Determinants Affecting Initiation of Continuous Positive Airway Pressure Treatment

Yaron S. Brin MD*, Haim Reuveni MD, Sari Greenberg MA, Asher Tal MD and Ariel Tarasiuk PhD
Sleep-Wake Disorders Unit, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

Key words: continuous positive airway pressure, obstructive sleep apnea syndrome, patient support, co-payment, socioeconomic status

Abstract

Background: Continuous positive airway pressure is the treatment of choice for patients with obstructive sleep apnea syndrome.

Objective: To determine the factors influencing treatment initiation with a CPAP device in a healthcare system in which co-payment is required.

Methods: A total of 400 adult patients with OSAS who required CPAP therapy completed questionnaires at three different stages of the diagnostic and therapeutic process: CPAP titration study (stage 1), patient adaptation trial (stage 2), and purchase of a CPAP device (stage 3). Logistic regression was used to analyze the variables influencing CPAP use at the different stages of the diagnostic and therapeutic processes.

Results: Only 32% of the patients who underwent CPAP titration study purchased a CPAP device. The number of subjects who purchased a CPAP device increased gradually as monthly income increased, 28% vs. 62% in the "very low" and "very high" income levels respectively. Reporting for the titration increased in patients with excessive daytime sleepiness and an Epworth Sleepiness Scale score above 9 (odds ratio = 1.9, P = 0.015). Higher socioeconomic status increased reporting to stage 2 (OR = 1.23, P = 0.03) and CPAP purchase (stage 3, OR = 1.35, P = 0.002). Excessive daytime sleepiness increased reporting to stage 2 (OR = 2.28, P = 0.006). Respiratory disturbance index above 35 increased CPAP purchasing (OR = 2.01, P = 0.022). Support from the bed partner, referring physician and sleep laboratory team increased CPAP purchasing.

Conclusions: A supportive environment for a patient with OSAS requiring CPAP is crucial to increase initiation of CPAP treatment. Minimizing cost sharing for the CPAP device will reduce inequality and may increase CPAP treatment initiation.

Some researchers have suggested that the respiratory disturbance index is the main predictor of compliance with CPAP therapy [3], while others found that the subject's gender, age and improvement in excessive daytime sleepiness could predict compliance [4]. Polysomnography findings might not be the only determinant for CPAP compliance. Subjects who were less obese and complained less of excessive daytime sleepiness before therapy were more likely to stop CPAP treatment [5]. Side effects and problems related to CPAP, including nasal blockage/dryness, cold air stream and patients' intolerance of the device, decreased long-term CPAP treatment [3,6,7]. CPAP support programs and patient education were found to increase patients' compliance during treatment initiation [8-10], since they ameliorate patients' symptoms and improve their quality of life, and therefore drive patients to seek therapy [9,11].

Due to the increased volume of referrals for sleep studies over the past decade, OSAS has attracted the attention of healthcare policymakers [12]. Various methods have been tried by healthcare providers to counteract this cost increase. Co-payment, the policy whereby patients cover part of the cost of their medication, is an accepted method of reducing costs [13]. Due to the known potential benefits of CPAP treatment, including reduction in healthcare utilization [14], some countries, such as Germany and the United Kingdom, several parts of Canada and some medical insurance companies in the United States, provide the CPAP device free of charge. In Israel, co-payment policy is determined by the Ministry of Health and the Ministry of Finance, and is implemented by the health management organizations. According to this policy, patients are required to pay between 20 and 50% of their average monthly income for a CPAP device, depending on the type of supplemental medical coverage they carry.

In the present study we investigated, in a health maintenance organization requiring co-payment, whether polysomnographic parameters, socioeconomic status, as well as subjective indices such as excessive daytime sleepiness and the bed partners' support, affect CPAP treatment initiation. We hypothesized that objective disease indices, patient and bed partner complaints and out-of-pocket payment for CPAP are barriers to treatment initiation. This in turn may increase inequity in the healthcare system.

Obstructive sleep apnea syndrome is a common condition that affects 2–4% of the adult population [1]. Continuous positive airway pressure is the treatment of choice. Other treatments may include surgical interventions such as oropharyngeal or tracheotomy in rare cases, weight reduction, and behavioral therapy. Although its therapeutic benefits have been recognized, compliance with CPAP can be low [2]. It is not clear what predicts CPAP acceptance, prescription and adherence. Early studies suggested that objective polysomnography data indicating improvement in sleep patterns during the titration study might predict acceptance of the therapy.

CPAP = continuous positive airway pressure
OSAS = obstructive sleep apnea syndrome
OR = odds ratio

*This study was conducted in partial fulfillment of the requirements for an MD degree.
 Patients and Methods
We conducted a cross-sectional study during the period April 2001 to March 2002 at the university-affiliated Sleep-Wake Disorders Center. The study population comprised 469 consecutive adult subjects with suspected OSAS who were referred for polysomnographic study. Four hundred patients with OSAS were recommended for CPAP therapy (mean age 53.7 ± 10.8 years, 68 females and 332 males) according to the following criteria: respiratory disturbance index ≥20/hour or RDI <20 if they had symptoms of excessive daytime sleepiness [4], and an Epworth Sleepiness Scale score of ≥9 [15]. We excluded from the study the following three diagnoses: chronic obstructive pulmonary disease that required bilevel positive airway pressure therapy, patients with facial abnormalities and patients with trisomy-21 syndrome. The Institutional Ethics Committee approved the protocol and informed consent was obtained from all subjects.

Data collection
- Questionnaire. We used validated self-administered questionnaires [9,11]. A supportive bed partner is defined as a spouse encouraging the patient to seek therapy. Socioeconomic level was evaluated according to: a) residential location clusters identified by the Israeli census according to mailing address, [16] with socioeconomic level 1 reflecting a population at the lowest level and level 10 a population at the highest socioeconomic level; b) patient income level relative to the average wage in Israel in October 2001 ($1,645 per individual and $3,290 per family) [16]; and c) education level.
- Polysomnographic study. Overnight PSG monitoring was performed according to previously described methods from our laboratory [17]. Patients are entitled to a PSG study, and all diagnostic and treatment information regarding OSAS are provided free of charge.
- CPAP support program. We used a modification of the approach previously described by Popescu et al. [10]. All subjects discussed the results of their PSG and CPAP titration study with a sleep physician up to 2 weeks following the completion of the study as a part of our laboratory routine. Upon receiving results of the CPAP titration study, patients were encouraged by sleep specialists to perform an adaptation trial in order to commence treatment. At this stage, patients were advised that the actual cost of both steps required out-of-pocket payment in addition to the cost participation by their health maintenance organization. Within one month after completion of the study, one of the investigators (Y.S.B) telephoned the patient and reported the results and the therapeutic approach suggested by the physician. If the patient agreed, he/she participated in a preadaptation session in the sleep laboratory with the presence of a sleep technician, during which patients received further explanation of the pathophysiology of OSAS, its risks and treatment, and an explanation of the upcoming adaptation trial. A 2 week period of adaptation with the CPAP device at home was offered and encouraged. During the pre-adaptation period, patients were fitted with an appropriate nasal mask selected from a variety of CPAP devices available in Israel. The patient was guided on how to use the device at home and received a brochure with helpful tips regarding common problems with CPAP use. During the following 2 week adaptation trial, patients used the device at home. A technician was in contact with the patient by phone at least once a week. In case of any problem – such as nasal dryness and congestion, feeling that the air that comes from the device is too cold, a noisy CPAP device, mask discomfort, difficulty in adapting to the pressure – the patients were encouraged to contact one of the investigators (Y.S.B) in order to resolve the problem. In about 10% of the patients the CPAP device was given for an additional 1–2 weeks to ensure the patient’s satisfaction. At the end of the 2 week period, initiation of CPAP treatment was discussed. On deciding to continue using the CPAP device, patients had to purchase a device.

Data and statistical analysis
We divided our analysis into three stages that represent the various steps of case management required for OSAS diagnosis and treatment: a) Titration study – a second polysomnogram whereby the therapeutic level of CPAP is determined (stage 1), b) CPAP adaptation – a 2 week trial at home using the CPAP therapeutic level with a mask fitted for the patient (stage 2), and c) purchase – when the patient pays his/her required portion of the CPAP device purchase price (stage 3). Following PSG, patients may accept or decline the CPAP titration study, accept or decline the adaptation trial, and purchase or decline the CPAP device.

All data were analyzed using SPSS software (Microsoft, USA). Normally distributed data were presented as mean ± SD. Logistic regression analysis was used to investigate variables influencing CPAP acceptance and adaptation and purchase. A conditional analysis of the data according to the three stages of diagnosis and treatment was performed. We used the chi-square test to determine the association between dichotomic variables, and the Pearson test for correlation values between continuous variables. In order to determine whether including more severe OSAS patients affects the percent of CPAP adaptation and purchase, data were analyzed retrospectively including only the severe OSAS patients (RDI >30/hr or RDI <30/hr and Epworth Sleepiness Scale >10), similar to Popescu et al. [10]. The null hypothesis was rejected at the 5% level.

Results
Patients
Figure 1 shows the number of patients in each group according to the therapeutic stage. We did not find any significant differences between the different groups in the therapeutic process in any of the variables (Tables 1 and 2). Table 1 describes patient characteristics and PSG findings, and Table 2 presents patients' co-morbidity and the main complaints for referral to the sleep center. Patient characteristics and co-morbidity were statistically similar in patients accepting CPAP titration (n=324) compared with patients (n=76) who declined CPAP titration; similarly, no statistical differences were found between patients undergoing CPAP adapta-
tion and patients purchasing a CPAP device. Thus, the 128 patients who purchased a CPAP device were similar with respect to OSAS severity and co-morbidity when compared with the total study population. Interestingly, 14.5% of OSAS patients reported having type 2 diabetes mellitus. Of these patients, 70.7% had a body mass index $>30$ and 69% reported having hypertension (RDI $40.7 \pm 24.1$). In 70% of cases, bed partners were aware of the sleep disturbance and encouraged the patient to see a physician. In only 30% of the cases was it the patient who was aware of the sleep disturbances. RDI correlated with arousal index ($r = 0.65, P < 0.001$) and oxygen desaturation index correlated with arousal index ($r = 0.49, P < 0.001$).

**Socioeconomic characteristics**

Table 2 describes the distribution of patients according to income level, education and area of residency. Income level was associated with education ($\chi^2 = 47.2, P < 0.001$) and socioeconomic status ($\chi^2 = 61.1, P < 0.001$). Education level was associated with socioeconomic status ($\chi^2 = 7.1, P = 0.008$).

**Adaptation and purchase**

Of the 183 patients who underwent the 2 week adaptation trial, 128 subjects purchased the CPAP device (32% of the total population who underwent CPAP titration study) [Figure 1]. Of the patients who purchased a CPAP device, 40.2% had an RDI $<30$, 14.3% had $30 \leq$ RDI $< 40$, and 45.5% had an RDI $>40$ events/hour. Referrals from physicians and bed partners or self-referral differed considerably (10–20% higher) in patients who purchased a CPAP device compared with patients who declined the adaptation trial and therapy. The reasons for purchasing are presented in Table 2. About 80% of the patients who purchased a CPAP device reported considerable improvement in their nocturnal symptoms and morning headaches on the first morning following the CPAP

![Table 2. Patient co-morbidity, main complaints, socioeconomic characteristics and reasons for CPAP purchase](image)
titration study. Patient recognition that ‘OSAS is a dangerous syndrome’ was associated with breathing difficulties during sleep ($\chi^2 = 11.2, P < 0.001$), excessive daytime sleepiness ($\chi^2 = 3.8, P = 0.05$) and encouragement of the bed partner ($\chi^2 = 27.6, P < 0.001$). Excessive daytime sleepiness was associated with Epworth Sleepiness Scale score ($\chi^2 = 14.1, P < 0.001$). Figure 2 presents income level and the percent of patients refusing adaptation, undergoing CPAP purchase, or declining treatment. The percentage of subjects who purchased a CPAP device increased gradually ($P < 0.03$) as monthly income increased (28% in the ‘very low’ income level category compared with 65% in the ‘very high’ income level category). The percent of subjects who declined CPAP device purchase was 72% (28% declined purchasing and 44% refused adaptation) in the ‘very low’ monthly income category and 35% (12% declined purchasing and 23% refused adaptation) in the ‘very high’ monthly income category. Patients who purchased the CPAP device were encouraged to do so by bed partners and physicians; 29.3% indicated that their primary physician referred them to the adaptation trial compared with 17% among the patients who declined purchase. The bed partner was mentioned as the reason for CPAP purchase in 16.4% of the cases compared with 2.1% among those who declined CPAP treatment.

**Scale effects on the diagnostic and therapeutic process**

Reporting to the CPAP titration study increased when the Epworth Sleepiness Scale was >9 (OR = 1.9, confidence interval = 1.13–3.2, $P = 0.015$). Reporting to adaptation CPAP increased in patients complaining of “breathing difficulties during sleep” (OR = 1.66, CI = 1.1–2.53, $P = 0.016$), patients complaining of daytime sleepiness (OR = 1.45, CI = 0.98–2.17, $P = 0.05$), patient recognition that OSAS is a serious condition (OR = 4.07, CI = 2.67–6.2, $P = 0.001$), higher socioeconomic status according to area of residence (OR = 1.14, CI = 1.01–1.29, $P = 0.032$), and encouragement of the bed partner (OR = 2.34, CI = 1.35–4.08, $P = 0.003$). CPAP purchase increased in patients complaining of breathing difficulties during sleep (OR = 1.58, CI = 1.03–2.45, $P = 0.04$), encouragement from the bed partner (OR = 3.27, CI = 1.89–5.69, $P = 0.001$), higher socioeconomic status according to the area of residency (OR = 1.2, CI = 1.06–1.36, $P = 0.05$), higher monthly income (OR = 1.19, CI = 0.99–1.43, $P = 0.05$), and patient recognition that OSAS is a serious condition (OR = 3.34, CI = 2.14–5.28, $P = 0.001$). Multivariate analysis of independent variables influencing CPAP adaptation and purchase revealed that the number of patients undergoing the CPAP adaptation trial increased with the patient complaint of “excessive daytime sleepiness” (OR = 2.28, CI = 1.27–4.09, $P = 0.006$) and with higher socioeconomic status according to the area of residence (OR = 1.23, CI = 1.02–1.40, $P = 0.03$). Other variables such as the Epworth Sleepiness Scale and the patient’s recognition that OSAS is a serious condition were most likely associated with CPAP device purchase. However, since both the Epworth Sleepiness Scale and patient recognition that OSAS is a serious condition were found to be statistically associated with the complaint of excessive daytime sleepiness ($\chi^2 = 14.1, P < 0.001$ and $\chi^2 = 3.8, P = 0.05$ respectively), they were not included in the model due to confounding effect. CPAP device purchase increased in patients having RDI >35/hr and higher socioeconomic status according to the area of residence. Higher monthly income most likely increased CPAP device purchase. However, since income was found to be in statistical association with socioeconomic status according to the area of residence ($\chi^2 = 61.1, P < 0.001$), it was not included in the model due to confounding effects.

**Severe OSAS group**

Retrospective analysis revealed that only 35% of the severe OSAS group (RDI >30/hr or RDI <30/hr and the Epworth Sleepiness Scale >10) purchased CPAP devices. There was no significant difference between the non-severe and the severe OSAS group (Table 1) with respect to age, gender, body mass index, smoking habits, percentage of healthy patients, socioeconomic status, and the reasons for purchasing a CPAP device (Table 2). Compliance with the CPAP titration study increased when the Epworth Sleepiness Scale was >9 (OR = 2.13, CI = 1.15–3.94, $P = 0.016$). Reporting to CPAP adaptation was increased in patients noting “breathing difficulties during sleep” (OR = 2.10, CI = 1.12–3.44, $P = 0.006$), encouragement of the bed partner (OR = 2.66, CI = 1.35–5.24, $P = 0.005$), patient’s recognition that OSAS is a serious condition (OR = 3.99, CI = 2.39–6.66, $P = 0.001$), and higher socioeconomic status (OR = 1.84, CI = 1.07–3.18, $P = 0.029$). CPAP device purchasing was increased in patients complaining of breathing difficulties during sleep (OR = 1.67, CI = 0.99–2.82, $P = 0.05$), encouragement from the bed partner (OR = 4.11, CI = 2.09–8.1, $P = 0.001$) and patient recognition that OSAS is a serious condition (OR = 2.89, CI = 1.72–4.87, $P = 0.001$). The number of patients undergoing the CPAP adaptation trial increased in subjects with a higher socioeconomic

---

CI = confidence interval
status. Purchase of a CPAP device increased in subjects with higher socioeconomic status and a supportive bed partner.

Discussion
We evaluated the determinants of CPAP treatment initiation in a health management organization that has a co-payment policy and found that only one-third of the patients with OSAS purchased a CPAP device (regardless of OSAS severity). The present study presents results of "typical" patients suffering from OSAS [1]. The patients were similar to OSAS patients in our region since our sleep center provides service to 65% of the enrollees in our referral area. The socioeconomic status and education level of our study group were similar to the general population in the southern region of Israel. According to the National Health Insurance Law, all patients have "free access" to polysomnographic studies for OSAS diagnosis. No barrier, except co-payment, exists for adults referred for a PSG study or CPAP purchase. Physicians do not have any economic incentive to prevent or deter patients from a PSG study or CPAP purchase.

Understanding obstacles to the use of CPAP by patients with OSAS is crucial to promoting successful adherence to therapy. Compliance with CPAP therapy is associated with a variety of parameters - severity of the syndrome, supportive bed partner and support from the sleep laboratory personnel and primary care physician [6, 9-11, 14, 18-20]. In the present study, we found that the same indices affect CPAP adaptation and purchase. The provision of basic information about the syndrome (possible therapeutic choices, costs and benefits) by the primary care physician and encouragement by the bed partner increased the number of patients purchasing CPAP devices, compared with those who declined CPAP therapy. It was demonstrated that the patients' main reason for seeking attention were symptoms that affect the bed partner rather than the patient [20]. These symptoms include poor subjective sleep quality and poor self-reported health status. Treatment with CPAP improved patients' subjective sleep quality and reduced their sleep disturbance. There is an association between a supportive bed partner and the patient's recognition that OSAS is a dangerous syndrome. Therefore, the bed partner serves an important role in determining the outcome of the adaptation trial, i.e., CPAP purchase.

A patient support protocol [10] was introduced to all patients and spouses since it relates to the factors (patient symptoms and mood) that drive patients to seek therapy [3, 9, 18]. The support protocol made treatment initiation easier for our patients, i.e., 95% developed a positive perception of the treatment benefits, which was similar to previous reports [20]. In spite of the support protocol and education on the negative outcomes of OSAS, only one-third of the patients began CPAP treatment. These patients were similar to patients who declined treatment, with respect to OSAS severity and co-morbidity. This result is in contrast to previous reports demonstrating that more than 70% of the patients receiving the patient support protocol, for whom a CPAP device was prescribed, commenced treatment [3, 4, 9, 10, 21]. Patients who began CPAP therapy had strong support from their primary care physicians in addition to their bed partner, both have an important role in determining CPAP treatment initiation [22]. Moreover, there is a statistical correlation between a supportive bed partner, patient education level, and the patient's recognition that OSAS is a dangerous syndrome. Greater involvement of primary care physicians in shared decision making improves treatment initiation. Finally, OSAS severity and its effects on daytime function may serve as additional impetuses to drive patients to seek therapy. However, in this study, OSAS severity did not explain poor CPAP acceptance.

In the Israeli healthcare system patients have to pay a co-payment for the CPAP device. The level of co-payment is constant, regardless of patient income level. The main argument supporting a co-payment policy is that sharing the cost of a service or medicine forces the patient to weigh the expected benefits and costs, thereby reducing unnecessary use of services [23]. From a purely economic viewpoint, co-payment is an administrative tool aimed at reducing drug expenditures on the part of the insurance carrier and thus preventing waste. Studies have shown that patients' co-payment leads to poor compliance in the purchase of prescription drugs, thus this policy discourages the purchase of prescribed drugs [13] and may lead to a negative social and medical influence. Lower income populations and those with low medical insurance coverage are the most vulnerable to this effect [13]. In this study, most of the patients had supplemental private medical insurance, which did not affect the purchase of the CPAP device. Low income level was a predictor of non-compliance, possibly due to cost (Figure 2). In contrast, patients with a higher monthly income are more likely to purchase CPAP devices. This study provides additional support to a concept presented by Becker and Maiman [24] that patients with higher socioeconomic levels are more likely to commence treatment than are patients with low socioeconomic levels. When Rauscher et al. [19] offered CPAP devices free, only 50% accepted. This could be due to offering the CPAP device to unsolicited patients with an RDI >15/hr (mild OSAS) and not using a support protocol. Income level and patient education are associated. Therefore, subjects who purchased CPAP devices were more exposed to information about their disease than patients with low income and education level.

We can presume that co-payment is a limiting factor of CPAP treatment, leading to increased inequality in a healthcare system in which co-payment is required. However, other factors such as poor patient education or unwillingness to comply with treatment cannot be completely excluded. To strengthen this presumption regarding co-payment as a limiting factor, at the conclusion of the study we conducted a telephone survey among the 161 patients (67%), clients of Clalit Health Services, who declined CPAP treatment. These patients who declined CPAP treatment represent all patients in the study group who declined CPAP treatment by socioeconomic characteristics. Of those, 40% acknowledged that cost was the barrier to purchasing the CPAP device, other causes mainly include side effects and discomfort from using the device. Therefore, it is possible that reducing cost sharing will increase CPAP treatment initiation. Further studies are needed to clarify the effect of co-payment as a limiting factor on CPAP treatment and the level of co-payment needed to achieve maximal compliance with CPAP treatment.
Conclusions
CPAP treatment initiation in Israel, where co-payment is required, is influenced by multiple factors – patient and spouse complaints, recognition that OSAS is a dangerous syndrome, PSG findings and socioeconomic parameters. In spite of a supportive environment by a bed partner and a physician, only one-third of the OSAS patients purchased CPAP devices and began treatment. Co-payment possibly affects CPAP treatment initiation especially among patients with low income. Therefore, further studies are needed to define whether minimizing the co-payment level will increase CPAP purchase and treatment initiation.

References

Correspondence: Dr A. Tarasiuk, Sleep-Wake Disorders Unit, Soroka University Medical Center, P.O. Box 151, Beer Sheva 84105, Israel. Phone: (972-8) 640-3049 Fax: (972-8) 640-3886 email: tarasiuk@bgu.ac.il

**Capsule**

**Blocking amyloid formation**
The inhibition of protein-protein interactions remains one of the “Holy Grails” of chemical biology and drug design. Gestwicki et al. describe a strategy to inhibit the protein-protein interactions that lead to amyloid beta (A) oligomerization and Alzheimer’s disease. The approach involves recruiting endogenous chaperones to aggregating A using bifunctional small molecules. Several model compounds were produced that acted as potent inhibitors of A aggregation.

*Science* 2004; 306:865 E. Israeli

**Capsule**

**Autophagy in health and disease**
Autophagy, the process by which cells sequester and degrade organelles and cytoplasm in times of stress, is being recognized as playing a role in a variety of disease processes. Shintani and Klionsky (*Science* 2004; 306:990) review the sometimes paradoxical roles of autophagy in human health, disease, and aging. Nakagawa et al. (p. 1037) describe how cells can clear an invading pathogen, group A Streptococcus, by targeting the cytosolic bacteria for destruction by the cellular autophagy machinery.

E. Israeli