

Effect of Telemedicine Education and Telemonitoring on Continuous Positive Airway Pressure Adherence

The Tele-OSA Randomized Trial

Dennis Hwang¹, Jeremiah W. Chang¹, Adam V. Benjafield², Maureen E. Crocker², Colleen Kelly³, Kendra A. Becker¹, Joseph B. Kim¹, Rosa R. Woodrum¹, Joanne Liang¹, and Stephen F. Derose^{1,4}

¹Division of Sleep Medicine, Southern California Permanente Medical Group, ²ResMed Science Center, ResMed Corporation, and ³Kelly Statistical Consulting, and ⁴Department of Research and Evaluation, Southern California Permanente Medical Group, Fontana, California

ORCID IDs: 0000-0002-4070-1640 (D.H.); 0000-0002-5150-7229 (M.E.C.).

Abstract

Rationale: Automated telemedicine interventions could potentially improve adherence to continuous positive airway pressure (CPAP) therapy.

Objectives: Examining the effects of telemedicine-delivered obstructive sleep apnea (OSA) education and CPAP telemonitoring with automated patient feedback messaging on CPAP adherence.

Methods: This four-arm, randomized, factorial design clinical trial enrolled 1,455 patients (51.0% women; age, 49.1 ± 12.5 yr [mean \pm SD]) referred for suspected OSA. Nine hundred and fifty-six underwent home sleep apnea testing, and 556 were prescribed CPAP. Two telemedicine interventions were implemented: 1) web-based OSA education (Tel-Ed) and 2) CPAP telemonitoring with automated patient feedback (Tel-TM). Patients were randomized to 1) usual care, 2) Tel-Ed added, 3) Tel-TM added, or 4) Tel-Ed and Tel-TM added (Tel-both).

Measurements and Main Results: The primary endpoint was 90-day CPAP usage. Secondary endpoints included attendance to OSA evaluation, and change in Epworth Sleepiness Scale score. CPAP average daily use at 90 days was 3.8 ± 2.5 , 4.0 ± 2.4 , 4.4 ± 2.2 , and 4.8 ± 2.3 hours in usual care, Tel-Ed, Tel-TM, and Tel-both groups. Usage was significantly higher in the Tel-TM and Tel-both groups versus usual care ($P = 0.0002$ for both) but not for Tel-Ed ($P = 0.10$). Medicare adherence rates were 53.5, 61.0, 65.6, and 73.2% in usual care, Tel-Ed, Tel-TM, and Tel-both groups (Tel-both vs. usual care, $P = 0.001$; Tel-TM vs. usual care, $P = 0.003$; Tel-Ed vs. usual care, $P = 0.07$), respectively. Telemedicine education improved clinic attendance compared with no telemedicine education (show rate, 68.5 vs. 62.7%; $P = 0.02$).

Conclusions: The use of CPAP telemonitoring with automated feedback messaging improved 90-day adherence in patients with OSA. Telemedicine-based education did not significantly improve CPAP adherence but did increase clinic attendance for OSA evaluation.

Clinical trial registered with www.clinicaltrials.gov (NCT02279901).

Keywords: disease management; patient compliance; telehealth

(Received in original form March 20, 2017; accepted in final form August 29, 2017)

Supported by a grant from the American Sleep Medicine Foundation. ResMed supported the study by providing use of the U-Sleep automated feedback platform. Medical writing support was provided by Nicola Ryan, independent medical writer, funded by ResMed. Biostatistical support was provided by Colleen Kelly, Ph.D., independent biostatistician, funded by ResMed. The steering committee oversaw the conduct of the trial and data analysis in collaboration with the sponsor according to a predefined statistical analysis plan. The trial was reviewed by an independent data and safety monitoring committee. The first draft of the manuscript was prepared by D.H., J.W.C., and S.F.D., who had unrestricted access to the data, with the assistance of C.K. and an independent medical writer funded by ResMed.

Author Contributions: All authors were involved in the conception and design of the study, data collection, and data analysis and interpretation. The article was initially drafted by D.H., with assistance from an independent medical writer. All authors provided critical revision of the article and approved the final version of the manuscript. The manuscript was reviewed and edited by all the authors. All authors made the decision to submit the manuscript for publication and assume responsibility for the accuracy and completeness of the analyses and for the fidelity of this report to the trial protocol.

Correspondence and requests for reprints should be addressed to Dennis Hwang, M.D., 9961 Sierra Avenue, Fontana, CA 92335. E-mail: dennis.x.hwang@kp.org.

This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

Am J Respir Crit Care Med Vol 197, Iss 1, pp 117–126, Jan 1, 2018

Copyright © 2018 by the American Thoracic Society

Originally Published in Press as DOI: 10.1164/rccm.201703-0582OC on August 31, 2017

Internet address: www.atsjournals.org

At a Glance Commentary

Scientific Knowledge on the

Subject: Although continuous positive airway pressure (CPAP) therapy is effective at improving outcomes and considered the treatment of choice for obstructive sleep apnea (OSA), optimizing adherence remains challenging. Strategies to improve adherence typically focus on enhancing OSA education and providing accountability through follow-up care; however, these activities are labor-intensive and difficult to deliver cost-effectively. Telemedicine is understood to be a necessary solution for the evolving healthcare environment. This study investigates whether telemedicine platforms with automated functions to provide education and accountability can be cost-effective solutions for sleep medicine.

What This Study Adds to the

Field: The results of this four-arm randomized clinical trial demonstrate that CPAP telemonitoring (which provides automated patient-messaging feedback based on CPAP use) significantly improved 90-day adherence. Furthermore, the improvement was observed without requiring additional provider intervention. In contrast, a remotely delivered automated education program did not improve adherence. However, it did improve attendance rates to appointments, demonstrating improved patient engagement despite no overt impact on CPAP use. The results suggest that these telemedicine mechanisms may be cost-effective solutions for the care of patients with OSA; furthermore, these mechanisms may be generalizable as solutions for other chronic diseases.

Obstructive sleep apnea (OSA) represents a significant disease and public health burden given its high prevalence, impact on quality of life, and association with cardiovascular disease (1, 2). Continuous positive airway pressure (CPAP) therapy is considered the “gold standard” treatment for OSA and is recommended as first-line

therapy in the majority of patients (3, 4). CPAP significantly decreases the number of respiratory events; improves daytime symptoms, quality of life, and neurocognitive function; reduces the risk of traffic accidents (5–11); and has beneficial effects on a number of cardiovascular comorbidities (12–19). However, regular and consistent device usage is required for the benefits of CPAP therapy to be realized, and optimizing CPAP adherence remains a significant challenge (14). Three months after initiation of therapy the proportion of patients who remain adherent to CPAP is typically only about 50 or 60% (20, 21).

Improvements in CPAP device technology have had little effect on improving adherence. Instead, interventions designed to enhance adherence have largely focused on engaging psychosocial factors that emphasize patient education and follow-up care (22–26). However, these approaches are labor-intensive, making them potentially difficult to deliver cost-effectively. Availability of sleep medicine specialists and overburdened primary care physicians create additional challenges.

Telemedicine—the remote delivery of care with the use of technology—is a potential solution for efficient delivery of education and enhanced follow-up care. Advances in CPAP technology have integrated wireless capabilities that enable transfer of CPAP data via a cellular signal for remote monitoring by medical providers. Furthermore, automated algorithms can analyze these data and send automated, individualized patient messages when use is suboptimal. In addition, web-based programs that inform patients about OSA can enable education outside the clinical setting.

The Tele-OSA study evaluated the impact of two telemedicine interventions (web-based OSA education and CPAP telemonitoring program with automated feedback messaging), alone and in combination, on CPAP adherence in patients with OSA. Some of the results of this study have been previously reported in the form of abstracts (27–29).

Methods

Study Design and Participants

The Tele-OSA study was a four-arm, randomized, factorial-design clinical trial conducted at a single sleep center that serves

a large medical center in Southern California. The study was conducted within the context of the sleep center’s usual clinical care procedures for the diagnosis and management of OSA (Figure 1). Most patients are referred by primary care physicians, and a sleep medicine physician triages appropriate patients to home sleep apnea testing (HSAT) after review of the referral information and electronic health record chart. HSAT classes (up to 13 people) are led by a sleep-trained respiratory therapist and sleep technologist and provide interactive OSA education and individualized HSAT setup. After a one-night test, each patient returns for an individual appointment with a respiratory therapist to review the results. Those with OSA are recommended to undergo a 1-week CPAP trial followed by an individual return appointment with a respiratory therapist to review CPAP data and patient experience. Patients willing to commit to CPAP therapy are immediately dispensed a device; otherwise CPAP troubleshooting or alternative treatments are discussed. Sleep medicine–boarded physicians supervise the workflow and review all sleep study and CPAP data. Clinicians providing routine care and study analysts were blinded to study arm assignment. The study protocol was approved by the Kaiser Permanente Southern California Institutional Review Board. Written informed consent requirement was waived after review determined that the study involved no more than minimal risk to subjects and that the waiver would not adversely affect the rights and welfare of subjects.

Consecutive patients referred to the Kaiser Permanente Fontana Sleep Disorders Center (Fontana, CA) for evaluation of suspected OSA and triaged to HSAT between November 2014 and August 2015 were enrolled into the study. Eligible patients were at least 18 years of age, had no previous sleep testing or trial of OSA therapy, and were eligible for HSAT. Patients were excluded if they were at risk of other sleep disorders (e.g., severe insomnia), had significant cardiopulmonary disease (e.g., heart failure, chronic respiratory failure), or did not indicate English as their preferred language.

All patients who were prescribed CPAP were provided an autotitrating device (AirSense 10; ResMed Corp) capable of wirelessly transmitting CPAP data daily via

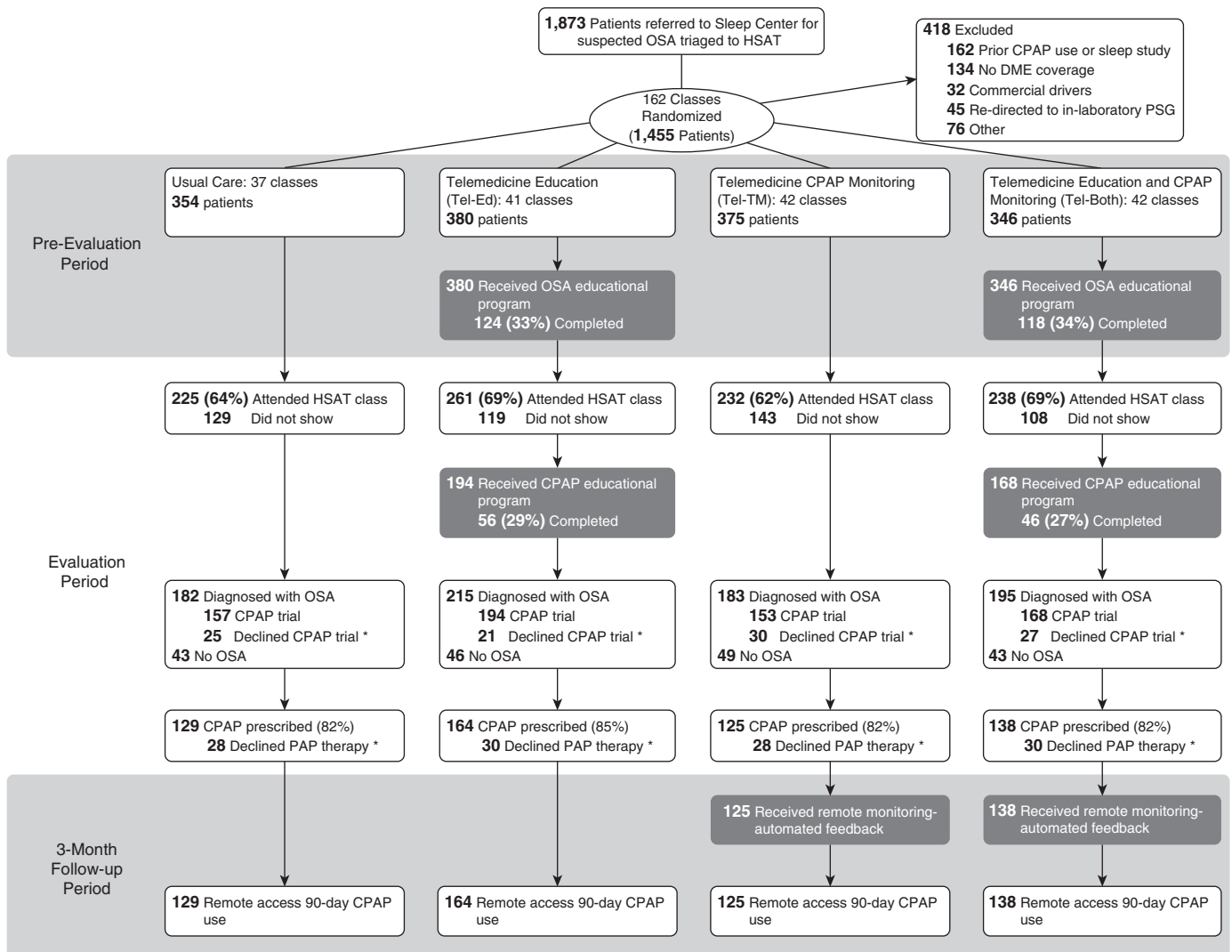


Figure 1. Study flowchart. CPAP = continuous positive airway pressure; DME = durable medical equipment; HSAT = home sleep apnea testing; OSA = obstructive sleep apnea; PAP = positive airway pressure; PSG = polysomnography; Tel-both = telemedicine-based education and telemonitoring; Tel-Ed = telemedicine-based education; Tel-TM = telemedicine-based telemonitoring. *Opted for conservative management or alternative therapy.

a cellular signal into a cloud database (U-Sleep; ResMed Corp).

Randomization and Masking

To conform to the sleep center's usual care procedures, groups of patients were randomized, with all participants in each HSAT class following the same treatment arm. Classes were randomized (1:1:1:1) to be managed using 1) usual care alone, 2) usual care plus telemedicine web-based education (Tel-Ed), 3) usual care plus CPAP telemonitoring with automated feedback messaging based on usage data for 90 days (Tel-TM), or 4) usual care plus both telemedicine-based education and telemonitoring with feedback messaging

(Tel-both). Randomization was performed for each HSAT class (not in blocks), using a computerized random number generator.

Interventions

The usual care pathway is shown in Figure 1. Briefly, all patients attended a 1-hour, small-group education class with HSAT setup. During the session, sleep apnea education was provided, CPAP therapy was briefly described, and the HSAT setup procedure was taught. Patients with an apnea-hypopnea index (AHI; hypopneas were associated with $\geq 4\%$ oxygen desaturation) of at least 5 per hour ($AHI \geq 5$) were provided a CPAP trial, typically for 1 week. After the trial, those

willing to continue CPAP were prescribed therapy and scheduled for a 3-month follow-up appointment.

The two telemedicine interventions in this study were designed to target different psychosocial factors: education and accountability. Two OSA-specific educational programs were used, developed by a company specializing in providing user-friendly patient education programs (Emmi; Emmi Solutions Inc.). In the Tel-Ed arm, patients were e-mailed a link to the OSA program 2 weeks before their HSAT class. All patients in all study groups received an appointment reminder call at that time. The first program included education about the pathophysiology of

OSA (including animated videos depicting airway narrowing), health-related risks such as cardiovascular disease and impact on daytime vigilance, an introduction to CPAP therapy, and details of the assessment process. In patients eventually determined to have OSA, a link to a second education program was e-mailed during their 1-week CPAP trial with focused education on how to properly use CPAP, potential benefits of treatment on health and daytime vigilance, methods of acclimating, and equipment care instructions (see example in Figure E1 in the online supplement). The education sessions were interactive and typically lasted 15 minutes, although patients were able to proceed at their preferred pace. Links to both programs were e-mailed to the patient with a personalized invitation that required date of birth verification for activation.

The Tel-TM intervention was based on automatic processing of device data by the cloud-based application (U-Sleep; ResMed Corp). When receiving their CPAP device, patients were educated about the automated feedback process and asked to state their preferred method for receiving messages (text messaging, e-mail, phone call, or a combination). During the 3-month study period, if CPAP usage thresholds were met, a message was automatically sent to the patient providing encouragement to improve use or positively reinforcing successful adherence (Table E1).

Patients randomized to the Tel-both arm received both the web-based education programs and the automated feedback messaging.

Assessments and Outcomes

Patient demographic and clinical characteristics were determined at baseline, and sleep study findings were recorded. Patients completed the Epworth Sleepiness Scale (ESS) and Functional Outcomes of Sleep Questionnaire (FOSQ-10) at baseline and at their 3-month follow-up appointment. CPAP usage data at 90 days were collected wirelessly from all patients. Also recorded was the 95th percentile of CPAP pressure, median mask leak, and residual AHI for population description. For patients in the Tel-Ed and Tel-both groups, educational program viewing status was determined for each patient. The number of clinical encounters (including office and telephone encounters) also was recorded.

The primary outcome was CPAP usage (days used, hours per day). Other adherence metrics were assessed including whether Medicare adherence (defined as a 30-d period during the first 3 mo of therapy in which CPAP use was ≥ 4 h/night on $\geq 70\%$ of days) was achieved. Secondary end points were attendance rates to the HSAT class and change in ESS and FOSQ-10 scores at 3-month follow-up. In a *post hoc* analysis, we examined long-term outcomes up to 360 days to determine whether the observed treatment effect persisted longer than the planned 90 days.

Statistical Analysis

To detect a 0.5-hour increase in average nightly CPAP usage with a standard deviation of 2.2 hours (as found in the Fox and colleagues study [30]) with 80% probability, it was estimated that 283 patients per group would be required at the 0.05 significance level. Power was estimated with Power Analysis and Sample Size (PASS) software version 14 (NCSS) using the one-way analysis of variance *F*-test procedure.

Mixed-effect general linear models were used to assess the effects of the interventions on the percentage of days that CPAP was used 4 hours or more in the first 90 days, the average hours of CPAP usage per day (all days) for the first 90 days, the average hours of CPAP usage per day (on days with CPAP use) for the first 90 days, change in ESS score, and change in FOSQ-10 score. The Tel-Ed and Tel-TM interventions were treated as fixed effects and the HSAT class in which each patient was enrolled was treated as a random effect nested in the treatment group (to account for potential correlations within classes). Similarly, mixed-effects logistic regression models were used to assess the effects of the intervention on Medicare adherence rates and HSAT class attendance rates, with effects as described above. An interaction term between Tel-Ed and Tel-TM was investigated for all outcome variables, but was not statistically significant ($P > 0.05$) for any variable and thus was not retained in the model. HSAT class attendance rates were compared between patients with the telemedicine education intervention and those without.

The percentage of days with CPAP use was compared between the combined groups with telemonitoring (Tel-TM and Tel-both) and the combined groups without

telemonitoring (usual care and Tel-Ed) at 30-day intervals up to 360 days. After 90 days, the telemonitoring arm was divided into two arms (feedback messaging continued vs. messaging discontinued). Means at each time point were compared by Student *t* tests adjusted with a Bonferroni correction. Relative changes in the percentage of days with CPAP use were calculated between time point “a” (0–30 d) and time point “b” (30–60 d), and between point “b” (30–60 d) and point “c” (60–90 d). Relative changes were then compared by Student *t* test and adjusted with a Bonferroni correction. A *P* value less than 0.05 was defined as statistically significant. All statistical analyses were performed with SAS versions 9.3 and 9.4 (SAS Institute).

Results

Study Population

Patients (1,873) were referred to the sleep center for suspected OSA and triaged to HSAT from November 2014 to August 2015. Recruitment closed when targeted accrual appeared to be reached. After excluding 418 patients who did not meet eligibility requirements (usually due to prior sleep study or CPAP use), 162 HSAT classes—accounting for 1,455 patients—were randomized (Figure 1). Overall, 66% showed up for the HSAT class and were tested, and 81.1% of those tested were diagnosed with OSA (AHI ≥ 5). Five hundred and fifty-six patients (38.2% of all randomized patients; 71.7% of all patients with OSA) were eventually prescribed CPAP, all of whom had 90-day usage data to be included for analysis. Baseline demographics, clinical characteristics, sleep study results, and CPAP trial data are shown in Table 1, and data for those prescribed CPAP therapy are shown in Table 2. The rate of CPAP prescriptions (among those randomized) and baseline characteristics for those prescribed CPAP were similar between the four arms.

Patient-selected formats for automated messages in the Tel-TM and Tel-both groups were e-mail (31.7%), text messaging (17.5%), phone (2.3%), or a combination (40.3%); 22 patients (8.4%) declined messaging but were included in the analysis for each group. Likewise, although the two education programs were accessed by only 27–34% of patients (Figure 1), all were also

Table 1. Baseline Characteristics of Study Patients

	All	Usual Care	Tel-Ed	Tel-TM	Tel-Both
Demographics	<i>n</i> = 1,455	<i>n</i> = 354	<i>n</i> = 380	<i>n</i> = 375	<i>n</i> = 346
Male, <i>n</i> (%)	713 (49.0)	163 (46.0)	186 (48.9)	193 (51.5)	171 (49.4)
Age, yr	49.1 ± 12.5	50.2 ± 12.7	49.1 ± 12.2	47.2 ± 12.5	49.7 ± 12.3
Ethnicity, <i>n</i> (%)					
African American	48 (3.3)	8 (2.3)	12 (3.2)	13 (3.5)	15 (4.3)
Asian	89 (6.1)	25 (7.1)	17 (4.5)	26 (6.9)	21 (6.1)
White	782 (53.8)	191 (54.0)	212 (55.8)	194 (51.7)	185 (53.5)
Hispanic	517 (35.5)	125 (35.3)	136 (35.8)	137 (36.5)	119 (34.4)
Other	19 (1.3)	5 (1.4)	3 (0.8)	5 (1.3)	6 (1.7)
Clinical data	<i>n</i> = 956	<i>n</i> = 225	<i>n</i> = 261	<i>n</i> = 232	<i>n</i> = 238
BMI, kg/m ²	34.0 ± 7.9	33.3 ± 7.8	34.8 ± 7.9	34.5 ± 8.4	33.5 ± 7.6
Sleep history					
Sleep time,* h	6.4 ± 1.3	6.3 ± 1.2	6.5 ± 1.2	6.4 ± 1.4	6.5 ± 1.4
Sleep latency,* min	27.8 ± 29.3	30.3 ± 27.5	27.1 ± 30.6	28.8 ± 31.1	25.4 ± 27.2
Wake instances,* <i>n</i>	2.7 ± 1.8	3.1 ± 2.1	2.7 ± 1.9	2.4 ± 1.6	2.5 ± 1.6
Caffeine servings,* <i>n</i>	1.9 ± 1.2	1.8 ± 1.0	1.9 ± 1.2	2.0 ± 1.3	1.9 ± 1.1
ESS score	9.1 ± 5.4	8.8 ± 5.1	9.4 ± 5.5	9.5 ± 5.7	8.5 ± 5.2
FOSQ-10 score	25.5 ± 10.2	26.9 ± 9.5	25.5 ± 9.9	24.8 ± 10.6	25.0 ± 10.5
Sleep study results	<i>n</i> = 956	<i>n</i> = 225	<i>n</i> = 261	<i>n</i> = 232	<i>n</i> = 238
AHI, h ⁻¹	22.7 ± 23.9	22.0 ± 23.4	22.6 ± 23.8	22.8 ± 25.2	23.2 ± 23.1
Supine AHI, h ⁻¹	32.7 ± 31.9	32.1 ± 36.9	33.7 ± 30.7	32.6 ± 31.4	32.1 ± 28.5
Nonsupine AHI, h ⁻¹	17.3 ± 24.1	16.6 ± 23.3	17.4 ± 23.2	18.0 ± 27.4	17.2 ± 22.4
ODI, h ⁻¹	20.3 ± 22.3	19.8 ± 22.2	20.6 ± 22.9	20.3 ± 23.0	20.4 ± 21.3
T90, %	13.9 ± 20.0	12.9 ± 17.8	14.6 ± 20.4	14.2 ± 21.7	13.8 ± 19.8
Minimum So ₂ , %	79.3 ± 9.0	80.1 ± 8.1	78.8 ± 9.5	79.5 ± 8.7	78.9 ± 9.6
Auto-CPAP trial	<i>n</i> = 672	<i>n</i> = 157	<i>n</i> = 194	<i>n</i> = 153	<i>n</i> = 168
Duration, d	9.9 ± 11.3	10.0 ± 8.3	8.5 ± 5.3	11.0 ± 18.2	10.2 ± 10.6
Days used, <i>n</i>	7.1 ± 4.5	7.1 ± 5.2	7.2 ± 4.2	7.1 ± 4.1	7.0 ± 4.3
Days used, %	85.4 ± 24.9	81.9 ± 28.5	87.7 ± 20.7	86.5 ± 24.4	85.1 ± 26.0
Days used for ≥4 h, %	63.0 ± 34.6	60.1 ± 36.6	64.8 ± 32.7	60.2 ± 36.1	66.3 ± 33.4
Average usage on all days, h	4.9 ± 2.5	4.6 ± 2.5	5.1 ± 2.5	4.8 ± 2.4	5.1 ± 2.4
Average usage on days used, h	5.3 ± 2.2	5.0 ± 2.4	5.5 ± 2.1	5.1 ± 2.2	5.5 ± 2.1
95th percentile pressure, cm H ₂ O	10.3 ± 2.5	10.0 ± 2.6	10.6 ± 2.3	10.2 ± 2.5	10.4 ± 2.4
Median leak, L/min	3.5 ± 6.8	4.0 ± 10.8	2.9 ± 5.0	3.7 ± 5.1	3.6 ± 5.0
Residual AHI, h ⁻¹	2.9 ± 3.2	2.6 ± 3.3	3.0 ± 3.2	3.0 ± 3.2	3.1 ± 3.3

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; ODI = oxygen desaturation index; So₂ = oxygen saturation; T90 = time with oxygen saturation less than 90%; Tel-both = telemedicine-based education and telemonitoring; Tel-Ed = telemedicine-based education; Tel-TM = telemedicine-based telemonitoring.

Values represent means ± SD, or number of patients (%).

*Self-reported.

included in the analysis. The mean number of telemonitoring messages was 18 (median, 8).

CPAP Usage and Adherence

CPAP adherence results are reported in Table 3. The effect of Tel-Ed was not statistically significant for any primary outcome ($P > 0.05$). In contrast, the Tel-TM and Tel-both groups showed a statistically significant increase in average usage across all days, compared with the usual care group (4.4 and 4.8 h vs. 3.7 h; $P = 0.0002$). The Tel-TM and Tel-both groups also showed a significant increase, compared with usual care, in the

proportion of days that CPAP was used (76.6 and 78.3% vs. 64.8%; $P < 0.0001$ and 0.0004) and in Medicare adherence rates (65.6 and 73.2% vs. 53.5%; $P = 0.003$ and 0.001). The odds of achieving Medicare adherence were 2.4 times higher (95% confidence interval, 1.4–4.0) in the Tel-both group and 1.7 times higher in the Tel-TM group (95% confidence interval, 1.2–2.4) than in the usual care group.

Self-Reported Sleep Symptoms

There were improvements in all study arms in the self-reported sleep symptoms (the ESS and the FOSQ-10) over 3 months (Table 3). Analyses did not reveal any differences in

the change in ESS or the FOSQ-10 scores in any intervention study arm versus usual care.

Healthcare Use

Attendance at the HSAT class was 1.3 times higher among patients who received the telemedicine education program compared with those who did not (Tel-Ed + Tel-both attendance, 68.5% vs. usual care + Tel-TM attendance, 62.7%; $P = 0.02$). The telemedicine program did not affect CPAP dispensation rates for patients with OSA, which ranged from 82 to 85% of those undergoing a CPAP trial across study arms (Figure 1). The number of sleep center

Table 2. Baseline Characteristics of Participants Prescribed Continuous Positive Airway Pressure

	All (n = 556)	Usual Care (n = 129)	Tel-Ed (n = 164)	Tel-TM (n = 125)	Tel-Both (n = 138)
Demographics					
Male, n (%)	325 (58.5)	73 (56.6)	91 (55.5)	76 (60.8)	85 (61.6)
Age, yr	50.5 ± 12.1	51.9 ± 13.1	50.3 ± 11.8	48.8 ± 11.8	50.7 ± 11.7
Ethnicity, n (%)					
African American	22 (4.0)	3 (2.3)	5 (3.0)	7 (5.6)	7 (5.1)
Asian	39 (7.0)	11 (8.5)	9 (5.5)	7 (5.6)	12 (8.7)
White	301 (54.1)	72 (55.8)	88 (53.7)	68 (54.4)	73 (52.9)
Hispanic	189 (34.0)	41 (31.8)	62 (37.8)	43 (34.4)	43 (31.2)
Other	5 (0.9)	2 (1.6)	0 (0.0)	0 (0.0)	3 (2.2)
Clinical data					
BMI, kg/m ²	34.5 ± 7.7	33.4 ± 7.4	35.4 ± 8.0	34.8 ± 7.8	34.3 ± 7.5
Sleep history					
Sleep time, h	6.4 ± 1.3	6.3 ± 1.2	6.5 ± 1.3	6.4 ± 1.3	6.5 ± 1.3
Sleep latency, min	27.6 ± 30.0	30.0 ± 27.5	26.7 ± 32.1	28.9 ± 32.0	25.6 ± 27.8
Wake instances, n	2.7 ± 1.8	3.1 ± 1.9	2.8 ± 2.0	2.3 ± 1.3	2.7 ± 1.6
Caffeine servings, n	1.9 ± 1.3	1.8 ± 1.0	1.9 ± 1.4	2.0 ± 1.5	1.9 ± 1.2
ESS score	9.6 ± 5.2	9.5 ± 4.9	9.6 ± 5.2	10.4 ± 5.5	8.7 ± 5.2
FOSQ-10 score	25.8 ± 9.8	27.6 ± 8.8	25.2 ± 10.0	25.6 ± 9.7	25.2 ± 10.3
Sleep study results					
AHI, per h	31.9 ± 25.8	31.5 ± 25.5	30.2 ± 25.9	33.5 ± 27.1	32.6 ± 24.7
Supine AHI, per h	42.8 ± 30.1	41.7 ± 30.8	41.1 ± 30.4	45.8 ± 31.0	43.3 ± 28.3
Nonsupine AHI, per h	24.4 ± 27.6	23.6 ± 27.1	22.8 ± 26.3	26.2 ± 31.7	25.4 ± 25.7
ODI, per h	28.5 ± 24.5	28.1 ± 24.3	27.9 ± 25.3	29.3 ± 25.2	28.9 ± 23.3
T90, %	18.8 ± 21.9	17.0 ± 18.5	18.7 ± 22.2	20.0 ± 23.7	19.5 ± 22.8
Minimum So ₂ , %	76.5 ± 9.2	77.8 ± 7.5	76.3 ± 10.0	76.0 ± 9.0	75.8 ± 10.0
Auto-CPAP trial					
Duration, d	8.2 ± 5.3	8.7 ± 6.4	8.4 ± 5.1	7.8 ± 4.4	8.0 ± 5.2
Days used, n	7.4 ± 4.3	7.6 ± 4.9	7.5 ± 4.2	7.1 ± 3.9	7.3 ± 4.3
Days used, %	92.6 ± 14.1	92.0 ± 14.7	91.7 ± 15.2	93.7 ± 12.8	93.2 ± 13.4
Days used for ≥4 h, %	71.9 ± 28.1	71.7 ± 28.5	69.6 ± 29.3	70.2 ± 29.3	76.4 ± 25.0
Average usage on all days, h	5.5 ± 2.0	5.4 ± 2.0	5.4 ± 2.3	5.4 ± 1.9	5.7 ± 1.9
Average usage on days used, h	5.8 ± 1.8	5.8 ± 1.8	5.7 ± 1.9	5.6 ± 1.8	6.1 ± 1.6
95th percentile pressure, cm H ₂ O	10.7 ± 2.3	10.4 ± 2.4	10.8 ± 2.3	10.7 ± 2.2	10.8 ± 2.2
Median leak, L/min	3.4 ± 5.0	3.2 ± 4.8	3.0 ± 5.0	3.8 ± 5.2	3.6 ± 5.1
Residual AHI, per h	2.9 ± 2.9	2.6 ± 2.7	2.8 ± 2.9	3.1 ± 3.3	3.0 ± 2.9

Definition of abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; ODI = oxygen desaturation index; So₂ = oxygen saturation; T90 = time with oxygen saturation less than 90%; Tel-both = telemedicine-based education and telemonitoring; Tel-Ed = telemedicine-based education; Tel-TM = telemedicine-based telemonitoring. Values represent means ± SD, or number of patients (%).

encounters (office visits or telephone calls) during the 90-day follow-up period was low and did not differ significantly between intervention groups. The median number of encounters per patient was zero, and all means were not more than 0.5 per person.

Temporal Analysis of Usage

Time trends in days of CPAP use were examined (Figure 2) for combined telemonitoring groups (Tel-TM + Tel-both) and combined nonmessaging groups (usual care + Tel-Ed). Telemonitoring with automated messaging had an early impact (0–30 d) with a higher percentage of days of CPAP use (83.3 vs. 76.2% of days; $P = 0.002$) (Figure 2). The CPAP usage rate

declined in all groups, although more slowly (from 0–30 to 30–60 d) in the groups with versus the groups without telemonitoring (–5.8 vs. –17.1%; $P = 0.04$). The rate of decline from 30–60 to 60–90 days was similar between groups, suggesting that the impact of telemonitoring with automated feedback messaging was primarily during the first 60 days after CPAP dispensation. Other usage metrics (e.g., percentage of days used ≥ 4 h, hours of use per day) showed similar findings (data not shown).

In a *post hoc* analysis, we decided to examine CPAP usage and adherence data at 1 year after CPAP dispensation (Figure 2). In doing so, we discovered that 73 patients

had telemessaging continued past the 90-day study outcome date because of a failure to turn off messaging. Insofar as we can tell, these errors were an arbitrary process (i.e., staff forgetting as rolling study completion dates were passed). In Figure 2, CPAP usage among patients who had automated feedback messaging discontinued after 90 days gradually declined to levels that appeared the same as those of patients who never had automated feedback messaging. In contrast, the 73 patients who mistakenly continued to receive automated feedback messaging appeared to sustain greater CPAP use than patients who never received messaging or had messaging discontinued (percentage

Table 3. CPAP Use and Subjective Outcomes 90 Days after CPAP Dispensation

	Usual Care	Tel-Ed	Tel-TM	Tel-Both	Tel-Ed Effect (95% CI), P Value	Tel-TM Effect (95% CI), P Value	Tel-Both Effect (95% CI), P Value
Days used, %	n = 129 64.8 ± 34.2	n = 163 68.6 ± 31.3	n = 125 76.6 ± 28.3	n = 138 78.3 ± 28.3	2.8 (-2.3 to 7.9), 0.28	10.6 (5.5 to 15.7), <0.0001	13.4 (6.1 to 20.8), 0.0004
Average usage on all days, h	3.8 ± 2.5	4.0 ± 2.4	4.4 ± 2.2	4.8 ± 2.3	0.3 (-0.1 to 0.7), 0.10	0.8 (0.4 to 1.15), 0.0002	1.1 (0.5 to 1.7), 0.0002
Average usage on days used, h	5.2 ± 1.8	5.2 ± 1.8	5.3 ± 1.7	5.8 ± 1.6	0.2 (-0.1 to 0.5), 0.13	0.4 (0.1 to 0.7), 0.006	0.6 (0.2 to 1.0), 0.003
Medicare adherence, n (%)	69 (53.5)	100 (61.0)	82 (65.6)	101 (73.2)	1.4* (1.0 to 2.0), 0.07	1.7* (1.2 to 2.4), 0.003	2.4* (1.4 to 3.9), 0.001
Change in ESS score [†]	n = 83 -3.7 ± 4.7	n = 113 -2.8 ± 6.4	n = 90 -3.7 ± 5.2	n = 93 -3.0 ± 3.7	0.8 (-0.2 to 1.9), 0.13	-0.14 (-1.2 to 0.9), 0.80	0.7 (-0.9 to 2.3), 0.38
Change in FOSQ-10 score [†]	-14.2 ± 10.3	-9.9 ± 12.9	-10.9 ± 11.2	-11.3 ± 12.8	1.9 (-0.8 to 4.5), 0.16	0.6 (-2.0 to 3.3), 0.64	2.5 (-1.3 to 6.4), 0.20

Definition of abbreviations: CI = confidence interval; CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; Tel-both = telemedicine-based education and telemonitoring; Tel-Ed = telemedicine-based education; Tel-TM = telemedicine-based telemonitoring. Values represent means ± SD or number of patients (%).

*Reported effect is an odds ratio.

[†]Although CPAP usage data were available for all patients, ESS and FOSQ-10 were available only for those who kept their 3-month follow-up appointment.

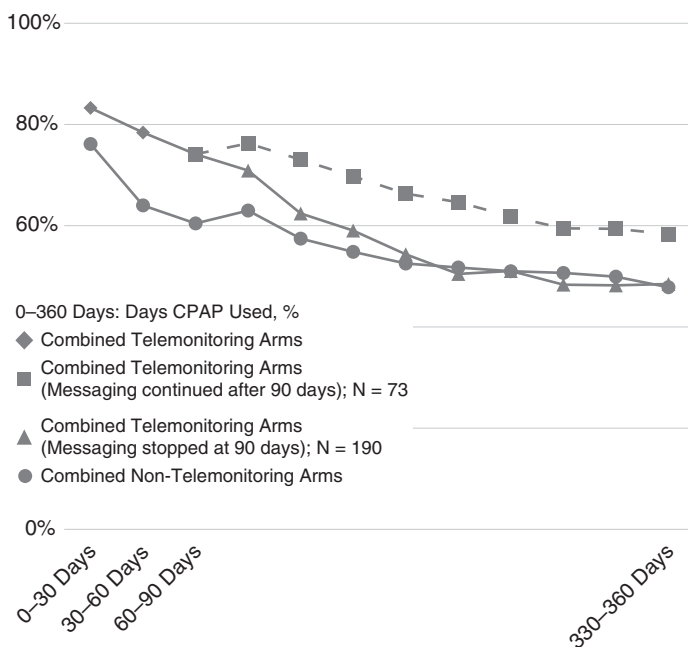


Figure 2. CPAP usage over 360 days. Because impact on CPAP adherence was limited to automated feedback messaging, this figure collapses four treatment arms into two arms to directly compare all patients with versus all patients without CPAP telemonitoring plus automated feedback messaging. Feedback messaging was arbitrarily not discontinued after 90 days in 73 patients. CPAP = continuous positive airway pressure.

of days used at 330–360 d was 58.4 ± 41.1 vs. $48.1 \pm 43.9\%$; $P = 0.05$).

Discussion

The Tele-Osa study showed that telemedicine-based automated feedback messaging improved 90-day CPAP use after therapy was prescribed. In contrast, telemedicine-based patient education had no significant effect on 90-day CPAP use, although the study was not powered to detect potentially small effects. Moreover, telemedicine education did increase attendance at the HSAT class even though the programs were not frequently accessed.

These findings suggest that accountability may be more effective than educational interventions at inducing changes in adherence behavior, although other factors could have contributed to the results. The timing of the intervention may be important, given that telemedicine-based feedback occurred during the follow-up period whereas telemedicine-education was provided before CPAP was prescribed. Another factor may have been the number of patient contacts for each intervention; access to education was provided twice,

whereas automated feedback messaging was delivered as many times as usage threshold criteria were met. Furthermore, patients could choose whether to view the educational material when they received the telemedicine-based prompt, whereas the automatic nature of messaging in the telemonitoring groups meant that patients always received messages, whether they wanted to or not. It is possible that higher viewing rates of the education programs could have improved the impact. Finally, the two telemedicine interventions could differ in their direct impact on behavioral psychology. Although education is likely necessary to provide foundational knowledge for behavior change, information and advice may not be enough to induce significant or sustained behavior changes (31). Instead, addition of motivational elements such as accountability (represented by the automated messaging in our study) or other methods such as personalized goal-setting may be essential.

Similar differences in effect of education and accountability have been seen in previous trials related to adherence to CPAP or other medical interventions. The TEXT ME trial reported that patients receiving four text messages per week (with

advice and reminders on lifestyle changes) had improved low-density lipoprotein cholesterol levels at 6 months compared with control subjects (32). In a CPAP study, Fox and colleagues demonstrated that patients randomized to CPAP remote monitoring had significantly improved 3-month adherence versus usual care (30). In that study, sleep medicine personnel manually reviewed CPAP use every weekday and contacted the patient to troubleshoot if use was less than 4 hours for two consecutive nights. On the other hand, there was no significant improvement in 3-month CPAP use in a study of an intensive 36-hour CPAP educational program that included individualized in-person discussions, focused workshops, and inclusion of spouses (33).

Another significant implication of the Tele-Osa study is that technology improved adherence without additional provider intervention, thus demonstrating the cost-effectiveness of this strategy. Follow-up care and education are labor-intensive, and automated tools such as those used in this study are likely to contribute to more efficient care delivery in the future. Although Fox and colleagues showed improved CPAP adherence with remote monitoring (30), their personnel-based approach would not be feasible in most clinical settings because of the high level of manual input and personnel time required. In contrast, our study showed benefits with automated feedback messaging without any resulting increase in patient encounters. This finding is supported by other studies demonstrating that telemedicine had equivalent CPAP outcomes to traditional follow-up but with reduced labor requirements, including one that compared a similar automated feedback messaging mechanism with personnel-based follow-up (34–37). Although the overall improvement in adherence with telemonitoring in this study was substantial, the degree of response varied between individual patients. Thus, the use of technology-based approaches should be considered as one solution among a larger set of management strategies to personalize the care for individuals (38). Finally, telemonitoring was well accepted by patients considering only a small minority of patients refused to receive messages, and no patients requested to discontinue messaging throughout the follow-up period.

This study applied two different interventions sequentially, allowing their relative impact on CPAP adherence to be assessed. Another strength of the study is the use of an established CPAP telemonitoring mechanism with established CPAP usage metrics to reliably and accurately collect objective data. There are a number of limitations that need to be taken into account. First, group rather than individual randomization was performed; nevertheless, treatment arm baseline characteristics were similar and within-group correlations were taken into account in analyses. Second, because randomization occurred before the initial diagnostic visit, there was a substantial number of “drop-outs” between randomization and CPAP prescription (primarily patients who did not have OSA or elected for non-CPAP therapies), thus limiting the ability to perform an intention-to-treat analysis and potentially introducing bias. However, the “drop-out” rate and baseline characteristics of patients prescribed CPAP were similar in the four arms and are appropriately reflective of clinical care in which many patients referred for suspected OSA are not eventually prescribed CPAP. Third, this

study was performed at a single center and health system, which may limit the generalizability of these results to other health sites and systems; however, this study had broad inclusion criteria, and study participants were representative of the sleep center’s typical patient population.

A number of important questions remain unanswered, including the impact of automated feedback messaging beyond the initial 3-month period. Longer term CPAP adherence past 90 days with ongoing automated feedback messaging was not formally assessed. Informally, in *post hoc* analyses, it appeared that continuation of messaging may be the optimal approach for sustained adherence. Additional questions include the potential impact of changing thresholds to increase message frequency or adding new triggers to provide more positive reinforcement; the possibility of personalizing automated messages for each patient, based specifically on what would motivate them the most; and whether the addition of mobile health applications that allow for individualized goal setting and self-direction of care would further enhance therapy adherence. It would also be useful to know whether implementing patient education

during the follow-up period (rather than before treatment initiation) would be more effective. Data from future trials in this new and evolving area of health care will help provide insight into these issues.

In conclusion, the use of CPAP telemonitoring with an automated feedback messaging mechanism linked to CPAP use improved 3-month CPAP adherence in patients with OSA. In this study, telemedicine-based education did not improve CPAP use to a statistically significant degree, but did improve adherence to OSA evaluation. This study supports the value of implementing automated telemedicine mechanisms into clinical sleep medicine and suggests that similar mechanisms may be useful in managing other chronic diseases. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

Acknowledgment: Additional biostatistical support was also provided by Raoul Burchette, M.S., Kaiser Permanente Department of Research and Evaluation. The authors also thank Dara Vega, R.N., and Julie DeWitte, B.S. (sleep center managers) for overseeing the clinical workflows during this study.

References

- Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, *et al.* Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study: Sleep Heart Health Study. *JAMA* 2000;283:1829–1836.
- Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. *JAMA* 2004;291:2013–2016.
- Qaseem A, Holty JE, Owens DK, Dallas P, Starkey M, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Management of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2013;159:471–483.
- Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, *et al.* Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009;5:263–276.
- Aloia MS, Ilniczky N, Di Dio P, Perlis ML, Greenblatt DW, Giles DE. Neuropsychological changes and treatment compliance in older adults with sleep apnea. *J Psychosom Res* 2003;54:71–76.
- Antonopoulos CN, Sergentanis TN, Daskalopoulou SS, Petridou ET. Nasal continuous positive airway pressure (nCPAP) treatment for obstructive sleep apnea, road traffic accidents and driving simulator performance: a meta-analysis. *Sleep Med Rev* 2011;15:301–310.
- Patel SR, White DP, Malhotra A, Stanchina ML, Ayas NT. Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. *Arch Intern Med* 2003;163:565–571.
- Stasche N. Selective indication for positive airway pressure (PAP) in sleep-related breathing disorders with obstruction. *GMS Curr Top Otorhinolaryngol Head Neck Surg* 2006;5:Doc06.
- Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep* 2010;33:1373–1380.
- Zimmerman ME, Arnedt JT, Stanchina M, Millman RP, Aloia MS. Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. *Chest* 2006;130:1772–1778.
- McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, *et al.* SAVE Investigators and Coordinators. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016;375:919–931.
- Fava C, Dorigoni S, Dalle Vedove F, Danese E, Montagnana M, Guidi GC, *et al.* Effect of CPAP on blood pressure in patients with OSA/hypopnea a systematic review and meta-analysis. *Chest* 2014;145:762–771.
- Haentjens P, Van Meerhaeghe A, Moscariello A, De Weerd S, Poppe K, Dupont A, *et al.* The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials. *Arch Intern Med* 2007;167:757–764.
- Martínez-García MA, Capote F, Campos-Rodríguez F, Lloberes P, Díaz de Atauri MJ, Somoza M, *et al.* Spanish Sleep Network. Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial. *JAMA* 2013;310:2407–2415.
- Fein AS, Shvilkin A, Shah D, Haffajee CI, Das S, Kumar K, *et al.* Treatment of obstructive sleep apnea reduces the risk of atrial fibrillation recurrence after catheter ablation. *J Am Coll Cardiol* 2013;62:300–305.
- Patel D, Mohanty P, Di Biase L, Shaheen M, Lewis WR, Quan K, *et al.* Safety and efficacy of pulmonary vein antral isolation in patients with obstructive sleep apnea: the impact of continuous positive airway pressure. *Circ Arrhythm Electrophysiol* 2010;3:445–451.

17. Cassar A, Morgenthaler TI, Lennon RJ, Rihal CS, Lerman A. Treatment of obstructive sleep apnea is associated with decreased cardiac death after percutaneous coronary intervention. *J Am Coll Cardiol* 2007;50:1310–1314.
18. Garcia-Rio F, Alonso-Fernández A, Armada E, Mediano O, Lores V, Rojo B, et al. CPAP effect on recurrent episodes in patients with sleep apnea and myocardial infarction. *Int J Cardiol* 2013;168: 1328–1335.
19. Milleron O, Pillière R, Foucher A, de Roquefeuil F, Aegerter P, Jondeau G, et al. Benefits of obstructive sleep apnoea treatment in coronary artery disease: a long-term follow-up study. *Eur Heart J* 2004;25: 728–734.
20. Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur V, et al. A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the HomePAP study. *Sleep* 2012;35: 757–767.
21. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993; 147:887–895.
22. Fuchs FS, Pittarelli A, Hahn EG, Ficker JH. Adherence to continuous positive airway pressure therapy for obstructive sleep apnea: impact of patient education after a longer treatment period. *Respiration* 2010;80:32–37.
23. Smith CE, Dautz E, Clements F, Werkowitch M, Whitman R. Patient education combined in a music and habit-forming intervention for adherence to continuous positive airway (CPAP) prescribed for sleep apnea. *Patient Educ Couns* 2009;74: 184–190.
24. Smith I, Nadig V, Lasserson TJ. Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines for adults with obstructive sleep apnoea. *Cochrane Database Syst Rev* 2009;2:CD007736.
25. Broström A, Fridlund B, Ulander M, Sunnergren O, Svanborg E, Nilsen P. A mixed method evaluation of a group-based educational programme for CPAP use in patients with obstructive sleep apnea. *J Eval Clin Pract* 2013;19:173–184.
26. Hoy CJ, Vennelle M, Kingshott RN, Engleman HM, Douglas NJ. Can intensive support improve continuous positive airway pressure use in patients with the sleep apnea/hypopnea syndrome? *Am J Respir Crit Care Med* 1999;159:1096–1100.
27. Hwang D, Chang J, Liang J, Becker K, Kim J, Woodrum R, et al. Impact of interactive web-based education and automated feedback program on CPAP adherence for the treatment of obstructive sleep apnea [abstract]. *Am J Respir Crit Care Med* 2016;193:A4186.
28. Chang J, Kim J, Becker K, Benjafield A, Crocker M, Woodrum R, et al. Impact of automated web-education and CPAP tele-monitoring on CPAP adherence at 3 months and 1 year: the Tele-OSA Randomized Clinical Trial [abstract]. *Sleep* 2017;40:A189–A190.
29. Chang J, Derose S, Benjafield A, Crocker M, Kim J, Becker K, et al. Acceptance and impact of telemedicine in patient sub-groups with obstructive sleep apnea: analysis from the Tele-OSA Randomized Clinical Trial [abstract]. *Sleep* 2017;40:A201–A202.
30. Fox N, Hirsch-Allen AJ, Goodfellow E, Wenner J, Fleetham J, Ryan CF, et al. The impact of a telemedicine monitoring system on positive airway pressure adherence in patients with obstructive sleep apnea: a randomized controlled trial. *Sleep* 2012;35:477–481.
31. EUFIC. Motivating behaviour change [2014 Jul 1; accessed 2016 Aug 2]. Available from: <http://www.eufic.org/en/healthy-living/article/motivating-behaviour-change>.
32. Chow CK, Redfern J, Hillis GS, Thakkar J, Santo K, Hackett ML, et al. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: a randomized clinical trial. *JAMA* 2015;314:1255–1263.
33. Golay A, Girard A, Grandin S, Métrailler JC, Victorion M, Lebas P, et al. A new educational program for patients suffering from sleep apnea syndrome. *Patient Educ Couns* 2006;60:220–227.
34. Isetta V, León C, Torres M, Embid C, Roca J, Navajas D, et al. Telemedicine-based approach for obstructive sleep apnea management: building evidence. *Interact J Med Res* 2014;3:e6.
35. Isetta V, Negrín MA, Monasterio C, Masa JF, Feu N, Álvarez A, et al. Spanish Sleep Network. A Bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: a multicentre randomised controlled trial. *Thorax* 2015;70:1054–1061.
36. Turino C, de Batlle J, Woehle H, Mayoral A, Castro-Grattoni AL, Gómez S, et al. Management of continuous positive airway pressure treatment compliance using telemonitoring in obstructive sleep apnoea. *Eur Respir J* 2017;49:1601128.
37. Munafò D, Hevener W, Crocker M, Willes L, Sridasome S, Muhsin M. A telehealth program for CPAP adherence reduces labor and yields similar adherence and efficacy when compared to standard of care. *Sleep Breath* 2016;20:777–785.
38. Sabate E. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003.