Online Supplement

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

An Official American Thoracic Society Clinical Practice Guideline

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METHODS

Panel Composition

The project was proposed by the chair and co-chairs through the American Thoracic Society (ATS) Sleep and Respiratory Neurobiology Assembly and was approved by the ATS Board of Directors. Potential panelists were identified by the chair and co-chairs based on their expertise in sleep disordered breathing, weight management, and/or behavioral science. All potential panelists disclosed their conflicts of interest to the ATS. Panelists determined to have no substantial conflicts of interest were "approved without limitation", while those with potential conflicts of interest that were considered manageable were "approved with management", allowing participation in discussions about the evidence but not in the formulation of recommendations related to their conflicts of interest. Potential panelists whose conflicts of interest were deemed not manageable were disqualified. The final guideline panel consisted of 20 members: a chair, a chairs, 10 additional experts in sleep-disordered breathing, 1 expert in weight management, 1 behavioral scientist, 3 patients, 1 lead methodologist, and 2 medical librarians. One sleep-disordered breathing expert and one librarian served as additional methodologists.

Questions

The chair and co-chair and lead methodologist drafted key clinical questions in a PICO (Population, Intervention, Comparator, and Outcome) format. The questions were then

discussed, modified, and approved by the full guideline panel. Outcomes that might be affected by each of the interventions were numerically rated (from 1 to 9) according to their importance. The evidence was assessed only for outcomes whose average rating fell into the "important" or "critical" categories. The primary outcomes evaluated were: Quality of life, mortality, weight loss, change in obstructive sleep apnea (OSA) severity, resolution of OSA, cardiovascular events or stroke, major and minor adverse events, daytime sleepiness, other OSA-related symptoms, sexual function, and glycemic control.

Literature search

The published literature was searched in the following databases: Medline, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, Cochrane Central Database of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), NHS Economic Evaluations Database, Database of Abstracts of Reviews of Effectiveness (DARE), and the Health Technology Assessment (HTA) Database. Search strategies consisted of controlled vocabulary terms (such as Medical Subject Headings), keyword terms, and phrases. Conceptual sets included 1) OSA and obesity and 2) OSA and weight loss interventions (e.g., drug therapy or surgery or exercise therapy or nutritional therapy or diet), which were combined using Boolean "OR." Filters were used as-needed to narrow the search results according to study design. Searches were not limited by publication date or language, and databases were searched from date of inception to search date. Searching was conducted in July and August 2015, and then updated in February 2017 and February 2018.

Grey literature searches consisted of searching Grey Matters (1), ClinicalTrials.gov (2), the World Health Organization's International Clinical Trials Registry Platform (3) , and the bibliographic databases on the websites of select organizations. The Grey Matters search encompassed the following: Australian Department of Health and Aging**,** Australia and New Zealand horizon scanning network (ANZHSN), http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/technologies-assessed-lp-2; Blue Cross Blue Shield Technology Evaluation Centre, http://www.bcbs.com/cce/; Canadian Agency for Drugs and Technologies in Health (CADTH) cadth.ca; Healthcare Improvement Scotland healthcareimprovementscotland.org; Institute for Clinical and Economic Review (ICER) http://icer-review.org ; Institute of Health Economics http://www.ihe.ca; Monash Health Centre for Clinical Effectiveness (CCE), Current Evidence Reviews, http://www.monashhealth.org/page/Health_Professionals/CCE/Evidence_reviews/Current/; TRIP Database https://www.tripdatabase.com; Washington State Health Care Authority http://www.hca.wa.gov; Sleep Research Society, http://www.sleepresearchsociety.org; European Sleep Research Society, www.esrs.**eu/**; National Sleep Foundation, http://sleepfoundation.org ; American Sleep Association, http://www.sleepassociation.org; Canadian Sleep Society, https://css-scs.ca/index.php; AHRQ (Agency for Healthcare Research and Quality), http://www.ahrq.gov; Obesity Society, http://www.obesity.org/meetings-and-events/annual-meeting.htm; and European Congress on Obesity, http://eco2015.easo.org. The bibliographic databases on the websites of the following organizations were also searched: National Institute for Health Care and Clinical Excellence, http://www.nice.org.uk; Scottish

Intercollegiate Guidelines Network, http://www.sign.ac.uk; National Guidelines Clearing House, http://www.guideline.gov.

Evidence synthesis

The lead methodologist reviewed all publications retrieved from the literature searches for relevance, initially screening based on title and/or abstract and then reviewing the full text of potentially relevant publications. Included and excluded studies lists of related systematic reviews were also reviewed. Published abstracts were utilized if they contained data on at least one of our outcomes of interest. Findings from relevant publications were extracted into structured data tables. Duplicate data abstraction was not performed. When data from individual studies were amenable to pooling, the random effects model of DerSimonian and Laird as implemented in the Cochrane Collaboration Review Manager, version 5.3 was used to pool results across studies (4, 5). Relative risk (RR) was used to report the results for dichotomous outcomes and the mean difference (MD) was used to report the results for continuous outcomes, each with an accompanying 95% confidence interval (CI). Statistical heterogeneity of the pooled results was measured using the I^2 and Chi^2 tests, considering an I^2 value of ≥50% or a Chi^2 p≤0.05 to indicate significant heterogeneity. Results from the meta-analyses are provided in the evidence tables.

We used the Grading, Recommendations, Assessment, Development, and Evaluation (GRADE) approach to assess certainty in the estimated effects (i.e., the quality of evidence) for each intervention on each outcome of interest (6). The lead methodologist created evidence profiles using the Guideline Development Tool (7), which categorized the overall certainty in the

evidence into one of four levels: high, moderate, low, or very low. Each level represents the certainty in the accuracy of the estimated effects for a specific intervention. The full guideline panel reviewed the evidence profiles and provided input and feedback.

Recommendations

The guideline panel met at the 2016 ATS International Conference in San Francisco and several subsequent conference calls to discuss the evidence profiles and develop recommendations to answer each PICO question using the Evidence-to-Decision (EtD) framework (8, 9). No relevant data could be identified for two of the initial PICO questions and so these were dropped from further consideration. These questions were: (1) Should both a reduced calorie diet and exercise/increased physical activity be recommended (rather than exercise alone) to patients with OSA who are overweight or obese?; and (2) Should weight loss medications be recommended to patients with OSA who are overweight or obese (rather than no weight loss intervention)?

The panelists made decisions about whether to recommend for or against an intervention based on: the balance of desirable consequences (benefits) and undesirable consequences (burdens, adverse effects, and costs), quality of evidence, cost and cost-effectiveness, feasibility, and acceptability to patients (i.e., patient values and preferences). Using the GRADE approach, the panelists rated each recommendation as either “strong” or “conditional”. All recommendations were formulated and graded by discussion and consensus; voting was never required.

Manuscript preparation

The initial draft of the manuscript was written by the chair and co-chair and lead methodologist. All members of the guideline panel reviewed the manuscript; comments were addressed by the chair and co-chair and the revised manuscript was redistributed to the full panel for further review. Once the manuscript was approved by the full panel, it was submitted for external peer review.

Peer review

External peer review was organized and overseen by the ATS Documents Editor. Comments from the reviewers were collated into a single decision letter and sent to the chair and co-chair. The manuscript was subsequently revised by the panel according to feedback received from the peer reviewers. Following several cycles of review and revisions, the manuscript was deemed satisfactory and sent to the ATS Board of Directors for further review and final approval.

EVIDENCE PROFILES

Evidence table E1: Exercise program vs. no exercise program

Bibliography: 1) Fanfulla F, Taurino AE, N DAL, Piran M, Scalvini S, Fracchia C. CPAP use and weight control in obese OSA patient improves by a tele-assistance program [Abstract]. *European Respiratory Society Annual Congress, Berlin, Germany*, 2008; 2) Kline CE, Crowley EP, Ewing GB, Burch JB, Blair SN, Durstine JL, Davis JM, Youngstedt SD. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. *Sleep* 2011; 34: 1631-1640; 3) Sengul YS, Ozalevli S, Oztura I, Itil O, Baklan B. The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. *Sleep Breath* 2011; 15: 49-56; 4) Ackel-D'Elia C, da Silva AC, Silva RS, Truksinas E, Sousa BS, Tufik S, de Mello MT, Bittencourt LR. Effects of exercise training associated with continuous positive airway pressure treatment in patients with obstructive sleep apnea syndrome. *Sleep Breath* 2012; 16: 723-735; 5) Schutz TC, Cunha TC, Moura-Guimaraes T, Luz GP, Ackel-D'Elia C, Alves Eda S, Pantiga G, Jr., Mello MT, Tufik S, Bittencourt L. Comparison of the effects of continuous positive airway pressure, oral appliance and exercise training in obstructive sleep apnea syndrome. *Clinics* 2013; 68: 1168-1174; 6) Desplan M, Mercier J, Sabate M, Ninot G, Prefaut C, Dauvilliers Y. A comprehensive rehabilitation program improves disease severity in patients with obstructive sleep apnea syndrome: a pilot randomized controlled study. *Sleep Med* 2014; 15: 906-912; 7) Gonzalez-Muniesa P, Lopez-Pascual A, de Andres J, Lasa A, Portillo MP, Aros F, Duran J, Egea CJ, Martinez JA. Impact of intermittent hypoxia and exercise on blood pressure and metabolic features from obese subjects suffering sleep apnea-hypopnea syndrome. *J Physiol Biochem* 2015; 71: 589-599; 8) Servantes DM, Pelcerman A, Salvetti XM, Salles AF, de Albuquerque PF, de Salles FC, Lopes C, de Mello MT, Almeida DR, Filho JA. Effects of home-based exercise training for patients with chronic heart failure and sleep apnoea: a randomized comparison of two different programmes. *Clin Rehabil* 2012; 26: 45-57; 9) Mendelson M, Lyons OD, Yadollahi A, Inami T, Oh P, Bradley TD. Effects of exercise training on sleep apnoea in patients with coronary artery disease: a randomised trial. *Eur Respir J* 2016; 48: 142-150.

Assessment of certainty in estimated effects							№ of patients		Effects		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Exercise**	**No exercise program**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality (follow up: range 4 weeks to 12 weeks)												
3	randomized trials	serious [a]	not serious	serious [b]	serious [c,d]	none	0/45 (0.0%)	0/35 (0.0%)	not estimable	**0 fewer per 1,000** (from 80 more to 80 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Serious adverse events (follow up: range 4 weeks to 12 weeks; assessed with: number of participants reporting an SAE)												
3	randomized trials	serious [a]	not serious	serious [b]	serious [c,d]	none	0/45 (0.0%)	0/35 (0.0%)	not estimable	**0 fewer per 1,000** (from 80 more to 80 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Weight loss (follow up: range 4 weeks to 6 months; assessed with: BMI at end of study)												
5	randomized trials	serious [a,e]	not serious [f]	serious [b]	serious [d,g]	none	50	55	-	MD **0.04 lower** (1.67 lower to 1.59 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Weight loss (follow up: range 12 weeks to 13 weeks; assessed with: weight (kg) at end of study)												
2	randomized trials	serious [a]	not serious	serious [b]	serious [d,g]	none	36	29	-	MD **2.14 higher** (4.29 lower to 8.56 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Weight loss (follow up: range 4 weeks to 12 weeks; assessed with: neck circumference (cm) at end of study)												

4	randomized trials	serious [a,e]	not serious [f]	serious [b]	serious [d,g]	none	52	44	-	MD **0.43 higher** (1.51 lower to 2.36 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Severity of OSA (follow up: range 4 weeks to 12 weeks; assessed with: AHI at end of study)												
5	randomized trials	very serious [a,e,h]	serious [i]	serious [b]	serious [d,g]	none	65	63	-	MD **0.77 lower** (13.36 lower to 11.82 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Daytime sleepiness (follow up: range 4 weeks to 6 months; assessed with: Epworth Sleepiness Scale (ESS) at end of study; Scale from: 0 to 24)												
5	randomized trials	serious [a,e]	not serious	serious [b]	serious [d]	none	62	54	-	MD **0.85 higher** (0.78 lower to 2.47 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Other OSA symptoms (sleep quality) (follow up: range 4 weeks to 12 weeks; assessed with: PSQI score at study end; Scale from: 0 to 21)												
2	randomized trials	serious [a]	not serious	serious [b]	serious [d]	none	35	25	-	MD **2.67 lower** (4.29 lower to 1.05 lower)	⨁◯◯◯ VERY LOW	IMPORTANT
Adverse events (follow up: range 4 weeks to 12 weeks; assessed with: number of participants reporting an AE)												
3	randomized trials	serious [a,e]	not serious	serious [b]	serious [d,g]	none	4/45 (8.9%)	0/35 (0.0%)	not estimable	**50 fewer per 1,000** (from 60 more to 160 fewer)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

a. None of the studies were blinded.

b. Short follow-up can be a source of indirectness.

c. Low number of events.

d. Sample size does not meet “optimum information size” criteria.

e. Some studies without descriptions of random sequence generation.

f. While heterogeneity statistics suggest inconsistency, this appears to be accounted for by the inclusion of one study with a 4-week inpatient rehabilitation program as the intervention, thus varying in intensity from other outpatient interventions.

g. Results do not exclude the possibility of significant benefit or significant harm.

h. Three studies with high dropout rates, two of which only reported data for study completers.

i. Significant heterogeneity detected across studies.

Evidence table E2: Comprehensive weight loss program (i.e., diet + behavioral intervention +/- exercise) vs. no program

Bibliography: 1) Foster GD, Borradaile KE, Sanders MH, Millman R, Zammit G, Newman AB, Wadden TA, Kelley D, Wing RR, Pi-Sunyer FX, Reboussin D, Kuna ST, Sleep ARGoLARG. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med* 2009; 169: 1619-1626; 2) Johansson K, Neovius M, Lagerros YT, Harlid R, Rossner S, Granath F, Hemmingsson E. Effect of a very low energy diet on moderate and severe obstructive sleep apnoea in obese men: a randomised controlled trial. *BMJ* 2009; 339: b4609; 3) Tuomilehto HP, Seppa JM, Partinen MM, Peltonen M, Gylling H, Tuomilehto JO, Vanninen EJ, Kokkarinen J, Sahlman JK, Martikainen T, Soini EJ, Randell J, Tukiainen H, Uusitupa M, Kuopio Sleep Apnea G. Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. *Am J Respir Crit Care Med* 2009; 179: 320-327; 4) Hood MM, Corsica J, Cvengros J, Wyatt J. Impact of a brief dietary self-monitoring intervention on weight change and CPAP adherence in patients with obstructive sleep apnea. *J Psychosom Res* 2013; 74: 170-174; 5) Chirinos JA, Gurubhagavatula I, Teff K, Rader DJ, Wadden TA, Townsend R, Foster GD, Maislin G, Saif H, Broderick P, Chittams J, Hanlon AL, Pack AI. CPAP, weight loss, or both for obstructive sleep apnea. *N Engl J Med* 2014; 370: 2265-2275; 6) Igelstrom H, Margareta E, Eva L, Pernilla A. Tailored behavioral medicine intervention for enhanced physical activity and healthy eating in patients with obstructive sleep apnea syndrome and overweight. *Sleep Breath* 2014; 18: 655-668; 7) Moss J, Tew GA, Copeland RJ, Stout M, Billings CG, Saxton JM, Winter EM, Bianchi SM. Effects of a pragmatic lifestyle intervention for reducing body mass in obese adults with obstructive sleep apnoea: a randomised controlled trial. *Biomed Res Int 2014*; 2014: 102164; 8) Nerfeldt P, Nilsson BY, Udden J, Rossner S, Friberg D. Weight reduction improves nocturnal respiration in obese sleep apnoea patients-A randomized controlled pilot study. *Obes Res Clin Pract* 2008; 2: 71-142. 9) Ng SS, Chan RS, Woo J, Chan TO, Cheung BH, Sea MM, To KW, Chan KK, Ngai J, Yip WH, Ko FW, Hui DS. A Randomized Controlled Study to Examine the Effect of a Lifestyle Modification Program in OSA. Chest 2015; 148: 1193-1203.

Assessment of certainty in estimated effects							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other consider-ations**	**Diet and/or exercise combined with behavioral intervention ("comprehensive weight loss program")**	**No such program**	**Relative (95% CI)**	**Absolute (95% CI)**		
Quality of Life (change in SF-12 physical component score) (follow up: 9 weeks; Scale from: 0 to 100)												
1	randomised trials	serious [a]	not serious	serious [b]	not serious [c]	none	30	33	-	MD **10.55 higher** (7.7 higher to 13.4 higher)	⊕⊕◯◯ LOW	CRITICAL
Quality of life (change in SF-12 mental component score) (follow up: 9 weeks; Scale from: 0 to 100)												
1	randomised trials	serious [a]	not serious	serious [b]	not serious [c]	none	30	33	-	MD **1.25 higher** (1.71 lower to 4.21 higher)	⊕⊕◯◯ LOW	CRITICAL
Mortality (follow up: range 9 weeks to 12 months)												
4	randomised trials	serious [a]	not serious	not serious [d]	serious [e]	none	0/154 (0.0%)	0/155 (0.0%)	not estimable	**0 fewer per 1,000** (from 20 more to 20 fewer)	⊕⊕◯◯ LOW	CRITICAL
Serious adverse events (follow up: range 9 weeks to 12 months; assessed with: number of participants with at least one SAE)												
4	randomised trials	serious [a]	not serious	not serious [d,f]	serious [e]	none	0/152 (0.0%)	0/156 (0.0%)	not estimable	**0 fewer per 1,000** (from 20 more to 20 fewer)	⊕⊕◯◯ LOW	CRITICAL
Weight loss with diets NOT including any meal replacement (follow up: range 12 weeks to 6 months; assessed with: change in weight (kg))[g]												

2 [h]	randomised trials	serious [a,i]	not serious	not serious [b]	serious [j,k]	none	58	59	-	MD **0.77 lower** (3.02 lower to 1.49 higher)	⊕⊕◯◯ LOW	CRITICAL
Weight loss with diets including any meal replacement (follow up: range 9 weeks to 12 months; assessed with: change in weight (kg))[l]												
4	randomised trials	serious [a]	serious [m]	not serious [d]	not serious	none	247	265	-	MD **11.58 lower** (17.84 lower to 5.31 lower)	⊕⊕◯◯ LOW	CRITICAL
Weight loss (follow up: 12 months; assessed with: change in neck circumference (cm))												
1	randomised trials	serious [a,i]	not serious	not serious	not serious	none	125	139	-	MD **1.3 lower** (1.85 lower to 0.75 lower)	⊕⊕⊕◯ MODERATE	CRITICAL
Resolution of OSA (follow up: 12 months; assessed with: Achieving AHI<5 as determined by blinded PSG)												
1	randomised trials	not serious [n]	not serious	not serious	serious [k]	none	20/35 (57.1%)	11/36 (30.6%)	**RR 1.87** (95% CI 1.06-3.31)	**266 more per 1,000** (from 36 more to 461 more)	⊕⊕⊕◯ MODERATE	CRITICAL
OSA Severity (follow up: range 9 weeks to 12 months; assessed with: change in AHI)												
4	randomised trials	not serious [n]	serious [m]	not serious [d]	not serious	none	251	252	-	MD **8.54 lower** (10.83 lower to 6.25 lower)	⊕⊕⊕◯ MODERATE	CRITICAL
Daytime sleepiness (follow up: range 9 weeks to 12 months; assessed with: change in Epworth Sleepiness Scale (ESS) score; MID has not been establish; Scale from: 0 to 24)												
2	randomised trials	serious [a]	not serious	not serious [d]	serious [k]	none	65	70	-	MD **2.43 lower** (5.37 lower to 0.51 higher)	⊕⊕◯◯ LOW	CRITICAL
Glycemic control (follow up: 24 weeks; assessed with: resolution in DM defined by cessation of glucose-lowering medications)												
1	randomised trials	serious [a,i]	not serious	serious [o]	serious [k]	none	0/46 (0.0%)	0/48 (0.0%)	not estimable	**0 fewer per 1,000** (from 40 more to 40 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Any adverse event (follow up: range 9 weeks to 12 months)												

4	randomised trials	serious [a,p]	serious [q]	serious [d,q]	not serious	none	Two studies reported number of participants experiencing any AE; there were 0 AEs across all participants for both studies. Four studies reported the number of events per group with 2 studies reporting no events (the same 2 studies also reporting no participants experiencing events), but 2 other studies reporting occurrences of AEs. In one of the latter two studies, there were 8 AEs in the intervention group and none in the control group. The the second of the latter two studies, many AEs were reported in both groups. When considering only those 2 studies reporting the occurrence of any AEs, the risk difference (pooled estimate) is 0.27 [0.15, 0.38] favoring control. When considering all 4 studies, together the risk difference (pooled estimate) is 0.12 [-0.07, 0.32].	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

a. Participants and personnel not blinded.

b. Short follow-up period can be a source of indirectness.

c. It is difficult to assess precision when MID is not known.

d. Varying lengths of follow-up (including some shorter follow-up periods) may be a source of indirectness.

e. Low number of events with overall small pooled sample size.

f. Lack of clear definition of what constituted an SAE in each study could be a source of indirectness.

g. One study also reported change in BMI: MD -0.50% [-1.12, 0.12].

h. One additional study (Ng, et al.) reported only change in BMI rather than weight. Results were similar with mean difference of -3.60 (95% CI -5.86, -1.34) between intervention and control groups over a 12-month follow-up period.

i. High dropout rate.

j. Results (confidence interval) do no exclude appreciable benefit with comprehensive weight loss vs. no difference.

k. Sample size does not meet OIS criteria.

l. Three studies also reported change in BMI (follow-up ranging from 9 weeks to 12 months) with MD (pooled esimate) of -4.13% [-6.28, -1.98]

m. One study with short-term (9 weeks) follow-up introduces significant inconsistency. Unclear if difference in length of follow-up from other studies fully explains inconsistency. This study also included only men.

n. PSG scorers and sleep technicians blinded. However, patients and personnel not blinded to intervention, and thus this could still represent risk of bias.

o. Unclear how many patients were using glucose-lowering medications at the start of the study. Patients with Type 1 DM were excluded; patients with Type 2 DM were only eligible if they had an A1C<=7% and had no medication changes in the last 3 months.

p. Variations in adverse events reporting could represent selective reporting, and thus a source of bias.

q. There is significant variability in adverse events reported. Adverse events are variably defined and reported across studies.

Evidence table E3: Bariatric surgery vs. no surgery

Bibliography: 1) Feigel-Guiller B, Drui D, Dimet J, Zair Y, Le Bras M, Fuertes-Zamorano N, Cariou B, Letessier E, Nobecourt-Dupuy E, Krempf M. Laparoscopic Gastric Banding in Obese Patients with Sleep Apnea: A 3-Year Controlled Study and Follow-up After 10 Years. *Obes Surg* 2015; 25(10):1886-1892; 2) Dixon JB, Schachter LM, O'Brien PE, Jones K, Grima M, Lambert G, Brown W, Bailey M, Naughton MT. Surgical vs. conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. *JAMA* 2012; 308(11):1142-1149.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considera-tions**	**Bariatric surgery**	**No surgery**	**Relative (95% CI)**	**Absolute (95% CI)**		
Mortality (follow up: range 2 to 3 years; assessed with: #events/group)												
2	randomized trials	serious [a]	not serious	not serious	serious [b]	none	0/60 (0.0%)	0/63 (0.0%)	not estimable	not estimable	⊕⊕◯◯ LOW	CRITICAL
Serious adverse events (follow up: range 2 to 3 years; assessed with: #events/group)												
2	randomized trials	serious [a]	not serious	not serious	serious [b]	none	5/60 (7.9%)	5/63 (8.3%)	RR 1.05 (0.32 to 3.44)	4 less per 1,000 (from 111 fewer to 101 more)	⊕⊕◯◯ LOW	CRITICAL
Weight loss (follow up: range 2 to 3 years; assessed with: change in weight in kg)												
2	randomized trials	serious [a]	not serious	not serious	not serious [c]	none	52	54	-	MD 11.0 lower (20.8 lower to 1.3 lower)	⊕⊕⊕◯ MODERATE	CRITICAL
Resolution of OSA (follow up: 3 years; assessed with: cessation of nocturnal NIV, not including nonadherence)												
1	randomized trials	very serious [a,d]	not serious	not serious	serious [b]	none	5/24 (20.8%)	3/22 (13.6%)	RR 1.53 (0.41 to 5.66)	72 more per 1,000 (from 80 fewer to 635 more)	⊕◯◯◯ VERY LOW	CRITICAL
Severity of OSA (follow up: range 2 to 3 years; assessed with: AHI at study end)												
2	randomized trials	serious [a]	not serious	not serious	serious [c]	none	50	50	-	MD 3.3 lower (13.6 lower to 7.1 higher)	⊕⊕◯◯ LOW	CRITICAL
Daytime sleepiness (follow up: 2 years; assessed with: ESS at study end)												
1	randomized trials	serious [a]	not serious	not serious	serious [c]	none	30	30	-	MD 2.4 lower (5.1 lower to 0.3 higher)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

a. Low number of events.
b. Lack of blinding of patients/personnel creates a risk of co-intervention.
c. Sample size does not meet OIS criteria.
d. High rate of dropout.

HIGH PRIORITY RESEARCH QUESTIONS

Specific research questions that the panel believes should be a high priority for future research include the following:

- What is the impact of weight loss on:
    - OSA severity
    - Reduction in continuous positive airway pressure (CPAP) pressure or need
    - Cardio-metabolic comorbidities
- Can overweight or obese OSA patients without excessive daytime sleepiness (with or without cardio-metabolic comorbidities) be treated with weight loss alone?
- Should weight management precede upper airway management in overweight or obese OSA patients?
- Can asymptomatic overweight or obese OSA patients in high-risk employment situations be treated with weight loss alone?
- Are there comorbidities and, if so, how severe do they need to be, to prohibit an initial attempt at weight management alone?
- When do more additional aggressive management tools need to be initiated in overweight or obese OSA patients if weight loss does not occur, or if weight is regained after initial loss?
- What are the long-term mortality, cardio-metabolic, and quality of life outcomes in overweight or obese OSA patients who are treated with weight loss strategies

alone, with upper airway management alone, or with a combination of weight loss and upper airway management?

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