PCR208

The Association of Intentional Weight Reduction with Symptom Burden and PRO Measures in Patients with Obstructive Sleep Apnea: A Systematic Literature Review

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BACKGROUND

- Obstructive sleep apnea (OSA) is a common sleep disorder that is characterized by repeated episodes of partial or complete upper airway obstruction during sleep.
- Obesity is a major risk factor for OSA. Weight reduction is an important management strategy for patients with OSA with obesity or overweight. However, a gap exists in understanding the correlation between weight loss and patient-reported outcomes (PROs) in patients with OSA.
- Accordingly, this systematic literature review (SLR) identified literature examining the association between intentional weight reduction (loss by exercise and diet, pharmaceuticals, bariatric surgery, etc.) and OSA symptom burden (e.g., dry mouth, morning headaches, difficulty remembering, extensive daytime sleepiness) and PRO measures among patients with OSA.

CONCLUSION

- Weight reduction interventions in patients with OSA have shown promising results in improving various PROs. However, further research is needed to better understand the relationship between weight reduction and PRO outcomes in patients with OSA and obesity/overweight, as well as to explore the impact of weight reduction interventions on other measures of QoL and sleep quality.

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METHODS

- Embase, MEDLINE, and the Cochrane Central Register of Controlled Trials were searched for English peer-reviewed articles (January 1998–September 2023).
- Clinical trials and observational studies in adults with OSA reporting changes in PRO measures or symptom burden following weight reduction treatment were included.
- Screening of records at title and abstract and full-text screening stage was conducted independently by two reviewers to determine its eligibility for inclusion in the SLR according to the population, intervention, comparator, outcome, and study design (PICOS) framework (**Table 1**). The protocol was registered in PROSPERO (CRD42023468169).
- Observational studies were assessed for risk of bias using the Newcastle-Ottawa Scale; quality assessment of randomized controlled trials was carried out using the Cochrane Risk-of-Bias Assessment Tool (version 2.0).

Table 1. PICOS Inclusion/Exclusion Criteria

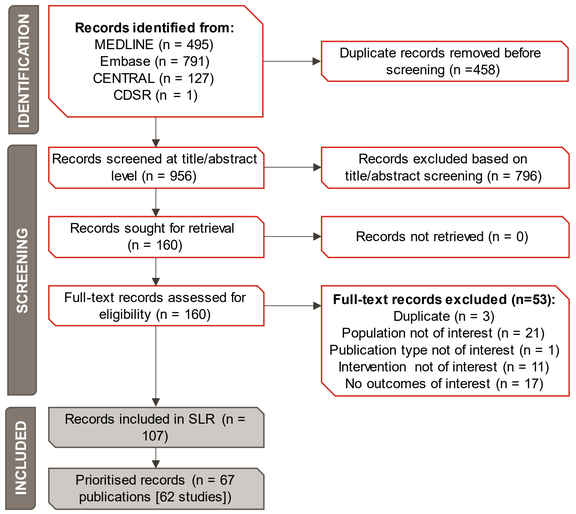
Criteria	Inclusion
Population	Adults with OSA (≥18 years old)
Interventions	Weight reduction treatment (diet, exercise, pharmacological*, surgical treatment)
Comparators	No restrictions
Outcomes	•Change in symptom burden (e.g., daytime sleepiness, dry mouth, headaches) •Change in PRO (e.g. ESS, SF-36) •Change in outcomes by degree of weight reduction
Study Design	•Observational studies •Clinical trials (PROs only) •Systematic reviews and meta-analyses (for citation chasing only)
Time Frame	No date restrictions applied for database searches except for conference abstracts (2021–2023)

*Refers to weight loss medications only.
Abbreviations: BMI = body mass index; ESS = Epworth Sleepiness Scale; NA = not applicable; OSA = obstructive sleep apnea; PRO = patient-reported outcome; SF-36 = 36-item Short Form Health Survey

RESULTS

- A total of 956 unique records were considered for title/abstract screening. One hundred and sixty abstracts deemed potentially relevant and assessed at the full-text level, of which 107 were included for data extraction. Among these publications, 62 studies (27 observational studies, 35 clinical trials), reported in 67 publications, were prioritized for data extraction based on sample size (n≥30) and date of publication (2013–2023) (**Figure 1**).

Figure 1: Database Searches

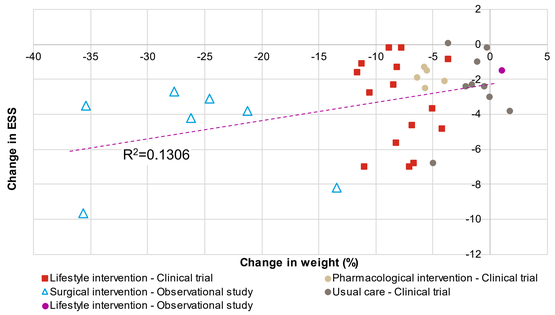


Abbreviations: CDSR = Cochrane Database of Systematic Reviews; CENTRAL = Cochrane Central Register of Controlled trials; SLR = systematic literature review

- Interventions for weight reduction included: bariatric surgery (n=25), lifestyle interventions (n=33), pharmacological interventions (n=2) or pharmacological and lifestyle interventions (n=2). Heterogeneity was observed for weight reduction interventions, study designs, patient characteristics, duration of intervention, and severity of OSA. Weight reduction ranged from 0% (standard of care) to 27.7% (bariatric surgery).
- **Relationship between Percent Weight Change and Epworth Sleepiness Scale (ESS) (Figure 2):**
  - Twenty-two studies reported ESS change in response to weight change. Of the 22 studies,18 reported the relationship between mean percent weight change and change in ESS. For study arms resulting in <5% weight reduction, change in ESS ranged from -4.8 to 0.1. In study arms resulting in >5% weight reduction, change in the ESS ranged from -9.7 to -0.2 and was not strongly correlated with weight reduction.
- **Relationship between Percent Weight Change and 36-item Short Form Health Survey (SF-36) (Figure 3 and Figure 4):**
  - Nine studies reported SF-36 quality of life (QoL) outcomes. Four of these reported on the relationship between percent weight change and SF-36 physical component summary (PCS) or mental component summary (MCS) with weak inverse correlation for both. For study arms resulting in < 5% weight reduction, change in the PCS score was reported in three studies and ranged from -0.02 to 7.8. For study arms reporting > 5% weight reduction, PCS score was reported in four studies and ranged from 2.9 to 10.8.
  - For study arms resulting in < 5% weight reduction, change in the MCS score was reported in three studies and ranged from -0.1 to 6.7. For study arms reporting > 5% weight reduction, MCS score was reported in four studies and ranged from -5.1 to 6.1.

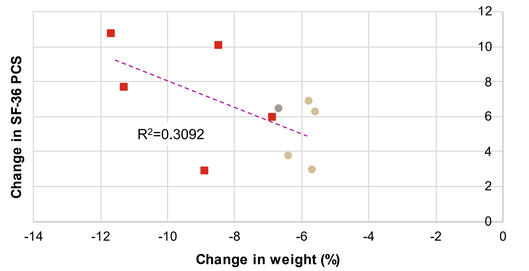
Results (continued)

Figure 2: Relationship between Percent Weight Change and Changes in ESS



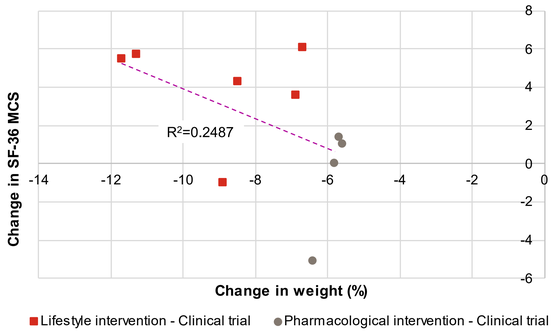
Abbreviations: ESS = Epworth Sleepiness Scale

Figure 3: Relationship between Percent Weight Change and Changes in SF-36 Physical Component Summary Score



Abbreviations: PCS = Physical Component Summary; SF-36 = 36-item Short Form Health Survey

Figure 4: Relationship between Percent Weight Change and Changes in SF-36 Mental Component Summary Score



Abbreviations: MCS = Mental Component Summary; SF-36 = 36-item Short Form Health Survey

- **Relationship between Percent Weight Change and Other PROs:**
  - **Functional Outcomes of Sleep Questionnaire:** Two studies reported greater improvements in the intervention compared to the control group (*P*=0.044 for moderate OSA in one study). Significant improvements in the 'activity level' domain were reported for the intervention group in another study (*P*=0.015). Three studies reported improvement in QoL following weight loss interventions but did not report percentage weight change.
  - **Pittsburgh Sleep Quality Index:** Two studies, including one with statistically significant results, found that weight reduction was accompanied by reduced PSQI in those receiving weight loss interventions (mean at 6 months of -2.5 and -3.6 vs -1.5 and 0.2 for no intervention, *P*=0.67 and *P*<0.001, respectively).
  - **Sleep Apnea QoL:** One study reported improvement in health-related QoL following weight loss intervention (mean at 6 months of 1.1 vs 0.1 for no intervention, *P*<0.001).
  - **Quebec Sleep Questionnaire:** One study reported no significant difference in the weight loss intervention arm compared to the control group.
- **Relationship between Percent Weight Change and Other PROs (continued):**
  - **Hamilton Depression Scale:** One study reported greater reduction in weight but not depression in intervention group compared to control group (*P*=0.66).
- **Relationship between Weight Reduction and OSA Symptom Burden:**
  - Limited data were identified for changes in OSA symptom burden in response to weight reduction. Three studies reported a decrease in the percentage of patients with excessive day time sleepiness (32–68% to 2–10% across studies) following weight reduction (*P*<0.0001 in 2 studies and P value NR in one study). Changes in other symptoms such as dry mouth, headaches in the morning, or difficulty remembering things were not identified. The only symptom burden reported was side effects of treatments, such as liraglutide and armodafinil.

Discussion

- The SLR identified various interventions for weight reduction in patients with OSA, including pharmacological, surgical, and lifestyle interventions. However, there was considerable heterogeneity in the specific interventions and control groups utilized across the studies. The SLR assessed the effect of weight reduction following interventions on a range of PRO and OSA symptom burden outcomes.
- The most extensive evidence available was for the ESS, in which 22 studies reported improvement in ESS following weight reduction in patients with OSA. Additionally, other measures such as the SF-36, FOSQ, PSQI, Quebec Sleep Questionnaire, and Hospital Anxiety and Depression Scale also demonstrated positive changes with weight reduction, although the evidence was more limited.
- In general, there was a positive association between the extent of weight reduction and the impact on PRO measures. The interventions reporting the maximum weight reduction (usually surgical interventions) were more likely to have higher impact on PRO measures.

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