Improving the Frequency and Quality of Sleep Apnea Care Management

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BACKGROUND:

Obstructive sleep apnea (OSA) is highly prevalent in the Veteran population given the risk factors of male gender, being overweight, and increasing age. OSA is caused by upper airway obstruction, resulting in arousals from sleep and hypoxia. While continuous positive airway pressure (CPAP) is a highly efficacious treatment for OSA, adherence with treatment is suboptimal. Because research is clear that adherence patterns are established early in treatment, we evaluated an mHealth intervention to facilitate early, productive interactions between patient and provider that improve the quality of care and ultimately improve adherence with therapy and outcomes. The mHealth interventional approach can allow for improved, more timely delivery of our Sleep Apnea Self-Management Program (SM).

OBJECTIVES:

The objective of this proposal was to evaluate an mHealth system for patients with Obstructive Sleep Apnea syndrome (OSA) that facilitates patient-centered, collaborative management for patients who are prescribed the gold-standard treatment, continuous positive airway pressure (CPAP).

DESIGN & METHODS:

The evaluative aspect of this proposal is designed as a randomized clinical trial-- Usual Care (Usual Care (control; UC); Self-Management Care (intervention 1; SM); and Self-Management via mHealth (intervention 2; SM-Mobile). The key feature of the SM-Mobile intervention is the use of a system that allows for receiving the SM via website at their convenience. The provider is able provide more directed feedback to the patient based on the telemedicine interaction, and the patient benefits from timely contact with the provider. Specific inclusion and exclusion criteria included: age > 18 years; confirmed diagnosis of moderate-severe OSA; being newly prescribed CPAP therapy; having chronic symptoms as noted on screening symptom checklist; and fluency in English. Patients were recruited from the VA San Diego Healthcare System Sleep Clinic. Participants were enrolled for a 4-month time period.

FINDING:

Overall Sample: The overall sample was aged 53.1±13.6, had a body mass index (BMI) of 32.6±5.7, apnea-hypopnea index (AHI) of 30.3±18.9, and a baseline Epworth Sleepiness Score (ESS) of 11.8±5.3. 90% of the sample were men. There were no significant differences between the groups on BMI, AHI, ESS, sleep apnea symptoms, insomnia symptoms or depressive symptoms.

Aim 1: To examine the effect of the Self-Management Care delivered by mHealth (SM-Mobile) intervention compared to Usual Care (UC) and Self-Management Care (SM) on level of CPAP adherence relative to Usual Care. The three groups were compared to see if there were differences on adherence. No statistically significant differences were found between UC, SM and SM-Mobile groups at the 2-month timepoint (4.0±2.2, 3.9±2.4, and 3.8±2.4 hours per night, respectively; F=.113; p=.893). or the 4-month timepoint (3.6±2.2, 3.6±2.5, and 3.6±2.5 hours per night, respectively; F=.041; p=.959).

In addition, we had CPAP efficacy metrics, including the residual Apnea-Hypopnea Index (AHI) and mask leak. At the 4-month time point, CPAP resulted in very good control of sleep apnea as evidenced by the mean AHI of 3.3 across the entire group. There were no group differences on residual AHI (UC, SM, and SM-Mobile of 3.0, 3.6 and 3.3, respectively). The same was true at the 2-month timepoint (mean residual AHI = 3.4; 3.2, 3.7 and 3.5, respectively). Mask leak was also well within normal limits at both the 2-month (mean = .14; .11, .15, and .16 lps) and 4-month timepoints (mean = 12; .12, .12, and .13 lps).

Aim 2: To examine the effect of the SM-Mobile intervention, compared to Usual Care and Self-Management Care, on the patient's experience of the quality of patient-centered, collaborative care (as measured by the Patient Assessment of Chronic Illness Care [PACIC]). The PACIC results in a total score and five subscale scores (Patient Activation, Delivery/support, Goal, Problem-solving, and Follow-up). The three intervention groups did not differ statistically (UC, SM, SM-Mobile) (3.3±1.1; 3.4±1.1; 3.4±1.1, respectively) on the PACIC Total Score. Higher scores indicated higher ratings of chronic illness care. The range of scores for the subscales was 2.6 to 3.7, with the higher overall scores on the Delivery/support subscale and the lowest on the Follow-up subscale. Overall, the scores were as high or higher than those reported in the literature for patients with similar chronic medical conditions, such as diabetes, asthma, depression and arthritis, indicating that the interventions studied in this project resulted in higher than average chronic illness care, as rated by patients.

Aim 3: To examine the effect of SM-Mobile, compared to UC and SM, on OSA apnea outcomes (e.g., OSA symptoms and OSA-specific health-related quality of life [HRQOL]). The Epworth Sleepiness Scale scores dropped from baseline to 2-months by 3.4 points and to 4-months by 4.0 points. Given that the cut-off for the ESS is 10 points (above which is considered sleepy; below which is considered within normal limits), all three interventions combined to reduce the sleepiness level of the sample from the sleepy range to the normal limits range (i.e., from mean ESS score of 11.8 to mean ESS score of 8.4 and 7.8 for 2-months and 4-months respectively). The mean ESS scores did not differ significantly between the groups at either the 2-month timepoint (8.3, 8.5, and 8.5 for the 3 groups respectively, UC, SM and SM-Mobile) or the 4-month timepoint (7.9, 7.4, and 8.2 for the 3 groups respectively, UC, SM and SM-Mobile). Sleep quality as measured by the Pittsburgh Sleep Quality Index was also significantly improved across all 3 groups from baseline (mean 11.9) to 2-months (2.8 points, mean 9.1) and to 4-months (2.9 points, mean 9.0). The mean PSQI scores did not differ significantly between the groups at either the 2-month timepoint (8.7, 9.4, and 9.5 for the 3 groups respectively, UC, SM and SM-Mobile) or the 4-month timepoint (8.5, 9.0, and 9.7 for the 3 groups respectively, UC, SM and SM-Mobile).

STATISTICAL ANALYSIS PLAN (SAP):

Data Analytic Plan. Preliminary analyses will begin with an examination of the distribution of variables to assess their characteristics (means, standard deviations, skewness, and kurtosis), to provide descriptive statistics of the study population, and to allow assessment of randomization. Continuous measures will be tested for normality and homogeneity of variance. Non-normally distributed variables will be transformed to meet the normal distribution assumption for linear statistical models.

The research question in the primary aim 1 will be addressed by comparing the CPAP adherence at post-intervention among the three intervention groups (UC, SM, SM-Mobile) and secondary aims 2 and 3 will be addressed by comparing the three intervention groups (UC, SM, SM-Mobile) on the changes in PACIC, OSA symptoms and OSA HRQOL from pre-intervention to post-intervention. The analytic model is based on an analysis of variance on the post-intervention measure (primary aim) or the change measures (secondary aims). For the change measures, the ANOVA will be accompanied by an analysis of covariance (ANCOVA) on the change scores with intervention as a main effect and the corresponding baseline measurement (baseline PACIC, OSA symptoms and OSA HRQOL) as the covariate. Adjustments will be made to correct for other baseline imbalances between groups, and to adjust for variables known to influence outcome independently of intervention. To explore this, univariate methods will be used. Each of the following variables will be assessed for imbalance between the three intervention groups and their association with each of the outcomes using a univariate analysis (ANOVA, Fisher's exact test or Spearman correlation coefficient as appropriate): age, gender, education and baseline OSA

severity. These variables will be included as covariates in the ANCOVA model if found to be moderately associated ($p<0.15$) with the outcome under study (CPAP adherence, CAHPS, PACIC, OSA symptoms and OSA HRQOL) or unbalanced ($p<0.10$) among intervention groups. The outcomes in secondary aims 2 and 3 will also be assessed by the random effects model, which is useful for examining changes in variables from clustered or longitudinal data and allows us to account for all levels of clustering when analyzing the data. It accommodates unequal time intervals and will include all available data, minimizing the effects of missing data on the analyses. The data analytic plan for secondary aim 4, which involves a cost analysis among three interventions [and a calcuation of the adherence level per intervention cost], is fully described in section D.7 below. An intent-to-treat analysis will be performed and no correction will be made for multiple comparisons. All above analyses will be performed in R.[110] Given below are detailed analysis plans for the primary aim and secondary aims 1 and 2.

Aim 1: An ANOVA will be used to assess the CPAP adherence at post-intervention among the three groups. Followed will be an ANCOVA by including potential covariates. Any variable that is significantly different at baseline ($p<0.10$) and found to be associated with response ($p<0.15$) as well as any clinically significant variables will be included as covariates.

Aim 2: An ANOVA will be used to assess the post vs. pre changes in PACIC among the three groups. An ANCOVA will be performed with treatment as a main effect and baseline score as a covariate. Any variable that is significantly different at baseline ($p<0.10$) and found to be associated with response ($p<0.15$) as well as any clinically significant variables will be included as covariates. As a secondary analysis, the change in PACIC will also be evaluated using a random effects model with a group, time and a group-by-time interaction term.

Aim 3: An ANOVA will be used to assess the post vs. pre changes in OSA symptoms and OSA HRQOL among the three groups. An ANCOVA will be performed with treatment as a main effect and baseline score as a covariate. Any variable that is significantly different at baseline ($p<0.10$) and found to be associated with response ($p<0.15$) as well as any clinically significant variables will be included as covariates. As a secondary analysis, a random effects model with a group-by-visit interaction term will be used to assess the rate of change in PACIC differs among three intervention groups.

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Principal Investigator:	**VAMC:**
Carl J. Stepnowsky, Jr., PhD	VA San Diego Healthcare System

Subject Name:	**Date:**

1) Purpose of this research study
Carl J. Stepnowsky, Jr., PhD and associates are conducting a research study to find out more about improving care provided to patients with sleep apnea. You have been asked to participate because you have a diagnosis of sleep apnea and have been prescribed continuous positive airway pressure (CPAP). There will be approximately 400 participants at this VA site. The funding source of this study is the Department of Veterans Affairs (VA) Health Services Research & Development Service (HSR&D).

2) How long the study will take
Your participation will take approximately 30-60 minutes each time you come to the VA hospital, and you will be expected to come to the hospital 1-5 times over a 4-month period. The entire study will take about 4 years.

3) What will happen to you in this study
If you agree to be in the study, the following will happen to you:

a. You will be randomized to one of three groups that are being studied using a random number generator.
b. The three groups will each differ on how the education and clinical support will be provided to you, but all three will be at or above the standard level of care.
c. You will be asked to follow an educational program that will help you learn to manage your sleep apnea using CPAP therapy.
d. You will be asked to complete questionnaires before you start CPAP therapy, and then again at two-months and at the end of the 4-month study period.
e. You will be set-up with the CPAP therapy device and fitted for a mask. You will be instructed on how to use the device and you will be able to call our Respiratory Therapist with any questions or problems you have with CPAP.
f. At a minimum, you will be called by the Respiratory Therapist during the first week and scheduled for a face-to-face visit at 1-month visit.

4) Which procedure(s) or treatment(s) are done for research only
Your treatment of sleep apnea with Continuous Positive Airway Pressure (CPAP) therapy is the standard of care for your condition, and it is not experimental in this study. What is experimental in this study is how the care is organized and delivered to you via two different communication methods, either by traditional face-to-face and telephone communication or by the use video teleconferencing via a mobile phone. Video teleconferencing includes the transmission of audio/video, and will be done using the VA-approved Clinical Video Teleconferencing Into the

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Home (CVTH) service. CVTH uses end-to-end encryption (Advanced Encryption Standard) for data security. You will be seen for all of your regularly scheduled clinic visits and will be treated at a minimum as you normally would in the Sleep Clinic – this represents the standard of care and is not experimental in this study.

5) RISKS reasonably to be expected
Participation in this program may involve some risks or discomforts. There is the possible risk of loss of confidentiality through participation in research because of access to your medical record. Safeguards will be taken to ensure that your confidentiality is not lost. A trained research staff member will access your medical record only to obtain data from your sleep study – the information the research study requires includes summary indices such as your apnea-hypopnea index (the number of breathing disturbances per hour of sleep), oxygen desaturation index (the number of times your oxygen drops ≥3% per hour of sleep), and total sleep time (the total amount of time in minutes that you are asleep). Use of the sleep recording device might results in (a) minor irritation to the skin caused by the electrode adhesive or (b) disrupted sleep from wearing the sleep equipment, which can result in sleepiness the next day.

Unforeseeable RISKS
Because this is an investigational study there may be some unknown risks that are currently unforeseeable. You will be informed if the researchers learn of any change in the amount of risk to you.

6) BENEFITS reasonably to be expected.
There may or may not be a direct benefit to you from these procedures. The study, however, may learn more about how best to organize and deliver care to patients with sleep apnea on CPAP.

7) Voluntary nature of participation and right to withdraw without penalty.
Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without jeopardy to the medical care you will receive at this institution or loss of benefits to which you are entitled.

8) Alternatives to the research procedure or treatment
The alternatives to participation in this study are: (a) to not participate; (b) to contact your current physician regarding any sleep apnea-related problems you may be experiencing, or (c) contacting your local A.W.A.K.E. group, which stands for **A**lert, **W**ell, **A**nd **K**eeping **E**nergetic, and is organized by the American Sleep Apnea Association. The goal of this informal group is to provide educational and emotional support from other sleep apnea patients – however, this does not replace the standard of care provided by your physician and his/her staff.

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9) Procedure for the orderly termination of a volunteer's participation
If you decide that you no longer wish to participate in this study please call Tania Zamora at 858-642-3269. You will be asked to come in for one final visit to complete the last set of questionnaires. You should come in for a final visit if you decide to stop participation in this study so that the investigators can ensure your health and well-being.

You may be withdrawn from the study by Dr. Stepnowsky for unanticipated circumstances. Though unlikely, these circumstances may include: cancellation of the study, you being unable to participate due to your health concerns or other reasons, or that your continuation may be harmful to you or to others. You may also be withdrawn from the study if you do not follow the instructions given you by the study personnel.

10) Information learned from the study will be shared with you
While you are a participant in this study you will be told if any important new information is found that may affect your wanting to continue.

If the results of this research might influence your medical care after you have completed your participation, the investigators will contact you to let you know these results.

11) Care provided if you are injured as a result of this study
The VA will provide necessary medical treatment should you be injured as a result of participating in this study and following study procedures. You will be treated for the injury by the VA at no cost to you or your insurance but no additional compensation is available. Every reasonable safety measure will be taken to protect your well-being.

12) Privacy and confidentiality
Participation in this study may involve a loss of privacy, but information about you will be handled as confidentially as possible. If study involves treatment, clinical resources, or potential for adverse events a CPRS note is required.

Your research records will be labeled with a code number. The list that matches your name with the code number will be kept in a locked file in the research team's office. The research records will be kept only as paper records in a secure VASDHS location, or as files behind the secure VASDHS computer firewall. Any presentations or publications from this information will not identify you.

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We will keep confidential all research and medical records that identify you to the extent allowed by law. However, you should know that there are some circumstances in which we may have to show your information to other people. For example, the Federal Office of Human Research Protections, the General Accounting Office, the VASDHS R&D Committee, the VASDHS Institutional Review Board, the VA Health Services Research & Development (the sponsor of this study) and federal compliance officers may look at or copy portions of records that identify you.

13) Payment

Costs to you or your insurance

There will be no costs to you or your insurance for any procedures or testing done only as part of this research study. If you receive a bill for services that you think could be related to your participation in this study, you should contact Dr. Stepnowsky at (858)642-1240.

Medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

You or your insurance company will be charged for any procedure or test that is medically necessary for the treatment of your illness, including the CPAP treatment, related tests and procedures. You will be responsible for all insurance co-payments and deductibles. The study test and procedures will be provided to you at no cost.

Payment for participating

You will receive payment for participating in this study. You will receive $20 for completion of the baseline questionnaires, $20 for completion of the 2-month questionnaire and $35 for completion of the final set of questionnaires for a total of $75 for the entire project.

14) Additional Information

The VA San Diego Healthcare System provides oversight and resources for this study.

15) RESEARCH SUBJECTS' RIGHTS: You have read or have had read to you all of the above. **You have been informed that you do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits to which you are entitled.**

In the event of illness or injury that you believe to be related to the study, or have questions about this research, you can call Dr. Stepnowsky at (858)642-1240 during the day. If you have

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any questions or concerns about your rights as a research subject, the validity of a research study, or research personnel you can contact the Research Compliance Officer at 858-642-3817, VA Research Service at 858-642-3657, VA Regional Counsel at 858-642-1540, or the VASDHS Human Research Protection Program at 858-642-6320.

_____ has explained the study to you and answered all of your questions. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You will receive a copy of this consent form and a copy of the Health Insurance Portability and Accountability Act (HIPAA) Authorization that you signed. You will also receive a copy of the California Experimental Subject's Bill of Rights.

By signing this form you indicate that you have been informed of your rights as a research subject, and that you voluntarily consent to participate in this study. You have been informed what the study is about and how and why it is being done.

_____ _____
Subject's Signature Date

_____ _____ _____
Signature of Researcher obtaining consent Name (print) Date