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# Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial

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## Summary

**Background** Obstructive sleep apnoea is associated with raised blood pressure. If blood pressure can be reduced by nasal continuous positive airway pressure (nCPAP), such treatment could reduce risk of cardiovascular disease in patients with obstructive sleep apnoea. Our aim was to see whether nCPAP for sleep apnoea reduces blood pressure compared with the most robust control intervention subtherapeutic nCPAP.

**Methods** We did a randomised parallel trial to compare change in blood pressure in 118 men with obstructive sleep apnoea (Epworth score >9, and a >4% oxygen desaturation index of >10 per h) who were assigned to either therapeutic (n=59) or subtherapeutic (59) nCPAP (about 1 cm $H_2O$ pressure) for 1 month. The primary outcome was the change in 24-h mean blood pressure. Secondary outcomes were changes in systolic, diastolic, sleep, and wake blood pressure, and relations between blood pressure changes, baseline blood pressure, and severity of sleep apnoea.

**Findings** Therapeutic nCPAP reduced mean arterial ambulatory blood pressure by 2·5 mm Hg (SE 0·8), whereas subtherapeutic nCPAP increased blood pressure by 0·8 mm Hg (0·7) (difference −3·3 [95% CI −5·3 to −1·3]; p=0·0013, unpaired t test). This benefit was seen in both systolic and diastolic blood pressure, and during both sleep and wake. The benefit was larger in patients with more severe sleep apnoea than those who had less severe apnoea, but was independent of the baseline blood pressure. The benefit was especially large in patients taking drug treatment for blood pressure.

**Interpretation** In patients with most severe sleep apnoea, nCPAP reduces blood pressure, providing significant vascular risk benefits, and substantially improving excessive daytime sleepiness and quality of life.

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## Introduction

In more-developed countries, 2–4% of adult men, and about 1% of adult women have detectable obstructive sleep apnoea,[1,2] and up to 1·5% of men in the UK have moderate or severe disease.[3] Sleep apnoea is caused by the collapse of the pharynx during sleep, which leads to airway occlusion and transient asphyxia. Asphyxia is reversed when the patient wakes and pharyngeal muscle tone returns to wake levels. These events are repetitive, with severely affected patients having hundreds of obstructive episodes and arousals every night. Both nocturnal and daytime blood pressure are raised in patients with obstructive sleep apnoea. This effect is seen in community-based epidemiological studies[4,5] and hospital clinic populations,[6] and is independent of obesity and other risk factors for raised blood pressure that are prevalent in this population.[4–6]

The standard treatment for sleep apnoea is nasal continuous positive airway pressure (nCPAP), and if this treatment reduces blood pressure it should also reduce vascular risk, which is high in patients with this disorder.[7] Results of observational cohort studies[8,9] and of a small crossover trial controlled by an oral placebo[10] suggest that blood pressure falls in patients with sleep apnoea who are given nCPAP. However, existing data[11,12] have been strongly criticised for not being adequately controlled, and vigorous debate about the effect of sleep apnoea treatment on vascular risk has resulted. For example, Phillipson[13] has described sleep apnoea as a vascular risk factor that is "as important as diabetes", whereas in another editorial,[14] the argument is that this disorder "may not be a disease at all". Wright and colleagues[11] have emphasised the need for methodologically robust trials to settle this debate, since the large symptomatic placebo effects seen with subtherapeutic nCPAP[15] probably change physical activity and diet, and hence blood pressure. We have addressed this uncertainty by comparing changes in ambulatory blood pressure when nCPAP treatment is used for obstructive sleep apnoea with those of the most robust control therapy available, subtherapeutic nCPAP.

## Methods

### *Design and setting*

We did a parallel, randomised, double-blind trial of patients in the Sleep and Respiratory Trials Units, Oxford Centre for Respiratory Medicine, Oxford, UK. The unit takes patients who have been referred with possible obstructive sleep apnoea from the surrounding region. About a third of patients are from the Oxford area. Referrals are made by general practitioners (36%); ear, nose, and throat surgeons (41%); or other hospital consultants (23%).

### Patients

Patients were eligible for the trial if they were men aged between 30 and 75 years who had excessive subjective daytime sleepiness (Epworth score >9[16]) and proven obstructive sleep apnoea with more than 10 dips of greater than 4% oxygen desaturation every hour. All eligible patients were offered entry into the study unless they chose alternative therapy (eg, weight loss, tonsillectomy), required urgent nCPAP therapy because of associated respiratory failure, were about to lose their jobs as a result of sleepiness, declined to participate, or were unable to give informed consent. Diagnosis of hypertension at presentation was not a factor in offering a patient entry to the trial. This study was approved by the central Oxford research ethics committee, and all participants gave written informed consent.

### Procedures

Obstructive sleep apnoea was diagnosed from a one-night respiratory polysomnographic sleep study in a hospital room that was decorated to resemble an ordinary bedroom. Patients' body movements, heart rate, and pulse transit time (PTT) changes were recorded as measures of arousal from sleep. The PTT signal and body movements recorded on video are robust markers of arousal.[17] Arterial oxygen saturation measurements, snoring, and increases in the respiratory swing in PTT were used as markers of breathing pattern and respiratory effort (Win-Visi monitoring system, Stowood Scientific Instruments, Oxford, UK). The PTT swing is a sensitive index of respiratory effort that accurately predicts change in pleural pressure and differentiates between central and obstructive apnoeas.[18] The results of the sleep study were scored automatically, with manual review as required to ensure accuracy of data. Obstructive sleep apnoea was diagnosed from a review of all data. The severity of sleep apnoea was then quantified as the number of dips in oxygen saturation of greater than 4% for every hour of study. This index is one of the best predictors of therapeutic response to nCPAP.[17]

24-h ambulatory blood pressure was measured with validated ambulatory recorders (TM 2420 and TM 2421, A & D Engineering, CA, USA).[19] A trained nurse fitted a cuff on the left arm, which was worn for the subsequent 24 h, during usual daily activities. Monitors were programmed to record blood pressure every 30 min, although patients were instructed to turn the monitor off while driving. Patients completed a diary card and pressed the event marker to identify sleep and wake periods. Data were included if the monitor had recorded at least 21 readings over the 24 h.[20] When two or more readings took place in the same half-hour (by pressing the event marker), these were averaged to give one value for every period.

Patients assessed their amount of sleepiness using the Epworth sleepiness score,[16] a self-completed questionnaire assessment of the tendency to fall asleep during various daytime situations. Objective sleepiness was measured with the Osler test,[21] a behavioural sleep resistance challenge, which formally tests the ability to remain awake when asked to do so, in a darkened room that is isolated from sound.

After baseline assessments, patients were admitted for a second night. A trained specialist nurse showed the patients a video about nCPAP, and taught them how to use the equipment. Patients were then randomly assigned to either therapeutic or subtherapeutic nCPAP by a series of presealed and numbered opaque envelopes. They then underwent a night of nCPAP titration, during which the signals recorded during the diagnostic study were again recorded, and nCPAP was used. For patients assigned to therapeutic nCPAP, the therapeutic airway pressure was derived from an overnight sleep study with the Devilbiss Horizon (Sunrise Medical, Wolleston, UK) or the Sullivan Autoset-T auto-adjusting (ResMed, Alingdon, UK) nCPAP machines, from which mask pressure was recorded and synchronised with the sleep-study signals. This record was reviewed manually the next morning, and the optimum therapeutic pressure to control snoring and sleep apnoea was confirmed by a technician. Patients assigned to subtherapeutic nCPAP used a machine that delivered less than 1 cm water of extra pressure, which is insufficient to hold open the pharynx.[15] In all other ways, subtherapeutic nCPAP was identical to therapeutic nCPAP. The subtherapeutic pressure was achieved by setting the nCPAP machine to its lowest pressure, insertion of a flow-restricting connector at the machine outlet, and insertion of six extra 4 mm holes in the collar of the main tubing at the end of the mask to allow air escape and to prevent re-breathing of carbon dioxide.

Patients were not aware of whether they were receiving therapeutic or subtherapeutic nCPAP, and the nurse who assigned patients to treatment group did not take part in outcome assessments. The investigators who assessed outcome were unaware of the randomisation status of the patients, and did not set up or maintain the machines, or assist the patients. Therefore, despite the physical nature of the treatment, the study was effectively double blind.

### Follow-up

The day after the assessment, patients were sent home with their therapeutic or subtherapeutic machine (Sullivan 6, ResMed, Abingdon, UK). A specialist nurse team helped all patients with advice by telephone, and masks were further adjusted if necessary. At 4 weeks, patients reattended for a repeat 24-h ambulatory blood pressure recording, Epworth sleepiness score, and Osler test. We also checked that any drugs being taken for hypertension had not been changed. Hour meters on the machines were read to calculate mean nightly use during the trial. At the end of this study, all patients had their nCPAP retitrated to establish their long-term therapeutic pressure.

### Data analysis

The primary endpoint was average 24-h mean arterial pressure, and change in this pressure was measured after therapeutic and subtherapeutic nCPAP. Secondary analyses assessed changes in systolic and diastolic blood pressure, changes in mean blood pressure during wake and sleep, and whether the size of any changes in blood pressure were associated with severity of baseline sleep apnoea, or baseline blood pressure, or compliance with treatment. We also did a subgroup analysis of treatment effects in patients who took drugs for hypertension to assess whether these patients behaved differently from the overall sample. Changes in blood pressure were assessed with unpaired *t* tests on an intention-to-treat basis, with no change being assumed when follow-up blood pressure data were missing, which makes the conclusions of the study conservative. The relations between baseline sleep apnoea severity, baseline blood pressure, and blood pressure change with nCPAP were assessed with Pearson's correlations. All analyses were

done with SPSS version 7.5.1. The randomisation code was broken only for the one planned interim analysis and then at the end of the study. Raw data can be obtained from the authors.

The study size was predicted from the results of previous uncontrolled studies assessing ambulatory blood pressure after nCPAP in patients with sleep apnoea. Results of these studies suggested that a difference in blood pressure of 5 mm Hg could be detected with an $\alpha$-level of 0·9 at 5% significance, with a sample size of 110. Allowing for a 10% loss to follow-up, we therefore expected to need 120 patients for randomisation. To check this power calculation, one planned interim data review was done after 50 patients had been randomly assigned to treatment.

*Role of the funding source*

The sponsors of the study had no role in study design, data collection, data analysis, or data interpretation, or in the writing of the report.

## Results

Figure 1 shows the trial profile. Of the 339 eligible patients, 67 had been included in our previous study of sleepiness in obstructive sleep apnoea.[15] Blood pressure measurement was added to this previous protocol after it had received ethical approval and after it was established to be manageable within the protocol. Patients who declined to take part did so mainly because of the extra time needed to participate, or the distance to travel. The severity of sleep apnoea was similar between these patients (mean oxygen saturation >4% dip rate 41·4 [SD 20·2], Epworth score 16·1 [3·6]) and those agreeing to enter the study (table 1). 137 patients had their baseline ambulatory blood pressure recorded, and in 19, the recording was inadequate (<21 data points per 24 h, maximum 48) and they were excluded. The remaining patients were randomly assigned to therapeutic or subtherapeutic nCPAP. 23 patients had an incomplete blood pressure recording at follow-up; 14 of these withdrew, and nine attended for the recording, but their recording was inadequate.

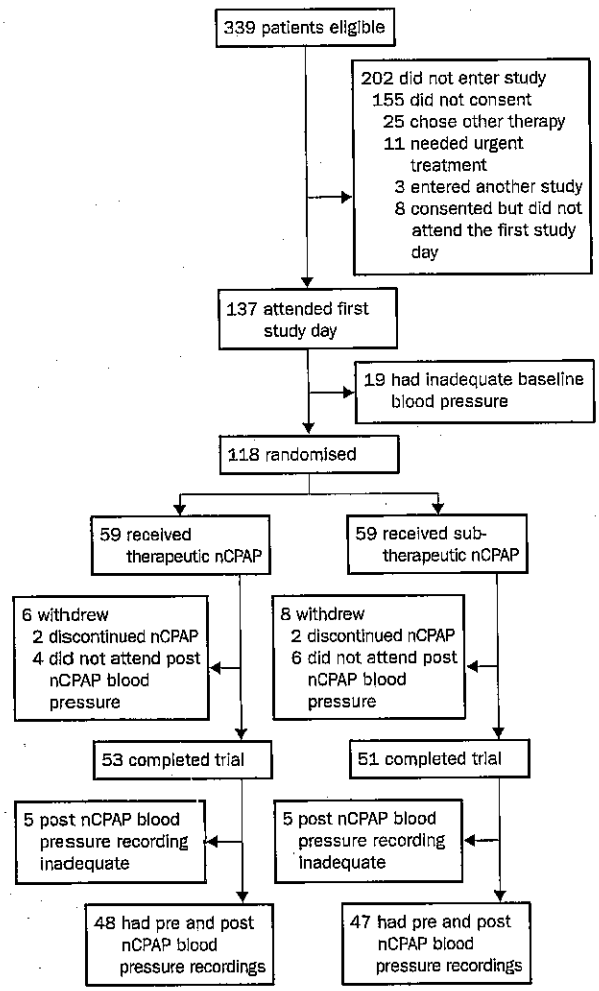


Figure 1: **Trial profile**

Therapeutic nCPAP significantly reduced overall 24-h mean blood pressure compared with sub-therapeutic control. Change in mean blood pressure with therapeutic nCPAP was −2·5 mm Hg (SE 0·8), and with sub-therapeutic nCPAP was +0·8 mm Hg (0·7) (difference −3·3 mm Hg [95% CI −5·3 to −1·3 mm Hg], p=0·0013, unpaired *t* test).

Mean ambulatory blood pressure fell with therapeutic nCPAP compared with subtherapeutic nCPAP, during both the wake and sleep periods as defined by the patient in their diary card. The magnitude of this fall was significant in both states (table 2, figure 2). The changes seen in the mean blood pressure were also evident in both systolic and diastolic blood pressure (table 2). The association between mean blood pressure change with treatment and severity of sleep apnoea at baseline differed between the two study groups. In the group receiving therapeutic nCPAP, blood pressure fall was greater as sleep apnoea severity increased (change in blood pressure −0·1 mm Hg, × desaturation rate +0·51, r=0·32 [95% CI 0·04–0·55], p=0·02). In the group receiving subtherapeutic nCPAP, the two variables showed no association (−0·004 mm Hg × desaturation rate +0·97, r=0·01 [−0·28 to 0·30], p=0·4).

Inspection of data showed that most patients whose blood pressure fell with therapeutic nCPAP had had more than 33 falls in arterial oxygen saturation of greater than 4% every hour, which was the median severity of sleep apnoea in the study sample. Figure 3 shows the change in blood pressure above and below

| | Subtherapeutic nCPAP (n=59) | Therapeutic nCPAP (n=59) |
|---|---|---|
| Age (years) | 51·0 (9·8) | 50·1 (10·4) |
| Weight (kg) | 109·0 (19·5) | 106·5 (21·3) |
| Body mass index (kg/m²) | 35·3 (6·0) | 34·6 (8·5) |
| Neck circumference (cm) | 45·7 (3·3) | 44·5 (4·1) |
| Waist/hip circumference ratio | 0·99 (0·06) | 0·99 (0·06) |
| Systolic blood pressure (mm Hg) | 134·9 (18·7) | 132·5 (15·3) |
| Mean blood pressure (mm Hg) | 101·7 (10·8) | 101·0 (9·8) |
| Diastolic blood pressure (mm Hg) | 85·1 (8·9) | 85·1 (8·7) |
| Oxygen saturation dips >4% (per h of sleep) | 35·9 (19·6) | 38·0 (19·8) |
| Baseline Epworth sleepiness score | 16·0 (3·1) | 16·3 (3·3) |
| Baseline Osler test (min) | 20·9 (13·3) | 21·6 (12·2) |
| nCPAP compliance (h per night) | 4·5 (2·4) | 4·9 (2·0) |
| Retitration treatment pressure (cm water) | 9·7 (2·2) | 9·8 (1·9) |

nCPAP machine compliance during trial period and retitration nCPAP pressures established at the end of the study are also shown. Values are mean (SD).

Table 1: **Patient characteristics**

| | Sub-therapeutic nCPAP* (n=59) | | Therapeutic nCPAP (n=59) | | Difference in blood pressure change (95% CI)* | p* |
|---|---|---|---|---|---|---|
| | Before | After | Before | After | | |
| 24-h mean blood pressure (mm Hg) | 101·7 (1·4) | 102·5 (1·4) | 101·0 (1·3) | 98·5 (1·2) | −3·3 (−5·3 to −1·3) | 0·0013 |
| Sleep period mean blood pressure (mm Hg) | 96·2 (1·6) | 95·8 (1·5) | 93·7 (1·6) | 90·3 (1·4) | −3·0 (−5·7 to −0·3) | 0·0298 |
| Wake period mean blood pressure (mm Hg) | 104·2 (1·4) | 106·1 (1·4) | 104·3 (1·3) | 101·9 (1·3) | −4·2 (−6·4 to −2·0) | 0·0002 |
| Overall systolic blood pressure (mm Hg) | 134·9 (2·4) | 135·9 (2·3) | 132·5 (2·0) | 130·2 (1·9) | −3·4 (−6·3 to −0·6) | 0·0190 |
| Overall diastolic blood pressure (mm Hg) | 85·1 (1·2) | 85·9 (1·1) | 85·1 (1·1) | 82·7 (1·2) | −3·3 (−5·3 to −1·2) | 0·0018 |

Values are mean (SE). *p values calculated with unpaired *t* test.

Table 2: **Changes in mean ambulatory blood pressure during sleep and wake as defined in the patient's diary and changes in overall systolic and diastolic blood pressure**

this median cut-off point for patients given therapeutic and subtherapeutic nCPAP. The blood pressure in the group with more severe sleep apnoea who were receiving therapeutic nCPAP was 5·1 mm Hg, (95% CI −2·1 to −8·1) less than that of controls, compared with a difference of 1·1 mm Hg (−1·5 to 3·6) in those with less-severe sleep apnoea.

Compared with controls, the fall in mean blood pressure with therapeutic nCPAP, was close between the two groups when divided according to whether they were above or below the median baseline mean blood pressure of 101·5 mm Hg, (fall above the median −3·9 [95% CI −1·0 to −6·6], p=0·008, fall below the median −2·8 [0·0 to −5·5 mm Hg], p=0·05). Thus, blood pressure fall was independent of baseline blood pressure. The reduction in mean blood pressure with therapeutic nCPAP was dependent on average nightly nCPAP use. In patients who used therapeutic nCPAP for longer than 5 h (above the median), mean blood pressure fell by 4·9 mm Hg (SE 1·1), compared with no change in pressure (0.0 mm Hg [0·8]) in those who used nCPAP for less than 5 h (below the median) (difference −4·9 mm Hg [−2·1 to −7·6], p=0·001).

11 patients from each group were taking drugs for hypertension. At baseline, the ambulatory blood pressure and severity of sleep apnoea in these patients were very similar to those of the whole sample. In the group receiving therapeutic nCPAP, mean blood pressure was 101·9 mm Hg (SD 8·6), and greater than 4% desaturation index was 39·1 per h (14·3). In the group receiving subtherapeutic nCPAP, mean blood pressure was 101·8 mm Hg (8·8) and the greater than 4% desaturation index was 35·4 per h (20·4) (compare with data for whole group in table 1). The 11 patients on antihypertensives who received subtherapeutic nCPAP showed little change in their blood pressure (−1·2 mm Hg; SE 1·1). By contrast, those who received therapeutic nCPAP showed a large fall (−7·9 mm Hg; 2·0) (difference 6·7 mm Hg [95% CI 1·9–11·4], p=0·01). Mean compliance with therapeutic (4·9 h every night, SD 2·0) and subtherapeutic nCPAP (4·5 h, 2·4) was similar (difference 0·4 h [95% CI −0·4 to 1·2] p=0·4).

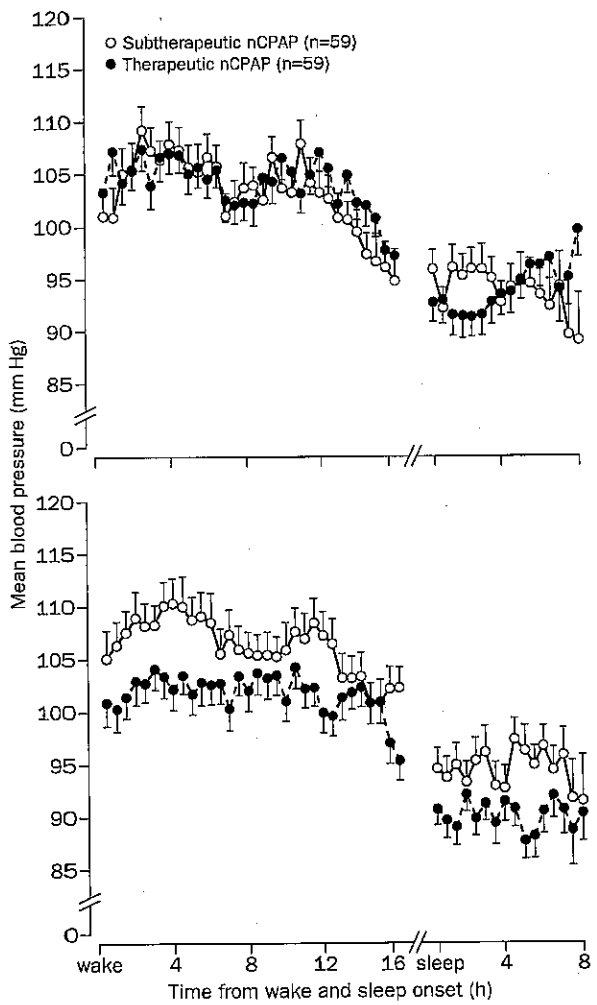


Figure 2: **Mean ambulatory blood pressure profile before (top) and after (bottom) treatment.**
Bars are SEs for every 30-min period, synchronised to wake and sleep times.

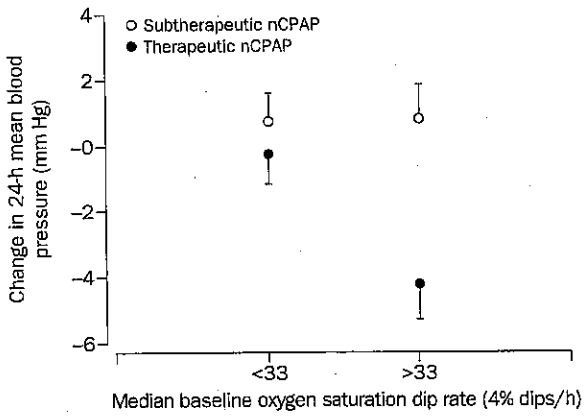


Figure 3: **Change in arterial blood pressure above and below the median of 33 episodes of >4% oxygen saturation dips every hour**
Groups were compared by unpaired *t* testing. Bars are 95% CIs. The difference between the therapeutic and subtherapeutic groups below the median was 1·1 mm Hg (95% CI−1·5 to 3·6; p=0·4). Above the median, the difference was 5·1 mm Hg (2·1–8·1; p=0·001).

## Discussion

Our results showed a significant fall from baseline of 3·3 mm Hg in mean ambulatory blood pressure in patients with moderate or severe obstructive sleep apnoea when given therapeutic nCPAP compared with patients on subtherapeutic nCPAP. Similar reductions were seen in systolic and diastolic blood pressure during both sleep and wake times. This result directly addresses a deficit in the evidence of the blood pressure response to nCPAP therapy in patients with sleep apnoea; specifically, the suggestion that falls in blood pressure seen in uncontrolled studies might be associated with a placebo effect of the nCPAP mask treatment.[11]

From large prospective studies, a blood pressure fall of 3·3 mm Hg would be expected to be associated with a stroke risk reduction of about 20% and a coronary heart disease event risk reduction of about 15%.[22] The estimated combined stroke and coronary event risk for patients with sleep apnoea such as those studied here is about 3% per year,[23] and up to 1·5% of adult men in the UK have sleep apnoea of this severity.[3] Therefore, these results suggest that effective treatment of sleep apnoea in the UK could prevent over 1000 coronary heart disease and stroke events yearly. Such a reduction in blood pressure is similar in magnitude to that seen in a study[24] of pharmacological treatments for control of hypertension, in which much of the expected mortality and morbidity benefit was evident within the first few years of treatment. This reduction is seen in both systolic and diastolic blood pressure, and during both wake and sleep, suggesting that the fall is associated with a general change in vascular pressure regulation and is not attributable solely to the correction of the acute haemodynamic effects of the sleeping apnoea/arousal cycle that characterises sleep that is disturbed by apnoea.[25]

The blood pressure profile of untreated sleep apnoea during sleep has other characteristics that might amplify the vascular risk benefit of nCPAP. Every instance of obstructive apnoea is associated with an acute rise in blood pressure, which can exceed 100 mm Hg,[25] pulse waveform peak pressure is increased and a fall in nocturnal blood pressure is sometimes absent.[26] These features are all independently important in vascular risk[27–29] and are corrected by nCPAP for sleep apnoea. nCPAP might also improve other vascular risk factors that are unrelated to blood pressure, including concentrations of fibrinogen, catecholamines, and frequency of arrhythmia.[30–32] Therefore, nCPAP treatment for sleep apnoea could, like β-receptor blockade after myocardial infarction,[33] produce a risk benefit greater than might be inferred from the straightforward blood pressure changes alone. The blood pressure fall with therapeutic nCPAP was consistent above and below the median of the baseline blood pressures studied. nCPAP is therefore probably correcting a sleep apnoea effect seen equally in patients, whatever their baseline blood pressure, rather than correcting a raised blood pressure that is present in only a subset of the study population.

The severity of patients' sleep apnoea was associated with their response to nCPAP. Patients with more severe disease showed a larger fall in blood pressure with therapeutic nCPAP than those with less severe disease. The blood pressure benefit seems to be mostly restricted to patients with more than 33 dips every hour of greater than 4% in oxygen saturation during sleep (figure 3). In such patients, this reduction would be predicted to reduce stroke risk by 35% and coronary heart disease event risk by 20%.[22] Up to 1·5% of adult UK men have sleep apnoea of the severity investigated in this study.[3] Until now, the main reason to treat these patients has been alleviation of excessive daytime sleepiness and impaired quality of life.[10,11] These symptomatic benefits might be accompanied by a reduction in cardiovascular risk, but criticism of the methods of studies showing such an association has been fierce.[11] To clarify the debate about nCPAP and vascular risk, we examined arterial blood pressure, since results of observational studies,[8,9] work with animals,[35] and epidemiological surveys[4,5] suggest that raised blood pressure is strongly associated with sleep apnoea. We measured 24-h ambulatory blood pressure because it is a better measure than single measurements of average pressures,[36] and it more accurately predicts left ventricular hypertrophy[37] and cardiovascular risk.[38] In reports of uncontrolled studies,[8,9] and in a small cross-over trial with an oral placebo,[10] nCPAP reduced ambulatory blood pressure. The results from our sizeable parallel trial with a robust placebo-treated control group lend support to such a reduction.

This trial was designed to produce data that could easily be applied to clinical practice. The severity of sleep apnoea in the study sample is representative of that for which nCPAP is generally used in this country, and sleep apnoea severity was quantified with one of the most widely used UK respiratory polysomnography systems. Baseline blood pressure was not used to select patients for study entry, so our results should estimate the blood pressure benefit likely to be seen across most patients with sleep apnoea receiving nCPAP.

Compared with controls, patients who had therapeutic nCPAP and were taking antihypertensive drugs had a particularly large fall in mean blood pressure of 6·6 mm Hg. We included only 22 such patients, randomly assigned equally to the two treatment groups. The interpretation of a finding in such a small sample must be cautious—but the magnitude of our recorded effect is substantial. These results suggest that benefits to this group of patients could be large, and could imply that untreated sleep apnoea antagonises the effectiveness of antihypertensives. Sleep apnoea is frequent in patients with hypertension who attend a hospital clinic.[8] However, in such patients, it is often mild, associated with few symptoms, and might not be as important as in those who we investigated. If treatment of this mild sleep apnoea did facilitate hypertensive drug therapy, it would be important for this challenging group of patients.

The overall blood pressure reduction might underestimate the true effect of nCPAP because of a confounding effect on sleepiness and, consequently, levels of physical activity. In patients receiving subtherapeutic nCPAP, blood pressure falls at about 10–12 h after waking (about 1800 h). By contrast, those on therapeutic nCPAP showed no fall until about 14 h after waking, (about 2130 h). Since sleep directly reduces blood pressure, the difference between the two groups is probably because patients receiving subtherapeutic nCPAP fell asleep earlier in the evening because of uncontrolled sleep apnoea,[39] whereas in patients receiving therapeutic nCPAP, the sleepiness is controlled, and their blood pressure does not fall. If this is correct, the physiological benefit from nCPAP is best measured from the morning and night-time periods, which keep differences in physical activity levels at a minimum between the groups. These are probably wake hours 0–10, in which all patients are probably awake and active, and the sleep hours, during which they are probably asleep and inactive. The difference in the mean blood pressure change between the groups for this period is about 6 mm Hg.

We have shown that therapeutic nCPAP for obstructive sleep apnoea reduces blood pressure after 1 month of treatment. Our results accord with those of Faccenda and colleagues,[10] who used an oral placebo tablet as a control for therapeutic nCPAP over 1 month. Results of long-term uncontrolled observational cohort series suggest that these blood pressure falls are sustained for longer periods than the 1 month investigated in our study. Results of three studies[8,40,41] including 37 patients, show ambulatory blood pressure falls of 5–20 mm Hg after 2–6 months of therapeutic nCPAP therapy, although Hedner and colleagues[42] recorded no difference in 12 patients after 1 year.

We have shown a clinically important lowering of blood pressure when patients with moderate or severe obstructive sleep apnoea are given therapeutic nCPAP. This result is confirmed by comparison with a robust control and is also seen in systolic and diastolic pressure, and during both wake and sleep. The reduction in blood pressure was independent of baseline pressure, but was mostly restricted to patients with more than 30 episodes of respiratory obstruction every hour, and was greater in patients with good nCPAP compliance. The patients studied were typical of those receiving nCPAP for obstructive sleep apnoea in the UK. We conclude that nCPAP treatment for obstructive sleep apnoea probably produces significant vascular risk benefits through reduced blood pressure, and substantially improves these patients' excessive daytime sleepiness and quality of life.[15]

### Contributors

J Pepperell coordinated the study and with S Ramdasingh-Dow, N Crosthwaite, and R Mullins, gathered, processed, and analysed the data. C Jenkinson, J Stradling, and R Davies designed the study and were responsible for funding. C Jenkinson prepared the randomisation code. J Stroding and R Davies supervised the study. All authors contributed to the writing of the report.

### Conflict of interest statement

None declared.

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