ORIGINAL ARTICLE

Cardiometabolic changes after continuous positive airway pressure for obstructive sleep apnoea: a randomised sham-controlled study

Camilla M Hoyos,1 Roo Killick,1 Brendon J Yee,1,2 Craig L Phillips,1,3 Ronald R Grunstein,2,4 Peter Y Liu1,5

ABSTRACT

Rationale and objectives Impaired insulin sensitivity (ISx), increased visceral abdominal fat (VAF) and liver fat are all central components of the metabolic syndrome and characteristics of men with obstructive sleep apnoea (OSA). The reversibility of these observed changes with continuous positive airway pressure (CPAP) treatment in men with OSA has not been systematically studied in a randomised sham-controlled fashion.

Methods 65 men without diabetes who were CPAP naive and had moderate to severe OSA (age=49±12 years, apnoea hypopnoea index (AHI)=39.9±17.7 events/h, body mass index=31.3±5.2 kg/m²) were randomised to receive either real (n=34) or sham (n=31) CPAP for 12 weeks. At 12 weeks, all subjects received real CPAP for an additional 12 weeks.

Measurements and main results Main outcomes were the change at week 12 from baseline in VAF, ISx and liver fat. Other metabolic outcomes were changes in the disposition index, total fat, and blood leptin and adiponectin concentrations. The AHI was lower on CPAP compared with sham by 33 events/h (95% CI—43.9 to —22.2, p<0.0001) after 12 weeks. There were no between-group differences at 12 weeks in VAF (—13.0 cm³, —42.4 to 16.2, p=0.37), ISx (—0.13 (min−1)μU/ml)−1, —0.40 to 0.14, p=0.33), liver fat (—0.5 cm³, —3.8 to 2.7, p=0.74) or any other cardiometabolic parameter. At 24 weeks, ISx (3.2×10^6 (min−1)μU/ml)−1, 0.9×10^6 to 6.0×10^6, p=0.009), but not VAF (—1.4 cm³, —19.2 to 16.4, p=0.87) or liver fat (—0.2 Hounsfield units, —2.4 to 2.0, p=0.83) were improved compared with baseline in the whole study group.

Conclusion Reducing visceral adiposity in men with OSA cannot be achieved with CPAP alone and is likely to require weight-loss interventions. Longer-term effects of CPAP on other cardiometabolic markers such as ISx require further investigation to fully examine time dependencies.

Trial Registration Number ACTRN1260800301369.

Key messages

What is the key question?

Does continuous positive airway pressure therapy, as practically applied in the community, improve central parameters of cardiometabolic risk in men with obstructive sleep apnoea?

What is the bottom line?

We found that CPAP may improve insulin sensitivity but does not decrease visceral adiposity or liver fat by 24 weeks.

Why read on?

Our results are of relevance to sleep medicine physicians who now cannot rely solely on CPAP therapy to improve cardiometabolic health.

Weight loss interventions are likely to be needed to reduce visceral adiposity in men with obstructive sleep apnoea.

INTRODUCTION

Obstructive sleep apnoea (OSA) is a common disorder that affects up to 25% of adult men.1 Untreated severe OSA increases the risk of all-cause and cardiovascular mortality.2–4 It is generally believed that these increased risks are partly due to obesity, increased visceral abdominal fat (VAF), insulin resistance (IR) and increased liver fat.2 This is because VAF, liver fat and IR (central components of the metabolic syndrome) are all independently associated with increased risk for cardiovascular disease and mortality in adults not selected for OSA.6–8 Furthermore, long-term CPAP treatment decreases mortality risk,6 but whether this is due to CPAP-induced improvements in IR or body fat distribution, including decreases in VAF and liver fat, has not been systematically studied. Indeed, the reversibility of IR, VAF and liver fat in OSA is still not known because few randomised controlled CPAP intervention studies have been performed.

Randomised studies investigating the effect of CPAP on VAF or liver fat are not yet available. However, we10 and others11 previously reported significant reductions in VAF volume after 3 and 6 months of CPAP treatment respectively, although other studies did not detect such changes.12–14 A single long-term (2–3 years) uncontrolled study showed that CPAP reduced liver fat but only in those who were CPAP compliant (n=6).15 Randomised controlled trials are required to fully address the question of whether CPAP alters VAF and liver fat.

Three randomised sham-controlled trials have examined the effect of CPAP therapy on IR, but the results are inconclusive. Only one of the three studies reported a statistically significant improvement in IR, but the controlled portion of this study was of 1 week duration, so that the durability of
these findings is not known. The other two studies did not show any change in IR with CPAP. However, one was performed specifically in diabetic men in whom the extent of reversibility may be limited and the other did not assess insulin resistance by a sensitive method. Additionally, none of these studies examined other important measures of glucose metabolism such as the disposition index (DI), a measure which combines impaired β-cell activity with IR and is useful in predicting future diabetes. Furthermore, the important inter-relationships among VAF, liver fat and IR may be limited and the other did not assess insulin resistance specifically in diabetic men. The extent of reversibility may also be limited and the other did not assess insulin resistance by a sensitive method. The other two studies did not fi...cally in diabetic men in whom the extent of reversibility may be limited and the other did not assess insulin resistance by a sensitive method. Additionally, none of these studies examined other important measures of glucose metabolism such as the disposition index (DI), a measure which combines impaired β-cell activity with IR and is useful in predicting future diabetes. Furthermore, the important inter-relationships among VAF, liver fat and IR may be limited...
then at 10, 20, 30, 60, 75, 90 and 120 min after a 75 g/300 ml oral glucose load following an established protocol. Additionally fasting samples were collected at 0, 6, 12, 24 weeks and the HOMA and QUICKI were calculated. Glucose, insulin, C peptide, leptin and adiponectin concentrations were all measured with commercially available assays. All samples were stored at −80°C for subsequent batched analysis and all samples from an individual patient were run within a single assay.

**Statistical analysis**

The study was powered to detect a standardised mean change in VAF of 0.78 using our previously published data. The total sample size (assuming 1:1 randomisation) required to detect this effect with 80% power at a two-tailed significance level of 5% was 52 men treated for 12 weeks.

The outcome variables were the calculated differences from baseline at 6, 12 and 24 weeks. Linear regression was used to determine between-treatment group differences of these calculated differences from baseline during the blinded period (6 and 12 weeks). Mixed model analysis was used for outcomes with repeated measurements. Further analyses explored the influence of treatment compliance, baseline severity (AHI), obesity (BMI and waist circumference) and sleepiness (ESS). These potential confounders were included as linear covariates. Additionally covariates with predefined cut points were included in separate mixed models as a dichotomised factor (compliance 4 h/night; AHI >30 events/h; BMI >30 kg/m²; ESS >10). The statistical significance of the interaction terms of treatment and each dichotomised variable were examined. These analyses were performed with and without these participants and there was no difference in findings. All findings presented here are of all participants with available data.

Analyses were performed using SAS V9.2 (SAS Institute). Data were considered significantly different at p < 0.05 (two sided) and are presented as mean differences (95% CI), mean (SD), or median (IQR) as indicated.

**RESULTS**

The flow of participants through the study is shown in figure 1. Sixty-nine men were enrolled of whom 65 were randomised to receive either real (n = 34) or sham (n = 31) CPAP treatment. Four participants could not complete home titration after multiple attempts and two other participants withdrew for personal reasons prior to starting real or sham CPAP (figure 1). Primary outcome data were available for 52 men at week 12 and 46 men at week 24. Baseline characteristics were comparable in the two treatment groups (table 1). The withdrawn subjects were comparable to those who completed, except for a significantly lower CPAP adherence rate (data not shown). None of the participants had physician-diagnosed diabetes at baseline, 92% were overweight, 70% had abdominal obesity and 55% were medically obese. Two participants without diagnosed diabetes during screening were randomised, and subsequently discovered to have diabetes after analysis of the oral glucose tolerance test at the end of the study. The analyses were performed with and without these participants and there was no difference in findings. All findings presented here are of all participants with available data.

During the blinded period, real CPAP use was 3.6 h per night and sham CPAP use was 2.8 h per night (p = 0.07). During the open-label period, CPAP use was 4 h per night for both groups (p = 0.72). CPAP use did not change during the open-label period in those initially randomised to CPAP therapy (p = 0.16) but increased by 1.1 h in those initially randomised to sham therapy (p = 0.04). All participants with available data, regardless of CPAP use, were included in the analysis.

The change in VAF or any other measurements of body composition at week 12 were not significantly different between groups (figure 2). At week 12 there was a within-group increase in lean muscle mass in the CPAP group (p = 0.001) compared to baseline. Sleep disordered breathing

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Figure 1 Study flow. CPAP, continuous positive airway pressure.
with a non-significant change after sham treatment (p=0.20). At week 24, lean muscle had increased in all participants but there were no changes in any other measures of body composition (figure 2 and table 3). Furthermore, the actual decrease in VAF at week 24 was 1.4 cm³ which corresponds to a standardised mean change in VAF of 0.08.

At week 12, real CPAP treatment significantly improved OSA parameters compared with sham CPAP (figure 5). The average nightly AHI as measured by the CPAP device, over the entire 12-week period, was 3.1 events/h in the real CPAP group (not available for sham group). The change in total sleep time was not different between groups, but rapid eye movement (REM) and non-REM sleep significantly increased and decreased respectively with real CPAP compared with sham (table 2). There were no between-group differences in the changes in subjective sleepiness (table 2). At week 24, OSA parameters had improved from baseline in all participants regardless of initial treatment allocation (figure 5).

We next assessed whether CPAP compliance, baseline age, AHI, BMI, waist circumference or sleepiness influenced treatment outcomes (namely, change in VAF, ISx and liver fat). We dichotomised age by the median, compliance by 4 h/night, AHI, BMI, waist circumference or sleepiness in dichotomised age by the median, compliance by 4 h/night, AHI, BMI, waist circumference or sleepiness in
dichotomised age by the median, compliance by 4 h/night, AHI, BMI, waist circumference or sleepiness in.

### Table 1: Baseline participant characteristics

<table>
<thead>
<tr>
<th>Baseline participant characteristics</th>
<th>Real CPAP (n=34)</th>
<th>Sham CPAP (n=31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.0 (12.3)</td>
<td>46.4 (10.4)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Sleep and breathing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST (min)</td>
<td>362 (308 to 400)</td>
<td>378 (329 to 406)</td>
<td>0.19</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>81.2 (67.4 to 88.7)</td>
<td>85.3 (76.9 to 92.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>REM (% TST)</td>
<td>14.0 (5.0)</td>
<td>17.0 (6.0)</td>
<td>0.08</td>
</tr>
<tr>
<td>Non-REM (% TST)</td>
<td>86.0 (5.0)</td>
<td>83.0 (6.0)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Anthropometry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>97.4 (20.7)</td>
<td>94.3 (17.9)</td>
<td>0.53</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.6 (5.3)</td>
<td>31.0 (5.1)</td>
<td>0.63</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>109.7 (13.3)</td>
<td>106.3 (13.0)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visceral abdominal fat (cm³)</td>
<td>307.4 (118.2)</td>
<td>299.2 (126.0)</td>
<td>0.72</td>
</tr>
<tr>
<td>Subcutaneous abdominal fat (cm³)</td>
<td>669.2 (239.7)</td>
<td>571.1 (225.4)</td>
<td>0.23</td>
</tr>
<tr>
<td>Liver fat (HU)</td>
<td>52.6 (13.3)</td>
<td>52.9 (8.8)</td>
<td>0.91</td>
</tr>
<tr>
<td>L/S ratio (HU)</td>
<td>1.1 (0.2)</td>
<td>1.0 (0.2)</td>
<td>0.19</td>
</tr>
<tr>
<td>Total fat (kg)</td>
<td>33.4 (12.6)</td>
<td>28.9 (10.8)</td>
<td>0.25</td>
</tr>
<tr>
<td>Total lean muscle (kg)</td>
<td>59.6 (8.1)</td>
<td>59.7 (8.6)</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Metabolic markers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISx (min⁻¹·(µU/ml)⁻¹)</td>
<td>7.1×10⁻⁴ (5.8×10⁻⁴)</td>
<td>5.5×10⁻⁴ (4.8×10⁻⁴)</td>
<td>0.44</td>
</tr>
<tr>
<td>DI (unit)</td>
<td>0.07 (0.09)</td>
<td>0.05 (0.07)</td>
<td>0.26</td>
</tr>
<tr>
<td>HOMA (unit)</td>
<td>2.9 (2.5)</td>
<td>2.9 (1.8)</td>
<td>0.70</td>
</tr>
<tr>
<td>QUICKI (unit)</td>
<td>0.3 (0.02)</td>
<td>0.4 (0.05)</td>
<td>0.36</td>
</tr>
<tr>
<td>Fasting glucose (mmol/litre)</td>
<td>5.3 (0.7)</td>
<td>5.2 (0.5)</td>
<td>0.56</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>11.8 (7.8)</td>
<td>12.5 (7.7)</td>
<td>0.81</td>
</tr>
<tr>
<td>Adiponectin (ng/ml)</td>
<td>7.3 (3.4)</td>
<td>7.0 (3.6)</td>
<td>0.59</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>15.9 (8.8)</td>
<td>14.5 (10.6)</td>
<td>0.58</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>11 (32)</td>
<td>11 (35)</td>
<td>0.80</td>
</tr>
<tr>
<td>Using antihypertensive, n (%)</td>
<td>11 (32)</td>
<td>11 (35)</td>
<td>0.80</td>
</tr>
<tr>
<td>Hypercholesterolaemia, n (%)</td>
<td>12 (35)</td>
<td>12 (39)</td>
<td>0.80</td>
</tr>
<tr>
<td>Using statins, n (%)</td>
<td>11 (32)</td>
<td>7 (23)</td>
<td>0.42</td>
</tr>
<tr>
<td>Pre-existing CVD, n (%)</td>
<td>5 (15)</td>
<td>3 (10)</td>
<td>0.71</td>
</tr>
<tr>
<td>Glucose intolerance, † n (%)</td>
<td>10 (29)</td>
<td>7 (23)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Values are mean (SD), median (IQR) or number (%) as appropriate. Between-group differences were assessed by t test after normalisation as required, or by rank-sum test as indicated with *.

AHI, apnoea-hypopnoea index; BMI, body mass index; CPAP, continuous positive airway pressure; CVD, cardiovascular disease; DI, insulin disposition index measured by minimal model analysis; ESS, Epworth Sleepiness Scale; HOMA, homeostasis model assessment of insulin resistance; HU, Hounsfield unit; ISx, insulin sensitivity measured by minimal model analysis; L/S, liver/spleen; ODI, oxygen desaturation index 3% pressure; QUICKI, quantitative insulin sensitivity check index; REM, rapid eye movement; SpO₂T90, time that the arterial oxygen saturation was <90%; TST, total sleep time; SWS, slow wave sleep.
DISCUSSION

This is, to our knowledge, the first randomised sham-controlled trial of the effect of CPAP treatment for OSA on VAF and liver fat, and the largest and longest trial of CPAP on ISx to date. We demonstrated that 12 weeks of CPAP did not improve VAF, liver fat or ISx compared with sham CPAP. Small-term improvements in ISx, but not VAF or liver fat, were observed but only in those who received a total of 6 months of CPAP treatment, albeit in a non-randomised phase. Furthermore, both the actual and standardised mean changes from baseline in VAF at 24 weeks were small. These data suggest that reducing visceral adiposity cannot be achieved with CPAP alone and that other interventions to reduce VAF will be required. This is important because reducing abdominal adiposity, rather than overall adiposity, is now recognised as the more metabolically relevant target. At present, lifestyle modification programmes to enforce weight loss would seem to be the most likely strategy to achieve this goal. CPAP may still be used in conjunction with lifestyle modification, but available options are becoming increasingly limited and the safety of any new drug would need to be firmly established in the OSA population.

Our finding that CPAP does not alter VAF after at least 3 months of CPAP treatment is consistent with uncontrolled intervention (week 12: $r^2=0.33, p=0.0008$; week 24: $r^2=0.55, p=0.0001$). There was no such correlation between BMI and adiponectin.
Sleep disordered breathing

Figure 4  Plot of mean and SE of the mean for (A) fasting insulin, (B) fasting blood glucose, (C) serum adiponectin concentrations and (D) serum leptin. The left-hand plot (line graph) shows the mean change at weeks 6 and 12 from baseline for the real continuous positive airway pressure (CPAP) (filled circles) and sham CPAP (open circles) groups. The p value above this graph denotes the between-group difference as determined by mixed model analysis. The right-hand plot (vertical bar graph) is the pooled mean change at week 24 from baseline in all participants regardless of initial treatment allocation. The p value above this graph denotes the significance of the change as determined by Student’s t test.

Table 2  Changes from baseline in real CPAP and sham CPAP groups and the between-group differences

- **Sleep architecture and sleepiness**
  - TST (min): 25.2 vs 26.9, Δ -1.7 (95% CI 39.9 to 43.2) p = 0.94
  - Sleep efficiency (% TST): 4.8 vs 2.8, Δ 2.0 (95% CI 9.8 to 5.9) p = 0.62
  - REM (% TST): 0.04 vs -0.02, Δ 0.06 (0.01 to 0.1) p = 0.02
  - Non-REM (% TST): -0.04 vs 0.02, Δ -0.06 (0.01 to 0.1) p = 0.02
  - SWS (% TST): 11.6 vs 4.5, Δ 7.1 (95% CI 14.3 to 0.04) p = 0.05
  - Subjective sleepiness (ESS, scale 0 to 18): -1.8 vs -1.7, Δ -0.1 (95% CI 1.6 to 1.9) p = 0.87
  - Objective sleepiness (OSLER, min): 4.5 vs 3.2, Δ 1.3 (95% CI 5.3 to 2.6) p = 0.19

- **Anthropometry**
  - BMI (kg/m²): 0.14 vs 0.08, Δ 0.06 (95% CI 0.3 to 0.4) p = 0.71
  - Weight (kg): 0.5 vs 0.3, Δ 0.2 (95% CI 1.2 to 0.7) p = 0.57
  - Waist circumference (cm): -0.5 vs -0.7, Δ 0.2 (95% CI 1.6 to 2.2) p = 0.79

- **Clinic blood pressure**
  - SBP (mm Hg): -4.75 vs -0.50, Δ -4.25 (95% CI 1.01 to 4.86) p = 0.12
  - DBP (mm Hg): 0.41 vs 0.04, Δ 0.37 (95% CI 4.28 to 3.38) p = 0.82
  - HR (beats/min): -1.48 vs 1.38, Δ -2.86 (95% CI 1.45 to 7.17) p = 0.19
  - MAP (mm Hg): -1.32 vs -0.30, Δ -1.01 (95% CI 2.47 to 4.49) p = 0.56

**Note:** Bold values are statistically significant (p < 0.05). Data are mean differences from baseline, between-group differences (and 95% CIs) and unadjusted p values. Between-group differences were determined by linear regression. Mixed model analysis was used for outcomes with repeated measures.

**Controls:** BMI, body mass index; CPAP, continuous positive airway pressure; DBP, diastolic blood pressure; ESS, Epworth Sleepiness Scale; HR, heart rate; MAP, mean arterial pressure; OSLER, the Oxford sleep resistance test; REM, rapid eye movement; SBP, systolic blood pressure; SWS, slow wave sleep; TST, total sleep time.
body weight alone would be expected to reduce VAF and metabolic syndrome. This finding that 3 months of CPAP can reduce total body weight has never previously been reported in any randomised sham-controlled trial and requires replication in other cohorts.

There was also no effect of CPAP on liver fat, which is in contrast to a previous uncontrolled study that showed 2–3 years of CPAP treatment can significantly decrease liver fat, but only in the subgroup of CPAP adherers (n=6) in whom other lifestyle modifications undertaken in conjunction with CPAP could have plausibly reduced liver fat.13 Furthermore the changes observed in this highly selected patient group may not be comparable to a general OSA population.

We found that CPAP therapy did not alter total body fat at any time, but significantly increased lean (muscle) mass at 6 months in all participants irrespective of initial treatment allocation. Our total body findings are consistent with an uncontrolled study showing that 8 months of CPAP did not alter total body fat but did significantly increase lean muscle mass.12 Increased lean body mass can have positive metabolic benefits if improvements over time and of sufficient magnitude. Potential improvements include increased exercise capacity, basal metabolic rate and ISx. Such improvements would occur even without changes in total or regional body fat.

The ISx findings are consistent with all previous randomised sham-controlled trials investigating 6–12 weeks of CPAP therapy.16 17 34 35 Although one sham-controlled trial showed improvement in ISx after just 1 week,34 a recent meta-analysis of randomised controlled studies46 (which included that trial) is consistent with our findings of no CPAP effect on ISx. Since the randomised controlled portion was of 1-week duration, that study was not designed to determine whether the improvement in ISx is maintained longer term. In contrast, we did not assess acute changes in ISx, so it remains possible that CPAP could acutely and transiently improve glucose metabolism.

Small long-term improvements in ISx were observed in those who received a total of 6 months of CPAP treatment, although there were no between-group differences. Other uncontrolled trials investigating the effect of CPAP on glucose metabolism of at least 6 months’ duration are available11 37–40 and report conflicting changes. Of these, only one formally measured ISx and this also showed an improvement.40 Our data, together with the published literature, suggest that CPAP therapy exceeding 3 months is required to improve ISx. We acknowledge that these longer-term analyses are uncontrolled and therefore a randomised controlled study of sufficient duration is needed to prove this.
Sleep disordered breathing

Our findings indicate that CPAP treatment does not change adiponectin levels and this finding is consistent with two previous randomised sham-controlled trials.\textsuperscript{16, 41} We also did not observe a change in leptin after CPAP, but did find a significant correlation between the change in BMI and leptin levels. This suggests that the association between OSA and leptin is mediated through obesity, as previously suggested.\textsuperscript{42} Our results are also consistent with some\textsuperscript{43, 44} but not other studies.\textsuperscript{45, 46}

Additionally there was no between-group difference in subjective sleepiness observed, however our participants were only mildly sleepy at baseline. Other randomised sham-controlled trials have also reported similar mild sleepiness at baseline.\textsuperscript{47, 48}

A strength of this study is the inclusion of a sham-control arm. A control group, blinded to treatment allocation, is important as participants enrolled in a study may alter behaviours, such as diet and exercise, as they are aware they are being monitored. These lifestyle changes could well alter many of the markers of metabolic function which were our primary outcomes. For these reasons, a sham control was considered essential.

The CPAP adherence observed in this study is comparable to other sham-controlled studies.\textsuperscript{16, 17, 47} CPAP adherence has been defined as the use of more than 4 h per night, five nights per week, which is equivalent to approximately 3 h per night. Our adherence rate was 3.6 h per night in the treatment arm. Our study was designed as a practical, intention-to-treat study that in turn could be generalisable to the greater OSA population. We did not include subjects based on their compliance nor did we include a run-in treatment arm to exclude the non-adherers which has been the case in other mechanistic studies.\textsuperscript{49} Our aim was to represent the general OSA population which we believe we have done as our rates are comparable to those of ‘real life’ CPAP studies that investigate methods to increase adherence.\textsuperscript{49}

Additionally our rates (3.6 h/night) are comparable to those reported by another 5-month sham-controlled study (3.5 h/night) investigating ISx.\textsuperscript{16} Interestingly, CPAP use increased by 1.1 h in those who initially received sham treatment, but was not significantly increased in those who initially received CPAP therapy. This illustrates the importance of recruiting CPAP-naïve individuals into a parallel rather than crossover study, as we have done here. A sham control is critical since placebo effects on subjective measures such as sleepiness were detected and have also previously been reported.\textsuperscript{48} Not only is our CPAP compliance comparable with other studies, but we also showed that CPAP compliance per se (as well as age, BMI, waist circumference and sleepiness) did not influence the treatment effect. Furthermore, the change in VAF that can be expected is small and demonstrating such a change would require a study of 5000 men assuming 80% power and two-sided α of 0.05 (post hoc analysis). Such a sham-controlled randomised controlled trial would be difficult to perform.

In conclusion, this study demonstrated that CPAP alone does not reduce visceral adiposity, even in the longer term. Obese men with severe OSA will most likely require weightloss interventions in conjunction with CPAP treatment to achieve this. Although 5 months of CPAP treatment did not improve ISx, longer-term treatment may produce beneficial changes but this requires further investigation.

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Contributors All authors equally contributed to the concept and design of the trial. PYL and RRG obtained funding. CMH was responsible for data collection, statistical analysis and the preparation of the manuscript. All authors participated in the overall analysis and interpretation of the data, revision of the manuscript and provided final approval of the submitted version.

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Competing interests None.

Ethics approval Ethics approval was provided by Sydney South West Area Health Service Human Research and Ethics Committee (RPAAH Zone).

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

Sleep disordered breathing


Correction


We have since realised that there were two transcription errors included in the manuscript that should ideally be corrected. Since these were transcription errors, neither had any influence on the statistical analyses presented.

► The study flow (figure 1) states that 28 in the CPAP groups and 24 in the sham group completed the 12 week treatment period. Actually, 29 completed CPAP and 23 completed sham CPAP. Furthermore, 2 men in the CPAP group and 3 men in the sham CPAP group withdrew prior to receiving the open-label CPAP treatment after week 12. The completion numbers of 26 in the CPAP group and 20 in the sham group at week 24 are correct.

► In table 1 and 2 for the results of insulin sensitivity (ISx) a negative sign (ie, ‘-’) was inadvertently left out (all the result should be $10^{-4}$ not $10^{4}$). Again this was a transcription error that had no influence on the statistical analyses presented.

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