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Does CPAP Use in the First 15 Days Predict its Use after 4 Months? A Prospective French Cohort Study

Thibaut Gentina[1], Elodie Gentina[2,*], Catherine Lamblin[1], François Jouniaux[1], François Codron[1] and Aiman Tulaimat[3]

[1]*Hôpital Privé La Louvière, Générale de Santé, Lille, France*
[2]*Skema Business School – Université de Lille, MERCUR Research, France*
[3]*Cook County Health and Hospital Systems, Division of Pulmonary, Critial Care, and Sleep Medicine, USA*

Abstract

Objective: Early prediction of which patients with obstructive sleep apnea will not adhere with CPAP can trigger physicians to correct possible causes or offer alternative therapies. This study aims to determine the ability of early CPAP use to predict long-term adherence with CPAP independent from its definition and to test previously described predictors of adherence.

Method: This is a prospective, observational cohort study that was performed in nine sleep disorder centers in France. Patients were newly diagnosed with obstructive sleep apnea and a CPAP was prescribed for the first time. We collected socioeconomic, medical, sleep, and psychological variables to be associated with adherence with CPAP. The patients were evaluated 15 days after CPAP set up and monthly for 4 months until they were adherent. We assessed potential predictors of CPAP adherence at 4 months with emphasis on CPAP use at 15 days. CPAP adherence was defined as an average daily use of at least 3, 4, 5, and 6 hours.

Results: We enrolled 420 patients. Early CPAP use and CPAP use at 4 months were similar. At 4 months, 94% of patients used a CPAP ≥3 hours and 49% of patients used it ≥6 hours. The area under the ROC curve for early CPAP use predicting adherence at 4 months was ≥0.85 for all adherence definitions. The optimal threshold for early CPAP use to predict adherence increased from 3.2 to 6.4 hours as the definition of CPAP adherence increased from 3 to 6 hours. CPAP use at 4 months was higher in older patients.

Conclusions: Early CPAP use was the single best predictor of CPAP adherence and was independent of how adherence was defined. Physicians must assess CPAP use no later than 2 weeks to address its causes or prescribe an alternative therapy.

Keywords: Obstructive sleep apnea (OSA); Continuous positive airway pressure (CPAP); Adherence; predictors

Introduction

Treatment of obstructive sleep apnea (OSA) with continuous positive airway pressure (CPAP) improves sleep quality, reduces sleepiness, enhances quality of life and reduces cardiovascular morbidities [1-3]. As in most medical conditions, the benefits of therapy are reaped only by adherent patients. Unfortunately, and as in other conditions, adherence to the use of a CPAP is suboptimal. In one study which defined adherence arbitrarily as using a CPAP ≥3 hours on 70% of nights, found that 54% of patients were non-adherent [4]. Understanding the barriers to and predictors of CPAP treatment uptake and long-term adherence is therefore critical for successfully establishing and maintaining patients on effective CPAP treatment [5]. It allows physicians to apply interventions that improve adherence early because waiting until patients declare themselves after few months of treatment to be non-adherent might be too late. It also allows physicians to select the patients that need these interventions instead of applying these interventions to all patients at a much higher cost. Knowing which patients are unlikely to adhere to the use of CPAP also prompts physicians to discuss alternative treatments early [6,7].

Socio-economic factors, disease severity, health problems, psychological variables, social variables, testing methods, side effects, and behavioural traits have been associated with adherence to the use of a CPAP. This large number of variables suggests that adherence is a complex process (Appendix 1).

This complexity underscores some of the limitations of published reports. First, the reports focus on one variable or a limited number of variables to predict CPAP adherence. Second, the samples of many of these studies are small. This not only reduces the generalizability of the findings, but also reduces the number of variables that can be reliably tested. Lastly, the sometimes vaguely described follow-up process of the patients reduces the reproducibility of the findings.

Furthermore, the definitions of adherence are arbitrary. The most frequently used definition is 4 hours per night and it is based on the improvement in consequences of OSA in patients that use CPAP for at least 4 hours. There is, however, growing interest in setting CPAP targets based on a patient needs [8-10].

Therefore, we conducted this study to validate a large number of variables as predictors of the adherence to CPAP use in a large sample of patients that were followed meticulously for 4 months. We focused on early use of CPAP and we defined adherence at 4 months in various ways.

***Corresponding author:** Elodie Gentina, 2SKEMA Business School – Université de Lille, MERCUR Research, France, Tel: 00 33(0)6 78 64 47 68; E-mail: elodie.gentina@skema.edu

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Materials and Methods

Study design

This prospective cohort study was performed in nine medical centers in the north of France. The protocol was approved by the French Research Ethics Board of The Patient Protection Committee. All patients provided written informed consent before participation.

Study sample

Adult patients (18-75 years old) were recruited from nine centers in France. Each center utilized the same method to recruit and follow their patients in order to avoid any differences between centers (Table 1).

All consecutive patients for whom CPAP had been prescribed for the first time for the treatment of OSA between March 2013 and June 2013 were eligible for the present study. We excluded patients that were cognitively deficient and unable to fill in the questionnaires, patients unable (or refused) to give their informed consent, patients unable to read and/or speak French, and patients with neuromuscular diseases.

Diagnosis of obstructive sleep apnea

The diagnosis was based on a full in-laboratory polysomnogram (PSG) or home sleep test (HST). The PSG was performed with the Alice 5 (Philips, Eindhoven, Netherlands) that included 6 EEG channels, 2 EOG channels, chin EMG, bilateral anterior tibialis EMG, nasal/oral thermister, nasal pressure transducer, chest and abdominal wall movements, EKG, and pulse oximetry. The PSG scoring was standardized across centers. HST was performed with Embletta polygraph (Resmed, San Diego, CA) that included nasal/oral thermister, nasal pressure transducer, chest and abdominal wall movements, heart rate, and pulse oximetry.

Sleep was scored with the Rechtschaffen and Kales criteria. Apneas, hypopneas, and arousals were scored according to the American Academy of Sleep Medicine 2007. The apnea hypopnea index that was calculated by dividing the number of apneas and hypopnea by the total sleep time (recording time for HST) in hours.

Prescription of CPAP

CPAP was prescribed if a patient met 1 of 2 conditions: 1) the apnea-hypopnea index (AHI) ≥30 events per hour, or 2) the AHI index was between 15 and 30 events per hour with respiratory arousal >10 per hour and at least 2 symptoms of OSA symptoms (snoring, choking or gasping during sleep, unrefreshing sleep, daytime fatigue, impaired concentration, or nocturia).

CPAP initiation and monitoring

Patients were seen by sleep physicians in consultation and then referred for a sleep study [11-13]. Because knowledge is a pre-condition for health behavior or a change in health behavior, patient were subjected to a specific educational intervention [14]. Before starting CPAP, each patient was educated by a physician and a technician about the health risk of OSA and about the use of the CPAP machine. Patients also watched a 10-min video about the definition of OSA, symptoms of OSA, CPAP machine, the sensation of wearing CPAP, and benefits of using CPAP [15]. The delay between seeing the physician and the sleep study was 15 days and between the sleep study and starting CPAP was less than 48 hours.

The CPAP devices include counters that measure machine-on time using a microprocessor. Patient adherence data was obtained on day 15 and at the end of the first month. Patients with CPAP use ≥3 hours at the end of the first month were evaluated at the end of fourth months. Patients with CPAP use <3 hours at the end of the first month were visited monthly until they became adherent. During each visit, the average nightly use CPAP hours over the last month was recorded (Table 1).

Data collected

Independent variables: The socio-economic variables were age, gender, marital status (married or living as a couple versus living alone), employment status (fulltime, part-time, or unemployed), type of health insurance (government or government insurance with private health insurance). The health variables were infarction, or arrhythmia. The psychological variables were assessed with two scales: The Pichot scale16 and the Epworth Sleepiness Scale (ESS17). The Pichot scale is divided in 2 subscales: depression (13 items) and fatigue (8 items). The ESS measures the level of sleepiness (8 items). OSA related variables were method of diagnosing OSA (PSG or HST), the apnea-hypopnea index (AHI), average nightly use of CPAP in the first 15 days (early CPAP use).

Dependent variable: Adherence was monitored using the smart card technology embedded in the CPAP machines and was defined as the average nightly use of CPAP at the set pressure.

Statistical analysis

To determine the ability of early CPAP use in predicting adherence with CPAP at 4 months, we calculated the area under the receiver operator characteristic curve (AU-ROC) for 4 adherence definitions (3, 4, 5, 6 hours).We determined the optimal thresholds of early CPAP use to predict adherence based on the Youden Index and calculated the sensitivity (Sn) and specificity (Sp) for these thresholds. We also determined, at each definition of adherence, the thresholds of early CPAP use that had a sensitivity of 90% (Sn90) or a specificity of 90% (Sp90). Bias-corrected bootstrapping of 1000 iterations was used to determine these thresholds and their confidence intervals.

The French government reimburses patients for CPAP if they use it for more than 3 hours per night. Therefore, we used the 3-hour definition for the rest of the analysis, with patients using CPAP ≥ 3 hours per day considered as adherent, patients using CPAP <3 hours considered as non-adherent.

We compared between adherent and non-adherent patients all other variables available for the physician before initiating CPAP (pre-CPAP predictors). We used the t-test or chi-squared as indicated by the data type. Differences were significant if the p value is ≤0.05. We tested the significant pre-CPAP predictors with early CPAP use in a multiple regression analysis to determine the smallest number of independent predictors of adherence.

Results

Patients

We give the study questionnaire to 465 patients: 429 patients responded, 9 were lost during the follow-up, and 420 patients were included in the final analysis (useable response rate of 92%). Most patients were men, obese, and had severe sleep apnea. The majority of patients had private insurance in addition to government insurance (Table 2).

Adherence CPAP use: early CPAP use (5.6 ± 2.0 hours) and CPAP use at 4 months (5.7 ± 1.7 hours) were similar, p=0.09. The correlation

Visit	Patients	Where	Personnel	What was done	Education
CPAP set up	All patients	Clinic	Physician	Questionnaire	A 15-min video about the definition of OSA, symptoms of OSA, CPAP machine, the sensation of wearing CPAP, and benefits of using CPAP. Discussion and demonstration
Visit 15 days	All patients	Home	Technician	Early CPAP use	Individualized and face to face education and specific information about OSA, performance, treatment relevance, symptom change with CPAP, troubleshooting advice… A written document on CPAP was provided Demonstration of the Website "Elia Medical Education http://eliamedical-education.com/
First month	All patients	Clinic	Physician	CPAP use	Discussion, demonstration and support
Second month	Non-adherent first month	Home	Technician	CPAP use	Discussion, demonstration and support
Third month	Non-adherent second month	Home	Technician	CPAP use	Discussion, demonstration and support
Fourth month	All patients	Clinic	Physician	CPAP use	Discussion, demonstration and support

Table 1: Visit types during the 1-4 month study.

between early CPAP use and CPAP use at 4 months was high (r=0.71, p<0.001). The linear regression equation for CPAP was use at 4 months (hours)=2.2 + 0.6 × early use of CPAP (hours).

Early CPAP use was equally predictive of use of CPAP at 4 months no matter what the threshold was (Table 3 and Figure 1). The accuracy of early CPAP in predicting adherence changed with the type of insurance. The AU-ROC was higher when patients had only government insurance than when they had additional private insurance (4-hours: 0.95 ± 0.04 versus 0.86 ± 0.02, p=0.04; 5-hours: 0.92 ± 0.06 versus 0.85 ± 0.02, p=0.2; 6-hours: 0.96 ± 0.03 versus 0.83 ± 0.02, p=0.002). We did not evaluate the 3 hours adherence because the sample was two small. The accuracy of early CPAP use in predicting adherence at 4 months was not affected by ESS, age, gender, employment, or marital status.

As the threshold to define CPAP adherence increased from 3 hours to 4 hours, the optimal threshold of early CPAP use increased, then was stable for adherence defined as 4 or 5 hours, and then increased again for adherence define as 6 hours. The ranges of thresholds for Sn90 (3.3-4.6 hours) and for Sp90 (5.5-6.5 hours) were narrow.

When the definition of adherence changes, the distribution of adherence status (remained adherent, became non-adherent, remained non-adherent, became adherent) at 4 months changes. When we used the same threshold to define adherence at 15 days and at 4 months, increasing the threshold for adherence from 3 to 6 hours increased the percentage of patients that remain non-adherent at 4 months and decreased the percentage remained adherent over the 4 month (Figure 2).

Pre-CPAP predictors of adherence at 4 months

Adherent patients were older than non-adherent patients (57 ± 12 versus 49 ± 11, p=0.002). The AU-ROC curve for age as a predictor of adherence was 0.67 and the optimal threshold was 53 years with a sensitivity of 0.62 and a specificity of 0.67. The threshold for a specificity of 90% was 67.

We divided patients into 2 groups: older patients>53 years (252 patients), and younger patients ≤ 53 years (168 patients). In comparison to the older patients, the younger patients had a higher BMI (34 ± 7 versus 31 ± 6), had a higher Pichot fatigue score (15 ± 8 versus 14 ± 8, p=0.01), and a higher ESS score (11, IQR 8-15 versus 10, IQR 6-14, p=0.03), and they used CPAP slightly less in the first 15 days (0.5 ± 0.2 hours). There was also a weak but significant correlation between the Pichot fatigue score and the drop in CPAP use from 15 days to 4 months (r=0.1, p=0.036).

When age and early use of CPAP were entered in a logistic regression, age became non-significant and early use of CPAP was the only predictor of adherence at 4 months. The odds ratio associated with every hour of early CPAP use for predicting CPAP adherence at 4 months was 2.1 (95% CI: 1.6-2.7, p<0.001). On the other hand, in a linear regression model with the hours of CPAP use as the dependent variable, age and early CPAP use were significant and the regression equation was CPAP use at 4 months=1.5+ [early CPAP use in hours × 0.62] + [age in years×0.01].

There was no correlation between CPAP use at 4 months and ESS (r=-0.05, p=0.3) or between CPAP use and AHI (r=0.09, p=0.06). Similarly, none of the other pre-CPAP variables (including the methods of diagnosing OSA) was associated with CPAP use at 4 months.

Discussion

In this relatively large sample of patient with OSA that was followed closely for 4 months, we found that early CPAP use was the strongest predictor of adherence at 4 months independent of its definition. Of the variables available for the physician before starting CPAP, age was the only variable associated, though weakly, with CPAP adherence at 4 months.

Our results complement the results reported by others that long-term CPAP adherence patterns are often established within the first weeks of therapy [15-18]. Budhiraj et al. [12] reported that CPAP use by the third day was predictive of CPAP use at 30 days. Popescu et al. [13] reported that CPAP use in the first 2 weeks predicts CPAP adherence at 1 year. Chai-Coetzer et al. [19] reported that adherence at one month predicted CPAP adherence at 1 year. McArdle et al. [5] reported that CPAP use at 3 months predicts adherence after 2 years. This composite of evidence suggests that adherence to CPAP use must be evaluated early and continuously after initiating therapy.

A novel and interesting finding of our study was the relationship between the area under the ROC curve for early CPAP use and the insurance type. It has been shown in the past that socioeconomic status (especially poverty) is associated with CPAP use (see appendix). In our study, early CPAP use was more predictive of long-term use in patients with government only (suggestive lower income). The type of insurance was not, however, associated the adherence itself. This finding deserves

Socio-economic variables	
Men, %	70
Age, years	56 ± 12
Married, %	78
Fully employed, %	59
Government insurance with private health insurance,%	94
Health variables	
Body mass index, kg/m^2	32 ± 6
Treated Hypertension, %	49
Heart disease (arrhythmia or congestive heart failure),%	12
Stroke,%	12
Myocardial infarction, %	11
Loss of libido, %	32
OSA related variables	
AHI	46 ± 19
Diagnosis made with HST, %	38
Daily CPAP use in the first 15 days	5.6±2
Psychological Variables	
Epworth Sleepiness Scale	10.7 ± 5
Pichot Fatigue Scale	14.2 ± 7
Pichot Depression Scale	4.7 ± 4

Table 2: Baseline characteristics of the patients at the onset of CPAP therapy (n=420).

Definition of adherence at 4 months	Adherence at 4 month based on definition	Threshold at 15 days	Sn	Sp	Sn_{90}	Sp_{90}
3 hours	94%	3.2 (2.2-3.9)	91%	70%	3.3	6.0
4 hours	81%	5.4 (3.3-5.6)	72%	86%	3.8	5.5
5 hours	69%	5.5 (5.1-5.5)	77%	83%	4.2	6.2
6 hours	49%	6.4 (5.7-6.8)	66%	89%	4.6	6.5

Table 3: The percentage of adherent patients at various definitions at four months, the optimal threshold of early use (15 days) to predict adherence based on bootstrap analysis, its sensitivity and specificity, and the threshold of early CPAP use with sensitivity of 90% (Sn_{90}) and specificity of 90% (Sp_{90}).

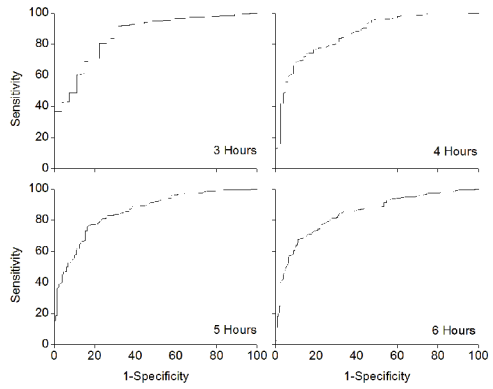

Figure 1: ROC curves for early CPAP use predicting adherence at the 4 thresholds at 4 months. The area was 0.86 (0.82-0.89) for 3 hours, 0.87 (0.83-0.89) for 4 hours, 0.86 (0.82-0.88) for 5 hours, and 0.85 (0.81-0.88) for 6 hours.

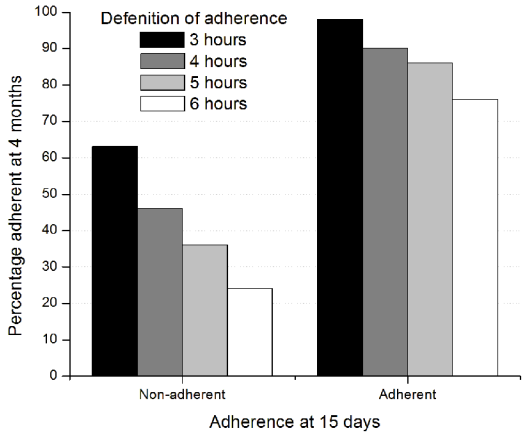

Figure 2: The relation between adherence on day 15 (x-axis) and adherence at 4 months defined with the same hours of CPAP use. When patients were non-adherent at 15 days, they are unlikely to be adherent at 4 months with a decreasing chance of adherence as the threshold for adherence increases. When patients were adherent at 15 days, the were likely to be adherent at 4 month but with a decreasing likelihood as the threshold for adherence increased; but, the lowest adherence rate, which was with a threshold of 6 hours, was still >70%.

further evaluation because it might reflect a motive behind the use of CPAP such as employment for drivers or just to avoid monetary penalty for not using CPAP.

Because the definition of CPAP adherence is arbitrary and studies have used definitions varying between 2 and 6 hours, we tested 3, 4, 5, and 6 hour thresholds. The AU- ROC curve for early CPAP use predicting later adherence was similar between all definitions of adherence. Therefore, our conclusions can be extended to settings where the criterion of adherence is different from that used in France, especially since Chai-Coetzer and colleagues have shown that the relation between early use and long-term adherence is independent from country [19].

Currently most clinicians rely on a single definition to identify patients not adherent to CPAP use. In the United States, patients are considered adherent if they use a CPAP for more than 4 hours most night of the week. This definition of adherence is required by Medicare to pay for CPAP. Nevertheless, to achieve maximal alertness and cognitive functioning, a reduction in carbon dioxide in patients with obesity hypoventilation syndrome, or a reduction in blood pressure, a patient must use a CPAP for more than 6 hours a day [20-22]. The thresholds we identified can help physicians predict if a patient will meet the required CPAP use. Therefore, for example, if a patient was a commercial driver that required maximal cognitive functioning, early CPAP use of less than 6.5 hours would be concerning and less than 4.5 hours would be very concerning.

Predicting non-adherent patients early helps physicians select patients that need attention and intensive follow-up. Of the patients that were using CPAP ≥3 hours in the first two weeks, 98% were using it ≥3 hours at 4 months. On the other hand, 37% of the patients that were using CPAP < 3 hours at 15 days were still using it <3 hours at 4 months. Thus, when the desired dose of CPAP use is low, only patients with very low early use should probably be followed closely for the first few months.

Variable	This study
Socio-economic variables	
Age [12,13]	Confirmed
Gender [30]	Not confirmed
Marital status [26,30]	Not confirmed
Employment status [26,31]	Not confirmed
Type of health insurance [32]	Not confirmed
Race [33]	Not tested
Life events [34]	Not tested
Health variables	
Treated Hypertension [35]	Not confirmed
Heart disorders [4]	Not confirmed
BMI [13,36]	Not confirmed
Stroke [37]	Not confirmed
Myocardial infarction [38]	Not confirmed
Nasal anatomy [39]	Not tested
Psychological or behavioural variables	
Epworth Sleepiness [17]	Not confirmed
Pichot Fatigue Scale [40]	Not confirmed
Pichot Depression scale [16]	Not confirmed
Self-efficacy [27,28]	Not tested
Coping-styles [41]	Not tested
Locus of control [29]	Not tested
Initial CPAP exposure variables	
CPAP use in the first 15 days [4,13]	Confirmed
Diagnosed with HST [42]	Not confirmed
AHI [43]	Not confirmed
Social variables	
Spousal involvement [27,44]	Not tested
Bed partner sleep quality [45,46]	Not tested
Technical variable	
Mask-interface [47]	Not tested
Heated vs. cold pass-over humidity [48]	Not tested
Flexible pressure on CPAP (C-Flex vs continuous positive airway pressure) [49]	Not tested
Claustrophobia [50]	Not tested
Side effect [19]	Not tested

Table 4: Summary of variables from prior studies on significant predictors of CPAP.

In contrast, 76% of patients using a CPAP more than 6 hours at 15 days were still doing so at 4 months and only 24% of patients using a CPAP less than 6 hours increased above this threshold. Therefore, when the desired dose of CPAP is high, as in drivers and patients with obesity hypoventilation, all patient should be followed closely.

Age was the only pre-CPAP variable predictor of adherence: older patients were more likely to use a CPAP than younger patients. Sin et al. [23] reported a similar relation between age and CPAP adherence. In fact they reported that CPAP use increased by 0.24 hours per decade, while in our study it was 0.34 hours in a univariate regression and 0.1 hours after adjustment for early CPAP use. Similarly, Budhiraja et al. [12] showed that adherent (defined as >4 hours) patients were on average 3 years older than non-adherent patients. If we use the 4 hour definition, adherent patients were 8 years older.

Although they were more fatigued and sleepy, younger patients used a CPAP less than older ones. This profile is similar to that report by Pepin et al. [24] as a predictor of residual sleepiness after treatment with a CPAP. Because of the correlation between the Pichot fatigue score and the drop in CPAP use from 15 days to 4 months, it is plausible that these young, fatigued patients gradually reduced their CPAP use because they did not feel better with it. This observation is also concerning because younger patients will live longer than older ones, and if they remain non-adherent, they are likely to suffer cardiovascular complications at a younger age, further leading to a larger societal impact of OSA.

Many investigators have reported that AHI [4,13] and the ESS4, [25] predicted adherence. We did not find such a relationship. This is not due to spectrum bias because the distribution of both AHI and ESS were wide. A larger sample size might have resulted in a weak correlation between AHI and adherence, but it would have been too weak to be useful predictor. Yet, patients with high AHI and ESS should receive special attention from physicians because they are more likely to benefit when they adhere to CPAP use than patients with lower AHI or ESS.

This study has two particular strengths. First, the sample is relatively large (only 5 other studies included more than 500 patients) and the patients were recruited from multiple centers. This allowed us to simultaneously test a large number of variables previously tested by other investigators (Table 4). Second, the patients were followed monthly if they remained non-adherent and at 4 months. In comparison, the study by Gagnadoux et al. [26] included more than 1000 patients that were followed at the end of the first week, and then at the end of the third month. The follow-up was not regular or based on adherence. Another study from Sin et al. [23] provided a very detailed follow-up of the patients but the sample was small.

Follow-up and adherence in this study was higher than what is reported by others. Two reasons might explain this observation. First, the study had a dedicated physician who was specifically involved in the coordination of data collection to monitor the quality of the collection processing. Second, the French government reimbursed patients for CPAP use if they used it for more than 3 hours per night, which encouraged the patients to use the CPAP. This is slightly different from reimbursement in the United States where Medicare purchases the CPAP machine once the patients is deemed adherent. In fact, the relationship between the accuracy of early CPAP use in predicting adherence and the type of insurance suggests that the reimbursement mechanism might play a role in the change in adherence between the first 15 days and 4 months.

There are several limitations in this study. The first limitation is that we did not test side effects. Early complaints of side effects have previously been associated with long-term non-adherence with CPAP [19]. We assume that they were addressed with the patients during the frequent visits and should have been resolved by the fourth months of follow-up. The second limitation is that we did not test coping, locus of control, and self-efficacy, which have previously been shown to predict adherence [19,20,21,26-29]. They are probably mechanisms that lead to early non-adherence that ultimately continues long-term. Once a patient is identified early on to be at risk of non-adherence, the clinician must evaluate that patient's coping and self-efficacy. Lastly, our follow-up was 4 months only. The longer the follow-up, the more events that can affect adherence: seasonal allergy, mask failure, change work hours, etc. The 4 four month follow-up is probably optimal to reduce external events that can affect adherence.

In conclusion, CPAP use in the first 15 days is the best predictor of adherence to the use of a CPAP at 4 months and it was more accurate in patients than in government only insured patients. The threshold of early CPAP use should be adjusted based on the desired long term adherence. These observations might assist physicians identify early the

patients that will not meets their target of CPAP use and these patients will be suitable for intensive follow-up or alternative therapy.

Contributions

Study conception and design: Thibaut Gentina. Thibaut Gentina designed the research plan and organized the study.

Acquisition of data: François Jounieaux, Catherine Lamblin and François Codron developed the methodology, participated in the collection of data and coordinated the data-analysis.

Analysis and interpretation of data: Elodie Dancoine and Aiman Tulaimat performed the analyses.

Drafting of manuscript: Thibaut Gentina, Elodie Dancoine and Aiman Tulaimat contributed to the writing of the manuscript.

Critical revision: Elodie Dancoine and Aiman Tulaimat.

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Conflict of Interest

There is not conflict of interest in this research.

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Appendix 1

Reference	Factors associated with compliance	Country	Sample (n)	threshold value to be adherent (/ night)
Socio-economic variables				
Mc Ardle et al. (1999)[1]	Age	U.K.	1211	2 hours
Krieger et al. (1996)[2]	Age	France	728	4 hours
Budhiraja et al. (2007)[3]	Age, race	U.S.	100	4 hours
Olsen et al. (2008)[4]	Age	Australia	77	2 hours
Popescu et al. (2001)[5]	Age, gender	England	209	
Sin et al. (2002)[6]	Age, gender	Canada	296	4 hours
Simon-Tuval et al. (2009)[7]	Age, monthly income	Israel	162	Not indicated
Young et al. (1993)[8]	Gender	U.S.	602	4 hours
Pelletier et al. (2001)[9]	Gender	France	163	3 hours
Lewis et al. (2004)[10]	Gender, marital status, life event	United Kingdom	82	4 hours
Ye et al. (2009)[11]	Gender	7 sleep centers in the U.S. and Canada	176	4 hours
Bakker et al.[12]	Age, gender, ethnicity, education, employment, annual income, type of health insurance, health literacy	New Zealand	126	4 hours
Ye et al. (2012)[13]	Marital status, race	U.S.	91	4 hours
Gagnadoux et al. (2011)[14]	Marital status, employment status	France	1141	4 hours
Scharf et al. (2004)[15]	Race	U.S.	128	Not indicated
Billings et al. (2011)[16]	Race	U.S.	191	2 hours
Platt et al. (2009)[17]	Race, employment status, Neighborhood of residence	U.S.	266	4hours
Hoffstein et al. (1992)[18]	Type of health insurance	U.S.	96	4 hours

Reference	Factors associated with compliance	Country	Sample (n)	threshold value to be adherent (/ night)
health variables				
Popescu et al. (2001)[5]	BMI	England	209	2 hours
Krieger et al. (1996)[2]	BMI	France	728	4 hours
Young et al. (1993)[8]	BMI	U.S.	602	4 hours
Pelletier et al. (2001)[9]	BMI	France	163	3 hours
Gagnadoux et al. (2011)[14]	BMI	France	1141	4 hours
Loredo et al. (2007)[19]	BMI, heart disorder	U.S.	76	6 hours
Wild et al. (2004) [20]	BMI	United Kingdom	119	3 hours
Olsen et al. (2008)[4]	BMI	Australia	77	4 hours
Redenius et al. (2008)[21]	BMI	U.S.	309	4 hours
Sugiera et al. (2007)[22]	BMI	Japan	77	5 hours
Reishten et al. (2010)[23]	Erectile dysfunction	U.S. and Canada	123	Not indicated
Margel et al. (2005)[24]	Erectile dysfunction	Israel	60	Not indicated
Mc Ardle et al. (1999)[1]	Treated Hypertension, heart disorder	U.K.	1211	2 hours
Hung et al. (1990)[25]	Treated Hypertension, myocardial infarction	Australia	101	Not indicated
Philips et al. (2013)[26]	Treated Hypertension	Spain	725	4 hours
Palombini et al. (2006)[27]	Stroke	Italy	50	4 hours
Martínez-García et al. (2012)[28]	Stroke, myocardial infarction	Italy	223	4 hours

Reference	Factors associated with compliance	Country	Sample (n)	threshold value to be adherent (/night)
osa related variables				
Mc Ardle et al. (1999)[1]	AHI	U.K.	1211	2 hours
Popescu et al. (2001)[5]	AHI	England	209	2 hours
Krieger et al. (1996)[2]	AHI	France	728	4 hours
Pelletier et al. (2001)[9]	AHI	France	163	3 hours
Gagnadoux et al. (2011)[14]	AHI	France	1141	4 hours
Wild et al. (2004)[20]	AHI	United Kingdom	119	3 hours
Palombini et al. (2006)[27]	AHI	Italy	50	4 hours
Hui et al. (2001)[29]	AHI	China	112	4 hours
Krieger (1992)[30]	AHI	France	233	Not indicated
Meurice et al. (1994)[31]	AHI	France	44	5 hours
Bollig (2010) [32]	AHI	Synthetical article		
Baron et al. (2011)[33]	AHI	U.S.	31	Not indicated
Hoffstein et al. (1992)[18]	Minimum nasal cross-sectional area + reduced volume	U.S.	96	4 hours
Sugiera et al. (2007)[22]	AHI, Minimum nasal cross-sectional area + reduced volume	Japan	77	5 hours
Morris et al. (2006)[34]	Minimum nasal cross-sectional area + reduced volume	U.S.	34	Not indicated
Fletcher et al. (1991)[35]	Minimum nasal cross-sectional area + reduced volume	U.S.	Not indicated	Not indicated
Bakker et al. (2011)[12]	AHI	USA	126	4 hours
Simon-Tuval et al. (2009)[7]	AHI	Israel	162	Not indicated

Reference	Factors associated with compliance	Country	Sample (n)	threshold value to be adherent (/ night)
psychological/ behavioral variables				
Mc Ardle et al. (1999)[1]	Epworth Sleepiness, Pichot Fatigue Scale	U.K.	1211	2 hours
Krieger et al. (1996)[2]	Epworth Sleepiness	France	728	4 hours
Pelletier et al. (2001)[9]	Epworth Sleepiness	France	163	3 hours
Lewis et al. (2004)[10]	Epworth Sleepiness	United Kingdom	82	4 hours
Ye et al. (2012)[11]	Epworth Sleepiness	U.S.	91	4 hours
Sin et al. (2002)[6]	Epworth Sleepiness, self-efficacy	Canada	296	4 hours

Loredo et al. (2007) [19]	Epworth Sleepiness	U.S.	76	6 hours
Wild et al. (2004)[20]	Epworth Sleepiness, self-efficacy	United Kingdom	119	3 hours
Meurice et al. (1994)[31]	Epworth Sleepiness	France	44	5 hours
Engleman et al. (1994)[36]	Epworth Sleepiness	U.K.	16	3.2 hours
Waldhorn et al. (1990)[37]	Epworth Sleepiness	U.S.	125	2 hours
Olsen et al. (2008)[4]	Pichot Fatigue Scale, Pichot Depression scale	Australia	77	4 hours
Yinghui et al. (2011)[38]	Pichot Fatigue Scale, Pichot Depression scale	U.S.	57	Not indicated
Bakker et al. (2011) [12]	Epworth Sleepiness, self-efficacy	USA	126	4 hours
Baron et al. (2011)[33]	Self-efficacy	U.S.	31	Not indicated
Sawyer et al. (2011)[39]	Self-efficacy	U.S.	66	20 minutes at effective pressure
Stepnowsky et al. (2002)[40]	Coping-styles	U.S.	23	Not indicated
de Zeeuw et al. (2007)[41]	Locus of control	Germany	85	Not indicated
Tyrrell et al. (2006)[42]	Locus of control	France	9	Not indicated

Reference	Factors associated with compliance	Country	Sample (n)	Minimum threshold value to be adherent (/night)
initial cpap exposure variables				
Mc Ardle et al. (1999)[1]	CPAP use (in the first 15 days stage <3 hours)	U.K.	1211	2 hours
Popescu et al. (2001)[5]	CPAP use (in the first 15 days stage <3 hours)	England	209	2 hours
Lewis et al. (2001)[10]	Initial problems with CPAP use (in the first night)	United Kingdom	82	4 hours
Balachandran et al.(2013)[43]	CPAP perception questionnaire over the first 30 days of therapy	U.S.	1226	4 hours
Rosen et al. (2012)[44]	Diagnosed with HST	U.S.	373	4 hours
Lettieri et al. (2011)[45]	Diagnosed with HST	U.S.	210	4 hours

Reference	Factors associated with compliance	Country	Sample (n)	Minimum threshold value to be adherent (/night)
social variables				
Baron et al. (2011)[33]	Spousal involvement	U.S.	31	Not indicated
Mc Ardle et al. (1999)[1]	Bed partner's sleep quality and overall quality of life	U.K.	1211	2 hours
Parish et al. (2003)[46]	Bed partner's sleep quality and overall quality of life	U.S.	51	6 hours (mean)
McArdle et al. (2001)[47]	Bed partner's sleep quality and overall quality of life	U.K.	49	Not indicated
Simon-Tuval et al. (2009)[7]	Partners sleeps separately and family and/or friends with positive experience of CPAP	Israel	162	Not indicated
Cartwright. (2008)[48]	Shared sleeping		20	
Ye et al. (2009)[49]	Spousal involvement	Synthetical article		

Reference	Factors associated with compliance	Country	Sample (n)	Minimum threshold value to be adherent (/night)
technical variables				
Anderson et al. (2003)[50]	Mask-interface (types of nasal vs face mask innovations)	New Zealand	11	Not indicated
Khanna et al. (2003)[51]	Mask-interface (types of nasal vs face mask innovations)	U.S.	38	4 hours

Massie et al. (2003)[52]	Mask-interface (types of nasal vs face mask innovations)	U.S.	39	4 hours
Mortimore et al. (1998)[53]	Mask-interface (types of nasal vs face mask innovations)	U.K.	30	Not indicated
Massie et al. (1999)[54]	Heated vs cold pass-over humidity	U.S.	38	1 hour
Aloia et al. (2005)[55]	Flexible pressure on CPAP adherence	U.S.	89	Not indicated
Pepin et al. (2009)[56]	Flexible pressure on CPAP adherence	France	218	4 hours
Chasen et al. (2005)[57]	Claustrophobia	U.S.	153	2 and 5 hours
Chai et al. (2013)[58]	Side effect	China, Australia, and New Zealand	275	3 hours

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