Primary Care Physicians Can Comprehensively Manage Patients with Sleep Apnea

A Noninferiority Randomized Controlled Trial

M. Ángeles Sánchez-Quiroga^{1,2}, Jaime Corral^{2,3}, Francisco J. Gómez-de-Terreros^{2,3}, Carmen Carmona-Bernal⁴, M. Isabel Asensio-Cruz⁴, Marta Cabello⁵, M. Ángeles Martínez-Martínez⁵, Carlos J. Egea⁶, Estrella Ordax⁷, Ferran Barbe^{2,8}, Javier Barca⁹, and Juan F. Masa^{2,3}; on behalf of the Spanish Sleep Network and Primary Care Group

¹Virgen del Puerto Hospital, Plasencia, Spain; ²Centro de Investigación en Red de Enfermedades Respiratorias, Instituto de Salud Carlos III, Madrid, Spain; ³San Pedro de Alcántara Hospital, Cáceres, Spain; ⁴Virgen del Rocío Hospital, Seville, Spain; ⁵Marqués de Valdecilla University Hospital, Santander, Spain; ⁶Organización Sanitaria Integrada, Bioaraba Research Institute, Araba University Hospital, Vitoria, Spain; ⁷Burgos University Hospital, Burgos, Spain; ⁸Arnau de Vilanova y Santa Maria Hospital, Lleida, Spain; and ⁹Extremadura University, Cáceres, Spain

Abstract

Rationale: General practitioners play a passive role in obstructive sleep apnea (OSA) management. Simplification of the diagnosis and use of a semiautomatic algorithm for treatment can facilitate the integration of general practitioners, which has cost advantages.

Objectives: To determine differences in effectiveness between primary health care area (PHA) and in-laboratory specialized management protocols during 6 months of follow-up.

Methods: A multicenter, noninferiority, randomized, controlled trial with two open parallel arms and a cost-effectiveness analysis was performed in six tertiary hospitals in Spain. Sequentially screened patients with an intermediate to high OSA probability were randomized to PHA or in-laboratory management. The PHA arm involved a portable monitor with automatic scoring and semiautomatic therapeutic decision-making. The in-laboratory arm included polysomnography and specialized therapeutic decision-making. Patients in both arms received continuous positive airway pressure treatment or sleep hygiene and dietary treatment alone. The primary outcome measure was the Epworth Sleepiness Scale.

Secondary outcomes were health-related quality of life, blood pressure, incidence of cardiovascular events, hospital resource utilization, continuous positive airway pressure adherence, and within-trial costs.

Measurements and Main Results: In total, 307 patients were randomized and 303 were included in the intention-to-treat analysis. Based on the Epworth Sleepiness Scale, the PHA protocol was noninferior to the in-laboratory protocol. Secondary outcome variables were similar between the protocols. The cost-effectiveness relationship favored the PHA arm, with a cost difference of €537.8 per patient.

Conclusions: PHA management may be an alternative to in-laboratory management for patients with an intermediate to high OSA probability. Given the clear economic advantage of outpatient management, this finding could change established clinical practice.

Clinical trial registered with www.clinicaltrials.gov (NCT 02141165).

Keywords: sleep apnea; portable monitor; cost-effectiveness; primary care

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A complete list of members of the Spanish Sleep Network and the Primary Care Group may be found before the beginning of the REFERENCES.

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Correspondence and requests for reprints should be addressed to Juan F. Masa, Ph.D., calle Rafael Alberti 12, 10005 Cáceres, Spain. E-mail: fmasa@separ.es.

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At a Glance Commentary

Scientific Knowledge on the

Subject: General practitioners (GP) manage less complex or less serious cases in common pathologies, such as bronchial asthma or hypertension. The lack of an easy diagnostic test for obstructive sleep apnea (OSA) and the necessity of a specialized training for treatment election process have led to a more passive role for GPs in OSA management. A previous study has shown similar effectiveness between a primary healthcare area and in-hospital management protocols, but the intensive training for GPs and nurses limits its generalization.

What This Study Adds to the

Field: The present study adds a simplification of the diagnosis and treatment election process by using a semi-automatic algorithm that markedly decreases the training necessity. Given that the primary healthcare area management had a similar effectiveness to in-hospital management, lower costs and a generalizable methodology can facilitate the integration of GPs in OSA management.

Obstructive sleep apnea (OSA) is a major health problem because of its high prevalence (1) and resultant cardiovascular problems (2, 3), role in traffic accidents (4, 5), and high health care costs (6). Other common pathologies, such as bronchial asthma or hypertension, are frequently treated by general practitioners (GPs), whereas specialist care is reserved for more complex or serious cases. The lack of an easy diagnostic test for OSA and a straightforward treatment selection process has led to a more passive role for GPs in OSA management. At present, GPs refer all patients with suspected OSA to a specialist.

The “gold standard” diagnostic test for OSA is polysomnography (PSG), but this test is expensive, time-consuming, and complex (7). Therapeutic decision-making (whether to prescribe continuous positive airway pressure [CPAP] or other treatments) is also a complex process (8) based on a wide range of variables and OSA severity. Therefore, OSA is usually managed by sleep specialists.

The type III portable monitoring (PM) device containing at least four channels is an abbreviated, accepted, and less expensive alternative for diagnosing OSA, although the test must be manually scored by an expert (9–12). Simpler PMs have been developed on the basis of a nasal pressure channel as a substitute for flow with and without oximetry. We previously published the results of a large study performed in the hospital setting that compared this home PM device, with automatic analysis, with PSG. The PM device yielded favorable diagnostic results and treatment selection for patients with an intermediate to high OSA probability (50% of patients with a low to high OSA suspicion) (13). A study including patients with similar levels of suspicion for OSA (14) did not find differences in effectiveness between a primary health care area (PHA) management protocol (diagnosis and treatment), using a simplified system (oximetry), and management by specialists using in-laboratory PSG. However, patients in the PHA arm were more frequently prescribed CPAP and more frequently discontinued this therapy. This outcome occurred despite moderately intensive training for GPs and nurses, which raised questions about the generalizability of the results.

On the basis of our previous study, we hypothesized that the use of a semiautomatic protocol integrating diagnosis and therapeutic decision-making based on a simple PM (automatic scoring) (13), which requires specific training for only some nurses in the PHA, could be as effective as in-laboratory care by specialists and offer improvements in cost and applicability.

We conducted a large, multicenter, noninferiority, randomized controlled trial with two open parallel arms that included a within-trial cost-effectiveness analysis in patients with an intermediate to high OSA probability. The goal was to compare the effectiveness of a PHA protocol based on a simple PM and an in-hospital specialized management protocol based on PSG. The follow-up period was 6 months. The primary outcome measure was the Epworth Sleepiness Scale (ESS).

Methods

Participants

From March 2014 to April 2016, we sequentially screened patients between

18 and 70 years of age who presented to 20 primary care centers corresponding to six tertiary hospitals in Spain for suspected OSA (*see the online supplement*). The inclusion criteria were chosen to select patients with intermediate to high OSA probability, being consistent with our previous study (13), and these were as follows: 1) snoring or sleep apnea observed by a partner, 2) an ESS score equal to or greater than 12 or previous cardiovascular disease (refractory hypertension, ischemic heart disease, or stroke), and 3) absence of clinical suspicion of any other sleep pathology that could cause daytime sleepiness. The exclusion criteria were as follows: 1) psychophysical inability to complete the questionnaires, 2) documented structural or coronary cardiac pathology that was not controlled by medical treatment, 3) Cheynes-Stokes syndrome, 4) patients who underwent uvulopalatopharyngoplasty, 5) severe nasal obstruction, 6) pregnancy, and 7) inability to provide informed consent. The ethics committees of the six centers approved the study (Comité Ético de Investigación Clínica). Written informed consent was obtained from all patients.

Intervention

Patients who fulfilled the inclusion criteria and none of the exclusion criteria were enrolled consecutively and randomized by GPs to the PHA or the in-laboratory arm, according to a simple randomization sequence generated by a database that remained hidden from the investigators until eligible patients were available. Patients randomized to the in-laboratory arm were referred to the sleep unit to follow the in-laboratory protocol. All randomized patients received instructions to maintain optimal sleep hygiene and to adhere to a hypocaloric diet if they were overweight or obese (*see the online supplement*). Patients randomized to the PHA or in-laboratory protocol were treated or not with CPAP based on PM or PSG test results and clinical symptoms (*see THERAPEUTIC DECISION-MAKING*). The patients treated with CPAP underwent titration at home with an auto-CPAP device (*see AUTO-CPAP TITRATION*).

PHA Arm

We used the same PM (ApneaLink Air; ResMed) in every primary health care center. This device determines airflow

through nasal pressure and includes oxygen saturation measurements. The automatic analysis included both flow channel and oximetry. We considered a study valid if either of the channels signaled for at least 3 hours (*see below*).

Each PHA had the equipment required for the PM and auto-CPAP. One nurse at each PHA received specific training for this purpose. *See the online supplement for more details.*

In-Laboratory Arm

We used standard protocols to perform in-laboratory PSG and to analyze the results (*see the online supplement*).

PSG and PM studies with less than three recorded hours were repeated on two other occasions, and the costs were included in the overall cost calculation. PSG was performed if the PM did not yield a valid recording, and the subsequent cost was added to the PHA arm (Figure E1 in the online supplement). For both devices (PM and PSG), apnea was defined as a reduction in flow greater than 90% for at least 10 seconds. For PSG, hypopnea was defined as a discernible reduction in flow ($>30\%$ and $<90\%$) or thoracoabdominal bands of at least 10 seconds accompanied by visible oxygen desaturation ($\geq 3\%$) or arousal (15). The analysis procedure used for the PM when both the flow and oximetry channels were analyzed together was the same but without the use of bands and the arousal criterion. If only the flow channel was analyzed because the oximetry channel failed, the procedure was the same as the procedure used for the flow channel without the desaturation criterion. If only oximetry was analyzed, apnea or hypopnea was defined as a decrease in oxygen saturation of at least 3%.

Therapeutic Decision-Making

In the PHA arm, the GP responsible for the patient made the therapeutic decision as defined in our previous study (13): 1) CPAP was recommended if the apnea-hypopnea index (AHI) was at least 20, and it was not recommended for patients with an AHI not exceeding 10, and 2) patients with an AHI between 10 and 20 were treated with CPAP when they had a body mass index (BMI) of at least 35 or were at least 55 years old. No other patients were treated with CPAP. When the nasal flow could not be analyzed but oximetry was reliable, the desaturation index was used as

an equivalent to the AHI as described above.

In the in-laboratory arm, a sleep physician in each center (always the same person) made therapeutic decisions based on a standardized set of variables, including clinical symptoms and the PSG results, using a standardized set of variables from a web-based database (*see the online supplement*). The treatment decision was guided by the Spanish Sleep Network guidelines (15). The sleep physician recommended CPAP treatment based on an AHI of at least 5 with significant clinical symptoms, prior cardiovascular disease that was potentially secondary to OSA, or an AHI of at least 30, in which case clinical symptoms were considered less important.

Auto-CPAP Titration

For the patients (both arms) who met the criteria for CPAP treatment, the optimal pressure for home use was determined from a single recorded automatic-CPAP home session (S9-AutoSet; ResMed) (*see the online supplement*) by a sleep physician blinded to the study arms in the coordinating center (centralized analysis). If the optimal pressure could not be determined after three attempts, the patients received polysomnographic titration at an additional cost.

Follow-up and Outcomes

Patients were evaluated on four occasions (*see the online supplement*) as follows: 1) at baseline, 2) after 1 and 3 months of follow-up, and 3) at the end of the follow-up period (6 mo). At baseline and after 6 months, we assessed the primary outcome (ESS) and several secondary outcomes, including blood pressure (*see the online supplement*) and health-related quality of life (HRQL) (EuroQol 5D thermometer and a visual analogical well-being scale [VAWS] with respect to the condition studied) (16, 17). Work- or traffic-related accidents, hospital admissions, length of admission, and emergency visits were evaluated 6 months before and after randomization. These data were obtained from patient interviews and the electronic medical record database. At the 6-month time point, new cardiovascular events, compliance, and side effects in the CPAP treatment groups and discontinuations were evaluated (*see definitions of discontinuation in the online supplement*). In the CPAP treatment groups, hourly

compliance according to the CPAP device, side effects, and discontinuations were recorded. In the groups that were not treated with CPAP, diet and sleep hygiene were recalled by the patients, and we insisted on compliance. Moreover, during the trial, patients in both arms received routine health care provided by the national health care system, including primary and specialized health care.

Sample-Size Calculation

On the basis of previous studies performed in patients treated with or without CPAP (13, 16), we calculated the sample size for an ESS change of 0 ± 5.7 between the arms, a noninferiority limit of -2 (14, 18), an α error of 0.025, and a power of 90%. The estimated sample size was 100 patients in each arm and 280 patients total after adjustment for a dropout rate of 30%.

Statistical Analysis

Missing values for the primary and secondary outcomes (dropouts included) were addressed using a multiple imputation method with iterative multivariable regression because the missing data had a missing-at-random pattern.

Primary outcome. The *a priori* noninferiority premise was -2 in the lower limit of the 95% confidence interval (CI) for the change in ESS between the arms. Considering that the intention-to-treat analysis could favor equivalence, we also performed a per-protocol analysis (patients who discontinued the study or who were missing ESS data were excluded from the analysis). We compared the change in ESS between the two arms using a two-sided analysis of covariance (ANCOVA) adjusted for the baseline value, center, age, sex, and BMI (hereafter called “basic adjustment”).

Secondary outcomes (inequality analysis). Intragroup changes in continuous variables from baseline to 6 months, or 6 months before and after randomization, and the observed effects in the two arms of the study (intergroup differences) were assessed using paired *t* tests. When the comparison was significant ($P < 0.05$), paired comparisons of the groups were performed by ANCOVA with basic adjustment. Categorical variables were compared between baseline and 6 months using the χ^2 test. These analyses were repeated in two subgroups of patients treated with and without CPAP.

Cost analysis. Only within-trial costs were analyzed. Figure E1 shows the cost

imputation procedure. The cost analysis was distributed into five cost groups.

Cost-effectiveness analysis. The cost difference between the arms was evaluated against the difference in effectiveness based on the primary outcome (ESS) and quality-adjusted life-years (QALYs) from the EuroQol questionnaire to determine the incremental cost-effectiveness ratio. We calculated the cost-effectiveness plane, in which the distribution of the incremental effectiveness and costs is displayed in an x - y plot. We also calculated the cost-effectiveness acceptability curve, in which the probability of preference for the PHA protocol is displayed as a function of the willingness to pay for one point on the ESS or a QALY,

using probabilistic Bayesian analysis (19). A sensitivity analysis was conducted according to percentiles of cost among centers.

Data management, imputation, statistical analyses, and Bayesian cost-effectiveness analyses were performed with EXCEL 2010 (Microsoft), SPSS software (version 22.0; IBM SPSS Statistics), and STATA 12 (StataCorp).

Results

Initially, 323 patients were selected. After 16 patients were excluded, 307 patients were randomized (159 to the PHA arm and 148

to the in-laboratory arm) (Figure 1). One patient in the PHA arm and four patients in the in-laboratory arm did not attend the corresponding sleep study and were excluded from the analysis. Similar numbers of patients in both arms had invalid PSG, PM, and autotitration tests after multiple repetitions (Figure E1), although PM was repeated more frequently than PSG (19.6% and 2.8%, respectively) (Table E2). Oximetry was the only valid parameter in 9% of the valid PM tests. The percentage of patients who met the indication for CPAP was similar between the two arms (68% in the PHA arm and 73% in the in-laboratory arm). Table 1 presents the

Figure 1. Flow chart of the study protocol. CPAP = continuous positive airway pressure; ITT = intention to treat; PHA = primary health care area.

Table 1. Anthropometric Characteristics, Alcohol and Smoking Habits, Comorbidities, and Sleep Studies

	ITT* (n = 303)	PHA (n = 158)	In-Laboratory (n = 145)	P Value	Imputed (%)
Sex, male, %	71.6%	71.5%	71.7%	0.97	0
Age, yr, median (IQR)	52 (15)	53 (14)	52 (15.5)	0.78	0
BMI, kg/m ² , median (IQR)	31 (7.6)	31.4 (8.4)	30.4 (7.4)	0.150	0
Neck circumference, cm, median (IQR)	41 (6)	42 (5.4)	41 (6)	0.43	2.6
Active drinker, %	16.2	17.7	14.5	0.45	0.3
Alcohol, g, median (IQR)	32 (25)	30 (23.5)	37.5 (26)	0.188	0
Active smoker, %	28.4	30.4	26.2	0.42	0
Pack-years, median (IQR)	19.8 (25.1)	20 (26.3)	19 (18.4)	0.37	0
Hypertension, %	43.9	45.6	42.1	0.54	0.3
Diabetes, %	11.9	13.3	10.3	0.43	0.7
Dyslipidemia, %	38.3	37.3	39.3	0.73	2.9
Ischemic heart disease, %	10.9	12.0	9.7	0.51	0
Arrhythmia, %	0.7	0.6	0.7	0.95	0
Stroke, %	0.7	0.6	0.7	0.79	0
Neoplasia, %	2.3	2.5	2.1	0.79	0.3
Depression, %	13.9	13.9	13.8	0.97	0
Anxiety, %	28.4	38.6	17.2	<0.001	0
Habitual unrefreshing sleep, %	66.0	72.8	58.6	0.009	0.3
Habitual snorer, %	95.4	96.2	94.5	0.48	0.7
Habitually observed apneas, %	59.7	69.6	49.0	<0.001	3.3
Recorded time, min, median (IQR)		426 (126)	420 (28)	0.57	1.3
Valid or total sleep time, min, median (IQR)		336 (156)	347 (77.4)	0.64	1.3
AHI, median (IQR)		22.3 (37.5)	29 (44.6)	0.036	1.6
DI, median (IQR)		25.8 (34)	15.3 (32.7)	0.41	2.3
SpO ₂ , median (IQR)		92 (4)	93 (4)	0.034	2.3

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; DI = desaturation index ($\geq 3\%$ oxygen saturation drop); IQR = interquartile range (difference between 1st and 3rd quartiles); ITT = intention to treat; PHA = primary health care area; SpO₂ = oxygen saturation.

*Randomization included in the intention-to-treat analysis.

population characteristics and sleep study parameters in each arm. In the PHA, subjects reported higher frequencies of anxiety, unrefreshing sleep, and observed apneic events.

Primary Outcome

In the per-protocol analysis, the intragroup ESS improvement between the PHA arm (-6.3 ; 95% CI, -7 to -5.5) and the in-laboratory arm (-6.4 ; 95% CI, -7.1 to -5.8) was not significantly different ($P = 0.737$). In both analyses, per protocol and

intention to treat, the lower limit of the 95% CI (-1.35 and -1.29 , respectively) was within our prespecified noninferiority margin (-2) (Table 2).

Secondary Outcomes

The changes in HRQL measures, blood pressure, and body mass indices were similar between the arms (Table 3). No significant differences were observed between the arms in hospital admissions, hospital days, emergency visits 6 months before and after randomization, and the cardiovascular

event incidence rate per 100 patient-years 6 months after randomization.

Compliance was similar between the arms, with a primary care mean of 4.3 (SE, 0.25) hours/day and an in-laboratory mean of 4.3 (SE, 0.23) hours/day (Figure 2).

The CPAP was similar between the arms (10.2 and 9.9 cm H₂O in the PHA and in-laboratory protocols, respectively). The secondary CPAP effects were similar between the arms with the exception of skin abrasions, which were more frequent in the PHA arm (Table E3).

Table 2. Noninferiority Analysis of the Primary Variable (Epworth Sleepiness Scale)

	ESS Mean (95% CI)		ESS Change Mean (95% CI)	Unadjusted Mean Difference (95% CI)	P Value	Adjusted Mean Difference (95% CI)	P Value
	Baseline	6 Months					
Per Protocol							
PHA (n = 146)	14.5 (14 to 15)	8.3 (7.6 to 9)	−6.3 (−7 to −5.5)	−0.18 (−1.22 to 0.86)	0.737	−0.41 (−1.35 to 0.54)	0.404
In-laboratory (n = 127)	14.5 (13.9 to 15)	8 (7.3 to 8.7)	−6.4 (−7.1 to −5.8)				
Intention to Treat							
PHA (n = 158)	14.5 (14.1 to 15)	8.3 (7.6 to 9)	−6.2 (−7 to −5.5)	−0.13 (−1.14 to 0.88)	0.798	−0.40 (−1.29 to 0.50)	0.389
In-laboratory (n = 145)	14.3 (13.9 to 14.8)	8 (7.3 to 8.7)	−6.4 (−7 to −5.7)				

Definition of abbreviations: CI = confidence interval; ESS = Epworth Sleepiness Scale; PHA = primary health care area.

Table 3. Baseline Measurements and Changes with Treatment with Respect to the Primary and Secondary Outcomes

	Baseline [Mean (SD)]		Intragroup Differences [Mean (SD)]		P Value of Intergroup Differences		Imputed (%)
	PHA	In-Laboratory	PHA	In-Laboratory	Unadjusted	Adjusted	
EuroQoL 5D	0.7 (0.2)	0.8 (0.2)	0 (0.2)	0 (0.2)	0.73	—	16.8
EuroQoL thermometer	61.6 (21.2)	63 (22.2)	4.8 (22.9)*	4.4 (23.8) [†]	0.90	—	16.8
VAWS	51.6 (20.8)	53.9 (22.6)	10.5 (24) [‡]	10.8 (26.8) [‡]	0.93	—	17.8
BMI, kg/m ²	32.2 (5.7)	31.2 (5.9)	−0.1 (1.5)	0.1 (1.4)	0.107	—	17.2
SBP, mm Hg	125.5 (16.4)	123.3 (15.6)	−1.8 (15.6)	−0.9 (16.7)	0.64	—	20.5
DBP, mm Hg	79.1 (11.8)	77.3 (11.6)	−1.8 (13.5)	−1.1 (14.8)	0.68	—	20.8
Cardiovascular event IR			12.3 (48.3)	4.7 (30.5)	0.127	—	0.0
Work/traffic accidents/patient [§]	0.06 (0.25)	0.09 (0.28)	−0.03 (0.33)	−0.06 (0.34)	0.41	—	0.0
Hospital admissions/patient [§]	0.12 (0.5)	0.08 (0.29)	−0.01 (0.94)	−0.02 (0.36)	0.92	—	0.0
Hospital days/patient [§]	0.27 (1.3)	0.53 (3.6)	−0.07 (1.7)	−0.36 (3.6)	0.37	—	0.0
Emergency visits/patient [§]	0.39 (0.83)	0.35 (1.1)	−0.09 (1)	−0.26 (1.1)	0.176	—	0.0

Definition of abbreviations: BMI = body mass index; DBP = diastolic blood pressure; IR = incidence rate (events per 100 patient-years); PHA = primary health care area; SBP = systolic blood pressure; VAWS = visual analogical well-being scale.

* $P = 0.010$; P values of intragroup differences (6 mo – baseline).

[†] $P = 0.026$; P values of intragroup differences (6 mo – baseline).

[‡] $P < 0.001$; P values of intragroup differences (6 mo – baseline).

[§] P values of intergroup differences unadjusted or adjusted by basic adjustment (baseline values of the variable analyzed, centers, age, sex, and BMI).

^{||} $P = 0.006$; P values of intragroup differences (6 mo – baseline).

Cost-Effectiveness Analysis

The cost per patient in the in-laboratory arm (€939.4) was more than double the cost in the PHA arm (€401.6) (Table E4), mainly due to the lower cost of the PM test (Figure E2). The average differences in effectiveness between the PHA and in-laboratory protocols were -0.13 as assessed by the ESS and -0.03 in the QALY analysis (Table E4). Because effectiveness (ESS and QALYs) was similar between the arms, the PHA protocol was

preferred because of its lower cost (Figures 3 and E3). The sensitivity analysis at the same level of effectiveness showed a minimum savings of €424.3 and a maximum savings of €620.9 (Table E5 and the additional results section in the online supplement). Figure 3 shows the sensitivity analysis based on a probabilistic Bayesian approach at the same level of effectiveness for the original mean cost and the 10th and 90th cost percentiles among centers.

Subgroup Analysis

Analysis of the primary and secondary variables in the PHA and in-laboratory arms for the subgroups of patients who received or did not receive CPAP treatment did not reveal any significant differences (Table E6).

Discussion

To the best of our knowledge, this study is the first to compare the long-term cost-effectiveness of semiautomatic PHA and in-laboratory management protocols in a large population of patients with an intermediate to high suspicion of OSA, some of whom were treated with CPAP. The principal findings are as follows: 1) the effectiveness of the PHA protocol as assessed by ESS was not inferior to the in-laboratory protocol; 2) HRQL, blood pressure, incidence of cardiovascular events, hospital resource utilization, and CPAP adherence were similar between the protocols; and 3) the cost-effectiveness relationship favored the PHA protocol.

In a previous randomized controlled trial of 787 patients with a suspicion of OSA ranging from low to high (13), we explored the usefulness of AHI cutoff points using a PM device (flow by nasal pressure; ApneaLink) for recommending CPAP treatment based on accordance with therapeutic decisions determined by sleep specialists

Figure 2. Differences between the arms in continuous positive airway pressure adherence at various periods of the study follow-up. The boxes represent tertiles, the transverse lines show medians, and central points show means. The lines outside the boxes indicate the maximum and minimum values. PHA = primary health care area.

Figure 3. (A) Cost-effectiveness plane. The probabilistic Bayesian analysis indicated that primary health care area management was preferable. Although in-laboratory management is slightly more effective, this approach is much more expensive. (B) Cost-effectiveness plane according to the original mean values and incremental cost percentiles (P10 and P90) based on a sensitivity analysis using a probabilistic Bayesian approach. ESS = Epworth Sleepiness Scale; P10 and P90 = 10th and 90th cost percentiles, respectively.

using in-laboratory PSG. Automatic PM scoring correlated well with the specialists' recommendations regarding CPAP only in the subgroup of more symptomatic patients based on selection criteria similar to the inclusion criteria applied in this study, which accounted for the 50% of all patients included with low to high OSA suspicion. CPAP was recommended when the PM AHI was at least 20, and it was not recommended

when the PM AHI was less than or equal to 10. Subjects with an AHI between 10 and 20 could not be classified. The previous study was conducted in a hospital environment. In this study, we wanted to validate this approach in PHAs using a new version of ApneaLink (nasal pressure and oximetry) and use an algorithm that could be applied in the unclassified group for decisions regarding CPAP.

Another study of 155 patients with a similar design (14) reported similar outcomes, although CPAP was recommended more frequently in the PHA group (90% in the PHA setting and 70% in the in-laboratory setting). CPAP was also more frequently discontinued in the PHA group (37% in the PHA group and 9% in the in-laboratory group). These differences occurred despite 6 hours of training for GPs and nurses and five additional days of training for nurses at the sleep center. Our semiautomatic approach does not require additional training for GPs; therefore, the results are less expensive, less complex, and more generalizable. In addition, our study included nearly twice as many patients, used a multicenter approach, added a noninferiority "per-protocol" analysis rather than an "intention-to-treat" analysis (which may favor equivalence between arms), included only sleep hygiene and dietary measures as CPAP alternatives to avoid "contamination" with other treatments (i.e., advanced mandibular devices), and incorporated a cost-effectiveness analysis including training costs to ensure that the results were more robust and applicable.

Both the previous study and our current study included patients with an intermediate to high clinical suspicion of OSA. However, because the criteria used to define this group were not uniform, the patient selection criteria differed between the studies. Nonetheless, the ESS, age, BMI, desaturation index, and percentage of patients who were prescribed CPAP by a specialist were similar (73% for this study and 70% for the previous study). Therefore, we inferred that OSA severity was similar in both studies.

Other studies performed in the PHA setting were designed to validate simplified diagnostic approaches without subsequent treatment follow-up (20, 21), or to validate CPAP treatment recommendations without incorporating diagnosis in the PHA (22). Two studies validated different clinical questionnaires using in-laboratory PSG versus the two ApneaLink channels (nasal flow and oximetry) with simultaneous in-laboratory PSG (20) or oximetry at home (21); both studies reported favorable results for the simplified regimens. Another randomized study (22) reported similar CPAP adherence after 6 months of follow-up in PHAs, including patients who were previously diagnosed in a hospital setting. This study confirms that comprehensive PHA management is noninferior to specialist

management in the hospital and has substantial cost benefits. Moreover, although other studies have compared the short-term (23) and medium-term (24) effectiveness of simpler portable monitoring devices (type IV) in ambulatory settings with in-laboratory PSG, these studies did not examine the implications for PHAs. The results were favorable for simplified management regimens.

We used nasal flow or oximetry to determine the AHI and prevent invalid PM tests and unnecessary test repetitions. Both nasal flow and oximetry from ApneaLink have been used for diagnosis (20, 25) and therapeutic decision-making (13) in patients with an intermediate to high suspicion of OSA. Some studies (26, 27) have even shown no advantage in performing the flow and oximetry analyses separately compared with only one analysis. However, performing both analyses does have some advantages. We were able to prevent the need for repeated tests in 9% of our valid PM recordings.

The AHI and the mean oxygen saturation during sleep were lower in the PHA group than in the in-laboratory group. This could be explained by the absence of hypopnea and desaturation associated with arousal and the inclusion of some awakening events as register times in the PM automatic analysis.

Although our trial protocol did not include specific treatments for other diseases that can lead to sleep problems (i.e., anxiety and depression) to avoid “contamination” between interventions, patients in both arms received standard, routine care provided by the public health system, including primary and specialized care, which may have resulted in medical treatment modifications. However, significant differences in effectiveness were not found between the arms overall or in the treatment subgroups (with and without CPAP treatment). Nevertheless, this result came from the overall study population, and we cannot exclude the possibility that some patients in both arms could have experienced additional benefits if our management had been more integrated and

specialized (see ADDITIONAL DISCUSSION in the online supplement).

Our study had the following limitations: 1) the researchers were not blinded because the diagnostic and therapeutic decisions were based on the PM or PSG results. Because the GPs were aware of the randomization of all included patients, the GPs may have provided some medical care to the patients randomized to the in-laboratory arm during the follow-up, which could have affected sleep problems. In addition, the patients were not blinded, although the application of the different diagnostic tests did not appear to have a significant impact on the patients; 2) management in a PHA or in a hospital by a specialist could affect patient confidence, but we did not detect differences in the analyzed outcome measures; and 3) the methodology included some variable decision nodes in decision-making for the in-laboratory arm and the use of autotitration to determine the visual CPAP level. Interobserver variability in therapeutic decisions was partially minimized by using the Spanish Sleep Network guidelines and a centralized assessment for the visual CPAP level.

In summary, the PHA management protocol was not inferior to the in-laboratory protocol and was substantially less expensive. Therefore, PHA management may be a less expensive alternative to in-laboratory management for patients with intermediate to high OSA suspicion, which represents approximately one-half of patients needing a sleep study for OSA suspicion. This finding may change established clinical practice based on the availability and applicability of an easy and generalizable diagnostic and treatment selection process and the clear economic advantage. Our results could also facilitate the integration of general practitioners in OSA management. ■

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Members of the Spanish Sleep Network and the Primary Care Group

Spanish Sleep Network: Galo Fernández-Zapata, M.D. (San Pedro de Alcántara Hospital, Cáceres, Spain), Ángeles Sánchez-Armengol, Ph.D. (Virgen del Rocío Hospital, Seville, Spain), Candela Caballero-Eraso, M.D. (Virgen del Rocío Hospital, Seville, Spain), Olga Cantalejo, M.D. (Marqués de Valdecilla University Hospital Santander, Spain), Roberto Ocon, M.D. (Marqués de Valdecilla University Hospital, Santander, Spain), Ainhoa Álvarez-Ruiz de Larrinaga, M.D. (Bioaraba Research Institute, Organización Sanitaria Integrada, Araba University Hospital, Vitoria, Spain), Mikel Azpiazu, M.D. (Bioaraba Research Institute, Organización Sanitaria Integrada, Araba University Hospital, Vitoria, Spain), and M. Luz Alonso-Alvarez, Ph.D. (Burgos University Hospital, Burgos, Spain; and CIBER of Respiratory Diseases [CIBERES], ISCIII, Madrid, Spain).

Primary Care Group: Luis Tobajas, M.D. (San Jorge Primary Care Center, Cáceres, Spain), Manuela Rubio, M.D. (Madroñera Primary Care Center, Madroñera, Cáceres, Spain), Amparo Gómez-Espárrago, M.D. (Zorita Primary Care Center, Zorita, Spain), Rafael Lebrero-Ferreiro, M.D. (Camas Clinical Management Unit, Camas, Seville, Spain), Teresa Hermosin-Bono, M.D. (Camas Clinical Management Unit, Camas, Seville, Spain), Julia Juan-Armas, M.D. (Camargo Costa Primary Care Center, Camargo, Santander, Spain), Pedro Crespo-Fidalgo, M.D. (Los Castros Primary Care Center, Santander, Spain), M. Hermosa De-la-Llama, M.D. (Camargo Interior Primary Care Center, Camargo, Spain), and M. Elena Vega-Dominguez, M.D. (Lakubizcarra Primary Care Center, Vitoria, Spain).

Collaborator Contributions

Substantial contribution to study conception and design, acquisition of data: Ángeles Sánchez-Armengol, Ph.D., M. Luz Alonso-Martínez, Ph.D., Ainhoa Álvarez-Ruiz de Larrinaga, M.D., Galo Fernández-Zapata, M.D., Candela Caballero-Eraso, M.D., Olga Cantalejo, M.D., Roberto Ocon, M.D., Mikel Azpiazu, M.D., Luis Tobajas, M.D., Manuela Rubio, M.D., Amparo Gómez-Espárrago, M.D., Rafael Lebrero-Ferreiro, M.D., Teresa Hermosin-Bono, M.D., Julia Juan-Armas, M.D., Pedro Crespo-Fidalgo, M.D., M. Hermosa De-la-Llama, M.D., and M. Elena Vega-Dominguez, M.D.

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