Sleep Breath (2013) 17:925–935
DOI 10.1007/s11325-013-0806-7

REVIEW

The impact of diet and lifestyle management strategies for obstructive sleep apnoea in adults: a systematic review and meta-analysis of randomised controlled trials

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Received: 2 October 2012 / Revised: 21 November 2012 / Accepted: 7 January 2013 / Published online: 30 January 2013

Abstract
Purpose To systematically evaluate the impact of diet, exercise and lifestyle modification programmes on indices of obesity, Obstructive Sleep Apnoea (OSA) parameters and quality of life (QoL) in adults with OSA.
Methods Electronic databases were searched to identify randomised controlled trials published in English with an intervention based on dietary weight loss, exercise and/or lifestyle programme in adults with OSA. Meta-analyses were conducted using random-effects models.
Results Twelve studies met the inclusion criteria with nine comparing similar interventions. Diet and diet plus continuous positive airway pressure (CPAP) therapy were compared in three studies (n=261), and intensive lifestyle programmes and routine care were compared in six studies (n=483). Diet with CPAP therapy reduced weight by −2.64 kg (95 % Confidence Interval (CI) −3.98, −1.30, I^2=0 %) compared with diet alone. No differences were observed for QoL or Epworth Sleepiness Scale. A significant reduction in weight was seen in participants receiving an intensive lifestyle intervention of −5.65 kg (95 % CI −10.91, −0.40, I^2=95.7 %) compared with controls. Reductions were also observed for waist circumference (−5.80 cm, 95 % CI −8.64, −2.96, I^2=77.7 %), body mass index (BMI) (−2.33 kg/m^2, 95 % CI −3.41, −1.24, I^2=78.8 %) and the Apnoea Hypopnoea Index (AHI) (−4.55 events/h, 95 % CI −7.12, −1.98, I^2=54.4 %) but with high levels of heterogeneity.
Conclusions Intensive lifestyle management can significantly reduce obesity indices and improve AHI. Future research is required to investigate this effect due to a limited number of studies identified.

Keywords Obstructive sleep apnoea · Diet · Lifestyle · Randomised controlled trial · Meta-analysis

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Introduction

The prevalence of Obstructive Sleep Apnoea (OSA) is currently estimated to be about 2 to 7 % in middle-aged adults in the general population [1]. Central obesity plays the leading role in the development and severity of chronic conditions including OSA. Approximately, 70 % of OSA subjects are obese, and incidence of OSA in obese men and women is estimated to be 40 % [2, 3]. Left untreated, mild OSA has a natural rapid progression to a moderate and/or severe state [4]. Risk factors for OSA include male gender, middle age, ethnicity, with obesity being the most important

modifiable risk factor [1]. In 2000, Peppard et al. reported that a weight gain of 10 % (n=39) was associated with a 32 % increase in the disease severity index (Apnoea-Hypopnoea Index (AHI)) while a 10 % weight loss (n=17) resulted in an AHI reduction of 26 % [5]. OSA is recognised as an independent risk factor for cardiovascular disease (CVD), hypertension and type 2 diabetes mellitus (T2DM) [6–14]. OSA and T2DM often coexist as both conditions share common risk factors including central obesity. The prevalence of undiagnosed OSA among obese diabetic patients is reported to be 86.6 % whilst prevalence of diabetes among patients with OSA is 40 % [14, 15]. As the epidemic of obesity increases worldwide, the prevalence of OSA is expected to increase further resulting in increased direct healthcare costs, associated additional societal costs relating to co-morbid conditions, absenteeism and accidents [16, 17].

Continuous positive airway pressure (CPAP) therapy is the 'gold standard' treatment for OSA [18]. Although the effectiveness of CPAP in ameliorating OSA-related symptoms, improving insulin sensitivity, reducing hypertension and improving quality of life is evident in the literature [19–21], it is not a curative therapy, and its efficacy relies on long-term compliance which remains a major challenge [22, 23]. Lifestyle modification interventions promoting physical activity and weight loss are actively encouraged in obese OSA subjects and are recommended by expert panels [24, 25]. However, the evidence to date of the effectiveness of lifestyle modification interventions with and without CPAP therapy from randomised controlled trials is conflicting [26–39]. A number of randomised trials have been conducted investigating the impact of intensive lifestyle modification intervention programmes in obese OSA subjects [34, 35, 37–39] which demonstrated weight loss can be sustained for 12 and 24 months post-intervention without additional support and further costs [40]. In contrast, a review assessing the impact of lifestyle modification interventions failed to identify associations between lifestyle management interventions and improved OSA parameters due to a lack of randomised controlled trials [41]. A systematic review and meta-analysis of both randomised and observational studies in obese OSA participants found a significant reduction in both BMI and AHI following weight loss with a dietary intervention [42]. A literature review comparing surgical and non-surgical interventions also showed reductions in BMI and AHI for the diet and lifestyle interventions [43]. To consolidate the evidence in this area, we conducted a systematic review and meta-analysis of randomised controlled trials aiming to evaluate the impact of weight loss through diet and lifestyle modification interventions with and without CPAP therapy on obesity indices (including BMI, weight, waist circumference), OSA parameters (AHI, ODI_4,) and quality of life (QoL) in adults with OSA.

Methods

Literature search

This systematic review and meta-analysis was conducted in accordance to the 'Preferred Reporting Items for Systematic reviews and Meta-Analyses' PRISMA guidelines [44]. The development of the systematic review protocol and search strategy was a collaborative approach between members of our research team and the university librarian. The search syntax coined three main MeSH terms including obstructive sleep apnoea (OSA), lifestyle (diet and/or physical exertion) and randomised controlled trials. Detailed individual search strategies for each of the following bibliographic databases were developed: OVIDSP Medline (1996 to October 2012), OVIDSP Embase (1996 to October 2012) the Cumulative Index to Nursing and Allied Health Literature-CINAHL (from inception to October 2012) and the Cochrane library including CENTRAL, CDSR and DARE databases (from inception to October 2012). Expert opinions were sought, and reference lists from eligible studies and review articles were cross-examined to identify relevant studies.

Study selection and inclusion criteria

Randomised controlled trials with an intervention based on dietary weight loss, exercise and/or lifestyle programme of at least 2 months follow-up in adult subjects (≥18 years of age) with OSA and a disease severity index of an AHI≥5 were eligible for inclusion. A language restriction was applied, and only studies in the English language which met the inclusion criteria were considered in this review. Studies prescribing CPAP therapy to their participants in addition to diet and lifestyle intervention were also included. Pilot studies were excluded from this review.

One reviewer performed the electronic searches (MAT) and two reviewers (MAT and EMB) independently screened titles and abstracts as well as citations retrieved by the electronic searches to assess eligibility. Following retrieval and scrutiny of full text articles, both reviewers independently assessed studies for inclusion based on the criteria for participants, intervention, comparator, outcomes and study design. We resolved disagreement by assigning a panel of three independent reviewers (KK, MJD and APH).

Data extraction and synthesis

Data were extracted independently by two reviewers (MAT and EMB) from those identified as eligible utilising a pretested data extraction form specifically designed to capture details of study design, participant characteristics, diet/lifestyle interventions and outcome measures. Upon completion of the data extraction, one reviewer (MAT) checked for data

reliability, and any disagreement was resolved by discussion with the second reviewer (EMB).

Validity assessment

Study quality was assessed independently by two reviewers (MAT and EMB) utilizing the Jadad scale [45]. The main quality criteria of interest were whether an adequate method of randomisation, blinding and flow of participants had been reported throughout the study. We assigned a maximum score of two points for each of the three main criteria if found to be adequate and allowed a score from zero to six (six indicating the highest quality).

Statistical methods

Meta-analyses were carried out of studies comparing similar interventions (1) diet weight loss programme or advice to reduce weight versus a diet plus CPAP therapy and (2) intensive lifestyle intervention programme (specific weight loss and/or exercise plan) versus routine care (based on dietary and/or exercise advice only) comparisons. The primary outcome was weight loss (kilograms), and secondary outcomes included AHI, ODI_4, BMI, waist circumference, Epworth Sleepiness Scale (ESS) and QoL. Continuous outcomes were reported in a variety of ways either as the mean change and standard deviation per arm from baseline to follow-up or the final absolute mean and standard deviation per arm; the differences between these were assumed to be equal. Data were pooled using a random-effect model to account for statistical heterogeneity between studies. The weight mean difference (WMD) statistic and 95 % confidence intervals were calculated. Heterogeneity was assessed with the chi-squared (χ^2) test, and variation between studies attributable to heterogeneity was calculated using the I^2 statistic. We predefined heterogeneity (I^2=0 % for no heterogeneity, I^2=25 % for low, I^2=50 % for medium and $I^2 \geq$ 75 % for high) [46]. Significance was set at $p<0.05$, and 95 % confidence intervals are indicated throughout. The data were analysed with Stata (StataCorp. 2007. *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP.)

Results

Search results

Figure 1 summarises the results of the search. Seven hundred sixty-five articles were identified of which only 18 articles investigated the impact of diet, exercise and lifestyle management strategies on OSA subjects. Three studies were excluded due to a non-randomised design [47–49]. One study included participants with sleep-related breathing disorders who underwent surgical treatments [50], one involved oral appliances [51] and another was a pilot study [30]. Consequently, these were excluded [30, 47–51]. Twelve eligible studies satisfying all the inclusion criteria for the systematic review were identified [27–29, 31–39], with one study [39] publishing ESS and QoL results in a second publication [52]. The baseline characteristics of these studies are shown in Table 1.

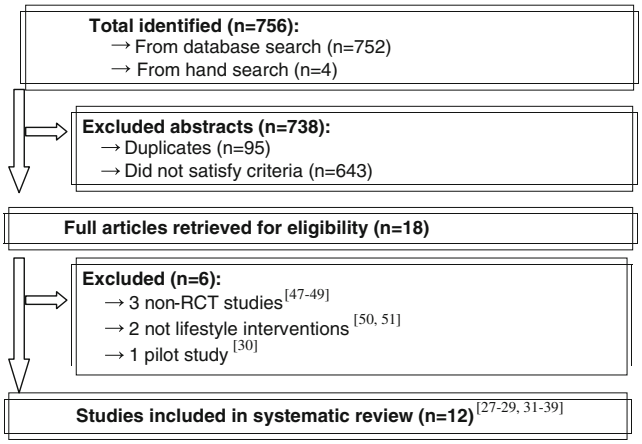

Fig. 1 Flow *diagram* of study selection

Intervention programmes

Three studies compared a diet programme with diet plus CPAP therapy [27–29]. Another six studies compared intensive lifestyle modification interventions which prescribed a specific dietary and/or exercise programme with routine care which included dietary and/or exercise advice only [33–35, 37–39]. One study compared a very low calorie diet with usual diet [36]; one study compared an exercise training programme based on breathing and aerobic exercises [32]; the final study compared a dietary advice programme with three different hypnotherapy options as a mean of weight loss [31]. All 12 studies employed multidisciplinary teams of highly trained staff to deliver the intervention programmes. All included regular follow-up appointments and assessments with the study participants. The length of diet, exercise and lifestyle interventions ranged from 2 to 18 months.

Study quality and publication bias

None of the studies met all the criteria of the quality assessment tool with all papers missing a full score for blinding. In addition, we identified one study in which the authors reported intention-to-treat analysis [28]; however, this was compromised as the lost-to-follow-up participants were not included in the analysis, and subsequently, it only gained a

Table 1 Baseline characteristics of the nine included studies (1) diet+CPAP; (2) intensive lifestyle intervention; (3) other

	Study details	Final sample size	Age (years)	Intervention	OSA diagnostic test	OSA severity index [AHI/ODI_4]	Body mass index [BMI, kg/m^2]	ESS	QoL	Treatment duration (months)	Jadad quality score	Included in meta-analysis
1	Ballester E[27] 1999 Spain	105 men and women	53±10 (mean±SEM)	Conservative treatment+CPAP (sleep hygiene and weight loss programme, home diet prescribed by a dietician) versus conservative treatment only	Partially attended Nighttime respiratory recording [NTRR]	*Severe* whole group 56±20 AHI (mean±SEM)	Whole group 32±6 (mean±SEM)	Whole group 12±5 (mean±SEM)	NHP sleep whole group 26.6.±3.5 (mean±SEM)	3	4	√
	Monasterio C[28] 2001 Spain	125 men and women	54±9 (mean±SD)	Conservative measures+CPAP (Weight loss programme following a home diet, avoidance of sedatives and alcohol consumption, avoidance of supine position during sleep and adequate hours of sleep) versus conservative measures only	PSG	*Moderate* Whole group 20±6 AHI (mean±SD)	Whole group 29±4 (mean±SD)	Whole group 12.6 ±4.6 (mean±SD)	NHP: whole group, 20.5±18 (mean±SD)	6	3	√
	Kajaste S[29] 2004 Finland	31 men	49.1±7.9 (mean±SD)	Weight reduction strategy+CPAP (individualised CBT approach and dietary counselling versus CBT, and dietary counselling	PSG	*Moderate* whole group 20±6 ODI_4 (mean±SD)	Whole group 43.8±5.4 (mean±SD)	Not assessed by ESS	Not assessed via NHP	24	3	√
2	Foster GD[34] 2009 USA	264 men and women	61.2±6.5 (mean±SD)	Intensive lifestyle intervention (group weight loss programme based on low-calorie diet and physical activity prescription of 175 min/week of moderate, developed specifically for obese T2DM patients) versus 3 group diabetes support education sessions focused on diet, physical activity and social support	Unattended PSG	*Moderate* whole group 23.2±16.5 AHI (mean±SD) 19.4±4.9 ODI_4 (mean±SD)	Whole group 36.7±5.7 (mean±SD)	Not assessed	Not assessed	12	5	√
	Tuomilehto HP[35] 2009 Finland	71 men and women	50.9±8.6 (mean±SD)	Lifestyle intervention (Individual tailored counselling weight reduction programme with emphasis placed on diet, exercise and modification of lifestyle focusing on eating behaviour) versus 1 dietary and exercise counselling session	Embletta.	*Mild* whole group 9.65±12 AHI (mean±SD)	Intervention, 33.4±2.8 (mean±SD) control, 31.4±2.7 (mean±SD)	10.9±9.8 (mean±SD)	Not assessed via NHP	12	4	√
	Kemppainen T[33] 2008 Finland	52 men and women	51±8.3 (mean±SD)	Lifestyle intervention (Individual tailored counselling and weight reduction programme with emphasis on diet, exercise and lifestyle modification focusing on eating behaviour.) versus 1 dietary and exercise counselling session	Embletta.	*Mild* whole group 10.1±6.3AHI (mean±SD)	Whole group 32.5±3.3 (mean±SD)	Not assessed	Not assessed via NHP	3	2	√
	Papandreou C[38] 2012 Greece	21 men and women	48.1±12.4 (mean±SD)	Intensive lifestyle intervention (individualised weight reduction programme based on a low-calorie Mediterranean diet and physical activity prescription of at least 30 min/day, developed specifically for obese OSA patients who were under CPAP treatment.) versus individualised weight reduction programme based on a low-calorie prudent diet and physical activity prescription of at least 30 min/day, developed specifically for obese OSA patients who were under CPAP treatment	PSG	*Severe* whole group 46.2±32.7AHI (mean±SD)	Whole group 36.6±3.7 (mean±SD)	Not assessed	Not assessed	6	4	√
	Kline C[39] 2011 USA	43 men and women	46.9±1.2 (mean±SE)	Intensive lifestyle intervention (group exercise training based on 150 min/week of moderate intensity aerobic activity followed by resistance training twice/week) versus stretching exercises	PSG	*Moderate* 28.3±5.6 AHI (mean±SE)	Whole group 34.8±0.9 (mean±SE)	Whole group 9.2±0.9 (mean±SE) **Data obtained from Kline 2012[52]	Not assessed via NHP	3	4	√

Table 1 (continued)

	Study details	Final sample size	Age (years)	Intervention	OSA diagnostic test	OSA severity index [AHI/ODI_4]	Body mass index [BMI, kg/m^2]	ESS	QoL	Treatment duration (months)	Jadad quality score	Included in meta-analysis
	Ackel-D'Elia C[37] 2012 Brazil	32 men	48.9±8.45 (mean±SD)	Intensive lifestyle intervention (2 month supervised aerobic exercise three times/week+CPAP therapy) versus CPAP therapy only	PSG	*Moderate* >15 AHI	Whole group 28.2±2.6 (mean±SD)	Whole group 13.5±4.4 (mean±SD)	Not assessed via NHP	2	3	√
3	Sengul Y[32] 2009 Turkey	20 men	51.2±7 (mean±SD)	Exercise training programme (breathing and aerobic exercises) versus no treatment	PSG	*Moderate* whole group 16.5±5.94 AHI (mean±SD)	Whole group 29.79±2.66 (mean±SD)	Whole group 5.81±5.6 (mean±SD)	Not assessed via NHP	6	2	x
	Stradling J[31] 1997 UK	46 men and women	≥18 , (adults, the authors do not provide this information)	*Intervention Arm 1:* dietary advice and hypnotherapy type 1 (with emphasis on ego strengthening centred on stress reduction) *Intervention Arm 2:* dietary advice and hypnotherapy type 2 (with emphasis on ego strengthening centred on altering attitudes to food using the Spiegel and Spiegel approach) versus dietary advice on two occasions only	Not stated	Not assessed	Whole group 39.2±6.7 (mean±SD)	Not assessed	Not assessed	18	2	x
	Johansson K[36] 2009 Sweden	63 men	49±7.3 (mean±SD)	Weight loss programme (very low-energy diet using a standard 2.3 MJ/day liquid energy intake protocol–Cambridge diet) versus usual diet	2 consecutive unattended sleep studies using a six-channel ambulatory polygraphy equipment	*Severe* whole group 37±15 AHI (mean±SD)	Whole group 34.6±2.9 (mean±SD)	Whole group 8±5 (mean±SD)	Not assessed	2.25	3	x

AHI Apnoea Hypopnoea Index (the number of apnoea–hypopnoea events with at least ≥4 % oxygen desaturation per hour of sleep), *ODI_4* Oxygen Desaturation Index (the number of oxygen desaturation events per hour of sleep exceeding 4 % from the baseline), *ESS* Epworth Sleepiness Scale questionnaire, *NHP* Nottingham Health Profile, *NHP Sleep* Nottingham Health Profile–domain: Sleep

single score on the flow of participants criterion. Publication bias was not assessed in this meta-analysis due to the small number of studies.

Systematic review results

Diet programmes with diet plus CPAP therapy (Table 1, "1")

Table 1 ("1") shows the study characteristics for the three European studies comparing diet programmes with diet plus CPAP (n=261) [27–29]. The sample sizes ranged from 31 to 125; the mean participant age from 49 to 54 years, and the mean BMI across the studies ranged from 29 to 43.8 kg/m^2. Weight (kilograms) was available in two studies only. The AHI was employed as the OSA severity index in two studies [27, 28] that was measured objectively by the in-built CPAP smart card reader with the 4 % oxygen desaturation index (ODI_4) reported in one study [29]. The cut-off points for AHI severity were set as mild=5−14 events/h, moderate=15−29 events/h and severe≥30 events/h. Daytime sleepiness using the ESS was measured in two studies, and quality of life was measured in two studies using the Nottingham Health Profile (NHP) questionnaire.

Ballester et al. [27] randomised 105 consecutive subjects with severe OSA (AHI=56±20 events/h) to receive either conservative measures including a weight loss diet plan plus CPAP or conservative measures only. The authors observed a greater relief of sleepiness and other OSA-related symptoms at 3 months post-intervention in the intervention group. The odds ratio of experiencing a treatment effect when receiving a diet plus CPAP compared with diet only was 6.52 based on the ESS, Sleep Apnoea Hypopnoea (SAHS)-related symptoms questionnaire and the energy domain from the NHP questionnaire. Although the weight loss achieved by the intervention group was only 1.1 kg when compared with 3.1 kg achieved by the control group, the authors observed a greater well-being and comfort of patients in the conservative measures plus CPAP group supporting CPAP as the treatment of choice for moderate to severe OSA.

Monasterio et al. [28] conducted a study of similar design to Ballester [27] and randomised 142 consecutive subjects with an AHI of 10–30 events/h to receive either conservative treatment including a weight loss diet plan plus CPAP or conservative treatment only. The overall weight loss reported at 6 months was 2.7±4.3 kg in the control group compared with no change in weight loss (+0.1±3.4 kg) in conservative treatment plus CPAP (p<0.001). However, the authors reported a significant improvement in SAHS directly related symptoms suggesting a potential role of CPAP in treating mild OSA patients on the basis of a beneficial effect on symptoms.

Kajaste et al. [29] randomised 31 obese OSA males (mean BMI 43.8±5.4 kg/m^2) to receive either a 2-year very low calorie diet (VLCD) and a cognitive behavioural therapy (CBT) weight reduction programme or a 2-year intervention which combined a VLCD, CBT with the addition of CPAP for the first 6 months. The mean weight loss reported was 19.1±10.2 kg for the whole group at 6 months, 18.3±13.2 kg at 12 months and 12.6±4.7 kg at 24 months. The addition of CPAP in the first 6 months to the weight reduction strategy did not result in greater weight loss at any time point.

Meta-analyses results

Diet programmes with diet plus CPAP therapy (Table 2, "1")

Meta analyses were conducted for the three identified studies [27–29], and the pooled results are shown in Table 2. A significant reduction in weight of −2.64 kg was observed

Table 2 Meta-analysis results: (1) diet+CPAP and (2) intensive lifestyle interventions

	Comparison	No. of studies	Cases/non-cases	Pooled WMD (95 % CI)	Heterogeneity	
					(I^2 %)	p value
(1)	Weight (kg)	3 [27–29]	151/110	−2.64 (−3.98 to −1.30)	0 %	0.657
	BMI (kg/m^2)	2 [28, 29]	83/73	−0.18 (−3.62 to −3.27)	57.4 %	0.126
	ESS	2 [27, 28]	134/96	−3.20 (−6.62 to 0.23)	82.7 %	0.016
	QoL	2 [27, 28]	134/96	−0.93 (−5.93 to 4.06)	0 %	0.481
(2)	Weight (kg)	4 [34, 35, 38, 39]	198/202	−5.65 (−10.91 to −0.40)	95.7 %	0.0001
	Waist circumference (cm)	4 [34, 35, 38, 39]	198/202	−5.80 (−8.64 to −2.96)	77.7 %	0.001
	BMI (kg/m^2)	3 [33, 34, 38]	171/186	−2.33 (−3.41 to −1.24)	78.8 %	0.003
	AHI (events/h)	6 [33–35, 37–39]	262/292	−4.55 (−7.12 to −1.98)	54.4 %	0.041
	ESS	2 [35, 39]	62 /52	−0.31 (−2.03 to −1.40)	33.5.%	0.220

in subjects receiving the diet plus CPAP intervention compared with the control which received diet only. No heterogeneity was observed for this group (I^2=0 %, p=0.657). A non-clinically significant reduction was observed for BMI (−0.18 kg/m^2 between groups). There was a significant reduction in ESS score of −3.19 points in the intervention group compared with the control; however, a high level for heterogeneity was observed for this outcome (I^2=82.7 %, p=0.016). No significant improvement in quality of life was seen in those receiving the intervention.

Systematic review results

Intensive lifestyle intervention programmes with usual care (Table 1, "2")

Table 1 ("2") shows the study characteristics of the six studies that compared intensive lifestyle intervention programmes with usual care (n=483). Two were conducted in Finland [33, 35], two in USA [34, 39], one in Brazil [37] and one in Greece [38]. The mean sample size ranged from 21 to 264; mean participant age ranged from 46.9 to 61 years, and BMI from 28.2 to 36.7 kg/m^2. Weight (kilograms) was available in four studies only [34, 35, 38, 39]. The AHI was used to measure OSA severity in all six studies that was measured objectively by the in-built CPAP smart card reader with two studies also reporting the ODI_4 [34, 52]. Daytime sleepiness measured using the ESS was reported in two studies only [35, 52].

Foster et al. [34] randomised 264 obese (mean BMI 36.7 ±5.7 kg/m^2) diabetic subjects with moderate OSA (mean AHI 23.2±16.5 events/h) to receive either an intensive lifestyle modification programme (ILI) based on a low calorie diet and moderate physical activity (175 min/week) or attended three diabetes support education sessions focused on diet, physical activity and social support over 1 year. A greater weight loss of 10.8 kg was observed in the ILI group post-1-year intervention when compared with the weight loss of 0.6 kg achieved by the control group (p<0.001).

Tuomilehto et al. [35] randomised 71 subjects with mild OSA and a BMI of 28 to 40 kg/m^2 to receive a VLCD programme with supervised lifestyle modification or routine lifestyle counselling on three occasions over 1 year. The mean change in weight post-1 year intervention was 10.7 kg in the intervention group and 2.4 kg in the control group (p<0.001).

Kemppainen et al. [33] randomised 52 subjects and followed them up for 3 months with a BMI of 24–40 kg/m^2 and mild OSA AHI≥5 events/h to receive a supervised, individual lifestyle intervention with a weight reduction counselling programme via consuming a very low calorie diet or to receive a single dietary and exercise session. The authors reported a greater reduction in BMI in the intervention group of 5.4 kg/m^2 compared with 0.49 kg/m^2 in the control group.

Ackel-D'Elia et al. [37] randomised 32 male subjects with a moderate to severe OSA diagnosis requiring CPAP treatment to receive a 2-month supervised aerobic exercise training or CPAP therapy only. The authors reported no significant differences in both groups on weight measurements. The study showed that both treatments were effective in improving subjective sleepiness. The authors reported that the intervention group showed lower values of tension and fatigue on the profile of mood state score and higher values of physical functioning, general health perceptions and vitality on the Short Form Health Survey (SF-36) quality-of-life questionnaire, suggesting exercise training as an adjunct intervention strategy in the management of patients with OSA.

Papandreou et al. [38] randomised 21 sedentary and obese (mean BMI 36.6±3.7 kg/m^2) subjects with a moderate to severe OSA diagnosis to receive CPAP therapy and a 6-month lifestyle intervention based on a low-calorie Mediterranean diet and physical activity or CPAP therapy and consuming a low calorie prudent diet. The authors reported a greater reduction in weight −10.8 kg, BMI −3.9 kg/m^2, waist circumference −9.9 cm and body fat percentage −4.7 % in the intervention group following the Mediterranean diet and CPAP therapy compared with the control group (p<0.05).

Kline et al. [39, 52] randomised 43 sedentary and obese subjects to receive a 12-week 150 min/week of moderate intensity aerobic activity followed by resistance training twice/week or low-intensity stretching exercises designed to increase whole body flexibility. The authors reported a significant reductions in AHI −7.6 events/h and ODI_4 −3 events/h in the intervention group compared with the control group (p<0.01 and p=0.03, respectively). The authors reported that the reductions observed in AHI and ODI_4 were achieved without a significant decrease in body weight. The intervention group also conferred significant improvements in depressive symptoms fatigue and vigour and QoL assessed by the SF-36 compared with the control group (p<0.05).

Meta-analyses results

Intensive lifestyle intervention (ILI) programmes with usual care (Table 2, "2")

Meta analyses were also carried out for the six identified studies [33–35, 37–39], and the pooled results are shown in Table 2. For the four studies reporting on weight loss, participants receiving the ILI had an overall weight loss of −5.65 kg (CI −10.91 to −0.40) with a high level of heterogeneity (I^2=95.7 %, p=0.0001) (Fig. 2). Significant reduction in waist circumference of −5.8 cm (CI −8.64 to −2.96)

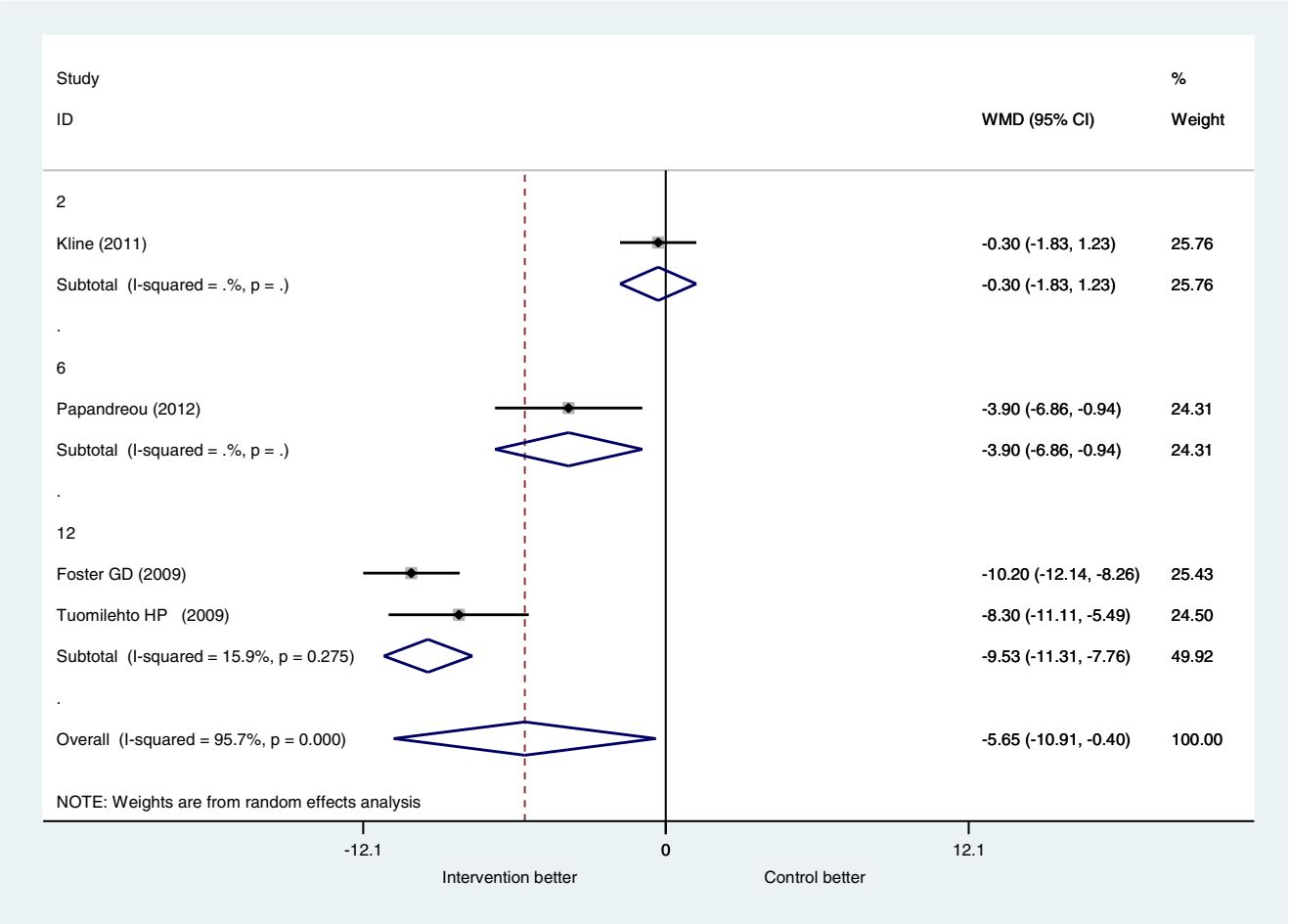

Fig. 2 Forest plot for change in weight (kilograms) by length of follow up (2, 6 and 12 months) following an intensive lifestyle programme versus usual care using the random-effects model. The *size* of the *box* indicates the study's relative weight based on standard error. The *diamond* reflects the 95 % confidence interval of the summary estimate

was also seen with high heterogeneity also observed for this outcome (I^2=77.7 %, p=0.001) and in BMI of −2.33 kg/m^2 with a high level of heterogeneity (I^2=78.8 %, p=0.003) observed. A significant reduction in the AHI was identified of −4.55 events/h in those subjects receiving an ILI compared with the control groups but with medium heterogeneity observed (I^2=54.4 %, p=0.041).A reduction in ESS score of −0.31 was observed with a medium level of heterogeneity (I^2=33.5 %, p=0.220).

Systematic review results

Other (Table 1, "3")

Breathing and aerobic exercise programme Sengul et al. [32] randomised 20 consecutive patients with mild to moderate OSA so to receive either a 12-week programme consisting of breathing and aerobic exercises or no exercise (Table 1). The author did not report any significant changes between the two groups.

Dietary advice and hypnotherapy programme Stradling et al. [31] randomised 46 OSA subjects in three parallel groups including dietary advice only, dietary advice and hypnotherapy (focused on stress reduction) and dietary advice with hypnotherapy type 2 (with specific suggestions about food) (Table 1). The authors reported no significant difference between the groups who achieved a weight loss of 2–3 % of their body weight at 3 months follow-up. However, 18 months post-follow-up, only the hypnotherapy with stress reduction group showed a small but significant mean weight loss (3.8 kg, p<0.02) compared with baseline.

Very low energy diet and usual diet Johansson et al. [36] randomised 63 obese (BMI, 30–40 kg/m^2) male subjects with moderately severe OSA (AHI≥15) to receive either a 9-week intervention programme based on a low-energy liquid diet or to adhere to their usual diet. The authors reported a greater improvement in both obesity and OSA severity indices compared with the control. A greater weight loss was reported in the intervention group of 18.7 kg

compared with 1.1 kg in the control group ($p<0.001$). In addition, a greater reduction in AHI was also reported in the intervention group when compared with the control.

Discussion

The current systematic review and meta-analysis showed that ILI programmes which employed caloric restriction and/or physical activity were effective in reducing indices of obesity and improve severity of OSA. Lower-intensity lifestyle modification programmes which combined dietary advice and CPAP therapy are also effective but to a lesser degree for these outcome measures.

The results indicate an additional benefit of CPAP therapy to the dietary advice. Although a significant weight reduction was observed in this group (−2.64 kg), the overall weight loss was not clinically significant (Table 2). However, the impact of CPAP therapy on this patient group is evident in the reported improvements observed in general well-being and alleviation of OSA-related symptoms leading to improvements in the quality of life. This is the first systematic review of non-surgical and non-pharmacological randomised controlled trials to our knowledge reporting the effectiveness of lifestyle modification interventions on indices of obesity and parameters of OSA in adult OSA subjects. A systematic review and meta-analysis of observational and randomised studies investigated the effects of dietary weight loss only on OSA [39]. It showed that these programmes were effective in reducing severity of OSA and BMI among obese OSA subjects. The review included in total six observational studies and only three randomised controlled trials representing 577 subjects. A comparison of non-surgical and surgical interventions also showed within group reductions in BMI and AHI after diet and lifestyle interventions (−4.51 kg/m^2 and −18.45 events/h, respectively) [40]. Both studies pose several limitations including the utility of randomised and non-randomised trials and the exploration of only a limited number of outcome measures. This systematic review, however, holds the exclusive design of utilising randomised controlled trials only with multiple outcome measures. We also observed a reduction in BMI and AHI in the intervention groups receiving diet and/or intensive lifestyle interventions but to a lesser degree. However, this may be due to the inclusion of both observational and randomised studies by Anandam et al. and Ashrafian et al. [42, 43] because observational studies tend to report higher reductions [53]. Therefore, the results need to be viewed with caution as the true effect may be overestimated. In our review, we included randomised controlled trials employing diet, physical activity and lifestyle management strategies only. The present study showed that weight reduction programmes based on caloric restriction and/or physical activity can induce significant weight loss. Concerns over the sustainability of weight loss produced by diet-related and lifestyle modification interventions have been widely expressed by several health-related taskforces which recommend their utility as an adjunct to CPAP therapy. In the present study, we also observed an additive effect of CPAP therapy on weight loss highlighting that a lifestyle modification intervention combined with CPAP therapy may confer additional benefits for this at risk population. CPAP therapy is the gold standard therapy in the treatment of moderate and severe OSA, and previous studies have demonstrated its effectiveness in reducing cardiovascular risk in ameliorating OSA symptoms and improving quality of life among OSA subjects [18]. Lifestyle modification programmes, however, may hold the key for better long-term outcomes as their primary goal is change in behaviours towards nutritional intake and physical activity offering counselling support and therefore enabling participants to understand the implications of obesity on OSA but also empowering them to change their lifestyle choices to further reduce the physiological and psychological impacts of this chronic condition. This approach emphasised how small changes in everyday living can potentially confer great changes in their health status. Weight reduction strategies in the form of diet or lifestyle modification programmes are effective in reducing weight and OSA indices among obese OSA subjects and their utility should be explored further.

Strengths and limitations

Limitations include significant heterogeneity between the included studies for some outcomes, and so, overall conclusions must be regarded with caution. However, for the primary outcome measure, no to high heterogeneity levels were observed. Another limitation is the difference in the length of follow-up between the studies ranging from 2 to 24 months. This difference in follow-up time had a great impact on the overall weight loss observed in the ILI group. In particular, when comparing the weight loss between the two studies with similar follow-up [34, 35], the mean weight reduction achieved was −9.53 kg, but when combining the results of other studies with shorter follow-up [38, 39], this reduced the overall effect resulting in lower weight reduction of −5.65 kg. Parameters of OSA severity were not routinely assessed in these studies, resulting in inability to perform a meta-analysis on AHI in the CPAP group. Given the limited number of studies, we were unable to assess publication bias. The pooled data are poorly representative of females, and therefore, the results may not be truly generalisable. An important strength in our study is the inclusion of randomised controlled trials only. A quality element was applied using the Jadad scale of which five of nine studies scored ≥4 which was set to denote good quality.

A systematic and broad search was carried out on multiple databases of both medical subject headings and keywords so as to capture all studies available in the literature that covered

OSA, lifestyle (diet and physical exertion) and randomised controlled trials. The methodological strengths of this study also include the independent data extraction carried out by two authors.

Future research

Intensive lifestyle programmes should be further explored in patients with OSA with several additional co-morbidities such as T2DM and CVD where intensive lifestyle interventions have proven effect. Furthermore, exploration of the utility of such programmes in newly diagnosed OSA subjects in primary healthcare is recommended as early intervention may prevent the progression rate and potentially cure OSA. The results highlight the effectiveness of lifestyle modification interventions in reducing weight and as a result improve OSA parameters among obese subjects. Further exploration into most effective type of intensive lifestyle management programmes is warranted. It is important to unravel which groups based on disease severity (AHI) such programmes are most effective in terms of overall weight loss, reduction in AHI and sustainability of these patient outcomes and indeed whether these programmes are cost-effective.

Conclusions

In conclusion, the results from our meta-analysis support the implementation of intensive lifestyle modification programmes as effective interventions for aggressive weight reduction and prevention of progression of OSA for those subjects with mild severity of the condition and in improving, if not curing, parameters of OSA in obese patients at high risk of cardiometabolic co-morbidities. This could potentially prove to be invaluable within the primary care setting. There is a call for research to assess the utility of such programmes in healthcare settings as well as to investigate further the role of CPAP therapy in improving metabolic parameters.

Financial Support Funding was provided by the Leicester Diabetes Centre and the Hanning Sleep Laboratory.

Disclosure The corresponding author and co-authors listed on this manuscript have no financial conflict of interest, and this research does not include off-label or investigational use of drugs or devices.

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