Sleep Medicine Reviews xxx (2018) 1–15

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

# The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis

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ARTICLE INFO

*Article history:*
Received 7 February 2018
Received in revised form
22 April 2018
Accepted 13 June 2018
Available online xxx

*Keywords:*
Obstructive sleep apnoea
Sleep disordered breathing
Surgical weight loss
Bariatric surgery

SUMMARY

This review aimed to examine the relationship between surgical weight loss and obstructive sleep apnoea (OSA) severity (i.e., apnoea-hypopnoea index [AHI]), and how this relationship is altered by the various respiratory events scoring (RES) criteria used to derive the AHI. A systematic search of the literature was performed up to December 2017. Before-and-after studies were considered due to a paucity of randomised controlled trials (RCTs) available to be reviewed in isolation. Primary outcomes included pre- and post-surgery AHI and body mass index (BMI). Secondary outcomes included sleep study type and RES criteria. Meta-analysis was undertaken where possible. Overall, surgical weight loss resulted in reduction of BMI and AHI, however, OSA persisted at follow-up in the majority of subjects. There was high between-study heterogeneity which was largely attributable to baseline AHI and duration of follow-up when analysed using meta-regression. There was insufficient data to evaluate the impact of different RES criteria on OSA severity. Therefore, more RCTs are needed to verify these findings given the high degree of heterogeneity and future studies are strongly encouraged to report the RES criteria used to enable fair and uniform comparisons of the impact of any intervention on OSA severity.

## Introduction

Obesity is a major worldwide problem as evidenced from a recent report by the World Health Organisation [1] suggesting that over 600 million people have a body mass index (BMI) $\geq 30$ kg/m$^2$. One of the major implications of obesity is the high prevalence of obstructive sleep apnoea (OSA) [2], and the risk for developing OSA increases by 1.14 (95% confidence interval [CI] 1.10, 1.19) times with every unit increase in BMI [3]. OSA is a serious condition, and is independently associated with excessive daytime sleepiness, workplace and motor vehicle accidents, depression, hypertension and cardiovascular disease [4]. Continuous positive airway pressure (CPAP) is considered the gold standard treatment for OSA and works by pneumatically splinting open the upper airway. However, evidence from randomised controlled trials (RCTs) shows that CPAP adherence is consistently low (~3.5 h use per night) [5] and as many as 50% of patients discontinue therapy after three months [6]. One of the most commonly recommended adjunctive treatments is weight reduction, either via lifestyle modifications or bariatric surgery. While weight loss can improve OSA severity, this does not always translate into complete resolution of OSA [7].

A recent systematic review and meta-analysis of RCTs showed that intensive lifestyle interventions (ILI) can result in weight loss

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https://doi.org/10.1016/j.smrv.2018.06.001
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Please cite this article in press as: Wong A-M, et al., The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis, Sleep Medicine Reviews (2018), https://doi.org/10.1016/j.smrv.2018.06.001

**Abbreviations**

| | |
|---|---|
| AASM | American Academy of Sleep Medicine |
| AHI | apnoea-hypopnoea index |
| BMI | body mass index |
| CI | confidence interval |
| CPAP | continuous positive airway pressure |
| DEXA | dual-energy X-ray absorptiometry |
| ESS | Epworth sleepiness scale |
| ILI | intensive lifestyle intervention |
| LAGB | laparoscopic adjustable gastric banding |
| MRI | magnetic resonance imaging |
| N | number of participants |
| non-RCT | non-randomised controlled trial |
| NREM | non-rapid eye movement |
| ODI | oxygen desaturation index |
| OHS | obesity hypoventilation syndrome |
| OSA | obstructive sleep apnoea |
| Pcrit | pharyngeal critical pressure |
| PSG | polysomnography |
| RCT | randomised controlled trial |
| RYGB | Roux-en-y gastric bypass |
| SG | sleeve gastrectomy |
| REM | rapid eye movement |
| RES | respiratory events scoring |
| WMD | weighted mean difference |

and reductions in OSA severity in comparison to conservative lifestyle interventions. However, the effects on both the apnoea-hypopnoea index (AHI) and weight reported in this review were modest [weighted mean difference (WMD) for change in AHI was −16.1 events/h (95%CI −25.6, −6.5; $I^2 = 92.2\%$) and WMD for weight change was −13.8 kg (95%CI −19.2, −8.3; $I^2 = 95.7\%$)] [8]. Similarly, a large prospective, non-randomised intervention trial comparing longitudinal outcomes of patients undergoing bariatric surgery to matched controls showed that patients who received bariatric surgery lost more weight than the control group two years after the intervention (−23% vs −0.1%) and weight loss was maintained at 10 y (−16% vs 1.6%) [9]. Therefore, bariatric surgery is an effective treatment option and can lead to more substantial and sustainable weight loss than lifestyle-based weight-loss methods (i.e., diet and/or exercise).

To date, two systematic reviews and meta-analyses have examined the effect of surgical weight loss on OSA [7,10]. Both reviews suggested that bariatric surgery resulted in significant reductions in both BMI and AHI [Greenburg et al. [7]: WMD for BMI −17.9 kg/m$^2$ (95%CI −19.3, −16.5) and WMD for AHI −38.2 events/h (95%CI −44.4, −31.9); Ashrafian et al. [10]: WMD for BMI −14.0 kg/m$^2$ (95%CI −16.4, −11.9) and WMD for AHI −29.0 events/h (95%CI −36.7, −22.4)]. However, there were two key limitations of these previous reviews. Firstly, the quality of studies included were low (i.e., non-RCTs), and since then, a number of higher-quality studies have been published. Secondly, the previous meta-analyses did not consider the impact of the type of respiratory events scoring (RES) criteria in the determination of the AHI – given that the AHI can vary by $\geq 30\%$ (median AHI) depending on the scoring criterion used [11]. Accordingly, the aims of the current work were to: a) re-examine the impact of surgical weight loss on the diagnosis and severity of OSA, and b) assess whether variable scoring of the respiratory events impacts on the findings.

## Materials and methods

### *Study protocol and registry registration*

The present systematic review and meta-analysis was performed in line with recommendations from the Cochrane Collaboration and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12]. The study protocol was developed and registered on PROSPERO (CRD42017062359).

### *Search strategy*

Keywords were grouped into two main areas, those regarding OSA (obstructive sleep apnoea, sleep disordered breathing) and those concerning surgical weight loss (bariatric surg*.mp, surg* weight loss, lap band.mp, gastric bypass.mp, sleeve gastrectomy, and bariatric adj5 surg*.mp). Electronic searches were performed on Ovid MEDLINE, Ovid MEDLINE including In-Process and Other Non-Indexed Citations, EMBASE Ovid, PubMed, Cochrane Library Review and ClinicalKey (http://www.clinicalkey.com.au) up to 18th December 2017. References of retrieved articles and of previously published systematic reviews, meta-analyses and reviews were also searched [7,10,13,14]. The complete search strategy is described in Fig. 1.

### *Eligibility criteria for study selection*

Studies were included (irrespective of design) if both of the following primary outcome measures were reported (before and after bariatric surgery):

- AHI or equivalent respiratory disturbance index (RDI) as determined using Type 1–3 sleep studies conducted in accordance with the American Academy of Sleep Medicine (AASM) guidelines [15].
- body mass index (BMI)

Studies were excluded from the review if: a) the patients had any other sleep-disordered breathing apart from OSA [e.g., obesity hypoventilation syndrome (OHS) (as this was considered as a different disease entity; i.e., different underlying physiological causes to patients with OSA alone)], b) the study was not published as a full paper, or c) if the English full text was not available.

After removal of duplicates, two study authors (AW and HB) independently selected studies for further examination by title and abstract review. Full text manuscripts of all potentially eligible studies were retrieved for further evaluation. Any disagreements were discussed with and resolved by one of the senior authors (GH). For publications originating from the same data, the study that best fitted the aim of this review, or was thought to best represent the data with the least amount of bias (e.g., selection, publication, follow-up) was included. If multiple publications from the same dataset were suspected, clarification was sought by contacting the corresponding authors. Lastly, individual participant data was sought from high quality publication studies (i.e., RCTs) where possible to enable more targeted analyses.

### *Data extraction and quality review*

Both authors independently extracted the data for all included studies using a standardised data extraction form. Extracted data were compared and checked by both authors. Any differences were discussed with and resolved by one of the senior authors (GH). The

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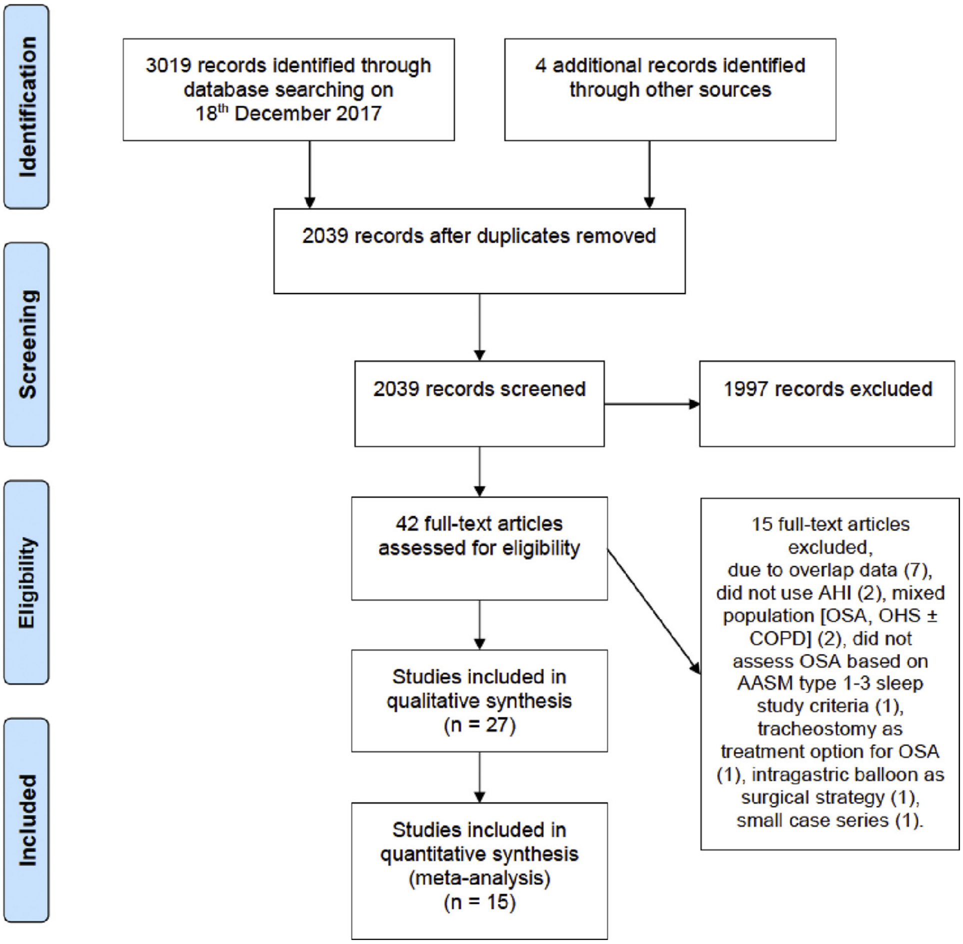

**Fig. 1.** Prisma flow diagram for identification of appropriate studies for inclusion. AASM: American Academy of Sleep Medicine; AHI: apnoea-hypopnoea index; COPD: chronic obstructive pulmonary disease; OHS: obesity hypoventilation syndrome.

primary data outcomes were AHI and BMI before and after bariatric surgery. The secondary outcomes included weight, Epworth sleepiness scale (ESS) scores, oxygen desaturation index (ODI), sleep study type and RES criteria used, type of bariatric surgery performed, and duration of follow-up (i.e., time from bariatric surgery to post-surgery sleep study). Where data had been published several times from the same study, data were extracted from the most recent publication with the longest follow-up period. If two follow-up end points were reported in the study, data with the longest follow-up parameters were used for analysis. However, data from an earlier follow-up time point was considered if there was a high drop-out rate (>75%) in the last follow-up. Relevant corresponding authors were contacted for additional data.

The quality of included studies was assessed using the following:

- RCTs using the Cochrane Risk of Bias (ROBINS2) assessment tool [16].
- non-randomised controlled trials (non-RCTs) using the Cochrane Risk of Bias in Non-Randomised Controlled Trials (ROBINS-I) assessment tool [17].
- before-and-after studies using the *Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group* [18].

An overall GRADE evaluation was performed to provide guidance to the readers on the quality of evidence of studies included in this review [19].

### *Results synthesis and statistical analysis*

All analyses were conducted using STATA (Version 14, StataCorp, 2013, College Station, Texas) and Review Manager®Version 5.3 (Revman) for Windows (The Cochrane Collaboration, Software Update, Oxford, UK). The relationship between surgical weight loss and effect on OSA severity as well as BMI was explored by meta-analysis where possible. Data were analysed using the random-effects models of DerSimonian and Laird to take into account the between-studies variation.

Statistical heterogeneity was assessed using the $I^2$ statistic, with $I^2$ of 0%, 25%, 50% and 75% indicative of nil, mild, moderate and severe heterogeneity respectively [20]. Potential explanations for heterogeneity were explored by sub-group analyses (type of sleep study, RES criteria used, time from bariatric surgery to post-surgery sleep study, publication year [i.e., before and ≥2007], ethnicity, type of bariatric surgery performed, study perspective [i.e., retrospective vs prospective], and study quality). The potential for publication bias was assessed using funnel plots and statistical tests

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described by Begg and Berlin [21] and Egger et al. [22]. Meta-regression was then performed to investigate for possible sources of heterogeneity [e.g., baseline AHI and BMI, change in BMI (WMD for BMI) as well as duration between bariatric surgery and post-surgery sleep study].

### *Individual participant data from RCTs*

Continuous variables were analysed using means and t-tests, and paired data using the Student's t-test. Non-parametric data were analysed using the Mann–Whitney U test, or Kruskal–Wallis rank sum test. A combination of STATA and Revman was used to calculate the overall WMD in AHI, BMI and weight at one-year post randomisation between those receiving bariatric surgery (intervention) and those receiving lifestyle intervention (control). A linear regression model was used to identify predictors of the change in AHI (age, gender, pre-surgery AHI and BMI) following weight loss.

## Results

### *Included studies*

A total of 3019 articles were identified (last search date 18th December 2017) followed by another four articles identified [23–26] via reviewing the reference list from other systematic reviews and meta-analyses [7,10,13,14] in this topic. After removing duplicate records and conducting title and abstract screening of the remaining 2039 articles, 42 full text articles were reviewed. Of these 42 articles, only 27 were included in the final systematic review representing 1169 participants (see Fig. 1 for details). Of the 27 articles included, only three were RCTs; two comparing bariatric surgery with ILI [27,28], and the third comparing bariatric surgery with CPAP [29]. The remaining 24 studies were either non-RCTs (one comparing bariatric surgery vs ILI [30], and the other comparing bariatric surgery vs CPAP [31]) or before-and-after studies with no control group.

Due to different study designs, we analysed data separately according to the following:

- Non-RCTs and before-and-after studies - only 15 studies (two non-RCTs and 13 before-and-after studies) provided sufficient data to be included in the group meta-analysis, with a total of 558 participants.
- RCTs - Individual participant data from patients with OSA from the two RCTs comparing bariatric surgery with ILI [27,28]. There was a total of 39 participants in each of the intervention and control arms (total n = 78).

Characteristics of the included studies and corresponding RES criteria used are shown in Table 1 (for non-RCTs and before-and-after studies) and Table 2 (for RCTs).

The overall quality of evidence across studies was very low, mainly due to a lack of RCTs, small sample sizes, lack of uniformity of inclusion criteria and follow-up, high dropout rates and the potential for all these factors to significantly alter the primary outcomes (See Supplementary Data Tables S1–4 for more details).

### *Systematic review*

Participants were middle-aged (range 30–60 y) and mostly female (range 25–88%). Study sample sizes ranged from eight to 205 participants, with the majority of studies enrolling between 20 and 40 participants. There was large variability in the time between bariatric surgery and first post-surgery sleep study. Most were performed at 12 mo or later, with a follow-up range of three months to five years. Five studies had collected data for two follow-up time points [27–29,31,32]. Study recruitment dates ranged from 1999 to 2015.

15 studies were conducted in participants who underwent malabsorptive bariatric surgery (e.g., sleeve gastrectomy [SG], Roux-en-Y gastric bypass [RYGB] etc.) whereas the remaining studies were performed in participants who received either restrictive bariatric surgery (open or laparoscopic adjustable gastric banding [LAGB]; eight studies), had a combination of malabsorptive and restrictive bariatric surgery (three studies), or the bariatric surgery type was not reported (one study).

A total of 22 (81%) studies conducted a type 1 sleep study [i.e., in-laboratory attended polysomnogram (PSG)] whereas the remainder conducted either type 2 (one study) or type 3 (four studies) studies. However, two studies performed type 3 studies in 26%–45% of participants instead of type 1 studies (for the remainder) due to financial and capacity restrictions [32,33].

While 20 (74%) studies reported the criteria used to score respiratory events, only 14 (70%) of these could be categorised into an equivalent and specific AASM RES criteria [15]. Furthermore, only one study reported how weight loss impacted the AHI when broken down by sleep stage [non-rapid eye movement (NREM) AHI vs rapid eye movement (REM) AHI] and by gender [25].

### *RCTs*

All three studies used LAGB surgery as the intervention arm [27–29]. Furthermore, all included participants with at least moderate OSA (Dixon et al. AHI $\geq$ 20 events/h [27], Feigel-Guiller et al. AHI > 30 events/h [28], Bakker et al. AHI $\geq$ 30 events/h if type 1 study and AHI $\geq$ 20 events/h if type 3 study [29]). Bakker et al. [29] scored the respiratory events based on the AASM 2012 recommended criteria, however, the criteria used in Dixon et al. [27] and Feigel-Guiller et al. [28] was not reported.

All studies were analysed using an intention-to-treat analysis. Of note, there was significant cross-over between groups in the bariatric surgery vs CPAP study [29]. Half of the participants (14/28 participants) in the bariatric surgery group did not receive surgery, with 10 participants receiving CPAP and the remaining four receiving neither intervention. In contrast, only 1/21 participants in the CPAP group crossed over to the bariatric surgery group.

Overall, participants who received bariatric surgery lost more weight and had greater improvements in OSA in comparison to participants who were treated with ILI [27,28]. In contrast, there was no significant difference in AHI and weight loss at 18 mo when bariatric surgery was compared with CPAP [29].

Furthermore, ESS scores improved in all participant groups (bariatric surgery vs ILI [27] and bariatric surgery vs CPAP [29]) with no significant between-group differences.

### *Non-RCTs and before-and-after studies*

All but two studies (i.e., 22 studies) were prospective in study design. Apart from common indication criteria for bariatric surgery, there were diverse inclusion criteria used across all studies with many reporting a high (>25%) dropout rate. Despite this, all studies consistently demonstrated a statistically significant reduction in AHI, BMI and weight after bariatric surgery. Ravesloot et al. was the only before-and-after study with two post-surgery sleep study time-points (see Table 1) [32]. They showed that after bariatric surgery, there was a significant reduction in AHI and BMI at 7.7 mo (n = 110), however, there was no significant difference when these parameters were reassessed at 16.9 mo (n = 50). These data should be interpreted with caution as there was 74% lost to follow-up at

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**Table 1**

Characteristics of included non-randomised controlled trials (non-RCTs) and before-and-after studies and sleep scoring criteria.

| Study and date of publication | Country | Study Design | Sam-ple size | Surgery type (% if reported) | Follow-up (mo) | BMI (kg/m$^2$) | | AHI (events/h) | | Hypopnoea definition | | Sleep scoring criteria (best fit) | Study notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Pre-op | Post-op | Pre-op | Post-op | Flow Reduction | Desat | | |
| Aguiar et al., 2014 [39] | Brazil | PPR | 16 | GBa | 3 | 48.2 (8.6) | 36.9 (6.7) | 15.7 (15.5) | 6.3 (7.5) | >50% | >3% | AASM2007alt (Assuming ≥3% desaturation criteria) | Parallel randomisation 1:2 (bariatric surgery: observation). Control group returns to bariatric surgery wait-list 3 mo later and did not have repeat PSG. |
| Bae et al., 2014 [73] | Korea | P | 10 | Lap RYGB | 13.9 | 39.9 (8.3) | 26.9 (4.4) | 51.0 (34.2) | 9.3 (12.9) | ≥30% | ≥3% | AASM2012rec | Potential for follow-up bias as only 10/37 (27%) participants who had pre-op PSG had a post-op PSG. |
| Bakker et al., 2014 [31] | USA | P<br>non-RCT | 12 | GBa or GBy | 6<br>12–18mo | #43.7 (42.0, 51.4) | #32.7 (30.1, 38.7)<br>#28.3 (25.3, 37.5) | #18.1 (16.3, 67.5) | #10.5 (5.0, 20.8)<br>#6.5 (1.9, 12.8) | ≥50% | 3% | AASM1999 | Participants with OSA (AHI ≥ 5) offered choice of CPAP or bariatric surgery. Surgical group did not use CPAP at any time during the study. |
| da Silva et al., 2013 [40] | Brazil | P | 17 | RYGB (88%) and SG (12%) | 3 | 46.0 (2.0) | 37.0 (2.0) | 19.0 (6.0) | 7.0 (1.0) | NS | NS | NS | Potential for selection bias as 17/26 (65%) completed the protocol, and 68 participants had fulfilled the inclusion criteria. |
| Dixon et al., 2005 [26] | Australia | P | 25 | LAGB | 17.7 (10.0) | 52.7 (9.5) | 37.2 (7.2) | 61.6 (31.9) | 13.4 (13) | >50% | ≥2% | NS | Potential for selection bias as only 25/49 (51%) who had pre-op PSG had a post-op PSG. Participants with baseline AHI ≥ 25 were included. |
| Del Genio et al., 2016 [43] | Italy | P | 36 | Lap SG | 60 | 51.3 (11.6) | 32.1 (6.6) | 32.8 (1.7) | 5.8 (1.2) | ≥30% | ≥4% | AASM2007rec | |
| de Raaff et al., 2016 [33] | The Netherlands | R | 205 | Lap RYGB | 8.6 | 46.0 (7.2) | 33.7 (5.5) | #32.3 (15.0–138) | #8.5 (0.0–53.6) | ≥30% | ≥4% | NS (Suspected to be AASM2007rec) | Potential for selection bias as only 205/437 (47%) participants who had pre-op PSG with AHI ≥ 15 had post-op PSG. |
| Fredheim et al., 2013 [30] | Norway | P<br>non-RCT | 44 | Lap RYGB | 12 | 47.5 (5.6) | 33.4 (4.8) | 29.3 (24.1) | 7.8 (9.7) | 50–90% | ≥3% | AASM2007alt | MOBIL study (still recruiting). Patients with OSA were offered either bariatric surgery or intensive lifestyle intervention. |
| Fritscher et al., 2007 [74] | Brazil | P | 12 | RYGB | 24.2 (6.4) | 55.5 (10.1) | 34.1 (8.1) | #46.5 (33.0–140.0) | #16 (0.9–87.0) | NS | NS | AASM1999 | Only one participant declined the post-op PSG. |
| Guardiano et al., 2003 [75] | USA | R | 8 | Vertical RYGB | 28 | 49 (12) | 34 (12) | 55 (31) | 14 (17) | ≥50% (in tidal volume) | 2 percentage percentage points and an arousal | NS | Small sample size and potential for follow bias as only 8/32 (24%) participants with pre-surgery OSA had |

(continued on next page)

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**Table 1** (*continued* )

| Study and date of publication | Country | Study Design | Sam-ple size | Surgery type (% if reported) | Follow-up (mo) | BMI (kg/m$^2$) | | AHI (events/h) | | Hypopnoea definition | | Sleep scoring criteria (best fit) | Study notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Pre-op | Post-op | Pre-op | Post-op | Flow Reduction | Desat | | |
| | | | | | | | | | | | | | post-op PSG. Participants were not excluded it they were noncompliant with nasal CPAP. |
| Haines et al., 2006 [46] | USA | P | 101 | 50% open and 50% Lap RYGB | #11 (6–42) | 56.0 (1.0) | 38.0 (1.0) | 51.0 (4.0) | 15.0 (2.0) | NS | NS | NS | Potential for follow-up bias as only 35% (101/289) participants with pre-op OSA had post-op PSG. |
| Krieger et al., 2012 [44] | USA | P | 24 | LAGB | 14.5 | 47.2 (11.0) | 35.6 (8.2) | 34.2 (35.0) | 19 (21.7) | NS | NS | AASM2007rec | 6/30 (20%) participants were lost to follow-up. |
| Lettieri et al., 2008 [36] | USA | P | 24 | GBa | 14 | 51 (10.4) | 32.1 (5.5) | 47.9 (33.8) | 24.5 (18.4) | NS | NS | AASM1999 | 25/118 (21%) participants who elected to have bariatric surgery were referred to the Sleep centre for evaluation due to sleep symptoms. |
| Morong et al., 2014 [35] | The Netherlands | R | 91 | NS | 7 | #44.8 (40, 49.6) | #35.7 (31.6, 40.2) | #21.2 (11.5, 34.9) | #6.3 (3.2, 12.3) | NS | NS | NS | Study objective was to determine prevalence of positional OSA. Potential for follow-up bias as 43/162 (27%) participants who had pre-op PSG were lost to follow-up. Subsequently, only 91/119 (76%) met the criteria to be included in analysis, hence there may be selection bias. |
| Pallayova et al., 2011 [25] | USA | P | 23 | RYGB, SG, BP | 13.7 (4.8) | 52.3 (7.4) | 35.7 (6.3) | #32.8 (11.4,75.7) | #4.7 (2.0, 12.9) | NS | NS | AASM1999 | Participants undergoing bariatric surgery at local institution, with clear inclusion criteria. |
| Peromaa-Haavisto et al., 2017 [34] | Finland | P | 132[a] | Lap RYGB with small gastric pouch | 12 | 43.9 (6.4) | 33 (5.1) | 27.6 (24.6) | 9.9 (11.2) | >30% | ≥4% | AASM2007rec | 119/132 (90%) participants who had pre-op PSG and OSA completed post-op PSG. |
| Priyadarshini et al., 2017 [45] | India | P | 27 | Lap SG or Lap RYGB | 5.2 (2.5) | 48.4 (8.2) | 41.2 (8.2) | 31.8 (20.4) | 20.2 (23.1) | NS | NS | AASM 2007 NS further | 26/27 (96%) participants at baseline had OSA on pre-op PSG. |
| Rao et al., 2009 [76] | Singapore | P | 46 | LAGB | 12.6 | 45.2 (33–60)[a] | 30 (23–40.3) | 38.11 (NS) | 13.18 (NS) | >50% | ≥2% | NS | Potential selection bias as only 75/161 (47%) participants who had pre-op PSG with AHI ≥ 15 were offered a post-op PSG using random selection. |

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| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ravesloot et al., 2014 [32] | The Netherlands | P | 110 | Lap RYGB (63.6%), LAGB (31.8%), SG (4.5%) | 7.7 | #44.0 (33.6–66.0) | #35.4 (24.9–55.0) | #27.3 (5.8–142.0) | #8.8 (0.2–96.0) | >30% | ≥4% | NS<br>-Suspected to be AASM2007rec | Potential for selection bias as 110/195 (56%) who had pre-op PSG and OSA had 1st post-op PSG, and only 50/110 (45%) had 2nd post-op PSG. Median values reported as were vastly different from the reported mean values. |
| | | | 50 (42 for BMI) | As above | 16.9 (4.3) | | #34.4 (23.4–54.0) | | #11.1 (1.3–66.0) | | | | |
| Shaarawy et al., 2016 [41] | Egypt | P | 22 | SG | 12 | 48.2 (7.3) | 35.9 (4.8) | 55.8 (8.3) | 12.8 (11.3) | NS | NS | NS | Participants had severe OSA and could not tolerate CPAP. 5/27 (19%) participants were lost to follow-up. |
| Suliman et al., 2016 [77] | Egypt | P | 20 | SG | 8.3 (1.0) | 60.5 (9.0) | 41.9 (6.0) | #18.0 (8.2–42.0) | #10.0 (3.0–22.0) | NS | NS | NS | Potential for selection bias because only 20/56 (36%) participants with OSA on pre-op PSG had post-op PSG. |
| Valencia-Flores et al., 2004 [42] | Mexico | P | 28 | RYGB (39.3%), Distal RYGB (39.3%), VBG (21.4%) | 13.7 | 56.5 (12.3) | 39.2 (8.5) | 53.7 (46.9) | 15.2 (22.5) | 20–50% | >3% | NS | Potential for selection bias as only 29/65 (45%) who attended pre-op evaluation at Sleep clinic agreed to have post-op evaluation at one year. |
| Xie et al., 2016 [78] | Ireland | P | 15 | Lap GBy, Lap SG, GBa | 6 | #47.9 (40.6–68.7) | #37.0 (28–53) | #45.6 (17.5–86.9) | #8.2 (0.0–44.2) | ≥30% | ≥4% | AASM2007rec | Possible selection bias as only participants with documented severe OSA (AHI ≥ 30 events/h) were invited for post-op PSG. 19/52 (36.5%) participants who had been utilising CPAP agreed to undergo post-op PSG, 4/19 (21%) did not have recorded pre-op AHI for comparison. |
| Zou et al., 2015 [37] | China | P | 44 | Lap RYGB | 9.7 | 31.1 (3.4) | 24.4 (2.6) | 22.4 (17.8) | 7.1 (9.4) | ≥30% | ≥4% | AASM2007rec | Participants had OSA and type 2 diabetes mellitus. Suspect some similar participant data from studies published by Xu et al. [38] and Jiao et al. [79]. 10/54 (19%) from initial 54 participants with pre-op PSG were lost to follow-up. |

1st: first; 2nd: second; AASM: American Academy of Sleep Medicine; AASM2007alt: AASM 2007 alternate criteria; AASM2007rec: AASM 2007 recommended criteria; AASM2012rec: AASM 2012 recommended criteria; BP: biliopancreatic diversion with duodenal switch; CPAP: continuous positive airway pressure; Desat: oxygen desaturation; GBa: gastric banding; GBy: gastric bypass; LAGB: laparoscopic adjustable gastric banding; MOBIL: Morbid Obesity treatment, Bariatric Surgery versus Intensive Lifestyle intervention Study, ClinicalTrials.gov number NCT00273104; Lap: laparoscopic; NS: not specified; SG: sleeve gastrectomy; P: prospective; Pre-op: prior bariatric surgery; Post-op: after bariatric surgery; PPR: prospective parallel randomisation; PSG: polysomnography; R: retrospective; RCT: randomised controlled trial; RYGB: Roux-en-Y gastric bypass; VBG: vertical banded gastroplasty. All values are presented as mean (standard deviation) unless indicated otherwise.

#median. If (x,y) = interquartile range, if (x-y) = range.

[a] Only 119 participants had post-op PSG, and only 128 participants had post-op BMI recorded.

**Table 2**

Characteristics of included randomised controlled trials (RCTs) and sleep scoring criteria.

| First Author | Country | Sample size (unless otherwise specified) | Intervention | Follow-up (months) | BMI (kg/m$^2$) | | | AHI (events/h) | | | Study notes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Baseline | 1$^{st}$ follow-up | 2$^{nd}$ follow-up | Baseline | 1$^{st}$ follow-up | 2$^{nd}$ follow-up | |
| Bakker et al., 2017 [29] | USA | 28 | LAGB | 9 mo and 18 mo | 39.1 (2.9) | 35.9 (3.5)<br>n = 25 | 35.7 (3.9)[a]<br>n = 24 | 51.5 (23.5) | 39.3 (26.4)[a]<br>n = 25 | 34.1 (24.6)<br>n = 24 | Participants had AHI ≥ 30 (type 1 study) and at least one OSA symptom. All participants in both arms were given a weight loss intervention (counseling on diet and exercise). There was a significant cross-over of participants from the bariatric surgery group to the CPAP group.<br>Sleep scoring criteria: Hypopnoea >30% flow reduction and ≥3% oxygen desaturation.<br>Suspected to be AASM2012rec. |
| | | 21 | CPAP | 9 mo and 18 mo | 38.7 (3.1) | 37.4 (3.7)<br>n = 18 | 37.4 (4.5)<br>n = 16 | 47.5 (31.5) | 34.7 (31.6)<br>n = 18 | 36.4 (23.2)<br>n = 16 | |
| Dixon et al., 2012 [27] | Australia | 30 | LAGB | 12 mo and 24 mo | 46.3 (5.8) | 38.2 (5.6) | 36.6 (5.7) | 64.8 (33.0) | 29.7 (24.8)<br>n = 24 | 36.7 (29.9)<br>n = 28 | Participants had AHI ≥ 20 on PSG within 6 mo of recruitment. Recruited from seven Melbourne Sleep clinics in Australia. Both groups had open access to a bariatric physician, sleep physician and dietitian, and were reviewed every 4–6 weeks throughout the 2-year trial. ILI group were offered a VLED program and a 500 kcal daily deficit. |
| | | 30 | ILI | 12 mo and 24 mo | 43.8 (5.1) | 36.6 (13.8)<br>n = 27 | 39.5 (11.8)<br>n = 28 | 57.2 (30.3) | 40.2 (28.7)<br>n = 22 | 42.7 (23.9)<br>n = 26 | Sleep scoring criteria not specified. All participants were provided APAP. There was a five-day CPAP wash-out period prior to any planned PSGs. |
| Feigel-Guiller et al., 2015 [28] | France | 19 | LAGB | 12 mo and 36 mo (120 mo had no PSG) | 47.8 (8.1) | 40.6 (5.4)<br>n = 17 | 41.6 (6.4)<br>n = 15 | 59.5 (19.9) | 28.3 (22.2)<br>n = 15 | 35.5 (22.0)<br>n = 14 | Participants had with AHI>30 (indication for NIV). Individual participant data (OSA only) were requested from the author (this trial had also recruited participants with OHS). Both treatment groups were advised to consume a low energy 1400 kcal/day diet and to perform physical exercise, and were reviewed by a registered dietician and physician monthly for first 6 mo, and every 2 y after. After a 3-year period, participants were free to use nutritional care or to undergo another bariatric procedure. Post-trial monitoring via phone was conducted at 10 y post enrolment, however, no clinical or sleep study was performed. |
| | | 19 (one drop-out) | INC | 12 mo and 36 mo (120 mo had no PSG) | 43.2 (6.3)<br>n = 19 | 39.6 (8.2)<br>n = 18 | 41.4 (8.3)<br>n = 14 | 52.6 (22.2)<br>n = 18 | 38.7 (18.8)<br>n = 17 | 46.0 (21.7)<br>n = 12 | Sleep scoring criteria was not specified. |

Results are presented as mean (standard deviation) unless otherwise specified.

1$^{st}$: first; 2nd: second; AASM2012rec: American Academy of Sleep Medicine 2012 recommended criteria; AHI: apnoea-hypopnoea index (events/h); APAP: automatic positive airway pressure; BMI: body mass index (kg/m$^2$); ILI: intensive lifestyle intervention; INC: intensive nutritional care; LAGB: laparoscopic adjustable gastric banding; mo: months; n: number of participants; OHS: obesity hypoventilation syndrome; PSG: polysomnography; VLED: very low energy diet.

[a] Data was log-transformed: AHI at 9 mo and BMI at 18 mo.

the second time-point when compared with the number of participants who had a pre-surgery sleep study.

*Impact of positional OSA and gender*: Interestingly, two before-and-after studies showed that weight loss improved non-supine AHI to a greater degree than the supine AHI [30,34]. Another study reported that 34% of their obese participants pre-bariatric surgery had positional OSA [35].

As for the impact of gender on the primary outcomes, one study observed that men experienced a higher level of reduction in AHI after bariatric surgery compared with women [36]. However, another study which was not included in the systematic review due to suspected overlap/duplication of the data contained within the publication by Zou et al. [37] did not observe any significant difference on change in AHI or BMI after surgery based on gender [38].

An expanded review of both positional OSA and impact of gender on OSA after bariatric surgery can be found in the Supplementary Data section.

## *Meta-analysis*

### *Impact of bariatric surgery on AHI*

Bariatric surgery was associated with a significant reduction in the AHI [WMD −25.1 events/h (95%CI −29.9, −20.2)] however, the $I^2$ value ($I^2 = 97.0\%$) indicated that significant heterogeneity was present (See Fig. 2). The pooled mean pre- and post-surgery AHI was 39.3 ± 15.1 events/h, and 12.5 ± 5.6 events/h respectively. A smaller reduction in AHI was observed in studies with a shorter follow-up time [39] and/or lower pre-surgery AHI [34,37,39,40]. By comparison, studies demonstrating greater reductions in AHI tended to have higher pre-surgical AHIs [27,41,42]. As an additional assessment of the impact that bariatric surgery has on OSA severity, we also conducted a meta-analysis on change in oxygen desaturation index 4% (ODI4%) in three studies [37,41,42]. There were insufficient studies to perform a similar analysis using ODI 3%. See Supplementary Data for further details.

### *Impact of bariatric surgery on BMI*

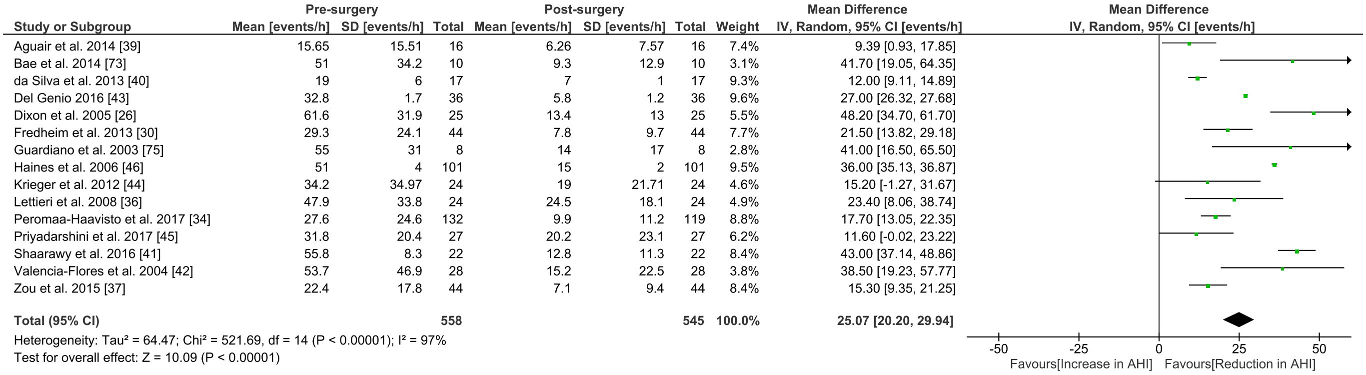
Bariatric surgery was associated with a significant reduction in BMI [WMD −13.2 kg/m$^2$ (95%CI −16.4, −10.0)], however, significant heterogeneity ($I^2 = 97.0\%$) was also present (See Fig. 3). Despite a significant reduction in BMI, the pooled mean post-surgery BMI was still within the obese range (pooled mean pre and post-surgery BMI was 47.8 ± 6.3 kg/m$^2$ and 34.5 ± 4.4 kg/m$^2$ respectively).

### *Impact of bariatric surgery on weight*

Only 12 of 15 studies had reported pre- and post-surgery weight for analysis [26,30,34,36,37,39–45]. In these studies, bariatric surgery was associated with a significant reduction in weight [WMD −35.4 kg (95%CI −41.7, −29.1)], again, with a substantial amount of heterogeneity ($I^2 = 84\%$) being present (See Supplementary Data Fig. S1). Despite significant weight loss, the pooled mean post-surgery weight remained high (95.6 ± 10.6 kg) (pooled mean pre-surgery weight was 133.2 ± 19.0 kg).

### *Impact of bariatric surgery on ESS*

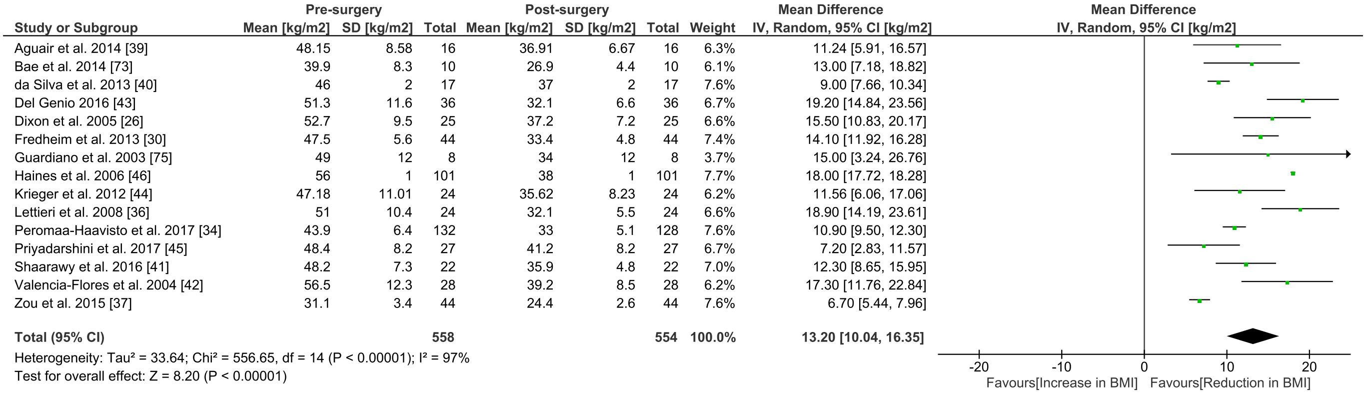
Pre- and post-surgery ESS was available in 10 studies [26,34,36,37,39,41–43,45,46]. There was a significant reduction in ESS [WMD −5.5 (95%CI −7.0, −4.1)] associated with bariatric



| | Pre-surgery | | | Post-surgery | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean [events/h] | SD [events/h] | Total | Mean [events/h] | SD [events/h] | Total | Weight | IV, Random, 95% CI [events/h] |
| Aguair et al. 2014 [39] | 15.65 | 15.51 | 16 | 6.26 | 7.57 | 16 | 7.4% | 9.39 [0.93, 17.85] |
| Bae et al. 2014 [73] | 51 | 34.2 | 10 | 9.3 | 12.9 | 10 | 3.1% | 41.70 [19.05, 64.35] |
| da Silva et al. 2013 [40] | 19 | 6 | 17 | 7 | 1 | 17 | 9.3% | 12.00 [9.11, 14.89] |
| Del Genio 2016 [43] | 32.8 | 1.7 | 36 | 5.8 | 1.2 | 36 | 9.6% | 27.00 [26.32, 27.68] |
| Dixon et al. 2005 [26] | 61.6 | 31.9 | 25 | 13.4 | 13 | 25 | 5.5% | 48.20 [34.70, 61.70] |
| Fredheim et al. 2013 [30] | 29.3 | 24.1 | 44 | 7.8 | 9.7 | 44 | 7.7% | 21.50 [13.82, 29.18] |
| Guardiano et al. 2003 [75] | 55 | 31 | 8 | 14 | 17 | 8 | 2.8% | 41.00 [16.50, 65.50] |
| Haines et al. 2006 [46] | 51 | 4 | 101 | 15 | 2 | 101 | 9.5% | 36.00 [35.13, 36.87] |
| Krieger et al. 2012 [44] | 34.2 | 34.97 | 24 | 19 | 21.71 | 24 | 4.6% | 15.20 [-1.27, 31.67] |
| Lettieri et al. 2008 [36] | 47.9 | 33.8 | 24 | 24.5 | 18.1 | 24 | 4.9% | 23.40 [8.06, 38.74] |
| Peromaa-Haavisto et al. 2017 [34] | 27.6 | 24.6 | 132 | 9.9 | 11.2 | 119 | 8.8% | 17.70 [13.05, 22.35] |
| Priyadarshini et al. 2017 [45] | 31.8 | 20.4 | 27 | 20.2 | 23.1 | 27 | 6.2% | 11.60 [-0.02, 23.22] |
| Shaarawy et al. 2016 [41] | 55.8 | 8.3 | 22 | 12.8 | 11.3 | 22 | 8.4% | 43.00 [37.14, 48.86] |
| Valencia-Flores et al. 2004 [42] | 53.7 | 46.9 | 28 | 15.2 | 22.5 | 28 | 3.8% | 38.50 [19.23, 57.77] |
| Zou et al. 2015 [37] | 22.4 | 17.8 | 44 | 7.1 | 9.4 | 44 | 8.4% | 15.30 [9.35, 21.25] |
| **Total (95% CI)** | | | **558** | | | **545** | **100.0%** | **25.07 [20.20, 29.94]** |

Heterogeneity: Tau² = 64.47; Chi² = 521.69, df = 14 (P < 0.00001); I² = 97%
Test for overall effect: Z = 10.09 (P < 0.00001)

**Fig. 2.** Pre-surgery compared to post-surgery for the primary outcome of ΔAHI forest plot. AHI: apnoea-hypopnoea index (events/h); SD: standard deviation; CI: confidence interval.



| | Pre-surgery | | | Post-surgery | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean [kg/m2] | SD [kg/m2] | Total | Mean [kg/m2] | SD [kg/m2] | Total | Weight | IV, Random, 95% CI [kg/m2] |
| Aguair et al. 2014 [39] | 48.15 | 8.58 | 16 | 36.91 | 6.67 | 16 | 6.3% | 11.24 [5.91, 16.57] |
| Bae et al. 2014 [73] | 39.9 | 8.3 | 10 | 26.9 | 4.4 | 10 | 6.1% | 13.00 [7.18, 18.82] |
| da Silva et al. 2013 [40] | 46 | 2 | 17 | 37 | 2 | 17 | 7.6% | 9.00 [7.66, 10.34] |
| Del Genio 2016 [43] | 51.3 | 11.6 | 36 | 32.1 | 6.6 | 36 | 6.7% | 19.20 [14.84, 23.56] |
| Dixon et al. 2005 [26] | 52.7 | 9.5 | 25 | 37.2 | 7.2 | 25 | 6.6% | 15.50 [10.83, 20.17] |
| Fredheim et al. 2013 [30] | 47.5 | 5.6 | 44 | 33.4 | 4.8 | 44 | 7.4% | 14.10 [11.92, 16.28] |
| Guardiano et al. 2003 [75] | 49 | 12 | 8 | 34 | 12 | 8 | 3.7% | 15.00 [3.24, 26.76] |
| Haines et al. 2006 [46] | 56 | 1 | 101 | 38 | 1 | 101 | 7.7% | 18.00 [17.72, 18.28] |
| Krieger et al. 2012 [44] | 47.18 | 11.01 | 24 | 35.62 | 8.23 | 24 | 6.2% | 11.56 [6.06, 17.06] |
| Lettieri et al. 2008 [36] | 51 | 10.4 | 24 | 32.1 | 5.5 | 24 | 6.6% | 18.90 [14.19, 23.61] |
| Peromaa-Haavisto et al. 2017 [34] | 43.9 | 6.4 | 132 | 33 | 5.1 | 128 | 7.6% | 10.90 [9.50, 12.30] |
| Priyadarshini et al. 2017 [45] | 48.4 | 8.2 | 27 | 41.2 | 8.2 | 27 | 6.7% | 7.20 [2.83, 11.57] |
| Shaarawy et al. 2016 [41] | 48.2 | 7.3 | 22 | 35.9 | 4.8 | 22 | 7.0% | 12.30 [8.65, 15.95] |
| Valencia-Flores et al. 2004 [42] | 56.5 | 12.3 | 28 | 39.2 | 8.5 | 28 | 6.2% | 17.30 [11.76, 22.84] |
| Zou et al. 2015 [37] | 31.1 | 3.4 | 44 | 24.4 | 2.6 | 44 | 7.6% | 6.70 [5.44, 7.96] |
| **Total (95% CI)** | | | **558** | | | **554** | **100.0%** | **13.20 [10.04, 16.35]** |

Heterogeneity: Tau² = 33.64; Chi² = 556.65, df = 14 (P < 0.00001); I² = 97%
Test for overall effect: Z = 8.20 (P < 0.00001)

**Fig. 3.** Pre-surgery compared to post-surgery for the primary outcome of ΔBMI forest plot. BMI: Body mass index (kg/m$^2$); SD: standard deviation; CI: confidence interval.

Please cite this article in press as: Wong A-M, et al., The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis, Sleep Medicine Reviews (2018), https://doi.org/10.1016/j.smrv.2018.06.001

surgery, however, there was significant heterogeneity ($I^2 = 92.0\%$). The pooled mean pre-surgery ESS was 11.1 ± 3.9 and post-surgery ESS was 5.6 ± 2.8. Similar to the results of the primary analysis, in this sub-group of studies, there was a significant improvement in AHI [WMD −26.4 events/h (95%CI −31.6, −21.2), $I^2 = 97.5\%$], BMI [WMD −13.6 kg/$m^2$ (95%CI −17.6, −9.6), $I^2 = 97.8\%$] and weight [only nine studies available for analysis: WMD −36.3 kg (95% CI −45.0, −27.6), $I^2 = 86.8\%$] after surgery.

### *Impact of respiratory events scoring criteria on surgical outcomes*

There were only enough studies to perform a meta-analysis in the AASM 2007 groups (four using the AASM 2007 recommended criteria and two using the AASM 2007 alternative criteria). The WMD for AHI was lower in studies using the AASM 2007 recommended [−19.7 events/h (95%CI −27.4, −12.0), $I^2 = 90.3\%$] and AASM 2007 alternate [−15.6 events/h (95%CI −27.4, −3.7); $I^2 = 76.8\%$] criteria compared with the WMD for AHI of all 15 studies [−25.1 events/h (95%CI −29.9, −20.2), $I^2 = 97\%$]. The WMD for BMI, however, was similar across all scoring criteria subgroups (range 11.4 kg/$m^2$ to 18.9 kg/$m^2$).

### *Publication bias and sensitivity analysis*

By excluding conference abstracts (due to lack of peer review) and non-English publications (only one article was excluded [47]) we may have introduced publication bias. However, there was no evidence of publication bias on the results of WMD for AHI, BMI or weight by visual inspection of the funnel plot, or using Begg's and Egger's statistics (see Supplementary Data Table S5 for Begg's and Egger's test p-values).

There was a high degree of heterogeneity between studies ($I^2 > 75\%$), hence, sensitivity analysis was conducted to determine if the AHI, BMI and weight outcomes differed when using different sub-group criteria. The length of time between bariatric surgery and post-surgery sleep studies was likely to explain some of the heterogeneity seen. Specifically, greater improvements in weight and AHI were associated with longer durations between the bariatric surgery and post-surgery sleep studies. Furthermore, less heterogeneity was observed when studies were sub-grouped by year of publication (before vs ≥ 2007). This may be due to participants in studies published before 2007 having lost more weight resulting in larger improvements in AHI. Heterogeneity was not explained by variations in study design, type of surgery (restrictive vs malabsorptive with endocrine effects), study quality or by ethnicity. Furthermore, reductions in both AHI and BMI were similar in participants who received either gastric banding (mainly restrictive) or malabsorptive surgery (e.g., laparoscopic or open RYGB, or SG).

Analysis by meta-regression revealed that baseline AHI was significantly related to the WMD of the AHI effect estimate (see Fig. 4), and it was the largest contributor to the heterogeneity seen in the meta-analysis with a p value of <0.001. Accounting for baseline AHI led to a significant reduction in heterogeneity with a reduction in $Tau^2$ from 64.5 to 4.7. Duration of follow-up (time from bariatric surgery to post-surgery sleep study) was only a significant factor when either baseline BMI or difference in BMI (before and after surgery) was adjusted for in the meta-regression model (p-value = 0.007), suggesting that BMI (baseline or the difference) is a likely confounder (see Supplementary Data Fig. S2 and S3).

### *Pooled analysis of individual participant data with OSA from two randomised controlled trials (RCTs) [bariatric surgery vs intensive lifestyle intervention (ILI)]*

In order to confirm our findings from the above meta-analysis, individual participant data from two RCTs comparing bariatric surgery with ILI were analysed [27,28]. Using a random-effects model, patients receiving bariatric surgery showed a greater improvement in AHI, BMI and weight loss in comparison with the non-surgical group [WMD for AHI −15.3 events/h (95% CI −27.0,−3.6), WMD for BMI −5.5 kg/$m^2$ (95%CI −7.5, −3.6) and WMD for weight −15.8 kg (95%CI −21.4, −15.8) respectively]. There was no significant heterogeneity between studies with an $I^2$ of 0%.

Although both bariatric surgery and ILI groups demonstrated significant reductions in AHI and BMI post-intervention, the percent reduction in AHI and BMI in the bariatric surgery group was two times greater than that achieved by the ILI group (AHI: −50.1% vs −23.7%; BMI: −17.9% vs −7.7%). Importantly, the majority of

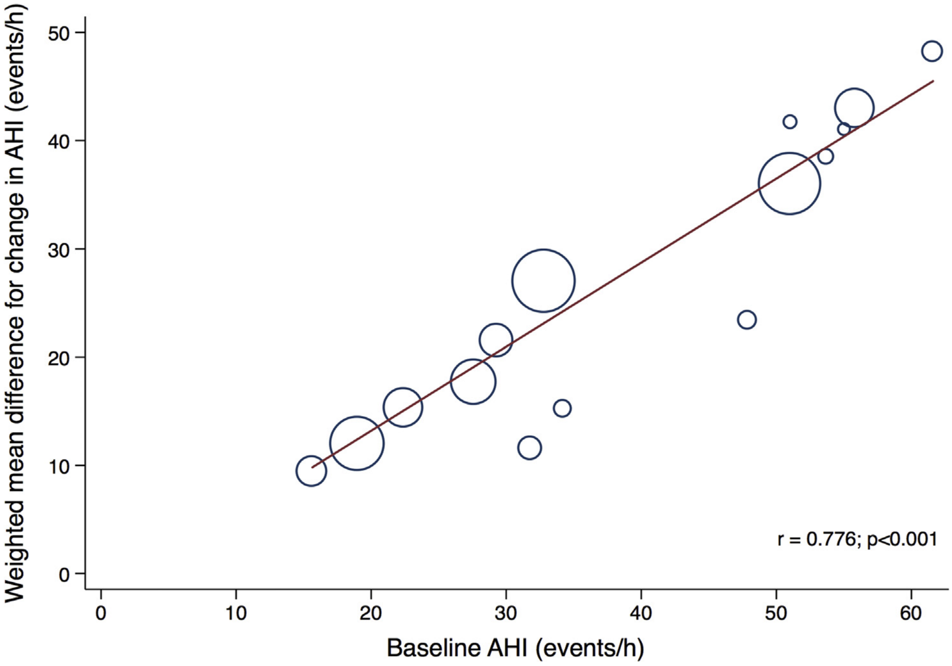


**Fig. 4.** Bubble plot of weighted mean difference for change in AHI versus baseline AHI. AHI: apnoea-hypopnoea index (events/h).

patients still had residual OSA (defined as AHI>5 events/hr) in both surgical (97.5%) and non-surgical (100%) weight loss groups at one year (see Supplementary Data Fig. S4–6).

Additionally, when further analysis was conducted in patients who only received bariatric surgery (n = 39), there was no relationship between the amount of weight loss and change in AHI (see Supplementary Data Fig. S7a–b). Linear regression did not identify any predictors of change in AHI using age, gender, baseline AHI and BMI as the independent variables. Results of the subgroup analysis performed from this dataset based on gender is also available in the supplementary (see Supplementary Data).

## Discussion

The major findings of the present review were that in OSA patients: a) bariatric surgery (regardless of type) can lead to substantial weight loss, significant reductions in OSA severity, as well as considerable improvement in daytime sleepiness (assessed using the ESS), b) surgical weight loss is more effective in reducing both AHI and BMI when compared to non-surgical weight loss strategies, c) higher baseline AHI and BMI, as well as a longer duration of follow-up, are associated with greater reductions in weight and AHI, d) there is no relationship between the amount of weight lost and the improvement in AHI, e) a significant proportion of patients still had residual OSA post-surgery despite improvements in clinical symptoms. There was also a lack of clear reporting of the RES criteria used in the studies included in our review which limited our ability to conduct further analyses on whether the use of different RES criteria affect the primary outcomes.

### *Comparison with previous systematic reviews and meta-analyses*

The findings in this review are similar with that of previous systematic reviews and meta-analyses [7,10], in that surgical weight loss is effective in improving OSA severity. However, there is high heterogeneity observed between studies. By contrast, the current work differs from previous systematic reviews and meta-analyses [7,10] as it contains the addition of more recent high-quality studies, which include three RCTs [27–29]. Furthermore, individual participant data from two of the RCTs [27,28] demonstrated that there was no relationship between the amount of weight loss and improvement in OSA. Meta-regression and subgroup analyses were also performed to explore the reasons for the high level of heterogeneity observed between studies. This exploration aided in drawing better conclusions from our findings as well as better treatment recommendations. This is also the first review to report on how respiratory events were scored across all studies and attempted to assess whether variable RES criteria influenced the primary outcomes.

### *Causes for high heterogeneity between studies – discussion of meta-regression findings*

A common observation between our review and the previous meta-analyses [7,10] is that there was a high level of heterogeneity between studies. This is despite the current review incorporating more stringent inclusion criteria and only including studies which performed pre- and post-surgery sleep studies and reported the AHI or equivalent. In order to assess the factors contributing towards this high degree of heterogeneity between studies, meta-regression of the WMD for AHI and BMI were performed. Of the various factors examined, baseline AHI was the most significant factor contributing to the heterogeneity. In other words, participants with more severe OSA prior to surgery had a larger improvement in AHI post-surgery. Therefore, baseline AHI may be useful as a general predictor of OSA response to bariatric surgery, but importantly, our analysis of the RCT data demonstrated that the amount of weight lost does not predict the amount of OSA improvement. When either baseline BMI or change in BMI (pre- and post-surgery) were included in the meta-regression model, the follow-up duration between surgery and post-surgery sleep study also significantly contributed to the increased heterogeneity observed. Following bariatric surgery, the period of peak weight loss is usually between 12 and 14 mo' post-surgery, hence, re-assessment of OSA at variable time points may influence the observed degree to which OSA severity improves. It is possible that in some studies the participants may not have yet achieved adequate weight loss for OSA improvement, depending on when the post-surgery sleep study was performed.

The observation that participants with a higher baseline AHI and BMI had a greater absolute and relative response than those with less severe OSA and obesity suggests that these participants may either have more “room” for improvement (i.e., are able to achieve a larger reduction in AHI and BMI post-surgical weight loss due to higher starting pre-surgery value), or may be reflective of a “floor effect” (i.e., the AHI cannot fall below a certain low level).

### *Other non-weight related factors mediating the improvement in OSA severity*

Although all studies showed significant weight loss and improvement in OSA after surgery, there was no relationship between the amount of weight loss and the improvement in OSA [27,28]. This lack of relationship helps explain why neither baseline BMI nor difference in BMI before and after surgery accounted for the heterogeneity seen in the meta-regression model. It suggests that there are likely other factors that may be contributing to the variability in AHI seen, apart from the effects of weight loss. Such factors may be influenced by a variety of mechanistic and/or technical factors discussed below:

### *Mechanistic factors*

#### *OSA pathophysiology*

Currently, it is unclear how obesity affects the non-anatomical physiological traits responsible for OSA and this may contribute to the non-linear relationship between weight loss and improvement in AHI. Prior research in OSA patients has shown that weight loss is associated with reductions in upper airway collapsibility when assessed using the critical closing pressure (Pcrit) technique [48]. Furthermore, near complete elimination of OSA has been shown to be dependent on the absolute levels to which Pcrit falls (i.e., $< -4$ cm $H_2O$) [48]. However, in addition to a compromised anatomy, there are several other additional physiological traits now recognised to contribute to the pathogenesis of OSA including: a) poor pharyngeal muscle response – an inability of the pharyngeal muscles to hold open or stiffen the airway during sleep, b) an oversensitive ventilatory control system (i.e., high loop gain), and c) a low respiratory arousal threshold [49]. How obesity alters these traits (in the same individual) and whether it involves primarily one or several of the mechanistic pathways is unknown and requires further research.

#### *Sleep stage dependence*

Another possible explanation for the variability in AHI is because OSA severity as measured by the AHI is sleep stage dependent [50]. In particular, OSA tends to worsen during REM sleep, and typically improves during slow wave sleep [50,51]. Furthermore, REM sleep disordered breathing has been reported to be more prevalent in women than in men, and more specifically, in obese women [52]. Therefore, the derived overall AHI may be influenced by both the composition of NREM and REM sleep sampled for each individual as well as by gender.

The majority of studies in this review did not report the AHI by sleep stage or gender to enable analyses of whether they contributed to significant differences in OSA severity and as such, suggest that this is an area that future research could focus on.

### *Interaction between OSA and sleeping position*

The presence of positional OSA may account for some of this variability in response to bariatric surgery because: a) OSA is frequently more prominent in supine sleep [53], with variability in the total AHI reported depending on the time spent in this position during sleep [54], and b) weight loss improves non-supine AHI by a greater degree than the supine AHI [55,56]. Furthermore, a post-hoc analysis of individual patient data in the RCT by Dixon et al. [27] conducted by Joosten et al. [56] showed that with weight loss there was a normalisation of non-supine AHI in 22% of patients compared with a normalisation of supine AHI in 0% of patients. The improvement in OSA in the lateral position has been shown to be due to more effective airway dilatation in the lateral position, improved caudal traction of the trachea secondary to improved lung volume, and a less collapsible airway (i.e., improved Pcrit) [57].

Combined body position analysis of individual patient data from the two RCTs [27,28] in the current review was not possible due to the lack of supine data in the second RCT reported by Feigel-Guiller et al. [28]. However, similar to the findings of Joosten et al. [56], one non-RCT [30] and one before-and-after study [34] reported greater improvement in non-supine AHI in comparison to supine AHI post-surgery. Collectively, the available evidence suggests that body position may play an important role in the variation of AHI seen before and after surgery, and highlights the potential for position modification therapy as a useful adjunct treatment for OSA in patients who have lost weight, but who still have residual OSA [58], or for those who have more position-dependent OSA.

### *Craniofacial features*

Craniofacial features and upper airway structure have been shown to influence individual OSA treatment response and may contribute to the variability seen in AHI in this review. For instance, Naughton et al. [59] showed that a greater fall in AHI was associated with a shorter jaw length in 57 patients who underwent a two-year randomised clinical weight loss trial (LAGB vs conventional treatment). Another study by Sutherland et al. [60] showed that participants with smaller craniofacial skeletons had greater reductions in AHI with weight loss compared with participants with larger maxillomandibular volumes. None of the studies included in the meta-analysis in this review examined the impact of craniofacial structure on the severity of OSA post weight loss and this is an important consideration for future studies.

### *Variable changes in fat distribution following weight loss*

The rate of weight loss and subsequent change in the amount and distribution of fat may be different for individual patients and hence may have a different impact on the severity of OSA. A number of studies have shown that by using sophisticated imaging in the form of dual-energy X-ray absorptiometry (DEXA) scanning [61] or magnetic resonance imaging (MRI) [62,63], the distribution of fat varies amongst individuals (including tongue fat) and can influence the development of OSA. What is unknown is how weight loss alters the distribution of fat, if there is a predictable pattern of change and whether this leads to improvements in OSA. These measurements were not examined by the studies included in this meta-analysis, but may help explain the lack of a clear relationship observed between weight loss and improvement in AHI.

### *Technical factors*

### *Differences in RES criteria*

Other potential sources of inconsistency in OSA response using the AHI may be related to the differences in RES criteria used across studies. Such variability is likely driven by either institution preference for particular scoring criteria, and/or reflects the changes in clinical practice in line with the AASM scoring criteria that have evolved over time [15]. The key issue with using different respiratory scoring criteria is that there can be more than 30% difference in median AHI for the same sleep study scored using different AASM scoring criteria [11]. Similarly, Duce et al. [64] showed that the NREM and REM AHI changed significantly depending on the AASM scoring criteria utilised, enough to alter the prevalence of REM-OSA.

In this current review, 20% of studies did not report how the respiratory events were scored and of the remaining studies, only 67% could be classified into a specific AASM criterion. Furthermore, only one study reported the AHI breakdown in NREM and REM sleep [25]. Given that these studies were conducted over a period of time in which the scoring criteria have changed, it is not clear if the same scoring criterion was applied to the same participant before and after surgery. Therefore, pooling AHI results from studies that used diverse scoring criteria may contribute to at least some of the heterogeneity observed in the present meta-analysis. Due to a lack of adequate studies available within each AASM scoring criteria, we were unable to systematically assess whether the use of different RES criteria impacted on OSA severity. As such, there needs to be a concerted effort in all future studies of this nature to consistently report the criteria used, as this would better facilitate fair and uniform comparisons of the impact of any intervention. In addition, reporting of other sleep study characteristics (e.g., AHI by sleep stage, ODI, stratification by gender etc.) would enable future analyses to determine whether knowledge of these characteristics would assist in determining which patients have their OSA resolved following weight loss.

### *Improvement in ESS despite residual OSA after surgery*

Across all studies in this review, there was a significant improvement in subjective daytime sleepiness, assessed using the ESS, of - 5.5 (95%CI −7.0, −4.1). This substantial improvement in ESS occurred despite a majority of patients having residual OSA after surgery. The mechanism behind this improvement in sleepiness (independent of OSA) is uncertain but may potentially relate to improvements in metabolic and humeral factors such as reductions in interleukin-6 [65,66]. Furthermore, ESS is a poor measure of sleepiness [67] and improvement may simply be associated with either a general improvement in quality of life due to weight loss (regardless of impact on AHI), or placebo effect from being enrolled in a clinical trial. Irrespective of the mechanism, the importance of symptomatic and therefore quality of life benefits from bariatric surgery in OSA patients should not be underestimated.

### *Bariatric surgery vs CPAP for treatment of OSA*

A recent RCT showed that surgical weight loss and CPAP therapy were equally effective in treating OSA [29]. Interestingly, the CPAP group lost weight over an 18-month period which contradicts data from a recent meta-analysis that suggested that CPAP promoted weight gain [68]. Further discussions on this topic is available in the Supplementary Data.

Please cite this article in press as: Wong A-M, et al., The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis, Sleep Medicine Reviews (2018), https://doi.org/10.1016/j.smrv.2018.06.001

*Study limitations*

The main limitation of this review is that the majority of data obtained are from before-and-after studies with high heterogeneity between studies, variable inclusion criteria which may lead to selection bias, high drop-out rates which may lead to attrition bias, and an overall low level of evidence using the GRADE classification.

Another limitation is the use of the AHI as the main parameter for OSA treatment outcomes. Firstly, there is a lack of standardised RES criteria used to derive the AHI. Secondly, the patient's symptoms (e.g., using the ESS) may not necessarily correlate with the severity of OSA as expressed by AHI [67]. Moreover, OSA is also linked with other important cardiometabolic outcomes (e.g., hypertension, insulin resistance and dyslipidaemia etc.) and the combined effects of weight loss and OSA alleviation may produce greater cardiometabolic benefits than either treatment alone [69]. However, these cardiometabolic outcomes were not universally reported in the studies in this review, hence the impact of weight loss and/or OSA alleviation on these outcomes were not able to be assessed.

Another concern is that there has been a shift in the bariatric surgery field towards SG whereas all of the high-quality studies (i.e., RCTs) and 27% of the studies included in the meta-analysis have utilised gastric banding (either LAGB or not further specified). This shift in practice may be due to SG providing superior weight loss than LAGB at two years [70], as well as the ability of SG to improve glucose tolerance and promote remission of type 2 diabetes [71]. Hence, the impact of surgical weight loss on OSA in this review may be underestimated and needs to be confirmed in patients having SG.

This review also focused on patients exclusively with OSA. There is a strong association between obesity and other complex sleep disordered breathing such as OHS [72], however, there were insufficient studies to make any meaningful analysis of this subpopulation and it would be an area of interest in future research.

Nevertheless, despite the above limitations, we feel the results are likely to be robust as all studies have shown uniform findings of improvement in AHI, BMI and weight after surgery regardless of surgery type with similar discoveries in the three new RCTs.

## Conclusion and clinical implications

In conclusion, bariatric surgery can be an effective treatment strategy in the management of OSA as it leads not only to weight loss, but also leads to improvement in OSA severity and daytime sleepiness. Although baseline OSA severity (i.e., baseline AHI) is a predictor of the absolute improvement in OSA with weight loss, there is no linear correlation between the amount of weight lost and the improvement in AHI, and some OSA frequently persists after surgery. Hence, sleep studies to document the presence and severity of OSA after surgery are recommended to guide accurate ongoing OSA management in these patients. In addition, further research into the impact of body position, influence of weight loss on change in fat distribution and how obesity and subsequent weight loss affect the pathophysiology responsible for OSA is warranted, as they may explain the lack of relationship between the extent of weight loss and improvement of OSA. Finally, future studies need to make a concerted effort to report how respiratory events are scored, as different scoring criteria used can significantly affect the AHI, and this would also enable comparable results of OSA diagnosis and severity across studies.

**Practice Points**

1.) Surgical weight loss significantly improves OSA severity and substantially improves OSA symptoms.
2.) The majority of patients have residual OSA following bariatric surgery, hence objective review of OSA severity using pre- and post-surgery sleep studies is recommended.
3.) There is no clear relationship between the extent of weight loss and improvement in AHI.

**Research Agenda**

1.) There is a need for more adequately powered RCTs exploring the effect of surgical (separated by surgical type) vs non-surgical weight loss on OSA and/or OHS, with both short and long-term data.
2.) Future research studies need to consistently report the RES criteria as well as other OSA characteristics (e.g., AHI based on different sleep stages, ODI etc.) in order to facilitate accurate comparison and interpretation of findings between studies.
3.) There is a need to develop a before bariatric surgery OSA screening protocol and after surgery review recommendations to guide objective reassessment of OSA despite symptom improvement post-surgery.
4.) It is important to measure OSA severity in supine and non-supine sleep, as positional therapy may be a useful adjunct in patients who experience a greater improvement in non-supine AHI with weight loss.
5.) Mechanistic studies aimed at elucidating key physiological and clinical predictors of those that gain the greatest benefit from weight loss are needed.
6.) Measurement of the effect of weight loss on the distribution of fat (body, tongue, visceral) using advanced radiological techniques (e.g., DEXA body composition scan and upper airway MRI) are needed.

## Conflicts of interest

Associate Professor Garun Hamilton has received equipment to support research from Resmed, Phillips Respironics and Air Liquide Healthcare.

## Acknowledgements

The authors wish to thank and acknowledge all the corresponding authors: Professor John Dixon, Dr. Liam Doherty, Dr. Barbara Feigel-Guiller, Dr. Jan Magnus Fredheim, Professor Jøran Hjelmesæth, Dr. Ana C. Krieger, Dr. Michel M. Murr, Dr. Sanjay Patel, Dr. Matilde Valencia-Flores and Professor J. Catesby Ware; for their generosity in providing information and enabling the production of this review. Furthermore, the authors also wish to thank Dr. StellaMay Gwini, Dr. Mehmet Ozmen, Dr. Matthew Page and Dr. Sanjeeva Ranasinha for statistical advice and review of the data, and Dr. Christian R. Osadnik for assistance with populating key meta-regression graphs. Dr. Ai-Ming Wong received an RTP stipend by Monash University for graduate research studies. Dr. Simon Joosten is supported by an NHMRC Early Career Fellowship (1139745). Dr. Shane Landry is supported by NeuroSleep, a NHMRC Centre of

Please cite this article in press as: Wong A-M, et al., The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis, Sleep Medicine Reviews (2018), https://doi.org/10.1016/j.smrv.2018.06.001

Research Excellence (1060992). Dr. Bradley Edwards is supported by a Heart Foundation of Australia Future Leader Fellowship (101167).

## Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.smrv.2018.06.001.

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Please cite this article in press as: Wong A-M, et al., The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis, Sleep Medicine Reviews (2018), https://doi.org/10.1016/j.smrv.2018.06.001