ACP Clinical Practice® American College of Physicians GUIDELINES

CLINICAL GUIDELINE

Management of Obstructive Sleep Apnea in Adults: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Jon-Erik C. Holty, MD, MS; Douglas K. Owens, MD, MS; Paul Dallas, MD; Melissa Starkey, PhD; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians*

Description: The American College of Physicians (ACP) developed this guideline to present the evidence and provide clinical recommendations on the management of obstructive sleep apnea (OSA) in adults.

Methods: This guideline is based on published literature from 1966 to September 2010 that was identified by using MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews. A supplemental MEDLINE search identified additional articles through October 2012. Searches were limited to English-language publications. The clinical outcomes evaluated for this guideline included cardiovascular disease (such as heart failure, hypertension, stroke, and myocardial infarction), type 2 diabetes, death, sleep study measures (such as the Apnea–Hypopnea Index), measures of cardiovascular status (such as blood pressure), measures of diabetes status (such as hemoglobin A_{1c} levels), and quality of life. This guideline grades the evidence and recommendations using ACP's clinical practice guidelines grading system.

Recommendation 1: ACP recommends that all overweight and obese patients diagnosed with OSA should be encouraged to lose weight. (Grade: strong recommendation; low-quality evidence)

Recommendation 2: ACP recommends continuous positive airway pressure treatment as initial therapy for patients diagnosed with OSA. (Grade: strong recommendation; moderate-quality evidence)

Recommendation 3: ACP recommends mandibular advancement devices as an alternative therapy to continuous positive airway pressure treatment for patients diagnosed with OSA who prefer mandibular advancement devices or for those with adverse effects associated with continuous positive airway pressure treatment. (Grade: weak recommendation; low-quality evidence)

Ann Intern Med. 2013;159. www.annals.org

For author affiliations, see end of text.

This article was published at www.annals.org on 24 September 2013.

Obstructive sleep apnea (OSA) is a common disorder that affects persons in all age groups, especially middle-aged and elderly persons (**Table 1**). Evidence shows that OSA rates are increasing, and this is probably because of escalating obesity rates (1). The goal of OSA treatment is to alleviate airway obstruction during sleep. The standard first-line OSA treatment involves continuous positive airway pressure (CPAP) devices, which deliver compressed air into the airway to keep it open. Many patients do not tolerate CPAP and often do not adhere to the instructions for many reasons, including discomfort, skin irritation, noise, and claustrophobia (2–4). To improve adherence, many technological modifications have been made to CPAP devices (mostly in alterations of when air pressure is delivered), although the utility of the modified devices is unknown. Because adherence is often an issue in OSA treatment, additional patient education or interventions may be warranted. Dental or mandibular advancement devices (MADs) that are worn while the patient is sleeping have been used to treat OSA. Alternative therapeutic strategies include surgical interventions to remove obstructive tissue, positional therapy, pharmacologic treatment, and weight-loss interventions for obese patients.

All interventions have the potential for adverse effects, and the purpose of this American College of Physicians (ACP) guideline is to present information on both the benefits and harms of interventions to assess the net benefits of available treatments. The target audience for this guideline includes all clinicians, and the target patient population comprises all adults with OSA.

METHODS

This guideline is based on a systematic evidence review sponsored by the Agency for Healthcare Research and

See also:

Web-Only
CME quiz

* This paper, written by Amir Qaseem, MD, PhD, MHA; Jon-Erik C. Holty, MD, MS; Douglas K. Owens, MD, MS; Paul Dallas, MD; Melissa Starkey, PhD; and Paul Shekelle, MD, PhD, was developed for the Clinical Guidelines Committee of the American College of Physicians. Individuals who served on the Clinical Guidelines Committee from initiation of the project until its approval were Paul Shekelle, MD, PhD (*Chair*); Roger Chou, MD; Molly Cooke, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forciea, MD; Robert H. Hopkins Jr., MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Douglas K. Owens, MD, MS; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; David S. Weinberg, MD, MSc; and Timothy Wilt, MD, MPH. Approved by the ACP Board of Regents on 17 November 2012.

Table 1. Terms and Definitions Related to OSA

Term	Definition
Apnea	Complete airflow cessation during sleep
Hypopnea	Reduced airflow during sleep
AHI	A measure of the number of apnea and hypopnea episodes per hour of monitored sleep. According to the American Academy of Sleep Medicine, an OSA diagnosis is defined by ≥15 events/h (with or without OSA symptoms) or ≥5 events/h with OSA symptoms. Severity of OSA classified according to AHI is defined as mild if 5–14 events/h, moderate if 15–30 events/h, and severe if >30 events/h.
ESS	A self-administered questionnaire in which patients rate their chances of dozing in various situations.
Arousal index	The frequency of arousals per hour of sleep, measured by electroencephalography.

AHI = Apnea–Hypopnea Index; ESS = Epworth Sleepiness Scale; OSA = obstructive sleep apnea.

Quality (AHRQ) (5) that addressed the following key questions related to OSA management:

1. What is the comparative effect of different treatments for OSA in adults?

a. Does the comparative effectiveness of treatments vary based on presenting patient characteristics, OSA severity, or other pretreatment factors? Are any of these characteristics or factors predictive of treatment success?

i. Characteristics: Age, sex, race, weight, bed partner, airway, other physical characteristics, and specific comorbid conditions.

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

iii. Other: Specific symptoms.

2. In patients with OSA who are prescribed nonsurgical treatments, what are the associations of pretreatment, patient-level characteristics with treatment adherence?

3. What is the effect of interventions to improve adherence to device use (positive airway pressure, oral appliances, and positional therapy) on clinical and intermediate outcomes?

The Tufts Evidence-based Practice Center conducted the systematic evidence review. The literature search included studies identified using MEDLINE (1966 to September 2010), the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews and included peer-reviewed studies on adult human patients published in English (6). Further details about the methods and inclusion and exclusion criteria applied in the evidence review are available in the full AHRQ report (5). No randomized, controlled trial (RCT) on OSA treatment with regard to mortality outcomes was identified. The ACP supplemented the AHRQ review (MEDLINE search, 1946 to October 2012) to identify English-language observational studies in humans reporting death or cardiovascular or cerebrovascular illness associated with OSA treatment strategies (that is, CPAP, surgery, or MADs), as well as more recent relevant RCTs. To guide our recommendations, we prioritized outcomes on the basis of clinical importance, starting with death and including cardiovascular outcomes. In the absence of statistically significant effects on clinical outcomes, we considered symptoms (such as Epworth Sleepiness Scale [ESS] scores) and other physiologic measures (such as the Apnea–Hypopnea Index [AHI]). This guideline rates the evidence and recommendations using ACP's grading system, which is based on the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system (**Table 2**). Details of ACP's guideline development process can be found in the methods paper (7).

Comparative Effectiveness of OSA Treatments

Evidence on the comparative effectiveness of OSA treatments is summarized in the **Appendix Table** (available at www.annals.org).

CPAP for OSA Treatment

Although moderate-quality evidence showed that CPAP improves sleep measures compared with control or sham devices in patients with at least moderate OSA (AHI score ≥15 events/h), there was little or no evidence on the effects of CPAP on other important clinical outcomes.

CPAP Versus Control Treatment

Twenty-two studies (reported in 23 articles) compared CPAP with control treatment, including patients with mean baseline AHI scores between 10 and 65 events per hour. These studies apply to many patients with OSA, and follow-up ranged from 1 to 24 months. Moderate-quality evidence showed that CPAP reduced AHI scores, improved ESS scores, reduced arousal index scores, and raised the minimum oxygen saturation compared with control

Table 2. The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) workgroup.

treatment (**Appendix Table**). Ten studies assessed the effect of CPAP on quality of life; however, they could not be compared because of the use of various quality-of-life subscales (8–17). Most studies found no statistically significant improvement with CPAP; however, some showed improvement in physical and vitality scales of the Short Form-36 Health Survey. Eight studies (9–11, 13, 15–18) evaluated neurocognitive and psychological test results, and most showed no improvement. None of the 7 studies (9, 10, 19–23) that addressed blood pressure differences or the 1 study (20) that assessed hemoglobin A_{1c} level differences found any statistically significant differences between CPAP and control treatment. A recent RCT in patients with OSA who did not have daytime sleepiness (24) showed no statistically significant difference in the incidence of hypertension or cardiovascular events for patients treated with CPAP compared with control treatment (incidence density ratio, 0.83 [95% CI, 0.63 to 1.1]; $P = 0.20$). Another RCT treated patients with acute stroke and OSA (AHI scores >10 events/h) with either CPAP or standard of care (25). Authors reported a statistically significant improvement in National Institutes of Health Stroke Scale scores at day 8 between patients randomly assigned to CPAP who were excellent users (CPAP device use >4 h for the first night and mean use >4 h/night for the first 3 nights; National Institutes of Health Stroke Scale score of 2.3 in 10 excellent CPAP users out of 25 total CPAP users) compared with those randomly assigned to standard of care (National Institutes of Health Stroke Scale score of 1.4 in 25 patients) ($P = 0.022$). Only 1 study examined a clinical outcome and found no statistically significant improvement of heart failure symptoms with CPAP compared with no specific treatment (8).

The literature review identified no RCTs evaluating the effect of CPAP on mortality rates. The ACP's supplemental search also identified no long-term RCT of CPAP in the general OSA population but did identify 1 recent trial that randomly assigned patients with OSA who previously had a stroke to CPAP treatment versus conservative therapy; however, no statistically significant improvement in cardiovascular mortality rates was reported at 24 months (0% vs. 4.3%; $P = 0.161$) (26). Five out of 8 identified observational studies of CPAP in general OSA populations reported statistically significant reductions in overall mortality rates associated with CPAP (or CPAP adherence) compared with no CPAP (or CPAP nonadherence) (27–35). Four out of 6 observational studies reported statistically significant reductions in cardiovascular mortality rates associated with CPAP (or CPAP adherence) (27, 29, 31, 32, 36, 37). Eight observational studies reported multivariate mortality analyses (overall or cardiovascular-specific death), and 7 of them reported statistically significant reductions in mortality rates associated with CPAP therapy (27, 30–32, 36–39).

CPAP Versus Sham CPAP

Twenty-four trials (reported in 30 articles) compared CPAP devices with sham CPAP treatment and included patients with mean baseline AHI scores between 22 and 68 events per hour. Follow-up ranged from 1 week to 3 months. These studies apply to many patients with OSA and included both fixed CPAP devices and autotitrating CPAP (auto-CPAP) devices, which involve a modification in which the machine increases positive pressure in response to airflow resistance. Moderate-quality evidence showed that CPAP was more effective than sham CPAP and reduced AHI scores, improved ESS scores, and reduced arousal index scores compared with sham CPAP (**Appendix Table**). One study (40) found better quality-of-life scores for auto-CPAP than for sham CPAP, although 5 other studies showed no benefit (41–45). No significant differences were found between CPAP and sham CPAP for oxygen saturation, sleep efficiency, Multiple Sleep Latency Test results, or sleep quality assessed by the Functional Outcomes of Sleep Questionnaire (5). Data on blood pressure were inconsistent across the 12 trials that assessed it (46–57), and no study compared CPAP with sham CPAP in regard to death or cardiovascular illness.

Oral CPAP Versus Nasal CPAP

Evidence from 3 small trials (46–48) to determine the comparative efficacy of oral CPAP versus nasal CPAP was insufficient. The trials reported inconsistent results, and effect estimates were generally imprecise, mostly because of the small sample sizes.

Auto-CPAP Versus Fixed CPAP

Twenty-one RCTs (58–78) compared auto-CPAP with fixed CPAP in patients with mean AHI scores between 15 and 55 events per hour and included many obese and overweight patients. These studies are mostly applicable to patients with AHI scores greater than 15 events per hour and body mass indices (BMIs) greater than 30 kg/m^2. Follow-up ranged from 3 weeks to 9 months. Despite some miniscule differences in ESS (0.5 point), minimum oxygen saturation (1%), and adherence (11 minutes), these differences are probably not clinically significant. Overall, moderate-quality evidence showed that auto-CPAP and fixed CPAP have similar adherence and treatment effects for patients with OSA (**Appendix Table**). The authors of the original evidence review published an updated review that included 3 additional studies and reported similar findings, concluding that the 2 treatments are similarly effective (79).

Bilevel CPAP Versus Fixed CPAP

Bilevel CPAP devices are designed to alleviate the difficulty and discomfort of exhaling against the fixed pressure of CPAP by delivering lower pressure during exhalation rather than during inhalation. Evidence from 5 trials (80,

81) to determine the comparative efficacy of bilevel CPAP versus fixed CPAP was insufficient. The studies were small and highly clinically heterogeneous, and most had imprecise treatment effect estimates and showed null findings. No study showed a difference in adherence between the devices.

Flexible Bilevel CPAP Versus Fixed CPAP

Flexible bilevel CPAP delivers reduced positive airway pressure at the end of inspiration and beginning of expiration, which is determined partly by the user's respiration. This differs from the fixed positive airway pressure delivered by CPAP and was designed to improve comfort. Evidence from 1 moderate-quality study (52) to determine the comparative efficacy of flexible bilevel CPAP versus fixed CPAP was insufficient.

C-Flex Versus Fixed CPAP

C-Flex (Philips Healthcare, Andover, Massachusetts) CPAP is a proprietary technology that slightly reduces the pressure at the beginning of exhalation. Four trials (53, 54, 82, 83) compared fixed CPAP with C-Flex CPAP in patients with mean baseline AHI scores between 35.4 and 53.3 events per hour. Follow-up ranged from 1.5 to 6 months. Low-quality evidence showed that C-Flex CPAP and fixed CPAP are similarly tolerated and efficacious for OSA treatment (**Appendix Table**).

CPAP With or Without Humidification

Evidence from 5 studies (55, 84–87) to determine the benefit of CPAP with or without humidification was insufficient. The studies were low- to moderate-quality, small, and clinically heterogeneous and reported inconsistent results. Although 2 trials reported improved adherence to humidification, the other 3 trials reported no significant difference.

MADs for OSA Treatment

MADs Versus No Treatment

Five trials (11, 12, 56, 88, 89) compared several MADs with no treatment in patients with mean baseline AHI scores between 19 and 34 events per hour. These studies generally apply to patients with AHI scores of 15 events or greater per hour, although patients with comorbid conditions or excessive sleepiness were excluded from some trials. Follow-up ranged from 4 to 23 weeks. Moderate-quality evidence showed that MAD use improved the signs and symptoms of sleep apnea, including AHI score, arousal index score, and minimum oxygen saturation (**Appendix Table**) compared with no treatment. No clear survival benefits or reductions in cardiovascular illness were associated with MADs.

MADs Versus Inactive Oral Devices

Five studies (reported in 7 publications) (56, 57, 90–94) compared MADs with inactive (sham) oral devices in patients with mean baseline AHI scores between 25 and 36 events per hour and excluded patients with significant comorbid conditions or periodontal disease. Follow-up ranged from 8 days to 6 weeks. Moderate-quality evidence showed that MAD use improves the signs and symptoms of sleep apnea (including AHI, ESS, and arousal index scores and minimum oxygen saturation) compared with inactive (sham) oral devices (**Appendix Table**). One study each showed improvements in quality of life and neurocognitive test results (56, 57, 90).

MADs Versus CPAP

Ten studies (reported in 11 articles) (11, 12, 95–103) compared the efficacy of CPAP with MADs in patients with mean baseline AHI scores between 18 and 40 events per hour. Follow-up ranged from 1 to 10 months. Moderate-quality evidence showed that CPAP are superior to MADs for improving sleep study measures, including AHI and arousal index scores and minimum oxygen saturation (**Appendix Table**). One study (98) showed improved adherence to MAD treatment (hours used per night and number of nights used) compared with CPAP treatment (**Appendix Table**).

Other OSA Treatment Strategies

Limited data, small studies, or heterogeneous data resulted in insufficient evidence to determine the efficacy or comparative efficacy of the following treatments of OSA: positional therapy versus CPAP, oropharyngeal exercise, palatal implants versus sham implants in patients with mild to moderate OSA, surgical interventions versus control treatment, CPAP or MADs, or atrial overdrive pacing (potential treatment option for patients who already have dual-chamber pacemakers, which have incidentally been shown to improve symptoms of breathing disorders) (5).

Weight-Loss Interventions Versus Control Treatment

Three studies (104–106) compared various weight-loss interventions with control treatment for patients with mean baseline AHI scores between 9 and 37 events per hour. These studies generally apply to patients with BMIs greater than 30 kg/m^2. Follow-up ranged from 2.3 to 12 months. Patients in the weight-loss groups lost 10.7 to 18.7 kg compared with patients in the control groups, who lost 0.6 to 2.4 kg. One study (104) randomly assigned patients with type 2 diabetes to a weight-loss program involving a portion-controlled diet and physical activity prescription or a diabetes support and education program that involved 3 educational sessions on diabetes management over 1 year involving diet, physical activity, and social support. Another study (105) compared patients on a 9-week low-energy diet with patients following their usual diets. The third study (106) randomly assigned obese patients to a very low-calorie diet complemented with lifestyle changes or general counseling on diet and exercise only.

The AHI scores were statistically significantly reduced (range, −4 to −23 events/h) in the groups receiving the weight-loss intervention in all 3 studies. Of the 2 studies (105, 106) that reported on ESS scores, only 1 (105) reported a statistically significant reduction in ESS scores in the weight-loss intervention group. This study also reported a statistically significant increase in minimum oxygen saturation for the low-energy diet group compared with the control group (5% [CI, 2% to 7%]; $P = 0.002$). Only 1 study evaluated cure of OSA as an outcome, defined by an AHI score less than 5 events per hour after 1 year of treatment, and found that a very low-calorie diet was associated with a 4-fold increase in the odds of OSA being cured (22 out of 35 with intervention vs. 13 out of 37 with control treatment; adjusted odds ratio, 4.2 [CI, 1.4 to 12.0]; $P = 0.011$) (106). Overall, low-quality evidence showed that some intensive weight-loss programs may effectively reduce signs and symptoms of OSA in obese patients with or without diabetes.

Drug Therapy Versus Control Treatment

Evidence from 7 RCTs (86, 107–112) showing that drug therapy, including mirtazapine, xylometazoline, fluticasone, paroxetine, pantoprazole, steroid plus CPAP (vs. CPAP alone), acetazolamide, and protriptyline, is superior to control treatment of OSA was insufficient. Each study reported on a different pharmacologic intervention, and outcomes were inconsistent across the studies.

Surgical Interventions Versus Control Treatment

Evidence from 7 studies (3 high-, 1 moderate-, and 3 low-quality [6 trials reported in 7 publications and 1 prospective nonrandomized, comparative study]) (18, 113–119) showing that surgical interventions (including uvulopalatopharyngoplasty [UPPP]; laser-assisted uvulopalatoplasty; radiofrequency ablation; and combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty, radiofrequency ablation of the inferior nasal turbinates, or combination nasal surgery) are more effective than control treatment was insufficient. Each study assessed a different surgical intervention, and outcomes were inconsistent, making it difficult to ascertain the benefit of surgery for OSA treatment. No RCT evaluating surgery versus conservative therapy in regard to death was identified. Two out of 3 observational studies of UPPP reported statistically significant reductions in mortality rates associated with surgery (32, 34, 35, 120–122). Two observational studies of tracheostomy versus conservative therapy reported statistically significant reductions in mortality rates (34, 35, 123, 124).

Surgical Interventions Versus CPAP

Evidence from 12 studies (1 high- and 11 low-quality) (119, 125–135) showing that surgical interventions, including temperature-controlled radiofrequency tissue-volume reduction of the soft palate, UPPP, maxillomandibular advancement osteotomy, and radiofrequency ablation, are more effective than CPAP for OSA treatment was insufficient. No RCT evaluating surgery versus CPAP with respect to death was identified. One of 4 observational studies reported a statistically significant survival advantage associated with UPPP compared with CPAP therapy for OSA (32, 34, 35, 136, 137).

Surgical Interventions Versus MADs

Only 1 moderate-quality trial (published in 3 articles) (138–140) compared UPPP with MADs; thus, evidence to determine which OSA treatment is more effective was insufficient. The study found that MAD treatment resulted in more significant reductions in AHI scores after 1 or 4 years of follow-up; however, the prognostic benefit is unclear.

Predictors of Adherence to OSA Treatment

Adherence to CPAP

Five studies (1 high-, 1 moderate-, and 3 low-quality) assessed adherence to CPAP in patients with mean baseline AHI scores between 44 and 50 events per hour, although adherence was defined differently in each study. Four studies (141–144) found a significant association with elevated baseline AHI scores and CPAP adherence over 1 to 4 years. Of the 3 studies that used baseline ESS as a predictor of CPAP adherence, 2 (143, 144) found a significant association between ESS greater than 10 and adherence, whereas the other (142) did not find a significant association when AHI score and age were adjusted for. One study (142) found that younger age was associated with greater CPAP adherence, although 2 other studies (54, 143) did not find the same result. One study (54) used the Grenoble Sleep Apnea Quality of Life test and found that greater baseline mean oxygen saturation and greater sleepiness were associated with adherence. Other predictors were inconsistent across studies, including snoring (141, 143), lower CPAP setting, and greater BMI (143, 144).

Overall, moderate-quality evidence showed that greater AHI and ESS scores are associated with greater adherence to CPAP treatment of OSA. Low-quality evidence showed that younger age, snoring, lower CPAP setting, greater BMI, greater mean oxygen saturation, and the sleepiness domain on the Grenoble Sleep Apnea Quality of Life test are each possible independent predictors of adherence.

Adherence to MAD Treatment

One low-quality retrospective cohort study (145) evaluated predictors for adherence to MAD treatment but did not find any significant associations with adherence. There were no data on interventions to improve adherence to MAD treatment.

Interventions to Improve Adherence

All 18 studies (2 high-, 8 moderate-, and 8 low-quality) (146–163) that assessed interventions were limited to adherence to CPAP. Overall, low-quality evidence showed that some interventions may help to improve CPAP adherence and that nurse-led care does not improve CPAP adherence.

Extra Support or Education

Nine studies (148, 149, 151, 153–156, 158, 162) assessed the effect of extra support or education on patient adherence to fixed or auto-CPAP. Follow-up ranged from 3 weeks to 1 year. Seven studies compared support protocols, such as phone calls and literature or education programs, with usual care, measuring adherence as hours of use per night. Three studies (148, 149, 153) found that intensive support or patient education literature significantly increased CPAP device use by an average of 1.1 to 2.7 additional hours per night. In contrast, 4 other studies (151, 154, 156, 158) found no significant differences. One study (161) found that audio-based intervention packets significantly decreased nonadherence at 1 month compared with placebo (11% vs. 45%; $P < 0.01$), but this effect was not seen at 6 months. One study (155) assessing return to the clinic for follow-up as a measure of adherence found that patients who received an educational video about appropriate use of CPAP returned more frequently than those in the control group (51% vs. 27%; $P = 0.02$). A single study (154) that assessed adherence rates between augmented support and basic support groups found no significant differences.

Telemonitoring Care

Telemonitoring care is a computer-based telecommunications system that monitors, educates, and counsels patients at home. Three studies (150, 162, 163) assessed the effect of telemonitoring care on patient adherence to CPAP. Follow-up ranged from 30 days to 2 months. Two studies (150, 162) reported that telemonitoring increased CPAP device use (average, 1.3 [$P = 0.07$] and 1.5 [$P = 0.08$] additional hours per night) compared with usual care, whereas the third study (163) found no significant difference.

Behavioral Interventions

One study (160) found that patients receiving cognitive behavioral therapy were 6.9 times more likely to adhere to CPAP device use at least 4 hours per night (CI, 2.8 to 18.2 hours) and used it for more hours per night compared with usual care (difference, 2.8 hours [CI, 1.8 to 3.9 hours]; $P < 0.001$) after 28 days of follow-up.

Other Interventions

One study (147) compared the effectiveness of an oral hypnotic agent (zolpidem, 10 mg) with placebo or standard care and found no significant differences in adherence or hours of CPAP use. Another study (157) found no significant differences in patients using CPAP with nasal pillows designed to improve comfort compared with regular CPAP. Two published RCTs not included in the AHRQ report showed statistically significant and clinically relevant improvements in CPAP adherence associated with eszopiclone compared with placebo (164, 165).

Care Models for Patients Who Use CPAP

Three studies (146, 152, 159) reported no significant difference in nurse-based care models compared with usual care for patients who use CPAP. Follow-up ranged from 3 months to 2 years.

Adverse Effects

Evidence on adverse effects related to various management strategies for OSA was sparse, especially from RCTs. The **Appendix Table** summarizes adverse effects associated with each treatment. The most serious effects were reported for surgical interventions, particularly for oronasopharyngeal or bariatric surgery. Tooth loosening, dental crown damage, and temporomandibular joint pain were the most commonly reported adverse effects with MADs; however, long-term consequences were not reported. Overall, approximately 5% to 15% of patients treated with CPAP reported adverse effects that they considered to be substantial, but these symptoms were potentially transient. In general, adverse effects in patients treated with CPAP could be alleviated with termination or modification of the treatment. No long-term adverse effects were reported for weight-loss interventions.

Summary

Management of OSA is based on symptoms, the severity of the disorder, and patient education about the risk factors and associated outcomes of OSA. Evidence on clinical outcomes of OSA interventions was very limited, and most of the data presented here focus on intermediate outcomes. Many studies included obese patients with AHI scores greater than 30 events per hour, so the generalizability of some data to the population at large may be difficult. The **Appendix Table** summarizes the various interventions for OSA treatment.

Moderate-quality evidence showed that CPAP was more effective than control or sham CPAP. However, no randomized trials evaluated the long-term clinical outcomes of CPAP use, such as death or cardiovascular illness, and evidence showing the effect of CPAP on quality of life was inconsistent and therefore inconclusive. Data to determine the comparative efficacy of most CPAP modifications were insufficient; however, moderate-quality evidence showed that fixed and auto-CPAP have overall similar efficacy and adherence despite small differences, and low-quality evidence showed that C-Flex and fixed CPAP were similarly efficacious.

There are various alternative therapeutic options to CPAP, including MADs, to manage OSA. Evidence showed that MADs could effectively lower AHI scores and

Figure. **Summary of the American College of Physicians guideline on management of OSA in adults.**

ACP Clinical Practice® American College of Physicians GUIDELINES

Summary of the American College of Physicians Guideline on Management of OSA in Adults

Disease/Condition	OSA
Target Audience	Internists, family physicians, and other clinicians
Target Patient Population	Adults with OSA
Interventions	Positive airway pressure machines, MADs, weight-loss programs, drug therapy, surgical interventions, atrial overdrive pacing, palatal implants, oropharyngeal exercises, tongue-retaining devices, positional alarms, bariatric surgery, nasal dilator strips, acupuncture, and auricular plaster
Outcomes	Cardiovascular disease (including congestive heart failure, hypertension, stroke, and myocardial infarction), type 2 diabetes mellitus, death, sleep study measures (e.g., AHI), measures of cardiovascular status (e.g., blood pressure), measures of diabetes status (e.g., hemoglobin A_{1c} levels), and quality of life
Recommendations	Recommendation 1: ACP recommends that all overweight and obese patients diagnosed with OSA should be encouraged to lose weight. (Grade: strong recommendation; low-quality evidence) Recommendation 2: ACP recommends continuous positive airway pressure treatment as initial therapy for patients diagnosed with OSA. (Grade: strong recommendation; moderate-quality evidence) Recommendation 3: ACP recommends mandibular advancement devices as an alternative therapy to continuous positive airway pressure treatment for patients diagnosed with OSA who prefer mandibular advancement devices or for those with adverse effects associated with continuous positive airway pressure treatment. (Grade: weak recommendation; low-quality evidence)
High-Value Care	Clinicians should target evaluation and treatment of OSA to patients with unexplained daytime sleepiness. Assessment of effectiveness is primarily based on improvement of daytime sleepiness; however, the effect on other clinical outcomes, including hypertension, cardiovascular events, and death, is uncertain. Adherence to therapies, especially CPAP treatment, is an important issue related to the effective treatment of OSA. Clinicians should keep patient preferences and adherence, specific reasons for nonadherence, and costs in mind before initiating CPAP treatment. Clinicians should encourage weight loss in obese patients because obesity is associated with increased risk for OSA, and weight loss may improve OSA symptoms and provide many other health benefits. Pharmacologic therapy is not currently supported by the available evidence and should not be prescribed for OSA treatment. Surgical treatments are associated with risks and harms. Current evidence evaluating surgery was limited and insufficient to show the benefits of surgery as an approach to treat OSA; therefore, surgery should not be used as an initial treatment of OSA.
Clinical Considerations	Management of a patient with OSA begins with diagnosis and establishing severity of the condition. There are no data to determine which patients benefit most from specific OSA treatment strategies. Behavioral modifications, such as weight-loss strategies, should be based on discussion with the patient and characteristics of the patient. Not all patients tolerate CPAP treatment, and these patients can be treated with MADs. It is important to stress adherence to OSA interventions. Patients with excessive daytime sleepiness should be warned to avoid such activities as driving or operating dangerous equipment.

AHI = Apnea–Hypopnea Index; CPAP = continuous positive airway pressure; MAD = mandibular advancement device; OSA = obstructive sleep apnea.

reduce sleepiness. However, CPAP more effectively reduced AHI and arousal index scores and increased the minimum oxygen saturation compared with MADs. Evidence on the long-term clinical outcomes, such as death or cardiovascular illness, associated with MAD therapy was insufficient. Evidence was also insufficient to determine which patients would benefit the most from either CPAP or MAD treatment or to determine the comparative efficacy of different oral devices.

Evidence to ascertain the efficacy or comparative efficacy of other OSA treatments, including positional therapy versus CPAP, oropharyngeal exercise, palatal implants versus sham implants in patients with mild to moderate OSA, surgical interventions versus control treatment, CPAP or MADs, pharmacologic therapy, or atrial overdrive pacing, was insufficient. Evidence to evaluate the relative efficacy of surgical interventions for OSA treatment was insufficient. Low-quality evidence indicated that weight-loss interventions improved sleep measures and should be recommended for obese patients with OSA.

Greater AHI and ESS scores may predict better adherence to CPAP, suggesting that patients with more severe

OSA may most readily adhere to treatment. Low-quality evidence also supported the association of younger age, snoring, lower CPAP setting, greater BMI, greater mean oxygen saturation, and the sleepiness domain on the Grenoble Sleep Apnea Quality of Life test with CPAP adherence. Data on the efficacy of various interventions to improve OSA treatment adherence (focused on CPAP) were often sparse and inconsistent. However, low-quality evidence showed that some of these interventions, such as telemonitoring care, may be helpful. See the **Figure** for a summary of the recommendations and clinical considerations.

Recommendations

Recommendation 1: ACP recommends that all overweight and obese patients diagnosed with OSA should be encouraged to lose weight. (Grade: strong recommendation; low-quality evidence)

Obesity is a risk factor for OSA, and evidence showed that intensive weight-loss interventions help reduce AHI scores and improve OSA symptoms. Weight loss is also associated with many other health benefits other than for OSA. Other factors, such as alcohol and opioid use, may be associated with adverse outcomes in patients with sleep apnea, but these factors were not addressed in the evidence review.

Recommendation 2: ACP recommends continuous positive airway pressure treatment as initial therapy for patients diagnosed with OSA. (Grade: strong recommendation; moderate-quality evidence)

In patients with excessive daytime sleepiness who have been diagnosed with OSA, CPAP is the most extensively studied therapy. This treatment has been shown to improve ESS scores, reduce AHI and arousal index scores, and increase oxygen saturation. However, CPAP has not been shown to increase quality of life. Evidence on the effect of CPAP on cardiovascular disease, hypertension, and type 2 diabetes was insufficient. Studies have evaluated various alternative CPAP modifications. Fixed and auto-CPAP, as well as C-Flex, have similar adherence and efficacy. Data were insufficient to determine the comparative efficacy of other CPAP modifications. Greater AHI and ESS scores were generally associated with better adherence to CPAP.

Recommendation 3: ACP recommends mandibular advancement devices as an alternative therapy to continuous positive airway pressure treatment for patients diagnosed with OSA who prefer mandibular advancement devices or for those with adverse effects associated with continuous positive airway pressure treatment. (Grade: weak recommendation; low-quality evidence)

Evidence showed that MADs have been used as an alternative to CPAP for treatment of OSA. Patients had AHI scores between 18 and 40 events per hour. Evidence to suggest which patients would benefit most from MADs was insufficient. However, MADs can be considered in patients with adverse effects or for those who do not tolerate or adhere to CPAP.

Inconclusive Areas of Evidence

Pharmacologic agents were evaluated as primary agents for OSA management, and current evidence from 1 study for each drug was insufficient to recommend the use of any of the agents. Pharmacologic agents included mirtazapine, xylometazoline, fluticasone, paroxetine, pantoprazole, steroid plus CPAP, acetazolamide, and protriptyline.

ACP High-Value Care

Clinicians should target evaluation and treatment of OSA to patients with unexplained daytime sleepiness. Assessment of effectiveness is based primarily on improvement of daytime sleepiness; however, the effect on other clinical outcomes, including hypertension, cardiovascular events, and death, is uncertain. Adherence to therapies, especially CPAP, is important for effective OSA treatment. Clinicians should keep patient preferences and adherence, specific reasons for nonadherence, and costs in mind before initiating CPAP. They should encourage weight loss in obese patients because obesity is associated with increased risk for OSA, and weight loss may reduce OSA symptoms and has many other health benefits. Pharmacologic therapy is not currently supported by evidence and should not be prescribed for OSA treatment. Surgical treatments are associated with risks and serious adverse effects. Current evidence evaluating surgery was limited and insufficient to show the benefits of surgery as treatment of OSA and thus should not be used as initial treatment.

From the American College of Physicians, Philadelphia, Pennsylvania; Stanford University, Stanford, California; Veterans Affairs Palo Alto Health Care System, Palo Alto, California; Virginia Tech University, Carilion School of Medicine, Roanoke, Virginia; and West Los Angeles Veterans Affairs Medical Center, Los Angeles, California.

Financial Support: Financial support for the development of this guideline comes exclusively from the ACP operating budget.

Potential Conflicts of Interest: Dr. Shekelle: *Personal fees:* ECRI Institute, Veterans Affairs; *Grants:* Agency for Healthcare Research and Quality, Veterans Affairs, Centers for Medicare & Medicaid Services, National Institute of Nursing Research, Office of the National Coordinator for Health Information Technology. All other authors have no disclo-

sures. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-3188. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm.

Requests for Single Reprints: Amir Qaseem, MD, PhD, MHA, American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106; e-mail, aqaseem@acponline.org.

Current author addresses and author contributions are available at www.annals.org.

References

1. **Young T, Peppard PE, Taheri S.** Excess weight and sleep-disordered breathing. J Appl Physiol. 2005;99:1592-9. [PMID: 16160020]
2. **Chasens ER, Pack AI, Maislin G, Dinges DF, Weaver TE.** Claustrophobia and adherence to CPAP treatment. West J Nurs Res. 2005;27:307-21. [PMID: 15781905]
3. **Parthasarathy S, Haynes PL, Budhiraja R, Habib MP, Quan SF.** A national survey of the effect of sleep medicine specialists and American Academy of Sleep Medicine Accreditation on management of obstructive sleep apnea. J Clin Sleep Med. 2006;2:133-42. [PMID: 17557485]
4. **Veasey SC, Guilleminault C, Strohl KP, Sanders MH, Ballard RD, Magalang UJ.** 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;29:1036-44. [PMID: 16944672]
5. **Balk EM, Moorthy D, Obadan NO, Patel K, Ip S, Chung M, et al.** Diagnosis and Treatment of Obstructive Sleep Apnea in Adults. Comparative Effectiveness Review No. 32. (Prepared by Tufts Evidence-Based Practice Center under contract 290-2007-100551.) AHRQ Publication No. 11-EHC052-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
6. **Agency for Healthcare Research and Quality.** Methods reference guide for effectiveness and comparative effectiveness reviews, version 1.0. Rockville, MD: Agency for Healthcare Research and Quality; 2010.
7. **Qaseem A, Snow V, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of Physicians.** The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010;153:194-9. [PMID: 20679562]
8. **Mansfield DR, Gollogly NC, Kaye DM, Richardson M, Bergin P, Naughton MT.** Controlled trial of continuous positive airway pressure in obstructive sleep apnea and heart failure. Am J Respir Crit Care Med. 2004;169:361-6. [PMID: 14597482]
9. **Monasterio C, Vidal S, Duran J, Ferrer M, Carmona C, Barbé F, et al.** Effectiveness of continuous positive airway pressure in mild sleep apnea-hypopnea syndrome. Am J Respir Crit Care Med. 2001;164:939-43. [PMID: 11587974]
10. **Barnes M, Houston D, Worsnop CJ, Neill AM, Mykytyn IJ, Kay A, et al.** A randomized controlled trial of continuous positive airway pressure in mild obstructive sleep apnea. Am J Respir Crit Care Med. 2002;165:773-80. [PMID: 11897643]
11. **Barnes M, McEvoy RD, Banks S, Tarquinio N, Murray CG, Vowles N, et al.** Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. Am J Respir Crit Care Med. 2004;170:656-64. [PMID: 15201136]
12. **Lam B, Sam K, Mok WY, Cheung MT, Fong DY, Lam JC, et al.** Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnoea. Thorax. 2007;62:354-9. [PMID: 17121868]
13. **Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ.** Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1999;159:461-7. [PMID: 9927358]
14. **Ballester E, Badia JR, Hernández L, Carrasco E, de Pablo J, Fornas C, et al.** Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1999;159:495-501. [PMID: 9927363]
15. **Engleman HM, Martin SE, Kingshott RN, Mackay TW, Deary IJ, Douglas NJ.** Randomised placebo controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. Thorax. 1998;53:341-5. [PMID: 9708223]
16. **Engleman HM, Martin SE, Deary IJ, Douglas NJ.** Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet. 1994;343:572-5. [PMID: 7906330]
17. **Engleman HM, Martin SE, Deary IJ, Douglas NJ.** Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. Thorax. 1997;52:114-9. [PMID: 9059469]
18. **Lojander J, Maasilta P, Partinen M, Brander PE, Salmi T, Lehtonen H.** Nasal-CPAP, surgery, and conservative management for treatment of obstructive sleep apnea syndrome. A randomized study. Chest. 1996;110:114-9. [PMID: 8681614]
19. **Barbé F, Durán-Cantolla J, Capote F, de la Peña M, Chiner E, Masa JF, et al; Spanish Sleep and Breathing Group.** Long-term effect of continuous positive airway pressure in hypertensive patients with sleep apnea. Am J Respir Crit Care Med. 2010;181:718-26. [PMID: 20007932]
20. **Comondore VR, Cheema R, Fox J, Butt A, John Mancini GB, Fleetham JA, 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. [PMID: 18795367]
21. **Drager LF, Bortolotto LA, Figueiredo AC, Krieger EM, Lorenzi GF.** Effects of continuous positive airway pressure on early signs of atherosclerosis in obstructive sleep apnea. Am J Respir Crit Care Med. 2007;176:706-12. [PMID: 17556718]
22. **Engleman HM, Gough K, Martin SE, Kingshott RN, Padfield PL, Douglas NJ.** Ambulatory blood pressure on and off continuous positive airway pressure therapy for the sleep apnea/hypopnea syndrome: effects in "non-dippers.". Sleep 1996;19:378-81. [PMID: 8843528]
23. **Kaneko Y, Floras JS, Usui K, Plante J, Tkacova R, Kubo T, et al.** Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med. 2003;348:1233-41. [PMID: 12660387]
24. **Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, et al; Spanish Sleep and Breathing Network.** Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;307:2161-8. [PMID: 22618923]
25. **Minnerup J, Ritter MA, Wersching H, Kemmling A, Okegwo A, Schmidt A, et al.** Continuous positive airway pressure ventilation for acute ischemic stroke: a randomized feasibility study. Stroke. 2012;43:1137-9. [PMID: 22198979]
26. **Parra O, Sánchez-Armengol A, Bonnin M, Arboix A, Campos-Rodríguez F, Pérez-Ronchel J, et al.** Early treatment of obstructive apnoea and stroke outcome: a randomised controlled trial. Eur Respir J. 2011;37:1128-36. [PMID: 20847081]
27. **Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I, Almeida-Gonzalez C, Catalan-Serra P, Montserrat JM.** Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med. 2012;156:115-22. [PMID: 22250142]
28. **Jennum P, Kjellberg J.** Health, social and economical consequences of sleep-disordered breathing: a controlled national study. Thorax. 2011;66:560-6. [PMID: 21199816]
29. **Korostovtseva LS, Sviryaev YV, Zvartau NE, Konradi AO, Kalinkin AL.** Prognosis and cardiovascular morbidity and mortality in prospective study of hypertensive patients with obstructive sleep apnea syndrome in St Petersburg, Russia. Med Sci Monit. 2011;17:CR146-53. [PMID: 21358601]
30. **Campos-Rodriguez F, Peña-Griñan N, Reyes-Nuñez N, De la Cruz-Moron I, Perez-Ronchel J, De la Vega-Gallardo F, et al.** Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. Chest. 2005;128:624-33. [PMID: 16100147]
31. **Doherty LS, Kiely JL, Swan V, McNicholas WT.** Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest. 2005;127:2076-84. [PMID: 15947323]
32. **Marti S, Sampol G, Muñoz X, Torres F, Roca A, Lloberes P, et al.** Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J. 2002;20:1511-8. [PMID: 12503712]

33. **Veale D, Chailleux E, Hoorelbeke-Ramon A, Reybet-Degas O, Humeau-Chapuis MP, Alluin-Aigouy F, 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. Eur Respir J. 2000;15:326-31. [PMID: 10706500]
34. **Roth T, Roehrs T, Kryger M.** Mortality in obstructive sleep apnea. Prog Clin Biol Res. 1990;345:347-51. [PMID: 2377641]
35. **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]
36. **Buchner NJ, Sanner BM, Borgel J, Rump LC.** Continuous positive airway pressure treatment of mild to moderate obstructive sleep apnea reduces cardiovascular risk. Am J Respir Crit Care Med. 2007;176:1274-80. [PMID: 17673692]
37. **Marin JM, Carrizo SJ, Vicente E, Agusti AG.** Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365:1046-53. [PMID: 15781100]
38. **Nakamura H, Kanemura T, Takara C, Tsukayama A, Tohyama K, Matsumoto T, et al.** A retrospective analysis of 4000 patients with obstructive sleep apnea in Okinawa, Japan. Sleep Biol Rhythms. 2009;7:103-12.
39. **Morrish E, Shneerson JM, Smith IE.** Why does gender influence survival in obstructive sleep apnoea? Respir Med. 2008;102:1231-6. [PMID: 18617382]
40. **Siccoli MM, Pepperell JC, Kohler M, Craig SE, Davies RJ, Stradling JR.** 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;31:1551-8. [PMID: 19014075]
41. **Barbé F, Mayoralas LR, Duran J, Masa JF, Maimó A, Montserrat JM, et al.** Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. a randomized, controlled trial. Ann Intern Med. 2001;134:1015-23. [PMID: 11388814]
42. **Egea CJ, Aizpuru F, Pinto JA, Ayuela JM, Ballester E, Zamarrón C, et al; Spanish Group of Sleep Breathing Disorders.** Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9:660-6. [PMID: 17904420]
43. **Marshall NS, Neill AM, Campbell AJ, Sheppard DS.** Randomised controlled crossover trial of humidified continuous positive airway pressure in mild obstructive sleep apnoea. Thorax. 2005;60:427-32. [PMID: 15860720]
44. **Montserrat JM, Ferrer M, Hernandez L, Farré R, Vilagut G, Navajas D, 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;164:608-13. [PMID: 11520724]
45. **Smith LA, Vennelle M, Gardner RS, McDonagh TA, Denvir MA, Douglas NJ, et al.** Auto-titrating continuous positive airway pressure therapy in patients with chronic heart failure and obstructive sleep apnoea: a randomized placebo-controlled trial. Eur Heart J. 2007;28:1221-7. [PMID: 17470670]
46. **Anderson FE, Kingshott RN, Taylor DR, Jones DR, Kline LR, Whyte KF.** A randomized crossover efficacy trial of oral CPAP (Oracle) compared with nasal CPAP in the management of obstructive sleep apnea. Sleep. 2003;26:721-6. [PMID: 14572126]
47. **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 Med. 2003;4:333-8. [PMID: 14592306]
48. **Mortimore IL, Whittle AT, Douglas NJ.** Comparison of nose and face mask CPAP therapy for sleep apnoea. Thorax. 1998;53:290-2. [PMID: 9741373]
49. **Khayat RN, Abraham WT, Patt B, Roy M, Hua K, Jarjoura D.** Cardiac effects of continuous and bilevel positive airway pressure for patients with heart failure and obstructive sleep apnea: a pilot study. Chest. 2008;134:1162-8. [PMID: 18641111]
50. **Piper AJ, Wang D, Yee BJ, Barnes DJ, Grunstein RR.** Randomised trial of CPAP vs bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation. Thorax. 2008;63:395-401. [PMID: 18203817]
51. **Reeves-Hoché MK, Hudgel DW, Meck R, Witteman R, Ross A, Zwillich CW.** Continuous versus bilevel positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med. 1995;151:443-9. [PMID: 7842204]
52. **Ballard RD, Gay PC, Strollo PJ.** Interventions to improve compliance in sleep apnea patients previously non-compliant with continuous positive airway pressure. J Clin Sleep Med. 2007;3:706-12. [PMID: 18198804]
53. **Dolan DC, Okonkwo R, Gfullner F, Hansbrough JR, Strobel RJ, Rosenthal L.** Longitudinal comparison study of pressure relief (C-Flex) vs. CPAP in OSA patients. Sleep Breath. 2009;13:73-7. [PMID: 18551327]
54. **Pépin JL, Muir JF, Gentina T, Dauvilliers Y, Tamisier R, Sapene M, et al.** Pressure reduction during exhalation in sleep apnea patients treated by continuous positive airway pressure. Chest. 2009;136:490-7. [PMID: 19567496]
55. **Neill AM, Wai HS, Bannan SP, Beasley CR, Weatherall M, Campbell AJ.** Humidified nasal continuous positive airway pressure in obstructive sleep apnoea. Eur Respir J. 2003;22:258-62. [PMID: 12952257]
56. **Petri N, Svanholt P, Solow B, Wildschiødtz G, Winkel P.** Mandibular advancement appliance for obstructive sleep apnoea: results of a randomised placebo controlled trial using parallel group design. J Sleep Res. 2008;17:221-9. [PMID: 18482111]
57. **Gotsopoulos H, Chen C, Qian J, Cistulli PA.** Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. Am J Respir Crit Care Med. 2002;166:743-8. [PMID: 12204875]
58. **Planès C, D'Ortho MP, Foucher A, Berkani M, Leroux K, Essalhi M, et al.** Efficacy and cost of home-initiated auto-nCPAP versus conventional nCPAP. Sleep. 2003;26:156-60. [PMID: 12683473]
59. **Randerath WJ, Schraeder O, Galetke W, Feldmeyer F, Rühle KH.** Auto-adjusting CPAP therapy based on impedance efficacy, compliance and acceptance. Am J Respir Crit Care Med. 2001;163:652-7. [PMID: 11254519]
60. **Resta O, Carratù P, Depalo A, Giliberti T, Ardito M, Marrone O, et al.** Effects of fixed compared to automatic CPAP on sleep in obstructive sleep apnoea syndrome. Monaldi Arch Chest Dis. 2004;61:153-6. [PMID: 15679008]
61. **Senn O, Brack T, Matthews F, Russi EW, Bloch KE.** 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: 1506-11. [PMID: 14525804]
62. **Teschler H, Wessendorf TE, Farhat AA, Konietzko N, Berthon-Jones M.** Two months auto-adjusting versus conventional nCPAP for obstructive sleep apnoea syndrome. Eur Respir J. 2000;15:990-5. [PMID: 10885414]
63. **Hudgel DW, Fung C.** A long-term randomized, cross-over comparison of auto-titrating and standard nasal continuous airway pressure. Sleep. 2000;23: 645-8. [PMID: 10947032]
64. **Marrone O, Resta O, Salvaggio A, Giliberti T, Stefano A, Insalaco G.** Preference for fixed or automatic CPAP in patients with obstructive sleep apnea syndrome. Sleep Med. 2004;5:247-51. [PMID: 15165530]
65. **Noseda A, Kempenaers C, Kerkhofs M, Braun S, Linkowski P, Jann E.** Constant vs auto-continuous positive airway pressure in patients with sleep apnea hypopnea syndrome and a high variability in pressure requirement. Chest. 2004; 126:31-7. [PMID: 15249439]
66. **Sériès 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. Ann Intern Med. 1997;127:588-95. [PMID: 9341056]
67. **To KW, Chan WC, Choo KL, Lam WK, Wong KK, Hui DS.** 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. [PMID: 18197915]
68. **Vennelle M, White S, Riha RL, Mackay TW, Engleman HM, Douglas NJ.** 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;33:267-71. [PMID: 20175411]
69. **Eskafi M.** Sleep apnoea in patients with stable congestive heart failure an intervention study with a mandibular advancement device. Swed Dent J Suppl. 2004:1-56. [PMID: 15638133]
70. **Benazzo M, Pagella F, Matti E, Zorzi S, Campanini A, Frassineti S, et al.** Hyoidthyroidpexia as a treatment in multilevel surgery for obstructive sleep apnea. Acta Otolaryngol. 2008;128:680-4. [PMID: 18568505]
71. **Esclamado RM, Glenn MG, McCulloch TM, Cummings CW.** Perioperative complications and risk factors in the surgical treatment of obstructive sleep apnea syndrome. Laryngoscope. 1989;99:1125-9. [PMID: 2530406]
72. **Friedman M, Ibrahim H, Joseph NJ.** Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope. 2004;114: 454-9. [PMID: 15091218]
73. **Friedman M, Lin HC, Gurpinar B, Joseph NJ.** Minimally invasive single-stage multilevel treatment for obstructive sleep apnea/hypopnea syndrome. Laryngoscope. 2007;117:1859-63. [PMID: 17713449]

74. **Grunstein RR, Stenlöf K, Hedner JA, Peltonen M, Karason K, Sjöström L.** Two year reduction in sleep apnea symptoms and associated diabetes incidence after weight loss in severe obesity. Sleep. 2007;30:703-10. [PMID: 17580591]
75. **Haavisto L, Suonpää J.** Complications of uvulopalatopharyngoplasty. Clin Otolaryngol Allied Sci. 1994;19:243-7. [PMID: 7923849]
76. **Harmon JD, Morgan W, Chaudhary B.** Sleep apnea: morbidity and mortality of surgical treatment. South Med J. 1989;82:161-4. [PMID: 2916139]
77. **Kezirian EJ, Weaver EM, Yueh B, Deyo RA, Khuri SF, Daley J, et al.** Incidence of serious complications after uvulopalatopharyngoplasty. Laryngoscope. 2004;114:450-3. [PMID: 15091217]
78. **Lundkvist K, Januszkiewicz A, Friberg D.** Uvulopalatopharyngoplasty in 158 OSAS patients failing non-surgical treatment. Acta Otolaryngol. 2009;129:1280-6. [PMID: 19863325]
79. **Ip S, D'Ambrosio C, Patel K, Obadan N, Kitsios GD, Chung M, et al.** Auto-titrating versus fixed continuous positive airway pressure for the treatment of obstructive sleep apnea: a systematic review with meta-analyses. Syst Rev. 2012;1:20. [PMID: 22587875]
80. **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;26:864-9. [PMID: 14655921]
81. **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. Med Sci Monit. 2003;9:CR353-8. [PMID: 12942031]
82. **Leidag M, Hader C, Keller T, Meyer Y, Rasche K.** Mask leakage in continuous positive airway pressure and C-Flex. J Physiol Pharmacol. 2008;59 Suppl 6:401-6. [PMID: 19218664]
83. **Nilius G, Happel A, Domanski U, Ruhle KH.** Pressure-relief continuous positive airway pressure vs constant continuous positive airway pressure: a comparison of efficacy and compliance. Chest. 2006;130:1018-24. [PMID: 17035433]
84. **Mador MJ, Krauza M, Pervez A, Pierce D, Braun M.** Effect of heated humidification on compliance and quality of life in patients with sleep apnea using nasal continuous positive airway pressure. Chest. 2005;128:2151-8. [PMID: 16236868]
85. **Massie CA, Hart RW, Peralez K, Richards GN.** Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure. Chest. 1999;116:403-8. [PMID: 10453869]
86. **Ryan S, Doherty LS, Nolan GM, McNicholas WT.** 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. J Clin Sleep Med. 2009;5:422-7. [PMID: 19961025]
87. **Salgado SM, Boléo-Tomé JP, Canhão CM, Dias AR, Teixeira JI, Pinto PM, et al.** Impact of heated humidification with automatic positive airway pressure in obstructive sleep apnea therapy. J Bras Pneumol. 2008;34:690-4. [PMID: 18982206]
88. **Bloch KE, Iseli A, Zhang JN, Xie X, Kaplan V, Stoeckli PW, et al.** A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. Am J Respir Crit Care Med. 2000;162:246-51. [PMID: 10903249]
89. **Kato J, Isono S, Tanaka A, Watanabe T, Araki D, Tanzawa H, et al.** Dose-dependent effects of mandibular advancement on pharyngeal mechanics and nocturnal oxygenation in patients with sleep-disordered breathing. Chest. 2000;117:1065-72. [PMID: 10767241]
90. **Gotsopoulos H, Kelly JJ, Cistulli PA.** Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. Sleep. 2004;27:934-41. [PMID: 15453552]
91. **Hans MG, Nelson S, Luks VG, Lorkovich P, Baek SJ.** Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). Am J Orthod Dentofacial Orthop. 1997;111:562-70. [PMID: 9155816]
92. **Johnston CD, Gleadhill IC, Cinnamond MJ, Gabbey J, Burden DJ.** Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. Eur J Orthod. 2002;24:251-62. [PMID: 12143089]
93. **Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA.** A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. Am J Respir Crit Care Med. 2001;163:1457-61. [PMID: 11371418]
94. **Naismith SL, Winter VR, Hickie IB, Cistulli PA.** Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. J Clin Sleep Med. 2005;1:374-80. [PMID: 17564405]
95. **Clark GT, Blumenfeld I, Yoffe N, Peled E, Lavie P.** A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. Chest. 1996;109:1477-83. [PMID: 8769497]
96. **Engleman HM, McDonald JP, Graham D, Lello GE, Kingshott RN, Coleman EL, 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;166:855-9. [PMID: 12231497]
97. **Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA.** 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;109:1269-75. [PMID: 8625679]
98. **Gagnadoux F, Fleury B, Vielle B, Pételle B, Meslier N, N'Guyen XL, et al.** Titrated mandibular advancement versus positive airway pressure for sleep apnoea. Eur Respir J. 2009;34:914-20. [PMID: 19324954]
99. **Hoekema A, Stegenga B, Wijkstra PJ, van der Hoeven JH, Meinesz AF, de Bont LG.** Obstructive sleep apnea therapy. J Dent Res. 2008;87:882-7. [PMID: 18719218]
100. **Hoekema A, Stel AL, Stegenga B, van der Hoeven JH, Wijkstra PJ, van Driel MF, 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. J Sex Med. 2007;4:1153-62. [PMID: 17081222]
101. **Randerath WJ, Heise M, Hinz R, Ruehle KH.** An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. Chest. 2002;122:569-75. [PMID: 12171833]
102. **Skinner MA, Kingshott RN, Jones DR, Taylor DR.** Lack of efficacy for a cervicomandibular support collar in the management of obstructive sleep apnea. Chest. 2004;125:118-26. [PMID: 14718430]
103. **Tan YK, L'Estrange PR, Luo YM, Smith C, Grant HR, Simonds AK, et al.** Mandibular advancement splints and continuous positive airway pressure in patients with obstructive sleep apnoea: a randomized cross-over trial. Eur J Orthod. 2002;24:239-49. [PMID: 12143088]
104. **Foster GD, Borradaile KE, Sanders MH, Millman R, Zammit G, Newman AB, et al; Sleep AHEAD Research Group of Look AHEAD Research Group.** A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. Arch Intern Med. 2009;169:1619-26. [PMID: 19786682]
105. **Johansson K, Neovius M, Lagerros YT, Harlid R, Rössner S, Granath F, 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. [PMID: 19959590]
106. **Tuomilehto HP, Seppä JM, Partinen MM, Peltonen M, Gylling H, Tuomilehto JO, et al; Kuopio Sleep Apnea Group.** Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. Am J Respir Crit Care Med. 2009;179:320-7. [PMID: 19011153]
107. **Carley DW, Olopade C, Ruigt GS, Radulovacki M.** Efficacy of mirtazapine in obstructive sleep apnea syndrome. Sleep. 2007;30:35-41. [PMID: 17310863]
108. **Clarenbach CF, Kohler M, Senn O, Thurnheer R, Bloch KE.** Does nasal decongestion improve obstructive sleep apnea? J Sleep Res. 2008;17:444-9. [PMID: 18710420]
109. **Kiely JL, Nolan P, McNicholas WT.** Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. Thorax. 2004;59:50-5. [PMID: 14694248]
110. **Kraiczi H, Hedner J, Dahlöf P, Ejnell H, Carlson J.** Effect of serotonin uptake inhibition on breathing during sleep and daytime symptoms in obstructive sleep apnea. Sleep. 1999;22:61-7. [PMID: 9989366]
111. **Suurna MV, Welge J, Surdulescu V, Kushner J, Steward DL.** Randomized placebo-controlled trial of pantoprazole for daytime sleepiness in GERD and obstructive sleep disordered breathing. Otolaryngol Head Neck Surg. 2008;139:286-90. [PMID: 18656731]
112. **Whyte KF, Gould GA, Airlie MA, Shapiro CM, Douglas NJ.** Role of protriptyline and acetazolamide in the sleep apnea/hypopnea syndrome. Sleep. 1988;11:463-72. [PMID: 3067313]
113. **Bäck LJ, Liukko T, Rantanen I, Peltola JS, Partinen M, Ylikoski J, 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;119:1621-7. [PMID: 19504550]

114. **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;167:15-9. [PMID: 12502473]
115. **Guilleminault C, Davis K, Huynh NT.** Prospective randomized study of patients with insomnia and mild sleep disordered breathing. Sleep. 2008;31: 1527-33. [PMID: 19014072]
116. **Koutsourelakis I, Georgoulopoulos G, Perraki E, Vagiakis E, Roussos C, Zakynthinos SG.** Randomised trial of nasal surgery for fixed nasal obstruction in obstructive sleep apnoea. Eur Respir J. 2008;31:110-7. [PMID: 17898015]
117. **Li HY, Lee LA, Wang PC, Fang TJ, Chen NH.** Can nasal surgery improve obstructive sleep apnea: subjective or objective? Am J Rhinol Allergy. 2009;23: e51-5. [PMID: 19793414]
118. **Lojander J, Kajaste S, Maasilta P, Partinen M.** Cognitive function and treatment of obstructive sleep apnea syndrome. J Sleep Res. 1999;8:71-6. [PMID: 10188139]
119. **Woodson BT, Steward DL, Weaver EM, Javaheri S.** A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg. 2003;128:848-61. [PMID: 12825037]
120. **Peker Y, Hedner J, Kraiczi H, Löth S.** Respiratory disturbance index: an independent predictor of mortality in coronary artery disease. Am J Respir Crit Care Med. 2000;162:81-6. [PMID: 10903224]
121. **Peker Y, Carlson J, Hedner J.** Increased incidence of coronary artery disease in sleep apnoea: a long-term follow-up. Eur Respir J. 2006;28:596-602. [PMID: 16641120]
122. **Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J.** Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. Am J Respir Crit Care Med. 2002;166:159-65. [PMID: 12119227]
123. **Partinen M, Jamieson A, Guilleminault C.** Long-term outcome for obstructive sleep apnea syndrome patients. Mortality. Chest. 1988;94:1200-4. [PMID: 3191760]
124. **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]
125. **Anand VK, Ferguson PW, Schoen LS.** Obstructive sleep apnea: a comparison of continuous positive airway pressure and surgical treatment. Otolaryngol Head Neck Surg. 1991;105:382-90. [PMID: 1945423]
126. **Ceylan K, Emir H, Kizilkaya Z, Tastan E, Yavanoglu A, Uzunkulaoglu H, 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. Arch Otolaryngol Head Neck Surg. 2009;135:915-9. [PMID: 19770425]
127. **Conradt R, Hochban W, Heitmann J, Brandenburg U, Cassel W, Penzel T, et al.** Sleep fragmentation and daytime vigilance in patients with OSA treated by surgical maxillomandibular advancement compared to CPAP therapy. J Sleep Res. 1998;7:217-23. [PMID: 9785277]
128. **Katsantonis GP, Schweitzer PK, Branham GH, Chambers G, Walsh JK.** Management of obstructive sleep apnea: comparison of various treatment modalities. Laryngoscope. 1988;98:304-9. [PMID: 3278184]
129. **Keenan SP, Burt H, Ryan CF, Fleetham JA.** Long-term survival of patients with obstructive sleep apnea treated by uvulopalatopharyngoplasty or nasal CPAP. Chest. 1994;105:155-9. [PMID: 8275724]
130. **Lin SW, Chen NH, Li HY, Fang TJ, Huang CC, Tsai YH, 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;116:1012-6. [PMID: 16735919]
131. **Robinson S, Chia M, Carney AS, Chawla S, Harris P, Esterman A.** Upper airway reconstructive surgery long-term quality-of-life outcomes compared with CPAP for adult obstructive sleep apnea. Otolaryngol Head Neck Surg. 2009;141: 257-263. [PMID: 19643262]
132. **Vicini C, Dallan I, Campanini A, De Vito A, Barbanti F, Giorgiomarrano G, et al.** Surgery vs ventilation in adult severe obstructive sleep apnea syndrome. Am J Otolaryngol. 2010;31:14-20. [PMID: 19944893]
133. **Weaver EM, Maynard C, Yueh B.** Survival of veterans with sleep apnea: continuous positive airway pressure versus surgery. Otolaryngol Head Neck Surg. 2004;130:659-65. [PMID: 15195049]
134. **Woodson BT, Nelson L, Mickelson S, Huntley T, Sher A.** A multi-institutional study of radiofrequency volumetric tissue reduction for OSAS. Otolaryngol Head Neck Surg. 2001;125:303-11. [PMID: 11593163]
135. **Zorick FJ, Roehrs T, Conway W, Potts G, Roth T.** Response to CPAP and UPPP in apnea. Henry Ford Hosp Med J. 1990;38:223-6. [PMID: 2086548]
136. **Keenan SP, Burt H, Ryan CF, Fleetham JA.** Long-term survival of patients with obstructive sleep apnea treated by uvulopalatopharyngoplasty or nasal CPAP. Chest. 1994;105:155-9. [PMID: 8275724]
137. **Weaver EM, Maynard C, Yueh B.** Survival of veterans with sleep apnea: continuous positive airway pressure versus surgery. Otolaryngol Head Neck Surg. 2004;130:659-65. [PMID: 15195049]
138. **Walker-Engström ML, Tegelberg A, Wilhelmsson B, Ringqvist I.** 4-year follow-up of treatment with dental appliance or uvulopalatopharyngoplasty in patients with obstructive sleep apnea: a randomized study. Chest. 2002;121:739-46. [PMID: 11888954]
139. **Walker-Engström ML, Wilhelmsson B, Tegelberg A, Dimenäs E, Ringqvist I.** 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. J Sleep Res. 2000;9:303-8. [PMID: 11012871]
140. **Wilhelmsson B, Tegelberg A, Walker-Engström ML, Ringqvist M, Andersson L, Krekmanov L, et al.** A prospective randomized study of a dental appliance compared with uvulopalatopharyngoplasty in the treatment of obstructive sleep apnoea. Acta Otolaryngol. 1999;119:503-9. [PMID: 10445069]
141. **Hui DS, Choy DK, Li TS, Ko FW, Wong KK, Chan JK, et al.** Determinants of continuous positive airway pressure compliance in a group of Chinese patients with obstructive sleep apnea. Chest. 2001;120:170-6. [PMID: 11451834]
142. **Krieger J, Kurtz D, Petiau C, Sforza E, Trautmann D.** Long-term compliance with CPAP therapy in obstructive sleep apnea patients and in snorers. Sleep. 1996;19:S136-43. [PMID: 9122571]
143. **McArdle N, Devereux G, Heidarnejad H, Engleman HM, Mackay TW, Douglas NJ.** Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1999;159:1108-14. [PMID: 10194153]
144. **Wild MR, Engleman HM, Douglas NJ, Espie CA.** Can psychological factors help us to determine adherence to CPAP? A prospective study. Eur Respir J. 2004;24:461-5. [PMID: 15358707]
145. **Izci B, McDonald JP, Coleman EL, Mackay TW, Douglas NJ, Engleman HM.** Clinical audit of subjects with snoring & sleep apnoea/hypopnoea syndrome fitted with mandibular repositioning splint. Respir Med. 2005;99:337-46. [PMID: 15733510]
146. **Antic NA, Buchan C, Esterman A, Hensley M, Naughton MT, Rowland S, 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: 501-8. [PMID: 19136368]
147. **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;130:1369-76. [PMID: 17099012]
148. **Chervin RD, Theut S, Bassetti C, Aldrich MS.** Compliance with nasal CPAP can be improved by simple interventions. Sleep. 1997;20:284-9. [PMID: 9231954]
149. **Damjanovic D, Fluck A, Bremer H, Müller-Quernheim J, Idzko M, Sorichter S.** Compliance in sleep apnoea therapy: influence of home care support and pressure mode. Eur Respir J. 2009;33:804-11. [PMID: 19129293]
150. **DeMolles DA, Sparrow D, Gottlieb DJ, Friedman R.** A pilot trial of a telecommunications system in sleep apnea management. Med Care. 2004;42: 764-9. [PMID: 15258478]
151. **Fletcher EC, Luckett RA.** The effect of positive reinforcement on hourly compliance in nasal continuous positive airway pressure users with obstructive sleep apnea. Am Rev Respir Dis. 1991;143:936-41. [PMID: 2024846]
152. **Holmdahl C, Schöllin IL, Alton M, Nilsson K.** CPAP treatment in obstructive sleep apnoea: a randomised, controlled trial of follow-up with a focus on patient satisfaction. Sleep Med. 2009;10:869-74. [PMID: 19179111]
153. **Hoy CJ, Vennelle M, Kingshott RN, Engleman HM, Douglas NJ.** Can intensive support improve continuous positive airway pressure use in patients with the sleep apnea/hypopnea syndrome? Am J Respir Crit Care Med. 1999; 159:1096-100. [PMID: 10194151]
154. **Hui DS, Chan JK, Choy DK, Ko FW, Li TS, Leung RC, et al.** Effects of augmented continuous positive airway pressure education and support on compliance and outcome in a Chinese population. Chest. 2000;117:1410-6. [PMID: 10807830]

155. **Jean Wiese H, Boethel C, Phillips B, Wilson JF, Peters J, Viggiano T.** CPAP compliance: video education may help!. Sleep Med. 2005;6:171-4. [PMID: 15716221]
156. **Lewis KE, Bartle IE, Watkins AJ, Seale L, Ebden P.** Simple interventions improve re-attendance when treating the sleep apnoea syndrome. Sleep Med. 2006;7:241-7. [PMID: 16564210]
157. **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;123:1112-8. [PMID: 12684301]
158. **Meurice JC, Ingrand P, Portier F, Arnulf I, Rakotonanahari D, Fournier E, et al; ANTADIR Working Group "PPC", CMTS ANTADIR.** A multicentre trial of education strategies at CPAP induction in the treatment of severe sleep apnoea-hypopnoea syndrome. Sleep Med. 2007;8:37-42. [PMID: 17157557]
159. **Palmer S, Selvaraj S, Dunn C, Osman LM, Cairns J, Franklin D, et al.** Annual review of patients with sleep apnea/hypopnea syndrome—a pragmatic randomised trial of nurse home visit versus consultant clinic review. Sleep Med. 2004;5:61-5. [PMID: 14725828]
160. **Richards D, Bartlett DJ, Wong K, Malouff J, Grunstein RR.** Increased adherence to CPAP with a group cognitive behavioral treatment intervention: a randomized trial. Sleep. 2007;30:635-40. [PMID: 17552379]
161. **Smith CE, Dauz E, Clements F, Werkowitch M, Whitman R.** Patient education combined in a music and habit-forming intervention for adherence to continuous positive airway (CPAP) prescribed for sleep apnea. Patient Educ Couns. 2009;74:184-90. [PMID: 18829212]
162. **Stepnowsky CJ, Palau JJ, Marler MR, Gifford AL.** Pilot randomized trial of the effect of wireless telemonitoring on compliance and treatment efficacy in obstructive sleep apnea. J Med Internet Res. 2007;9:e14. [PMID: 17513285]
163. **Taylor Y, Eliasson A, Andrada T, Kristo D, Howard R.** The role of telemedicine in CPAP compliance for patients with obstructive sleep apnea syndrome. Sleep Breath. 2006;10:132-8. [PMID: 16565867]
164. **Lettieri CJ, Collen JF, Eliasson AH, Quast TM.** Sedative use during continuous positive airway pressure titration improves subsequent compliance: a randomized, double-blind, placebo-controlled trial. Chest. 2009;136:1263-8. [PMID: 19567493]
165. **Lettieri CJ, Shah AA, Holley AB, Kelly WF, Chang AS, Roop SA; CPAP Promotion and Prognosis-The Army Sleep Apnea Program Trial.** Effects of a short course of eszopiclone on continuous positive airway pressure adherence: a randomized trial. Ann Intern Med. 2009;151:696-702. [PMID: 19920270]

Current Author Addresses: Drs. Qaseem and Starkey: 190 N. Independence Mall West, Philadelphia, PA 19106.
Drs. Holty and Owens: Stanford University, 117 Encina Commons, Stanford, CA 94305.
Dr. Dallas: Carilion School of Medicine, 1906 Bellview Avenue, Roanoke, VA 24014.
Dr. Shekelle: West Los Angeles Veterans Affairs Medical Center, 11301 Wilshire Boulevard, Los Angeles, CA 90073.

Author Contributions: Conception and design: A. Qaseem, D.K. Owens.
Analysis and interpretation of the data: A. Qaseem, J.E.C. Holty, D.K. Owens, P. Dallas, M. Starkey, P. Shekelle.
Drafting of the article: A. Qaseem, P. Dallas, M. Starkey.
Critical revision for important intellectual content: A. Qaseem, J.E.C. Holty, D.K. Owens, P. Dallas, M. Starkey, P. Shekelle.
Final approval of the article: A. Qaseem, J.E.C. Holty, D.K. Owens, P. Dallas, P. Shekelle.
Provision of study materials or patients: A. Qaseem.
Statistical expertise: A. Qaseem.
Obtaining of funding: A. Qaseem.
Administrative, technical, or logistic support: A. Qaseem, M. Starkey.
Collection and assembly of data: A. Qaseem, J.E.C. Holty.

166. **Chakravorty I, Cayton RM, Szczepura A.** Health utilities in evaluating intervention in the sleep apnoea/hypopnoea syndrome. Eur Respir J. 2002;20:1233-8. [PMID: 12449179]
167. **Ip MS, Tse HF, Lam B, Tsang KW, Lam WK.** Endothelial function in obstructive sleep apnea and response to treatment. Am J Respir Crit Care Med. 2004;169:348-53. [PMID: 14551167]
168. **Faccenda JF, Mackay TW, Boon NA, Douglas NJ.** 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;163:344-8. [PMID: 11179104]
169. **Redline S, Adams N, Strauss ME, Roebuck T, Winters M, Rosenberg C.** Improvement of mild sleep-disordered breathing with CPAP compared with conservative therapy. Am J Respir Crit Care Med. 1998;157:858-65. [PMID: 9517603]
170. **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;164:1459-63. [PMID: 11704596]
171. **Hukins C.** Comparative study of autotitrating and fixed-pressure CPAP in the home: a randomized, single-blind crossover trial. Sleep. 2004;27:1512-7. [PMID: 15683142]
172. **Nussbaumer Y, Bloch KE, Genser T, Thurnheer R.** Equivalence of auto-adjusted and constant continuous positive airway pressure in home treatment of sleep apnea. Chest. 2006;129:638-43. [PMID: 16537862]
173. **Becker HF, Jerrentrup A, Ploch T, Grote L, Penzel T, Sullivan CE, et al.** Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. Circulation. 2003;107:68-73. [PMID: 12515745]
174. **Haensel A, Norman D, Natarajan L, Bardwell WA, Ancoli-Israel S, Dimsdale JE.** Effect of a 2 week CPAP treatment on mood states in patients with obstructive sleep apnea: a double-blind trial. Sleep Breath. 2007;11:239-44. [PMID: 17503102]
175. **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;116:1545-9. [PMID: 10593774]
176. **Loredo JS, Ancoli-Israel S, Kim EJ, Lim WJ, Dimsdale JE.** Effect of continuous positive airway pressure versus supplemental oxygen on sleep quality in obstructive sleep apnea: a placebo-CPAP-controlled study. Sleep. 2006;29:564-71. [PMID: 16676791]
177. **Mills PJ, Kennedy BP, Loredo JS, Dimsdale JE, Ziegler MG.** Effects of nasal continuous positive airway pressure and oxygen supplementation on norepinephrine kinetics and cardiovascular responses in obstructive sleep apnea. J Appl Physiol. 2006;100:343-8. [PMID: 16357087]
178. **Norman D, Loredo JS, Nelesen RA, Ancoli-Israel S, Mills PJ, Ziegler MG, et al.** Effects of continuous positive airway pressure versus supplemental oxygen on 24-hour ambulatory blood pressure. Hypertension. 2006;47:840-5. [PMID: 16585412]
179. **Spicuzza L, Bernardi L, Balsamo R, Ciancio N, Polosa R, Di Maria G.** Effect of treatment with nasal continuous positive airway pressure on ventilatory response to hypoxia and hypercapnia in patients with sleep apnea syndrome. Chest. 2006;130:774-9. [PMID: 16963674]
180. **Campos-Rodriguez F, Grilo-Reina A, Perez-Ronchel J, Merino-Sanchez M, Gonzalez-Benitez MA, Beltran-Robles M, et al.** Effect of continuous positive airway pressure on ambulatory BP in patients with sleep apnea and hypertension: a placebo-controlled trial. Chest. 2006;129:1459-67. [PMID: 16778262]
181. **Coughlin SR, Mawdsley L, Mugarza JA, Wilding JP, Calverley PM.** Cardiovascular and metabolic effects of CPAP in obese males with OSA. Eur Respir J. 2007;29:720-7. [PMID: 17251237]
182. **Hui DS, To KW, Ko FW, Fok JP, Chan MC, Ngai JC, et al.** Nasal CPAP reduces systemic blood pressure in patients with obstructive sleep apnoea and mild sleepiness. Thorax. 2006;61:1083-90. [PMID: 16928705]
183. **Jenkinson C, Davies RJ, Mullins R, Stradling JR.** Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet. 1999;353:2100-5. [PMID: 10382693]
184. **Lam JC, Lam B, Yao TJ, Lai AY, Ooi CG, Tam S, et al.** A randomised controlled trial of nasal continuous positive airway pressure on insulin sensitivity in obstructive sleep apnoea. Eur Respir J. 2010;35:138-45. [PMID: 19608589]
185. **Robinson GV, Smith DM, Langford BA, Davies RJ, Stradling JR.** Continuous positive airway pressure does not reduce blood pressure in nonsleepy hypertensive OSA patients. Eur Respir J. 2006;27:1229-35. [PMID: 16455835]
186. **West SD, Kohler M, Nicoll DJ, Stradling JR.** The effect of continuous positive airway pressure treatment on physical activity in patients with obstructive sleep apnoea: A randomised controlled trial. Sleep Med. 2009;10:1056-8. [PMID: 19427263]
187. **West SD, Nicoll DJ, Wallace TM, Matthews DR, Stradling JR.** Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. Thorax. 2007;62:969-74. [PMID: 17557769]
188. **Fietze I, Glos M, Moebus I, Witt C, Penzel T, Baumann G.** Automatic pressure titration with APAP is as effective as manual titration with CPAP in patients with obstructive sleep apnea. Respiration. 2007;74:279-86. [PMID: 17337881]
189. **Galetke W, Anduleit N, Richter K, Stieglitz S, Randerath WJ.** Comparison of automatic and continuous positive airway pressure in a night-by-night analysis: a randomized, crossover study. Respiration. 2008;75:163-9. [PMID: 17148931]
190. **Hussain SF, Love L, Burt H, Fleetham JA.** A randomized trial of autotitrating CPAP and fixed CPAP in the treatment of obstructive sleep apnea-hypopnea. Respir Med. 2004;98:330-3. [PMID: 15072173]
191. **Massie CA, McArdle N, Hart RW, Schmidt-Nowara WW, Lankford A, Hudgel DW, et al.** Comparison between automatic and fixed positive airway pressure therapy in the home. Am J Respir Crit Care Med. 2003;167:20-3. [PMID: 12406840]
192. **Meurice JC, Cornette A, Philip-Joet F, Pepin JL, Escourrou P, Ingrand P, et al; ANTADIR "PPC" Working Group.** Evaluation of autoCPAP devices in home treatment of sleep apnea/hypopnea syndrome. Sleep Med. 2007;8:695-703. [PMID: 17638595]
193. **Nolan GM, Doherty LS, Mc Nicholas WT.** Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. Sleep. 2007;30:189-94. [PMID: 17326544]
194. **Patruno V, Aiolfi S, Costantino G, Murgia R, Selmi C, Malliani A, 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;131:1393-9. [PMID: 17494789]
195. **Riley RW, Powell NB, Guilleminault C.** Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. Otolaryngol Head Neck Surg. 1993;108:117-25. [PMID: 8441535]
196. **Riley RW, Powell NB, Guilleminault C, Pelayo R, Troell RJ, Li KK.** Obstructive sleep apnea surgery: risk management and complications. Otolaryngol Head Neck Surg. 1997;117:648-52. [PMID: 9419093]
197. **Steward DL, Huntley TC, Woodson BT, Surdulescu V.** Palate implants for obstructive sleep apnea: multi-institution, randomized, placebo-controlled study. Otolaryngol Head Neck Surg. 2008;139:506-10. [PMID: 18922335]
198. **Stuck BA, Starzak K, Verse T, Hörmann K, Maurer JT.** Complications of temperature-controlled radiofrequency volumetric tissue reduction for sleep-disordered breathing. Acta Otolaryngol. 2003;123:532-5. [PMID: 12797590]

Appendix Table. Evidence Summary for Interventions for OSA*

Intervention	Overall Effect†	Strength of Evidence	Summary of Evidence					Potential AE
			AHI Score Difference	ESS Score Difference	AI Score Difference	Minimum Oxygen Saturation	Other	
CPAP								
CPAP vs. no treatment CPAP vs. sham	CPAP superior CPAP superior	Moderate	−19.85 events/h (95% CI, −26.06 to −13.65 events/h); $P < 0.001$; $I^2 = 86.0\%$ (8, 9, 11, 12, 23, 166, 167) −46.39 events/h (95% CI, −56.97 to −35.81 events/h); $P < 0.001$; $I^2 = 69.6\%$ (42, 173–179)	−2.37 events/h (CI, −3.23 to −1.51 events/h); $P < 0.001$; $I^2 = 66.0\%$ (8, 9, 11–15, 17, 19, 166, 168, 169) −2.5 events/h (CI, −3.5 to −1.5 events/h); $P < 0.001$ (40–45, 173, 176, 180–187)	−14.71 events/h (CI, −22.23 to −7.19 events/h); $P < 0.001$; $I^2 = 83.5\%$ (11, 12, 23, 167, 170) −27 events/h (CI, −42 to −12 events/h; $P < 0.001$) (173, 175, 176)	12.05% (CI, 6.35% to 17.74%); $P < 0.001$; $I^2 = 75.1\%$ (8, 11, 12, 23, 167) NA	22 trials (11 moderate and 11 low-quality) No significant improvement in sleep efficiency (11, 166) Overall, no consistent benefit in quality-of-life or neurocognitive measures 24 trials (5 high-, 13 moderate-, and 6 low-quality). Overall, no consistent benefit in quality-of-life or neurocognitive measures.	Claustrophobia, skin irritation, nasal irritation or obstruction, dry nose or mouth, excess salivation, minor or moderate sore gums or lips, minor aerophagia, abdominal distention, minor chest wall discomfort, pressure discomfort, and transient or minor epistaxis (46, 47, 87, 131, 171, 172).
Oral CPAP vs. nasal CPAP	–	Insufficient	NA	NA	NA	NA	3 small trials (1 moderate- and 2 low-quality) had inconsistent results and generally imprecise effect estimates (46–48); 1 study found increased adherence to nasal CPAP treatment; 2 studies found no significant difference (46–48).	
Auto-CPAP vs. fixed CPAP	Interventions equal	Moderate	0.23 events/h (CI, −0.18 to 0.64 events/h); $P = 0.268$; $I^2 = 0\%$ (58–62, 149, 172, 188–194)	−0.48 events/h (CI, −0.86 to −0.11 events/h); $P = 0.012$; $I^2 = 12.7\%$ (58–61, 63–68, 149, 172, 189–193)	−1.09 events/h (CI, −2.4 to 0.2 events/h); $P = 0.10$; $I^2 = 0\%$ (58–60, 149, 189, 190, 193)	−1.34 h total sleep time (CI, −2.24 to −0.45); $P = 0.03$; $I^2 = 0\%$ (59, 60, 189, 190, 192–194)	21 trials (1 high-, 10 moderate-, and 1 low-quality) Difference in adherence, 0.19 h (95% CI, 0.06 to 0.33); $P = 0.006$; $I^2 = 16.4\%$ (58–68, 149, 171, 172, 188–194) No consistent difference in quality-of-life metrics	
Bilevel CPAP vs. fixed CPAP	–	Insufficient	NA	NA	NA	NA	5 small, heterogeneous trials (1 moderate- and 4 low-quality) with mostly imprecise effect estimates showed mostly null findings for efficacy and no difference for adherence (49–51, 81).	
Flexible bilevel CPAP vs. fixed CPAP	–	Insufficient	NA	NA	NA	NA	1 moderate-quality study (85) showed that more patients used flexible bilevel CPAP devices for >4 h per night (49% vs. 28%; $P = 0.03$) and for more hours per night (3.7 vs. 2.9 h/night; $P < 0.05$) compared with fixed CPAP devices.	

Continued on following page

Appendix Table—**Continued**

Intervention	Overall Effect†	Strength of Evidence	Summary of Evidence					Potential AE
			AHI Score Difference	ESS Score Difference	AI Score Difference	Minimum Oxygen Saturation	Other	
C-Flex vs. fixed CPAP	Interventions equal	Low	NA	−0.23 events/h (CI, −0.74 to 0.27 events/h); $P = 0.36$	NA	NA	4 studies (2 low- and 2 moderate-quality) showed no significant differences for adherence, AHI score, minimum oxygen saturation, arousals, sleep stages, or quality of life (53, 54, 82, 83).	
CPAP with or without humidification	–	Insufficient	NA	NA	NA	NA	5 small, clinically heterogeneous studies (3 moderate- and 2 low-quality) reported inconsistent results (55, 84–87).	
MADs								
MADs vs. no treatment	MADs superior	Moderate	−11 events/h (CI, −15 to −8 events/h); $I^2 = 55.3\%$ (11, 12, 56, 88)	−1.2 events/h (CI, −1.7 to −0.6 events/h); $I^2 = 45.0\%$ (11, 12, 56, 88)	−7.9 events/h (CI, −14 to −1.3 events/h); $I^2 = 80.4\%$ (11, 12, 88)	2.98% (CI, 0.43% to 5.54%); $I^2 = 37.8\%$ (11, 12)	5 studies (4 moderate- and 1 low-quality) Overall, no significant differences for quality-of-life assessments 1 small observational study ($n = 25$) found no significant mortality difference between MAD treatment–adherent (30.8%) vs. MAD treatment–nonadherent (66.7%; $P = 0.073$) patients with congestive heart failure OSA (69).	Sleep disruption, sensations of pressure in the mouth, mucosal erosions, excessive salivation, dental crown damage, teeth loosening, tooth, mouth and jaw damage, TMJ pain (2%–4% of patients) (56, 92, 96, 97, 138).
MADs vs. sham	MADs superior	Moderate	14.04 events/h (CI, −20.06 to −8.02 events/h); $I^2 = 0\%$ (92–94)	−1.95 events/h (CI, −2.93 to −0.97 events/h); $I^2 = 0.0\%$ (91, 92, 94)	−10 events/h (CI, −16 to −5 events/h); $P = 0.001$ (93, 94)	3.1% (CI, 1.4% to 4.8%); $I^2 = 37.8\%$ (93, 94)	5 studies (4 moderate- and 1 low-quality) 1 study (132, 133) showed improvements in the Multiple Sleep Latency Test results ($P = 0.01$), somatic items on the Beck Depression Inventory scale ($P < 0.05$), choice reaction time task on the neuropsychological test ($P < 0.001$), and reductions in 24-h SBP ($P < 0.05$) and DBP ($P < 0.001$) with MADs compared with control treatment.	

Continued on following page

Appendix Table—Continued

Intervention	Overall Effect†	Strength of Evidence	Summary of Evidence					Potential AE
			AHI Score Difference	ESS Score Difference	AI Score Difference	Minimum Oxygen Saturation	Other	
MADs vs. CPAP	CPAP superior	Moderate	7.7 events/h (CI, 5.3 to 10.1 events/h); $P < 0.001$; $I^2 = 60.3\%$ (11, 12, 95, 97–99, 101–103)	1.27 events/h (CI, −0.23 to 2.77 events/h); $P = 0.098$; $I^2 = 89.3\%$ (11, 12, 96, 98, 99, 102, 103)	3.5 events/h (CI, 1.5 to 5.5 events/h); $P = 0.001$; $I^2 = 47\%$ (11, 12, 101–103)	−3.5% (CI, −4.6% to −2.4%); $P < 0.001$; $I^2 = 34.5\%$ (11, 12, 95, 97, 99, 101, 102)	10 moderate-quality studies 1 study found that although CPAP treatment was better at improving quality of life as determined by SAQLI, patients had more treatment-related symptoms (12). 1 study assessed adherence and found that patients used MADs more than CPAP devices for more hours during the night (7.0 vs. 6.0 h/night; $P < 0.01$) and for more nights (98% vs. 90% of nights; $P < 0.01$) (98). 2 studies assessed treatment effect as a dichotomous outcome; 1 found that CPAP treatment more effectively achieved an AHI score of <5 events/h (normal AHI score range) in all patients compared with MADs (risk difference, −20% [CI, −3% to −2%]; $P = 0.02$) (78). The other study found no differences (98).	
Weight loss vs. control	Weight loss superior	Low	NA	NA	NA	NA	3 trials (1 high- and 2 moderate-quality) found reductions in AHI scores with intensive weight-loss programs (104–106).	None
Drug therapy vs. control	–	Insufficient	NA	NA	NA	NA	7 trials (1 low-, 5 moderate-, and 1 high-quality) (86, 107–112) assessed mirtazapine, xylometazoline, fluticasone, paroxetine, pantoprazole, steroid plus CPAP treatment (vs. CPAP treatment alone), acetazolamide, and protriptyline. Only 1 study assessed each drug.	Acetazolamide had the most reported AEs, including paresthesia. Protriptyline was associated with severe dry mouth, visual upset, urinary symptoms, and altered sexual potency. Paroxetine was associated with ejaculation disturbance, decreased libido, headache, and constipation. Patients taking zolpidem had episodes of sleepwalking (110, 112, 147).

Continued on following page

Appendix Table—Continued

Intervention	Overall Effect†	Strength of Evidence	Summary of Evidence					Potential AE
			AHI Score Difference	ESS Score Difference	AI Score Difference	Minimum Oxygen Saturation	Other	
Surgical interventions								
Surgery vs. control	–	NA	NA	NA	NA	7 studies (3 high-, 1 moderate-, and 3 low-quality) (18, 113–119) each assessed different interventions, and results were inconsistent. 12 studies (1 high- and 11 low-quality) (119, 125–135) each assessed different interventions compared with CPAP treatment, and results were inconsistent. 1 moderate-quality study was available, which found that MADs improved AHI scores compared with surgery with UPPP (138–140).	AEs related to surgical interventions varied. The most serious AEs occurred in patients having oronasopharyngeal or bariatric surgery, including perioperative deaths. Others from surgical interventions included major postsurgical complications, such as hemorrhage, nerve palsies, emergency surgical treatments, cardiovascular events, respiratory failure, and rehospitalizations. Long-term AEs included speech or voice changes, difficulties swallowing, and airway stenosis (18, 70–78, 114, 125, 134, 138, 195–198).	
Surgery vs. CPAP	–	NA	NA	NA	NA			
Surgery vs. MADs	–	NA	NA	NA	NA			

AE = adverse effect; AHI = Apnea–Hypopnea Index; AI = arousal index; CPAP = continuous positive airway pressure; DBP = diastolic blood pressure; ESS = Epworth Sleepiness Scale; MAD = mandibular advancement device; NA = not available; SBP = systolic blood pressure; SAQLI = Sleep Apnea Quality of Life Index; TMJ = temporomandibular joint; UPPP = uvulopalatopharyngoplasty.

* Data were derived from a meta-analysis of relevant randomized, controlled trials.

† For comparisons with insufficient evidence, differentiations could not be made between the interventions.