EFFECT OF PRIMARY CARE VERSUS SPECIALIST SLEEP CENTER MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA ON DAYTIME SLEEPINESS AND QUALITY OF LIFE: A RANDOMISED TRIAL

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ABSTRACT

Context: Due to rising demand for sleep services, there has been growing interest in ambulatory models of care for obstructive sleep apnea (OSA). With appropriate training and simplified management tools, primary care physicians (PCPs) are ideally positioned to take on a greater role in the diagnosis and treatment of OSA.

Objective: To compare the clinical efficacy and cost-effectiveness of a simplified model of diagnosis and care for OSA in primary care relative to that in specialist sleep centres.

Design: A randomised, controlled, non-inferiority study.

Setting: Primary care practices in metropolitan Adelaide and 3 rural regions of South Australia and a university hospital sleep medicine centre in Adelaide, Australia.

Patients: A total of 155 patients with OSA (identified by screening questionnaire and home oximetry) and Epworth Sleepiness Scale (ESS) ≥8 or resistant hypertension were randomised into the study between September 2008 to June 2010. 81 patients were randomly assigned to the primary care arm and 74 patients to the specialist arm.

Interventions: Primary care management of OSA led by a PCP and community-based nurse versus usual care in a specialist sleep centre. Treatments for OSA employed in both arms included continuous positive airway pressure (CPAP), mandibular advancement splints or conservative measures only.

Main Outcome Measures: The primary outcome was the change in ESS after 6 months, and was assessed for non-inferiority using an a priori determined non-inferiority margin of -2.0 points. The ESS is scored from 0 (no daytime sleepiness) to
24 points (high level of daytime sleepiness). Secondary outcomes included disease-specific and general quality of life measures, OSA symptoms, CPAP compliance, patient satisfaction and health care costs.

**Results:** There were significant improvements in ESS scores from baseline to 6 months in both the primary care arm (12.8 [baseline] to 7.0 [6 months], p<0.001) and specialist arm (12.5 to 7.0, p<0.001). Primary care management was non-inferior to specialist management for the mean change in ESS (5.8 vs 5.4; adjusted difference -0.13 [lower bound of one-sided 95% confidence interval : -1.5], p=0.43) using a non-inferiority margin of -2.0. There were no differences in secondary outcomes measures between groups. More patients withdrew from the study in the primary care arm (17 [21%] vs 6 [8%]).

**Conclusions:** Among patients with OSA, treatment under a primary care model compared with a specialist model did not result in worse sleepiness scores.

**Trial Registration:** Australian New Zealand Clinical Trials Registry, ACTRN 12608000514303, http://www.anzctr.org.au/
INTRODUCTION

Obstructive sleep apnea (OSA) with accompanying daytime sleepiness was estimated during the early 1990s to affect 2-4% of middle-aged adults\(^1,2\). With growing awareness of the public health implications of untreated disease\(^3-6\) and rising obesity rates that have increased the prevalence of OSA\(^7\), there has been a steady rise in the demand for sleep service provision in specialist centres and growing waiting lists for sleep physician consultation and laboratory-based polysomnography (PSG). As a result, there has been increasing interest in the use of screening questionnaires, home sleep monitoring, and auto-titrating continuous positive airway pressure (CPAP)\(^8-10\), and greater involvement of other health care professionals in providing care\(^11\).

One-third of primary care patients report symptoms suggestive of OSA\(^12\). With appropriate training and simplified management tools, primary care physicians (PCPs) and practice nurses might be ideally positioned to take on a greater role in OSA diagnosis and management. Several randomised controlled studies have shown that ambulatory management of OSA in specialist sleep centres using home testing and auto-titrating CPAP produce comparable patient outcomes to standard laboratory-based sleep study methods\(^8-11\). However, whether an ambulatory approach would be non-inferior in a primary care setting is unknown. The aim of this study was to compare the clinical efficacy of OSA management provided in primary care by a PCP and a community-based nurse versus currently recommended management in a specialist sleep centre.
METHODS

Design Overview
A randomised, controlled, non-inferiority study was conducted to compare an ambulatory, primary care-based management strategy for OSA versus standard care in a specialist sleep centre. The research protocol was approved by institutional research ethics committees at the Repatriation General Hospital and Flinders Medical Centre, South Australia and the study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12608000514303). Patients and PCPs provided written, informed consent.

Settings and Participants
Patients aged 25 to 70 years attending a primary care consultation for any reason were screened for eligibility by 34 PCPs between September 2008 to June 2010. Participants were recruited from 4 geographical locations in South Australia consisting of: (1) metropolitan Adelaide (6 primary care practices; 2 community nurse clinics); and 3 rural regions (2) South Coast (2 primary care practices; 1 community nurse clinic); (3) Barossa Valley (4 primary care practices; 1 community nurse clinic) and (4) Riverland (4 primary care practices; 1 community nurse clinic). All patients were screened for moderate-severe OSA using a validated two-step method\(^{15}\) that consisted of a screening OSA50 questionnaire which, if positive (i.e. score $\geq 5$ out of 10 points), was followed by overnight oximetry (ApneaLink, ReMed). Inclusion criteria were: (1) high diagnostic likelihood of moderate-severe OSA defined as an OSA50 questionnaire score $\geq 5$ and overnight 3% oxygen desaturation index ($\geq 3\%\text{ODI}$) $\geq 16$/hr; and (2) Epworth Sleepiness Scale (ESS)\(^{16}\) $\geq 8$ or persistent hypertension despite $\geq 2$ antihypertensive agents. The ESS subjectively assesses
excessive daytime sleepiness by asking patients to rate their chance of dozing off from 0 (would never doze) to 3 (high chance of dozing) for eight commonly-encountered scenarios, giving a total score out of 24. A cut-off score ≥8 suggests the presence of at least mild daytime sleepiness. Exclusion criteria were: (1) severe morbid obesity (body mass index [BMI] >50kg/m²); (2) neuromuscular disease; (3) unstable psychiatric disease or cognitive impairment considered likely to prevent the patient complying with instructions, completing the study and/or managing CPAP; (4) hospitalisation in the previous 3 months for myocardial infarction, unstable angina, cardiac failure or cerebrovascular accident, or New York Heart Association Class III or IV symptoms; or (5) lung disease with awake resting oxygen saturation <92%. Demographic and anthropometric data were collected, including gender, age, geographical region, weight, height, BMI, and waist circumference.

Randomisation and Interventions

Patients meeting eligibility criteria were randomised into either: (1) Primary care management; or (2) Specialist sleep centre management. Randomisation was conducted by a telephone call to a clinical trials pharmacist independent of the study, using a computer-generated random numbers list.

(1) Primary care management

Patients were managed by their PCP and a community-based nurse who participated in a six-hour education program on OSA and its management. The education program was developed and presented by sleep physicians and a specialist nurse from the university hospital sleep medicine centre, and accredited by the Royal Australasian College of General Practitioners. Patients were reviewed in-
person by one of four nurses who held clinics at five community locations (2 nurse clinics in metropolitan Adelaide and 1 nurse clinic in each of the three rural regions) to review progress and provided with advice on managing CPAP-related side effects, encouraged to maintain ongoing compliance with therapy, advised to discuss alternative treatment options with PCPs if necessary, educated about lifestyle changes to improve OSA and asked to complete relevant research questionnaires. One nurse had 15 years of experience in a tertiary care sleep medicine service and managed patients at the 2 metropolitan-based clinics and the South Coast clinic. The other 3 nurses were newly trained in OSA management, but had worked as rural-based practice nurses prior to their involvement (1 nurse managed patients at the Barossa Valley clinic and the other 2 nurses managed patients at the Riverland clinic). In addition to the 6 hour education program which they attended alongside the PCPs, the sleep training provided to the community-based nurses also involved 5 days of in-service training with specialist nurses at the tertiary sleep centre. Home auto-titrating CPAP (REMstar Auto, Respironics or S8 AutoSet Spirit, ResMed) was used over 3 consecutive nights to determine a fixed treatment pressure based on the 90th (REMstar Auto) or 95th (S8 AutoSet Spirit) percentile pressure. CPAP devices were converted to a fixed pressure mode for the remainder of the study. Patients were followed up by their nurse with a telephone call within two weeks of commencing therapy and in-person at 1, 3 and 6 months, and seen by their PCP at 3 and 6 months. CPAP adherence was objectively recorded by each device and information from data cards were downloaded at 1, 3 and 6 month reviews. Although CPAP was considered the primary treatment, PCPs were educated about and could initially prescribe, or at a subsequent review, switch to alternative therapies for OSA if deemed appropriate, including lifestyle measures, a mandibular advancement
splint (MAS) or upper airway surgery. PCPs were provided with contact details of a
dentist expert in the fashioning of mandibular advancement splints (SomnoDent
MAS, SomnoMed Ltd, Crows Nest, New South Wales, Australia). CPAP and MAS
were available free of charge to participants. PCPs were advised that a sleep
physician could be contacted for advice or to request a formal consultation.

**(2) Specialist sleep centre management**

Patients were referred to one of nine sleep specialists at the Adelaide Institute for
Sleep Health, South Australia, for ongoing management. Sleep specialists had
completed their Fellowship of the Royal Australasian College of Physicians, having
undertaken at least 3 years of respiratory medicine training including 1 year of full-
time sleep medicine training. Sleep specialists were provided with the patient’s
overnight oximetry trace. Further investigations, including full or split-night laboratory
PSG, and treatment recommendations were left to the discretion of the treating
physician. CPAP titration, if recommended, was conducted manually during
laboratory PSG or by home auto-titration. Experienced nurses at the specialist centre
provided support for CPAP set-up and education. The same models of CPAP
machines were used as in the primary care arm. In-person follow-ups occurred at the
same time points as the primary care arm. As in the primary care arm, CPAP was
considered the primary treatment, but sleep specialists could initially prescribe, or at
a subsequent review, switch to alternative therapies for OSA if deemed appropriate
including lifestyle measures, a MAS or upper airway surgery.
Outcomes and Follow-up
The primary outcome measure was the change in ESS from baseline to 6 months\textsuperscript{16}. Secondary outcome measures were the Functional Outcomes of Sleep Questionnaire (FOSQ)\textsuperscript{17}, Sleep Apnea Symptoms Questionnaire (SASQ)\textsuperscript{18}, Short-Form 36 Health Survey (SF-36)\textsuperscript{19} vitality and mental health components, CPAP compliance, blood pressure and weight which were measured at baseline and 6 months. Vitality and mental health components of the SF-36 have been most responsive in previous CPAP studies\textsuperscript{20, 21}, therefore, only changes in these two scores are reported. A Visit-Specific Satisfaction Questionnaire (VSQ-9)\textsuperscript{22} was also completed at 6 months. See online supplement for a detailed description of questionnaires.

Statistical Analysis
Statistical analyses were performed using STATA/IC 11.2 for Windows (StataCorp LP, College Station, Texas, USA). Missing values for the main outcome measures were replaced by multiple imputation with multivariate normal regression using demographic and baseline outcome data, and with creation of 10 complete data sets. Comparisons between groups for the mean change in ESS, FOSQ, SASQ, SF-36, weight and blood pressure after 6 months were conducted in an intention-to-treat manner including all patients randomised using analysis of covariance with adjustment for baseline scores and region. Results for data analysed by carrying forward baseline observations for missing values, and by inclusion of patients with complete data have also been conducted as a sensitivity analysis. A Student’s t-test was used to evaluate for group differences in CPAP use and VSQ-9 scores. The difference in the mean change in ESS scores after 6 months was evaluated for non-
inferiority of the primary care arm using an *a priori* determined non-inferiority margin of -2.0 based on past literature on minimal clinically important differences for health-related quality of life instruments\textsuperscript{23}, clinical studies which have assessed natural variations in ESS scores and ESS responses to placebo CPAP in OSA patients\textsuperscript{24-26}, and consensus amongst sleep physicians in a previously published study\textsuperscript{11}. For the non-inferiority analysis, significance testing using a one-sided p-value of 0.05 was used to determine the probability of rejecting the null hypothesis of inferiority. Statistical significance for secondary outcomes was determined using a two-sided alpha of 0.05.

*Sample size*

The study was powered to assess for non-inferiority of the primary care arm relative to the specialist arm in the mean change in ESS score after 6 months. A sample size of 138 patients (69 patients in each arm) was required for a study with 90% power and a Type I error of 5%, assuming a non-inferiority margin of -2.0 and a standard deviation of 4.0 for the change in ESS. A total of 155 patients were recruited to allow for potential withdrawals and loss to follow-up.

*Within-Trial Costs*

Within-trial sleep diagnostic and treatment costs were collected and compared during the 6 month follow-up for nurse consultations, PCP and sleep physician consultations, travel costs, sleep study costs and treatment-related costs. Within-trial costs were also calculated for the US context and reported in US dollars. See online supplement for a detailed description of how costs were calculated.
RESULTS

A flow diagram outlining the recruitment and randomisation pathway is shown in Figure 1. 402 patients were referred by PCPs after initial screening to community-based nurses for review of eligibility criteria and oximetry monitoring. 301 patients agreed to and were eligible for overnight oximetry. 155 patients were found to have a $\geq 3\% ODI \geq 16/hr$ and were randomised into the study.

Baseline Characteristics

81 patients (Adelaide n=27; South Coast n=3; Barossa Valley n=24; Riverland n=27) were randomised to the primary care arm, and 74 patients (Adelaide n=18; South Coast n=1; Barossa Valley n=26; Riverland n=29) to the specialist arm. The two groups were comparable and consisted of predominantly middle-aged, obese males from rural regions with at least mild daytime sleepiness (Table 1).

Treatment

The principal treatment recommended to patients at baseline and used at 6 months are outlined in Table 2. At baseline, almost all patients (90%) in the primary care arm were commenced on CPAP. Fewer patients in the specialist arm were commenced on CPAP (70%) and a higher proportion of patients were managed with conservative measures only. In the specialist arm, 73 of 74 patients had a laboratory-based full (n=38) or split-night (n=35) PSG. Three (4%) patients in the primary care arm were referred for sleep specialist consultation during the study, one of whom had a laboratory full night diagnostic PSG.
After 6 months follow-up, the proportions of patients using CPAP were similar in the primary care and specialist arms (63% and 61%, respectively). More patients withdrew from the study in the primary care arm. Baseline demographic, anthropomorphic and OSA severity indices were similar in patients who withdrew and those who completed the study in each study arm (see eTable 1 in the online supplement).

**Outcomes**

*Daytime Sleepiness: Epworth Sleepiness Scale (ESS)*

The mean ESS for the entire study population was 12.6 (95%CI: 12.0 to 13.3). There were significant improvements in the mean ESS scores from baseline to 6 months in both the primary care arm (12.8 [baseline] to 7.0 [6 months], adjusted mean difference 5.8 [95%CI: 4.4 to 7.2], p<0.001) and specialist arm (12.5 to 7.0, adjusted mean difference 5.4 [95%CI: 4.2 to 6.6], p<0.001), see Table 3). After controlling for baseline ESS and region, the adjusted difference in mean change in ESS was -0.13 (lower bound of one-sided 95%CI: -1.5, p=0.43). Sensitivity analyses using baseline observations carried forward for missing values and using data only from patients who completed the study produced similar outcomes. For the analysis using baseline observations carried forward for missing data, the adjusted difference in mean change in ESS was -0.63 (lower bound of one-sided 95%CI: -1.80, p=0.19). When including only patients who completed the study (primary care arm, n=64; specialist arm, n=68), the adjusted difference in the mean change in ESS was -0.14 (lower bound of one-sided 95%CI: -1.28, p=0.42). These results support non-inferiority of primary care management as the lower bound of the one-sided 95% confidence
interval for all analyses were greater than the pre-specified non-inferiority margin of -2.0.

**Secondary Outcomes**
Secondary outcomes measures are shown in Table 4. After 6 months, there were significant improvements in the mean FOSQ, SASQ or SF-36 scores in both primary care and specialist groups compared to baseline (p<0.001 for all measures), but no difference was evident between groups.

CPAP compliance in patients using CPAP at 6 months was no different between the two groups, with mean usage of 4.8 ± 2.1 hours per night in the primary care arm (n=51) and 5.4 ± 0.3 hours per night (n=44) in the specialist arm (p=0.11). No differences in systolic or diastolic blood pressure, or weight were evident in either primary care or specialist arms after 6 months, and there was no difference between groups in the mean change. There were small, but statistically significant, differences in 5 out of 9 items in the VSQ-9 patient satisfaction survey in favour of the primary care arm (see eTable 2 in the online supplement) although no difference in overall satisfaction was evident. Furthermore, effect sizes for the 9 items were small (range 0.14 to 0.41) and may not therefore be clinically significant.

**Within-Trial Costs**
Comparison of within-trial sleep diagnostic and treatment costs revealed a total average cost per randomised patient of AUS$1606.48 in the primary care arm and AUS$2576.47 in the specialist arm (see eTable 3 in the online supplement). When considered in the US context, the equivalent total average costs per patient were
estimated at US$1819.44 in the primary care arm and US$3067.86 in the specialist arm. Sleep study costs, sleep physician consultations and travel costs appeared to be the main contributors to the increased within-trial costs in the specialist arm.
COMMENTS

In this study, patients identified by a two-step screening process as having a high likelihood of moderate-severe OSA and who were at least mildly sleepy, were randomised to either primary care or specialist management. Clinically significant improvements in the primary outcome measure, daytime sleepiness, were observed following treatment in both settings\(^2^7\) and outcomes for patients managed in primary care were not inferior to those treated in a specialist centre. No differences between groups were found in secondary outcomes, including change in OSA symptoms, quality of life, CPAP adherence and overall patient satisfaction.

These results extend the findings of previously published studies of ambulatory models of care for OSA deployed in specialist sleep centres. Mulgrew et al\(^8\) utilised a strategy of portable monitoring and auto-titrating CPAP and found no differences in major outcomes, including change in ESS and quality of life, compared to laboratory-based care. Furthermore, CPAP adherence was higher in the ambulatory care arm. Berry et al\(^9\) conducted a similar study in a veteran population where patients with OSA were randomised to either portable monitoring and auto-titrating CPAP, or to laboratory PSG and CPAP titration. After 6 weeks, no differences were observed in CPAP compliance, change in ESS or FOSQ scores, patient satisfaction with CPAP or residual AHI. Kuna et al\(^1^0\) found that functional outcomes and CPAP adherence were not inferior to laboratory-based care when using an ambulatory strategy for OSA. None of these studies assessed the relative costs of the simplified management strategies.

More recent studies evaluating ambulatory strategies for OSA have examined within-
study costs. Andreu et al\textsuperscript{28} randomised patients into either: (1) home sleep monitoring and follow-up; (2) hospital PSG and follow-up; or (3) home monitoring and hospital follow-up. They found no differences in CPAP compliance, ESS, FOSQ or symptom scores after 6 months. They also reported significant cost savings for home diagnosis and follow-up (mean €590 ± SD 43) and home diagnosis with hospital follow-up (€644 ± 93) compared to laboratory PSG and hospital follow-up (€849 ± 11). Rosen et al\textsuperscript{29} showed that home diagnosis and auto-titrating CPAP was associated with higher CPAP adherence, similar to the study by Mulgrew et al, with no difference in the change in ESS or functional outcomes after 3 months compared to laboratory-based management. Within-trial costs were 25% cheaper in the home treatment arm.

We previously conducted a randomised controlled trial to evaluate a simplified model of care for OSA led by sleep-trained nurses in a tertiary care setting\textsuperscript{11}. The primary outcome, mean change in ESS at 3 months, for patients managed using the nurse-led approach was not inferior to specialist-led management and had within-study cost savings of AUD$1,111 per patient. These results led us to consider the potential role of primary care physicians and nurses in the diagnosis and management of OSA.

The present study which recruited patients from metropolitan and rural communities had a longer period of follow-up than previous studies (i.e. 6 months compared to 1-3 months). We believe that important elements in the success of the study were the training given to PCPs and nurses and access to specialist support. Thus, while PCPs and community nurses were encouraged to take primary responsibility for
patient management, this simplified strategy was designed as a “hub-and-spoke”-like model of care, with a central specialist sleep centre overseeing and supporting a number of primary care-based OSA clinics. Of note though is that PCPs cross-referred only 3 of 81 (4%) patients to sleep specialists for a second opinion. This could be because two-thirds of the study population were recruited in rural regions located 90 to 240km from the city-based specialist sleep service. However, only 1 out of 21 (5%) metropolitan-based patients enrolled in the primary care arm were cross-referred suggesting perhaps that, at least in the context of the research study, PCPs and nurses were reasonably confident in their management decisions.

At baseline, CPAP was recommended more frequently in the primary care arm. However, by 6 months a considerable number of patients in the primary care arm had stopped using CPAP, and the proportion of patients on CPAP was similar to the specialist arm. Average daily CPAP use at 6 months was no different between arms. These observations could suggest that specialists, who have additional information from laboratory PSG and are more experienced at OSA management, may be better at predicting which patients will adhere to CPAP in the long term. Alternatively, attendance at a specialist and/or nurse review in a tertiary sleep centre may itself have had an influence on long term adherence. There could also be an effect of experience such that with time, the PCPs may become more confident with managing sleep apnea and thus promote greater CPAP adherence, or recommend alternative therapies such as a MAS or conservative measures earlier in the course of treatment for patients who are reluctant to use or are intolerant of CPAP. However, it is interesting to note that, in spite of the different approaches to management, patient outcomes were ultimately similar in the two arms.
Analysis of within-trial sleep-related diagnostic and treatment costs revealed that primary care management of OSA was approximately 40% cheaper than specialist care in both the Australian and US contexts. However, our study reports within-trial sleep management-related costs only and not indirect costs nor does it assess the longer term economic implications of an ambulatory strategy in primary care. Recent debate has been sparked by a study by Pietzsch et al\textsuperscript{30} which showed full-night PSG to be more cost-effective than unattended home monitoring in the management of OSA, due to its superior diagnostic accuracy. It was pointed out in an accompanying editorial\textsuperscript{31}, however, that several assumptions used in their modelling could have magnified the effects of false positive and negative results and elevated the costs of portable monitoring. More detailed cost-effectiveness analyses which take into account increased access and reduced waiting lists, the impact of false positive and negative tests, potential adverse health consequences of untreated disease and benefits of therapy, and indirect costs of ambulatory, primary care-based management strategies for OSA are needed.

Several limitations of our study are acknowledged. We excluded patients with a BMI>50kg/m\textsuperscript{2}, significant respiratory or cardiac disease, and serious psychiatric illness or cognitive impairment. Thus, the results of this study cannot be generalised to these populations. It is possible that patients with predominantly central sleep apnea, including Cheynes Stokes respiration, may have been misdiagnosed in the primary care arm, since only oximetry was used to identify patients with disease. However, we excluded patients with disorders prone to central sleep apnea (e.g. heart failure) plus residual AHI was monitored on CPAP devices and, at 6 months,
only 1 patient in the primary care arm had a residual AHI exceeding 15/hr.

One of the community-based nurses in the primary care arm who predominantly managed patients in the metropolitan region had 15 years of prior experience in a tertiary care sleep medicine service whilst the other three rural-based community nurses were newly-trained in OSA management. The more experienced nurse was included in the primary care arm to assist in the training and to mentor the newly recruited nurses. We would anticipate that if such a model of care were to be translated into real practice, that some nurses employed to manage OSA patients in a community-based clinic would likely have some prior experience in OSA management, particularly in the metropolitan region where there is a larger pool of experienced, CPAP-trained nursing staff. The more experienced nurse managed a total of 30 (37%) patients in the primary care arm who were based in the metropolitan and rural South Coast regions, whilst the three less experienced nurses managed the other 51 (63%) patients located in the rural Barossa Valley and Riverland regions. We have attempted to account for the difference in nurse experience by adjusting for geographical region in addition to baseline ESS in our analyses. Furthermore, withdrawal rates, change in ESS from baseline to 6 months, 6 month CPAP adherence and auto-CPAP titration results were not significantly different between the experienced versus newly-trained nurses. Therefore, we do not believe that inclusion of an experienced nurse in the primary care arm significantly biased our results.

For reasons which are not entirely clear, more patients withdrew from the primary care arm. It is possible that patients were more inclined to remain in the study if they
were receiving specialist consultations. Alternatively, participants may have had less faith in the advice of the primary care team and the greater number of withdrawals in the primary care arm may be because PCPs were less skilled in educating patients about OSA and treatment options. Although overall patient satisfaction was no different between groups, the opinions of patients who withdrew were not sampled. Interestingly, one-half of patients who withdrew from the primary care arm did so because of “CPAP intolerance" whilst this was not cited as a reason in the specialist group. The higher number of withdrawals in the primary care arm may have biased study results by excluding data from patients with worse outcomes. However, we believe our findings are robust since in both the primary analysis using multiple imputation for missing values and in two sensitivity analyses, patient outcomes in the primary care arm remained clinically non-inferior.

In conclusion, this prospective, randomised controlled study demonstrates that a simplified management strategy for OSA based in primary care is not clinically inferior to standard care in a specialist sleep centre and can likely be delivered at a lower cost. Thus, with adequate training of PCPs and practice nurses and appropriate funding models to support an ambulatory strategy, primary care management of OSA has the potential to improve patient access to sleep services. This would be particularly beneficial for rural and remote regions, as well as developing nations, where access to specialist services can be limited. However, some caution needs to be exercised in extrapolating these findings to actual practice where PCPs may not be as skilled and motivated as the PCPs who participated in this randomised controlled trial and where, conceivably, patient outcomes may not be as good as those observed in this study. Our comparison of within-trial costs
cannot be considered a cost-effectiveness analysis and further investigation is needed in this regard.
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Author contributions: Dr Chai-Coetzer had full access to all of the data in the study and takes responsibility for the integrity of data and the accuracy of the data analysis.

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Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Chai-Coetzer reported that she has received research funding from the National Health and Medical Research Council of Australia, Flinders Medical Centre Clinicians Trust and Flinders Medical Centre Foundation, and equipment donations from ResMed, Philips Respironics and SomnoMed. Associate Professor Antic has reported that he has received research funding from the National Health and Medical Research Council of Australia, Philips Respironics and Fisher and Paykel, equipment donations from ResMed, Philips Respironics and SomnoMed, and lecture fees and payment for development of educational presentations from ResMed. Mrs Rowland has reported that she has received research funding from the National Health and Medical Research Council of Australia and equipment donations from ResMed, Philips Respironics and SomnoMed. Professor Reed reported that he has received research funding from the National Health and Medical Research Council of Australia. Associate Professor Catcheside has reported that he has received research funding from the National Health and Medical Research Council of Australia, and equipment support from Philips Respironics, Apnex Medical, and Gorman Promed Pty Ltd. Dr Williams has reported that she is Director on the Board of the Australian Commission.
for Safety and Quality in Health Care and Chair of the Primary Care Clinical Committee, is employed by the SAFKI Medicare Local as Executive Clinical Director, Southern Adelaide Local health Network as the Presiding Member of the Governing Council, and the Russell Clinic where she is practicing as a general practitioner, and she has previously been employed by the Royal District Nursing Society of South Australia as the Chair of the Clinical Governance Committee. In addition, the National Prescribing Service has paid for her accommodation to attend the National Medicines Symposium 2012. Professor Dunn has reported that she has received research funding from the National Health and Medical Research Council of Australia and equipment donations from ResMed, Philips Respironics and SomnoMed. Professor McEvoy has reported that he has received research funding from the National Health and Medical Research Council of Australia, Philips Respironics, and Fisher and Paykel, equipment donations from ResMed, Philips Respironics and SomnoMed, and lecture fees from Philips Respironics. Professor Esterman, Professor Eckermann and Dr Vowles have reported no conflicts of interest.

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REFERENCES


Figure 1. Flow diagram of participant recruitment and randomisation
Table 1. Baseline characteristics of patients in primary care and specialist arms

<table>
<thead>
<tr>
<th>Description</th>
<th>Model A: Primary Care Arm (n=81)</th>
<th>Model B: Specialist Arm (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>69 (85%)</td>
<td>57 (77%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>57.2 ± 10.9</td>
<td>54.5 ± 11.8</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metropolitan, n (%)</td>
<td>21 (33%)</td>
<td>18 (24%)</td>
</tr>
<tr>
<td>South Coast, n (%)</td>
<td>3 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Riverland, n (%)</td>
<td>27 (33%)</td>
<td>29 (39%)</td>
</tr>
<tr>
<td>Barossa Valley, n (%)</td>
<td>24 (30%)</td>
<td>26 (35%)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>33.1 ± 5.5</td>
<td>33.7 ± 5.6</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>111.2 ± 13.6</td>
<td>113.1 ± 14.5</td>
</tr>
<tr>
<td>OSA50 questionnaire score</td>
<td>8.2 ± 1.5</td>
<td>8.1 ± 1.7</td>
</tr>
<tr>
<td>ESS total score</td>
<td>12.8 ± 3.9</td>
<td>12.5 ± 3.9</td>
</tr>
<tr>
<td>ApneaLink ≥3%ODI, events/hr</td>
<td>32.7 ± 18.2</td>
<td>35.7 ± 17.4</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%)
BMI = body mass index; ESS = Epworth Sleepiness Scale; ≥3%ODI = 3% oxygen desaturation index
Table 2. Principal treatment recommended to patients at baseline and used at 6 months

**Recommended at Baseline:**

<table>
<thead>
<tr>
<th>Principal treatment</th>
<th>Model A: Primary care (n=81)</th>
<th>Model B: Specialist sleep centre (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td>73 (90%)</td>
<td>52 (70%)</td>
</tr>
<tr>
<td>Conservative measures only</td>
<td>2 (2%)</td>
<td>18 (24%)</td>
</tr>
<tr>
<td>MAS</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Patient withdrew</td>
<td>5 (7%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

**Used at 6 months:**

<table>
<thead>
<tr>
<th>Principal treatment</th>
<th>Model A: Primary Care (n=64*)</th>
<th>Model B: Specialist sleep centre (n=68**)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td>51 (63%)</td>
<td>45 (61%)</td>
</tr>
<tr>
<td>Conservative measures only</td>
<td>7 (9%)</td>
<td>12 (16%)</td>
</tr>
<tr>
<td>MAS</td>
<td>6 (7%)</td>
<td>11 (15%)</td>
</tr>
</tbody>
</table>

Data is presented as n (%)
CPAP = continuous positive airway pressure; MAS = mandibular advancement splint
*At 6 months, 17 patients had withdrawn from primary care arm
**At 6 months, 6 patients had withdrawn from specialist arm
Table 3. Change in Epworth Sleepiness Scale score at 6 months

<table>
<thead>
<tr>
<th></th>
<th>Model A: Primary Care Arm (n=81)</th>
<th>Model B: Specialist Arm (n=74)</th>
<th>(^\dagger) Adjusted difference in mean change</th>
<th>(^\dagger\dagger) p value</th>
<th>Lower bound of one-sided 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ESS</td>
<td>12.8 (12.0 to 13.6)</td>
<td>12.5 (12.4 to 13.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 month ESS*</td>
<td>7.0 (6.0 to 8.0)</td>
<td>7.0 (6.0 to 8.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in ESS</td>
<td>5.8** (4.4 to 7.2)</td>
<td>5.4** (4.2 to 6.6)</td>
<td>-0.13</td>
<td>0.43</td>
<td>-1.50</td>
</tr>
</tbody>
</table>

ESS = Epworth Sleepiness Scale; 95%CI = 95% confidence interval

*Missing values replaced by multiple imputation

**p<0.001 for paired t-test comparison of ESS examining change from baseline to 6 months.

\(^\dagger\)Based on analysis of co-variance with adjustment for baseline ESS and region.

\(^\dagger\dagger\)1-sided p value
## Table 4. Secondary outcome measures at 6 months

<table>
<thead>
<tr>
<th></th>
<th>Primary Care Arm</th>
<th></th>
<th>Specialist Arm</th>
<th></th>
<th>*Adjusted difference in mean change (95%CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Baseline (95%CI)</td>
<td>Mean change at 6 months (95%CI)</td>
<td>n</td>
<td>Baseline (95%CI)</td>
<td>Mean change at 6 month (95%CI)</td>
</tr>
<tr>
<td>FOSQ</td>
<td>81</td>
<td>14.7 (14.1 to 15.4)</td>
<td>2.8 (2.0 to 3.6)</td>
<td>74</td>
<td>14.2 (13.5 to 14.8)</td>
<td>2.8 (2.2 to 3.4)</td>
</tr>
<tr>
<td>SASQ</td>
<td>81</td>
<td>71.2 (66.5 to 75.9)</td>
<td>-29.7 (-23.0 to -36.4)</td>
<td>74</td>
<td>72.1 (67.4 to 76.7)</td>
<td>-31.2 (-23.8 to -38.6)</td>
</tr>
<tr>
<td>SF-36 vitality</td>
<td>81</td>
<td>43.6 (39.1 to 48.1)</td>
<td>16.1 (11.0 to 21.2)</td>
<td>74</td>
<td>34.6 (30.3 to 38.9)</td>
<td>19.9 (14.4 to 25.4)</td>
</tr>
<tr>
<td>SF-36 mental health</td>
<td>81</td>
<td>66.5 (62.4 to 70.7)</td>
<td>7.9 (4.0 to 11.8)</td>
<td>74</td>
<td>61.6 (57.2 to 66.1)</td>
<td>8.4 (4.5 to 12.3)</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>81</td>
<td>134.0 (130.3 to 137.8)</td>
<td>-2.2 (-6.3 to 1.9)</td>
<td>74</td>
<td>135.9 (132.1 to 139.7)</td>
<td>-4.4 (-9.1 to 0.3)</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>81</td>
<td>84.5 (82.0 to 86.9)</td>
<td>-1.4 (-4.3 to 1.5)</td>
<td>74</td>
<td>85.23 (82.7 to 87.8)</td>
<td>-0.5 (-3.6 to 2.6)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>81</td>
<td>101.9 (97.9 to 105.9)</td>
<td>-0.1 (-2.5 to 2.3)</td>
<td>74</td>
<td>103.2 (98.9 to 107.5)</td>
<td>0.3 (-1.5 to 2.1)</td>
</tr>
</tbody>
</table>

FOSQ = Functional Outcomes of Sleep Questionnaire – measures disease-specific quality of life by assessing the impact of daytime sleepiness on activities of daily living, total score out of a possible 20 points with higher scores indicating higher levels of functioning.

SASQ = Sleep Apnea Symptoms Questionnaire – measures the frequency of 14 commonly reported OSA symptoms on a 10cm visual analogue scale, total score out of a possible 140 points, with higher scores indicating greater severity of OSA symptoms.

SF-36 = Short Form 36 Health Survey – measures the general health status of a patient using 8 subscales which each have a total score out of a possible 100 points, with higher scores indicating a higher level of functioning. Only 2 of the 8 SF-36 subscales (i.e. vitality and mental health) are reported here.

BP = blood pressure; BMI = body mass index; 95%CI = 95% confidence interval

*Based on analysis of covariance with adjustment for baseline measure and region.

†p<0.001 for paired t-test comparison of outcome measures examining change from baseline to 6 months.