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Diagnosis and Initial Management of Obstructive Sleep Apnea without Polysomnography

A Randomized Validation Study

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Background: Polysomnography (PSG), despite limited availability and high cost, is currently recommended for diagnosis of obstructive sleep apnea and titration of effective continuous positive airway pressure (CPAP).

Objective: To test the utility of a diagnostic algorithm in conjunction with ambulatory CPAP titration in initial management of obstructive sleep apnea.

Design: A randomized, controlled, open-label trial that compared standard PSG with ambulatory CPAP titration in high-risk patients identified by a diagnostic algorithm.

Setting: A tertiary referral sleep disorders program in Vancouver, British Columbia, Canada.

Patients: 68 patients with a high pretest probability of moderate to severe obstructive sleep apnea (apnea–hypopnea index [AHI] >15 episodes/h) identified by sequential application of the Epworth Sleepiness Scale (ESS) score, Sleep Apnea Clinical Score, and overnight oximetry.

Intervention: Patients were randomly assigned to PSG or ambulatory titration by using a combination of auto-CPAP and overnight oximetry. They were observed for 3 months.

Measurements: Apnea–hypopnea index on CPAP, ESS score, quality of life, and CPAP adherence.

Results: The PSG and ambulatory groups had similar median BMI (38 kg/m^2), age (55 years), ESS score (14 points), and respiratory disturbance index (31 episodes of respiratory disturbance/h). Each episode is determined by a computer algorithm based on analysis of oxygen saturation measured by pulse oximetry. After 3 months, there were no differences in the primary outcome, AHI on CPAP (median, 3.2 vs. 2.5; difference, 0.8/h [95% CI, −0.9 to 2.3]) (P = 0.31), between the PSG and ambulatory groups, or in the secondary outcomes, ESS score, Sleep Apnea Quality of Life Index, and CPAP. Adherence to CPAP therapy was better in the ambulatory group than in the PSG group (median, 5.4 vs. 6.0; difference, −1.12 h/night [CI, −2.0 to 0.2]) (P = 0.021).

Conclusions: In the initial management of patients with a high probability of obstructive sleep apnea, PSG confers no advantage over the ambulatory approach in terms of diagnosis and CPAP titration. The ambulatory approach may improve adherence to treatment. When access to PSG is inadequate, the ambulatory approach can be used to expedite management of patients most in need of treatment.

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Symptomatic obstructive sleep apnea is a common, underdiagnosed condition that occurs in 4% of men and in 2% of women (1). Patients with obstructive sleep apnea have considerable comorbid conditions, including excessive daytime sleepiness; concentration difficulties; and an increased risk for motor vehicle accidents, hypertension (2), coronary artery disease, and strokes. Obstructive sleep apnea may result in a systemic inflammatory state that predisposes the patient to cardiac and cerebrovascular conditions (3). Continuous positive airway pressure (CPAP) is an effective treatment that is commonly prescribed for symptomatic patients with obstructive sleep apnea: It is cost-effective (4) and reduces daytime sleepiness, rates of motor vehicle accidents, and blood pressure.

The American Thoracic Society (5) and the American Academy of Sleep Medicine (6) recommend supervised polysomnography (PSG) in the sleep laboratory over 2 nights for diagnosis of obstructive sleep apnea and initiation of CPAP. This approach to a highly prevalent condition results in inevitable discrepancies between the demand for services and the current capacity of sleep laboratories (7). Various strategies have been proposed to expedite diagnosis and treatment for obstructive sleep apnea (8). Predictive algorithms (9–15) and widespread use of overnight home monitoring, such as oximetry, have improved access to diagnostic testing (16–22). Several algorithms have been used to determine optimal CPAP (23, 24). Ambulatory use of autotitrating CPAP machines is effective in determining therapeutic CPAP (25) and as a treatment method.

To our knowledge, this is the first study to examine a combined ambulatory diagnostic and treatment algorithm without PSG in initial management of obstructive sleep apnea. To do so, we performed 2 parallel validation studies: 1) a cross-sectional study in patients screened by the

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Context

Overnight polysomnography in a sleep laboratory is normal practice for diagnosing obstructive sleep apnea (OSA) but it is expensive and can delay diagnosis.

Contribution

The authors combined standard clinical scales and overnight home oximetry to ensure a pretest probability of OSA of 90% or greater. Sixty-eight patients were randomly assigned to usual care (polysomnography obtained before continuous positive airway pressure [CPAP]) or ambulatory management (start CPAP without doing polysomnography). After 3 months, the 2 groups had the same results on overnight polysomnography.

Cautions

The study was done in a single tertiary care center.

Implications

Most patients with a probability of OSA of 90% or greater do not require polysomnography before starting CPAP.

—The Editors

diagnostic algorithm to test its use in identifying high-probability patients using PSG as the gold standard, and 2) a randomized trial of PSG versus ambulatory CPAP titration in high-probability patients identified by the diagnostic algorithm. Our study asked whether the conventional PSG approach was superior to the ambulatory approach in terms of controlling obstructive sleep apnea as measured by the apnea–hypopnea index (AHI) on CPAP after 3 months of treatment. We also wanted to determine whether there was any difference between the 2 management strategies in terms of sleepiness, quality of life, treatment adherence, and CPAP after 3 months of treatment.

METHODS

Study Design

We designed a randomized, controlled, open-label clinical trial to compare PSG with an ambulatory algorithm for titration of effective CPAP in patients with a high probability of moderate to severe obstructive sleep apnea.

Patient Selection

Participants were recruited from among adult patients referred from the catchment area of the Sleep Disorders Program at University of British Columbia Hospital, Vancouver, British Columbia, Canada, between May 2004 and November 2005, for assessment of suspected obstructive sleep apnea. Consecutive patients who, on the basis of a routine clinical evaluation by their sleep physician, were suspected of having moderate to severe obstructive sleep apnea, met the inclusion criteria, and were referred for possible participation in the trial, were considered for recruitment. Eligible patients had a high pretest probability of moderate to severe obstructive sleep apnea, were medically stable, and were not taking any sedative medications. We excluded patients who were pregnant or who had abnormal results on spirometry (predicted forced vital capacity or FEV_1 <70%); a known cause of daytime sleepiness; a major psychiatric disorder; a life-threatening comorbid illness, such as unstable coronary artery disease or chronic lung disease; a motor vehicle accident attributable to hypersomnolence in the preceding 5 years; previous treatment for obstructive sleep apnea; a contraindication to nasal CPAP therapy; or the inability to provide informed consent. Each eligible patient provided written informed consent, and our institutional ethics review committees approved the protocol. Patients were enrolled by the research coordinator who collected the baseline data.

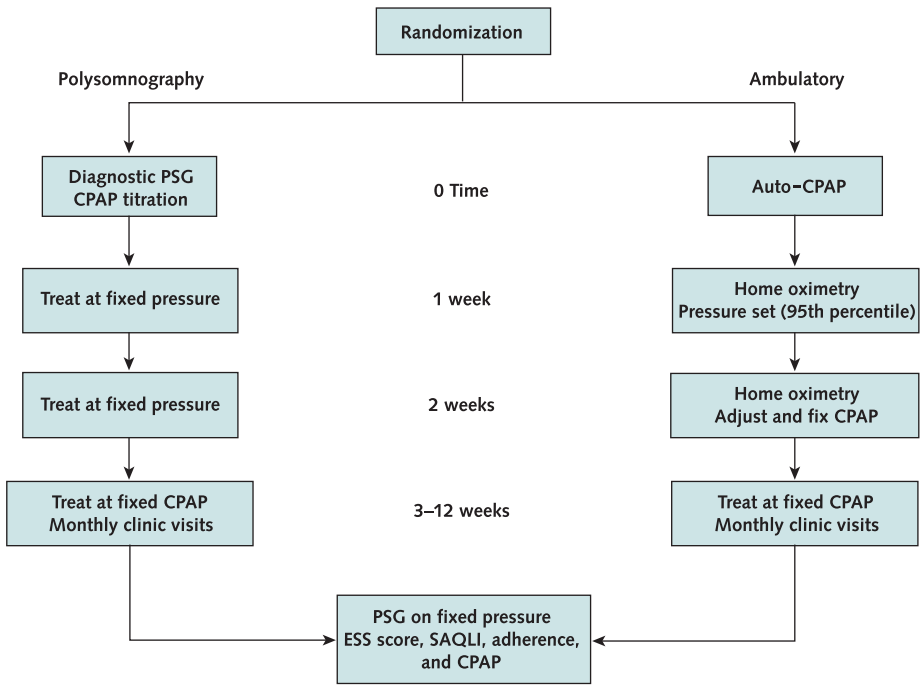
Determining Pretest Probability

High-probability patients were identified by sequential application of the Epworth Sleepiness Scale (ESS), Sleep Apnea Clinical Score (SACS) (11), and overnight oximetry in the home. The range of possible scores on the ESS is 0 to 24. In a retrospective case series of all patients ($n = 798$) referred to our sleep clinic with suspected obstructive sleep apnea who had a full diagnostic overnight PSG between 1 January 2001 and 31 December 2001 (26), the prevalence of moderate to severe obstructive sleep apnea (AHI >15/h) was 49% among patients with an ESS score of 10 or greater. The SACS is a screening tool based on snoring, witnessed episodes of apnea, neck circumference, and systemic hypertension that can be used to calculate likelihood ratios for the presence of obstructive sleep apnea (11). A score of 15 or greater gives a likelihood ratio of 4.45 of having moderate to severe sleep apnea (11). The Remmers Sleep Recorder (SagaTech Electronics Inc., Calgary, Alberta, Canada) is an easy-to-use, multichannel portable device that measures oxygen saturation, respiratory effort, airflow, snoring, and leg movements. This device calculates a respiratory disturbance index (RDI) on the basis of oxygen desaturation events. An RDI of 15/h or greater measured by the Remmers Sleep Recorder has a sensitivity of 98% and a specificity of 88% for diagnosis of moderate to severe obstructive sleep apnea, giving a likelihood ratio of 8.1 (18). Starting with pretest odds of approximately 1:1 on the basis of an ESS score of 10 or greater, we used Bayes theorem and assumed no interaction between components of the algorithm. The combined likelihood ratio conditional on a SACS of 15 or greater and an oximetry RDI of 15/h or greater yielded an estimated pretest probability of moderate to severe obstructive sleep apnea greater than 95%.

Protocol

Before randomization, all recruited patients completed the Sleep Apnea Quality of Life Index (SAQLI)—a comprehensive survey with a high degree of internal consistency, face validity, and construct validity designed to mea-

Figure 1. **Design of the clinical study.**



CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Scale; PSG = polysomnography; SAQLI = Sleep Apnea Quality of Life Index.

sure outcomes of clinical trials in sleep apnea (27, 28). All patients received a one-on-one orientation and education session from a dedicated CPAP coordinator who provided information in a standardized fashion regarding nasal CPAP therapy. This session included mask fitting and a trial of CPAP while the patient was awake to ensure that he or she could tolerate the device (**Appendix**, available at www.annals.org).

The CPAP coordinator randomly assigned patients to standard PSG or the ambulatory algorithm (**Figure 1**), using a stratified block randomization with a block size of 20. The stratification factors were an ESS score less than 15 versus an ESS score 15 or greater and oximetry RDI less than 30 episodes per hour versus RDI 30 episodes per hour or greater. Four large envelopes were prepared, 1 for each block. There were 20 folded cards in each envelope, 10 for the PSG group and 10 for the ambulatory group. Patients who consented to participate were assigned to a block according to their ESS and RDI scores. Each patient picked 1 card from the designated envelope; the CPAP coordinator noted the treatment allocation and destroyed the card. Blinding patients to their treatment allocation was not possible, but all patients were treated in an identical manner, including follow-up, aside from the interventions being studied. The ResMed AutoSet Spirit (ResMed Inc., Sydney, Australia) autotitrating CPAP machine was used in all patients. Together with the ResMed Autoscan software, this device is capable of storing and downloading data on compliance; mask leak; and CPAP, including the 95th percentile pressure (29)—the pressure at or below which the patient spent 95% of the time. Final CPAP was determined according to treatment group.

Polysomnography Group

A trained technologist supervised PSG. Obstructive sleep apnea was confirmed during a regularly scheduled overnight PSG in the sleep laboratory at our hospital. Final CPAP was determined according to a standard protocol during a CPAP titration PSG performed on the following night (**Appendix**, available at www.annals.org). There was no subsequent adjustment to the fixed CPAP in the PSG group.

Ambulatory Group

The AutoSet Spirit was set to autotitrate at pressures between 4 and 20 cm H_2O. After being used for 1 week, the ResMed Autoscan software was interrogated for efficacy data, including CPAP, mask leak, residual respiratory events, and use. The 95th percentile pressure was taken as the initial effective pressure if no residual sleep-disordered breathing was identified. The patient continued treatment at this pressure in fixed CPAP mode for another week. On days 6 and 13, overnight oximetry using a single-channel device (Ohmeda Biox 3400, Ohmeda, Milan, Italy) was performed. The following day, patients returned to the clinic where ResMed Autoscan interrogation was performed. If residual respiratory events or oxygen desatura-

tion was observed during either night, the initial 95th percentile pressure or the fixed CPAP was increased by 1 to 2 cm H_2O as tolerated. The final pressure was set on day 14 by the CPAP coordinator in consultation with the study physician; this was deemed to be the effective pressure and was not changed for the remainder of the study. The study physician was responsible for monitoring adverse events and ensuring patient safety (**Appendix**, available at www.annals.org).

Measurements

Baseline measurements on all patients included the SACS and RDI by using the Remmers Sleep Recorder. Baseline diagnostic PSG was performed only in the PSG group. At baseline and after 3 months of therapy, all patients completed the ESS (a decreasing score reflected less sleepiness) and were administered the SAQLI questionnaire (an increasing score reflected improved quality of life). After 3 months of treatment, the CPAP machines were interrogated for the patient's adherence and CPAP. All patients then had overnight PSG to measure the primary outcome: AHI while CPAP was used at the effective pressure. The primary outcome was, therefore, a measure of the efficacy of the chosen CPAP in eliminating sleep-disordered breathing. Secondary outcomes were ESS and SAQLI after 3 months of treatment, adherence to CPAP averaged over 3 months, and final CPAP.

Sample Size and Statistical Analyses

The primary outcome of interest was AHI on CPAP after 3 months of treatment. We calculated that a sample size of 30 patients in each group would be needed to detect a clinically important minimum between-group difference of 5/h or more in AHI on treatment (AHI <5/h was considered normal [30]), at the 0.05 level (2-sided) with 95% power, assuming a standard deviation for AHI of 5 on the basis of previously published data (24, 31–34). This sample size provided 85% power to detect a clinically important minimum difference of 1 in the SAQLI. All analyses were performed by using GraphPad Prism, version 4 (GraphPad Software Inc., San Diego, California) and Stata, version 9.2 (Stata Corporation, College Station, Texas). We expressed normally distributed baseline data as means (SD) and nonnormally distributed baseline data as medians (interquartile range). Most outcomes (AHI, ESS score, SAQLI, and CPAP adherence) had floor and ceiling effects, which resulted in moderately to severely skewed distributions. We used the Wilcoxon rank-sum test to compare the 2 treatment groups for these outcomes; point and interval estimates for the difference between medians were calculated using the Hodges–Lehmann method. We used the 2-sample *t*-test to compare CPAP, and point and interval estimates were calculated for the average difference between groups. The primary outcome was AHI on CPAP after 3 months of treatment. We used a complete case analysis for primary and secondary outcomes and performed additional sensitivity analyses using worst-case and best-case scenarios to address the impact of missing data. We used Fisher exact test to assess the performance of the diagnostic algorithm. We collected baseline data before randomization and analyzed outcome data with the treatment allocation concealed.

Role of Funding Sources

The funding sources played no role in the conception or design of the study, in analysis or interpretation of the data, in writing of this report, or in the decision to submit the manuscript for publication.

RESULTS

Figure 2 shows the details of study enrollment and outcomes. The baseline characteristics of patients who were not enrolled were similar to those who were randomly assigned (**Appendix Table 1**, available at www.annals.org). Baseline characteristics of the patients who were randomly assigned were comparable between the 2 groups (**Table 1**). In general, patients were middle-aged, predominantly male, moderately obese, and hypersomnolent and had moderate to severe obstructive sleep apnea.

Performance of the Diagnostic Algorithm

Of 79 patients screened by the diagnostic algorithm, 2 declined enrollment, 9 were ineligible because of an RDI less than 15/h, and 68 were eligible for randomization. Of these 68 patients, 35 were assigned to the PSG group (**Figure 2**). Of the patients who were screened, 41 had a baseline diagnostic PSG: 34 patients were part of the randomized trial and 7 ineligible patients as part of routine care. In these patients, the PSG served as the gold standard for assessment of performance of the diagnostic algorithm. Of the 36 patients with an ESS score of 10 or greater, SACS 15 or greater, and RDI 15/h or greater who had a baseline PSG, 34 had an AHI greater than 15 h/night. Thus, the probability of moderate to severe obstructive sleep apnea was 0.94 (95% CI, 0.81 to 0.99), conditional on an ESS score of 10 or greater, a SACS of 15 or greater, and an RDI of 15/h or greater.

Apnea–Hypopnea Index

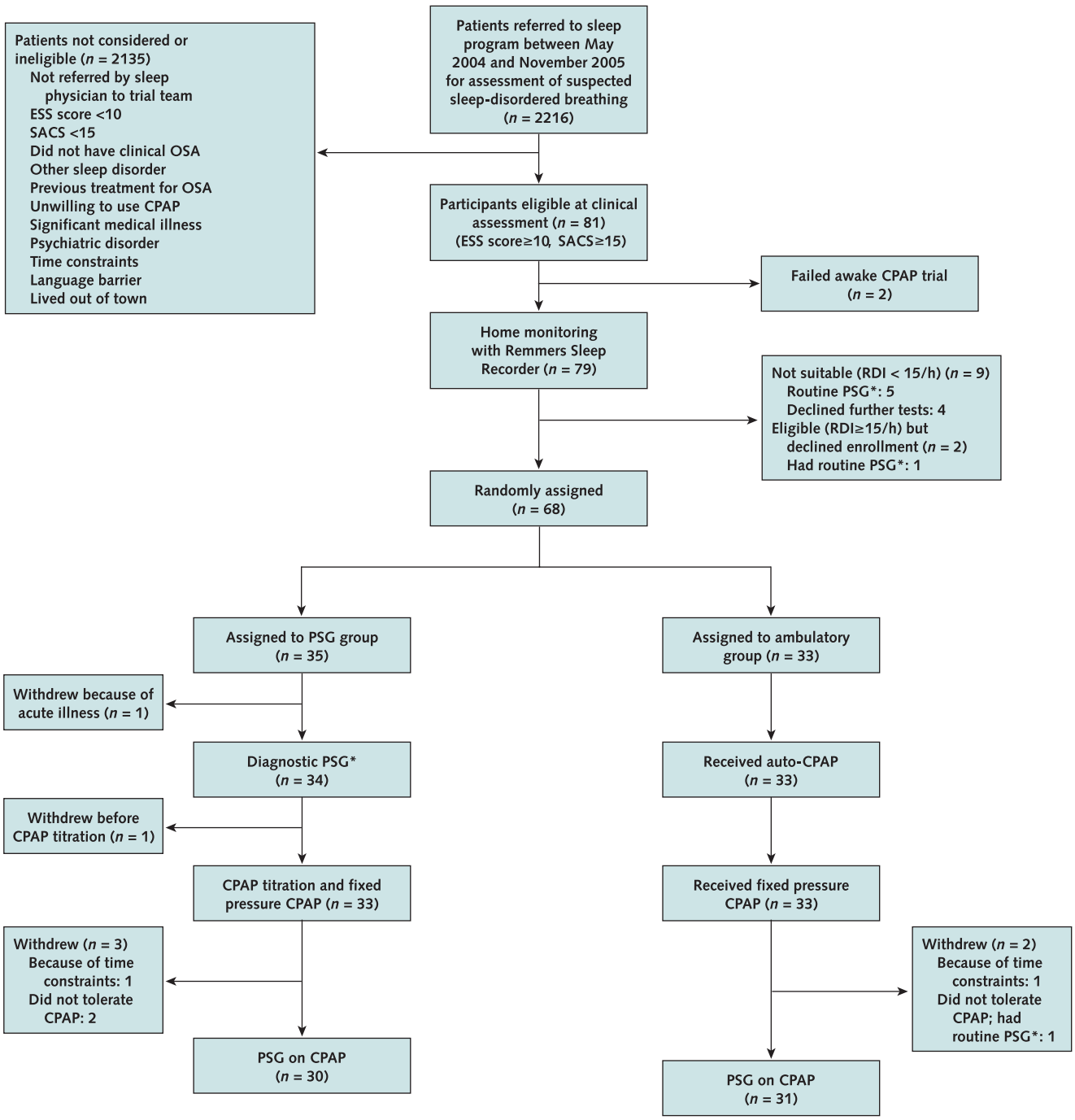
After 3 months of treatment, there was no difference in AHI on CPAP therapy between the groups (**Figure 3**). The median difference in AHI was 0.8/h (CI, −0.9 to 2.3) (**Table 2**). One patient in the PSG group who had mixed central and obstructive sleep apnea and an AHI of 90/h on baseline PSG had a residual AHI greater than 30/h but had a good clinical response to CPAP.

One patient in the ambulatory group with Cheyne-Stokes respiration and a baseline RDI of 43/h had a residual AHI of 27/h. He remained symptomatic and had poor adherence to CPAP therapy throughout the study.

Epworth Sleepiness Scale and Sleep Apnea Quality of Life Index

The changes from baseline did not differ between the groups for ESS score (1 [range, −1 to 4]) ($P = 0.26$) or SAQLI (0.17 [range, −0.6 to 0.9]) ($P = 0.69$) (**Table 2**).

Figure 2. **Study flow diagram.**



CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Scale; OSA = obstructive sleep apnea; PSG = polysomnography; RDI = respiratory disturbance index; SACS = Sleep Apnea Clinical Score. *Baseline PSG was used to assess the performance of the diagnostic algorithm.

After 3 months of treatment, there was no difference between groups in ESS score (0.0 [range, −2.0 to 2.0]) (P = 0.86) or SAQLI (−0.19 [range, −0.7 to 0.3]) (P = 0.41) (**Figure** 4). Scores on the ESS and SAQLI improved in all patients who completed the study, except for the person with Cheyne-Stokes respiration.

Adherence and Continuous Positive Airway Pressure

Overall compliance was good. Compliance was better in the ambulatory group (median, 6.0 [interquartile range, 5.1 to 7.1] h/night) than in the PSG group (median, 5.4 [interquartile range, 3.7 to 6.4] h/night): The difference between the PSG and ambulatory groups (−1.12 [CI,

Table 1. **Baseline Characteristics of the Patients Who Were Randomly Assigned***

Variable	Group	
	Polysomnography (n = 35)	Ambulatory (n = 33)
Mean age (SD), *y*	52 (11)	55 (10)
Men, %	75	79
Mean body mass index (SD), *kg/m²*	38 (8)	39 (9)
Median ESS score (interquartile range)	14 (11–19)	14 (12–16)
Median SACS (interquartile range)	30 (18–42)	32 (22–48)
Median RDI (interquartile range)	31 (21–47)	27 (17–57)
Median SAQLI (interquartile range)	2.8 (2.1–4.2)	3.5 (2.8–4.1)

* The Epworth Sleepiness Scale (ESS) has a range of 0 to 24, and the Sleep Apnea Quality of Life Index (SAQLI) has a maximum score of 7. RDI = respiratory disturbance index; SACS = Sleep Apnea Clinical Score.

−2.0 to − 0.2] h/night) was statistically significant (P = 0.021). There was no difference in the CPAP between the PSG and ambulatory groups (**Figure 4**).

Sensitivity Analyses

For AHI, we performed the sensitivity analysis for a worst-case scenario by assigning the observed 75th percentile value to the patients in the ambulatory group who withdrew and the observed 25th percentile value to the patients in the PSG group who withdrew, and vice versa for a best-case scenario. We performed similar analyses for adherence to therapy and CPAP. For the sensitivity analyses on ESS score and SAQLI at 3 months, we used the baseline value for a worst-case scenario. **Appendix Table 2** (available at www.annals.org) shows the analyses, which indicated no clinically significant change in our results after accounting for missing data.

Patient Satisfaction

All patients expressed overall satisfaction with their diagnosis and treatment at the end of the study. Given the opportunity, the majority (62%) of patients in the PSG group would have preferred home management, whereas only 6% of patients in the ambulatory group would have preferred sleep laboratory management.

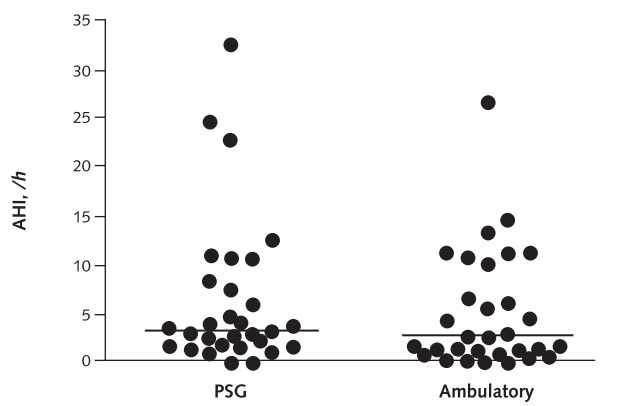
DISCUSSION

Our results show that a clinical strategy using exclusively ambulatory techniques can be substituted for PSG to establish the diagnosis and determine the effective CPAP in patients who are sleepy and have a high probability of obstructive sleep apnea. In determining effective CPAP, polysomnography was not superior to our ambulatory strategy, which combined a standardized clinical assessment to identify high-probability patients together with portable sleep monitoring and autotitration.

Previous studies have shown the use of diagnostic algorithms in obstructive sleep apnea (9–15). Several studies have demonstrated the ability of auto-CPAP to determine effective CPAP in patients in whom the diagnosis of obstructive sleep apnea has been confirmed by PSG (23, 25, 31, 35, 36). To our knowledge, this is the first study to examine a sequential strategy for diagnosis and treatment by using an entirely ambulatory clinical algorithm in which auto-CPAP was initiated without a polysomnographically confirmed diagnosis of obstructive sleep apnea. We felt that the small risk for misdiagnosis in the ambulatory approach would be offset by the potential benefits of expedited care. After 3 months of treatment, there were no differences in residual sleep-disordered breathing, sleepiness, quality of life, or CPAP between patients managed conventionally using PSG and those managed with an ambulatory strategy. Patients in the ambulatory group adhered more to CPAP therapy than did those in the PSG group. The American Academy of Sleep Medicine (6) and the American Thoracic Society (5) currently recommend supervised PSG in a sleep laboratory for diagnosis of obstructive sleep apnea and for CPAP titration, based on the premise that the early establishment of optimal CPAP improves adherence to treatment. Our results indicate that PSG offers no advantage in this regard for patients with a high probability of obstructive sleep apnea. The ambulatory strategy offers the potential for expedited care in settings in which access to PSG is inadequate. Our results lend support to the notion that expedited treatment may lead to better adherence.

Although the possibility of misdiagnosis is an obvious potential hazard, the diagnostic algorithm proved to be highly effective. The algorithm yielded a probability of 0.94 (CI, 0.81 to 0.99) for the diagnosis of moderate to severe obstructive sleep apnea (AHI >15/h). Only 1 patient in the ambulatory group was misdiagnosed as having

Figure 3. **Apnea–hypopnea index (*AHI*) on continuous positive airway pressure after 3 months of treatment in the polysomnography (*PSG*) (n =30) and ambulatory (n = 31) groups.**



The horizontal bars are the median values.

Table 2. **Comparison of Outcomes after 3 Months of Treatment with Continuous Positive Airway Pressure***

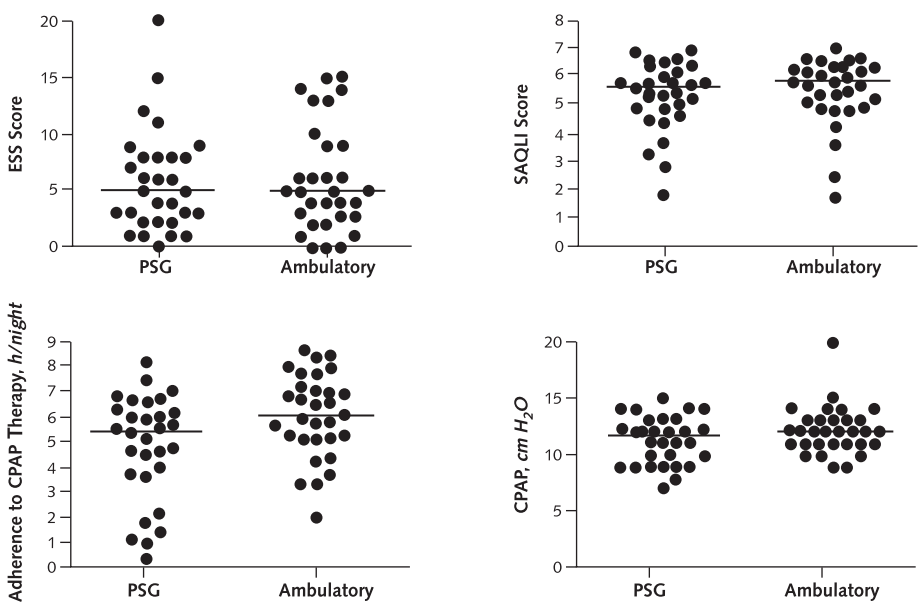
Variable	Outcome at 3 Months		Difference at 3 Months	
	Polysomnography Group (n = 30)	Ambulatory Group (n = 31)	Difference between Polysomnography Group and Ambulatory Group (95% CI)	*P* Value
Median AHI (interquartile range), episodes/*h*	3.2 (1.7 to 8.4)	2.5 (0.9 to 10.1)	0.8 (−0.9 to 2.3)†	0.31‡
Median ESS score (interquartile range)	5.0 (2.0 to 8.0)	5.0 (3.0 to 9.0)	0.0 (−2.0 to 2.0)†	0.86‡
Decrease of ESS score from baseline	10.0 (6.0 to 12.0)	8.0 (4 .0 to 12.0)	1.0 (−1 to 4)†	0.26‡
Median SAQLI (interquartile range)	5.5 (4.8 to 6.2)	5.8 (4.9 to 6.3)	−0.19 (−0.7 to 0.3)†	0.41‡
Increase of SAQLI from baseline	2.2 (1.2 to 3.4)	1.9 (1.1 to 3.0)	0.17 (−0.6 to 0.9)†	0.69‡
Median CPAP adherence (interquartile range), *h/night*	5.4 (3.7 to 6.4)	6.0 (5.1 to 7.1)	−1.12 (−2.0 to −0.2)†	0.021‡
Mean CPAP (SD), *cm* H_2O	11.2 (2.1)	12.1 (2.1)	−0.9 (−2.0 to 0.1)§	0.082‖

* Based on a complete case analysis with additional sensitivity analyses including worst-case and best-case scenarios to account for the impact of missing data. The Epworth Sleepiness Scale (ESS) has a range of 0 to 24, and the Sleep Apnea Quality of Life Index (SAQLI) has a maximum score of 7. AHI = apnea–hypopnea index; CPAP = continuous positive airway pressure.
† Calculated by using the Hodges–Lehmann estimate for difference in medians.
‡ Rank-sum test.
§ Mean difference.
‖ 2-sample *t*-test.

obstructive sleep apnea when in fact he had Cheyne-Stokes respiration. This patient was identified within the first 2 weeks of treatment because he did not improve clinically. If we allow a lower prevalence of 25% for patients with an AHI greater than 15/h and an ESS score of 10 or greater and use the same cutoff values for SACS of 15 or greater and RDI of 15/h or greater, the estimated pretest probability would be greater than 0.90 (**Appendix Figure 1**, available at www.annals.org). If the prevalence is 50% but the cutoff values of SACS and RDI are reduced to 10, the estimated pretest probability would be greater than 0.85 (**Appendix Figure 2**, available at www.annals.org). Thus, even if less rigorous criteria are used, the algorithm would have a low likelihood of misdiagnosis. We believe, therefore, that patients with a very high probability of obstructive sleep apnea can be safely and effectively treated with CPAP after ambulatory titration. We recommend, however, that patients treated with the ambulatory approach be reassessed clinically after a 2-week trial of CPAP (**Figure 5**). Those who do not improve symptomatically should have definitive diagnostic testing.

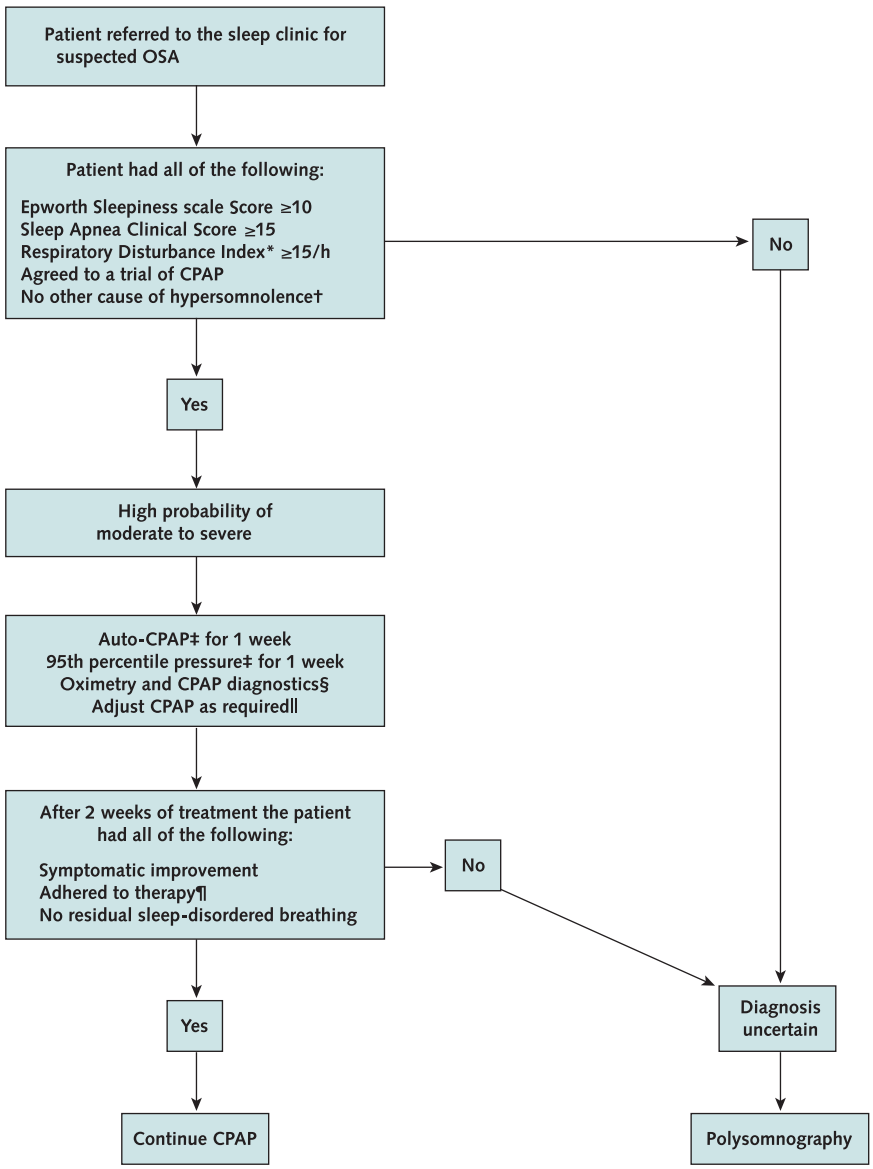
Adherence to treatment is a key issue for successful

Figure 4. **Secondary outcomes on continuous positive airway pressure (*CPAP*) after 3 months of treatment in the polysomnography (*PSG*) (n = 30) and ambulatory (n = 31) groups.**



The horizontal bars are the median values for Epworth Sleepiness Scale (*ESS*) score, Sleep Apnea Quality of Life Index (*SAQLI*), and adherence to CPAP therapy and the mean values for CPAP.

Figure 5. **Clinical algorithm for management of patients with a high probability of obstructive sleep apnea (*OSA*).**



CPAP = continuous positive airway pressure. * Based on offline analysis of oxygen desaturation recorded using the Remmers Sleep Recorder (formerly Snoresat, SagaTech Electronics, Inc., Calgary, Alberta, Canada). † Other causes of hypersomnolence, such as disorders of sleep fragmentation (for example, periodic limb movement disorder; psychiatric disorders; medications ([for example, sedative hypnotics]); endocrine disorders (for example, hypothyroidism); circadian rhythm disturbances; and sleep deprivation. ‡ Auto-CPAP initial pressure (range, 4-20 cm H_2O). ‡ 95th percentile pressure recorded by the appropriate software at or below which the patient spent 95% of the time while using auto-CPAP. § CPAP diagnostics downloaded from the CPAP machine and analyzed by using the appropriate proprietary software. ‖ Upward adjustment in CPAP in 1- to 2-cm H_2O increments to eliminate any residual sleep-disordered breathing on oximetry or CPAP diagnostics. ¶ Compliance of fewer than 3 hours per night suggests a diagnosis other than obstructive sleep apnea or predicts ultimate failure of CPAP therapy.

care of patients with obstructive sleep apnea. Initial experience with CPAP is important in predicting future compliance, and patterns of adherence are often established within the first week of therapy (34, 37). Krieger and colleagues (38) found that using a simplified diagnostic procedure with ambulatory monitoring was associated with lower adherence to CPAP and a higher withdrawal rate compared with standard PSG. In contrast, we found that the ambulatory group had better adherence to CPAP treatment, with a difference in adherence of more than 1 hour between groups, which is undoubtedly clinically significant. The reasons for the difference in adherence are not clear. Both groups were treated in an identical manner (apart from the interventions being studied) and were supported equally by study personnel. We speculate that the more expeditious commencement of effective CPAP therapy, and possibly the lower mean CPAP during the first week of treatment, may have contributed to better adher-

ence in the ambulatory group. We believe this issue warrants further study.

Our study has several limitations. First, it was a superiority trial and we cannot claim formal equivalence between the 2 strategies. Nonetheless, the 95% confidence bounds of the outcomes between groups indicate that the range of plausible differences includes a PSG advantage of 0.9/h in AHI and 2 cm H_20 in CPAP, values that we believe are not important clinically. In the case of ESS score and SAQLI, the confidence bounds for the change in value from baseline include a PSG advantage of 4 in ESS score and 0.9 in SAQLI, values that could be clinically important. However, the final values of ESS score and SAQLI after 3 months of treatment were not different between the groups (**Table 2**), which suggests that the upper confidence bound on the changed scores may be an artifact of the floor and ceiling effects associated with these measures (39). The PSG group had more patients with high ESS scores at baseline and lower SAQLI scores; thus, they had more room to improve. The difference in adherence to CPAP therapy between the groups was statistically significant and clearly favored the ambulatory approach. We are confident, therefore, that the ambulatory approach is safe and effective and can be recommended for patients with a high probability of obstructive sleep apnea. We conducted a complete case analysis, thereby excluding patients who did not have PSG after 3 months of treatment. To account for patients who withdrew, we conducted sensitivity analyses (**Appendix Table 2**, available at www.annals.org). The results for AHI were as follows: difference worst-case scenario 0.30/h (CI, −1.4 to 1.60) ($P = 0.602$) and best-case scenario 1.2/h (CI, −0.4 to 2.9) ($P = 0.147$), and for adherence to CPAP therapy, worst-case scenario − 0.97 h/night (CI, −1.88 to 0.01) ($P = 0.055$) and best-case scenario − 1.15 h/night (CI, −2.1 to − 0.15) ($P = 0.023$). These results confirmed that even in the worst-case scenario, the ambulatory approach was safe and could be recommended.

It was not possible to blind the patients to treatment allocation. Data collection and analysis, however, were conducted without knowledge of group allocation. Apart from the interventions being studied, patients in each group were handled in an identical fashion. Although we cannot be certain, it is unlikely that the lack of blinding introduced a systematic bias in patients' responses to the ESS and SAQLI questionnaires. The intensive follow-up of patients during the first 2 weeks of the study could have increased overall adherence to CPAP, and it is possible that the study interventions of overnight oximetry, CPAP downloads, and CPAP adjustments contributed to better adherence in the ambulatory group. If given the choice, almost two thirds of patients in the PSG group would have preferred ambulatory management, whereas only 6% of those in the ambulatory group would have preferred management on the basis of PSG. We do not know whether there is any relationship between these preferences expressed at the end of the study and adherence during the study.

The prevalence of moderate to severe obstructive sleep apnea may vary considerably among sleep clinics. Also, our assumption regarding independence of the components of the diagnostic algorithm is probably incorrect. We have addressed these limitations by providing estimates of pretest probability on the basis of a prevalence of 25% and lower scores for SACS and RDI. Given the variability in the characteristics of currently available oximeters and autotitrating CPAP equipment, it is possible that the use of alternative devices might have affected the performance of our diagnostic and treatment algorithms. Finally, the patients in the ambulatory group did not have a diagnostic PSG; therefore, we do not know their baseline AHI. Because the oximetry RDI was similar in both groups (**Table 1**) and because patients were randomly assigned, it is likely that the baseline AHI was comparable. Sleep specialists who were supported by a dedicated CPAP coordinator conducted the study at a tertiary care sleep disorders program. We focused exclusively on high-probability patients with substantial daytime sleepiness (ESS score of ≥10). In our experience, these patients are more motivated to seek therapy, improve to a greater degree with CPAP, and are more adherent to treatment. It remains to be determined whether the ambulatory strategy would be as effective in patients who are less sleepy or in those who have less severe obstructive sleep apnea.

On the basis of our results, we suggest a clinical algorithm for use in patients who have a high probability of obstructive sleep apnea, with the caveat that patients who do not fulfill the criteria for high probability in the diagnostic algorithm, or who do not respond appropriately to CPAP, should undergo PSG (**Figure 5**). In the context of scarce resources, the ambulatory approach provides an opportunity to expedite care for patients most in need of urgent treatment while conserving PSG slots. We believe this approach should be considered in sleep clinics with inadequate access to PSG.

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Appendix: Supplementary Information on Methodology, Baseline Characteristics, and Sensitivity Analyses

Role of the Continuous Positive Pressure Coordinator

The CPAP coordinator provided information regarding therapy to all patients in a standardized fashion. To ensure that patients understood and would be able to tolerate CPAP, a supervised CPAP trial with the patient awake was conducted before home oximetry. This trial was conducted in the coordinator's office and involved fitting patients with a suitable mask, which allowed them to experience a range of pressures for a 30-minute period. A second, more in-depth orientation took place at the time patients were randomly assigned into PSG or ambulatory groups. Once therapy began, the coordinator maintained regular telephone contact with all patients for the first 2 weeks. Patients also were scheduled for 2 office visits with the coordinator, at which time any problems with therapy or mask fit were addressed, and CPAP machines were interrogated and downloaded. At the end of the initial 2-week treatment period, the coordinator stopped actively contacting patients but remained available in case of ongoing problems.

Role of the Study Physician

The study physician had no involvement in the clinical care of study patients before entry into the trial. The study physician confirmed the eligibility of all patients entering the trial and participated in the process of informed consent. During the initial 2-week treatment period, the study physician reviewed material downloaded from CPAP machines and home oximetry results to determine fixed CPAP for patients in the ambulatory group. Any adverse events related to therapy were reported to the study physician and nasal corticosteroid spray was prescribed for upper airway side effects if necessary. After the initial 2-week period, patients were scheduled for 3 monthly clinic visits with their regular sleep physicians. Sleep physicians were provided with standardized forms to record any adverse events. The study physician reviewed these records to determine safety and suitability to continue in the trial. No patient was withdrawn from the trial because of safety concerns.

Determining Fixed Continuous Positive Airway Pressure

Polysomnography Group

Continuous positive airway pressure was determined during standard CPAP titration PSG as recommended by the American Academy of Sleep Medicine (6). Patients attended the University of British Columbia Hospital Sleep Laboratory and had PSG under the supervision of a trained technologist. Continuous positive airway pressure was initiated at 4 cm H_2O and increased by remote control in increments of 1-cm H_2O as tolerated. The effective pressure was defined as the lowest tolerated CPAP that eliminated all obstructed breathing events in all body positions and in all sleep stages. The CPAP machines were provided to patients on the morning after CPAP titration and were set to the effective pressure by the coordinator. Patients entered the initial 2-week period of intensive follow-up supervised by the CPAP coordinator and the study physician. The effective CPAP was maintained unchanged until the end of the study.

Ambulatory Group

The study physician determined CPAP after reviewing the data from CPAP machines and oximeters. Patients were initially placed on autotitrating CPAP. After 1 week, the pressure was fixed, usually at the 95th percentile of pressure delivered during the previous week. However, if CPAP machines or oximeters indicated residual sleep-disordered breathing while the patient was receiving CPAP, a pressure 1 cm H_2O higher than the 95th percentile was chosen. At the end of the second week, the recorded data were again reviewed and the fixed pressure was increased by 1 to 2 cm H_2O as tolerated if ongoing sleep-disordered breathing was noted.

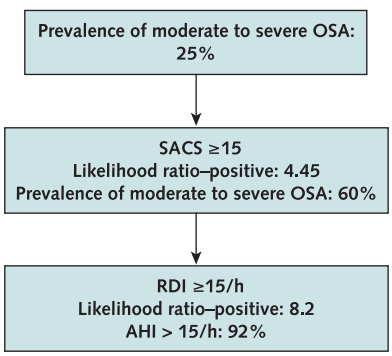
Although not as well standardized or validated as PSG CPAP titration, the ambulatory approach has the advantage that it incorporates information from several nights of sleep in the home environment, thus avoiding problems of night-to-night variability that may be encountered with single-night studies.

Appendix Table 1. **Baseline Characteristics of Patients Who Were Randomly Assigned Compared with Those Who Were Not Enrolled***

Variable	Patients Who Were Randomly Assigned (n = 68)	Patients Who Were Not Enrolled (n = 13)	*P* Value
Median age (range), *y*†	55 (46–59)	52 (40–57)	0.36
Median BMI (range), kg/m^2†	38 (33–43)	39 (31–41)	0.30
Median ESS score (range)	14 (12–17)	14 (13–16)	0.81
Median SACS (range)‡	31 (20–46)	30 (17–46)	0.46

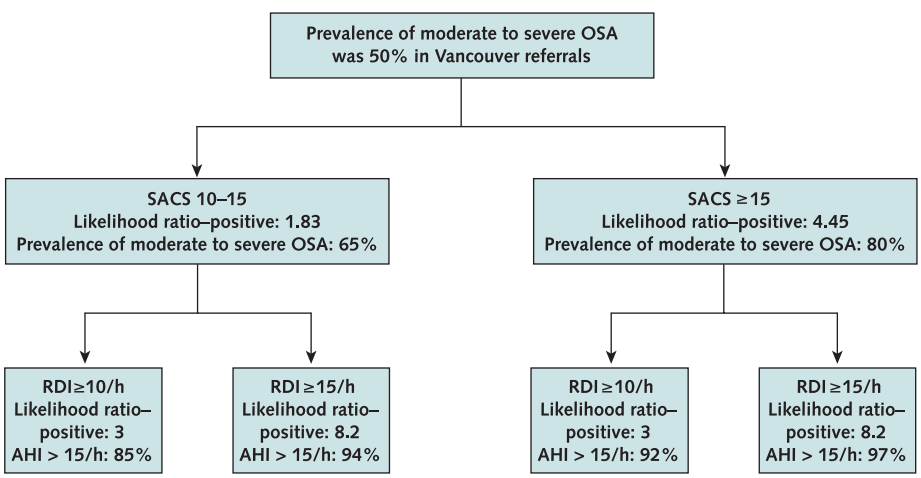
* Values are presented as median (25th–75th percentile). The Epworth Sleepiness Scale (ESS) has a range of 0 to 24. BMI = body mass index; SACS = Sleep Apnea Clinical Score.
† Normally distributed variables were analyzed by the *t*-test.
‡ Nonparametrically distributed variables were analyzed by the Mann–Whitney test.

Appendix Figure 1. **Pretest probability estimate for an obstructive sleep apnea (*OSA*) prevalence of 25%.**



AHI = apnea–hypopnea index; RDI = respiratory disturbance index; SACS = Sleep Apnea Clinical Score.

Appendix Figure 2. **Pretest probability estimates for different values of Sleep Apnea Clinical Score (*SACS*) and Respiratory Disturbance Index (*RDI*).**



AHI = apnea–hypopnea index; OSA = obstructive sleep apnea.

Appendix Table 2. **Sensitivity Analyses of Outcomes at 3 Months to Account for Missing Data***

Variable	Difference between Polysomnography and Ambulatory Groups at 3 Months			
	Worst-Case Scenario (95% CI)	*P* Value	Best-Case Scenario (95% CI)	*P* Value
Median AHI, */h*	0.30 (−1.4 to 1.6)	0.602	1.2 (−0.4 to 2.9)	0.147
Median ESS score	0 (−2 to 3)	0.854		
Median SAQLI	−0.28 (−0.83 to 0.25)	0.302		
Median CPAP adherence, *h/night*	−0.97 (−1.88 to 0.01)	0.055	−1.15 (−2.1 to −0.15)	0.023
Mean CPAP (SD), *cm H_20*	−1.12 (−2.1 to −0.15)	0.025	−0.77 (−1.75 to 0.22)	0.124

* The Epworth Sleepiness Scale (ESS) has a range of 0 to 24, and the Sleep Apnea Quality of Life Index (SAQLI) has a maximum score of 7. AHI = apnea–hypopnea index; CPAP = continuous positive airway pressure.