AMERICAN THORACIC SOCIETY DOCUMENTS

The Role of Weight Management in the Treatment of Adult Obstructive Sleep Apnea

An Official American Thoracic Society Clinical Practice Guideline: Executive Summary

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Background: Overweight/obesity is a common, reversible risk factor for obstructive sleep apnea severity (OSA). The purpose of this guideline is to provide evidence-based recommendations for the management of overweight/obesity in patients with OSA.

Methods: The Grading of Recommendations, Assessment, Development and Evaluation approach was used to evaluate the literature. Clinical recommendations were formulated by a panel of pulmonary, sleep medicine, weight management, and behavioral science specialists.

Results: Behavioral, pharmacological, and surgical treatments promote weight loss and can reduce OSA severity, reverse common comorbidities, and improve quality of life, although published studies have methodological limitations. After considering the quality of evidence, feasibility, and acceptability of these interventions, the panel made a strong recommendation that patients with OSA who are overweight or obese be treated with comprehensive lifestyle intervention consisting of *1*) a reduced-calorie diet, *2*) exercise or increased physical activity, and *3*) behavioral guidance. Conditional recommendations were made regarding reduced-calorie diet and exercise/increased physical activity as separate management tools. Pharmacological therapy and bariatric surgery are appropriate for selected patients who require further assistance with weight loss.

Conclusions: Weight-loss interventions, especially comprehensive lifestyle interventions, are associated with improvements in OSA severity, cardiometabolic comorbidities, and quality of life. The American Thoracic Society recommends that clinicians regularly assess weight and incorporate weight management strategies that are tailored to individual patient preferences into the routine treatment of adult patients with OSA who are overweight or obese.

Keywords: obstructive sleep apnea; obesity; comprehensive lifestyle intervention; weight-loss medications; bariatric surgery

Contents

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Overview

Although previously developed guidelines on the treatment of adult obstructive sleep apnea (OSA) recommended weight loss for patients who are overweight or obese, detailed analyses of the impact of weight-loss therapies on OSA and its sequelae, as well as recommendations on specific weight management strategies, were not provided. The purpose of this clinical practice guideline is to *1*) review the evidence of the impact of weight-loss interventions on OSA severity, quality of life, and associated comorbidities and *2*) provide specific recommendations for weight management in adult patients with OSA who are overweight or obese, as defined as a body mass index (BMI) greater than or equal to 25 kg/m^2. A panel of sleep and pulmonary physicians, weight management experts, and behavioral scientists developed seven therapy-related questions, reviewed the relevant literature, and used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to summarize the outcomes and shortcomings of the literature. On the basis of this analysis, evidence-based recommendations were made for the management of overweight/obesity in adults with OSA.

The following questions were developed for the evidence-based review:

Question 1: Should a reduced-calorie diet be recommended (rather than no diet) to patients with OSA who are overweight or obese?

Question 2: Should exercise/increased physical activity be recommended (rather than no exercise) to patients with OSA who are overweight or obese?

Question 3: Should both a reduced-calorie diet and exercise/increased physical activity be recommended (rather than a reduced-calorie diet alone) to patients with OSA who are overweight or obese?

Question 4: Should a comprehensive lifestyle intervention (i.e., a program that includes a reduced-calorie diet, exercise/increased physical activity, and behavioral counseling) be recommended (rather than no weight-loss intervention) to patients with OSA who are overweight or obese?

Question 5: Should a comprehensive lifestyle intervention (i.e., a program that includes a reduced-calorie diet, exercise/increased physical activity, and behavioral counseling) be recommended (rather than a reduced-calorie diet alone) to patients with OSA who are overweight or obese?

Question 6: Should weight-loss medications be recommended (rather than comprehensive lifestyle intervention alone) to patients with OSA who are overweight or obese and who have been unsuccessful in losing weight with lifestyle intervention?

Question 7: Should bariatric surgery be recommended (rather than comprehensive lifestyle intervention alone) to patients with OSA who are overweight or obese and who have been unsuccessful in losing weight with lifestyle intervention?

Summary of Recommendations

1. For patients with OSA who are overweight or obese (i.e., BMI $\geqslant$25 kg/m^2):
   a. We **recommend** participation in a comprehensive lifestyle intervention program that includes a reduced-calorie diet, exercise/increased physical activity, and behavioral counseling rather than no program (strong recommendation, very low certainty in the estimated effects).
   b. We **suggest** participation in a comprehensive lifestyle intervention program that includes a reduced-calorie diet, exercise/increased physical activity, and behavioral counseling rather than a program that includes only a reduced-calorie diet, with or without exercise/increased physical activity (conditional recommendation, very low certainty in the estimated effects).
   c. We **suggest** participation in a reduced-calorie diet (with or without exercise/increased physical activity) rather than no diet (conditional recommendation, very low certainty in the estimated effects).
   d. We **suggest** exercise/increased physical activity rather than no exercise or increased physical activity (conditional recommendation, very low certainty in the estimated effects).
2. For patients with OSA with a BMI greater than or equal to 27 kg/m^2, whose weight has not improved despite

participating in a comprehensive weight-loss lifestyle program, and who have no contraindications including no active cardiovascular disease, we **suggest** an evaluation for antiobesity pharmacotherapy (conditional recommendation, very low certainty in the estimated effects).

3. For patients with OSA with a BMI greater than or equal to 35 kg/m^2, whose weight has not improved despite participating in a comprehensive weight-loss lifestyle intervention program, and who have no contraindications, we **suggest** referral for bariatric surgery evaluation (conditional recommendation, very low certainty in the estimated effects).

Note: In recommending weight management strategies for patients with OSA who are overweight or obese, it is recommended that clinicians discuss options and involve patients in shared decision-making, considering their values and preferences (*see* Discussion section below).

Introduction

The relationship between weight gain and the development and worsening of OSA is well established (1–4). Furthermore, obesity and OSA are complexly intertwined because obesity is an aggravating factor for many of the known metabolic and cardiovascular comorbidities of OSA (5, 6). Published guidelines for the management of OSA acknowledge obesity as an exacerbating factor for OSA and mention weight loss as an adjunctive therapeutic tool (7–10). However, none provides detailed recommendations about how to achieve weight loss. Perhaps the absence of specific clinically relevant recommendations has contributed to limited implementation of weight-loss counseling in the routine care of patients with OSA who are overweight or obese.

To address this knowledge gap, this project was developed by the chair and co-chair and approved by the board of directors of the American Thoracic Society (ATS). A panel of pulmonary and sleep medicine specialists, weight management experts, behavioral scientists, and patients was created to summarize the relevant evidence and make recommendations regarding weight-loss interventions in the care of patients with OSA who are overweight or obese. Overweight was defined as a BMI of 25.0–29.9 kg/m^2 (or in some studies BMI of 27.0–29.9 kg/m^2) and obesity as a BMI greater than or equal to 30 kg/m^2, which can be further divided into grade I obesity (BMI, $\geqslant$30.0–34.9 kg/m^2), grade II obesity (BMI, $\geqslant$35–39.9 kg/m^2), and grade III obesity (BMI, $\geqslant$40.0 kg/m^2). The cutoffs used in various regions of the world for categorizing people as overweight or obese may be different based on ethnic and/or racial differences defining the risks for weight-related disorders in different populations.

Methods

This guideline was developed in accordance with ATS standards, which included a systematic review for each question and use of the GRADE approach to appraise the quality of evidence, formulate and write the recommendations, and rate the strength of each recommendation (11–16). These methods are described in detail in the online supplement. The meanings of "strong" and "conditional" recommendations are described in Table 1, and the methods employed are summarized in Table 2.

Results

Question 1: Should a Reduced-Calorie Diet Be Recommended (Rather Than No Diet) to Patients with OSA Who Are Overweight or Obese?

Summary of the evidence from non-OSA literature. The NIH/NHLBI guideline found a strong and consistent effect of reduced-calorie diets consisting of approximately 1,000–1,200 kcal/d in inducing weight loss, with a mean weight loss of 8% of body weight compared with control (17). The American Heart Association/American College of Cardiology (AHA/ACC) guideline found no difference in weight loss between diet types once the amount of caloric deficit was controlled (18).

Summary of the evidence from OSA-specific literature. Our literature search identified two relevant randomized trials and an abstract (19–21); the abstract reported on a study in progress and did not include sufficient data for analysis (19). The trials could not be pooled, because they reported outcomes differently.

Table 1. Implications of Strong and Conditional Recommendations

	Strong Recommendation	Conditional Recommendation
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for different patients and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful in helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
For policy makers	The recommendation can be adopted as policy in most situations, including for use as performance indicators.	Policy making will require substantial debate and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

Table 2. Summary of Guideline Development Methods

Activity	Yes	No
Panel assembly included experts for relevant clinical and nonclinical disciplines	X	
Included a methodologist with appropriate expertise (documented expertise in conducting systematic reviews to identify the evidence base and the development of evidence-based recommendations)	X	
Included an individual who represents the views of patients and society at large	X	
Literature review performed in collaboration with librarian	X	
Searched multiple electronic databases; reviewed reference lists of retrieved articles	X	
Evidence synthesis applied prespecified inclusion and exclusion criteria	X	
Evaluated included studies for sources of bias	X	
Used GRADE to describe quality of evidence	X	
Generation of recommendations used GRADE to rate the strength of recommendations	X	

Definition of abbreviation: GRADE = Grading of Recommendations, Assessment, Development and Evaluation.

The earlier trial randomly assigned 23 moderately obese patients with snoring and excessive daytime sleepiness to either caloric restriction or no dietary changes (20). Weight-loss group patients lost weight relative to control individuals (mean difference [MD], 11.0 kg more in the weight-loss group; 95% confidence interval [CI], 39.5 kg more to 17.5 kg less), and they had decreases in the apnea–hypopnea index (AHI) during non-REM and REM sleep (MD, 30.3 fewer events/h; 95% CI, 1.9 to 58.7 fewer events/h).

A later trial found similar results after 4 months in 29 patients with obesity and OSA by a reduction in calorie consumption by 800 kcal/d for 4 months (21). Patients in the weight-loss group lost weight (MD, 6.0 kg more weight loss; 95% CI, 16.7 kg more to 4.7 kg less weight loss) and BMI (MD, 2.0 kg/m^2 lower; 95% CI, 3.4 to 0.5 kg/m^2 lower), and they had decreases in neck circumference (MD, 0.8 cm smaller; 95% CI, 0.1 to 1.5 cm smaller) and AHI (7.35 fewer events/h; 95% CI, 0.8 to 13.9 fewer events/h), with control individuals having minimal changes in these variables. All of the changes in assessed variables noted above were statistically significant, except the weight loss in kilograms (20, 21).

Neither trial reported on quality of life, daytime sleepiness, other OSA-related symptoms, glycemic control, cardiovascular events, mortality, or adverse events. The panel's confidence in the estimated effects was very low because the trials were small with a serious risk of bias due to the absence of blinding and high dropout rates.

Conclusions. In patients with OSA who are overweight or obese, a weight-loss program focusing on reduced-calorie diet alone was associated with decreases in body weight and neck circumference and a reduction in OSA severity. Adverse effects were not reported. The panel judged that the benefits of a weight-loss program focusing on diet outweigh the risks, burdens, and costs, but the panel's confidence was tempered by its very low certainty in the estimated effects.

Recommendation. For patients with OSA who are overweight or obese, we **suggest** participation in a reduced-calorie diet (with or without exercise/increased physical activity) rather than no diet (conditional recommendation, very low certainty in the estimated effects).

Question 2: Should Exercise/Increased Physical Activity Be Recommended (Rather Than No Exercise) to Patients with OSA Who Are Overweight or Obese?; and Question 3: Should Both a Reduced-Calorie Diet and Exercise/Increased Physical Activity Be Recommended (Rather Than a Reduced-Calorie Diet Alone) to Patients with OSA Who Are Overweight or Obese?

Summary of the evidence from non-OSA literature. The NIH/NHLBI review evaluated studies assessing the impact of increased physical activity, typically aerobic activities, with or without diet (17). Further study found that exercise plus diet versus diet alone led to a significantly greater weight loss than occurred with diet alone, but only in studies lasting more than 1 year (22). In addition, aerobic exercise has been found to produce a clinically significant reduction in blood pressure (23, 24).

Summary of the evidence from OSA-specific literature. Eight published papers (25–30) were identified assessing exercise versus no exercise, although two of these studies were not analyzed further because of lack of recruitment specifically of patients with OSA (30, 31). There were no trials comparing exercise plus reduced-calorie diet versus reduced-calorie diet alone. Measured outcomes of interest included weight, AHI, daytime sleepiness, sleep quality, mortality, and adverse events (*see* Table E1 in the online supplement).

When the trials were pooled, exercise was not associated with weight loss (MD, +2.1 kg; 95% CI, −4.3 to +8.6 kg), change in BMI (MD, −0.04 kg/m^2; 95% CI, −1.7 to +1.6 kg/m^2), or change in neck circumference (MD, +0.4 cm; 95% CI, −1.5 to +2.4 cm). There were also no changes in the AHI (MD, −0.8 events/h; 95% CI, −13.4 to +11.8 events/h), mortality, daytime sleepiness, or adverse events. The only significant change among the pooled outcomes was a minimal improvement in sleep quality, as measured by the Pittsburgh Sleep Quality Index (MD, −2.7; 95% CI, −4.3 to −1.0), with the postexercise value remaining in the poor sleep range (32). Improvements in depression, fatigue, vigor, vitality, and physical functioning (25) as well as serum glucose (26) were found in single studies. The panel's confidence in these estimated effects was very low because the trials were small with a serious risk of bias due to the absence of blinding and short durations of follow-up.

Conclusions. For patients with OSA who are overweight or obese, exercise/increased physical activity does not produce clinically significant weight loss or improvement in OSA severity. Exercise/increased physical activity is associated with a minimal improvement in sleep quality, serum glucose, depression, fatigue, vigor, vitality, and physical functioning, and there is evidence for a benefit in blood pressure in the general

obesity literature. The panel judges that the benefits of exercise/increased physical activity likely outweigh the risks and burdens in most patients with OSA who are overweight or obese. The effects of exercise are applicable to general well-being rather than to OSA *per se*. The panel's certainty was tempered by its very low confidence in the estimated effects.

Recommendation. For patients with OSA who are overweight or obese, we **suggest** exercise/increased physical activity, rather than no exercise/increased physical activity, regardless of whether a reduced-calorie diet is added (conditional recommendation, very low certainty in the estimated effects).

Question 4: Should a Comprehensive Lifestyle Intervention (i.e., a Program That Includes a Reduced-Calorie Diet, Exercise/Increased Physical Activity, and Behavioral Counseling) Be Recommended (Rather Than No Weight-Loss Intervention) to Patients with OSA Who Are Overweight or Obese?; and Question 5: Should a Comprehensive Lifestyle Intervention (i.e., a Program That Includes a Reduced-Calorie Diet, Exercise/Increased Physical Activity, and Behavioral Counseling) Be Recommended (Rather Than a Reduced-Calorie Diet Alone) to Patients with OSA Who Are Overweight or Obese?

Summary of the evidence from non-OSA literature. The NIH/NHLBI review showed that three of four trials found the addition of a behavioral intervention increased the amount of weight lost at the end of the intervention at 1 year (17); however, this difference disappeared at 5-year follow-up, suggesting that behavioral interventions need to be maintained long term to minimize weight regain. There was no difference in outcomes of the different behavioral strategies used, but greater intensity of sessions predicted greater weight loss. This finding was verified by the AHA/ACC guideline with 14 or more visits resulting in greater weight loss than 6–12 visits or fewer than 6 lifestyle intervention visits over 6 months (18).

Summary of the evidence from OSA-specific literature. Nine randomized trials compared comprehensive lifestyle interventions composed of reduced-calorie diets and behavioral modification with no intervention in patients with OSA who were overweight or obese (33–41). Some of the trials also included formal exercise programs (supervised or unsupervised) as part of the lifestyle intervention (35, 37, 39, 40). In contrast, no studies were found comparing a comprehensive lifestyle intervention with reduced-calorie diet alone. The trials ranged in size from 11 patients (34) to 264 patients (39). Behavioral interventions were wide ranging and included various combinations of self-determination, goal setting, stimulus control, self-monitoring, self-regulation, group support, problem solving, and relapse prevention. The trials' durations ranged from 9 weeks to 12 months.

Comprehensive lifestyle interventions improved multiple outcomes (Table E2). These programs induced weight loss, regardless of whether the accompanying diet involved meal replacement, although weight loss was greater with meal replacement (MD, −11.6 kg; 95% CI, −17.8 to −5.3 kg) than without meal replacement or substitution (MD, −0.8 kg; 95% CI, −3.0 to +1.5 kg). Similarly, weight loss was observed in interventions that did or did not include exercise/increased physical activity compared with control (MD, −9.0 kg; 95% CI, −10.5 to −7.4 kg in interventions with exercise vs. MD, −7.2 kg; 95% CI, −19.9 to 5.6 kg in interventions without exercise), with considerable heterogeneity and inconsistency among studies without an exercise intervention. Comprehensive lifestyle interventions were associated with reduced OSA severity (MD, −8.5 events/h; 95% CI, −10.8 to −6.3 events/h), increased the resolution of OSA (defined as AHI <5 events/h at end of study) (57.1% vs. 30.6%; relative risk [RR], 1.87; 95% CI, 1.06–3.31), reduced daytime sleepiness as measured by the Epworth Sleepiness Scale (MD, −2.1 points; 95% CI, −4.1 to −0.2 points), reduced snoring as measured by the Snore Outcomes Survey (MD, 7.2 points; 95% CI, 1.4 to 13.1 points), and reduced neck circumference (in one study, MD, −1.3 cm; 95% CI, −1.9 to −0.8 cm; in another study, MD, −4.2 cm; 95% CI, −4.8 to −3.6 cm). There were no OSA-related deaths, and comprehensive lifestyle interventions did not affect adverse event occurrence. Notably, the decrease in AHI correlated with the magnitude of weight loss (34, 39, 41).

The beneficial effects of comprehensive lifestyle modification were further supported by two randomized trials in individuals who were overweight and had OSA that were published after the completion of our evidence synthesis (42, 43). In both trials, individuals who received the comprehensive lifestyle modification had a larger decrease in their AHI.

The panel's confidence in the estimated effects ranged from very low to moderate, depending on the outcome. Reasons for the panel's diminished confidence included imprecision due to small sample size and few events, as well as risk of bias due to lack of blinding, short durations of follow-up, failure to describe concealment, failure to adequately describe randomization procedures, and high dropout rates.

Conclusions. Comprehensive lifestyle interventions that combine reduced-calorie diet (especially meal substitution), exercise/increased physical activity, and behavioral modifications are associated with numerous desirable consequences, including weight loss, reductions in OSA severity, and improvement in daytime sleepiness, in patients with OSA who are overweight or obese. They may also decrease neck circumference, reduce snoring, and lead to resolution of OSA. Moreover, comprehensive lifestyle interventions have no significant demonstrable harm and, therefore, minimal undesirable consequences. As a result, the panel was certain that the balance of desirable to undesirable consequences of a comprehensive lifestyle intervention greatly exceeds the balance for no intervention, because there is no reason to expect benefits from no intervention. The panel was less certain that the balance of desirable to undesirable consequences of a comprehensive lifestyle intervention exceeds the balance for a reduced-calorie diet, but they believed that it was likely. The panel's lack of certainty reflected the absence of randomized controlled studies comparing comprehensive lifestyle intervention with reduced-calorie diets in patients with OSA and, therefore, the need to inform the recommendation with indirect evidence from the general obese population.

Recommendations. For patients with OSA who are overweight or obese, we **recommend** participation in a comprehensive lifestyle intervention program that includes a reduced-calorie diet, exercise/increased physical activity,

and behavioral counseling rather than no program (**strong** recommendation, very low certainty in the estimated effects).

For patients with OSA who are overweight or obese, we **suggest** participation in a comprehensive lifestyle intervention program that includes a reduced-calorie diet, exercise/increased physical activity, and behavioral counseling rather than a program that includes only a reduced-calorie diet, with or without exercise/increased physical activity (**conditional** recommendation, very low certainty in the estimated effects).

Question 6: Should Weight-Loss Medications Be Recommended (Rather Than Comprehensive Lifestyle Intervention Alone) to Patients with OSA Who Are Overweight or Obese and Who Have Been Unsuccessful in Losing Weight with Lifestyle Intervention?

Summary of the evidence from non-OSA literature. All recent authoritative guidelines agree that patients who are unable to achieve or sustain weight loss through a comprehensive lifestyle intervention may be offered the option to add pharmacotherapy if their BMI is greater than or equal to 30 kg/m^2 or their BMI is greater than or equal to 27 kg/m^2 with weight-related comorbidities, unless otherwise contraindicated (17, 44).

We conducted a systematic review of U.S. Food and Drug Administration–approved weight-loss medications: phentermine, orlistat, lorcaserin, liraglutide, naltrexone/bupropion, and phentermine/topiramate extended release (ER). Our initial search was limited to studies that specifically enrolled patients with OSA, and this yielded three studies (45–47); however, one was an abstract only that did not report enough data for analysis (47). Because of this limited data pool, our search was expanded to include studies that did not specifically recruit patients with OSA. Forty-six additional randomized controlled trials (RCTs) were identified across the six medications of interest, although one trial of naltrexone/bupropion was excluded from analysis because it was stopped early owing to breach of confidentiality (48). The majority of the additional studies were conducted with orlistat (49–72); others comprised four studies of liraglutide (73–76), two studies of phentermine/topiramate (77, 78), three studies of lorcaserin (79–81), four studies of naltrexone/bupropion (82–85), and eight studies of phentermine (86–93). The duration of these studies ranged from 20 to 56 weeks. Combined, these trials included over 30,000 patients, more than half of whom received medications. The overall quality of the included studies was low because the existing data were generated largely by manufacturer-funded trials and/or limited by high dropout rates (30–50% in most studies). In addition, there was significant variability regarding the effect of these medications on weight loss. Across studies, the use of weight-loss medications was associated with greater reductions in body weight than placebo, diet, or lifestyle modifications alone (*see* Table 3 for details).

In general, an increased incidence of adverse cardiovascular events was not identified in these studies. However, most trials excluded patients with known cardiovascular disease, and trial durations were most commonly 6–12 months. Both factors likely limited the ability to identify incident cardiovascular events during these trials.

Summary of the evidence from OSA-specific literature. Three studies of cohorts of patients with OSA evaluated the effects of phentermine/topiramate ER (45), liraglutide (46), and orlistat (65, 66). Outcome measures reflecting the impact of these agents on OSA included assessments of changes in weight and BMI, reduction in the AHI, daytime sleepiness, quality-of-life variables, and adverse events. Overall, only minimal decreases in AHI, with little to no improvement in daytime somnolence or quality-of-life measures, were observed in patients receiving weight loss–promoting medications as compared with placebo. The panel's confidence in the estimated effects from these trials was low because several estimates were imprecise, and most trials received pharmacological industry funding.

Conclusions. Limited randomized trial data support the idea that the addition of a weight-loss medication to a behavioral weight-loss program (i.e., reduced-calorie diet, exercise/increased physical activity, and behavioral counseling) improves sleep quality and possibly OSA severity and other OSA-related outcomes. Available medications vary in their efficacy and side effect profiles. The panel weighed the potential benefits versus risks and costs and determined that the addition of a weight-loss medication may be worthwhile for individuals without contraindications who are not improving despite participation in a comprehensive lifestyle intervention weight-loss program. The panel's certainty in its judgment was diminished because the potential desirable and undesirable consequences were finely balanced, and its confidence in the estimated effects on which it relied to make its judgment was low.

The reason for limiting this recommendation to patients who do not have active cardiovascular disease is the persistent uncertainty about the safety of phentermine, phentermine/topiramate ER, lorcaserin, and naltrexone/bupropion in patients with underlying cardiovascular disease. These agents may increase heart rate and myocardial oxygen demand, which, in theory, could have negative consequences in such patients. However, liraglutide has recently been found to be cardioprotective in doses administered to those with type 2 diabetes mellitus (94). Providers treating overweight or obese patients with OSA should be knowledgeable about these medications, including their indications, risks, and potential benefits.

Recommendation. For patients with OSA with a BMI greater than or equal to 27 kg/m^2 who have not lost sufficient weight despite participating in a comprehensive lifestyle weight management program and have no contraindications or active cardiovascular disease, we **suggest** an evaluation for potential antiobesity pharmacotherapy (conditional recommendation, very low certainty in the estimated effects).

REMARKS. "Active cardiovascular disease" refers to a myocardial infarction or cerebrovascular accident within the past 6 months, uncontrolled hypertension, life-threatening arrhythmias, or decompensated congestive heart failure.

Question 7: Should Bariatric Surgery Be Recommended (Rather Than Comprehensive Lifestyle Intervention Alone) to Patients with OSA Who Are Overweight or Obese and Who Have Been Unsuccessful in Losing Weight with Lifestyle Intervention?

Summary of the evidence from non-OSA literature. RCTs in obese populations not

Table 3. Studies of Weight-Loss Medications

Medication	No. of Studies Reviewed/No. of Subjects	Follow-up (*Range*)	Effect on Weight *[Mean (95% CI) Difference in kg, or as Specified]*	No. of Studies with OSA as Outcome/No. of Subjects	Effect on OSA *[Mean (95% CI) Difference in AHI, or as Specified]*	No. of Studies with QOL Outcome
Phentermine	8 studies/169 D, 171 C	12 d to 24 wk	−2.1 (−3.1 to −1.0)	0 studies	No data	No data
Orlistat	25 studies/6,831 D, 6,388 C	26 wk to 3 yr	−2.9 (−3.5 to −2.3)	3 studies	12 patients on CPAP had reduction in pressure of 0.55 cm H_2O	2 studies mention improvement in OSA QOL, but minimal data provided
Lorcaserin	3 studies/3,447 D, 3,441 C	52 wk	−2.9 (−3.4 to −2.5)	0 studies	No data	3 studies, minimal improvement in IWQoL-Lite
Liraglutide 3 mg	5 studies/3,341 D, 1,924 C	20 to 68 wk	−4.7 (−5.7 to −3.7)	1 study/176 D, 179 C	−6.1 (−11.4 to −0.8)	1 study, modest improvement in IWQoL-Lite
Naltrexone/bupropion	4 studies/2,489 D, 1,432 C	56 wk	−4.5 (−5.0 to −3.9)	0 studies	No data	3 studies, modest improvement in IWQoL-Lite
Phentermine/topiramate ER	3 studies/1,515 D, 1,516 C	28 to 56 wk	−8.7% (−9.7% to −7.7%)	1 study/22 D, 23 C	−14.9 (−26.5 to −3.3)	1 study, improvement in SF-36

Definition of abbreviations: AHI = apnea–hypopnea index; C = control; CI = confidence interval; CPAP = continuous positive airway pressure; D = drug; ER = extended release; IWQoL-Lite = Impact of Weight on Quality of Life–Lite instrument; OSA = obstructive sleep apnea; QOL = quality of life; SF-36 = 36-item Short Form Health Survey.

selected for OSA have established that weight loss, glycemic control, resolution of diabetes, and improvements in quality of life are greater with bariatric procedures than nonsurgical interventions and that gastric bypass surgery has greater effects than gastric banding (18, 95).

Only two RCTs of the impact of bariatric surgery, gastric banding, on OSA were identified (96, 97). In 13 RCTs not specific to OSA (98–110), the panel found that bariatric surgery resulted in significant improvement in glycemic control (HbA1c concentration, −1.6%; 95% CI, −2.0% to −1.2%) compared with control individuals. The resolution of diabetes was 9.6-fold more likely with bariatric surgery (RR, 9.6; 95% CI, 5.3 to 17.3). No deaths occurred, and serious adverse were not significantly higher than in control individuals (Table E3).

Summary of the evidence from OSA-specific literature. Two RCTs assessed patients with OSA and a BMI greater than or equal to 35 kg/m^2, both comparing gastric banding with comprehensive lifestyle intervention (96, 97). These studies showed that surgery decreased body weight (MD, −11.0 kg; 95% CI, −20.8 to −1.3 kg) more than nonsurgical treatment but that AHI was not significantly improved (MD, −3.3 events/h; 95% CI, −13.6 to +7.1 events/h), nor was the rate of OSA resolution (20.8% vs. 13.6%; RR, 1.5; 95% CI, 0.4–5.7). Sleepiness as assessed by Epworth Sleepiness Scale tended toward improvement (MD, −2.4 points; 95% CI, −5.1 to +0.3). No deaths were reported, and one patient had a surgical complication that required reoperation (111) (Table E3).

These findings are supported by a randomized trial that was published after completion of our evidence synthesis. The trial compared gastric banding with positive airway pressure therapy in patients with severe OSA (AHI, ⩾30 events/h) and a BMI of 35–45 kg/m^2 (112). Similar to the trials mentioned above, gastric banding had a greater effect on weight loss, but not on OSA-related outcomes, when compared with an alternative intervention.

Conclusions. Gastric banding does not appear to reduce OSA severity to a greater degree than lifestyle interventions alone or positive airway pressure therapy alone. In patient groups not defined as having OSA, gastric banding is associated with decreases in weight, improvement in glycemic control (including resolution of diabetes), and improved quality of life over lifestyle intervention alone. Severe adverse events are uncommon. There are no randomized trial data available for other bariatric procedures in OSA, but weight loss overall was less after gastric banding than after other bariatric procedures. Bariatric surgery has been found to be cost-effective (113). Taken together, the panel concluded that for patients with a BMI greater than or equal to 35 kg/m^2 who have failed a comprehensive lifestyle intervention program for weight loss, bariatric surgery should be considered, based on patient preferences, because the benefits likely outweigh the risks and burdens in most patients with OSA if one considers benefits beyond OSA-specific outcomes. Of note, discussion about bariatric surgery with their sleep provider is welcomed by a substantial proportion of patients with OSA who are obese (114).

Recommendation. For patients with OSA with a BMI greater than or equal to 35 kg/m^2 and whose weight has not improved despite participating in a comprehensive lifestyle intervention program for weight loss and who have no contraindications, we **suggest** referral for bariatric surgery evaluation (conditional recommendation, very low certainty in the estimated effects).

Discussion

What Others Are Saying

Weight loss in OSA. Our recommendations extend those offered in other guidelines. Others recommend weight loss for patients with OSA who are overweight or obese, but they focus primarily on educating patients on the relevance of excess weight to OSA risk without specific recommendations on strategies to accomplish weight loss beyond consideration of bariatric surgery (7–9, 115). For example, the American Academy of Sleep Medicine proposed a set of quality measures in adult OSA management in 2015 that include two related to weight management: measuring weight at every clinical visit and annual discussion with a healthcare provider on weight status (116). However, no assessment or discussion on excess weight is suggested. Our recommendations are consistent with those of major obesity management guidelines in recommending comprehensive lifestyle intervention with three components—reduced-calorie diet, exercise/increased physical activity, and behavioral guidance—as the most potentially successful treatment of overweight/obesity (17, 18, 44).

Weight loss in diabetes. Diabetologists have learned that weight loss, usually induced by comprehensive lifestyle intervention, or bariatric surgery improves the severity of, if not the resolution of, type 2 diabetes mellitus (117–120). In the Look AHEAD (Action for Health in Diabetes) study of weight loss in patients with type 2 diabetes who also had OSA, not only did the diabetes improve but also OSA severity diminished, remaining stable despite a weight regain (121). This study also demonstrated a clinically important improvement in cardiovascular risk in the subgroup losing at least 10% of initial weight (122). Clinicians caring for patients with OSA who are overweight or obese potentially may gain from the knowledge and experience of diabetology colleagues, potentially enrolling patients with OSA in weight-loss programs that have been established in diabetes centers or duplicating those programs in sleep centers.

Putting It All Together

Weight loss is consistently associated with improvement in OSA severity, regardless of

Table 4. Specific Advice for Diet as Part of a Comprehensive Weight-Loss Intervention*

Key aspect of successful diet is reduction in caloric intake
Options for doing so include: • General recommendation for 1,200–1,500 kcal/d for women and 1,500–1,800 kcal/d for men • Reducing caloric intake by 500–1,000 kcal/d
No specific dietary composition (e.g., low fat, low carbohydrate, high protein) proven to be more successful for weight loss
Tailor diet composition to patient preference to maximize adherence

*Recommendations taken from Reference 18.

how the weight is reduced. Behavioral approaches to weight loss have essentially no risk, whereas pharmacological and surgical therapies have mild risks. Taken together, weight loss should be a goal of all clinicians who take care of overweight or obese patients with OSA. However, there are some basic factors to be considered that may enhance the clinician's approach to these patients with OSA.

Diagnosis of overweight/obesity and discussion of this state with patients. Even though most clinicians recognize obesity in their patients and are aware of the benefits of weight loss, the diagnosis of overweight or obesity is often not made, and therefore a weight management program is never recommended (123, 124). Furthermore, even when the need for weight loss is discussed, evidence suggests that physicians fail to recommend the most effective interventions when counseling on weight-loss strategies (125). Thus, it is important to make this specific diagnosis and discuss this issue with patients.

Terminology when discussing the diagnosis of overweight or obesity is important. Patients are generally accepting of the discussion, except for some morbidly obese individuals (126, 127). Descriptors such as "weight problem" and "excess weight" are preferred over "fatness," "excess fat," "large size," "obesity," and "heaviness" (128, 129). The term "adiposity-based chronic disease," or ABCD, has been devised to remove any "judgmental" aspect related to the term "obesity" (130).

Treatment of overweight/obesity. Before recommending a weight-loss program, the clinician should first assess the "reasons and motivation for weight reduction; previous history of successful and unsuccessful weight-loss attempts; family, friends, and work-site support; the patient's understanding of the causes of obesity and how obesity contributes to several diseases; attitude toward physical activity; capacity to engage in physical activity; time availability for weight-loss intervention; and financial considerations" (131). Once this information has been assessed, referral to a specific weight management program that might assist a patient can be made. Results may be superior than if patients are referred to a generic program or simply advised to lose weight (132–134).

Specific recommendations for incorporation of comprehensive lifestyle intervention into a weight management program have been presented by the NIH/NHLBI and AHA/ACC guidelines (*see* details in Tables 4–6) (17, 18). A comprehensive program that combines a reduced-calorie diet, exercise, and counseling should be prescribed as soon as the patient is willing to begin (18, 131). The key feature of a weight management program is creating an energy deficit by restricting caloric intake; the specific type of diet used to generate that deficit does not seem important. The calorie reduction diet should be tailored to patient preference. Secondarily, increased physical activity of at least 150 min/wk, progressing to 200–300 min/wk, should be added. Third, the behavioral science component is essential, together with follow-up. We also agree with a guideline developed by the American Association of Clinical Endocrinologists and the American College of Endocrinology that discusses adding weight-loss medications to a weight management program in the appropriate patients. The weight-loss goal with medication should be at least 7–11% of total body weight or more (135).

Once weight loss has occurred, continued frequent contact (at least once per month for ⩾14 times over 6 mo) with care providers has been found to be important. Monthly maintenance sessions have been demonstrated to minimize weight regain in the long term. To initiate such a program, clinicians caring for these patients need to have knowledge of locally available programs providing these components. Several commercial programs have proven successful and are accessible in most geographic regions (136, 137). As an alternative to external referral, clinicians might consider providing weight management services within their own practices. Many large centers employ cognitive behavioral therapy practitioners who may be able to apply their behavioral expertise in developing and conducting weight-loss programs.

The clinician might consider using the 5-A framework that is used during smoking cessation: assess, advise, agree, assist, and arrange (138). Motivational interviewing has been shown to be effective (139–141). Patients who lose weight as part of a comprehensive lifestyle intervention should be encouraged to remain engaged in long-term weight maintenance programs to minimize weight regain and related comorbidities, including OSA.

In addition to face-to-face weight management programs, Internet-based weight management programs enhance weight loss (142–144). Other broad societal strategies that may facilitate weight loss include improved nutritional labeling of foods and taxing sugar-sweetened beverages (145).

Cost-effectiveness. It has been found that participation in a successful external weight management program was more cost-effective than an in-house program (146). The analysis predicted that such programs could reduce diabetes mellitus prevalence by 20% and cardiovascular disease incidence by 5%.

Table 5. Specific Advice for Exercise/Physical Activity as Part of a Comprehensive Weight-Loss Intervention*

Increased aerobic activity (e.g., brisk walking) for ⩾150 min/wk
Avoid ambulatory conveniences such as elevators when possible
Tailor activity to patient preference to maximize adherence
In the long term, increase physical activity to 200–300 min/wk to minimize weight regain

*Recommendations taken from Reference 18.

Table 6. Specific Advice for Behavioral Counseling as Part of a Comprehensive Weight-Loss Intervention*

At least 14 sessions (individual or group) over the first 6 mo
Monthly booster sessions (in person or by phone) after the first 6 mo
Regular self-monitoring of food intake, physical activity, and weight
If in-person programs are not feasible, consider Internet-based programs

*Recommendations taken from Reference 18.

Future Research

Our analysis of the applicable literature suggests that OSA can be improved with weight loss and even resolved in some cases, although the quality of the evidence is modest, and there is still much work to be done. Small sample sizes, short study durations, high dropout rates, and a lack of blinding were common methodological weaknesses identified. In addition, many studies evaluated individuals incidentally noted to have OSA rather than patients presenting for OSA treatment. Similarly, many studies failed to evaluate outcomes relevant to patients with OSA. Resolution of these study design defects is not easy to accomplish, but we anticipate that their identification will aid investigators in the design of future studies in this area. The panel encourages further research into the behavioral, pharmacological, and surgical treatment of excess weight, not only as adjunctive therapy but also as a potential primary treatment of OSA in patients who are overweight or obese. Specific research questions that the panel believes should be a high priority for future research are listed in the online supplement.

Conclusions

Despite evidence that weight loss can reduce OSA severity, weight management is still not a mainstay of OSA treatment in that existing clinical practice guidelines (7–9) and a recent NIH symposium (147) make only cursory reference to the benefits of weight management and do not offer specific therapeutic recommendations on how to achieve weight loss. However, our guideline demonstrates that clinicians caring for patients with OSA who are overweight or obese should view excess weight as a major potentially modifiable contributing factor to OSA severity and engage in health education and shared decision-making with patients about evidence-based strategies to address excess weight. When indicated, discussion should include participation in a comprehensive lifestyle modification program and, if needed, exploration of additional options such as pharmacotherapy or bariatric surgery, based on patient preferences and needs. ■

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