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CLINICAL GUIDELINE

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

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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)

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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

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* 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.

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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.	

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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.	

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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).

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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	–	Insufficient	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	–	Insufficient	NA	NA	NA	NA		
Surgery vs. MADs	–	Insufficient	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.