 (IQR: 0.2–352.8)	+15.5 (difference of medians)	nd	NS	0	C
				Refused preoperative PSG	205	nd	Median 29.3 (IQR: 0.1–299.8)					

Table 3.3. Postsurgical outcomes in comparative studies of preoperative screening with PSG

Study PMID	Outcome	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	n Event	N Total	Outcome metric	Result *	95% CI	P Btw	Dropout, %	Study Quality
Hallowell, 2007[110] 17950355	ICU admission	nd	nd	Immediate post-operative (retro-spective chart review)	Mandatory PSG	11	318	RR	0.62	0.32, 1.22	nd	0	C
					Indicated PSG	32	576						
	Respiratory related ICU admission				Mandatory PSG	1	318	RR	0.16	0.02, 1.27	nd		
					Indicated PSG	11	576						
Chung, 2008[97] 18431117	ICU admission	20 (6) [nd]	nd	30 d (case series)	Preop PSG	13	211	RR	3.16	1.05, 9.52	nd	0	C
					No Preop PSG	4	205						
	Total complications				Preop PSG	48	211	RR	1.55	1.03, 2.35	0.03		
					No Preop PSG	30	205						
	Respiratory complication				Preop PSG	39	211	RR	1.52	0.95, 2.41	0.08		
					No Preop PSG	25	205						
	Cardiac complication				Preop PSG	12	211	RR	1.94	0.74, 5.08	0.11		
					No Preop PSG	6	205						
	Neurologic complication				Preop PSG	2	211	RR	0.65	0.11, 3.84	0.68		
					No Preop PSG	3	205						
	Prolonged O_2 therapy				Preop PSG	24	211	RR	1.46	0.80, 2.66	0.22		
					No Preop PSG	16	205						
	Additional monitoring				Preop PSG	9	211	RR	1.46	0.53, 4.02	0.46		
					No Preop PSG	6	205						
	Readmission within 30 d				Preop PSG	4	211	RR	0.78	0.21, 2.85	0.75		
					No Preop PSG	5	205						
	ED visit within 30 d				Preop PSG	1	211	RR	0.24	0.03, 2.15	0.21		
					No Preop PSG	4	205						

* Top row intervention vs. bottom row intervention. Calculated from reported data.

Table 4.1. Multivariable analyses of AHI as a predictor of all-cause mortality: study characteristics

Study PMID	Design Country (study years)	eligibility	N (followup)	Factor	Value	Quality
Lavie 2005[111] 15738297	Retrospective Israel (1991-2000)	Men, >20 yr, OSA symptoms	13,853 (4.7 yr)	**Male**	100%	A
				Age	48 yr	
				BMI (kg/m^2)	28.8	
Punjabi 2009[2] 19688045	Prospective US (1995-1998)	≥40 yr, no Tx	6441 (8.2 yr)	**Male**	47%	B
				Age	63 yr	
				BMI	28.4	
Young 2008[1] 18714778	Prospective US (1988-nd)	General population	1522 (14 yr)	**Male**	55%	A
				Age	48 yr	
				BMI	28.6	
Lavie 1995[112] 7610310	Retrospective Israel (1976-1988)	Men, apnea index ≥10	1140 (2-14 yr)	**Male**	100%	A
				Age	48 yr	
				BMI	nd	

Table 4.2. Results of multivariable analyses of AHI as a predictor of all-cause mortality

Study PMID	Baseline AHI	n/	N	Adjusted HR	95% CI	P Trend	Other Predictors: Significant	P	NS	nd P *	NS Univariable †	Interactions
Lavie	≤10	34/	3227	Ref		0.0001				Age		nd
2005[111]	11-20	88/	4154	1.52	NS					BMI (kg/m^2)		
15738297	21-30	65/	2601	1.34	NS							
	31-40	50/	1204	2.13	1.36-3.34							
	>40	126/	2667	2.59	1.73-3.87							
Punjabi	**All**						Age	<0.05	Cholesterol	Sex		No substantive difference with addition of other predictors Interaction of Age x AHI significant P<0.005 Interaction of Sex x AHI implied
2009[2]	<5	477/	3429	Ref		<0.05 ‡				Race		
SHHS	5-15	320/	1797	0.93	0.80-1.08					BMI		
19688045	15-30	165/	727	1.17	0.97-1.42					Smoking		
	≥30	86/	341	1.46	1.14-1.86					BP		
	Men≤70 §									HTN		
	<5	91/	985	Ref		<0.05 **				Diabetes		
	5-15	82/	694	1.24	0.90-1.71					CVD		
	15-30	47/	322	1.45	0.98-2.14							
	≥30	28/	168	2.09	1.31-3.33							
	Men>70											
	<5	125/	277	Ref		NS						
	5-15	111/	282	0.92	0.70-1.20							
	15-30	67/	140	1.23	0.90-1.68							
	≥30	36/	75	1.27	0.86-1.86							
	Women											
	<5	261/	2167	Ref		NS						
	5-15	126/	821	0.83	0.66-1.04							
	15-30	51/	265	1.01	0.73-1.38							
	≥30	22/	99	1.40	0.89-2.22							
Young,	<5	46/	1157	Ref		0.008			Age			nd
2008[1]	5-15	16/	220	1.6	0.9-2.8				Sex			
WSCS	15-30	6/	82	1.4	0.6-3.3				BMI (kg/m^2)			
18714778	≥30	12/	63	3.0	1.4-6.3							
Lavie 1995[112] 7610310	Per unit ††	51/	1140	OR=1.012	1.001 - 1.024	0.04	Older age	0.0001	Diabetes			No substantive difference with addition of comorbidities
							Higher BMI	0.006				
							HTN	0.009				
							CVD	<0.04				
							Lung dz	<0.01				

* Included in multivariable analysis. No data on whether statistically significant independent predictor.
† Not statistically significant in univariable analysis. Not included in multivariable analysis.
‡ Implied
§ Results also reported for all men combined, and women divided above and below age 70 yr.
** Implied
†† Analyzed in a multivariable logistic regression with apnea index (continuous) included as a predictor.

Table 4.3. Multivariable analyses of AHI as a predictor of cardiovascular events: study characteristics

Study PMID	Design Country (study years)	eligibility	N (followup)	Factor	Value	Quality
CVD Death						
Marin 2005[6] 15781100	Prospective Spain (1992-1994)	Men, healthy w/ SDB	1651 (10 yr)	**Male**	100%	A
				Age	50 yr	
				BMI (kg/m^2)	28.7	
Young, 2008[1] 18714778	Prospective US (1988-nd)	General population	1522 (14 yr)	**Male**	55%	A
				Age	48 yr	
				BMI	28.6	
Nonfatal CVD						
Marin 2005[6] 15781100	Prospective Spain (1992-1994)	Men, healthy w/ SDB	1651 (10 yr)	**Male**	100%	A
				Age	50 yr	
				BMI	28.7	
Stroke						
Arzt 2005[113] 16141444	Prospective US (≥1988)	30-60 yr, no stroke	1475 (4, 8, 12 yr)	**Male**	55%	B
				Age	47 yr	
				BMI	30	

Table 4.4. Results of multivariable analyses of AHI as a predictor of cardiovascular events

Study PMID	Baseline AHI	n/	N	Adjusted HR	95% CI	P trend	Other Predictors					
							Significant	P	NS	nd P*	NS Univariable †	Interactions
CVD Death												
Marin, 2005[6] 15781100	"Healthy"	12/	264	Ref		nd	Older age	0.001	HTN		BMI (implied) (kg/m^2)	No substantive difference in AHI with or without CVD and HTN in model
	<5	22/	377	1.03	0.31, 1.84		CVD	0.02	Diabetes			
	5-30	36/	403	1.15	0.34, 2.69		Higher SBP	0.04	Dyslipidemia			
	≥30	50/	235	2.87	1.17, 7.51		Smoker	0.04	Alcohol use			
	CPAP	24/	372	1.05	0.39, 2.21				DBP			
									Glucose			
									TC & Tg			
									Prescriptions ‡			
Young, 2008[1] WSCS 18714778	<5	12/	1157	Ref		0.12			Age			nd
	5-15	6/	220	1.8	0.7, 4.9				Sex			
	15-30	2/	82	1.2	0.3, 5.8				BMI (kg/m^2)			
	≥30	5/	63	2.9	0.8, 10.0							
Nonfatal CVD												
Marin, 2005[6] 15781100	"Healthy"	8/	264	Ref		nd	Older age	0.001	HTN		BMI (implied) (kg/m^2)	No substantive difference in AHI with or without CVD and HTN in model
	<5	13/	377	1.32	0.64, 3.01		CVD	0.005	Diabetes			
	5-30	22/	403	1.57	0.62, 3.16				Dyslipidemia			
	≥30	25/	235	3.17	1.12, 7.52				Smoking			
	CPAP	13/	372	1.42	0.52, 3.40				Alcohol use			
									BP			
									Glucose			
									TC & Tg			
									Prescriptions §			
Stroke												
Arzt, 2005[113] 16141444	<5	9/	1121	Ref		nd				Age		AHI≥20 significant w/o BMI in model
	5-20	1/	255	0.29	0.04, 2.36					Sex		
	≥20	4/	99	3.08	0.74, 13.0					BMI		

* Included in multivariable analysis. No data on whether statistically significant independent predictor.
† Not statistically significant in univariable analysis. Not included in multivariable analysis.
‡ Antihypertensive, lipid-lowering, and antidiabetic drugs.
§ Antihypertensive, lipid-lowering, and antidiabetic drugs.

Table 4.5. Multivariable analyses of AHI as a predictor of incident HTN: study characteristics

Study PMID	Design Country (study years)	eligibility	N (followup)	Factor	Value	Quality
O'Connor 2009[114] 19264976	Prospective US (1995-1998)	≥40 y	2470 (5 yr)	**Male**	45%	A
				Age	60 yr	
				BMI (kg/m^2)	27.9	
Peppard 2000[11] 10805822	Prospective US (1989-1995)	No CVD	709 (4, 8 yr)	**Male**	46%	B
				Age	47 yr	
				BMI	29	

Table 4.6. Results of multivariable analyses of AHI as a predictor of incident HTN

Study PMID	Baseline AHI	n/	N	Adjusted OR	95% CI	P Trend	Other Predictors: Significant P	NS	nd P *	NS Univariable †	Interactions
O'Connor 2009[114] SHHS 19264976	**All**										
	<5	**296/**	**1510**	**Ref**		NS			Age		AHI significant without BMI in model.
	5-15	156/	629	0.94	0.73-1.22				Sex		
	15-30	77/	234	1.09	0.77-1.54				Race		
	≥30	33/	97	1.50	0.91-2.46				BMI		No substantive change with WHR or girth
									WHR		
									Neck girth		
	Men										AHI x sex interaction term NS P=0.09
	<5	nd	**505**	**Ref**		nd			Age		
	5-15	nd	341	0.96	0.68-1.36				Race		
	15-30	nd	155	0.89	0.57-1.39				BMI (kg/m^2)		
	≥30	nd	56	1.10	0.57-2.10						
	Women										
	<5	nd	**950**	**Ref**		nd					
	5-15	nd	261	0.83	0.59-1.18						
	15-30	nd	72	1.59	0.95-2.64						
	≥30	nd	31	2.27	1.07-4.80						
	BMI≤27.3										AHI x BMI interaction term NS P=0.36
	<5	nd	**887**	**Ref**		nd			Age		
	5-15	nd	213	0.89	0.59-1.34				Sex		
	15-30	nd	58	0.93	0.46-1.90				Race		
	≥30	nd	21	2.71	1.24-5.93				BMI		
	BMI>27.3										
	<5	nd	541	Ref		nd					
	5-15	nd	378	0.92	0.67-1.27						
	15-30	nd	164	1.13	0.76-1.68						
	≥30	nd	65	1.18	0.64-2.19						
	Age≤59 yr										No difference in association stratified by age
	<5	nd	**879**	**Ref**		nd			Sex		
	5-15	nd	262	1.02	0.70-1.50				Race		
	15-30	nd	96	1.79	1.08-2.95				BMI		
	≥30	nd	33	1.47	0.64-3.37						
	Age>59 yr										
	<5	nd	576	Ref		nd					
	5-15	nd	340	0.85	0.62-1.16						
	15-30	nd	131	0.82	0.53-1.26						
	≥30	nd	54	1.53	0.84-2.79						

Table 4.6. Results of multivariable analyses of AHI as a predictor of incident HTN (continued)

Study PMID	Baseline AHI	n/	N	Adjusted OR	95% CI	P Trend	Other Predictors					
							Significant P	NS	nd P ‡	NS Univariable §	Interactions
O'Connor SHHS 2009[114] (cont.)	**ESS≤11**											
	<5	nd	**1189**	**Ref**		nd			Age Sex Race BMI (kg/m^2)		AHI x ESS interaction term NS P=0.11
	5-15	nd	472	0.83	0.63-1.09						
	15-30	nd	178	0.90	0.62-1.31						
	≥30	nd	58	1.57	0.87-2.83						
	ESS>11										
	<5	nd	221	Ref		nd					
	5-15	nd	119	1.31	0.72-2.38						
	15-30	nd	47	2.32	1.09-4.97						
	≥30	nd	27	1.50	0.58-3.85						
Peppard, 2000[11] WSCS 10805822	0	**32/**	**187**	**Ref**		0.002			Baseline HT N Age Sex BMI Neck girth Waist girth Alcohol use Smoking		No substantive changes in association with addition of predictors. No interaction terms were significant.
	<5	142/	507	1.42	1.13-1.78						
	5-15	64/	132	2.03	1.29-3.17						
	≥15	40/	67	2.89	1.46-5.64						

* Included in multivariable analysis. No data on whether statistically significant independent predictor.
† Not statistically significant in univariable analysis. Not included in multivariable analysis.
‡ Included in multivariable analysis. No data on whether statistically significant independent predictor.
§ Not statistically significant in univariable analysis. Not included in multivariable analysis.

Table 4.7. Multivariable analyses of AHI as a predictor in incident type 2 diabetes: study characteristics

Study PMID	Design Country (study years)	eligibility	N (followup)	Factor	Value	Quality
Reichmuth 2005[115] 16192452	Prospective US (1988)	30-60 yr, no DM	978 (4 yr)	**Male**	56%	B
				Age	49 yr	
				BMI (kg/m^2)	28.9	
Botros 2009[116] 19958890	Prospective US (2000-2005)	SDB, no DM	544 (2.7 yr)	**Male**	93%	A
				Age	62 yr	
				BMI	33.2	

Table 4.8. Results of multivariable analyses of AHI as a predictor in incident type 2 diabetes

Study PMID	Baseline AHI	n/	N	Adjusted OR/HR	95% CI	P trend	Other Predictors: Significant	P	NS	nd P *	NS Univariable †	Interactions
Reichmuth 2005[115] WSCS 16192452	<5	nd	nd	**Ref (OR)**		nd				Age, sex, waist girth		AHI significant w/o waist girth in the model
	5-15	nd	nd	1.56	0.80-3.02							
	≥15	nd	nd	1.62	0.67-3.65							
Botros 2009[116] 19958890	<8	6/	142	Ref (HR)		0.008	Glucose	<0.001	Age Sex Race BMI ‡			AHI similar with or without adjustment
	≥8	55/	402	1.43	1.10-1.86							

* Included in multivariable analysis. No data on whether statistically significant independent predictor.
† Not statistically significant in univariable analysis. Not included in multivariable analysis.
‡ Change in BMI during follow-up was statistically significant

Table 4.9. Multivariable analyses of AHI as a predictor of quality of life SF-36: study characteristics

Study PMID	Design Country (study years)	eligibility	N (followup)	Factor	Value	Quality
Silva 2009[117] 19725256	Prospective US (1995)	All	3078 (5 yr)	**Male**	45%	A
				Age	62 yr	
				BMI (kg/m^2)	28.7	

Table 4.10. Results of multivariable analyses of AHI as a predictor of quality of life (SF-36)

Study PMID	Baseline AHI	N	Score *	Adjusted RR	95% CI	P Trend	Other Predictors: Significant	P	NS	nd P †	NS Univariable ‡	Interactions
Silva 2009[117] 19725256	**PCS**			**Continuous**			Age, sleeping pills	<0.001, 0.003	BMI (kg/m^2), CHD, Resp dz, Smoking, Sex			nd
	<5	1662	49/48	1.008	nd	NS						
	5-15	893	48/46									
	15-30	339	47/45									
	≥30	154	45/44									
	MCS			**Continuous**			Smoking	0.02	Age, BMI, CHD, Resp dz, Sex			
	<5	1662	54/55	0.98	nd	NS						
	5-15	893	54/55									
	15-30	339	55/54									
	≥30	154	55/56									

* Baseline / Final

† Included in multivariable analysis. No data on whether statistically significant independent predictor.

‡ Not statistically significant in univariable analysis. Not included in multivariable analysis.

Table 5.1.1. Randomized clinical trials of CPAP vs. control: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Ballester 1999[118] 9927363	CPAP +conservative measures Conservative measures	Auto (separate)	53	88	32.7		Spain (nd)	No power calculation
Barbe 2010[130] 20007932	CPAP + conservative treatment Conservative treatment	Auto (Separate)	55	82	32	Hypertensive patients	Spain (2004-2006)	
Barnes 2004[140] 15201136	CPAP Placebo	nd (nd)	47	80	31.1		Australia (nd)	
Barnes 2002[131] 11897643	CPAP Placebo	nd (nd)	46	86	30.9		Australia (nd)	
Chakravorty 2002[119] 12449179	CPAP Lifestyle intervention	Auto (separate)	50	nd	37		UK (1998-1999)	No power calculation
Comondore 2009[132] 18795367	CPAP No treatment	Auto (nd)	56	69	31.1		Canada (nd)	Multiple comparisons in a small pilot study
Drager 2007[120] 17556718	C-flex CPAP No treatment	Manual (separate)	46	100	29.8	Severe OSA patients free of co-morbidities	Brazil (2004-2006)	
Engleman 1994[133] 7906330	CPAP Placebo	Manual (separate)	49	74	33		UK (nd)	Baseline data not reported, no wash out period, nd on blinding
Engleman 1996[134] 8843528	CPAP Placebo	Manual (separate)	51	85	36		UK (nd)	No power calculation
Engleman 1997[135] 9059469	CPAP Placebo	Manual (separate)	52	85	29.8		UK (nd)	Baseline data not reported, no wash out period, nd on blinding
Engleman 1998[136] 9708223	CPAP Placebo	Manual (separate)	47	91	30		UK (nd)	No adverse event data
Engleman 1999[137] 9927358	CPAP Placebo	Manual (separate)	44	62	30		UK (nd)	

Table 5.1.1. Randomized clinical trials of CPAP vs. control: study characteristics (continued)

Study PMID	Interventions	CPAP Pressure† (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Faccenda 2001[138] 11179104	CPAP Placebo	Auto (separate)	50	81	30		UK (nd)	No wash out period, but no measurements were made until 26 days after crossover; no power calculations reported.
Ip 2004[121] 14551167	CPAP No treatment	Manual (unclear)	43	100	29.4	Very healthy	Hong Kong (nd)	
Kajaste 2004[122] 15033131	CPAP No treatment	Manual (separate)	49	100	43.8	Obese male	Finland (nd)	No power calculation
Kaneko 2003[123] 12660387	CPAP Optimal drug treatment	Manual (separate)	56	88	31.4	Symptomatic, stable, optimally treated CHF	Canada (nd)	No power calculation
Lam 2007[129] 17121868	CPAP + conservative measures Conservative measures	nd (nd)	47	79	27.3		Hong Kong (nd)	
Lojander 1996[124] 8681614 Lojander 1999[125] 10188139	CPAP Conservative measures	Manual (separate)	51	93	31.1		Finland (1987-1992)	Large drop out; expert panel decided patients would be more suitable for nasal CPAP but no objective criteria stated
Mansfield 2004[126] 14597482	CPAP No treatment	Manual (separate)	58	95	33.5	Symptomatic, stable, optimally treated CHF	Australia (nd)	No power calculation
McArdle 2001[139] 11704596	CPAP Placebo	nd (separate)	53	87	31		Australia (nd)	
Monasterio 2001[127] 11587974	CPAP + conservative measures Conservative measures	Manual (separate)	54	86	29.4		Spain (nd)	Did not enroll enough to meet power calculations
Redline 1998[128] 9517603	CPAP Conservative measures	Manual (separate)	48	52	33		US (nd)	Power calculation: needed sample size -112; no. analyzed- 97

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

† Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.1.2. AHI (events/hr) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Lam 2007[129] 17121868	19 (17) [>5]	12.0 (8.8)	10 wk (PL)	CPAP + conservative measures	34	23.8 (16.7)	2.8 (9.7)	-22.2	-27.6, -16.7	<0.001	0	B
				Conservative measures	33	19.3 (16.7)	20.5 (21.9)					
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + conservative measures	66	20.0 (6.0)	6.0 (8.0)	-10	-12.8, -7.2	<0.001	12	C
				Conservative measures	59	21 (6.0)	17.0 (10.0)					
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0 (4.2)	3 mo (PL)	AutoCPAP	32	55 (28.7)	8 (28)	-46	-59.0, -32.9	<0.001	25	C
				Lifestyle intervention	21	35 (19.1)	34 (21)					
Mansfield 2004[126] 14597482	27 (21) [>5]	8.8 (0.9)	3 mo (PL)	CPAP	19	25 (17.9)	2.9 (3.5)	-13.7	-24.4, -3.0	0.012	27	C
				No treatment	21	26.6 (20.6)	18.2 (12.8)					
Ip 2004[121] 14551167	46 (15) [>15]	11.1 (6.2)	1 mo (PL)	CPAP	14	47.7 (15.3)	1.7 (1.8)	-16.8	-27.9, -5.7 †	0.003	7	C
				No treatment	14	45.1 (14.3)	15.9 (15.5)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	37.1 (22.2)	8.3 (9.9)	-28.3	-45.2, -11.4 ‡	0.001	0	C
				Optimal drug treatment	12	45.2 (18.4)	44.7 (23.6)					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	21.3 (11.6)	4.8 (4.5)	-15.5	-18.7, -12.2	<0.001	23	B
				Placebo			20.3 (9.8)					

* Estimated from reported data.
† Estimated from reported P value.
‡ Estimated from reported P value.

Table 5.1.3. ESS in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Barbe 2010[130] 20007932	43 (19) [>19]	6.4 (2.4)	12 mo (PL)	CPAP + conservative treatment	178	6.4 (2.3)	4.87 (nd)	-1.26	-1.9, -0.6	nd	4	B
				Conservative treatment	181	6.4 (2.4)	6.13 (nd)					
Ballester 1999[118] 9927363	58 (20) [>15]	11.4 (5.0)	3 mo (PL)	AutoCPAP + conservative measures	68	12.1 (8.2)	5.6 (nd)	-5.7	-8.1, -3.3	<0.001	0	B
				Conservative measures	37	11.4 (3.6)	10.6 (nd)					
Redline 1998[128] 9517603	12 (10) [>5]	10.6 (5.6)	10 wk (PL)	CPAP	51	10.4 (4.3)	nd	-1.1	-2.5, 0.3	nd	15	B
				Conservative measures	46	10.6 (5.6)	nd					
Lam 2007[129] 17121868	19 (17) [>5]	12.0 (8.8)	10 wk (PL)	CPAP + conservative measures	34	12 (8.8)	7 (8.8)	-3	-5.7, -0.2 †	0.034	0	B
				Conservative measures	33	12 (8.8)	10 (8.8)					
Drager 2007[120] 17556718	65 (22) [>30]	13.0 (5.0)	4 mo (PL)	C-Flex	12	14.0 (4.0)	7.0 (2.0)	-7	-10.2, -3.7	<0.001	0	B
				No treatment	12	13.0 (5.0)	13.0 (4.0)					
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + conservative measures	66	12.1 (4.9)	9.6 (5.5)	-1.1	-2.9, 0.7	NS	12	C
				Conservative measures	59	13.2 (4.3)	11.8 (5.2)					
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0(4.2)	3 mo (PL)	AutoCPAP	32	16 (5.6)	8 (6.4)	-5.0	-7.9, -2.1	0.001	25	C
				Lifestyle intervention	21	14 (4.2)	11 (5.0)					
Mansfield 2004[126] 14597482	27 (21) [>5]	8.8 (0.9)	3 mo (PL)	CPAP	19	9.5 (3.9)	6.9 (4.5)	-4.2 ‡	-7.4, -1.0 §	0.01	27	C
				No treatment	21	8.8 (3.9)	9.9 (4.5)					

Table 5.1.3. ESS in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI **	P Btw	Dropout, %	Study Quality
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	10.7 (3.6)	9.2 (3.6)	-1	-2.1, 0.1	NS	23	B
				Placebo			10.2 (3.6)					
Faccenda 2001[138] 11179104	35 (15-129) [>15]	15 (6-24)	1 mo (XO)	AutoCPAP	68	nd	10.1 (0.7)	-2.0	-3.2, -0.8 ††	0.001	5	B
				Placebo			12.5 (0.8)					
Engleman 1999[137] 9927358	10 (nd) [>5]	13.0 (3.0)	4 wk (XO)	CPAP	34	13.0 (3.0)	8.0 (4.0)	-3	-4.8, -1.2 ‡‡	0.001	8	B
				Placebo			11.0 (4.0)					
Engleman 1998[136] 9708223	43 (nd) [>15]	12.0 (4.0)	4wk (XO)	CPAP	23	12.0 (4.0)	6.0 (3.0)	-6	-9.5, -2.4 §§	0.001	0	B
				Placebo			12.0 (4.0)					
Barnes 2002[131] 11897643	13 (6) [>5]	11.3 (5.0)	8 wk (XO)	CPAP	28	11.2 (5.0)	-2.7 ***	-0.6	nd	NS	33	C
				Placebo			-2.1 †††					
Engleman 1997[135] 9059469	11 (4) [>5]	nd	4 wk (XO)	CPAP	16	nd	10.1 (5.6)	0.1	-3.5, 3.7	NS	11	C
				Placebo			10.0 (4.8)					

* Estimated from reported data
† Estimated from reported P value.
‡ Based on reported within-group changes.
§ Estimated from reported P value.
** Estimated from reported data
†† Estimated from reported P value.
‡‡ Estimated from reported P value.
§§ Estimated from reported P value.
*** Reported change.
††† Reported change.

Table 5.1.4a. Arousal index (events/hr) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Lam 2007[129] 17121868	19 (17) [>5]	12.0 (8.8)	10 wk (PL)	CPAP + conservative measures	34	21.6 (14.9)	16.3 (15.7)	-10.6	-16.3, -4.83	<0.001	0	B
				Conservative measures	33	23.5 (19.3)	28.8 (21.9)					
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0 (4.2)	3 mo (PL)	AutoCPAP	32	64.0 (28.0)	38.9 (28.6)	-9.8	-25.4, 4.9	nd	25	C
				Lifestyle intervention	21	52.2 (28.5)	36.9 (21.5)					
Ip 2004[121] 14551167	46 (15) [>15)	11.1 (6.2)	1 mo (PL)	CPAP	14	33.4 (17.2)	17.5 (10.7)	-17.6	-29.3, -5.9	0.003	7	C
				No treatment	14	33.8 (15.0)	35.5 (17.7)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	31.4 (21.1)	12.6 (5.9)	-18.0	-33.7, -2.3	0.025	0	C
				Optimal drug treatment	12	42.9 (19.1)	42.3 (21.5)					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	22.0 (10.7)	18.3 (8.0)	-6.9	-9.9, -3.8	<0.001	23	B
				Placebo			25.2 (9.8)					
McArdle 2001[139] 11704596	40 (25-65) [>15]	14.0 (10-17)	1 mo (XO)	CPAP	22	nd	21.0	-24.0	-38.3, -9.7 †	<0.001	4	B
				Placebo			45.0					

* Estimated from reported data.
† Estimated from reported P value.

Table 5.1.4b. Minimum O_2 saturation (%) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Lam 2007[129] 17121868	19 (17) [>5]	12.0 (8.8)	10 wk (PL)	CPAP + conservative measures	34	75.0 (12.3)	87.2 (25.4)	10.9	4.2, 17.7	0.002	0	B
				Conservative measures	33	76.1 (22.8)	77.4 (17.5)					
Mansfield 2004[126] 14597482	27 (21) [>5]	8.8 (0.9)	3 mo (PL)	CPAP	19	79.6 (11.3)	91.1 (3.9)	11.5	2.9, 20.1	0.008	27	C
				No treatment	21	77.2 (17.8)	77.2 (16.0)					
Ip 2004[121] 14551167	46 (15) [>15)	11.1 (6.2)	1 mo (PL)	CPAP	14	64.9 (11.9)	91.4 (2.6)	26.6	17.4, 35,8	<0.001	7	C
				No treatment	14	66.6 (12.2)	66.5 (15.0)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	82.3 (4.2)	89.6 (3.8)	8.8	2.2, 15.3	0.009	0	C
				Optimal drug treatment	12	78.4 (7.6)	76.9 (12.4)					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	86.7 (5.4)	91.9 (2.7)	6.5	4.9, 8.0	<0.001	23	B
				Placebo			85.4 (5.4)					

* Estimated from reported data

Table 5.1.4c. Sleep efficiency (% total sleep time) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	79.5 (9.83)	82.1 (7.15)	1.4	-1.4, 4.2	NS	23%	B
				Placebo tablets		79.5 (9.83)	80.7 (8.04)					
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0 (4.2)	3 mo (PL)	AutoCPAP	32	67.7 (18.2)	67.5 (15.7)	-3	-10.8, 4.8	nd	25	C
				Lifestyle intervention	21	71.6 (12.8)	74.4 (11.1)					

* Estimated from reported data

Table 5.1.4d. Slow wave sleep (% total sleep time or minutes) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0 (4.2)	3 mo (PL)	AutoCPAP	32	16.6% (nd)	21.0 (nd)	-1	nd	nd	25	C
				Lifestyle intervention	21	18.7% (nd)	22.0 (nd)					
				AutoCPAP	32	64.7 min (50.2)	69.5 (50.1)	0.7	-26.7, 28.1	nd		
				Lifestyle intervention	21	81.2 min (52.5)	85.3 (46.6)					
Mansfield 2004[126] 14597482	27 (21) [>5]	8.8 (0.9)	3 mo (PL)	CPAP	19	5% (4.4)	7.0 (8.7)	4.0	0.1, 7.9	0.046	27	C
				No treatment	21	6% (4.6)	4.0 (4.6)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	10.0% (9.0)	12.7 (11.4)	3.2	-5.5, 11.9	NS	0	C
				Optimal drug treatment	12	8.5% (10.4)	8.0 (3.5)					
McArdle 2001[139] 11704596	40 (25-65) [>15]	14 (10-17)	1 mo (XO)	CPAP	22	nd (min)	41.0 (nd)	18	4.9, 31.1 †	0.007	4	B
				Placebo			23.0 (nd)					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	17.9% (10.7)	20.7 (9.8)	2.2	-1.1, 5.5	NS	23	B
				Placebo			18.5 (10.7)					

* Estimated from reported data.
† Estimated from reported P value.

Table 5.1.4e. REM sleep (% total sleep time or minutes) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Chakravorty 2002[119] 12449179	35 (19) [>15]	14.0 (4.2)	3 mo (PL)	AutoCPAP	32	20.7% (nd)	24.9 (nd)	nd	nd	nd	25	C
				Lifestyle intervention	21	20.1% (nd)	23.9 (nd)					
				AutoCPAP	32	80.6 min (39.3)	81.9 (35.8)	-4.1	-27.2, 19.0	nd		
				Lifestyle intervention	21	87.1 min (40.5)	92.5 (47.8)					
Mansfield 2004[126] 14597482	27 (21) [>5]	8.8 (0.9)	3 mo (PL)	CPAP	19	14.0% (4.4)	13.0 (8.7)	0	-4,8, 4.8	NS	27	C
				No treatment	21	12.0% (9.2)	11.0 (4.6)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	7.7% (5.5)	12.2 (7.3)	5.9	-0.1, 11.9	NS	0	C
				Optimal drug treatment	12	13.2% (6.2)	11.6 (9.4)					
McArdle 2001[139] 11704596	40 (25-65) [>15]	14 (10-17)	1 mo (XO)	CPAP	22	nd (min)	86.0 (30.0)	12	-2.3, 26.3 †	NS	4	B
				Placebo			74.0 (29.0)					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	18.8% (6.2)	18.9 (4.4)	0	-1.8, 1.8	NS	23	B
				Placebo			18.9 (5.3)					

* Estimated from reported data.
† Estimated from reported P value.

Table 5.1.5a. Multiple sleep latency test (min) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Redline 1998[128] 9517603	12 (10) [>5]	10.6 (5.6)	10 wk (PL)	CPAP	51	9.9 (4.8)	nd	0.39	-1.7, 2.5	nd	15	B
				Conservative measures	46	10.3 (5.0)	nd					
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + Conservative measures	40	10.0 (5.0)	10.0 (5.0)	0	-2.2, 2.2	NS	12	C
				Conservative measures		11.0 (5.0)	11.0 (5.0)					
Engleman 1998[136] 9708223	43 (nd) [>15]	12.0 (4.0)	4wk (XO)	CPAP	23	nd	9.2 (3.9)	2.4	0.8, 4.0	<0.001	0	B
				Placebo			6.8 (4.3)					
Engleman 1994[133] 7906330	28 (7-129) [>5]	nd	1 mo (XO)	CPAP	32	nd	7.2 (4.0)	1.1	0.1, 2.1 †	0.03	9	C
				Placebo			6.1 (4.0)					
Barnes 2002[131] 11897643	13 (6) [>5]	11.3 (5.0)	8 wk (XO)	CPAP	28	12.5 (4.8)	-1.8 ‡	-1.0	nd	NS	33	C
				Placebo			-0.8 §					
Engleman 1997[135] 9059469	11 (4) [>5]	nd	4 wk (XO)	CPAP	16	nd	10.0 (4.8)	0.1	-3.6, 3.9	NS	11	C
				Placebo			9.9 (6.0)					

* Estimated from reported data
† Estimated from reported P value
‡ Reported change
§ Reported change

Table 5.1.5b. Maintenance of wakefulness test (min) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Engleman 1999[137] 9927358	10 (nd) [>5]	13.0 (3.0)	4 wk (XO)	CPAP	34	nd	16.2 (10.6)	1.8	-4.2, 7.8*	NS	8	B
				Placebo tablet			14.4 (8.5)					

* Estimated from reported data.

Table 5.1.6a. FOSQ in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + conservative measures	66	101 (18) †	106 (20) ‡	3	-3.6, 9.6	NS	12	C
				Conservative measures	59	100 (15) §	102 (21) **					
Barnes 2004[140] 15201136	21 (12) [>5]	10.7 (3.5)	3 mo (XO)	CPAP	80	3.1 (0.9) ††	3.3 (0.9) ‡‡	0	-0.3, 0.3	NS	27	B
				Placebo			3.3 (0.9) §§					
Faccenda 2001[138] 11179104	35 (15-129) [>15]	15 (6-24)	1 mo (XO)	AutoCPAP	68	nd	12.4 (4.1) ***	+0.8	-0.2, 1.4 †††	NS	5	B
				Placebo			11.6 (5.7) ‡‡‡					
Barnes 2002[131] 11897643	13 (6) [>5]	11.3 (5.0)	8 wk (XO)	CPAP	28	0.8 (0.1) §§§	+0.07 ****	+0.01	nd	NS	33	C
				Placebo			+0.06 ††††					

* Estimated from reported data.
† Total summed score of FOSQ responses.
‡ Total summed score of FOSQ responses.
§ Total summed score of FOSQ responses.
** Total summed score of FOSQ responses.
†† Weighted average of FOSQ subscale scores.
‡‡ Weighted average of FOSQ subscale scores.
§§ Weighted average of FOSQ subscale scores.
*** Summed score of FOSQ subscale averages.
††† Estimated from reported P value.
‡‡‡ Summed score of FOSQ subscale averages.
§§§ Ratio of total summed score over maximum possible score.
**** Reported change.
†††† Reported change.

Table 5.1.6b. Quality of life in randomized controlled trials of CPAP vs. control

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference: Net difference	95% CI *	Test range "Worst"	Test range "Best"	P Btw	Study Quality
Ballester 1999[118] 9927363	AHI 58 (20)	3 mo (PL)	AutoCPAP + CM	68	SAHS-related symptoms questionnaire	AutoCPAP	-12.3	-14.6, -9.9	15	-16	<0.001	B
	ESS 11.4 (5.0)		CM	37	NHP – Emotional reactions	0						
					NHP - Sleep	0						
					NHP - Physical	0						
					NHP – Social isolation	0 †	-3.7	-11.2, 3.8	0	100	0.33	
					NHP – Pain	0						
					NHP - Energy	AutoCPAP	-20.6	-33.1, -8.1	0	100	<0.001	
Lam 2007[129] 17121868	AHI 19 (17)	10 wk (PL)	CPAP + CM	34	SAQLI summary score (A-D)[a]	CPAP	1	0.7, 1.2	0	7	<0.001	B
	ESS 12 (8.8)		CM	33	SAQLI summary score (A-E)[a]	CPAP	nd	nd	0	7	<0.05	
					SF-36 Physical function	CPAP	6.9	1.6, 12.1 ‡	0	100	<0.05	
					SF-36 Bodily Pain	CPAP	11.7		0	100	<0.05	
Monasterio 2001[127] 11587974	AHI 21 (5)	6 mo (PL)	CPAP + CM	66	SAHS related symptoms	CPAP	-5	-6.4, -3.6	8	32	<0.001	C
	ESS 13.2 (4.3)		CM	59	NHP	0					NS	
Mansfield 2004[126] 14597482	AHI 27 (21)	3 mo (PL)	CPAP	19	SF-36 role-physical	0					NS	C
	ESS 8.8 (0.9)		No treatment	21	SF-36 vitality	CPAP	20	5.2, 34.8	0	100	0.008	
					SF-36 mental health	0					NS	

Table 5.1.6b. Quality of life in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference: Net difference	95% CI §	Test range "Worst"	Test range "Best"	P Btw	Study Quality
Barnes 2002[131] 11897643	AHI 13 (6) ESS 11.3 (5.0)	8 wk (XO)	CPAP Placebo	28	SF-36 physical functioning	0					NS	B
					SF-36 mental health	0					NS	
Barnes 2004[140] 15201136	AHI 21 (12) ESS 10.7 (3.5)	3 mo (XO)	CPAP Placebo	80	SF-36 mean score	0					NS **	B
Engleman 1994[133] 7906330	AHI 28 (7-129) ESS nd	1 mo (XO)	CPAP Placebo	32	GHQ 28 total score	CPAP	-3.4	-5.6, -1.2 ††	0	28	0.003	C
Engleman 1997[135] 9059469	AHI 11 (4) ESS nd	4 wk (XO)	CPAP Placebo	16	GHQ 28 total score	0					NS	C
Engleman 1998[136] 9708223	AHI 43 (nd) ESS 12.0 (nd)	4 wk (XO)	CPAP Placebo	23	UMACL Energetic Arousal Score	0					NS	B
					GHQ-28	0					NS	
					NHP Part 2 score	0					NS	
Engleman 1999[137] 9927358	AHI 10 (nd) ESS 13.0 (3.0)	4 wk (XO)	CPAP Placebo	34	SF-36 Role-physical	CPAP	17	0.9, 33.0	0	100	0.038	B
					SF-36 mental health	0					NS	
					SF-36 Vitality	CPAP	12	2.6, 24.1	0	100	0.014	
					UMACL Energetic Arousal Score	0					NS	
					NHP Part 2 score	0					NS	

* Estimated from reported data.
† Contrary to the reported P-value for this outcome (P=0.03), our calculations showed no statistical significance (P=0.33).
‡ Estimated from reported P value.
§ Estimated from reported data.
** Our estimated does not match with reported statistical significance.
†† Estimated from reported P value.

Table 5.1.7. Neurocognitive and psychological tests in randomized controlled trials of CPAP vs. control

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				P Btw	Study Quality
							Net Difference	95% CI	Test Range "Worst"	Test Range "Best"		
Monasterio 2001[127] 11587974	AHI 21 (5)	6 mo (PL)	CPAP + CM	66	Attention - digit symbol (WAIS) SS	0					NS	C
	ESS 13.2 (4.3)		CM	59	Attention - digits forward and backward (WAIS) SS	0					NS	
					Attention - mental control (WMS) p	0					NS	
					Memory - verbal paired associated (WMS) p	0					NS	
					Memory - visual memory (WMS), SS	0					NS	
					Executive function - Verbal fluency, p	0					NS	
					Executive function - Block Design (WAIS), SS	0					NS	
					Trailmaking A (sec)	0					NS	
					Trailmaking B (sec)	0					NS	
					PASAT 4-s,	0					NS	
					PASAT 3-s	0					NS	
					PASAT 2-s	0					NS	
					PASAT 1-s	0					NS	
					Vigilance - Steer-clear, % hits	0					NS	

Table 5.1.7. Neurocognitive and psychological tests in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				P Btw	Study Quality
							Net Difference	95% CI	Test Range "Worst"	Test Range "Best"		
Lojander 1996, 1999[125,124] 8681614, 10188139	nd	12 mo (PL)	CPAP + CM	23	Wechsler Verbal	0					NS	C
			CM	21	Wechsler Performance	0					NS	
					Wechsler Memory	0					NS	
Barnes 2004[140] 15201136	AHI 21 (12) ESS 10.7 (3.5)	3 mo (XO)	CPAP	80	Beck Depression Inventory	0					NS	B
			Placebo									
Engleman 1999[137] 9927358	AHI 10 (nd) ESS 13 (3)	4 wk (XO)	CPAP	34	SteerClear	0					NS	B
			Placebo		Trailmaking A and B	0					NS	
					Digit symbol	CPAP	0.5*	nd			0.004	
					Block Design score	0					NS	
					Performance IQ score	0					NS	
					HADS anxiety score	0					NS	
					HADS depression score	CPAP	0.41†		0	21	0.003	
					PASAT 2-s	CPAP	0.36‡				0.02	

Table 5.1.7. Neurocognitive and psychological tests in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				P Btw	Study Quality
							Net Difference	95% CI	Test Range "Worst"	Test Range "Best"		
Barnes 2002[131] 11897643	AHI 13 (6) [>5]	8 wk (XO)	CPAP	28	Word pair memory recall	0					NS	B
	ESS 11.3 (5.0)		Placebo		WMS-R visual reproduction	0					NS	
					Trailmaking A (sec)	0					NS	
					Trailmaking B (sec)	0					NS	
					Digital symbol substitution test	0					NS	
					Controlled oral word association test	CPAP	+2.7	0.43, 4.97 §			0.02	
					Psychomotor vigilance task	0					NS	
					Stroop color association test	0					NS	
					POMS	0					NS	
					Mood- Beck depression inventory	0					NS	

Table 5.1.7. Neurocognitive and psychological tests in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				P Btw	Study Quality
							Net Difference	95% CI	Test Range "Worst"	Test Range "Best"		
Engleman 1998[136] 9708223	AHI 43 (nd) ESS 12.0 (nd)	4 wk (XO)	CPAP	23	SteerClear	0					NS	B
			Placebo		Trailmaking B	0					NS	
					Digit symbol substitution	0					NS	
					Block Design	0					NS	
					Performance IQ decrement	0					NS	
					HADS anxiety score	0					NS	
					Rapid visual information processing	0					NS	
					HADS depression score	0					NS	
					PASAT 2-s	0					NS	
Engleman 1994[133] 7906330	AHI 28 (7-129) ESS nd	1 mo (XO)	CPAP	32	IQ decrement score	CPAP	-3.2	-6.3, -0.1 **	NA	NA	0.04	C
			Placebo		Trailmaking B (sec)	CPAP	-9	-16.5, -1.4 ††	NA	NA	0.02	
					PASAT	0					NS	
					HADS anxiety score	CPAP	-1.2	-2.2, -0.2	0	21	0.02	
					HADS depression score	CPAP	-1.9	-3.1, -0.7 ‡‡	0	21	0.002	

Table 5.1.7. Neurocognitive and psychological tests in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline Test (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				P Btw	Study Quality
							Net Difference	95% CI	Test Range "Worst"	Test Range "Best"		
Engleman 1997[135] 9059469	AHI 11 (4)	4 wk (XO)	CPAP	16	IQ decrement score	0					NS	C
	ESS nd		Placebo		Trailmaking B (sec)	CPAP	-13.6	-25.1, -2.1	NA	NA	0.02	
					PASAT	0					NS	
					Verbal fluency total words	0					NS	
					HADS anxiety score	0					NS	
					HADS depression score	CPAP	-1.6	-3.0, -0.2	0	21	0.03	

* Reported Effect size (final difference/standard deviation of difference)
† Reported Effect size (final difference/standard deviation of difference)
‡ Reported Effect size (final difference/standard deviation of difference)
§ Estimated from reported P value.
** Estimated from reported P value.
†† Estimated from reported P value.
‡‡ Estimated from reported P value.

Table 5.1.8a. Blood pressure measurements (mm Hg) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Systolic Blood Pressure												
Barbe 2010[130] 20007932	43 (19) [>19]	6.4 (2.4)	12 mo (PL)	CPAP + conservative treatment	178	141 (5)	134.7 (nd)	-2.09	-5.6, 1.4	nd	4	B
				Conservative treatment	181	141 (15)	136.8 (nd)					
Diastolic Blood Pressure												
Barbe 2010[130] 20007932	43 (19) [>19]	6.4 (2.4)	12 mo (PL)	CPAP + conservative treatment	178	85 (11)	82.8 (nd)	0.46	-2.0, 2.9	nd	4	B
				Conservative treatment	181	86 (10)	83.3 (nd)					
Daytime Systolic Blood Pressure												
Drager 2007[120] 17556718	65 (22) [>30]	13.0 (5.0)	4 mo (PL)	C-Flex	12	122 (5)	119 (9)	-1	-8.2, 6.2	NS	0	B
				No treatment	12	124 (11)	122 (9)					
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + conservative measures	66	126.0 (17.0)	122.0 (22.0)	-2	-8.4, 4.4	NS	12	C
				Conservative measures	59	132.0 (17.0)	130.0 (16.0)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	126 (20.8)	116 (17.3)	-16	-34.4, 2.4	NS	0	C
				Optimal drug treatment	12	128 (24.2)	134 (27.7)					
Barnes 2002[131] 11897643	13 (6) [>5]	11.3 (5.0)	8 wk (XO)	CPAP	28	132.0 (11.0)	-0.7 (25.6) †	-2.1	-11.2, 7.0	0.65	33	C
				Placebo			2.2 (9.8) ‡					
Comondore 2009[132] 18795367	28 (nd) [>15]	6.8 (nd)	4 wk (XO)	AutoCPAP	13	139.3 (nd)	131.9 (nd)	-3.6	-18.5, 11.3	0.50	0	C
				No treatment			133.6 (nd)					
Engleman 1996[134] 8843528	49 (32) [>5]	nd	3 wk (XO)	CPAP	13	nd	138.0 (14.4)	-0.1	-10.8, 8.7	nd	19	C
				Placebo			139.0 (10.8)					

Table 5.1.8a. Blood pressure measurements (mm Hg) in randomized controlled trials of CPAP vs. control (continued)

Study PMID	Baseline AHI (SD) [min]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI §	P Btw	Dropout, %	Study Quality
Nighttime Systolic Blood Pressure												
Drager 2007[120] 17556718	65 (22) [>30]	13.0 (5.0)	4 mo (PL)	C-Flex	12	108.0 (9.0)	105.0 (10.0)	-4	-11.6, 3.6	NS	0	B
				No treatment		109 (10.0)	113.0 (9.0)					
Daytime Diastolic Blood Pressure												
Drager 2007[120] 17556718	65 (22) [>30]	13.0 (5.0)	4 mo (PL)	C-Flex	12	79.0 (4.0)	75.0 (7.0)	-1	-4.6, 6.6	NS	0	B
				No treatment	12	78.0 (9.0)	75.0 (6.0)					
Kaneko 2003[123] 12660387	45 (5) [>20]	5.7 (0.9)	1 mo (PL)	CPAP	12	62.0 (13.9)	59.0 (6.9)	-1	-10.8, 8.8	NS	0	C
				Optimal drug treatment	12	60.0 (13.9)	58.0 (10.4)					
Monasterio 2001[127] 11587974	21 (5) [>10]	13.2 (4.3)	6 mo (PL)	CPAP + conservative measures	66	81.0 (12.0)	80.0 (10.0)	-1	-4.9, 2.9	NS	12	C
				Conservative measures	59	84.0 (11.0)	84.0 (11v)					
Barnes 2002[131] 11897643	13 (6) [>5]	11.3 (5.0)	8 wk (XO)	CPAP	28	84.0 (7.8)	-0.5 (25.6) **	-2.6	-11.7, -6.5	0.57	33	C
				Placebo			+2.1 (9.8) ††					
Comondore 2009[132] 18795367	28 (nd) [>15]	6.8 (nd)	4 wk (XO)	AutoCPAP	13	82.7 (nd)	79.0 (nd)	-0.7	-8.5, 7.1	0.84	0	C
				No treatment		84.8 (nd)	81.8 (nd)					
Engleman 1996[134] 8843528	49 (32) [>5]	nd	3 wk (XO)	CPAP	13	nd	84.0 (3.0)	-2	-4.3, 0.3	nd	19	C
				Placebo		nd	86.0 (3.0)					
Nightime Diastolic Blood Pressure												
Drager 2007[120] 17556718	65 (22) [>30]	13.0 (5.0)	4 mo (PL)	C-Flex	12	67.0 (8.0)	63.0 (8.0)	-1	-7.7, 5.7	NS	0	B
				No treatment	12	69.0 (7.0)	66.0 (10.0)					

* Estimated from reported data.
† Reported change.
‡ Reported change
§ Estimated from reported data.
** Reported change.
†† Reported change.

Table 5.1.8b. HbA1C (%) in randomized controlled trials of CPAP vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Comondore 2009[132] 18795367	28 (nd) [>15]	6.8 (nd)	4 wk (XO)	AutoCPAP	13	5.91 (nd)	5.94 (nd)	0.04	-0.27, 0.34	NS	0	C
				No treatment		5.85 (nd)	5.85 (nd)					

Table 5.2.1. Characteristics of randomized controlled trials comparing CPAP with sham control

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Arias 2005[141] 16009798	CPAP Sham CPAP	Auto (separate)	52	100	30.5		Spain (nd)	
Barbe 2001[142] 11388814	CPAP Sham CPAP	Manual (separate)	53	91	29	Non-sleepy	Spain (1999-2000)	N <30
Becker 2003[143] 12515745	CPAP Sham CPAP	Manual (separate)	53	91	33.4	67% with HTN	Germany (nd)	No power calculation, no allocation concealment, high dropout rate
Campos-Rodriguez 2006[144] 16778262	CPAP Sham CPAP	Manual (separate)	57	60	34.8	30-70 yr with primary HTN and on treatment	Spain (nd)	Unclear randomization
Coughlin 2007[145] 17251237	CPAP Sham CPAP	Auto (split)	49	100	36.1	Healthy obese males	UK (nd)	
Cross 2008[146] 18390635	CPAP Sham CPAP	Auto (separate)	48	96	37	22% on aspirin, statins, or beta blockers	UK (nd)	
Egea 2008[147] 17904420	CPAP Sham CPAP	Manual (split)	64	94	31.1	Stable heart failure patients with sleep apnea	Spain (nd)	PSG results included 17% central sleep apnea subjects, but sleepiness and QoL measures only included OSA subjects
Haensel 2007[148] 17503102	CPAP Sham CPAP	Manual (separate)	49	80	33.4		US (nd)	relatively small samples, no power calculation
Henke 2001[149] 11282765	CPAP Sham CPAP	Manual (separate)	50	56	42.6		US (nd)	No power calculation; one-way cross over
Hui 2006[150] 16928705	CPAP Sham CPAP	Auto (separate)	51	80	27.2		Hong Kong (nd)	Underpowered; Non-ITT analyses; likely selection bias; questionable patient blinding
Jenkinson 1999[151] 10382693 Hack 2000[152] 10679542	CPAP Sham CPAP	Auto (separate)	49	100	35.1		UK (1997-98)	
Lam 2010[169] 19608589	CPAP Sham CPAP	Auto (separate)	46	100	27.5		China (2002-2007)	

Table 5.2.1. Characteristics of randomized controlled trials comparing CPAP with sham control (continued)

Study PMID	Interventions	CPAP Pressure † (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	CPAP Sham CPAP	Manual (separate)	48	75	31.3		US (nd)	
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	CPAP Sham CPAP	Manual (separate)	48	83	31.8		US (2002-04)	Poorly reported results, with much missing data, incomplete analyses
Marshall 2005[159] 15860720	CPAP Sham CPAP	Manual (separate)	51	76	31.5		New Zealand (2001-03)	Allocation concealment: yes – assessors; no - patients
Mills 2006[160] 16357087 Lim 2007[161] 17694727	CPAP Sham CPAP	Manual (separate)	48	85	31.9		US (nd)	No power calculation
Montserrat 2001[162] 11520724	CPAP Sham CPAP	Manual (separate)	54	91	32.0		Spain (nd)	Needed sample size 48 but had only 45
Norman 2006[163] 16585412	CPAP Sham CPAP	Manual (separate)	50	85	30.8			No power calculation
Robinson 2006[164] 16455835	CPAP Sham CPAP	Auto (split)	54	89	33.2	HTN with significant OSA, but without sufficient daytime hypersomnolence	UK (nd)	
Siccolli 2008[165] 19014075	CPAP Sham CPAP	Auto (separate)	48	100	35.2		UK (nd)	
Smith 2007[166] 17470670	CPAP Sham CPAP	Auto (split)	61	88	31	CHF	UK (nd)	
Spicuzza 2006[167] 16963674	CPAP Sham CPAP	Manual (separate)	56	80	32.1		Italy (nd)	
West 2007[168] 17557769	CPAP Sham CPAP	Auto (split)	56	100	37.8	Diabetes mellitus	UK (2004-05)	
West 2009[170] 19427263	CPAP Sham CPAP	Auto (separate)	55	100	36.7	Type 2 diabetes	UK (nd)	No power calculation; unclear how many patients were randomized

[*] Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoPAP is the intervention). In parentheses: split (CPAP introduced in a split night study); separate (CPAP introduced on a separate full night than the diagnostic sleep study).

[†] Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoPAP is the intervention). In parentheses: split (CPAP introduced in a split night study); separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.2.2. AHI (events/hr) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Lam 2010[169] 19608589	39.7 (22.1) [≥15]	10.3 (4.9)	1 wk (PL)	AutoCPAP	30	33.4 (nd)	0.6 (nd)	-24.6	nd *	<0.001	0	A
				Sham CPAP	31	31.3 (nd)	19.7 (nd)					
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	27	43.7 (22.9)	10.8 (11.4)	-25.6	-36.5, -14.6 †	<0.0001 ‡	18	B
				Sham CPAP	29	35.3 (16.7)	28 (24.8)					
Haensel 2007[148] 17503102	58 (30) [≥15]	nd	2 wk (PL)	CPAP	25	65.9 (28.6)	3.5 (3.4)	-58.3	-74.9, -41.7 §	<0.001	0	B
				Sham CPAP	25	57.5 (32.1)	53.4 (32.9)					
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	44 (25) [RDI≥20]	nd	1 wk (PL)	CPAP	23	56.4 (24.1)	3.3 (3.8)	-37.2	-51.6, -22.7 **	<0.001	14	B
				Sham CPAP	18	44.2 (25.3)	28.3 (22.7)					
Mills 2006[160] 16357087 Lim 2007[161] 17694727	61 (33) [>15]	nd	2 wk (PL)	CPAP	17	65.0 (34)	2.56 (2.4)	-58.5	-84.0, -33.0 ††	nd	nd	B
				Sham CPAP	16	61.2 (41)	57.3 (41)					
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	57 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	65.9 (28.6)	3.0 (4.7)	-57.9	-76.2, -39.6 ‡‡	<0.001	nd	C
				Sham CPAP	19	57.5 (32.1)	52.5 (37.5)					

Table 5.2.2. AHI (events/hr) in randomized controlled trials of CPAP vs. sham control (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Norman 2006[163] 16585412	54 (30) [>15]	12.0 (6.6)	2 wk (PL)	CPAP	18	66.1 (29.1)	3.4 (3.0)	-58.9	-79.2, -38.6 §§	<0.05	nd	C
				Sham CPAP	15	53.9 (29.8)	50.1 (32.1)					
Becker 2003[143] 12515745	65.0 (26.7) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	62.5 (17.8)	3.4 (3.1)	-27.5	-43.4, -11.6 ***	0.001	47	C
				Sham CPAP	16	65.0 (26.7)	33.4 (29.2)					
Spicuzza 2006[167] 16963674	59 (17) [>5]	nd	1 mo (PL)	CPAP	15	55.3 (11.9)	2.1 (0.3)	-51.0	-62.0, -40.0 †††	<0.005	nd	C
				Sham CPAP	10	59.2 (17.3)	57.0 (8.6)					

* Only IQR were reported.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data.
** Estimated from reported data.
†† Estimated from reported data.
‡‡ Estimated from reported data.
§§ Estimated from reported data.
*** Estimated from reported data
††† Estimated from reported data.

Table 5.2.3. ESS in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Drop-out %	Study Quality
West 2007[168] 17557769	nd	14 (3.5)	3 mo (PL)	AutoCPAP	19	15 (3.5)	-6.6 (4.5) *	-4.0	-7.0, -0.9	0.01	5	A
				Sham CPAP	21	17 (3.5)	-2.6 (4.9) †					
Coughlin 2007[145] 17251237	40 (14) [>15]	14 (4.9)	6 wk (XO)	CPAP	34	14 (4.9)	nd	-3.1	-4.5, -1.7	<0.01	3	A
				Sham CPAP	34	14 (4.9)						
Robinson 2006[164] 16455835	nd	5.3 (IRQ 3.0-7.0)	1 mo (XO)	AutoCPAP	32	5.3 (nd)	-1.4 (nd) ‡	-1.1	-2.0, -0.17 §	<0.02	9	A
				Sham CPAP	32	5.3 (nd)	-0.3 (nd) **					
Lam 2010[169] 19608589	39.7 (22.1) [≥15]	10.3 (4.9)	1 wk (PL)	AutoCPAP	30	10.3 (4.9)	10.5 (5.2)	+0.7	-0.76, 2.06 ††	NS	0	A
				Sham CPAP	31	10.8 (5.5)	10.5 (5.6)					
Smith 2007[166] 17470670	36 (23) [≥15]	10 (5)	6 wk (XO)	AutoCPAP	23	10 (5)	7 (4)	-1.0	-1.9, 0	0.04	12	A
				Sham CPAP	23	10 (5)	8 (5)					
Jenkinson 1999[151] 10382693 Hack 2000[152] 10679542	nd	17.0 (nd)	4 wk (PL)	AutoCPAP	52	15.5 (nd)	7.0 (nd)	-7.0	-10.5, -3.5 ‡‡	<0.0001	6	B
				Sham CPAP	49	15.0 (nd)	13.0 (nd)					
Siccolli 2008[165] 19014075	nd	15.2 (4.0)	4 wk (PL)	CPAP	50	15.8 (4.0)	6.8 (5.1)	-5.9	-7.8, -3.95	<0.0001	3	B
				Sham CPAP	49	15.0 (4.0)	11.9 (5.9)					
Campos-Rodriguez 2006[144] 16778262	60 (22) [≥10]	13.6 (3.6)	4 wk (PL)	CPAP	34	15.0 (3.9)	11.2 (3.0)	-2.4	-4.0, -0.81 §§	0.003	6	B
				Sham CPAP	34	13.6 (3.6)	12.2 (2.2)					
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	7 (2.2)	8 (3.2)	+1.0	-1.0, 3.0 ***	NS	2	B
				Sham CPAP	25	7 (2.0)	8 (5.0)					

Table 5.2.3. ESS in randomized controlled trials of CPAP vs. sham control (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Drop-out %	Study Quality
Hui 2006[150] 16928705	30 (16) [≥5]	10.7 (3.3)	3 mo (PL)	CPAP	23	10.2 (4.8)	7.0 (4.8)	-0.04	-2.94, 2.86	NS	18	B
				Sham CPAP	23	11.2 (5.5)	8.1 (5.0)					
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	20	8.6 (3.6)	5.0 (3.6)	-1.9	-4.1, 0.3 †††	NS	18	B
				Sham CPAP	25	6.9 (4.0)	5.2 (4.0)					
Montserrat 2001[162] 11520724	54 (19) [>10]	16.9 (5.6)	6 wk (PL)	CPAP	23	16.1 (4.8)	6.7 (3.4)	-7.21	-10.1, -4.4 ‡‡‡	<0.001	6	B
				Sham CPAP	22	16.9 (6.0)	14 (5.5)					
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	58 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	11.6 (4.9)	8.2 (4.4)	-1.7	-5.2, 1.8 §§§	NS	nd	B
				Sham CPAP	19	12.3 (6.7)	10.6 (6.4)					
Marshall 2005[159] 15860720	22 (nd) [nd]	12.5 (4.3)	3 wk (XO)	CPAP	29	12.5 (4.3)	9.7 (3.8)	-2.4	-4.2, -0.6	0.04	6	B
				Sham CPAP	29	12.5 (4.3)	12.0 (3.8)					
West 2009[170] 19427263	nd	13.4 (2.6)	3 mo (PL)	AutoCPAP	16	13.4 (2.6)	-6.1 (4.4) ****	-3.3	-6.5, -0.1 ††††	0.04	nd	B
				Sham CPAP	20	13.3 (3.4)	-2.8 (5.1) ‡‡‡‡					
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	14.4 (2.5)	5.1 (3.8)	-4.1	-6.8, -1.4 §§§§	0.009	47	C
				Sham CPAP	16	14.1 (3.2)	8.9 (5.0)					

* Change from baseline (SD)
† Change from baseline (SD)
‡ Change from baseline (SD)
§ Estimated from reported P value
** Change from baseline (SD)
†† Estimated from reported data.
‡‡ Estimated from reported data.
§§ Estimated from reported data.
*** Estimated from reported data.
††† Estimated from reported data.

‡‡‡ Estimated from reported data.
§§§ Estimated from reported data.
**** Change from baseline (SD)
†††† Estimated from reported data
‡‡‡‡ Change from baseline (SD)
§§§§ Estimated from reported data

Table 5.2.4. Arousal index (events/hr) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	44 (25) [RDI≥20]	nd	1 wk (PL)	CPAP	23	55.1 (24.4)	1.4 (9.5)	-38.6	-53.5, -23.7 *	0.001	14	B
				Sham CPAP	18	48.6 (28.2)	33.5 (23.2)					
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	58 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	41 (28.4)	10.5 (1.0)	-27.2	-45.9, -8.4 †	<0.001	nd	C
				Sham CPAP	19	43.8 (32.6)	40.5 (8.0)					
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	58.7 (21.9)	24.1 (9.8)	-13.8	-30.2, 2.6 ‡	nd	47	C
				Sham CPAP	16	62.0 (28.0)	41.2 (27.2)					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported data

Table 5.2.5. Sleep efficiency (%TST) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Haensel 2007[148] 17503102	58 (30) [≥15]	nd	2 wk (PL)	CPAP	25	80.3 (2.3)	87.5 (1.5)	3.3	2.3, 4.3 *	NS	0	B
				Sham CPAP	25	82.0 (1.6)	85.9 (1.6)					
Loredo 1999[153] 10593774	44 (25) [RDI≥20]	nd	1 wk (PL)	CPAP	23	83.7 (10.7)	88.1 (8.6)	2.9	-4.1, 9.9 †	NS	14	B
Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548				Sham CPAP	18	82.2 (11.8)	83.7 (12.9)					

* Estimated from reported data.
† Estimated from reported data.

Table 5.2.6. Slow wave sleep (% TST) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	27	7.9 (8.3)	7.2 (10.4)	3.2	-1.9, 8.3 *	NS	18	B
				Sham CPAP	29	9.7 (10.2)	5.8 (9.7)					
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	44 (25) [RDI≥20]	nd	1 wk (PL)	CPAP	23	7.4 (8.7)	12.5 (10.6)	-1.6	-8.7, 5.5 †	NS	14	B
				Sham CPAP	18	6.3 (8.6)	13.0 (14.5)					
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	58 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	5.0 (6.9)	7.1 (6.2)	1.5	-2.2, 5.2 ‡	NS	nd	B
				Sham CPAP	19	4.1 (5.1)	4.7 (5.8)					
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL	CPAP	16	6.2 (7.2)	15.2 (7.1)	3.4	-1.8, 8.6 §	NS	47	C
				Sham CPAP	16	6.0 (8.4)	11.6 (6.7)					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data

Table 5.2.7. REM sleep (% TST) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net Diff or diff*	95% CI	P Btw	Dropout, %	Study Quality
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	27	15.7 (9.9)	12.2 (6.2)	-2.8	-6.9, 1.3 †	NS	18	B
				Sham CPAP	29	12.9 (7.0)	12.2 (7.0)					
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	44 (25) [RDI≥20]	nd	1 wk (PL)	CPAP	23	19.0 (7.9)	26.2 (7.0)	5.7	0.85, 10.6 ‡	NS	14	B
				Sham CPAP	18	17.7 (8.0)	19.2 (8.3)					
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	58 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	14.3 (6.9)	22 (9.4)	7.5	3.5, 11.5 §	<0.05	nd	C
				Sham CPAP	19	15.3 (4.8)	15.5 (4.4)					
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	11.4 (6.8)	22.3 (5.7)	4.1	-0.8, 9.0 **	NS	47%	C
				Sham CPAP	16	14.3 (6.3)	21.1 (8.8)					

* In crossover studies, if only data on the final values and the difference in final values are reported (as opposed to changes from baseline and net change), these data are italicized.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data.
** Estimated from reported data

Table 5.2.8. Maintenance of wakefulness test (min) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (SD)	Net diff	95% CI	P Btw	Dropout, %	Study Quality
West 2007[168] 17557769	nd	14 (3.5)	3 mo (PL)	AutoCPAP	19	22 (13) *	+10.6 (14)	+15.3	6.5, 24	0.001	5	A
				Sham	21	32 (11) †	-4.7 (12)					
Jenkinson 1999[151] 10382693 Hack 2000[152] 10679542	nd	17.0 (nd)	4 Wk (PL)	AutoCPAP	52	23 (nd)	32.9 (nd)	+6.8	2.0, 11.5 ‡	0.005	6	B
				Sham	49	20 (nd)	23.5 (nd)					
Marshall 2005[159] 15860720	22 (nd) [nd]	12.5 (4.3)	3 wk (XO)	CPAP	29	20.9 (2.5)	23.1 (10.8)	+5.2	-0.6, 11	0.09	6	B
				Sham	29	20.9 (2.5)	17.9 (10.8)					
West 2009[170] 19427263	nd	13.4 (2.6)	3 mo (PL)	AutoCPAP	16	23.5 (12.7)	+10.4 (14.4)	+15.4	-2.1, 52.1	NS	nd	B
				Sham CPAP	20	33.9 (9.2)	-5.0 (12.0)					

* Significantly different between group at baseline
† Significantly different between group at baseline
‡ Estimated from reported data.

Table 5.2.9. FOSQ in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff	95% CI	P Btw	Dropout, %	Study Quality
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	102 (16)	108 (11)	+4.0	-3.3, 11.3 *	NS	2	B
				Sham CPAP	25	107 (15)	110 (10)					
Montserrat 2001[162] 11520724	54 (19) [>10]	16.9 (5.6)	6 wk (PL)	CPAP	23	85 (22)	109 (13)	+10.48	-2.6, 23.6 †	NS	6	B
				Sham CPAP	22	86 (28)	101 (22)					
Marshall 2005[159] 15860720	22 (nd) [nd]	12.5 (4.3)	3 wk (XO)	CPAP	29	12.6 (1.6)	13.6 (1.8)	-0.3	-1.1, 0.5	NS	6	B
				Sham CPAP	29	12.6 (1.6)	13.3 (1.8)					

* Estimated from reported data.
† Estimated from reported data.

Table 5.2.10. Quality of life in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors *	If Significant Difference				P Btw	Dropout, %	Study Quality
								Net Diff	95 CI	Test Range "Worst"	Test Range "Best"			
Smith 2007[166] 17470670	36 (23) [≥15]	10 (5)	6 wk (XO)	AutoCPAP	23	SF-36 PCS	0					NS	12	A
				Sham	23									
						SF-36 MCS	0					NS		
Siccolli 2008[165] 19014075	nd	15.2 (4.0)	4 wk (PL)	CPAP	50	SF-36 PCS	CPAP	8.2	0.4, 16.0 †	0	100	0.01	3	B
				Sham CPAP	49									
						SF-36 MCS	CPAP	10.8	2.8, 18.8 ‡	0	100	0.002		
						Calgary SAQLI total score	CPAP	0.9	0.4, 1.4 §	0	7	0.001		
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	20	SF-36 PCS	0					NS	18	B
				Sham CPAP	25									
						SF-36 MCS	0					NS		
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	SF-36 PCS	0					NS	2	B
				Sham CPAP	25									
						SF-36 MCS	0							
Montserrat 2001[162] 11520724	54 (19) [>10]	16.9 (5.6)	6 wk (PL)	CPAP	23	SF-36 PCS	0					NS	6	B
				Sham CPAP	22									
						SF-36 MCS	0					NS		
Marshall 2005[159] 15860720	22 (nd) [nd]	12.5 (4.3)	3 wk (XO)	CPAP	29	SF-36 PCS	0					NS	6	B
				Sham CPAP	29									
						SF-36 MCS	0					NS		

* The noted intervention statistically significantly favors the patient (net better score on test). 0 = no difference.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data.

Table 5.2.11. Neuropsychological outcomes in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors*	If Significant Difference				Dropout, %	Study Quality
								Net Diff	95 CI	Test Range "Worst"	Test Range "Best"	P Btw	
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	Trial Making A test	0					NS	2	B
				Sham CPAP	25	Trial Making B test	0					NS		
						WAIS- Digital symbols	0					NS		
						WAIS- block design	0					NS		
						WAIS- digit span	0					NS		
						WMS- mental control	0					NS		
						WMS- verbal paired associated	0					NS		
						PASAT 1	0					NS		
						PASAT 2	0					NS		
						PASAT 3	0					NS		
						PASAT 4	0					NS		
Haensel 2007[148] 17503102	58 (30) [≥15]	nd	2 wk (PL)	CPAP	25	POMS total score	0					NS	0	B
				Sham CPAP	25									
Loredo 1999[153] 10593774 Yu 1999[154] 10504011 Bardwell 2001[155] 11485111 Profant 2003[156] 12571548	44 (25) [RDI≥20]	nd	11 d (PL)	CPAP	23	POMS- TMD	0					NS	14	B
				Sham CPAP	18	All Cognitive tests	0					NS		
						MOS	0					NS		
Loredo 2006[157] 16676791 Bardwell 2001[155] 11485111	58 (32) [≥15]	12.3 (6.7)	2 wk (PL)	CPAP	22	BSI GSI	0					NS	nd	B
				Sham CPAP	19	BSI Depression	0					NS		

Table 5.2.11. Neuropsychological outcomes in randomized controlled trials of CPAP vs. sham control (continued)

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors †	If Significant Difference					Dropout, %	Study Quality
								Net Diff	95 CI	Test Range "Worst"	Test Range "Best"	P Btw		
Mills 2006[160] 16357087 Lim 2007[161] 17694727	61 (33) [>15]	nd	2 wk (PL)	CPAP	17	All neuropsychological tests except the one below	0					NS	nd	B
				Sham CPAP	14									
						Digit Vigilance	CPAP	-15.3	nd			0.02		
Marshall 2005[159] 15860720	22 (nd) [nd]	12.5 (4.3)	3 wk (XO)	CPAP	29	Hospital Anxiety and Depression scale	0					NS	6	B
				Sham CPAP										
Henke 2001[149] 11282765	68 (25) [>10]	16.0 (4.8)	2 wk (PL)	CPAP	27	Trial Making A test	0					NS	0	C
				Sham CPAP	18									
						Trial Making B test	0					NS		
						WAIS- Digital symbols	0					NS		
						WAIS- complex figure	0					NS		
						WAIS- digit span	0					NS		
						Hits on steer clear test	0					NS		

* The noted intervention statistically significantly favors the patient (net better score on test). 0 = no difference.
† The noted intervention statistically significantly favors the patient (net better score on test). 0 = no difference.

Table 5.2.12. Blood pressure outcomes (mm Hg) in randomized controlled trials of CPAP vs. sham control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff	95% CI	P Btw	Dropout, %	Study Quality
MAP												
Coughlin 2007[145] 17251237	40 (14) [>15]	14 (4.9)	6 wk (XO)	CPAP	34	nd	103.1 (8.7)	-5.5	-8.2, -2.8	<0.01	3	A
				Sham	34		108.6 (9.9)					
Robinson 2006[164] 16455835	nd	5.3 (IRQ 3.0-7.0)	1 mo (XO)	AutoCPAP	32	106 (14)	105.6 (13.2)	+1.1 *	-2.9, +5.1	NS	9	A
				Sham	32	109 (13)	107.6 (13.6)					
Campos-Rodriguez 2006[144] 16778262	60 (22) [≥10]	13.6 (3.6)	4 wk (PL)	CPAP	34	100.8 (10.7)	99.8 (10.1)	-0.8	-3.1, 4.9	NS	6	B
				Sham CPAP	34	98.9 (10.0)	98.9 (11.2)					
Hui 2006[150] 16928705	30 (16) [≥5]	10.7 (3.3)	3 mo (PL)	CPAP	23	98.9 (10.1)	96.9 (10.1)	-2.2	-6.2, +1.9	NS	18	B
				Sham CPAP	23	98.1 (10.1)	98.3 (11.5)					
Norman 2006[163] 16585412	54 (30) [>15]	12.0 (6.6)	2 wk (PL)	CPAP	18	Change (SD): -3.1 (5.5)		-6.4	-11.1, -1.7 †	<0.05	nd	C
				Sham CPAP	15	Change (SD): +3.3 (7.2)						
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	103.6 (16.1)	93.6 (11.3)	-11.3	-20, -2.7	0.01	47	C
				Sham CPAP	16	103.5 (12.1)	104.8 (10.6)					
SBP												
Coughlin 2007[145] 17251237	40 (14) [>15]	14 (4.9)	6 wk (XO)	CPAP	34	nd	135.7 (11.7)	-6.7	-10, -1.7	<0.01	3	A
				Sham	34		142.4 (14.0)					
Lam 2010[169] 19608589	39.7 (22.1) [≥15]	10.3 (4.9)	1 wk (PL)	AutoCPAP	30	131 (14.7)	127 (15.9)	-0.94	-5.2, 3.3 ‡	NS	0	A
				Sham CPAP	31	130 (16.5)	127 (15.9)					
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	130 (10.8)	127 (10.8)	-2	-8.5, 4.5 §	NS	2	B
				Sham CPAP	25	127 (10.0)	124 (10.0)					

Table 5.2.12. Blood pressure outcomes (mm Hg) in randomized controlled trials of CPAP vs. sham control (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff	95% CI	P Btw	Dropout %	Study Quality
Hui 2006[150] 16928705	30 (16) [≥5]	10.7 (3.3)	3 mo (PL)	CPAP	23	129.1 (14.4)	126.8 (14.4)	-2.5	-8.2, +3.2	NS	18	B
				Sham CPAP	23	127.7 (14.4)	128.0 (16.3)					
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	20	124.3 (18.8)	124.3 (21.9)	+1.6	-8.9, 12.1 **	NS	18	B
				Sham CPAP	25	125.0 (13.5)	123.4 (14)					
Mills 2006[160] 16357087 Lim 2007[161] 17694727	61 (33) [>15]	nd	2 wk (PL)	CPAP	17	155.2 (18.6)	145.1 (21.0)	-8.0	-22.4, 6.4 ††	nd	nd	B
				Sham CPAP	16	149.0 (23.2)	146.9 (21.2)					
Cross 2008[146] 18390635	63.0 (26) [>15]	nd	6 wk (XO)	AutoCPAP	27	143.0 (17.1)	141 (16.1)	-3.8	-10.5, 2.9 ‡‡	0.07	13	B
				Sham CPAP	27	143.0 (17.1)	144.8 (19.2)					
Norman 2006[163] 16585412	54 (30) [>15]	12.0 (6.6)	2 wk (PL)	CPAP	18	Change (SD): -2.2 (5.5)		-5.7	-11.2, -0.2 §§	<0.05	nd	C
				Sham CPAP	15	Change (SD): +3.5 (9.7)						
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL)	CPAP	16	140.1 (17.6)	132.1 (15.7)	-10.3	-20.6, 0.1	0.05	47	C
				Sham CPAP	16	141.0 (13.8)	143.2 (11.2)					
Arias 2005[141] 16009798	44 (28) [≥10]	nd	12 wk (XO)	AutoCPAP	25	127 (50)	127 (40)	0	-18, 18 ***	NS	7	C
				Sham CPAP	25	127 (50)	127 (60)					

Table 5.2.12. Blood pressure outcomes (mm Hg) in randomized controlled trials of CPAP vs. sham control (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff	95% CI	P Btw	Dropout %	Study Quality
DBP												
Coughlin 2007[145] 17251237	40 (14) [>15]	14 (4.9)	6 wk (XO)	CPAP	34	nd	86.8 (8.7)	-4.9	-8.0, -1.8	<0.01	3	A
				Sham	34		91.7 (9.3)					
Lam 2010[169] 19608589	39.7 (22.1) [≥15]	10.3 (4.9)	1 wk (PL)	AutoCPAP	30	80 (10.8)	76 (8.2)	-0.61	-4.1, 2.9 †††	NS	0	A
				Sham CPAP	31	82 (11.6)	79 (11.8)					
Barbe 2001[142] 11388814	57 (15) [≥30]	7.0 (2)	6 wk (PL)	CPAP	29	82(5.4)	81 (5.4)	-1	-5.4, 3.4 ‡‡‡	NS	2	B
				Sham CPAP	25	80 (10.0)	80 (10.0)					
Hui 2006[150] 16928705	30 (16) [≥5]	10.7 (3.3)	3 mo (PL)	CPAP	23	84.3 (10.1)	82.3 (9.6)	-1.8	-5.3, +1.8	NS	18	B
				Sham CPAP	23	83.6 (10.1)	83.4 (9.1)					
Egea 2008[147] 17904420	35 (17) [>10]	7.3 (4.5)	3 mo (PL)	CPAP	20	75.6 (10.3)	76.0 (12.5)	-0.8	-8.9, 7.3 §§§	NS	18	B
				Sham CPAP	25	75.8 (12)	77.0 (18.5)					
Mills 2006[160] 16357087 Lim 2007[161] 17694727	61 (33) [>15]	nd	2 wk (PL)	CPAP	17	84.2 (10.7	79.5 (13.2)	-4.0	-12.5, 4.5 ****	nd	nd	B
				Sham CPAP	16	83.6 (14.0)	82.9 (12.4)					
Cross 2008[146] 18390635	63.0 (26) [>15]	nd	6 wk (XO)	AutoCPAP	27	80.4 (10.5)	82.3 (9.9)	0	-3.5, 3.5 ††††	NS	13	B
				Sham CPAP	27	80.4 (10.5)	82.3 (8.8)					
Norman 2006[163] 16585412	54 (30) [>15]	12.0 (6.6)	2 wk (PL)	CPAP	18	Change (SD): -2.6 (4.7)		-5.2	-9.3, -1.1 ‡‡‡‡	<0.05	nd	C
				Sham CPAP	15	Change (SD): +2.6 (6.5)						
Becker 2003[143] 12515745	65 (27) [≥5]	14.1 (3.2)	9 wk (PL	CPAP	16	86.4 (16.1)	75.8 (11.6)	-11.2	-19.5, -2.8	0.01	47	C
				Sham CPAP	16	85.4 (12.3)	85.9 (10.6)					
Arias 2005[141] 16009798	44 (28) [≥10]	nd	12 wk (XO)	AutoCPAP	25	79 (25)	78 (25)	0	-11, 11 §§§§	NS	7	C
				Sham CPAP	25	79 (25)	78 (30)					

* Median
† Estimated from reported data.
‡ Estimated from reported data.

§ Estimated from reported data.
** Estimated from reported data.
†† Estimated from reported data.
‡‡ Estimated from reported data.
§§ Estimated from reported data.
*** Estimated from reported data.
††† Estimated from reported data.
‡‡‡ Estimated from reported data.
§§§ Estimated from reported data.
**** Estimated from reported data.
†††† Estimated from reported data.
‡‡‡‡ Estimated from reported data.
§§§§ Estimated from reported data.

Table 5.3.1. Randomized controlled trials of oral vs. nasal CPAP: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Anderson 2003[171] 14572126	oral CPAP nasal CPAP	manual (both)	46	nd	43	high BMI	New Zealand (nd)	small sample
Mortimore 1998[172] 9741373	oral CPAP nasal CPAP	manual (separate?)	52	nd	32	-	UK (nd)	study inclusion criteria not stated
Khanna 2003[173] 14592306	oral CPAP nasal CPAP	manual (separate)	52	63	34.6	-	US (2000-01)	incomplete reporting

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, eg if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.3.2. Compliance (mean hr/ night) in randomized controlled trials of oral vs. nasal CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Change (final)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Anderson 2003[171] 14572126	85 (36) [>20]	17 (2.3)	1 mo (XO)	oral CPAP	21	3.5	-0.3	-1.1, 0.5 *	0.50	16	B
				nasal CPAP	21	3.8					
Mortimore 1998[172] 9741373	35 (23) [nd]	nd	1 mo (XO)	oral CPAP	20	4.3	-1.0	-1.8, -0.3	0.01	0	C
				nasal CPAP	20	5.3					
Khanna 2003[173] 14592306	60 † (39) [>15]	13.3 (3.6)	1 mo (PL)	oral CPAP	21	5.8	0	-0.73, 0.73 ‡	NS	29	C
				nasal CPAP	17	5.8					
			2 mo (PL)	oral CPAP	15	5.8	0.1	-1.2, 1.4 §	NS		
				nasal CPAP	12	5.7					

* Estimated from reported P value
† RDI
‡ Estimated from reported data
§ Estimated from reported data

Table 5.3.3. ESS in randomized controlled trials of oral vs. nasal CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Anderson 2003[171] 14572126	85 (36) [>20]	17 (2.3)	1 mo (XO)	oral CPAP	21	17 (2.3)	-10.0	0.7	-1.7, 3.1	0.20	16	B
				nasal CPAP	21	17 (2.3)	-11.0					
Mortimore 1998[172] 9741373	35 (23) [nd]	nd	1 mo (XO)	oral CPAP	20	nd	9.8	1.6	0.38, 2.82*	<0.01	0	C
				nasal CPAP	20	nd	8.2					

* Estimated from reported P value

Table 5.4.1. Randomized controlled trials of autoCPAP vs. CPAP: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Damjanovic 2009[174] 19129293	autoCPAP CPAP	auto/manual (separate)	57	78	31.1	-	Germany (nd)	
Meurice 2007[177] 17638595	autoCPAP CPAP	auto/manual (separate)	55	nd	30.8	-	France (nd)	pt recruitment unclear
Patruno 2007[180] 17494789	autoCPAP CPAP	manual (separate)	48	81	36.5	some with HTN	Italy (nd)	incomplete reporting
Planes 2003[193] 12683473	autoCPAP CPAP	manual (separate)	54	77	32.4	-	France (1998-99)	pt recruitment unclear
Series 1997[191] 9341056	autoCPAP est./meas. CPAP	manual (separate)	36-65 (range)	nd	36.4	-	Canada (1995-96)	potential selection bias
Fietze 2007[175] 17337881	autoCPAP CPAP	auto/manual (separate)	54	95	30.9	-	Germany (nd)	incomplete reporting; pt selection unclear
Resta 2004[188] 15679008	autoCPAP CPAP	manual (nd)	33	90	36.7	-	Italy (nd)	incomplete reporting
Vennelle 2010[194] 20175411	autoCPAP CPAP	auto/manual (separate)	50	77	34.5	-	UK	-
Hukins 2004[183] 15683142	autoCPAP CPAP	manual (nd)	50	87	35.2	-	Australia (nd)	-
Randerath 2001[190] 11254519	autoCPAP CPAP	manual (separate)	55	87	32.4	-	Germany	-
Massie 2003[186] 12406840	autoCPAP CPAP	manual (both)	49	82	32	-	Australia, UK, U.S.	incomplete reporting
To 2008[181] 18197915	autoCPAP CPAP	auto/manual (separate?)	46	nd	28.7	severe OSA	China (nd)	-
Nussbaumer 2006[179] 16537862	autoCPAP CPAP	manual (separate)	49	90	31.1	-	Switzerland (nd)	-
Senn 2003[189] Switzerland 14525804	autoCPAP (2 modes) CPAP	auto/manual (separate)	53	79	33.3	-	Switzerland (nd)	-
Nolan 2007[178] 17326544	autoCPAP CPAP	auto/manual (separate?)	53	90	29.9	-	Ireland (nd)	-

Table 5.4.1. Randomized controlled trials of autoCPAP vs. CPAP: study characteristics (continued)

Study PMID	Interventions	CPAP Pressure † (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Noseda 2004[187] 15249439	autoCPAP CPAP	manual (separate)	49	96	32.3	high variability in pressure required during 2 wk autoCPAP run-in	Belgium (nd)	-
Hudgel 2000[182] 10947032	autoCPAP CPAP	auto/manual (both)	46	54	42	-	U.S.	incomplete reporting; 35% drop out
Marrone 2004[185] 15165530	autoCPAP CPAP	auto/manual (separate)	53	95	32.9	-	Italy	small sample & no power calc
Galetke 2008[176] 17148931	autoCPAP CPAP	auto/manual (separate)	56	80	29.3	-	Germany (nd)	incomplete reporting; small sample & no power calc
Hussain 2004[184] 15072173	autoCPAP CPAP	manual (separate)	45	90	35.9	-	Pakistan and Canada (nd)	pt recruitment method unclear; small sample & no power calc
Teschler 2000[192] 10885414	autoCPAP CPAP	manual/auto (separate)	52	100	33.8	-	Germany (nd)	incomplete reporting; small sample; ?power calc

* Method for choosing CPAP Pressure: manual (during sleep study), auto (determined with AutoCPAP); Algorithm (by an algorithm); nd = no data reported; NA = not applicable (e.g., if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study), Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

† Method for choosing CPAP Pressure: manual (during sleep study), auto (determined with AutoCPAP); Algorithm (by an algorithm); nd = no data reported; NA = not applicable (e.g., if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study), Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.4.2. Compliance (mean hr/night) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	P Btw	Dropout, %	Study Quality
Damjanovic 2009[174] 19129293	44 (25) [≥15]	8.8 (5.2)	3 mo (PL)	autoCPAP	46	5.4	0	-0.7, 0.7	nd	8	B
				CPAP	46	5.4					
			9 mo (PL)	autoCPAP	34	5.2	0.1	-0.9, 1.1	nd	22	
				CPAP	44	5.1					
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	3 mo (PL)	autoCPAP (AutoSet)	15	6.0	-0.1	-0.786, 0.586	nd	15	B
				CPAP	14	6.1					
			6 mo (PL)	autoCPAP (AutoSet)	15	6.1	-0.4	-1.28, 0.48	nd	15	
				CPAP	14	6.5					
Patruno 2007[180] 17494789	46 (14) [>20]	15 (2.7)	3 mo (PL)	autoCPAP	15	6.2	0.2	-0.25, 0.65	nd	23	C
				CPAP	16	6.0					
Planes 2003[193] 12683473	59 (17) [≥30]	15.1 (3.9)	2 mo (PL)	autoCPAP	16	4.5	-0.8	nd	NS	14	C
				CPAP	14	5.3					
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	nd *	-	-	NS	0	C
				CPAP	12	nd					
				autoCPAP meas.	12	nd †	-	-	NS		
				CPAP	12	nd					
Fietze 2007[175] 17337881	42 (26) [≥10]	nd	1.5 mo (PL)	autoCPAP	20	5.0	0.8	nd	NS	0	C
				CPAP	21	4.2					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	5.2	-0.1	-1.12, 0.92	nd	0	C
				CPAP	10	5.3					
Vennelle 2010[194] 20175411	33 (18) [≥15]	14 (3)	6 wk (XO)	autoCPAP	181	4.2	0.2	0.003, 0.397	0.047	9.5	A
				CPAP	181	4.0					
Hukins 2004[183] 15683142	56 (nd)	12.5 (nd)	1–2 mo (XO)	autoCPAP	46	5.05	0.19	-0.062, 0.442 ‡	0.14	16	B
				CPAP	46	4.86					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?)	5.26	0	-0.44, 0.44	nd	12	B
				CPAP	52 (46?)	5.26					
Massie 2003[186] 12406840	nd [≥15]	nd	1.5 mo (XO)	autoCPAP	44	5.1	0.58	0.18, 0.99 §	0.005	4	B
				CPAP	44	4.52					

Table 5.4.2. Compliance (mean hr/night) in randomized controlled trials of autoCPAP vs. CPAP (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	P Btw	Dropout, %	Study Quality
To 2008[181] 18197915	54 (nd) [>30]	13.4 (nd)	1 mo (XO)	autoCPAP	41	4.3	0.5	0.02, 0.98 **	0.04	5	B
				CPAP	41	3.8					
			2 mo (XO)	autoCPAP	41	4.4	0.7	0.17, 1.23 ††	0.01		
				CPAP	41	3.7					
Nussbaumer 2006[179] 16537862	41 (20) [>10]	12.7 (3.3)	1 mo (XO)	autoCPAP	30	5.1	0.3	-0.29, 0.89	nd	12	B
				CPAP	30	4.8					
Senn 2003[189] Switzerland 14525804	46 (23) [>10]	14.2 (3.8)	1 mo (XO)	autoCPAP (Autoset T)	29	5.5	-0.1	nd	NS	7	B
				autoCPAP (AutoAdjust)	29	5.5	-0.1	nd	NS		
				CPAP	29	5.6					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4.0)	2 mo (XO)	autoCPAP	29	4.9	0	nd	0.94	15	B
				CPAP	29	4.9					
Noseda 2004[187] 15249439	51 (25) [>20]	10.7 (2.4)	2 mo (XO)	autoCPAP	24	5.3	-0.2	-0.89, 0.49	nd	11	B
				CPAP	24	5.5					
Hudgel 2000[182] 10947032	30 (25) [nd]	16.0 (5.0)	3 mo (XO)	autoCPAP	14	6.0	0.5	0.02, 0.98 ‡‡	<0.04	35	C
				CPAP	19	5.5					
Marrone 2004[185] 15165530	68 (12) [30]	16.3 (5.0)	1 mo (XO)	autoCPAP	22	4.9	0.5	-0.26, 1.26	nd	0	C
				CPAP	22	4.4					
Galetke 2008[176] 17148931	33 (19) [>10]	10.3 (5.7)	2 mo (XO)	autoCPAP	20	6.37	-0.01	-0.82, 0.8	nd	0?	C
				CPAP	20	6.38					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	4.3	0.6	-0.84, 2.04	nd	0	C
				CPAP	10	3.7					
Teschler 2000[192] 10885414	53 (26) [>20]	nd	2 mo (XO)	autoCPAP	10	6.3	0.2	-0.7, 1.1	nd	0?	C
				CPAP	10	6.1					

* directions of changes were not reported in the study
† directions of changes were not reported in the study

‡ Estimated from reported P value
§ Estimated from reported P value
** Estimated from reported P value
†† Estimated from reported P value
‡‡ Estimated from reported P value

Table 5.4.3. AHI (events/hr) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Damjanovic 2009[174] 19129293	44 (25) [≥15]	8.8 (5.2)	3 mo (PL)	autoCPAP	46	41.8 (23.7)	-37.0	1.8	-7.14, 10.74	nd	8	B
				CPAP	46	45.5 (24.4)	-38.8					
			9 mo (PL)	autoCPAP	34	41.8 (23.7)?	-38.2	1.9	-6.86, 10.66	nd	22	
				CPAP	44	45.5 (24.4)?	-40.1					
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	6 mo (PL)	autoCPAP (AutoSet)	15	53.4 (15.1)	-51.1	2.6	-8.88, 14.08	nd	15	B
				CPAP	14	56.1 (21.4)	-53.7					
Patruno 2007[180] 17494789	46 (14) [>20]	15 (2.7)	3 mo (PL)	autoCPAP	15	47.3 (14.7)	-41.3	2.7	-7.01, 12.41	nd	23	C
				CPAP	16	46.0 (14.6)	-44.0					
Planes 2003[193] 12683473	59 (17) [≥30]	15.1 (3.9)	2 mo (PL)	autoCPAP	16	57.5 (16.5)	-49.9	0.7	-10.06, 11.46	nd	14	C
				CPAP	14	61.0 (17.4)	-50.6					
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	61.5 (27.9)	nd †	-	-	NS	0	C
				CPAP	12	50.1 (14.5)	nd					
				autoCPAP meas.	12	46.8 (22.3)	nd ‡	-	-	NS		
				CPAP	12	50.1 (14.5)	nd					
Fietze 2007[175] 17337881	42 (26) [≥10]	nd	1.5 mo (PL)	autoCPAP	20	43.3 (30.2)	-38.9	0.5	-1.19, 2.19	nd	0	C
				CPAP	21	40.4 (26.1)	-36.5					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	48.0 (14.3)	-39.7	-2.8	-12.96, 7.36	nd	0	C
				CPAP	10	45.3 (10.7)	-36.9					

Table 5.4.3. AHI (events/hr) in randomized controlled trials of autoCPAP vs. CPAP (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI §	P Btw	Dropout, %	Study Quality
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?)	35.1 (26)	-30.1	0.7	-0.88, 2.28	nd	12	B
				CPAP	52 (46?)	35.1 (26)	-30.8					
Massie 2003[186] 12406840	nd [≥15]	nd	1.5 mo (XO)	autoCPAP	44	nd	nd	-1.1	-2.89, 0.69	nd	4	B
				CPAP	44	nd	nd					
Nussbaumer 2006[179] 16537862	41 (20) [>10]	12.7 (3.3)	1 mo (XO)	autoCPAP	30	41.1 (19.7)	-36.5	-0.8	-1.7, 3.3 **	nd	12	B
				CPAP	30	41.2 (19.7)	-35.7					
Senn 2003[189] Switzerland 14525804	46 (23) [>10]	14.2 (3.8)	1 mo (XO)	autoCPAP (Autoset T)	29	45.8 (22.6)	-39.8	0.7	-1.26, 2.66	nd	7	B
				autoCPAP (AutoAdjust)	29	45.8 (22.6)	-38.1	2.4	-0.34, 5.14	nd		
				CPAP	29	45.8 (22.6)	-40.5					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4.0)	2 mo (XO)	autoCPAP	29	14.7 (8)	-12.0	-0.8	-1.89, 0.29 ††	0.15	15	B
				CPAP	29	14.7 (8)	-11.2					
Galetke 2008[176] 17148931	33 (19) [>10]	10.3 (5.7)	2 mo (XO)	autoCPAP	20	32.9 (19.1)	-27.3	1.0	-0.45, 2.45	nd	0?	C
				CPAP	20	32.9 (19.1)	-28.3					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	47.2 (35.6)	-34.1	3.5	-1.02, 8.02	nd	0	C
				CPAP	10	47.2 (35.6)	-37.6					
Teschler 2000[192] 10885414	53 (26) [>20]	nd	2 mo (XO)	autoCPAP	10	52.9 (25.6)	-48.9	0.3	-0.29, 0.89	nd	0?	C
				CPAP	10	52.9 (25.6)	-49.2					

* Estimated from reported data
† Directions of changes were not reported in the study
‡ Directions of changes were not reported in the study
§ Estimated from reported data
** Actual reported data
†† Estimated from reported P value

Table 5.4.4. ESS in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Damjanovic 2009[174] 19129293	44 (25) [≥15]	8.8 (5.2)	3 mo (PL)	autoCPAP	46	8.5 (5.42)	-2.6	-0.3	-2.32, 1.72	nd	8	B
				CPAP	46	9.3 (4.75)	-2.3					
			9 mo (PL)	autoCPAP	34	8.5 (5.42) ?	-2.6	0.1	-1.92, 2.12	nd	22	
				CPAP	44	9.3 (4.75) ?	-2.7					
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	3 mo (PL)	autoCPAP (AutoSet)	15	12.9 (4.3)	-9.1	-3.3	-6.68, 0.08	NS	15	B
				CPAP	14	10.6 (5.2)	-5.8					
			6 mo (PL)	autoCPAP (AutoSet)	15	12.9 (4.3)	-7.7	-3.0	-6.44, 0.44	NS	15	
				CPAP	14	10.6 (5.2)	-4.7					
Patruno 2007[180] 17494789	46 (14) [>20]	15 (2.7)	3 mo (PL)	autoCPAP	15	15.8 (3.5)	nd	nd	nd	NS	23	C
				CPAP	16	14.1 (1.7)	nd					
Planes 2003[193] 12683473	59 (17) [≥30]	15.1 (3.9)	2 mo (PL)	autoCPAP	16	15.5 (4.7)	-8.0	-0.9	-3.72, 1.92	nd	14	
				CPAP	14	14.7 (3.9)	-7.1					
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	17.0 (4.1)	-9.1	-0.8	-4.28, 2.69	nd	0	C
				CPAP	12	16.1 (4.5)	-8.3					
				autoCPAP meas.	12	13.5 (4.7)	-6.5	1.8	-1.78, 5.38	nd		
				CPAP	12	16.1 (4.5)	-8.3					
Fietze 2007[175] 17337881	42 (26) [≥10]	nd	1.5 mo (PL)	autoCPAP	20	nd	nd	nd	nd	NS	0	C
				CPAP	21	nd	nd					

* Estimated from reported data

Table 5.4.4. ESS in randomized controlled trials of autoCPAP vs. CPAP (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	15.7 (5.1)	-10.5	-2.6	-5.84, 0.64	nd	0	C
				CPAP	10	12.0 (3.2)	-7.9					
Vennelle 2010[194] 20175411	33 (18) [≥15]	14 (3)	6 wk (XO)	autoCPAP	181	14 (3)	-4.5	-0.5	-0.95, -0.05	0.031	9.5	A
				CPAP	181	14 (3)	-4					
Hukins 2004[183] 15683142	56 (nd) [≥5]	12.5 (nd)	1 – 2 mo (XO)	autoCPAP	46	12.5 (nd)	-4.5	-0.2	nd	NS	16	B
				CPAP	46	12.5 (nd)	-4.3					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?)	11.1 (5.1)	-3.3	-1	-2.26, 0.26	nd	12	B
				CPAP	52 (46?)	11.1 (5.1)	-2.3					
Massie 2003[186] 12406840	nd [≥15]	nd	1.5 mo (XO)	autoCPAP	44	nd	nd	-1	-2.06, 0.06 †	0.065	4	B
				CPAP	44	nd	nd					
To 2008[181] 18197915	54 (nd) [>30]	13.4 (nd)	1 mo (XO)	autoCPAP	41	13.4 (5.76)	-4.9	0.3	-1.46, 2.06	nd	5	B
				CPAP	41	13.4 (5.76)	-5.2					
			2 mo (XO)	autoCPAP	41	13.4 (5.76)	-4.9	0	-1.76, 1.76	nd		
				CPAP	41	13.4 (5.76)	-4.9					
Nussbaumer 2006[179] 16537862	41 (207) [>10]	12.7 (3.29)	1 mo (XO)	autoCPAP	30	12.7 (0.6)	-6.6	0	-1.6, 1.1	nd	12	B
				CPAP	30	12.7 (0.6)	-6.6					
Senn 2003[189] Switzerland 14525804	46 (23) [>10]	14.2 (3.77)	1 mo (XO)	autoCPAP (Autoset T)	29	14.2 (3.77)	-5.2	0.8	-0.49, 2.09	nd	7	B
				autoCPAP (AutoAdjust)	29	14.2 (3.77)	-6.2	-0.2	-1.68, 1.28	nd		
				CPAP	29	14.2 (3.77)	-6.0					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4.0)	2 mo (XO)	autoCPAP	29	12.3 (4.0)	-3.7	0.9	-0.99, 2.79 ‡	0.35	15	B
				CPAP	29	12.3 (4.0)	-4.6					

Table 5.4.4. ESS in randomized controlled trials of autoCPAP vs. CPAP (continued)

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Noseda 2004[187] 15249439	nd [>20]	10.7 (2.4)	2 mo (XO)	autoCPAP	24	10.7 (2.4)	nd	-1	-1.76, -0.24 §	<0.01	11	B
				CPAP	24	10.7 (2.4)	nd					
Hudgel 2000[182] 10947032	30 (25) [nd]	16.0 (5.0)	3 mo (XO)	autoCPAP	39	16.0 (5.0)	-7.0	1	-0.96, 2.96	nd	35	C
				CPAP	39	16.0 (5.0)	-8.0					
Marrone 2004[185] 15165530	68 (12) [30]	16.3 (5.0)	1 mo (XO)	autoCPAP	22	16.3 (5.0)	-12.4	-1	-2.4, 0.4	nd	0	C
				CPAP	22	16.3 (5.0)	-11.4					
Galetke 2008[176] 17148931	33 (19) [>10]	10.3 (5.7)	2 mo (XO)	autoCPAP	20	10.3 (5.7)	-5.4	-1.7	-3.76, 0.36	nd	0	C
				CPAP	20	10.3 (5.7)	-3.7					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	11.1 (6.4)	-3.1	1.4	-2.2, 5.0	nd	0	C
				CPAP	10	11.1 (6.4)	-4.5					

* Estimated from reported data
† Estimated from reported P value
‡ Estimated from reported P value
§ Estimated from reported P value

Table 5.4.5. Arousal index (events/hr) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Damjanovic 2009[174] 19129293	44 (25) [≥15]	8.8 (5.18)	3 mo (PL)	autoCPAP	46	30.6 (22.4)	-18.3	-0.2	-7.92, 7.52	nd	8	B
				CPAP	46	34.5 (21.0)	-18.1					
				autoCPAP	34	30.6 (22.4)?	-17.7	3.6	-4.09, 11.29	nd	22	
				CPAP	44	34.5 (21.0)?	-21.3					
Planes 2003[193] 12683473	59 (17) [≥30]	15.1 (3.9)	2 mo (PL)	autoCPAP	16	44.4 (19.1)		3.3	-7.14, 12.74	nd	14	C
				CPAP	14	48.5 (14.2)						
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	nd	nd †	-	-	NS	0	C
				CPAP	12	nd	nd					
				autoCPAP meas.	12	nd	nd ‡	-	-	NS		
				CPAP	12	nd	nd					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	43.1 (11.9)	-35.7	0.1	-8.29, 8.49	nd	0	C
				CPAP	10	43.1 (9.1)	-35.8					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?)	34 (21.7)	-23.1	-1.7	-3.7, 0.3	nd	12	B
				CPAP	52 (46?)	34 (21.7)	-21.4					
Nolan 2007[178] 17326544	15 (8) [≥5]	12.3 (4)	2 mo (XO)	autoCPAP	29	16.0 (14.0)	-14.0	-3.0	-5.7, -0.29 §	0.03	15	B
				CPAP	29	16.0 (14.0)	-11.0					
Galetke 2008[176] 17148931	33 (19) [>10]	10.3 (5.7)	2 mo (XO)	autoCPAP	20	17.6 (9.2)	-4.0	1.0	-2.52, 4.52	nd	0?	C
				CPAP	20	17.6 (9.2)	-5.0					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	17.3 (17.7)	-11.4	1.0	-2.5, 4.5	nd	0	C
				CPAP	10	17.3 (17.7)	-12.4					

* Estimated from reported data
† Directions of changes were not reported in the study
‡ Directions of changes were not reported in the study
§ Estimated from reported P value

Table 5.4.6. Minimum O_2 saturation (%) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net Diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	6 mo (PL)	AutoCPAP (AutoSet)	15	82.1 (12.8)	0.2	-2.9	-7.1, 7.5	nd	15	B
				CPAP	14	82.3 (9.9)	0.5					
Patruno 2007[180] 17494789	46 (14) [>20]	15 (2.7)	3 mo (PL)	AutoCPAP	15	71.7 (10.6)	16.4	-4.4	-11.8, 3.0	nd	23	C
				CPAP	16	70.0 (11.7)	20.8					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	AutoCPAP	10	72.4 (10.5)	15.9	0.9	-7.4, 9.2	nd	0	C
				CPAP	10	74.1 (10.8)	15.0					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	AutoCPAP	52 (46?)	81 (8.0)	7.0	-1.0	-2.1, 0.1	nd	12	B
				CPAP	52 (46?)	81 (8.0)	8.0					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4)	2 mo (XO)	AutoCPAP	29	79 (11.5)	8.5	4.8	-7.4, 17.0 †	0.44	15	B
				CPAP	29	79 (11.5)	3.7					
Galetke 2008[176] 17148931	33 (19) [>10]	10.3 (5.7)	2 mo (XO)	AutoCPAP	20	77.8 (8.4)	8.7	-1.8	-3.8, 0.2	nd	0?	C
				CPAP	20	77.8 (8.4)	10.5					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	AutoCPAP	10	67.8 (12.5)	14.0	-3.9	-7.3, -0.5	nd	0	C
				CPAP	10	67.8 (12.5)	17.9					

* Estimated from reported data
† Estimated from reported P value

Table 5.4.7. Sleep efficiency (%) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	86.9 (8)	-0.5	-2.5	-8.89, 3.89 *	nd	0	C
				CPAP	10	84.2 (4.9)	2					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4)	2 mo (PL)	autoCPAP	29	79 (9)	4	-1	-4.34, 2.34 †	0.39	15	B
				CPAP	29	79 (9)	5					

* Estimated from reported data
† Estimated from reported P value

Table 5.4.8. REM sleep (%) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	6 mo (PL)	autoCPAP (AutoSet)	15	18.9 (6.6)	-2.4	-2.9	-7.49, 1.69	nd	15	B
				CPAP	14	19.1 (5.9)	0.5					
Planes 2003[193] 12683473	59 (17) [≥30]	15.1 (3.9)	2 mo (PL)	autoCPAP	16	12.4 (7.0)	4.2	0.5	-5.44, 6.44	nd	14	C
				CPAP	14	13.7 (9.3)	3.7					
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	nd	nd *	-	-	NS	0	C
				CPAP	12	nd	nd					
				autoCPAP meas.	12	nd	nd †	-	-	NS		
				CPAP	12	nd	nd					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	15.0 (8.1)	6.7	-2	-10.31, 6.31	nd	0	C
				CPAP	10	15.9 (4.2)	8.7					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?) ‡	11 (8)	6.0	1	-0.63, 2.63	nd	12	B
				CPAP	52 (46?) §	11 (8)	5.0					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4)	2 mo (XO)	autoCPAP	29	17.6 (5.1)	-0.5	-2.5	-5.11, 0.11 **	0.06	15	B
				CPAP	29	17.6 (5.1)	2.0					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	15 (7.0)	4.0	-1	-4.72, 2.72	nd	0	C
				CPAP	10	15 (7.0)	5.0					

* Directions of changes were not reported in the study
† Directions of changes were not reported in the study
‡ Unclear
§ Unclear
** Estimated from reported P value

Table 5.4.9. Stage 3 or 4 sleep (%) in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI *	P Btw	Dropout, %	Study Quality
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	6 mo (PL)	autoCPAP (AutoSet)	15	25.5 (14.7)	-4.4	-5.2	-13.51, 3.11	nd	15	B
				CPAP	14	17.1 (7)	0.8					
Series 1997[191] 9341056	44 (20) [nd]	15.5 (4.5)	0.75 mo (PL)	autoCPAP est.	12	nd	nd †	-	-	NS	0	C
				CPAP	12	nd	nd					
				autoCPAP meas.	12	nd	nd ‡	-	-	NS		
				CPAP	12	nd	nd					
Resta 2004[188] 15679008	47 (11) [>30]	13.9 (3.2)	1 mo (PL)	autoCPAP	10	19.8 (10.9)	14	7.3	-2.35, 16.95	nd	0	C
				CPAP	10	22.8 (12.5)	6.7					
Randerath 2001[190] 11254519	35 (26) [≥10]	11.1 (5.1)	1.5 mo (XO)	autoCPAP	52 (46?) §	14 (11)	0	-1	-3.45, 1.45	NS	12	B
				CPAP	52 (46?) **	14 (11)	1.0					
Nolan 2007[178] 17326544	15 (8) [≥5)	12.3 (4)	2 mo (XO)	autoCPAP	29	13.7 (7.8)	1.3	0.3	-3.29, 3.89 ††	0.87	15	B
				CPAP	29	13.7 (7.8)	1.0					
Hussain 2004[184] 15072173	47 (36) [>15]	11.1 (6.4)	1 mo (XO)	autoCPAP	10	14 (25)	-4.0	-8	-18.32, 2.32	nd	0	C
				CPAP	10	14 (25)	4.0					

* Estimated from reported data
† directions of changes were not reported in the study
‡ directions of changes were not reported in the study
§ Unclear
** Unclear
†† Estimated from reported P value

Table 5.4.10. Quality of life and functional outcomes in randomized controlled trials of autoCPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If significant difference: Net difference	95% CI	Test range "Worst"	Test range "Best"	P Btw	Dropout, %	Study Quality
Vennelle 2010[194] 20175411	33 (18) [≥15]	14 (3)	6 wk (XO)	autoCPAP	181	SF-36-M	0						9.5	A
				CPAP	181	SF-36-P	0							
						Vigilance (OSLER)	0							
						Vigilance (Psychomotor)	0							
Meurice 2007[177] 17638595	55 (10) [nd]	11.8 (4.9)	3 mo (PL)	autoCPAP (AutoSet)	15	SF-36-M	0						15	B
				CPAP	14									
						SF-36-P	0							
			6 mo (PL)	autoCPAP (AutoSet)	15	SF-36-M	0						15	
				CPAP	14									
						SF-36-P	0							
Hukins 2004[183] 15683142	56 (nd) [≥5]	12.5 (nd)	2 mo (XO)	autoCPAP	46	SF-36-M	0						16	B
				CPAP	46									
						SF-36-P	0							
Massie 2003[186] 12406840	nd [≥15]	nd	1.5 mo (XO)	autoCPAP	44	SF-36 - MH	autoCPAP	5	0.16, 9.8 *	0	100	<0.05	4	B
				CPAP	44									
						SF-36 - vitality	autoCPAP	7	0.6, 13.4 †	0	100	<0.05		
						SF-36 – remainder	0							
To 2008[181] 18197915	54.3 (nd) [>30]	13.4 (nd)	1 mo (XO)	autoCPAP	41	SAQLI	0						5	B
				CPAP	41									
			2 mo (XO)	autoCPAP	41	SAQLI	0							
				CPAP	41									
Nussbaumer 2006[179] 16537862	41 (20) [>10]	12.7 (3.3)	1 mo (XO)	autoCPAP	30	SF-36 all	0						12	B
				CPAP	30									
Senn 2003[189] 14525804	46 (23) [>10]	14.2 (3.8)	1 mo (XO)	autoCPAP (Autoset T)	29	SF-36 all	0						7	B
				autoCPAP (AutoAdjust)	29									
				CPAP	29									
						Vigilance (OSLER)	0							
Fietze 2007[175] 17337881	42 (26) [≥10]	nd	1.5 mo (XO)	autoCPAP	20	SF-36 all	0						0	C
				CPAP	21									

* Estimated from reported P value
† Estimated from reported P value

Table 5.5.1. Characteristics of randomized controlled trials of bilevel CPAP vs. CPAP or autoCPAP

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Piper 2008[197] 18203817	Bilevel CPAP CPAP	manual (nd)	50	64	53	morbidly obese	Australia (nd)	unclear % of central apnea
Reeves-Hoche 1995[198] 7842204	Bilevel CPAP CPAP	manual (separate)	47	73	39.4	-	US (nd)	differential drop out
Gay 2003[195] 14655921	Bilevel CPAP CPAP	manual (split)	44	81	35.2	-	US (nd)	unclear conduct of randomization
Khayat 2008[196] 18641111	Bilevel CPAP CPAP	manual? (separate)	53	nd	33.6	AHA II or III	US (2005-07)	small sample; possible selection bias
Randerath 2003[199] 12942031	Bilevel CPAP AutoCPAP	manual (separate)	57	85	33.5	intolerance to CPAP	Germany (nd)	assumptions on missing pts unclear

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.5.2. Compliance (mean hr/night) in randomized controlled trials of bilevel CPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Compliance (hr/night)	Difference	95% CI	P Btw	Dropout, %	Study Quality
Piper 2008[197] 18203817	nd	14.5 (IQR = 12-19)	3 mo (PL)	Bilevel CPAP	18	6.1	0.33	-1.8, 1.2	NS	0	B
				CPAP	18	5.8					
Reeves-Hoche 1995[198] 7842204	52 (3) [≥10]	nd	12 mo (PL)	Bilevel CPAP	26	4.9	-0.1	-0.52, 0.32*	NS	25	C
				CPAP	36	5.0					
Gay 2003[195] 14655921	44 (24) [>10]	12 (3.4)	1 mo (PL)	Bilevel CPAP	12	5.6	0	nd	NS	0	C
				CPAP	15	5.6					
Khayat 2008[196] 18641111	32 (16) [>10]	12.6 (6.3)	3 mo (PL)	Bilevel CPAP	13	4.5	0.9	-1.6, 3.4	NS	4	C
				CPAP	11	3.6					
Randerath 2003[199] 12942031	49 (27) [≥10]	12.1 (5.1)	1.5 mo (XO)	Bilevel CPAP	27 (?)	94.4% days used	4.8	-3.14, 12.74†	NS	26	C
				AutoCPAP	27 (?)	89.6% days used					

* Estimated from reported data
† Estimated from reported data

Table 5.5.3. ESS in randomized controlled trials of bilevel CPAP vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or diff	95% CI	P Btw	Dropout, %	Study Quality
Piper 2008[197] 18203817	nd	14.5 (IQR = 12-19)	3 mo (PL)	Bilevel CPAP	18	14 (IQR 12-19)	-9.0	-2.89	-7.56, 1.78	NS	0	B
				CPAP	18	15 (IQR 8-17)	-6.0					
Gay 2003[195] 14655921	44 (24) [>10]	12 (3.4)	1 mo (PL)	Bilevel CPAP	12	14.2 (3.4)	-6.4	-0.9	-3.88, 2.08 *	NS	0	C
				CPAP	15	13.5 (3.4)	-5.5					
Khayat 2008[196] 18641111	32 (16) [>10]	12.6 (6.3)	3 mo (PL)	Bilevel CPAP	13	11.8 (SE 1.8)	-2.6	2.1	-2.7, 6.9	NS	4	C
				CPAP	11	13.5 (SE 1.8)	-4.7					
Randerath 2003[199] 12942031	49 (27) [≥10]	12.1 (5.1)	1.5 mo (XO)	Bilevel CPAP	27 (?)	12.1 (5.1)	-3.7	1.2	-0.63, 3.03 †	NS	26	C
				AutoCPAP	27 (?)	12.1 (5.1)	-4.9					

* Estimated from reported data
† Estimated from reported data

Table 5.5.4. Quality of life and functional outcomes in randomized controlled trials of bilevel CPAP vs. CPAP

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome measure	Favors	If significant difference: Net difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw	Dropout, %	Study Quality
Piper 2008[197] 18203817	nd	14.5 (IQR = 12-19)	3 mo (PL)	Bilevel CPAP CPAP	18 18	SF-36 Mental	0						0	B
						SF-36 Physical	0							
Piper 2008[197] 18203817	nd	14.5 (IQR 12-19)	3 mo (PL)	Bilevel CPAP CPAP	18 18	mean of slowest 10% reaction	Bilevel CPAP	net diff of median 0.65				0.03	0	B
						Lapses	0							
						Median (ms)	0							
Gay 2003[195] 14655921	44 (24)	12	1 mo (PL)	Bilevel CPAP CPAP	12 15	FOSQ	0						0	C
Khayat 2008[196] 18641111	32 (16)	12.6 (6.3)	3 mo (PL)	Bilevel CPAP CPAP	13 11	MLHFQ	0						4	C

Table 5.7.1. Characteristics of randomized controlled trials of C-Flex™ vs. CPAP

Study PMID	Interventions	CPAP Pressure * (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Pepin 2009[203] 19567496	C-Flex CPAP	auto/manual (separate)	56	72	31		France (nd)	
Nilius 2006[202] 17035433	C-Flex CPAP	manual (separate)	57	88	32.7		Germany (nd)	Recruitment unclear
Dolan 2009[201] 18551327	C-Flex CPAP	nd (both)	48	75	34.9		US; Germany (nd)	Incomplete reporting
Leidag 2008[204] 19218664	C-Flex CPAP	manual (separate)	55	73	32		Germany	High drop out rate

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.7.2. Compliance (mean hr/night) in randomized controlled trials of C-Flex™ vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Compliance (hr/night)	Difference	95% CI *	P Btw	Dropout, %	Study Quality
Pepin 2009[203] 19567496	44 (22) [≥15]	11.6 (5.2)	3 mo (PL)	C-Flex	83	4.98	0.07	-0.4, 0.6	NS	24	B
				CPAP	82	4.91					
Nilius 2006[202] 17035433	53 (21) [>20)	10.5 (nd)	1.75 mo (PL)	C-Flex	25	5.3	0.1	-15.5, 15.7 †	0.99	2	B
				CPAP	26	5.2					
Dolan 2009[201] 18551327	52 (28) [≥10]	14.9 (3.6)	6 mo (PL)	C-Flex	92	6.23	0.18	-0.03, 0.39	NS	0?	C
				CPAP	92	6.05					
Leidag 2008[204] 19218664	35 (25) [≥5]	nd	1.5 mo (XO)	C-Flex	25	5.78	-0.05	-0.52, 0.42	NS	40	C
				CPAP	23	5.83					

* Estimated from reported data
† Estimated from reported P value

Table 5.7.3. ESS in randomized controlled trials of C-Flex™ vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff	95% CI	P Btw	Dropout, %	Study Quality
Pepin 2009[203] 19567496	44 (22) [≥15]	11.6 (5.2)	3 mo (PL)	C-Flex	83	11.7 (5.1)	-3.9	-0.5	-2.1, 1.1 *	NS	24	B
				CPAP	82	11.4 (5.2)	-3.4					
Nilius 2006[202] 17035433	53 (21) [>20)	10.5 (nd)	1.75 mo (PL)	C-Flex	25	10.9 (nd)	-5.1	-1.0	-10.1, 8.1 †	NS	2	B
				CPAP	26	10.2 (nd)	-4.1					
Dolan 2009[201] 18551327	52 (28) [≥10]	14.9 (3.6)	6 mo (PL)	C-Flex	92	nd	-6.6	-0.2	-0.7, 0.3 ‡	NS	0?	C
				CPAP	92	nd	-6.4					

* Estimated from reported data
† Estimated from reported P value
‡ Estimated from reported P value

Table 5.8.1. Randomized controlled trials comparing different aspects of humidification with CPAP or autoCPAP: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Ryan 2009[205] 19961025	Heated humidity + CPAP CPAP	nd (nd)	49	94	34.4	-	Ireland (nd)	-
Neill 2003[208] 12952257	Heated humidity + CPAP CPAP	manual (both)	49	89	34.8	-	New Zealand (nd)	-
Massie 1999[209] 10453869	Heated humidity + CPAP Cold passover humidity + CPAP	manual (both)	44	79	37.6	-	New Zealand (nd)	Differential dropouts between arms; washout period used as control
Mador 2005[206] 16236868	Heated humidity + CPAP CPAP + heated humidity as needed only	manual (both)	59	97	36	-	US	Unclear analysis
Salgado 2008[207] 18982206	Heated humidity + AutoCPAP AutoCPAP	manual (nd)	56	74	nd	-	Portugal	Incomplete reporting

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.8.2. Compliance (mean hr/night) in randomized controlled trials comparing different aspects of humidification with CPAP or autoCPAP

Study PMID	Baseline AHI (SD) [minimum]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Compliance (hr/night)	Difference	95% CI	P Btw	Dropout, %	Study Quality
Ryan 2009[205] 19961025	36 (22) [≥10]	12.7 (5)	1 mo (PL)	Heated humidity + CPAP	42	5.21	0	nd	NS	10	B
				CPAP	39	5.21					
Neill 2003[208] 12952257	50 (26) [≥9]	12.1 (5.1)	0.75 mo (XO)	Heated humidity + CPAP	37	5.7	0.4	0.05, 0.76	0.03	12	B
				CPAP	37	5.3					
Massie 1999[209] 10453869	54 (38) [≥10]	nd	0.75 mo (XO)	Heated humidity + CPAP	38	5.52	0.37	nd	NS	19	B
				Cold passover humidity + CPAP	38	5.15					
			0.5 mo (washout as control CPAP)	Heated humidity + CPAP	38	5.52	0.59	0.15, 1.03 *	0.008		
				CPAP	38	4.93					
			0.5 mo (washout as control CPAP)	Cold passover humidity + CPAP	38	5.15	0.22	nd	NS		
				CPAP	38	4.93					
Mador 2005[206] 16236868	46 (30) [≥10]	13.5 (5.3)	1 mo (PL)	Heated humidity + CPAP	49	4.3	0	nd	NS	21	C
				CPAP + heated humidity as needed only	49	4.3					
			12 mo	Heated humidity + CPAP	nd	4.3	-0.5	nd	NS		
				CPAP + heated humidity as needed only	nd	4.8					
Salgado 2008[207] 18982206	28 (20) [nd]	11.6 (6.3)	1 mo (PL)	Heated humidity + AutoCPAP	17	5.3	0.1	nd	NS	22	C
				AutoCPAP	22	5.2					

* Estimated from P value

Table 5.8.3. ESS in randomized controlled trials comparing different aspects of humidification with CPAP or autoCPAP

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff*	95% CI	P Btw	Dropout, %	Study Quality
Ryan 2009[205] 19961025	36 (22) [≥10]	12.7 (5)	1 mo (PL)	Heated humidity + CPAP	42	13 (6)	-5	-2	nd	NS	10	B
				CPAP	39	12 (5)	-3					
Neill 2003[208] 12952257	50 (26) [≥9]	12.1 (5.1)	0.75 mo (XO)	Heated humidity + CPAP	37	12.1 (5.1)	-8	-0.4	-1.28, 0.48 †	0.37	12	B
				CPAP	37	12.1 (5.1)	-7.6					
Massie 1999[209] 10453869	54 (38) [≥10]	nd	0.75 mo (XO)	Heated humidity + CPAP	38	nd	6.2	-1	nd	NS	19	B
				Cold passover humidity + CPAP	38	nd	7.2					
			0.5 mo (washout as control CPAP)	Heated humidity + CPAP	38	nd	6.2	-0.5	nd	NS		
				CPAP	38	nd	6.7					
			0.5 mo (washout as control CPAP)	Cold passover humidity + CPAP	38	nd	7.2	0.5	nd	NS		
				CPAP	38	nd	6.7					
Mador 2005[206] 16236868	46 (30) [≥10]	13.5 (5.3)	1 mo (PL)	Heated humidity + CPAP	49	12.9 (5.2)	-2.4	0.6	nd	NS	21	C
				CPAP + heated humidity as needed only	49	14.1 (5.3)	-3					
			12 mo	Heated humidity + CPAP	nd	12.9 (5.2)	-3.9	1.4	nd	NS		
				CPAP + heated humidity as needed only	nd	14.1 (5.3)	-5.3					
Salgado 2008[207] 18982206	28 (20) [nd]	11.6 (6.3)	1 mo (PL)	Heated humidity + autoCPAP	17	11.2 (5.8)	-4.3	-0.9	nd	NS	22	C
				autoCPAP	22	11.9 (6.3)	-5.2					

* In crossover studies, if only data on the final values and the difference in final values are reported (as opposed to changes from baseline and net change), these data are italicized.
† Estimated from reported P value

Table 5.9.1. Randomized controlled trials of mandibular devices vs. control: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Bloch 2000[210] 10903249	MAD-1 piece or MAD-2 piece No treatment	51	nd	27.4		Switzerland	Patient not blinded, selection bias likely, compliance not accounted for, power not reported, no washout
Barnes 2004[140] 15201136	Mandibular advancement splint Placebo tablet	47	80	31.1		Australia (nd)	
Kato 2000[211] 10767241	Oral appliance 2 mm, oral appliance 4 mm, or oral appliance 6 mm No oral appliance	49	nd	28.7		Japan (nd)	Interventions not adequately described
Lam 2007[129] 17121868	Conservative management plus MAD Conservative management	47	79	27.3		Hong Kong (nd)	
Petri 2008[212] 18482111	Mandibular advancement appliance No treatment	50	81	31.1		Denmark (nd)	

Table 5.9.2. AHI (events/hr) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	26.7 (3.3)	-18.8	-14.7	-20.0, -9.4 *	<0.05	0	B
				No treatment	24	26.7 (3.3)	-4.1					
				MAD-2 piece	24	26.7 (3.3)	-18	-13.9	-19.2, -8.6 †	<0.05		
				No treatment	24	26.7 (3.3)	-4.1					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	21.3 (1.3, SE)	-16.5	-6.3	-10.1, -2.5 ‡	0.001	14	B
				Placebo tablet	80	21.3 (1.3, SE)	-7.3					
Lam 2007[129] 17121868	19 (11) [5-40]	12 (5.7)	10 wk (PL)	MAD + conservative management	34	20.9 (1.7, SE)	-10.3	-11.5	-17.0, -6.1 §	<0.001	13	B
				Conservative management	33	19.3 (1.9, SE)	1.2					
Petri 2008[212] 18482111	34 (26) [>5]	10.7 (4.6)	4 wk (PL)	Mandibular advancement appliance	27	39.1 (23.8)	-14.1	-13.1	-26.6, 0.4 **	nd	9	B
				No treatment	29	34.3 (26.3)	-0.9					
Kato 2000[211] 10767241	nd	nd	8 nights (PL)	Oral appliance 2 mm	37	26.0, ODI	17.3 ††	-8.7	nd	<0.05	13	C
				No oral appliance	37	26.0	26					
				Oral appliance 4 mm	37	26.0	14.7	-11.3	nd	<0.05		
				No oral appliance	37	26.0	26					
				Oral appliance 6 mm	37	26.0	10.8	-15.2	nd	<0.05		
				No oral appliance	37	26.0	26					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported P value.
§ Estimated from reported data.
** Estimated from reported data.
†† Median

Table 5.9.3. ESS in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	11.9 (0.8)	9 median	-4.5 *	nd	<0.001	0	B
				No treatment	24	11.9 (0.8)	13.5 median					
				MAD-2 piece	24	11.9 (0.8)	9 median	-4.5	nd	<0.001		
				No treatment	24	11.9 (0.8)	13.5 median					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	10.7 (0.4)	-1.5	-1	-1.6, -0.4 †	0.001	14	B
				Placebo tablet	80	10.7 (0.4)	-0.5					
Lam 2007[129] 17121868	19 (11) [5-40]	12 (5.7)	10 wk (PL)	MAD + conservative management	34	12 (1)	-3	-1	-1.5, -0.5 ‡	<0.05	13	B
				Conservative management	33	12 (1)	-2					
Petri 2008[212] 18482111	34 (26) [>5]	10.7 (4.6)	4 wk (PL)	Mandibular advancement appliance	27	11.7 (4.3)	-3.3	-2.6	-3.3, 0.1 §	<0.05	9	B
				No treatment	29	10.7 (4.6)	-0.7					

* Difference of medians
† Estimated from reported P value.
‡ Estimated from reported data.
§ Estimated from reported data.

Table 5.9.4a. Minimum oxygen saturation (%) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Kato 2000[211] 10767241	nd	nd	8 nights (PL)	Oral appliance 2 mm	37	87.2	(89.2) medians	2.0 *	nd	<0.05	13	C
				No oral appliance	37		(87.2)					
				Oral appliance 4 mm	37		(89.5)	2.3	nd	<0.05		
				No oral appliance	37		(87.2)					
				Oral appliance 6 mm	37		(89.6)	2.4	nd	<0.05		
				No oral appliance	37		(87.2)					
Lam 2007[129] 17121868	19 (11) [5-40]	12 (5.7)	10 wk (PL)	MAD + conservative management	34	73.8 (1.9, SE)	7.2	5.9	0.1, 11.7 †	NS	13	B
				Conservative management	33	76.1 (2.6)	1.3					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	86.7 (0.6)	1.1	2.4	1.0, 3.8 ‡	0.001	14	B
				Placebo tablet	80	86.7 (0.6)	-1.3					

* Differences between final median values.
† Estimated from reported data
‡ Estimated from reported P value.

Table 5.9.4b. Arousal index (events/hr) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	36 (4.3)	26.5	-14.5	-22.6, -6.4 *	<0.05	0	B
				No treatment	24	36 (4.3)	41					
				MAD-2 piece	24	36 (4.3)	30.9	-10.1	-17.9, -2.3 †	NS		
				No treatment	24	36 (4.3)	41					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	22.0 (1.2)	1.8	-1.4	-3.6, 0.8 ‡	NS	14	B
				Placebo tablet	80	22.0 (1.2)	3.2					
Lam 2007[129] 17121868	19 (11) [5-40]	12 (5.7)	10 wk (PL)	MAD + conservative management	34	24.5 (2.2)	-2.9	-8.2	-14.8, -1.6 §	<0.05	13	B
				Conservative management	33	23.5 (2.2)	5.3					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data.

Table 5.9.4c. Sleep efficiency (%) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	85 (2)	3	-1	-4.9, 2.9 *	NS	0	B
				MAD-2 piece	24	85 (2)	4	0	-3.4, 3.4 †	NS		
				No treatment	24	85 (2)	4					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	79.5 (1.1)	2.5	1.3	-0.6, 3.2 ‡	NS	14	B
				Placebo tablet	80	79.5 (1.1)	1.2					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported data

Table 5.9.4d. Slow wave sleep (%) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	nd	18	nd	nd	<0.05	0	B
				MAD-2 piece	24	nd	16	nd	nd	NS		
				No treatment	24	nd	12					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	17.9 (1.2)	2.8	0.6	-0.6, 3.8 *	NS	14	B
				Placebo tablet	80	17.9 (1.2)	2.2					

* Estimated from reported data

Table 5.9.4e. REM sleep (%) in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Bloch 2000[210] 10903249	27 (16) [≥5]	11.9 (3.9)	1 wk (XO)	MAD-1 piece	24	13 (1)	2	1	-1.0, 3.0 *	NS	0	B
				MAD-2 piece	24	13 (1)	3	2	0.04, 4.0 †	NS		
				No treatment	24	13 (1)	1					
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	18.8 (0.7)	0.1	0.9	-0.3, 2.1 ‡	NS	14	B
				Placebo tablet	80	18.8 (0.7)	1					
Petri 2008[212] 18482111	34 (26) [>5]	10.7 (4.6)	4 wk (PL)	Mandibular advancement appliance	27	18.4 (5.6)	0.3	-0.7	-2.1, 2.4 §	nd	9	B
				No treatment	29	17.5 (6.2)	1					

* Estimated from reported data.
† Estimated from reported data.
‡ Estimated from reported data.
§ Estimated from reported data.

Table 5.9.5. Quality of life outcomes in randomized controlled trials of mandibular devices vs. control

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference					Dropout, %	Study Quality
								Net Diff	95% CI	Test Range "Worst"	Test Range "Best"	P Btw		
Barnes 2004[140] 15201136	21 (13) [nd]	10.7 (4.1)	3 mo (XO)	Mandibular advancement splint	80	Beck Depression Inventory	0						14	B
				Placebo tablet	80									
						FOSQ social domain outcome	0							
Lam 2007[129] 17121868	19 (11) [5-40]	12 (5.7)	10 wk (PL)	Conservative management plus MAD	34	SAQLI-social interactions, treatment-related symptoms	0						13	B
				Conservative management	33	SAQLI score*	Conservative management plus MAD	0.7	0.6, 0.8†	1	7	<0.001		
						SF-36 All	0							

* Domain A-D, not including treatment-related symptoms
† Estimated from reported data

Table 5.10.1. Randomized controlled trials of mandibular advancement devices vs. inactive oral devices: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Hans 1997[213] 9155816	MAD Sham oral appliance	51	83	29	--	US (nd)	Blinding not reported; no power analysis; dropout rate 30%
Johnston 2002[216] 12143089	MAD MAD Placebo	55	81	32	--	Ireland (nd)	
Mehta 2001[218] 11371418	MAD Lower dental plate	48	79	29	--	Australia (nd)	Blinding not reported
Naismith 2005[217] 17564405 Gotsopoulos 2002[214]12204875 Gotsopoulos 2004[215]15453552	MAD Single upper plate	48	81	29	--	Australia (nd)	
Petri 2008[212] 18482111	MAD Non-advancement MAD	50	81	31	--	Denmark (nd)	

Table 5.10.2. AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Johnston 2002[216] 12143089	31 (nd) [nd]	30.7 (nd)	4-6 wk (X0)	AHI	MAD	20	31.9 (21.2)	-9.07	-14.8	-26.2, -3.4	0.011	5	B
					MAD Placebo	20	31.9 (21.18)	5.75					
Mehta 2001[218] 11371418	27 (17) [10-68]	nd	1 wk (XO)	AHI	MAD	24	27 (17)	-13	-16	-24.1,-7.9 *	<0.0001	14	B
					Lower dental plate	24	27 (17)	3					
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5)	4 wk (X0)	AHI	MAD	73	26.9 (15.4)	-14.7	-13.2	-21.1, -5.3 †	<0.001	0	B
					Single upper plate	73	26.9 (15.4)	-1.5					
Petri 2008[212] 18482111	35 (nd) [>5]	11.0 (nd)	4 wk (PL)	AHI	MAD	27	39.1 (23.8)	-14.1	-13.1	-26.0, 0.0 ‡	<0.05	9	B
					Non-advancement MAD	25	32.6 (22)	-0.9					
Hans 1997[213] 9155816	RDI 36 (43) [RDI <30]	12.5 (5.7)	2 wk (X0)	RDI	MAD-A	17	28.4 (21.1)	-14.5	-24.8	-41.9, -7.6 §	<0.0045	29	C
					Sham oral	17	43.7 (46.8)	10.3					

* Estimated from reported P value
† Estimated from reported P value
‡ Estimated from reported P value
§ Estimated from reported P value

Table 5.10.3. ESS in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Johnston 2002 [216] 12143089	31 (nd) [nd]	30.7 (nd)	4-6 wk (X0)	MAD	18	13.9 (6.39)	-2.29	-0.94	-3.32,1.43	NS	5	B
				MAD Placebo	18	13.9 (6.39)	-1.34					
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MAD	73	10.9 (4.8)	-3.8	-2	-3.1, -0.8 *	<0.001	0	B
				Single upper plate	73	10.9 (4.8)	-1.8					
Petri 2008[212] 18482111	35 (nd) [>5]	11.0 (nd)	4 wk (PL)	MAD	27	11.7 (4.3)	-3.3	-2.1 †	-4.4,0.2 ‡	nd	9	B
				Non-advancement MAD	25	10.8 (4.6)	-1.2					
Hans 1997[213] 9155816	RDI 36 (43) [RDI <30]	12.5 (5.7)	2 wk (X0)	MAD-A	17	12.1 (3.9)	-3.8	-3.3	-6.4,-0.2 §	NS	29	C
				Sham oral	17	13.0 (4.5)	-0.5					

* Estimated from reported P value
† Estimated from reported P value
‡ Estimated from reported data
§ Estimated from reported P value .our estimates does not match reported NS

Table 5.10.4. Minimum oxygen saturation (%) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Intervention	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Mehta 2001[218] 11371418	27 (17) [10-68]	nd	1 wk (XO)	MAD	24	85 (8)	6	4	1.9, 6.0 *	<0.0001	14	B
				Lower dental plate	24	85 (8)	2					
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MAD	73	85.7 (5.6)	3	2.3	0.5, 4.0 †	<0.01	0	B
				Single upper plate	73	85.7 (5.6)	0.7					

* Estimated from reported P value
† Estimated from reported P value

Table 5.10.5. Arousal index (events/hr) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Mehta 2001[218] 11371418	27 (17) [10-68]	nd	1 wk (XO)	MAD	24	nd	27	-14	-21.1, -6.6 *	<0.0001	14	B
				Lower dental plate	24	nd	41					
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MAD	73	35 (13.5)	-10	-8.1	-12.4, -3.2 †	<0.001	0	B
				Single upper plate	73	35 (13.5)	-1.9					

* Estimated from reported P value
† Estimated from reported P value

Table 5.10.6. Sleep efficiency (%) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Mehta 2001[218] 11371418	27 (17) [10-68]	nd	1 wk (XO)	MAD	24	nd	85	-2	nd	nd	14	B
				Lower dental plate	24	nd	87					
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MAD	73	80.6 (12)	3	1.8	-2.1, 5.6 *	nd	0	B
				Single upper plate	73	80.6 (12)	1.2					

* Estimated from reported data

Table 5.10.7. Changes in REM and slow wave sleep (%) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net diff or Diff	95% CI	P Btw	Dropout %	Study Quality
Mehta 2001[218] 11371418	27 (17) [10-68]	nd	1 wk (XO)	REM	MAD	24	nd	21	5	1.5, 8.5 *	<0.005	14	B
					Lower dental plate	24	nd	16					
Petri 2008[212] 18482111	35 (nd) [>5]	11.0 (nd)	4 wk (PL)	REM	MAD	27	18.4 (5.6)	0.3	-0.4	-3.7, 2.9 †	nd	9	B
					Non-advancement MAD	25	16.8 (7.5)	0.7					
				Stage 3	MAD	27	7 (5)	2.1	2.9	0.1, 5.7 ‡	nd		
					Non-advancement MAD	25	9.9 (5.1)	-0.8					
				Stage 4	MAD	27	10.2 (10.5)	2.2	-1.2	-6.6, 4.2 §	nd		
					Non-advancement MAD	25	9.6 (10.3)	3.4					

* Estimated from reported P value
† Estimated from reported data
‡ Estimated from reported P value
§ Estimated from reported data

Table 5.10.8. Other outcomes (see 5th column) in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Naismith 2005[217] 17564405 Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MSLT	MAD	73	nd	10.3(0.5)	nd	nd	0.01	0	B
					Single upper plate	73	nd	9.1(0.5)					
				24 hour systolic BP	MAD	61	127.3 (1.3) *	-2.1	-1.5	-3.0, -0.0 †	0.05		
					Single upper plate	61	127.3 (1.3) ‡	-0.6					
				24 hour diastolic BP	MAD	61	77 (0.9) §	-1.3	-1.6	-2.5, -0.6 **	0.001		
					Single upper plate	61	77 (0.9) ††	0.3					

* Mean(SE)
† Estimated from reported P value
‡ Mean(SE)
§ Mean(SE)
** Estimated from reported P value
†† Mean(SE)

Table 5.10.9. Functional outcomes in randomized controlled trials of mandibular advancement devices vs. inactive oral devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference					Dropout, %	Study Quality
								Net diff	95% CI	Test Range "Worst"	Test Range "Best"	P Btw		
Petri 2008[212] 18482111	35 (nd) [>5]	11.0 (nd)	4 wk (PL)	MAD	27	SF-36 Vitality *	MAD	18.7	nd	0	100	0.001	9	B
				Nonadvance-ment MAD	25									
Naismith 2005[217] 17564405	25 (13) [≥10]	11.0 (5.0)	4 wk (X0)	MAD	73	Neuro-psychological † (speed/vigilance-Choice reaction time)	MAD	-0.019	nd			0.001	0	B
				Single upper plate	73									
Gotsopoulos 2002[214] 12204875 Gotsopoulos 2004[215] 15453552						Beck Depression inventory (somatic items) ‡	MAD	-0.6	nd			<0.05		

*P value for all other domains Not Significant

† P value for other Neuropschological tests Not Significant.

‡ P value for other items on Beck Depression Inventory Not significant

Table 5.11.1. Randomized controlled trials of mandibular advancement devices vs. mandibular advancement devices: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Campbell 2009[219] 18989715	MAD objective * / MAD subjective †	47	86	28.0	BMI<35 Kg/m^2	New Zealand (nd)	-
Deane 2009[222] 19480232	MAD / TSD	49	59	29.3		Australia (nd)	-
Dort 2008[223] 18461376	Suction TRD / Non suction TRD	48	69	29.4		Canada (nd)	-
Vanderveken 2008[221] 17673699	MAD $_{cm}$ ‡ / MAD $_{tp}$ **	47	84	28.0	SDB, history of surgery §	Belgium (2003-04)	-
Walker Engstrom 2003[220] 14569523	50% MAD †† / 75% MAD ‡‡	46	100	30.2	--	Sweden 1998-2000)	-

* "objective adjustment" at 3 weeks following PSG-based feedback
† self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
‡ Custom made mandibular advancement device
§ Some patients had refused CPAP treatment and others had a history of unsuccessful UPPP
** Pre- molded thermoplastic mandibular advancement device
†† 50% mandibular advancement (mean mandibular advancement 5.0 mm)
‡‡ 75% of mandibular advancement (mean mandibular advancement 7.2 mm)

Table 5.11.2. AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. mandibular advancement devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95 % CI	P Btw	Dropout, %	Study Quality
Campbell 2009[219] 18989715	25 (7) [10-40]	11.6 (4.7)	6 wk (PL)	MAD objective *	12	26.6 (12)	-14.9	-3.8	-11.4, 3.9 †	nd	6	B
				MAD subjective ‡	16	25.4 (7.4)	-11.1					
Vanderveken 2008[221] 17673699	13 (11) [<40]	8.0 (5.0)	4 mo (XO)	MAD $_{cm}$ §	23	14 (12)	-8	-5	-8.5, -1.5 **	nd	8	B
				MAD $_{tp}$ ††	23	14 (12)	-3					
Walker Engstrom 2003[220] 14569523	50 (4) [≥20]	11.5 (3.1)	6 mo (PL)	50% MAD ‡‡	37	47.0 (5.1)	-29.6	5.2	2.7,7.6 §§	NS	8	B
				75% MAD ***	40	50.4 (4.7)	-34.8					

* objective adjustment at 3 weeks following PSG-based feedback
† Estimated from reported data
‡ self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
§ Custom made mandibular advancement device
** Estimated from reported data
†† Pre- molded thermoplastic mandibular advancement device
‡‡ 50% mandibular advancement (mean mandibular advancement 5.0 mm)
§§ Estimated from reported data; our estimates do not match with reported NS
*** 75% of mandibular advancement (mean mandibular advancement 7.2 mm)

Table 5.11.3. AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. mandibular advancement devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	n Event	N Total	Outcome Metric	Result*	95% CI	P Btw	Dropout, %	Study Quality
Campbell 2009[219] 18989715	25 (7) [10-40]	11.6 (4.7)	6 wk (PL)	AHI<5	MAD objective †	3.9	12	%	33.0 vs.12.5	nd	NS	6	B
					MAD subjective ‡	1.9	16						
				Improvement percentage §	MAD objective **	5.0	12	%	42.0 vs. 56.2	nd	NS		
					MAD subjective ††	8.9	16						
				Failure percentage ‡‡	MAD objective §§	3.0	12	%	25.0 vs. 31.2	nd	NS		
					MAD subjective ***	4.9	16						

* Top row intervention vs. bottom row intervention.
† objective adjustment at 3 weeks following PSG-based feedback
‡ self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
§ >50% reduction in AHI but still >5/hr
** objective adjustment at 3 weeks following PSG-based feedback
†† self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
‡‡ AHI decreased by <50%
§§ objective adjustment at 3 weeks following PSG-based feedback
*** self-adjustment of mandibular advancement device during the entire study duration (6 weeks)

Table 5.11.4. ESS in randomized controlled trials of mandibular advancement devices vs. mandibular advancement devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Campbell 2009[219] 18989715	25 (7) [10-40]	11.6 (4.7)	6 wk (PL)	MAD objective *	12	11.0(5.3)	-1.5	2.3	-1.4, 6.0 †	nd	6	B
				MAD subjective ‡	16	11.6(4.7)	-3.8					
Vanderveken 2008[221] 17673699	13 (11) [<40]	8 (5)	4mo (XO)	MAD_{cm} §	23	7(5)	-2	0	-1.6, 1.6 **	nd	8	B
				MAD_{tp} ††	23	7(5)	-2					
Walker Engstrom 2003[220] 14569523	50 (4) [≥20]	11.5 (3.1)	6 mo (PL)	50% MAD ‡‡	37	11.7(3.1)	-3.1	0.9	-0.4, 2.2	nd	8	B
				75% MAD §§	40	11.5(3.1)	-4					

* objective adjustment at 3 weeks following PSG-based feedback
† Estimated from reported data
‡ self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
§ Custom made mandibular advancement device
** Estimated from reported data
†† Pre- molded thermoplastic mandibular advancement device
‡‡ 50% mandibular advancement (mean mandibular advancement 5.0 mm)
§§ 75% of mandibular advancement (mean mandibular advancement 7.2 mm)

Table 5.11.5. Other outcomes reported in randomized controlled trials of mandibular advancement devices vs. mandibular advancement devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Campbell 2009[219] 18989715	25 (7) [10-40]	11.6 (4.7)	6wk (PL)	Arousal index	MAD objective *	12	33.6(10)	-9.4	0.5	-7.3,8.3 †	nd	6	B
					MAD subjective ‡	16	32.1(13.3)	-9.9					
Vanderveken 2008[221] 17673699	13 (11) [<40]	8 (5)	4 mo (XO)	Minimum oxygen saturation	MAD_{cm} §	23	83 (7)	-1	0	-3.2,3.2 **	nd	8	B
					MAD_{tp} ††	23	83 (7)	-1					
				Sleep efficiency	MAD_{cm} ‡‡	23	78(11)	2	-1	-5.7,3.7 §§	nd		
					MAD_{tp} ***	23	78(11)	3					

* objective adjustment at 3 weeks following PSG-based feedback
† Estimated from reported data
‡ self-adjustment of mandibular advancement device during the entire study duration (6 weeks)
§ Custom made mandibular advancement device
** Estimated from reported data
†† Pre- molded thermoplastic mandibular advancement device
‡‡ Custom made mandibular advancement device
§§ Estimated from reported data
*** Pre- molded thermoplastic mandibular advancement device

Table 5.11.6. Outcomes randomized controlled trials of mandibular advancement devices vs. tongue-retaining devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Deane 2009[222] 19480232	27.0(nd) [>10]	nd	1 wk (XO)	AHI	MAD	22	27 (17)	-15	-1	-9.7, 7.7 *	nd	19	B
					TSD	22	27 (17)	-14					
				Minimum O_2 sat	MAD	22	84 (7)	3	-1	-4.7, 2.7 †	nd		
					TSD	22	84 (7)	4					
				Arousal index	MAD	22	33 (16)	-12	0	nd	nd		
					TSD	22	33 (16)	-12					
				Sleep efficiency	MAD	22	80 (11)	-2	-1	-8.7, 6.7 ‡	nd		
					TSD	22	80 (11)	-1					
				REM	MAD	22	nd	18	1	nd	NS		
					TSD	22	nd	17					

* Estimated from reported data
† Estimated from reported data
‡ Estimated from reported data

Table 5.11.7. Outcomes randomized controlled trials of tongue-retaining devices vs. tongue-retaining devices

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Dort 2008[223] 18461376	nd [RDI 5-30]	12.4 (nd)	1 wk (XO)	SQALI	Suction TRD	32	3.9 (1.2)	0.3	0.28	-0.93,0.31	NS	nd	C
					Non suction TRD	32	3.9 (1.2)	0					
				AHI	Suction TRD	32	15.5(17.6)	-6.6	-4.9	-8.9,-0.85	0.019		
					Non suction TRD	32	15.5(17.6)	-2.0					
				ESS	Suction TRD	32	12.4(4.5)	-1.5	0.65	-0.47, 1.8	NS		
					Non suction TRD	32	12.4(4.5)	-21					

Table 5.12.1. Randomized controlled trials of mandibular advancement devices vs. CPAP: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Barnes 2004[140] 15201136	MAD (Medical Dental Sleep Appliance) CPAP	nd (nd)	47	80	31.1	Excluded diabetes	Australia (nd)	
Clark 1996[224] 8769497	MAD, custom CPAP	nd (separate)	47	100	28.1	--	Israel (1991-92)	Failed crossover design
Engleman 2002[225] 12231497	MAD, custom CPAP	nd (split)	46	75	nd	--	UK (nd)	
Ferguson 1996[226] 8625679	MAD (Snore-Guard) CPAP	nd (separate)	46	88	30.4	--	Canada (1991-94)	
Gagnadoux 2009[227] 19324954	MAD (AMC) CPAP	manual (split)	50	61	26.7	--	France (nd)	
Hoekema 2007[231] 17081222 Hoekema 2008[230] 18719218	MAD (Thornton Adjustable Positioner) CPAP	nd (separate)	49	89	33.3	--	Netherlands (2002-05)	
Lam 2007[129] 17121868	MAD, custom CPAP	nd (nd)	45	78	27.5	Excluded previous surgery	Hong Kong (nd)	
Randerath 2002[228] 12171833	MAD (Hinz IST) CPAP	manual (nd)	57	80	31.2	--	Germany (1999)	
Skinner 2004[232] 14718430	Cervicomandibular support collar AutoCPAP	auto (nd)	49	80	34.1	--	New Zealand (nd)	Study stopped with ½ sample size due to lack of objective benefit
Tan 2002[229] 12143088	MAD, custom CPAP	manual (nd)	51	83	31.9	Excluded recent CVD	UK (nd)	

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, eg if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 5.12.2. Treatment response in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome (subgroup)	Interventions	n Event	N Total	Metric	Result *	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR 60-88 d] (PL)	Effective Treatment † (Total)	MAD	39	51	RD	-6.2%	-22, 9.4	NS	4	B
					CPAP	43	52						
				(AHI≤30)	MAD	21	25	RD	+4.0%	-18, 25	NS		
					CPAP	20	25						
				(AHI>30)	MAD	18	26	RD	-1.6%	-37, 6.8	NS		
					CPAP	23	27						
				AHI<5 (Total)	MAD	29	51	RD	-20.0%	-37, -1.9	0.02 ‡		
					CPAP	40	52						
				(AHI≤30)	MAD	21	25	RD	+4.0%	-18, 25	NS		
					CPAP	20	25						
				(AHI>30)	MAD	8	26	RD	-43.3%	-62, -17	<0.001 §		
					CPAP	20	27						
				AHI<10 ** (Total)	MAD	31	44	RD	-4.5%	-23, 14	NS		
					CPAP	33	44						
				(AHI≤30)	MAD	16	18	RD	+18.3%	-8.7, 43	NS		
					CPAP	12	17						
				(AHI>30)	MAD	15	26	RD	-20.1%	-42, 4.9	NS		
					CPAP	21	27						
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	Complete Response ††	MAD	12	28	RD ‡‡	-28.6%	-53, -3.8	0.02 §§	0	B
					CPAP	20	28						
				Partial *** or Complete Response	MAD	26	28	RD †††	-3.6%	-15, 8.2	NS ‡‡‡		
					CPAP	27	28						

* Top row intervention vs. bottom row intervention.
† AHI<5 or >50% reduction to an AHI<20 without symptoms
‡ Estimated from confidence interval
§ Estimated from confidence interval
** Excluding 15 participants who had AHI<10 at baseline.
†† ≥50% reduction in AHI to <5
‡‡ Calculated from reported data
§§ Calculated from reported data
*** ≥50% reduction in AHI to ≥5
††† Calculated from reported data
‡‡‡ Calculated from reported data

Table 5.12.3. AHI (events/hr) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47*	39.4 (30.8)	2.2 (0, 9.5)†	--	--	0.006‡	4	B
				CPAP	52/47	40.3 (27.6)	0 (0, 3.0)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	21.3 (11.6)	14.0 (9.8)	9.2	7.3, 11.1§	<0.05	23	B
				CPAP			4.8 (4.5)					
Lam 2007[129] 17121868	24 (6) [5-40]	12 (6)	10 wk (PL)	MAD	34	20.9 (9.9)	10.6 (9.9)	10.7	6.1, 15.4**	<0.001	0	B
				CPAP	34	23.8 (11.1)	2.8 (6.4)					
Ferguson 1996[226] 8625679	25 (9) [15-50]	nd	4 mo (XO)	MAD	19	19.7 (13.8)	9.7 (7.3)	4.0	-3.7, 11.7††	nd	24	B
				CPAP	20	17.6 (13.2)	3.6 (1.7)					
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	MAD	28	34.2 (13.0)	6 (nd)	4	1.6, 6.4‡‡	0.001	0	B
				CPAP			2 (nd)					
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	22.2 (9.6)	8.0 (10.9)	4.9	1.0, 8.8§§	NS	12	B
				CPAP			3.1 (2.8)					
Randerath 2002[228] 12171833	18 (8) [5-30]	nd	6 wk (XO)	MAD	20	17.5 (7.7)	13.8 (11.1)	10.6	2.5, 18.7***	0.01	0	B
				CPAP			3.2 (2.9)					
Clark 1996[224] 8769497	34 (14) [≥10]	nd	2 wk (XO)	MAD	21	33.86 (14.30)	19.94 (12.75)	8.8	4.0, 13.6†††	nd	4	C
				CPAP			11.15 (3.93)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	29.4 (13.4)	26.9 (17.2)	16.9	6.8, 27.0‡‡‡	0.001	0	C
				AutoCPAP			9.9 (8.0)					

* Baseline/Final
† Median (IQR)
‡ Statistical analysis of final values. By Mann-Whitney test. Skewed distribution.
§ Estimated from reported SE's.

** Estimated from reported SE's.
†† Estimated from reported SD's.
‡‡ Estimated from reported P value.
§§ Estimated from reported SD's. Our estimate does not match with reported significance.
*** Estimated from reported P value.
††† Estimated from reported SD's.
‡‡‡ Estimated from reported P value.

Table 5.12.4. ESS in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47 *	12.9 (5.6)	6.9 (5.5)	2.3	0.2, 4.4 †	0.53 ‡	4	B
				CPAP	52/47	14.2 (5.6)	5.9 (4.8)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	10.7 (3.6)	9.2 (3.6)	0	-0.8, 0.8 §	NS	23	B
				CPAP			9.2 (3.6)					
Lam 2007[129] 17121868	24 (5.8) [5-40]	12 (6)	10 wk (PL)	MAD	34	12 (6)	9 (6)	2	-1, 5 **	<0.05	0	B
				CPAP	34	12 (6)	7 (6)					
Engleman 2002[225] 12231497	31 (26) [≥5]	14 (4)	8 wk (XO)	MAD	48	13 (4)	12 (5)	6	4.2, 7.8 ††	<0.001	6	B
				CPAP		15 (3)	8 (5)					
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	MAD	28	10.6 (4.5)	7.7 (4.0)	-0.5	-2.0, 1.0 ‡‡	<0.05	0	B
				CPAP			8.2 (3.9)					
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	13.4 (4.6)	9.0 (5.1)	0.9	-1.0, 2.8 §§	NS	12	B
				CPAP			8.1 (4.1)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	13.2 (4.9)	9.4 (5.5)	-1.9	-4.9, 1.1 ***	0.22	0	C
				AutoCPAP			11.3 (4.6)					

* Baseline/Final
† Estimated from reported SD's.
‡ Statistical analysis of comparison of final values.
§ Estimated from reported SD's.
** Estimated from reported SE's Our estimate does not match with reported significance.
†† Estimated from reported SD's.
‡‡ Estimated from reported SD's.
§§ Estimated from reported SD's.
*** Estimated from reported P value.

Table 5.12.5a. AI (events/hr) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	22.0 (10.7)	23.8 (10.7)	5.5	3.4, 7.6 *	<0.05	23	B
				CPAP			18.3 (8.0)					
Lam 2007[129] 17121868	24 (5.8) [5-40]	12 (6)	10 wk (PL)	MAD	34	24.5 (12.8)	21.6 (14.6)	2.4	-3.4, 8.2 †	NS	0	B
				CPAP	34	21.6 (9.9)	16.3 (10.5)					
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	19.3 (9.6)	11.6 (5.6)	1.8	-0.7, 4.3 ‡	NS	12	B
				CPAP			9.8 (6.6)					
Randerath 2002[228] 12171833	18 (8) [5-30]	nd	6 wk (XO)	MAD	20	21.8 (9.9)	17.0 (5.1)	2.9	0.7, 5.1 §	NS	0	B
				CPAP			14.1 (5.1)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	27.7 (9.0)	31.7 (22.8)	15.2	-1.4, 31.7 **	0.072	0	C
				AutoCPAP			16.5 (5.9)					

* Estimated from reported SE's.
† Estimated from reported SE's.
‡ Estimated from reported SD's.
§ Estimated from reported SD's. Our estimate does not match with reported significance.
** Estimated from reported P value.

Table 5.12.5b. Minimum oxygen saturation (%) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47 *	78.0 (8.5)	87.7 (6.3)	-2.1	-5.3, 1.1	NS †	4	B
				CPAP	52/47	77.9 (9.9)	89.7 (5.8)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	86.7 (5.4)	87.8 (3.6)	-4.1	-4.9, -3.4 ‡	<0.05	23	B
				CPAP			91.9 (2.7)					
Lam 2007[129] 17121868	24 (5.8) [5-40]	12 (6)	10 wk (PL)	MAD	34	73.8 (11.1)	81.0 (9.3)	-5.0	-11.0, 1.0 §	NS	0	B
				CPAP	34	75.0 (8.2)	87.2 (16.9)					
Ferguson 1996[226] 8625679	25 (9) [15-50]	nd	4 mo (XO)	MAD	19	83.0 (7.4)	83.8 (7.3)	-5.3	-9.3, -1.3 **	nd	24	B
				CPAP	20	82.6 (6.0)	88.7 (2.5)					
Randerath 2002[228] 12171833	18 (8) [5-30]	nd	6 wk (XO)	MAD	20	54.5 (25.9)	85.3 (3.1)	-3.7	-5.1, -2.3 ††	<0.05	0	B
				CPAP			89.0 (3.4)					
Clark 1996[224] 8769497	34 (14) [≥10]	nd	2 wk (XO)	MAD	21	84.3 (6.77)	90.2 (4.36)	-0.9	-3.3, 1.5 ‡‡	nd	4	C
				CPAP			91.1 (6.40)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	84.3 (4.4)	81.0 (12.0)	-9.8	-20.6, 1.0 §§	0.076	0	C
				AutoCPAP			90.8 (3.0)					

* Baseline/Final
† Statistical analysis of comparison of final values.
‡ Estimated from reported SE's.
§ Estimated from reported SE's.
** Estimated from reported SD's.
†† Estimated from reported SD's.
‡‡ Estimated from reported SD's.
§§ Estimated from reported P value.

Table 5.12.5c. Sleep efficiency (%TST) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47*	88.3 (9.7)	86.1 (8.1)	-2.9	-7.4, 1.6†	NS‡	4	B
				CPAP	52/47	85.5 (15.5)	86.2 (10.0)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	79.5 (9.8)	82.0 (8.9)	-0.1	-1.9, 1.7§	NS	23	B
				CPAP			82.1 (7.2)					
Ferguson 1996[226] 8625679	25 (9) [15-50]	nd	4 mo (XO)	MAD	19	88.0 (5.4)	86.5 (10.6)	-1.8	-7.1, 3.5**	nd	24	B
				CPAP	20	87.8 (7.7)	88.1 (7.3)					
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	81.6 (10.4)	83.2 (8.1)	-4	-7.2, 0.8††	NS	12	B
				CPAP			87.2 (8.1)					
Clark 1996[224] 8769497	34 (14) [≥10]	nd	2 wk (XO)	MAD	21	87.1 (10.7)	89.9 (5.5)	0.4	-2.4, 3.2‡‡	NS	4	C
				CPAP			89.5 (7.3)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	81.9 (7.9)	78.6 (11.8)	0.2	-7.1, 7.5§§	0.97	0	C
				AutoCPAP			78.4 (11.6)					

* Baseline/Final
† Estimated from reported SD's.
‡ Statistical analysis of comparison of final values.
§ Estimated from reported SE's.
** Estimated from reported SD's.
†† Estimated from reported SD's.
‡‡ Estimated from reported SD's.
§§ Estimated from reported SD's.

Table 5.12.5d. Slow wave sleep (% TST) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47 *	13.7 (9.0)	20.4 (7.7)	-2.1	-5.8, 1.6 †	NS ‡	4	B
				CPAP	52/47	13.0 (11.5)	21.8 (8.0)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	17.9 (10.7)	20.1 (9.8)	-0.6	-2.8, 1.6 §	NS	23	B
				CPAP			20.7 (9.8)					
Randerath 2002[228] 12171833	18 (8) [5-30]	nd	6 wk (XO)	MAD	20	14.2 (10.6)	14.1 (10.8)	-2.1	-6.5, 2.3 **	NS	0	B
				CPAP			16.2 (9.1)					
Clark 1996[224] 8769497	34 (14) [≥10]	nd	2 wk (XO)	MAD	21	12.4 (7.8)	13.4 (8.0)	-1.8	-4.9, 1.2 ††	nd	4	C
				CPAP			15.2 (5.6)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	20.4 (8.2)	20.1 (13.4)	-3.9	-11.2, 3.4 ‡‡	0.30	0	C
				AutoCPAP			24.0 (8.9)					

* Baseline/Final
† Estimated from reported SD's.
‡ Statistical analysis of comparison of final values.
§ Estimated from reported SE's.
** Estimated from reported SD's.
†† Estimated from reported SD's.
‡‡ Estimated from reported SD's.

Table 5.12.5e. REM sleep (% TST) in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47 *	21.0 (7.8)	26.5 (6.7)	0.6	-2.2, 3.4 †	NS ‡	4	B
				CPAP	52/47	19.2 (7.4)	24.1 (5.7)					
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	18.8 (6.3)	19.8 (5.4)	0.9	-0.2, 2.0 §	NS	23	B
				CPAP			18.9 (4.5)					
Ferguson 1996[226] 8625679	25 (9) [15-50]	nd	4 mo (XO)	MAD	19	14.3 (6.5)	20.0 (12.3)	6.1	0.3, 11.9 **	nd	24	B
				CPAP	20	16.5 (8.2)	16.1 (6.1)					
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	12.7 (5.8)	13.8 (5.6)	-4.7	-7.0, -2.4 ††	NS	12	B
				CPAP			18.5 (6.1)					
Randerath 2002[228] 12171833	18 (8) [5-30]	nd	6 wk (XO)	MAD	20	15.1 (5.9)	14.8 (7.3)	-0.5	-3.6, 2.6 ‡‡	NS	0	B
				CPAP			15.3 (6.8)					
Clark 1996[224] 8769497	34 (14) [≥10]	nd	2 wk (XO)	MAD	21	5.9 (5.8)	20.9 (7.5)	0.2	-2.9, 3.3 §§	NS	4	C
				CPAP			20.7 (6.7)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	20.4 (4.6)	19.7 (5.1)	-0.7	-5.0, 3.6 ***	0.82	0	C
				AutoCPAP			20.4 (8.0)					

* Baseline/Final
† Estimated from reported SD's.
‡ Statistical analysis of comparison of final values.
§ Estimated from reported SE's.
** Estimated from reported SD's.
†† Estimated from reported SD's. Our estimate does not match with reported significance.
‡‡ Estimated from reported SD's.
§§ Estimated from reported SD's.
*** Estimated from reported SD's.

Table 5.12.6. Wakefulness tests in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Test	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Engleman 2002[225] 12231497	31 (26) [≥5]	14 (4)	8 wk (XO)	MAD	48	MWT (min)	nd	22 (12)	-2	-7.3, 2.7 *	0.46	6	B
				CPAP				24 (12)					
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	MAD	28	OSLER (sec)	2094 (674)	2312 (322)	12	-122, 146 †	NS	0	B
				CPAP				2300 (391)					

* Estimated from reported P value.
† Estimated from reported SD's.

Table 5.12.7a. FOSQ in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Final (SD)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/49 *	13.7 (3.1)	16.6 (2.8)	0.1	-1.1, 1.3	NS †	4	B
				CPAP	52/50	13.9 (3.7)	16.7 (3.1)					
Engleman 2002[225] 12231497	31 (26) [≥5]	14 (4)	8 wk (XO)	MAD	48	12 (2)	13 (3)	-3	-4.8, -1.2 ‡	0.001	6	B
				CPAP		10 (3)	14 (2)					
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	12.2 (3.1)	12.7 (3.1)	-0.1	-1.2, 1.0 §	0.85	0	C
				AutoCPAP			12.8 (2.7)					

* Baseline/Final
† Statistical analysis of comparison of final values.
‡ Estimated from reported P value.
§ Estimated from reported P value.

Table 5.12.7b. Quality of life in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference: Net Difference	Estimated 95% CI	Test Range "Worst"	Test Range "Best"	P Btw	Dropout, %	Study Quality
Hoekema 2008[230] 18719218	40 (28) [≥5]	14.2 (5.6)	78 d [IQR = 60-88 d] (PL)	MAD	51/47 *	SF-36 (all 8 components)	0						4	B
						Hospital Anxiety Scale	0							
				CPAP	52/47	Hospital Depression Scale	0							
Barnes 2004[140] 15201136	21 (12) [nd]	10.7 (3.6)	3 mo (XO)	MAD	80	SF-36 (mean score)	0						23	B
				CPAP		Beck Depression Index	0							
Lam 2007[129] 17121868	24 (5.8) [5-40]	12 (6)	10 wk (PL)	MAD	34	SF-36 Bodily Pain	CPAP	-16	-17, -14	0	100	<0.05	0	B
						SF-36 (other components)	0							
						SAQLI (A,B,C,D) †	0							
						SAQLI A-D ‡	CPAP	-0.3	-0.4, -0.2	1	7	<0.05		
				CPAP	34	SAQLI E §	MAD	-0.8	-0.9, -0.7	7	1	<0.05		
						SAQLI A-E **	0							
Engleman 2002[225] 12231497	31 (26) [≥5]	14 (4)	8 wk (XO)	MAD	48	SF-36 Health transition	CPAP	0.52	nd	Effect size (SD units)		0.001	6	B
						SF-36 PCS	CPAP	0.35	nd			0.02		
						SF-36 MCS	CPAP	0.34	nd			0.008		
						Hospital Anxiety Score	0							
				CPAP		Hospital Depression Score	0							
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	MAD	28	Nottingham Health Profile (6 components)	0						0	B
				CPAP										
Tan 2002[229] 12143088	22 (10) [<50]	13.4 (4.6)	2 mo (XO)	MAD	24	General Health ††	0						12	B
				CPAP										
Skinner 2004[232] 14718430	29 (13) [10-60]	13.2 (4.9)	1 mo (XO)	CMS collar	10	SF-36 PCS	0						0	C
				AutoCPAP		SF-36 MCS	0							
						SQ	0							

* Baseline/Final
† A: Daily functioning; B: Social interactions; C: Emotional; D: Symptoms
‡ Summary score for components A-D.
§ E: Treatment-related symptoms
** Summary score for components A-E.
†† Flemons WW, Whitelaw WA, Brant R, Remmers JE. 1994. Likelihood ratios for a sleep apnea clinical prediction rule. Am J Resp Crit Care Med. 150: 1279-1285

Table 5.12.8. Cognitive function tests in randomized controlled trials of mandibular advancement devices vs. CPAP

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors *	If Significant Difference				Dropout, %	Study Quality
								Net Difference	Estimated 95% CI	Test Range "Worst"	Test Range "Best"	P Btw	
Engleman 2002[225] 12231497	31 (26) [≥5]	14 (4)	8 wk (XO)	MAD	48	Performance IQ	0						6	B
						Trailmaking B	0							
				CPAP		SteerClear	0							
						PASAT 2s	0							
Gagnadoux 2009[227] 19324954	34 (13) [10-60]	10.6 (4.5)	2 mo (XO)	MAD	28	OSLER Errors	0						0	B
				CPAP		Trailmaking A	0							
						Trailmaking B	0							

* The noted intervention statistically significantly favors the patient (net better score on test). 0 = no difference.

Table 5.16.1. Randomized controlled trials of positional therapy vs. CPAP: study characteristics

Study PMID	Interventions	CPAP Pressure * (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Jokic 1999[235] 10084491	Positional treatment CPAP	Manual (Split)	51	nd	30	nd	Canada (nd)	No washout
Skinner 2004[233] 15611894	SHEP † CPAP	Auto (Split)	54	85	34	nd	New Zealand	Patient not blinded, multicenter not accounted for in analysis, no power analysis reported
Skinner 2008[234] 18713092	TASB ‡ CPAP	Auto (Separate)	56	nd	30.7	Positional OSA	New Zealand	Patient not blinded

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, eg if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).
† Shoulder-head elevation pillow
‡ Thoracic anti-supine band

Table 5.16.2a. AHI (events/hr) in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Difference	95% CI	P Btw	Dropout, %	Study Quality
Jokic 1999[235] 10084491	18 (nd) [4-33]	13.4 (nd)	2 wk (XO)	Positional therapy	13	17.9 (nd)	-8.4	6.1	2, 10.2	0.007	7	B
				CPAP	13		-14.5					
Skinner 2004[233] 15611894	27 (12) [13-50]	11.9 (4.6)	1 mo (XO)	SHEP	14	27 (12)	-6	16	4.2, 27.8 *	0.008	7	B
				nCPAP	13		-22					
Skinner 2008[234] 18713092	23 (12) [6-51]	13.6 (50.5)	1 mo (XO)	TASB	20	22.7	-10.7	7.1	1.1, 13.1 †	0.02	0	B
				nCPAP	20		-17.8					

* Estimated from reported P value
† Estimated from reported P value

Table 5.16.2b. AHI ≤10 events/hr in randomized controlled trials of positional therapy

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	n Event	N Total	Outcome Metric	Result *	95% CI	P Btw	Dropout, %	Study Quality
Skinner 2008[234] 18713092	23 (12) [6-51]	13.6 (50.5)	1 mo (XO)	TASB	13	18	RR	0.81	0.58, 1.13	0.004 †	0	B
				CPAP	16	18						

* Top row intervention vs. bottom row intervention. Estimated based on reported data.
† Per article, by Wilcoxin sign-rank test.

Table 5.16.3. ESS in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Difference	95% CI	P Btw	Dropout, %	Study Quality
Jokic 1999[235] 10084491	18 (nd) [4-33]	13.4 (nd)	2 wk (XO)	Positional therapy	13	13.4 (nd)	9.5	1.5 *	-2.9, 0.8	0.2	7	B
				CPAP	13		8.75					
Skinner 2004[233] 15611894	27 (12) [13-50]	11.9 (4.6)	1 mo (XO)	SHEP	14	10.2 (5.0)	-1.7	0.7	-2.8, 4.2 †	0.69	7	B
				nCPAP	14	9.5 (4.0)	-2.4					
Skinner 2008[234] 18713092	23 (12) [6-51]	13.6 (50.5)	1 mo (XO)	TASB	20	13.6	50.5	1.2		NS	0	B
				nCPAP	20		50.5					

* median
† Estimated from reported P value.

Table 5.16.4. Other sleep study and related outcomes in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Jokic 1999[235] 10084491	18 (nd) [4-33]	13.4 (nd)	2 wk (XO)	Arousal index (events/hr)	Positional therapy	13	24.5 (nd)	-5.0	4.5	(-0.7, 9.4)	0.08	7	B
					CPAP	13		-9.5					
				Sleep efficiency (%)	Positional therapy	13	nd	82	-4	nd	0.51		C *
					CPAP	13		84					
				Slow wave sleep (%)	Positional therapy	13	nd	20	-2	nd	0.31		
					CPAP	13		22					
				REM (%)	Positional therapy	13	nd	24	-2	nd	0.71		
					CPAP	13		26					
				MWT (min)	Positional therapy	13	nd	31.2	-1.7	(-1.9, 5.3)	0.32		
					CPAP	13		32.9					

* No baseline data

Table 5.16.5. Quality of life in randomized controlled trials of positional therapy vs CPAP

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference: Net Difference	95% CI	Test Range: "Worst"	Test Range: "Best"	P Btw	Dropout, %	Study Quality
Jokic 1999 10084491	17.9 (nd) [4.4-32.8]	13.4	2 wk (XO)	Positional Therapy	13	General Health Questionnaire	0						7%	B
				CPAP	13									
Skinner 2004[233] 15611894	27 (12) [13-50]	11.9 (4.6)	1 mo (XO)	SHEP	14	SF-36 physical	0							
				TASB	14	SF-36 mental	0							
Skinner 2008[234] 18713092	23 (12) [6-51]	13.6 (50.5)	1 mo (XO)	SHEP	20	SF-36 physical	0							
				TASB	20	SF-36 mental	0							

Table 5.16.6. FOSQ in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Difference	95% CI	P Btw	Dropout, %	Study Quality
Skinner 2004[233] 15611894	27 (12) [13-50]	11.9 (4.6)	1 mo (XO)	SHEP *	14	12.1 (1.9)	1.1	-0.3	nd	0.93	7	B
				CPAP	14		1.4					

* Shoulder-head elevation pillow

Table 5.16.7. Neurocognitive tests in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference: Net difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw	Dropout, %	Study Quality
Jokic 1999[235] 10084491	17.9 (nd) [4.4-32.8]	13.4	2 wk (XO)	Positional Therapy	13	Wechsler Memory Scale	0						7	B
				CPAP	13	Purdue Pegboard	0							
						Trail-Making test	0							
						Symbol Digit Modalities	0							
						Consonant Trigram	0							
						Concentration Endurance Test	0							
						Nottingham Health Profile Energy	CPAP	-1		0	3	0.04		
						Nottingham Health Profile Others	0							
						Hospital Anxiety Scale	0							
						Hospital Depression Scale	0							
						UWIST adjective checklist	0							

Table 5.17.1. Randomized controlled trials of weight loss: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Foster 2009[236] 19786682	Intensive lifestyle intervention Diabetes support and education	61	42	36.7	Diabetics	US (nd)	Unclear if outcome data included all initial participants, and if so, unclear how data were imputed.
Johansson 2009[237] 19959590	Low energy diet Usual diet	50	100	34.8	No	Sweden (2009)	
Tuomilehto 2009[238] 19011153	VLCD with lifestyle changes General counseling	51	74	31.4	Obese	Finland (2004-06)	

Table 5.17.2. Patients with OSA cure in 1 year in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	n Event	N Total	Outcome metric	Result *	95% CI †	P Btw	Dropout, %	Study Quality
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	22	35	OR (adjusted) ‡	4.17	(1.41, 12.34)	0.011	11	B
				General counseling	13	37						

* Top row intervention vs. bottom row intervention.
† Estimated from reported P value
‡ Adjusted OR for age, sex, BMI and baseline AHI.

Table 5.17.3. AHI (events/hr) in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Johansson 2009[237] 19959590	37 (14) [≥15]	7.0 (5.0)	9 wk (PL)	Low energy diet	30	37 (17)	-25	-23	-30, -15	<0.001	3	A
				Usual diet	33	37 (14)	-2					
Foster 2009[236] 19786682	24 (15) [nd]	nd	1 yr (PL)	Intensive lifestyle intervention	125	22.9 (18.0)	-5.4	-9.7	-13.6, -5.7	<0.001	17	B
				Diabetes support and education	139	23.5 (15.0)	4.2					
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	40	11 (3.6)	-4	-4.3	-7.6, -1.0	0.011	11	B
				General counseling	41	9 (2.7)	0.3					

Table 5.17.4. ESS in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Johansson 2009[237] 19959590	37 (14) [≥15]	7.0 (5.0)	9 wk (PL)	Low energy diet	30	9 (5)	-3	-4	-6, -2	<0.001	3	A
				Usual diet	33	7 (5)	1					
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	40	10.1 (5)	-3.1	-1	-2.7, 0.7 †	0.25	11%	B
				General counseling	41	9.9 (4.8)	-2.1					

* Estimated from reported data.
† Estimated from reported data.

Table 5.17.5. Minimum oxygen saturation (%) in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Johansson 2009[237] 19959590	37 (14) [≥15]	7.0 (5.0)	9 wk (PL)	Low energy diet	30	82 (6)	5	5	2, 7	0.002	3	A
				Usual diet	33	82 (5)	0					

Table 5.17.6. Blood pressure (mm Hg) in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Systolic blood pressure												
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	40	131.2 (10.2)	-1.7	-0.6	-8.4, 7.2	0.88	11	B
				General counseling	41	130.0 (12.8)	-1.9					
Diastolic blood pressure												
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	40	81.8 (8.9)	-1.9	-1.5	-7.4, 4.4	0.62	11	B
				General counseling	41	80.7 (7.8)	-0.4					

Table 5.17.7. Hemoglobin A1c (%) in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI †	P Btw	Dropout, %	Study Quality
Foster 2009[236] 19786682	24 (15) [nd]	nd	1 yr (PL)	Intensive lifestyle intervention	125	7.1 (0.9)	-0.7	-0.5	-0.8, -0.2	<0.001	17	B
				Diabetes support and education	139	7.3 (1.1)	-0.2					

* Estimated from reported data.
† Estimated from reported data.

Table 5.17.8. Weight change (kg) in randomized controlled trials of weight loss

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI *	P Btw	Dropout, %	Study Quality
Johansson 2009[237] 19959590	37 (14) [≥15]	7.0 (5.0)	9 wk (PL)	Low energy diet	30	113.4 (14.8)	-18.7	-19.8	-21.4, -18.2	nd	3	A
				Usual diet	33	111.7 (13.7)	1.1					
Foster 2009[236] 19786682	24 (15) [nd]	nd	1 yr (PL)	Intensive lifestyle intervention	125	102.9 (19.6)	-10.8	-10.2	-12.1, -8.3	<0.001	17	B
				Diabetes support and education	139	102.0 (17.1)	-0.6					
Tuomilehto 2009[238] 19011153	9 (3) [>5]	9.9 (4.8)	1 yr (PL)	VLCD with lifestyle changes	40	101.2 (11.9)	-10.7	-8.3	-11.1, -5.5	<0.001	11	B
				General counseling	41	92.3 (11.3)	-2.4					

* Estimated from reported data.

Table 5.18.1. Randomized controlled trials of oropharyngeal exercises: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Guimaraes 2009[240] 19234106	Oropharyngeal exercise Sham therapy	48	73	31.0	-	Brazil (nd)	
Randerath 2004[241] 15124719	Tongue training Sham training	53	66	28.9	-	Germany (2002)	
Puhan 2005[239] 16377643	Didgeridoo No intervention	49	84	25.8	-	Switzerland (2004-05)	

Table 5.18.2. AHI (events/hr) in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Puhan 2005[239] 16377643	20 (5) [≥15]	11.5 (nd)	4 mo (PL)	Didgeridoo	14	22.3 (5.0)	-10.7	-6.2	-12.3, -0.1	0.05	0	A
				No treatment	11	19.9 (4.7)	-4.5					
Guimaraes 2009[240] 19234106	22 (5) [≥15]	14 (7)	3 mo (PL)	Oropharyngeal exercise	16	22.4 (5.4)	-8.7	-12.2	-19, -5 *	<0.001	10	B
				Sham therapy	15	22.4 (5.4)	3.5					
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Tongue training	33	24.7 (8.6)	0.6	0.4	-5.6, 6.4 †	NS	8	A
				Sham training	24	27.7 (6.3)	0.2					

* Estimated from reported P value
† Estimated from reported data

Table 5.18.3. ESS in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Puhan 2005[239] 16377643	20 (5) [≥15]	11.5 (nd)	4 mo (PL)	Didgeridoo	14	11.8 (3.5)	-4.4	-2.8	-5.7, -0.3	0.04	0	A
				No treatment	11	11.1 (6.4)	-1.4					
Guimaraes 2009[240] 19234106	22 (5) [≥15]	14 (7)	3 mo (PL)	Oropharyngeal exercise	16	14 (5)	-6	-4	-8, -0.02 *	<0.05	10	B
				Sham therapy	15	14 (7)	-2					
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Tongue training	33	10.2 (4.9)	-1.5	-0.2	-2.6, 2.4 †	NS	8	A
				Sham training	24	10.5 (5.1)	-1.3					

* Estimated from reported P value
† Estimated from reported data

Table 5.18.4. Minimum oxygen saturation (%) in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Guimaraes 2009[240] 19234106	22 (5) [≥15]	14 (7)	3 mo (PL)	Oropharyngeal exercise	16	83 (6)	85 (7)	4	0.2, 7.8 *	NS	10	B
				Sham therapy	15	82 (4)	80 (4)					
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Tongue training	33	81.7 (6.8)	-0.3	1.1	-2.4, 4.6 †	NS	8	A
				Sham training	24	82.3 (5.8)	-1.4					

* Estimated from reported data
† Estimated from reported data

Table 5.18.5. Sleep efficiency (%) in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Guimaraes 2009[240] 19234106	22 (5) [≥15]	14 (7)	3 mo (PL)	Oropharyngeal exercise	16	87 (8)	-1	-2	-8.8, 4.8 *	0.58	10	B
				Sham therapy	15	86 (10)	1					

* Estimated from reported data.

Table 5.18.6. Other sleep study outcomes in randomized controlled trials of positional therapy vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Slow wave sleep	Tongue training	33	19.1 (13.6)	6.8	11	-1.3, 21.5 *	NS	8	A
					Sham training	24	23.5 (9.8)	-4.2					
				REM sleep	Tongue training	33	11 (4.7)	1.1	-0.3	-3.0, 2.2 †	NS		
					Sham training	24	12.9 (5.2)	1.4					
				Arousal index	Tongue training	33	23.7 (9.5)	-0.7	-1.9	-6.9, 3.5 ‡	NS		
					Sham training	24	23 (9.8)	1.2					

* Estimated from reported data
† Estimated from reported data
‡ Estimated from reported data

Note: There is no Table 5.18.7.

Table 5.18.8. FOSQ in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Tongue training	33	84.8 (32.5)	4.2	1.6	-20.4, 13.6 *	NS	8	A
				Sham training	24	74.2 (36.9)	2.6					

Table 5.18.9. Quality of life outcomes in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference Net Difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw	Dropout, %	Study Quality
Puhan 2005[239] 16377643	20 (5) [≥15]	11.5 (nd)	4 mo (PL)	Didgeridoo	14	PQoSI	0						0	A
				No treatment	11									
						SF-36- all domains	0							
Guimaraes 2009[240] 19234106	22 (5) [≥15]	14 (7)	3 mo (PL)	Oropharyngeal exercise	16	Pittsburgh Quality of Sleep Index	Oropharyngeal exercise	-3.4	nd	21	0	<0.01	10	B
				Sham therapy	15									

Table 5.18.10. Neurocognitive tests in randomized controlled trials of oropharyngeal exercises

Study PMID	Baseline AHI (SD)	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference Net Difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw	Dropout, %	Study Quality
Randerath 2004[241] 15124719	28 (6) [10-40]	9.4 (4.7)	8 wk (PL)	Tongue training	33	Attention Test	0						0	A
				Sham training	24									

* Estimated from reported data

Table 5.19.1. Randomized controlled trials of palatal implants vs. control: study characteristics

Study PMID	Interventions	Mean Age (yr)	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Friedman 2008[242] 18241718	Palatal implants Placebo	39 (9)	53	28.7 (2.3)	-	US (2005-06)	-
Steward 2008[243] 18922335	Soft palate implants Sham implants	49 (nd)	79	27.6 (nd)	-	US (nd)	-

Table 5.19.2a. AHI (events/hr) in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Friedman 2008[242] 18241718	20 (4) [5-40]	11.7 (2.7)	3 mo (PL)	Palatal implants	29	23.8 (5.5)	-7.1	-8.8	5.3, 12.2	<0.0001	11	A
				Placebo	26	20.1 (4.0)	+0.9					
Steward 2008[243] 18922335	17 (nd) [10-40]	10.6 (nd)	3 mo (PL)	Soft palate implants	47	17.2 (nd)	2.9	-6	0.9, -13	NS	1	B
				Sham implants	50	16.7(nd)	8.9					

Table 5.19.2b. Fifty percent reduction in AHI to ≤ 20 events/hr in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	n Event	N Total	Outcome Metric	Result *	95% CI	P Btw	Dropout, %	Study Quality
Steward 2008[243] 18922335	16 (nd) [10-40]	10.6(nd)	3 mo (PL)	Soft palate implants	13	50	RR	2.60	1.00, 6.75	0.04 †	1	B
				Sham implants	5	50						

* Top row intervention vs. bottom row intervention.
† Per article, by chi-squared test.

Table 5.19.3. ESS in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Friedman 2008[242] 18241718	20 (4) [5-40]	11.7 (2.7)	3 mo (PL)	Palatal implants	31	12.7(2.7)	-2.4	-1.9	1.0, 2.9	0.0002	11	A
				Placebo	31	11.7(2.7)	-0.5					
Steward 2008[243] 18922335	17 (nd) [10-40]	10.6 (nd)	3 mo (PL)	Soft palate implants	47	10.6(nd)	-1.8	-0.3	-1.8, 1.1	NS	1	B
				Sham implants	49	10.7(nd)	-1.5					

Table 5.19.4. Minimum oxygen saturation in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Friedman 2008[242] 18241718	20 (4) [5-40]	11.7 (2.7)	3 mo (PL)	Palatal implants	28	88.3 (3.0)	-1.3	-0.6	-2.2, 1.0	NS	11	A
				Placebo	23	89.6 (2.5)	-0.7					
Steward 2008[243] 18922335	17 (nd) [10-40]	10.6 (nd)	3 mo (PL)	Soft palate implants	46	nd	0.1	-2.9	-0.8, -5.0	0.007	1	B
				Sham implants	48	nd	3					

Table 5.19.5. REM sleep in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Friedman 2008[242] 18241718	20 (4) [5-40]	11.7 (2.7)	3 mo (PL)	Palatal implants	29	16.1 (3.3)	-0.8	-2	-4.0, 0.01	NS	11	A
				Placebo	26	12.9 (3.7)	1.2					

Table 5.19.6. FOSQ total in randomized controlled trials of palatal implant vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Steward 2008[243] 18922335	17 (nd) [10-40]	10.6 (nd)	3 mo (PL)	Soft palate implants	49	15.5(nd)	1.4	0.83	0.0,1.6	NS	1	B
				Sham implants	49	16.1(nd)	0.6					

Table 5.20.1. Studies of surgery vs. control: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (Enrollment years)	Major quality issues
Back 2009[244] 19504550	RFA (Soft palate) Sham surgery	30-65 (range)	100	25.6 (median)	BMI ≤35 kg/m^2	Finland (nd)	
Ferguson 2003[245] 12502473	LAUP No treatment	44	78	31.6	-	Canada (nd)	
Guilleminault 2008[248] 19014072	Surgery combo * Cognitive behavioral therapy for insomnia	32	40	23.9	-	US (2002-03)	First phase †
Koutsourelakis 2008[246] 17898015	Surgery ‡ Sham surgery	37	59	29.9	Deviated nasal septum	Greece (nd)	
Li 2009[249] 19793414	Nasal surgery Conservative treatment	38	95	26.2	Nasal obstruction	Taiwan (nd)	Not randomized; no data on followup duration
Lojander 1996[124] 8681614 Lojander 1999[125] 10188139	UPPP Conservative treatment	47	97	31.0	BMI ≤40kg/m^2	Finland (1987-92)	
Woodson 2003[247] 12825037	RFA (tongue & palate) Sham RFA RFA (nd where)	46	70	28.5	-	US (nd)	

* combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
† Paper was presented as a crossover study between behavioral therapy and surgery. Only the first phase (prior to crossover) evaluated here.
‡ Submucous resection of the deviated septum and bilateral resection of inferior turbinates

Table 5.20.2. AHI or oxygen desaturation index (events/hr) in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcomes	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Back 2009[244] 19504550	12 (5–8)* [5-15]	8.0 (3.0-16.0)†	4 mo (PL)	AHI	RFA	17	11 (5-15)‡	2	3	-9.1, 15.1§	NS	0	A
					Sham surgery	15	12.0 (5.0-8.0)**	-1					
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40]††	11.6(3.5)	2 mo (PL)	AHI	RFA	24	21.3 (11.1)	-4.5	-2.7	-9.9,4.5	NS	13	A
					Sham RFA	28	15.4 (7.8)	-1.8					
Koutsourelakis 2008[246] 17898015	31 (14) [≥5]	13.7 (4.4)	4 mo (PL)	AHI	Surgery‡‡	27	31.5 (16.7)	0	-1.5	-10.3, 7.3§§	nd	3	A
					Sham surgery	22	30.6 (13.8)	1.5					
Ferguson 2003[245] 12502473	16 (4) [10-25]	10.0 (5.2)	8 to15 mo (PL)	AHI	LAUP	21	18.6 (4.3)	-3.9	-10.5	-20.5, -0.4***	nd	1	B
					No treatment	23	16.1 (4.0)	6.6					
Lojander, 1996[124] 8681614	nd	(nd)	12 mo (PL)	ODI_4†††	UPPP	16	45	-31	-20	nd	NS	3	C
					Conservative treatment	10	34	-11					
				ODI_{10}‡‡‡	UPPP	16	17	-14	-6	nd	NS		
					Conservative treatment	10	14	-8					
Guilleminault 2008[248] 19014072	10 (6) [nd]	6.6 (1.2)	3 mo (XO first phase)	AHI	Surgery combo§§§	15	9.7 (5.7)	-5.2	-6.2	-9.3,-3.1****	<0.0001	33	C
					Cognitive behavioral therapy	15	9.7 (5.7)	1					
Li 2009[249] 19793414	26 (27) [≥5]	10.2 (5.2)	nd (PL)	AHI	Nasal surgery	44	36.4 (29.1)	1.1	2.6	-11.0, 16.2††††	NS	0	C
					Conservative treatment	22	25.9 (27.0)	-1.5					

* Median (range)
† Median (range)
‡ Median (range)
§ Estimated from reported P value
** Median (range)
†† Two parts of methods section disagree with each other
‡‡ Patients had submucous resection of the deviated septum and bilateral resection of inferior turbinates
§§ Estimated from reported data
*** Estimated from reported data
††† no. of desaturation of ≥4% per hr in bed
‡‡‡ no. of desaturation of ≥10% per hr in bed
§§§ combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
**** Estimated from reported P value
†††† Estimated from reported data

Table 5.20.3. ESS in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Back 2009[244] 19504550	12 (5–8) * [5-15]	8.0 (3.0-16.0) †	4 mo (PL)	RFA	17	10 (3-21) ‡	-3	0	nd	NS	0	A
				sham surgery	15	8.0 (3.0–16.0) §	-3					
Koutsourelakis 2008[246] 17898015	31 (14) [≥5]	13.7 (4.4)	4 mo (PL)	Surgery **	27	13.4 (2.9)	-1.7	-0.5	-2.5, 1.5 ††	nd	3	A
				Sham surgery	22	13.7 (4.4)	-1.2					
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] ‡‡	11.6(3.5)	2 mo (PL)	RFA	26	11.9 (4.6)	-2.1	-1.2	-3.1,0.8	NS	13	A
				Sham RFA	28	11.6 (3.5)	-1.0					
Ferguson 2003[245] 12502473	16 (4) [10-25]	10.0 (5.2)	8 to15 mo (PL)	LAUP	21	10.7 (3.7)	1.4	-2.2	-5.8, 1.4 §§	nd	1	B
				No treatment	23	10.0 (5.2)	-0.8					
Guilleminault 2008[248] 19014072	10 (6) [nd]	6.6 (1.2)	3 mo (XO first phase)	Surgery combo ***	15	6.6 (1.2)	-1.8	-1.2	-1.8, -0.5 †††	0.005	33	C
				Cognitive behavioral therapy	15	6.6 (1.2)	-0.6					
Li 2009[249] 19793414	26 (27) [≥5]	10.2 (5.2)	nd (PL)	Nasal surgery	44	10.6 (3.9)	-3.0	-3.6	-6.1, -1.1 ‡‡‡	0.02	0	C
				Conservative treatment	22	10.2 (5.2)	0.6					

* Median(range)
† Median(range)
‡ Median(range)
§ Median(range)
** Patients had submucous resection of the deviated septum and bilateral resection of inferior turbinates
†† Estimated from reported data
‡‡ two parts of methods section disagree with each other
§§ Estimated from reported data
*** combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
††† Estimated from reported P value
‡‡‡ Estimated from reported data

Table 5.20.4. Minimum oxygen saturation (%) in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Back 2009[244] 19504550	12 (5–8) * [5-15]	8.0 (3.0-16.0) †	4 mo (PL)	RFA	17	82.0 (68.0-88.0) ‡	0	0	nd	NS	0	A
				sham surgery	15	83.0 (69.0-88.0) §	0					
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] **	11.6(3.5)	2 mo (PL)	RFA	24	86.3 (7.6)	-0.6	-1.2	-3.8, 1.4	NS	13	A
				Sham RFA	28	88.3 (3.9)	0.6					
Guilleminault 2008[248] 19014072	10 (6) [nd]	6.6 (1.2)	3 mo (XO first phase)	Surgery combo ††	15	91.3 (1.9)	4.7	4.4	2.1,6.6 ‡‡	<0.0001	33	C
				Cognitive behavioral therapy	15	91.3 (1.9)	0.3					
Li 2009[249] 19793414	26 (27) [≥5]	10.2 (5.2)	nd (PL)	Nasal surgery	44	78.3 (11.6)	0.8	0.3	2.1,6.6 §§	NS	0	C
				Conservative treatment	22	82.7 (8.5)	0.5					

* Median(range)
† Median(range)
‡ Median(range)
§ Median(range)
** Two parts of methods section disagree with each other
†† combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
‡‡ Estimated from reported P value
§§ Estimated from reported data

Table 5.20.5. Sleep stage changes (%) in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Guilleminault 2008[248] 19014072	10 (6) [nd]	6.6 (1.2)	3 mo (XO first phase)	REM	Surgery combo *	15	13.1(1.8)	3.7	3.1	1.5, 4.6 †	<0.0001	33	C
					Cognitive behavioral therapy	15	13.1(1.8)	0.6					
				Stage 3 and 4	Surgery combo ‡	15	11.5(1.5)	4.5	3.5	1.7, 5.3 §	<0.0001		
					Cognitive behavioral therapy	15	11.5(1.5)	1					
Li 2009[249] 19793414	26 (27) [≥5]	10.2 (5.2)	nd (PL)	REM	Nasal surgery	44	13.7 (5.7)	0.9	-0.1	-3.9, 1.9 **	NS	0	C
					Conservative treatment	22	13.9 (4.6)	1.0					
				Stage 3 and 4	Nasal surgery	44	6.3 (7.0)	-0.2	-1.0	-3.0, 2.8 ††	NS		
					Conservative treatment	22	2.4 (3.8)	0.8					

* combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
† Estimated from reported P value
‡ combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty and RFA of the inferior nasal turbinates
§ Estimated from reported P value
** Estimated from reported data
†† Estimated from reported data

Table 5.20.6. FOSQ in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] *	11.6(3.5)	2 mo (PL)	RFA	24	16.5(2.0)	1.2	0.9	-0.1, 1.9	0.04	13	A
				Sham RFA	27	16.8(2.1)	0.4					

* Two parts of methods section disagree with each other

Table 5.20.7. Functional Outcomes in randomized controlled trials of surgery vs. control

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference					Dropout, %	Study Quality
								Net Difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw		
Back 2009[244] 19504550	12 (5–8) * [5-15]	8.0 (3.0-16.0) †	4 mo (PL)	RFA	17	SF-36 (all domains)	0						0	A
				sham surgery	15									
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] ‡	11.6(3.5)	2 mo (PL)	RFA	24	SF-36 (all domains)	0						13	A
				Sham RFA	27									
Ferguson 2003[245] 12502473	16 (4) [10-25]	10.0 (5.2)	8 to15 mo (PL)	LAUP	21	SAQLI	0						1	B
				No treatment	23									
Lojander, 1999[125] 10188139	nd	(nd)	12 mo (PL)	UPPP	10	Wechsler verbal	0						3	C
				Conservative treatment	10									
						Wechsler performance	0							
						Wechsler memory	0							

* Median (range)
† Median (range)
‡ Two parts of methods section disagree with each other

Table 5.21.1. Studies of surgery vs. CPAP: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Anand 1991[255] 1945423	UPPP CPAP	53 (nd)	60	nd	--	US (1983-90)	No eligibility criteria. Retrospective.
Ceylan 2009[254] 19770425	TCRFVTR CPAP	46 (nd)	89	28.8	--	Turkey (2003-06)	Small sample size. Prospective nonrandomized.
Conradt 1998[251] 9785277	MMO CPAP	42 (10)	100	26.7	Craniofacial abnormalities	Germany (1993-96)	No eligibility criteria. Prospective nonrandomized.
Katsantonis 1988[256] 327 8184	UPP Orthognathic device Tracheostomy Medication(TCA) Tongue retaining device CPAP	49 (19-78) *	81	nd	--	US (1982-86)	No eligibility criteria. Retrospective.
Keenan 1994[257] 8275724	UPPP CPAP	52 (12)	79	36.0	--	Canada (1984-90)	Significant difference between followup durations. Retrospective.
Lin 2006[258] 16735919	Extended UPP CPAP	48 (nd)	nd	27.2	--	Taiwan (2000-01)	Significant differences in baseline characteristics. Retrospective.
Robinson 2009[259] 19643262	Stepwise surgery CPAP	56 (nd)	88	31.6		Australia (2003-04)	Incomplete results. Retrospective.
Vicini 2010[250] 19944893	MMA CPAP	48 (10)	86	30.2	AHI >30 events/hr	Italy (nd)	No exclusion criteria
Weaver 2004[260] 15195049	UPPP CPAP	57 (nd)	98	nd	--	US (1997-2001)	No details on OSA severity. Retrospective.
Woodson 2001[252] 11593163	TCRFVTR CPAP	48 (9)	77	31.2	BMI <35 kg/m^2, Anesthesia risk group ASA class I, II, or III	US (nd)	No eligibility criteria. Prospective nonrandomized.
Woodson 2003[247] 12825037	RFA (tongue & palate) CPAP	53 (nd)	60	nd	--	US (nd)	
Zorick 1990[253] 2086548	UPPP CPAP	46 (nd)	89	28.8	--	US (nd)	Dropout rate >20%. No eligibility criteria. Prospective nonrandomized

* Range

Table 5.21.2. Categorical outcomes in studies of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	n Event	N Total	Outcome Metric	Result *	95% CI	P Btw	Dropout, %	Study Quality
Weaver 2004[260] 15195049	nd [nd]	nd	6 y (NRCS, retrospective)	Mortality	UPPP	nd	2072	HR	1.31	1.03, 1.67	0.03	NA	C
					CPAP	nd	20826						
Katsantonis 1988[256] 327 8184	70 UPPP 80 CPAP [nd]	nd	18 mo (retrospective)	50% improvement in AHI and 85% improvement in severity index	UPPP	37	98	%	38 vs. 100	nd	nd	NA	C
					CPAP	53	53						
Keenan 1994[257] 8275724	nd [≥5]	nd	28 to 43 mo (NRCS, retrospective)	Survival	UPPP	6	149	%	4 vs. 2	nd	NS	NA	C
					CPAP	3	126						
Anand 1991[255] 1945423	(nd) [nd]	nd	16 d to 87mo (NRCS, retrospective)	Increased MSLT score ≥3 min	UPPP	13	43	%	30 vs. 41	nd	nd	NA	C
					CPAP	12	29						

* Top row intervention vs. bottom row intervention.

Table 5.21.3. Survival in studies of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Keenan 1994[257] 8275724	nd [≥5]	nd	28 to 43 mo (NRCS, retrospective)	Age adjusted 5 y probability of survival	UPPP	149	nd	0.94 (0.02) *	-0.01	nd	NS	NA	C
					CPAP	126	nd	0.95 (0.03) †					
Weaver 2004[260] 15195049	nd [nd]	nd	4 y (NRCS, retrospective)	Survival (years)	UPPP	2072	nd	2.81	0.06	0.0, 0.1 ‡	0.03	NA	C
					CPAP	20, 826	nd	2.75					

* Mean (SE)
† Mean (SE)
‡ Estimated from reported P value

Table 5.21.4. AHI or RDI in studies of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Ceylan 2009[254] 19770425	28 (6) [5-40]	11.1 (3.1)	12 mo (NRCS, prospective)	AHI	TCRFTVR	26	29.6 (7.8)	-13.5	-0.7	-4.8, 3.4*	NS	0	C
					CPAP	21	28.5 (6.9)	-12.8					
Conradt 1998[251] 9785277	RDI 59 (24) [nd]	nd	3 mo (NRCS, prospective)	RDI	MMA	24	59.4 (24.1)	-53.8	0.3	-11.7, 12.3†	NS	0	C
					CPAP	24	59.4 (24.1)	-54.1					
Katsantonis 1988[256] 327 8184	70 UPPP 80 CPAP [nd]	nd	18 mo (retrospective)	AHI	UPPP	98	~70 (nd)	-20	35	nd	nd	NA	C
					CPAP	53	~80 (nd)	-55					
Lin 2006[258] 16735919	RDI 65 (24) vs. 44 (30) [nd]	14.1 (4.4) vs. 11.8 (5.5)	6 mo (NRCS, retrospective)	RDI	Extended UPP	55	43.6 (29.7)	-31.5	31.1	12.5, 49.6	<0.001	NA	C
					CPAP	54	65.3 (24.7)	-62.6					
Vicini 2010[250] 19944893	50 (12) [>30]	11.2 (1.6)	12 mo (PL RCT)	AHI	MMA	25	56.8 (16.5)	-48.7	-4.7	-11.9, 2.5	NS	12% CPAP	C
					CPAP	25	50.3 (12.4)	-44					

* Estimated from reported P value
† Estimated from reported data

Table 5.21.5. ESS in studies of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] *	11.6 (3.5)	2 mo (PL RCT)	RFA	26	11.9 (4.6)	-2.1	-0.2	-2.4, 2.8	NS	13	A
				CPAP	25	12.6 (5.0)	-2.3					
Ceylan 2009[254] 19770425	28 (6) [5-40	11.1 (3.1)	12 mo (NRCS prospective)	TCRFTVR †	26	10.8 (3.2)	-2.6	+0.1	-0.7, 0.9 ‡	NS	0	C
				CPAP	21	11.1 (3.1)	-2.7					
Lin 2006[258] 16735919	RDI 65 (24) vs. 44 (30) [nd]	14.1 (4.4) vs. 11.8 (5.5)	6 mo (NRCS, retrospective)	Extended UPP	55	11.1 (3.72)	-3.78	+1.09	nd	NS	NA	C
				CPAP	54	14.1 (4.43)	-4.87					
Robinson 2009[259] 19643262	RDI 45 (nd) [>15]	10.5 (8.75) §	20-46 mo (NRCS, retrospective)	Surgery, stepwise approach	77	9 (7) **	-5	1.5	-8.7, 11.7 ††	NS ‡‡	NA	C
				CPAP	89	10.5 (8.75) §§	-6.5					
Vicini 2010[250] 19944893	50 (12) [>30]	11.2 (1.6)	12 mo (PL RCT)	MMA	25	11.6 (2.8)	-3.9	1.4	-0.74, 3.5	NS	12% CPAP	C
				CPAP	25	11.2 (2.6)	-5.3					
Woodson 2001[252] 11593163	40 (21) [15-60]	11.8 (nd)	8-12 wk (NRCS, prospective)	TCRFTVR ***	50	11.1 (nd)	-3.7	0.7	nd	nd	15	C
				CPAP	74	11.8 (nd)	-4.4					

* two parts of methods section disagree with each other
† temperature controlled RF tissue volume reduction and septoplasty ± nasal valve suspension (somnoplasty)
‡ Estimated from reported P value
§ Median (IQR)
** Median (IQR)
†† Estimated from reported P value
‡‡ adjusted for age, RDI, Epworth, length of followup
§§ Median (IQR)
*** temperature controlled radiofrequency tissue volume reduction of the soft palate

Table 5.21.6. Other continuous outcomes in studies of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] *	11.6 (3.5)	2 mo (PL RCT)	FOSQ	RFA	26	16.5 (2.0)	1.2	-0.29	-1.35, 0.77	NS	13	A
					CPAP	25	16.0 (2.6)	1.5					
Conradt 1998[251] 9785277	RDI 59 (24)	nd	3 mo (NRCS, prospective)	Sleep efficiency	MMA	24	80.2 (9.91)	4	-1	-6.2, 4.2 †	NS	0	C
					CPAP	24	80.2 (9.91)	5					
				Arousal index	MMA	24	54.3 (20.0)	-34.6	0.4	-10.3, 11.1	NS		
					CPAP	24	54.3 (20.0)	-35					
Ceylan 2009[254] 19770425	28 (6) [5-40	11.1 (3.1)	12 mo (NRCS, prospective)	Minimum O_2 saturation	TCRFTVR	26	86.8 (8.9)	7.8	2.7	-4.7, 10.2 ‡	NS	0	C
					CPAP	21	88.4 (8.5)	5.1					
Woodson 2001[252] 11593163	40 (21) [15-60]	11.8 (nd)	8-12 wk (NRCS, prospective)	FOSQ	TCRFTVR	18	72.3 (13.8)	7.8	-4.4	-10.2, 1.4 §	NS	15	C
					CPAP	74	69.9 (19.7)	12.2					
Zorick 1990[253] 2086548	nd [nd]	nd	6 wk (NRCS, prospective)	MSLT	UPPP	46	4.1 (0.9)	1.4	-4.5	-8.9, -0.02 **	<0.05	nd	C
					CPAP	46	4.4 (1.1)	5.9					

* Two parts of methods section disagree with each other
† Estimated from reported data
‡ Estimated from reported P value
§ Estimated from reported P value
** Estimated from reported data

Table 5.21.7. Sleep stage in randomized controlled trials of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (Final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Conradt 1998[251] 9785277	RDI 59 (24)	nd	3 mo (NRCS, prospective)	REM	MMA	24	19.6 (7.38)	1.7	0.1	-3.7, 3.9 *	NS	0	C
					CPAP	24	19.6 (7.38)	1.6					
				Stage 3 and 4	MMA	24	8.0 (6.08)	6.4	-3.8	-8.9,1.3 †	NS		
					CPAP	24	8.0 (6.08)	10.2					
Zorick 1990[253] 2086548	nd [nd]	nd	6 wk (NRCS, prospective)	REM	UPPP	46	10 (5)	3	-8	-15.9,-0.03 ‡	<0.05	nd	C
					CPAP	46	10 (6)	11					
				Stage 3 and 4	UPPP	46	4.0 (6)	1	--7	-13.9, -0.03 §	<0.05		
					CPAP	46	1.0 (3)	8					

* Estimated from reported data
† Estimated from reported data
‡ Estimated from reported data
§ Estimated from reported data

Table 5.21.8. Quality of life outcomes in randomized controlled trials of surgery vs. CPAP

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Outcome	Favors	If Significant Difference				Dropout, %	Study Quality
								Net Difference	95% CI	Test Range "Worst"	Test Range "Best"	P Btw	
Woodson 2003[247] 12825037	15 (7) [10-30 or 5-40] *	11.6 (3.5)	2 mo (PL RCT)	RFA (tongue & palate)	24	SF-36 (PCS, MCS)	0						13	A
				CPAP	24									
Lin 2006[258] 16735919	RDI 65 (24) [nd]	14.1 (4.4)	6 mo (NRCS, retrospective)	Extended UPP	55	SF-36 (all domains)	0						NA	C
				CPAP	54									
Woodson 2001[252] 11593163	40 (21) [15-60]	11.8 (nd)	8-12 wk (NRCS, prospective)	TCRFVTR	nd	SF-36 (all domains)	0						NA	C
				nCPAP	nd									

* Two parts of methods section disagree with each other

Table 5.23.1. Randomized controlled trials of drug interventions: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Carley 2007[264] 17310863	Mirtazapine 4.5 or 15 mg Placebo	41	58	37.8	Most pts with HTN excluded	US (nd)	-
Clarenbach 2008[269] 18710420	Xylometazoline Placebo	49	87	30.7	nd	Switzerland (2004-05)	-
Kiely 2004[265] 14694248	Fluticasone placebo	47	nd	29.8	Snorers	Ireland (nd)	-
Kraiczi 1999[266] 9989366	Paroxetine Placebo	53	100	28.7	No	Sweden (nd)	-
Suurna 2008[268] 18656731	Pantoprazole Placebo	51	42	31	All patients have GERD	US (2004-06)	-
Ryan 2009[205] 19961025	Steroid + CPAP Dry CPAP	48	94	34	nd	Ireland (nd)	-
Whyte 1988[267] 3067313	Acetazolamide or Protriptyline Placebo	nd	80	nd	nd	UK (nd)	No information on exclusion criteria

Table 5.23.2. AHI (events/hr) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	13.5	-8.8	-14.8, -2.8 *	0.004	0	B
				Mirtazapine 15 mg	12	nd	11.4	-10.9	-18.3, -3.5 †	0.004		
				Placebo	12	nd	22.3					
Clarenbach 2008[269] 18710420	33 (25) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	32.6 (24.5)	29.3 (32.5)	-2.9	-21.4, 15.6 ‡	NS	0	A
				Placebo	12	32.6 (24.5)	32.2 (32.8)					
Kiely 2004[265] 14694248	26 § (27) **	12 (nd)	4 wk (XO)	Fluticasone	13	26.5 (26.9) ††	23.3	-6.5 ‡‡	-29.5, 1.8	<0.05	0	B
				Placebo	13	26.5 (26.9)	30.3					
				Fluticasone	18 §§	nd	17	-5.6 ***	-22.6, -0.7	0.01		
				Placebo	13 †††	nd	24.3					
Kraiczi 1999[266] 9989366	nd	nd	6 wk (XO)	Paroxetine	17	nd	30.2	-6.1	-17.9, 0.6	0.021	15	B
				Placebo	17	nd	36.3					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	26	-24	nd	nd	0	C
				Protriptyline	10	nd	46	-4	nd	nd		
				Placebo	10	nd	50					

* Estimated from reported P value
† Estimated from reported P value
‡ Estimated from reported data
§ Median
** Quartile range
†† Median (quartile range)
‡‡ Median
§§ Using definition of AHI ≥ 5 instead of AHI ≥10
*** Median
††† Using definition of AHI ≥ 5 instead of AHI ≥10

Table 5.23.3. ESS in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Clarenbach 2008[269] 18710420	33 (24) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	nd	10.5 (3.8)	-1.3	-3.6, 1.0 *	NS	0	A
				Placebo	12	nd	11.8 (4.4)					
Suurna 2008[268] 18656731	10 (8) [≤30]	14 (3.5)	2 wk (XO)	Pantoprazole	57	14 (3.5)	-1.8	-0.5	-0.98, -0.02 †	0.04	16	B
				Placebo	57	14 (3.5)	-1.3					
Ryan 2009[205] 19961025	36 (22) [≥10]	12 (5)	4 wk (PL)	Steroid + CPAP	42	13 (6)	-4	-1	-4.0, 2.0 ‡	nd	9	B
				Dry CPAP	39	12 (5)	-3					

* Estimated from reported data.
† Estimated from reported P value.
‡ Estimated from reported data.

Table 5.24.4. Arousal index (events/hr) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	41.9	0.8	nd	NS	0	B
				Mirtazapine 15 mg	12	nd	28.1	-13.0	-24, -2 *	0.02		
				Placebo	12	nd	41.1					
Clarenbach 2008[269] 18710420	33 (24) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	nd	54	-2	nd	NS	0	A
				Placebo	12	nd	56					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	16	-10	nd	nd	0	C
				Protriptyline	10	nd	21	-5	nd	nd		
				Placebo	10	nd	26					

* Estimated from reported P value

Table 5.24.5. Sleep efficiency (%) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	87.7	4.8	nd	NS	0	B
				Mirtazapine 15 mg	12	nd	90.1	8.2	nd	0.05		
				Placebo	12	nd	82.9					
Clarenbach 2008[269] 18710420	33 (24) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	nd	86 (12)	-2	nd	NS	0	A
				Placebo	12	nd	88 (6)					
Kraiczi 1999[266] 9989366	nd	nd	6 wk (XO)	Paroxetine	17	nd	77.2	-2.9	-10.6,4.3	0.411	15	B
				Placebo	17	nd	80.3					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	82 *	12	nd	nd	0	C
				Protriptyline	10	nd	78 †	8	nd	nd		
				Placebo	10	nd	70 ‡					

* Estimated from Figure 4 in paper
† Estimated from Figure 4 in paper
‡ Estimated from Figure 4 in paper

Table 5.23.6. Slow wave sleep (%) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	7.5	2.4	nd	NS	0	B
				Mirtazapine 15 mg	12	nd	7.2	2.1	nd	NS		
				Placebo	12	nd	5.1					
Clarenbach 2008[269] 18710420	33 (24) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	nd	9 (8)	-2	nd	NS	0	A
				Placebo	12	nd	7 (6)					
Kraiczi 1999[266] 9989366	nd	nd	6 wk (XO)	Paroxetine	17	nd	12.2	-0.6	-6.4, 4.7	0.411	15	B
				Placebo	17	nd	12.8					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	14 *	-1	nd	nd	0	C
				Protriptyline	10	nd	15 †	0	nd	nd		
				Placebo	10	nd	15 ‡					

* Estimated from Figure 4 in paper
† Estimated from Figure 4 in paper
‡ Estimated from Figure 4 in paper

Table 5.23.7. REM sleep (%) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [Eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	15.6	-6.6	nd	NS	0	B
				Mirtazapine 15 mg	12	nd	16.6	-5.6	nd	0.04		
				Placebo	12	nd	22.2					
Clarenbach 2008[269] 18710420	33 (24) [>10]	11.8 (4.5)	1 wk (XO)	Xylometazoline	12	nd	10 (5)	-1	nd	NS	0	A
				Placebo	12	nd	11 (5)					
Kiely 2004[265] 14694248	26.5 * (26.9) †	12 (nd)	4 wk (XO)	Fluticasone	13	nd	10.9	0.4 ‡	nd	NS	0	B
				Placebo	13	nd	10.5					
Kraiczi 1999[266] 9989366	nd	nd	6 wk (XO)	Paroxetine	17	nd	9.7	nd	-7.4, 1.4	0.191	15	B
				Placebo	17	nd	12.9					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	23	4	nd	nd	0	C
				Protriptyline	10	nd	18	-1	nd	nd		
				Placebo	10	nd	19					

* Median
† Quartile range
‡ Median

Table 5.23.8. Minimum oxygen saturation (%) in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Carley 2007[264] 17310863	23 (17) [nd]	nd	7 d (XO)	Mirtazapine 4.5 mg	12	nd	81.1	-0.6	nd	NS	0	B
				Mirtazapine 15 mg	12	nd	80.8	-0.9	nd	NS		
				Placebo	12	nd	81.7					
Kiely 2004[265] 14694248	26.5 * (26.9) †	12 (nd)	4 wk (XO)	Fluticasone	13	nd	2.1	-0.1	nd	NS	0	B
				Placebo	13	nd	2.2					
Whyte 1988[267] 3067313	nd [>15]	nd	2 wk (XO)	Acetazolamide	10	nd	72	2	nd	nd	0	C
				Protriptyline	10	nd	77	7	nd	nd		
				Placebo	10	nd	70					

Table 5.23.9. FOSQ in randomized controlled trials of drug interventions

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Suurna 2008[268] 18656731	10 (8) [≤30]	14 (3.5)	2 wk (XO)	Pantoprazole	57	nd	-8.1	-2.6	-5.3, 0.1 ‡	0.06	16	B
				Placebo	57	nd	-5.5					

* Median
† Quartile range
‡ Estimated from reported P value.

Table 5.24.1. Randomized controlled trials of atrial overdrive pacing: study characteristics

Study PMID	Interventions	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Other quality issues
Melzer 2006[270] 17040007	AOP 75 bpm AOP 45 bpm	69	84%	29.5	nd	Germany, Switzerland (nd)	Dropout >20%, patient not blinded.
Simantirakis 2005[271] 16354893	AOP CPAP	60	75%	nd	Bradyarrhythmia (pacer)	Greece	No description of how pressure was titrated.

Table 5.24.2. AHI (events/hr) in randomized controlled trials of atrial overdrive pacing

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Melzer 2006[270] 17040007	27 * (nd) [>15]	9.0 (3.9)	1 wk (XO)	AOP 75 bpm	19	nd	23.0	-3.8	-14.6, 7.0 †	0.49	5	A
				AOP 45 bpm	19	nd	26.8					
Simantirakis 2005[271] 16354893	49 (19) [nd]	15.7 (nd)	1 mo (XO)	AOP	16	49.0 (19)	0.2	46.5	-9.8, 27.8 ‡	nd	0	B
				CPAP	16	49.0 (19)	-46.3					

* Estimated from control value
† Estimated from reported P value.
‡ Estimated from reported data.

Table 5.24.3. ESS in randomized Controlled trials of atrial overdrive pacing

Study PMID	Baseline AHI (SD) [range]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Simantirakis 2005[271] 16354893	**49.0 (nd)**	**15.7 (nd)**	**1 mo (XO)**	AOP	**16**	**15.7 (nd)**	**0.1**	**10.3**	**nd**	**nd**	**0%**	**B**
				CPAP	16	15.7 (nd)	-10.2					

Table 5.24.4. REM and Slow Wave Sleep (%) in randomized controlled trials of atrial overdrive pacing

Study PMID	Baseline AHI (SD) [eligibility]	Baseline ESS (SD)	Duration (design)	Outcome	Interventions	No. Analyzed	Baseline (SD)	Change (final)	Net Diff or Diff	95% CI	P Btw	Dropout, %	Study Quality
Melzer 2006[270] 17040007	nd	9.0 (3.9)	1 wk (XO)	REM (%)	AOP 75 bpm	19	nd	0	0	nd	0.93	5%	A
					AOP 45 bpm	19	nd	0					
				Slow wave sleep (%)	AOP 75 bpm	19	nd	14	-3.8	-46.0, 38.4 *	0.86		
					AOP 45 bpm	19	nd	13					

* Estimated from reported P value.

Table 5.25.1. Positive airway pressure devices, reported major adverse events * †

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Robinson, 2009[259] 19643262	CPAP	2-4 mo	73	Claustrophobia	1	1.4%
Hukins, 2004[183] 15683142	CPAP	2 mo	55	Pressure intolerance	5	9.2%
	AutoCPAP				2	3.6%
Salgado, 2008[207] 18982206	AutoCPAP, humidified	4 wk	17	Epistaxis	0	0
	AutoCPAP, nonhumidified		22		2	9.1%
Khanna, 2003[173] 14592306	Nasal CPAP	1 mo	17	Excessive nasal dryness	2	12%
			17	Epistaxis	2	12%
		2 mo	15	Excessive pressure	2	13%
			13	Severe claustrophobia	3	23%
	Oral CPAP	1 mo	21	Excessive oral dryness	11	52%
			21	Severe gum pain	3	14%
			21	Excessive pressure	4	19%
Nussbaumer, 2006[179] 16537862	AutoCPAP	1 mo	34	Claustrophobia	1	2.9%
Anderson, 2003[171] 14572126	Nasal CPAP	1 mo	21	Claustrophobia	1	4.8%
	Oral CPAP	1 mo	21	Dry mouthr/throat (major problem)	3	14%
				Excess salivation (major problem)	1	4.8%
				Sore gums/lips (major problem)	2	9.5%

* Reporting of no events excluded (unless N≥100), except Salgado 2008 because the direct comparison between humidified and nonhumidified CPAP was reported.
† Other adverse events (or side effects or harms) reported by studies included: skin irritation, nasal irritation or obstruction, dry nose or mouth, excess salivation, minor or moderate sore gums or lips, minor aerophagia, abdominal distension, minor chest wall discomfort, pressure discomfort, and transient or minor epistaxis.

Table 5.25.2. Mandibular advancement devices, reported major adverse events * †

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Engleman, 2002[225] 12231497	Custom-made (80% maximal comfortable mandibular protrusion, 2-4 mm interdental clearance)	8 wk	48	Dental crown damaged	3	6.3%
Walker-Engstrom 2002[262] 11888954	Custom-made (50% maximal mandibular advancement, 5 mm vertical opening)	4 yr	45	Tooth malocclusion and TMJ pain	1	2.2%
				Aphthous ulcer due to acrylic polymer allergy	1	2.2%
Petri, 2008[212] 18482111	Custom-made (maximal comfortable mandibular advancement, 5 mm vertical opening)	4 wk	31	Teeth loosening	1	3.2%
				TMJ pain	1	3.2%
Ferguson 1996[226] 8625679	Snore-Guard (mandible 3 mm posterior to maximal acceptable advance, 7 mm opening)	4 mo	25	Moderate to severe jaw discomfort	1	4.0%
Johnston, 2002[216] 12143089	Custom-made (75% maximal comfortable mandibular protrusion, 4 mm interincisal clearance)	4-6 wk	19	Persistent daytime TMJ discomfort	1	5.2%

* Reporting of no events excluded (unless N≥100).

† Other adverse events (or side effects or harms) reported by studies included: pressure sensation in the mouth, transient morning mouth and TMJ discomfort or sounds, minor sore teeth or jaw, transient mild mucosal erosions, minor excessive salivation, tooth grinding, and sleep disruption.

Table 5.25.3. Surgical intervention (UPPP primarily), reported major adverse events*†

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Kezirian, 2004[277] 15091217	UPPP ± tonsil, nasal, turbinate surgery	30 days	3130	Death	7	0.2%
				Reintubation	17	0.5%
				Emergency tracheotomy	7	0.2%
				Ventilation >48 hr	6	0.2%
				Pneumonia	11	0.4%
				Cardiovascular complication	8	0.3%
				Hemorrhage	9	0.3%
				Deep vein thrombosis	0	0%
				Kidney failure	0	0%
				Total serious complications (including death)	51	1.6%
Lundkvist 2009[278] 19863325	UPPP (with tonsillectomy)	1 yr	158	Bleeding from tonsillectomy, profuse	2	1.3%
				Laryngeal edema, substantial	2	1.3%
				Long-term sequelae from complications	0	0%
				Death	0	0%
Esclamado 1989[279] 2530406	UPPP ± tonsil, nasal surgery, tracheostomy	24 hr	135	Reintubation (long-term sequelae = 0/135)	7	5.2%
				Death	1	0.7%
				Pulmonary edema	1	0.7%
				Hemorrhage, requiring surgical intervention	3	2.2%
Friedman, 2004[280] 15091218	UPPP	Perioperative	134	Airway complication	0	0%
				Abscess requiring surgical intervention	0	0%
				Rehospitalization	0	0%
Harmon 1989[281] 2916139	UPPP ± nasal, adenoid, tracheostomy	3 mo	126	Oropharyngeal hemorrhage	7	5.5%
				Voice change (rhinolalia)	2	0.6%
				Nasopharyngeal reflux	0	0%
				Pharyngeal infection	0	0%
			132‡	Pneumonia	2	1.5%
				Death	2	1.5%
				Emergency tracheotomy	2	1.5%
				Intubation difficulty and/or pulmonary edema or respiratory arrest	6	4.5%
Haavisto 1994[282] 7923849	UPPP	Postoperative	101	Hemorrhage requiring surgical intervention	5	5.0%
				Tracheostomy	4	4.0%
				Asystole, post-extubation	1	1.0%
				Infection	0	0%
				Arrhythmia	0	0%
		1 yr	91	Nasopharyngeal regurgitation	22	24%
				Difficulty swallowing	9	10%
				Difficulty with speech or change in voice quality	14	15%
				Loss of taste	2	2.2%
				Breathing difficulty	5	5.5%
				Hemorrhage	1	1.1%

Table 5.25.3. Surgical intervention (UPPP primarily), reported major adverse events§ (continued)**

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Anand 1991[255] 1945423	UPPP ± nose, turbinate, tonsil, epiglottis surgery, tracheostomy	16 d – 7.25 yr	66	Velopharyngeal incompetence >1 mo	8	12%
				Voice change, long term	1	1.5%
				Choanal stenosis, unilateral	1	1.5%
				Bleeding, requiring surgical intervention	1	1.5%
				Reintubation	1	1.5%
				Death	1	1.5%
				Nasal synechiae	2	3.0%
				Tracheal stenosis	1	1.5%
Walker-Engstrom 2002[262] 11888954	UPPP	4 yr	40	Nasopharyngeal regurgitation of fluids (pronounced)	3	8%
				Difficulty swallowing (pronounced)	4	10%
Ferguson, 2003[245] 12502473	LAUP	nd	21	Swallowing difficulty, persistent, moderate	1	4.8%
				Bleeding, requiring medical attention	1	4.8%
Lojander, 1996[124] 8681614	UPPP ± osteotomy	12 mo	18	Tracheotomy x 1 mo	1	5.6%
				Infection, requiring surgical intervention	2	11%
				Velopharyngeal incompetence	2	11%

* Reporting of no events excluded (unless N≥100).
† Other adverse events (or side effects or harms) reported by studies included: unplanned medications, mild transient pain and swallowing difficulty, postoperative (minor) hematomas or ulcerations, mild bleeding, mild and transient tongue deviation, transient swelling sensation, pharyngeal dryness, nasal regurgitation (transient), increased mucus secretion, gagging, cough, infection (self-limited), antibiotic-related diarrhea, burning sensation, anosmia, temporary vocal quality change, and difficulty singing, playing saxophone, etc.
‡ Including patients who received tracheostomy, tonsillectomy, and/or septoplasty without UPPP.
§ Reporting of no events excluded (unless N≥100).
** Other adverse events (or side effects or harms) reported by studies included: unplanned medications, mild transient pain and swallowing difficulty, postoperative (minor) hematomas or ulcerations, mild bleeding, mild and transient tongue deviation, transient swelling sensation, pharyngeal dryness, nasal regurgitation (transient), increased mucus secretion, gagging, cough, infection (self-limited), antibiotic-related diarrhea, burning sensation, anosmia, temporary vocal quality change, and difficulty singing, playing saxophone, etc.

Table 5.25.4. Radiofrequency ablation, reported major adverse events * †

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Stuck 2003 ‡[283] 12797590	RFVTR, tongue base or soft palate or turbinates or combination ± other oropharyngeal, nasal, hyoid surgery	3-8 days	497	Tongue base ulceration, requiring surgical intervention	3	0.6%
				Soft palate mucosa ulceration, requiring surgical intervention	1	0.2%
				Dysphagia requiring hospitalization	4	0.8%
				Hypoglossal nerve palsy, temporary	1	0.2%
				Tongue base abscess, requiring surgical intervention	1	0.2%
		>8 days	422	Long-term complications	0	0%
Woodson, 2001[252] 11593163	RFVTR, tongue base	6 wk	73	Severe, suppurative tongue base infection (2 required surgical intervention, 2 drained spontaneously)	4	5.5%
				Tongue abscess	1	1.4%
				Infection or cellulitis	7	9.6%

* Reporting of no events excluded (unless N≥100).
† Other adverse events (or side effects or harms) reported by studies included: unplanned medications, mild transient pain and swallowing difficulty, postoperative (minor) hematomas or ulcerations, mild and transient tongue deviation, transient swelling sensation, and asymptomatic fibrotic narrowing.
‡ Complication rate decreased over time, 1999-2002.

Table 5.25.5. Combination or various surgeries, reported major adverse events * †

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Riley, 1993[284] 8441535	UPPP + MO/GAHM ‡	Postoperative	233	Bleeding requiring anesthesia	3	1.3%
		9 mo		Long-term speech or swallowing problem	0	0%
Riley, 1997[285] 9419093	UPPP + GA + HS § UPPP ± GA ± HS ± MMO	3-7 days	182 **	Bleeding (not described)	4	1.9%
				New onset atrial fibrillation	4	1.9%
				New unstable angina	1	0.5%
				Death	0	0%
Friedman, 2004[280] 15091218	UPPP + Tongue RFA	Perioperative	143	Hypoglossal nerve paralysis	1	0.7%
				Nerve paralysis (transient)	2	1.4%
				Airway complication	0	0%
				Abscess requiring surgical intervention	0	0%
				Rehospitalization	0	0%
Friedman, 2007[286] 17713449	3-level: Tongue RF, Pillar implants, partial uvulectomy, nasal, turbinate surgery	nd	122	Major complication	0	0%
				Nasal septum perforation, tongue mucosal ulceration, & hypoglossal nerve weakness <1 month	1	0.8%
				Turbinate bone exposure	2	1.6%
				Pillar extrusion requiring removal and replacement	5	4.1%
Benazzo, 2008[287] 18568505	HS + nasal, turbinate, palate surgery	6 mo	109	"Major complication"	0	0%
Robinson, 2009[259] 19643262	Stepwise UPPP, GA, TAP, HS, Tongue RFA	nd	64	Paresthesia	11	17%
				Dysphagia	7	11%
				Voice change	2	3.1%
				Taste alteration	1	1.6%
				Wound dehiscence	1	1.6%
				Infection	2	3.1%
				Palatal fistula (transient)	1	1.6%

* Reporting of no events excluded (unless N≥100).
† Other adverse events (or side effects or harms) reported by studies included: aspiration, neck seroma, transient dysphagia, transient tongue base ulceration, suture removal for foreign body reaction, and transient facial anesthesia.
‡ Small number with only UPPP or only MO/GAHM.
§ Mostly
** 210 procedures in 182 patients

Table 5.25.6. Surgical implant, reported major adverse events*

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Steward, 2008[243] 18922335	Pillar implant	1 wk	50	Infection	1	2%
				Extrusion	2	4%

* Reporting of no events excluded (unless N≥100). Other reported adverse events included sore throat and foreign body sensation.

Table 5.25.7. Bariatric surgery, reported major adverse events*

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Grunstein, 2007[272] 17580591	Vertical banded gastroplasty (72%) Gastric banding (20%) Gastric bypass (8%)	Perioperative	1592	Perioperative mortality	~3	0.21%
				Bleeding, embolus and/or thrombosis, wound complications, deep infections, pulmonary, and other complications	~207	13.0%

* Reporting of no events excluded (unless N≥100).

Table 5.25.8. Weight loss diet, reported major adverse events*

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Johansson, 2009[237] 19959590	Liquid, very low energy diet	9 wk	30	Elevated alanine aminotransferase concentration (transient)	2	6.7%
				Gout (transient)	1	3.3%

* Reporting of no events excluded (unless N≥100). Other reported adverse events included dizziness, dry lips, and constipation.

Table 5.25.9. Drugs, reported major adverse events*

Study PMID	Intervention details	Followup duration	No. Analyzed	Adverse event	n	%
Bradshaw, 2006[288] 17099012	Zolpidem	4 wk	72	Sleep walking	1	1.4%
Kraiczi, 1999[266] 9989366	Paroxetine †	6 wk	20	Ejaculation disturbance	3	15%
				Decreased libido	2	10%
				Headache	1	5%
				Constipation	1	5%
Whyte, 1988[267] 3067313	Protriptyline	2 wk	10	Severe dry mouth requiring discontinuation	2	20%
				Visual upset	1	10%
				Urinary symptoms	1	10%
				Altered sexual potency & testicular discomfort	1	10%
	Acetazolamide	2 wk	10	Paresthesia, intolerable	1	10%
				Paresthesia, any	8	80%

* Reporting of no events excluded (unless N≥100).
† Other reported adverse events included, fatigue, mouth dryness, somnolence, and dizziness (with both paroxetine and placebo); and sweating, nervousness, infectious pneumonia and Lyme disease (during paroxetine treatment).

Table 6.1a. Predictors of compliance with CPAP: study characteristics

Study PMID	Design Country (study years)	eligibility	N	Factor	Value	Treatment	CPAP Pressure [A] (type)	Ancillary care	(Lack of) Compliance definition
McArdle 1999[289] 10194153	Prosp Scotland, UK (1986-97)	Starting CPAP	1103	**Male** **Age** **BMI** **AHI**	86% 50 [C] yr 30 [C] 50 (18-53) [D]	CPAP various	Manual (separate)	2 weeks with nurse specialist [B]	<2 hr/night x 1 mo or voluntarily discontinued
Krieger 1996[290] 9122571	Prosp France (1984-95)	Starting CPAP	608	**Male** **Age** **BMI** **AHI**	nd 54 yr 31.9 70	CPAP	nd (separate)	Questionnaire: If use <3 hr/night then f/up	<1 hr/night
Pepin 2009[203] 19567496	Prosp (RCT) France (nd)	Starting CPAP	218	**Male** **Age** **BMI** **AHI**	72% 56 yr 31 44	C-Flex vs. CPAP	Auto (separate)	nd	"Objective compliance" not defined (measured by CPAP)
Wild 2004[291] 15358707	Prosp Scotland, UK (nd)	Starting CPAP	119	**Male** **Age** **BMI** **AHI**	79% 51 yr 33 45	CPAP	nd (separate)	Pretitration training Support x2 wk	Adherence = >3 hr/night
Hui 2001[292] 11451834	Prosp Hong Kong (1997-98)	Starting CPAP	112	**Male** **Age** **BMI** **AHI**	90% 46 yr 29.3 48	AutoCPAP	Auto (separate)	Initial education, brochure & training session	hr/night (continuous)

[A] Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, eg if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

[B] 2 weeks contact with nurse specialist. At reviews, if objective CPAP use <2 h, confronted with usage data to encourage increase use. If still <2 h at 1 month f/up visit, CPAP machine reclaimed.

[C] Median

[D] Median (interquartile range)

Table 6.1b. Predictors of compliance with CPAP, multivariable analyses

Study PMID	Outcome	Overall outcome rate	Follow-up	Predictor	Baseline predictor	HR/OR	95% CI	P	Quality
McArdle [A] 1999[289] 10194153	Discontinue CPAP	16%	(12 mo)	ESS ≤10 [B]	40%	1.92	1.41-2.61	<0.001	A
		32%	(4 yr)	AHI <15 [C]	nd	2.48	1.79-3.46	<0.001	
			22 mo, mean	Nonsnorer	2%	2.76	1.29-5.95	0.009	
				CPAP use at 3 mo <2 hr	*nd*	*13.8*	*8.86-21.5*	*<0.001*	
				AHI <30	~50%			NS	
				Arousal Index <32	~50%			NS	
				No witnessed apneas	17%			NS	
				No somnolence	19%			NS	
				No driving problem	64%			NS	
				Coexisting COPD	10%			NS	
				Pressure <8 cm H2O	~50%			NS	
				Female	14%			NS	
				Age ≥50 y	~50%			NS	
				BMI ≤30	~50%			NS	
Krieger [D] 1996[290] 9122571	CPAP withdrawn	14%	3.2 yr	AHI ≤15	5%	nd		<0.05	C
				Age (continuous [E])	50	nd		<0.05	
				MSLT (continuous [E])	16.5 min			NS	
				ESS (continuous [E])	8.8			NS	
				Respiratory symptoms (nd)				NS	
Pepin [F] 2009[203] 19567496	"Objective compliance" [G]	5 hr/night	3 mo	Mean SaO2, per %	93%	1.22	1.03-1.45	0.02	C
				GrenobleSAQOL Sleepiness [H], per scale unit	~15	1.13	1.04-1.24	<0.01	
				Age, per 10 y	56 y	0.9	0.54-1.34	NS	
				GrenobleSAQOL Treatment, efficacy [J] per unit (3 mo)	*nd*	*1.16*	*1.02-1.32*	*0.02*	
				Noise (3 mo, not defined)	*nd*	*0.74*	*0.98-1.02 [K]*	*nd*	
				Feel exhalation resistance (3 mo)	*nd*	*1.02*	*1.00-1.04*	*0.1 [L]*	
Wild [M] 2004[291] 15358707	Adherence [G]	nd	3 mo	AHI (continuous [E])	45	1.02	nd	0.02	B
				CPAP Pressure (continuous [E])	9 cm H_2O	0.82	nd	0.05	
				BMI (continuous [E])	33	1.09	nd	0.02	
				ESS (continuous [E])	13	1.09	nd	0.04	
Hui [N] 2001[292] 11451834	hr/night use	5.4 hr/night	1 mo	AHI (continuous [E])	48	nd	nd	0.006	C
				Snoring		nd	nd	NS	
		5.4 hr/night	3 mo	AHI (continuous [E])	48	nd	nd	0.004	
				Snoring		nd	nd	NS	

Predictors measured after baseline are italicized.

[A] Occupation, referral source, collar size, alcohol consumption, smoking status, diagnostic test type, and CPAP titration method were not associated with discontinuing CPAP by univariable analysis.

[B] Also reported that lower ESS (analyzed as a continuous variable) predicted less compliance across the range of ESS.

[C] Also reported that lower AHI (analyzed as a continuous variable) predicted less compliance across the range of AHI.
[D] No data on which tested variables were not associated with CPAP withdrawal by univariable analysis.
[E] Implied.
[F] No data on which tested variables were not associated with "objective compliance" by univariable analysis.
[G] Note that in contrast to most other studies, the outcome is compliance/adherence, not lack of compliance.
[H] Grenoble Sleep Apnea Quality of Life. 25 point scale (implied), with higher scores indicating worse conditions.
[J] This outcome is not defined or included in the list of domains in Grenoble Sleep Apnea Quality of Life. Higher scores indicate worse conditions.
[K] These illogical OR and confidence interval were what was reported. The reported beta and standard error of the beta did not match any of these values.
[L] Although this P value does not match with the reported beta, standard error of the beta, OR, or 95% CI, it is what was reported.
[M] Also analyzed with psychological variables (Multidimensional locus of control scale). Results for AHI, CPAP Pressure, BMI, and ESS were similar. Higher health value scale (measure of how much patient values his/her health) was associated with increased compliance (OR=1.40, P=0.02). Other psychological tests were not significantly associated. Age, alcohol intake, current cigarette use, marital status, and minimum O2 saturation were not associated with adherence by univariable analysis.
[N] Frequent awakenings, witnessed apneas, and other symptoms were not associated with adherence at 1 or 3 months by univariable analyses.

Table 6.2a. Mandibular advancement device as predictors of compliance: Study characteristics

Study PMID	Design Country (study years)	eligibility	N	Factor	Value	Treatment	Description	Ancillary Care	(Lack of) Compliance Definition
Izci 2005[293] 15733510	Retro Scotland, UK (nd)	MAD after PSG	144	**Male** **Age** **BMI** **AHI**	79% 51 yr nd 23	Individually fitted mandibular repositioning splint	~80 maximal comfortable mandibular protrusion 2-4 mm interdental clearance	Standard education Adjusted until workable	Compliance hr/night and/or nights/wk (unclear)

Table 6.2b. Pre-treatment predictors of compliance with mandibular advancement device, univariable analysis*

Study PMID	Outcome	Overall Outcome Rate	Follow-up	Predictor	Quality
Izci, 2005[293] 15733510	Compliance	nd	31 mo	Not associated with compliance on univariable analysis (nd): Age, Sex, Occupation, "Marital situation", Snoring, Refreshment after sleep, Daytime somnolence, Driving problems, ESS, AHI, CPAP failure or refusal	C

* No studies performed multivariable analyses.

Table 7.1. Randomized controlled trials of interventions to improve compliance with CPAP use: study characteristics

Study PMID	Interventions	CPAP Pressure* (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Extra Support or Education								
Chervin 1997[294] 9231954	Telephone calls Literature Standard care	nd (nd)	52	64	nd	Either new to CPAP (31%) or continuous CPAP users (69%)	US (1995)	Different follow-up durations between comparative groups.
Damjanovic 2009[174] 19129293	Intensive support Standard support	Auto and manual (separate)	57	78	31	Newly diagnosed OSA	Germany (nd)	Large dropout rate. Assumed non-compliance for dropout patients.
Fletcher, 1991[296] 2024846	Telephone reinforcement about OSA and CPAP use Usual care	Manual (separate)	52	100	Mean IBW = 158%	New CPAP users	US (nd)	Inconsistent reporting; primarily relying on self-reported readings for CPAP use
Hoy 1999[297] 10194151	Intensive educational programs and nursing support Usual care	Manual (separate)	58	98	33	New CPAP users	UK (nd)	
Hui 2000[298] 10807830	Augmented education and support Basic education and support	Auto (separate)	45	90	30	Newly diagnosed OSA	Hong Kong (nd)	More missing data on objective CPAP use in the intervention group than the control group due to technical problems.
Wiese 2005[299] 15716221	Educational videotape No intervention	nd (nd)	48	53	38	Newly diagnosed OSA	US (nd)	More dropouts in the control group than intervention group. Assumed non-compliance for dropout patients.
Lewis 2006[300] 16564210	Extra early support Usual care	Auto (separate?)	51	86	36	New CPAP users	UK (nd)	More dropouts in the control group than intervention group.
Meurice 2007[301] 17157557	RP+RH RP+SH SP+RH SP+SH	Manual (separate)	58	nd	33	New CPAP users	France (nd)	Potential center effects were not controlled fro in the analyses.
Smith 2009[303] 18829212	Habit-promoting experimental audio intervention: CPAP everyday Placebo control audio-based intervention	Auto (nd)	63	58	82% >30	Newly diagnosed OSA and new CPAP users	US (nd)	Assumed non-compliance for dropout patients.

Table 7.1. Randomized controlled trials of interventions to improve compliance with CPAP use: study characteristics (continued)

Study PMID	Interventions	CPAP Pressure † (type)	Mean Age, yr	Male, %	Mean BMI, kg/m^2	Other Patient Characteristics	Country (enrollment years)	Major quality issues
Telehealth or telemonitoring care								
DeMolles 2004[295] 15258478	Telephone-linked communications for CPAP Usual care	nd (nd)	46	nd	38	New CPAP users	US (nd)	How CPAP use data were collected was not described. "Usual care" was not described.
Stepnowsky 2007[304] 17513285	Wireless telemonitoring clinical care Usual care	Auto (nd)	59	98	32	Newly diagnosed OSA and new CPAP users	US (2004-06)	Small sample size
Taylor 2006[305] 16565867	Telemedicine support Usual care	nd (nd)	45	69	nd	New CPAP users	US (2002-03)	Patients who had difficulties to use telemedicine support were excluded from the analyses.
Behavioral interventions								
Richards 2007[302] 17552379	Cognitive behavioral therapy Usual care	Manual (nd)	56	86	30	nd	Australia (2005)	
Miscellaneous interventions								
Bradshaw 2006[288] 17099012	Oral hypnotic agent (zolpidem), 10 mg Placebo pill Standard care (no zolpidem or placebo pill)	nd (both)	38	100	32	New CPAP users	US (2001-03)	Patients in the standard care had more severe OSA based on AHI; not blinded.
Massie 2003[306] 12684301	Nasal pillows Nasal mask	Manual (both)	49	82	36	New CPAP users	US (nd)	
Different care models								
Antic 2009[307] 19136368	Simplified nurse-led model of care Usual care	Auto and manual (separate) manual (nd)	50	74	35	nd	Australia (2004-06)	Different CPAP titrations between groups by study design
Holmdahl 2009[308] 19179111	Simplified nurse-led model of care Usual care	Manual (nd)	58	85	35	CPAP-treated patients with OSAS in a stable condition	Sweden (nd)	More patients dropped out in the control group. How CPAP use data were collected was not reported.
Palmer 2004[309] 14725828	A home visit from a specialist nurse A visit to a consultant led clinic	nd (nd)	55	86	nd	The mean duration of CPAP therapy = 2.99 yr	UK (2001)	Baseline patient characteristics were unclear. Dropout and unusable CPAP use data were excluded form the analyses.

* Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).
† Method for choosing CPAP Pressure: Manual (during sleep study); Auto (determined with AutoCPAP); Algorithm (by an algorithm); nd (no data reported); NA (not applicable, e.g. if AutoCPAP is the intervention). In parentheses: Split (CPAP introduced in a split night study); Separate (CPAP introduced on a separate full night than the diagnostic sleep study).

Table 7.2. Compliance (hr/night) in randomized controlled trials of interventions to improve CPAP use

Study PMID	Baseline AHI (SD) [minimum]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Final	SD	Diff	95% CI	P Btw	Dropout, %	Study Quality
Extra Support or Education												
Hoy 1999[297] 10194151	58 (33) [>15]	13 (6)	6 mo (PL)	Intensive support	40	5.4	1.9	+1.6	0.62, 2.58 *	0.003	0	A
				Usual care	40	3.8	2.5					
Meurice 2007[301] 17157557	58 (24) [>30]	11.3 (5.4)	3 mo (PL)	RP+RH	27	5.6	2.4	+0.9	-0.38, 2.18 †	NS	16	B
				RP+SH	30	4.7	2.2	0	-1.20, 1.20 ‡			
				SP+RH	28	5.1	2.5	+0.4	-0.90, 1.70 §			
				SP+SH	27	4.7	2.4					
			12 mo (PL)	RP+RH	23	5.8	2.8	+0.3	-1.16, 1.76	NS	19	
				RP+SH	22	6.3	2.2	+0.8	-0.49, 2.09			
				SP+RH	21	5.7	2.2	+0.2	-1.09, 1.49			
				SP+SH	25	5.5	2.4					
Damjanovic 2009[174] 19129293	44 (25) [≥15]	8.8 (5.2)	3 mo (PL)	Intensive support	50	5.5	1.4	+0.1	-0.61, 0.81 **	NS	0 ††	B
				Standard support	50	5.4	2.1					
			9 mo (PL)	Intensive support	50	5.7	1.4	+1.1	0.22, 1.98 ‡‡	<0.05		
				Standard support	50	4.6	2.8					
Hui 2000[298] 10807830	48 (24) [≥10]	12.5 (5.1)	3 mo (PL)	Augmented support	45	5.3	0.3	0	-0.7, 0.7 §§	NS	10	B
				Basic support	52	5.3	0.2					
Lewis 2006[300] 16564210	42 (27) [nd]	15.7 (4.3)	1 mo (PL)	Extra early support	36	5.2	nd	-0.2	nd	nd	6	C
				Usual care	32	5.4	nd					
			12 mo (PL)	Extra early support	30	4.6	nd	-0.5	nd	nd	17	
				Usual care	30	5.1	nd					
Chervin 1997[294] 9231954	49 (39) [nd]	10.9 (5.1)	1-2.5 mo (PL)	Telephone calls	12	5.7	2.3	+1.3	-1.45, 4.05 ***	0.02	18	C
				Literature	14	7.1	1.8	+2.7	0.35, 5.05 †††			
				Standard care	7	4.4	3.4					
Fletcher, 1991[296] 2024846	49 (26) [nd]	nd	3 mo (XO)	Telephone reinforcement	10	5.95	2.7	-0.05	-1.76, 1.66 ‡‡‡	NS	0	C
				Usual care	10	6.0	2.8					

Table 7.2. Compliance (hr/night) in randomized controlled trials of interventions to improve CPAP use (continued)

Study PMID	Baseline AHI (SD) [minimum]	Baseline ESS (SD)	Duration (design)	Interventions	No. Analyzed	Final	SD	Diff	95% CI	P Btw	Dropout, %	Study Quality
Telehealth or telemonitoring care												
Stepnowsky 2007[304] 17513285	41 (16) [≥15]	12.6 (5.5)	2 mo (PL)	Wireless telemonitoring	20	4.1	1.8	+1.3	-0.05, 2.5 §§§	0.07	12	B
				Usual care	20	2.8	2.2					
Taylor 2006[305] 16565867	41% severe OSA [>4]	14 (4)	30 d (PL)	Telemedicine support	47	4.3	2.2	+0.07	-0.77, 0.91 ****	NS	16	C
				Usual care	49	4.2	2.1					
DeMolles 2004[295] 15258478	42 (38) [nd]	nd	2 mo (PL)	Telephone-linked CPAP communication	15	4.4	3.0	+1.5	-0.53, 3.53 ††††	0.08	0	C
				Usual care	15	2.9	2.4					
Behavioral interventions												
Richards 2007[302] 17552379	26 (22) [>5]	10.5 (5.3)	28 days (PL)	Cognitive behavioral therapy	48	5.4	2.6	+2.8	1.8, 3.9 ‡‡‡‡	<0.0001	4	A
				Usual care	48	2.5	2.7					
Miscellaneous interventions												
Bradshaw 2006[288] 17099012	43 (28) [≥5]	15.4 (3.5)	Days 1-14 (PL)	Zolpidem 10 mg	24	11.1	3.7	+1.6 §§§§	-0.83, 4.03 *****	NS	0	B
				Placebo pill	24	9.5	4.6					
				Standard care †††††	24	12.1	3.2					
			Days 15-28 (PL)	Zolpidem 10 mg	24	9.5	4.6	+1.2 ‡‡‡‡‡	-1.65, 4.05 §§§§§	NS		
				Placebo pill	24	8.3	5.2					
				Standard care ******	24	10.8	3.9					
Massie 2003[306] 12684301	47 (35) [≥15]	12.8 (4.9)	3 wk (XO)	Nasal pillows	39	5.6	1.3	+0.2	-3.8, 4.2 ‡‡‡‡‡‡	NS	7	B
				Nasal mask	39	5.4	1.6					
Different care models												
Antic 2009[307] 19136368	68 (27)	13 (3.9)	3 mo	Simplified nurse-led model of care	94	4.1	2.7	-0.45	-1.26, 0.36	NS	10	B
				Usual care	83	4.6	2.7					
Palmer 2004[309] 14725828	nd [nd]	8.5 (5.5)	12 mo	One home visit by special nurse	63	5.9	2.7	+0.21	-0.40, 0.82 §§§§§§	NS	28	C
				One consultant clinic visit	63	5.6	2.5					

* Estimated from reported SE's
† Estimated from reported SD's
‡ Estimated from reported SD's
§ Estimated from reported SD's
** Estimated from reported SE's
†† Compliance parameters were set to zero when patients did not appear for their follow-up visit (8% and 22% dropout at 3 and 9 mo, respectively)
‡‡ Estimated from reported SE's
§§ Estimated from reported SE's
*** Estimated from reported SD's
††† Estimated from reported SD's
‡‡‡ Estimated from reported SD's
§§§ Estimated from reported SD's
**** Estimated from reported SD's
†††† Estimated from reported SD's
‡‡‡‡ Estimated from reported SD's
§§§§ Compared to placebo
***** Estimated from reported SD's
††††† Patients in the standard care had more severe OSA based on AHI [mean = 54.8 (28 SD), P=0.012 compared to other groups]
‡‡‡‡‡ Compared to placebo
§§§§§ Estimated from reported SD's
****** Patients in the standard care had more severe OSA based on AHI [mean = 54.8 (28 SD), P=0.012 compared to other groups]
†††††† Estimated from reported SD's
‡‡‡‡‡‡ Estimated from reported changes (SD) from baseline

Table 7.3. Non-compliance outcome in randomized controlled trials of interventions to improve CPAP use

Study PMID	Baseline AHI (SD) [minimum]	Baseline ESS (SD)	Duration (design)	Definition of non-compliance	Interventions	n Event	N Total	Outcome metric	Result *	95% CI †	P Btw	Dropout, %	Study Quality
Extra Support or Education													
Hui 2000[298] 10807830	48 (24) [≥10]	12.5 (5.1)	3 mo (PL)	Mean CPAP use ≤4 hr and ≤70% of nights	Augmented support	16	54	RD	-0.04	-0.13, 0.21	NS	10	B
					Basic support	14	54						
Smith 2009[303] 18829212	50 (nd) [≥20]	nd	1 mo (PL)	CPAP use <4 hr/night and less than 80% use rate	Habit-promoting experimental audio intervention	6	55	RD	-0.34	-0.52, -0.17	<0.01	0 ‡	B
					Placebo control audio-intervention	19	42						
			6 mo (PL)	CPAP use <4 hr/night and less than 80% use rate	Habit-promoting experimental audio intervention	14	55	RD	-0.03	-0.21, 0.15	NS		
					Placebo	12	42						
Wiese 2005[299] 15716221	9 (nd) [>4]	13 (6)	1 mo (PL)	Not return to clinic at 4 weeks	Educational videotape	14	51	RD	-0.24	-0.42, -0.05	0.02	39 §	C
					No intervention	25	49						
Behavioral interventions													
Richards 2007[302] 17552379	26 (22) [>5]	10.5 (5.3)	28 d (PL)	CPAP use <4 hr/night at 28 days	Cognitive behavioral therapy	9	48	Adjusted OR **	0.14	0.05, 0.36	<0.0001	4	A
					Usual care	33	48						

Table 7.3. Non-compliance outcome in randomized controlled trials of interventions to improve CPAP use (continued)

Study PMID	Baseline AHI (SD) [minimum]	Baseline ESS (SD)	Duration (design)	Definition of non-compliance	Interventions	n Event	N Total	Outcome metric	Result [††]	95% CI [‡‡]	P Btw	Dropout, %	Study Quality
Miscellaneous interventions													
Bradshaw 2006[288] 17099012	43 (27) [≥5]	15.4 (3.5)	4 wk (PL)	Mean CPAP use ≤4 hr	Zolpidem 10 mg	7	24	RD	-0.17 [§§]	-0.44, 0.10	NS	0	B
					Placebo pill	11	24						
					Standard care [***]	7	24						
			4 wk (PL)	Receiving CPAP ≤70% of nights	Zolpidem 10 mg	8	24	RD	-0.13 [†††]	-0.40, 0.15	NS		
					Placebo pill	11	24						
					Standard care [‡‡‡]	4	24						
			4 wk (PL)	Mean CPAP use ≤4 hr and ≤70% of nights	Zolpidem 10 mg	10	24	RD	-0.08 [§§§]	-0.36, 0.20	NS		
					Placebo pill	12	24						
					Standard care [****]	9	24						
Different care models													
Holmdahl 2009[308] 19179111	nd [>15]	nd	2 yr (PL)	<6 hr CPAP use per night	Simplified nurse-led model of care	23	95	RD	-0.02	-0.14, 0.11	NS	16	C
					Usual care	23	89						
			2 yr (PL)	<4 hr CPAP use per night	Simplified nurse-led model of care	5	95	RD	-0.02	-0.08, 0.05	NS		
					Usual care	6	89						

[*] Top row intervention vs. bottom row intervention.
[†] Estimated from the reported number of events and total number of patients, unless otherwise noted.
[‡] ITT analysis: all dropouts due to lost to contact were also counted as non-adherent patients
[§] Lost-to follow-up rate were used as measure of non-compliance
[**] Adjusted for sex
[††] Top row intervention vs. bottom row intervention.
[‡‡] Estimated from the reported number of events and total number of patients, unless otherwise noted.
[§§] Compared to placebo pill
[***] Patients in the standard care had more severe OSA based on AHI [mean = 54.8 (28 SD), P=0.012 compared to other groups]
[†††] Compared to placebo pill
[‡‡‡] Patients in the standard care had more severe OSA based on AHI [mean = 54.8 (28 SD), P=0.012 compared to other groups]

§§§ Compared to placebo pill
**** Patients in the standard care had more severe OSA based on AHI [mean = 54.8 (28 SD), P=0.012 compared to other groups]