STUDY PROTOCOL

Diagnosis and Treatment of Sleep Apnea in Women Veterans

VA HSR&D Project

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INTRODUCTION

Sleep apnea (SA) is associated with significant adverse consequences including cardiovascular disease, which remains the leading cause of death for women worldwide, as well as low quality of life and high mortality risk.[2-4] Although SA is more common among men, 17.4% of women in the population meet the minimum diagnostic criteria for SA.[5] Our preliminary work suggests nearly half of women Veterans with poor sleep have SA, with nearly 1/3 having moderate to severe disease (see Preliminary Data). While SA is a well-studied condition with known treatments, the existing literature has not focused on understanding this disorder among women. There is reason to suspect that men and women with this sleep disease differ in important ways. Much like heart disease, women with SA present differently. Women are more likely to present with insomnia, fatigue, depression or hypothyroidism, while men are more likely to present with excessive sleepiness, snoring or hypertension.[6;7] These differences likely contribute to the fact that 90% of women with SA remain undiagnosed and therefore untreated.[7-9]

The most effective and widely used treatment for SA is positive airway pressure (PAP) therapy.[10;11] While PAP has demonstrated benefits, such as reducing blood pressure and improving daytime sleepiness, patients encounter numerous barriers to using PAP. Studies in the US show that women have lower PAP adherence rates than men.[12;13] PAP adherence interventions that are focused on patient education, cognitive-behavioral therapy and motivational enhancement do increase adherence;[14] however, a significant proportion of patients (>30%) remain non-adherent after intervention. Women are significantly underrepresented in this research. In addition, since women with SA have more sleep disturbance than men with SA, improving PAP adherence among women may require addressing sleep quality prior to PAP initiation.

We have been studying sleep disorders among women Veterans since 2010,[15] focusing on treatment preferences and adherence to psychological treatments for sleep disorders (e.g., cognitive-behavioral therapy for Insomnia; CBT-I). In treating insomnia, we found that the initial discomfort created by traditional CBT-I (e.g. sleep restriction therapy) may contribute to treatment discontinuation and non-adherence to recommendations among women Veterans. We therefore developed an insomnia intervention incorporating Acceptance and Commitment Therapy (ACT). ACT centers on mindfulness and focused choices consistent with a patient's values as reasons for implementing behavioral changes. ACT, which is currently being disseminated by VA as a treatment for depression and anxiety through an Evidence-Based Psychotherapy roll out, involves helping patients learn strategies for tolerating temporary discomfort in pursuit of values-based goals. We propose to use an ACT-based intervention to improve PAP adherence among women Veterans with SA.

The proposed study is a randomized controlled trial (RCT) to test the efficacy of an ACT-based program for improving PAP adherence called “ABC-SA” or “Acceptance and the Behavioral Changes to treat Sleep Apnea.” This 6-session intervention differs from current approaches in two important ways. First, we will begin working on improving sleep quality before PAP therapy is initiated. Second, the ACT approach and techniques will address initial discomfort, link treatment to the patient’s values and incorporate methods for accepting the behavioral changes required to treat SA (i.e. accepting and using PAP therapy). The main study outcomes will be assessed 3 months after PAP initiation, and PAP adherence will be monitored for 12 months. The 6-session “control” intervention will be modeled after “usual care” PAP education programs.

SPECIFIC AIMS

Aim 1: Test the efficacy of the ABC-SA program in improving PAP adherence, compared to a control program modeled after usual care, for women Veterans with SA.

Hypothesis 1a: Women who receive the ABC-SA program will show higher rates of PAP adherence (% of nights with ≥4 hours of use) during the first 3 months of PAP use compared to those who receive the control program. Exploratory Hypothesis 1b: These effects will be sustained for up to 12 months.

Aim 2: Test the efficacy of the ABC-SA program for improving objectively-measured and patient-reported sleep quality, compared to the control program.

Hypothesis 2a: Women who receive the ABC-SA program will have better objectively-measured sleep quality at 3-months compared to those who receive the control program. Hypothesis 2b: Women who

receive the ABC-SA program will have better self-reported sleep quality at 3-months compared to those who receive the control program.

Exploratory Aim 3: Test the efficacy of the ABC-SA program for improving quality of life and **symptoms of depression, compared to the control program.**

Hypothesis 3a: Women who receive the ABC-SA program will demonstrate better quality of life at 3-months compared to those who receive the control program. Hypothesis 3b: Women who receive the ABC-SA program will demonstrate reduced symptoms of depression and fatigue at 3-months compared to those who receive the control program.

RESEARCH DESIGN AND METHODS

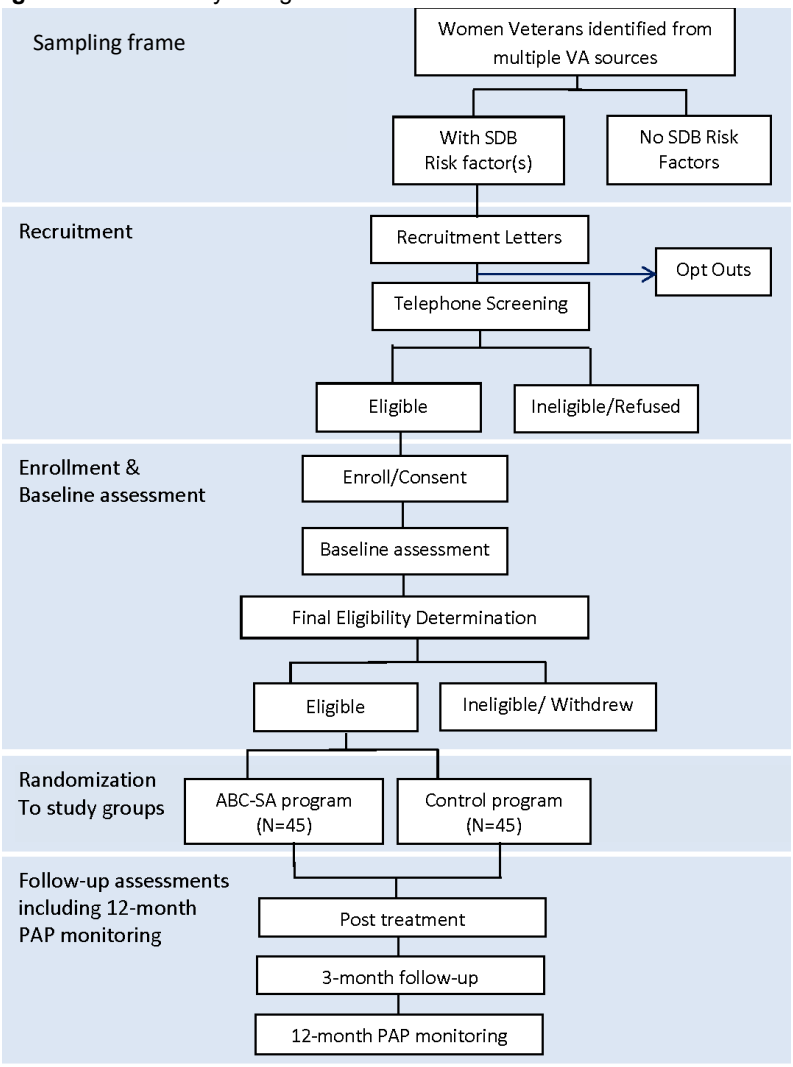
Basic Study Design (Figure 1)

The proposed study is a 4-year randomized controlled trial (RCT) to test the effectiveness of Acceptance and the Behavioral Changes to treat Sleep Apnea (ABC-SA), an ACT-based approach to improve PAP therapy adherence among women Veterans with SA. We anticipate enrolling 300 women to achieve the proposed sample of 90 randomized participants (45 ABC-SA and 45 controls).

Participants will complete a comprehensive sleep, mental health and physical health assessment at baseline (baseline), immediately after the intervention ends (post-treatment; approximately 1 month after PAP initiation), and 3 months after PAP initiation (primary endpoint). We will gather PAP adherence data for one year.

Primary outcomes will focus on differences in PAP adherence and patient-reported and objectively measured (wrist actigraphy) sleep quality at the 3-month follow-up. Data will be analyzed in an intention to treat analysis.

Figure 1: Basic Study Design



Setting The study will be carried out within VAGLAHS. In-person study assessments and intervention sessions will be completed at the Sepulveda Ambulatory Care Center (SACC) or West Los Angeles (WLA) campuses. Unattended sleep recordings (home sleep apnea testing; wrist actigraphy) will take place at participants' homes using study-provided equipment.

Study participants Participants in this study will be women Veterans over the age of 18 years old who receive care at VA GLA. To enhance the relevance of our findings, we have focused our sampling frame on women who would likely receive the ABC-SA intervention in routine clinical care. We have based the number of participants expected at each phase of recruitment, screening and enrollment on our current study with women Veterans (Martin project #0008).

Recruitment

Sources of potential participants

We will employ two methods to recruit participants to ensure that we obtain a representative sample of women Veterans with SA:

1. VA Corporate Data Warehouse (CDW) data

   Authorized VA project team member(s) will work with VINCI programmers to pull a sample using the VA Corporate Data Warehouse (CDW). Study inclusionary criteria will be applied to select eligible Veterans for recruitment. To help capture eligible patients with fresh contact information, this process will be repeated 2-3 time during the study recruitment period.

   The sample file will include women Veterans who have had a recent visit at VA GLA and have one or more of the common SA risk factors such as obesity, hypertension or age>50. The variables in the sample file will include the following:

Table 1: Data variables requested from CDW
• **Unique patient identifiers** (e.g. Scrambled SSN, Patient ICN, PatientSID, etc.)
• **Contact information** (e.g. Name, residential address, zip code, telephone numbers-cell/work/residence, etc.)
• **Demographic and Veteran Characteristics information** (e.g. dob, gender, race/ethnicity, dod, Veteran status, military service cohort, combat exposure, service-connected status, military sexual trauma expose, income, etc.)
• **Treatment and Diagnosis** (e.g. clinic stop codes, station codes, encounter dates, ICD9/ICD10 codes, date of diagnosis, weight/height, BMI, etc.)

   A Link File will be created using the sample file to associate the project specific study ID with the Veterans' unique identifier (PatientICN/PatientSID, or scrambled SSN) which can be used to access VA VINCI/CDW data. The new records pulled with each additional sample pull will be added to our link file to create a single cumulative file of all sampled Veterans. All records will be assigned a study ID number that will serve as the primary key for matching data from the additional sources. The Link File will be stored on a restricted-access folder on the CSHIIP secure server behind the VA firewall and is never transferred during the project, nor will it be accessible to anyone other than authorized VA project team member(s).

   These women Veterans will be mailed a recruitment letter (see Recruitment Letter for CDW sample) that will introduce the study. Enclosed in the letter will be an 'opt-out' card (see Opt-out Card) that they can return within 7 days to indicate if they want further contact from the research team. Veterans who do not return the card within 7 days of the letter mail date may be contacted by telephone by study staff (see Telephone Screening Script). The purpose of this telephone call will be to further explain the study and to administer a brief questionnaire (see Telephone Screening Questionnaire) to screen for study eligibility. A waiver of consent and waiver of HIPAA authorization are required to access these data.

2. Women Veterans referred to VA GLA Sleep Medicine clinics

   Women Veterans referred to VA GLA Sleep Medicine clinics for evaluation will be mailed a recruitment letter (see Recruitment letter for Sleep Disorders Center patients) and opt-out card. The same protocol will be followed for contacting these women as described above. A waiver of consent and waiver of HIPAA authorization will be obtained for these data.

3. Women Veterans previously enrolled in Dr. Martin's project #0008

   A subset of women Veterans who were previously enrolled in Dr. Martin's project #0008, had symptoms of sleep apnea (AHI > 5 and/or excessive daytime sleepiness), and who agreed to be contacted about future research, will be mailed a recruitment letter and opt-out card. The same protocol will be followed for contacting these women as described above. A waiver of consent and waiver of HIPAA authorization will be obtained for using the previously collected contact and sleep apnea screening data.

Telephone screening

Women Veterans who are contacted by research staff and express interest in participating in the study will be asked to provide verbal consent prior to administration of the screening questionnaire (see Telephone Screening Script). The Telephone Screening Questionnaire includes questions to confirm inclusion criteria and inquire about exclusion criteria (see Table 2).

A waiver of documentation of consent and waiver of HIPAA authorization will be obtained for the telephone screening phase of the study.

Table 2: Inclusion and exclusion criteria for study enrollment
Inclusion criteria
1) Female
2) community-dwelling
3) aged 18 years or older
Exclusion criteria
1) current treatment for SA
2) current pregnancy
3) active substance use or in recovery with< 90 days sobriety
4) too ill to engage in study procedures (e.g., unable to attend in-person meetings)
5) no access to transportation to the medical center
6) unable to self-consent
7) unstable housing (since we may be unable to retrieve study monitoring equipment).

Enrollment and informed consent

Following completion of the telephone screening questionnaire, eligible and interested women Veterans will be scheduled for an initial in-person meeting to obtain written informed consent. Potential participants also will be informed that they can receive a blank written informed consent form in the mail to provide them with sufficient time to consider participation and discuss participation with family members, should they so desire.

Prior to the in-person visit, research staff will access each potential participant's VA electronic medical record to review previous sleep study results, sleep apnea treatments, and medical diagnoses that might indicate ineligibility for study enrollment. Potential participants who are found to be ineligible will be informed by study staff and the consent visit will be cancelled.

When an eligible potential participant comes to the consent visit, a trained research staff member will review the details of the study and answer any questions. Potential participants will be shown the wrist actigraph and WatchPat monitoring equipment to ensure that they become familiar and comfortable with this equipment.

As part of the consent presentation, potential participants will be provided with information about SA and how PAP is used to treat SA. They will be informed that while PAP is not the only available treatment for SA (e.g., some mild SA can be treated with oral appliances), this study is designed specifically for participants who are prescribed PAP. During the consent process, PAP equipment will be available for participants to see, and they will be informed that if they are diagnosed with sleep apnea and are prescribed PAP therapy, they will receive a PAP as part of the study protocol. Participants will also be informed that they will receive usual follow-up care for their SA in the VA Sleep Disorders Center.

Capacity to provide informed consent will be evaluated with a brief questionnaire (Evaluation to Sign A Consent Form for Research), previously approved by the IRB, that asks the Veteran to recount major procedures and risks of the study. Veterans who are unable to provide informed consent will be excluded; proxy consent will not be pursued. Participants who can provide informed consent will be asked to sign the written informed consent form and HIPAA authorization and will be provided with copies.

COVID-19 amendment to obtain consent through mail and video/telephone options

While in-person research visits are restricted due to COVID-19 guidelines, we will modify the consent process accordingly:

- Following completion of the telephone screening questionnaire, eligible and interested women Veterans will be scheduled for a consent review appointment. The consent appointment will occur via a VA approved video telehealth platform (e.g, VA Video Connect-VVC) or telephone. Prior to the appointment Veterans will be mailed the informed consent form, HIPAA authorization, and an

information sheet that summarizes the major study procedures and provides pictures of the wrist actigraph and WatchPat device.

- During the video/telephone consent appointment, research staff will follow the same protocol as described above. Veterans who agree to participate in the study will be instructed to sign the informed consent and HIPAA authorization forms and return them by mail or by dropping them off at the Sepulveda or WLA campus.

If Veterans prefer to drop off the consent form, research staff will arrange to meet the Veteran in a VA parking lot or in the lobby of Building 25.

Procedures

Baseline assessment

Once enrolled, participants will complete a 9-day baseline assessment consisting of 3 visits to the study site (Table 3). This is similar to the number of visits needed to diagnose and initiate treatment for SA in clinical care. At the first visit (30 minutes following the consent process), the participant will be administered Part 1 of the baseline questionnaire. They will also be provided with a WatchPAT recording device to wear overnight to screen for SA. Participants will view an instructional video on use of the WatchPAT equipment, and they will be given a toll-free number to call if difficulties arise with equipment overnight.

Table 3: Enrollment and baseline data collection process

	Day 1 Visit 1	Night 1	Day 2 Visit 2	Nights 2-8	Day 9 Visit 3
Consent; Questionnaires Part 1	X				
WatchPAT monitoring*	X	X	X		
Questionnaires: Part 2			X		
Wrist actigraphy* and sleep diary			X	XXXXXXX	X
Questionnaires: Part 3					X

*Equipment worn at participant's home

On Day 2 (visit 2; 30-45 minutes), the participant will return the WatchPAT device, and will be administered Part 2 of the baseline questionnaire. She will also be provided with a wrist actigraph to wear at home for one week and a sleep diary to complete each day while wearing the wrist actigraph (see Sleep Diary).

One week later, the participant will return for Visit 3 (60-90 minutes) and will return the wrist actigraph and diary and complete Part 3 of the baseline questionnaire. A description of the questionnaires and data collected at baseline are included in Table 5.

COVID-19 amendment for baseline data collection

In lieu of in-person visits, we will administer the baseline questionnaires using a VA approved video telehealth platform or by telephone. Participants will receive and return the WatchPAT, actigraph, and sleep diary either by mail or by meeting research staff in a VA parking lot or in the lobby of Building 25. If devices are mailed, we will use UPS and will provide participants with a return box and a pre-paid label.

Determination of Sleep Apnea

Initial screening for SA will be part of research activities in this study. However, the diagnosis of SA and any prescription for SA treatment will occur within the VA GLA Sleep Disorders Center (SDC) and will be documented in the participant's VA medical record. Following a process previously used in Dr. Alessi's study (project #0015) and approved by Dr. Zeidler (SDC Director and co-investigator), SDC physicians will review WatchPAT results. The reviewing physicians will determine whether the participant has sleep apnea based on International Classification of Sleep Disorders definition[67] or requires additional testing (e.g., repeat of a home sleep test or a laboratory polysomography (PSG)). Following standard clinical practices, the participant will be informed of her diagnosis by an SDC physician or other clinic staff member, who will discuss treatment options. The treating physician will prescribe the appropriate treatment and establish the initial pressure settings for PAP for patients who accept this treatment.

Eligibility determination for randomization

Participant's baseline assessment results will be reviewed during a weekly investigators' meeting to determine eligibility for randomization to receive the study intervention. The meeting will include Dr. Martin (a psychologist

specializing in Behavioral Sleep Medicine) plus one of the Board Certified Sleep Medicine physicians (Drs. Alessi, Fung or Zeidler), and a member of the study team who completed baseline assessments. These investigators will review the baseline assessment and medical record to determine if a participant meets the inclusion criteria for randomization (AHI>5 from overnight sleep apnea recording, a diagnosis of SA and a prescription for PAP therapy) and does not meet any of the following exclusionary criteria that would make them ineligible for randomization:

(1) no SA (AHI<5) found on overnight monitoring
(2) another untreated sleep disorder that accounts for sleep difficulties (e.g., untreated restless legs syndrome)
(3) unstable medical or psychiatric conditions (e.g., chemotherapy, untreated schizophrenia)
(4) prior participation in a structured PAP adherence program or our ABC-I intervention
(5) no sleep-related complaints or symptoms on baseline assessments
(6) refusal to attempt PAP therapy

Participants with stable psychiatric/medical conditions, and those using medications for sleep will not be excluded. Participants determined to be ineligible for the study will be notified by mail (see Participant Ineligibility Letter).

Randomization

Participants approved for randomization will be randomly assigned to the ABC-SA (n=45) or control program (n=45), following CONSORT guidelines.[47] Randomization sequences will be created using a computerized random number generator. Stratified randomization will help insure that groups (ABC-SA and control) are balanced in the severity of SA (AHI 5-15, and AHI≥15). Furthermore, within each strata, the randomization sequences will be “blocked” using a block size of n=4. The study statistician will generate the stratified randomization sequence and transfer it to a series of "security envelopes". These envelopes, containing the group assignment, will be stored in a secure location that only authorized “unblinded” staff can access. This will assure random allocation concealment, which is critical to the integrity of randomized trials.

Study groups

- **ABC-SA for women Veterans with SA (Table 4)**

Participants randomized to ABC-SA group will receive the Acceptance and the Behavioral Changes to treat Sleep Apnea (ABC-SA) program that we developed to improve PAP adherence among women Veterans. The ABC-SA program melds strategies to improve sleep (stimulus control, targeted sleep hygiene, sleep compression) and increase PAP adherence (SA and PAP education) with psychological principles of ACT (e.g., using metaphors, linking behavior change to values, strategies for accepting discomfort). The program includes 6 weekly face-to-face meetings with the study interventionist, plus ongoing monitoring and support. Sessions are designed to last ≤45 minutes each. Issues specific to women’s health are incorporated into ABC-SA, such as discussion of social factors that might impact PAP adherence (e.g., interpersonal relationships) and health issues among women (e.g., heart health, menopause and SA). Sessions are interactive to facilitate participant engagement. A written outline with the specific, individualized recommendations documented in clear language will be provided after each session. Interventionists will also complete session summaries for the participants to review at home.

The ABC-SA program focuses on psychological flexibility, using ACT-based exercises, to increase adherence to behavioral recommendations (i.e., use of PAP and improved sleep habits). Each week begins with a metaphor, and each session uses the patient’s core values as potential motivating factors for adherence. A major focus of the program will involve troubleshooting commonly occurring problems with PAP, tailored to the participant’s ongoing experiences, in addition to understanding how specific aspects of an individual’s use of PAP relates to her own targeted outcomes. At the end of each session, the patient will be provided with written materials and a diary for monitoring progress. During each of the planned sessions, the interventionist will review the patient’s Encore Anywhere Detailed Summary Report captured by remote PAP monitoring, which includes average and total use statistics as well as the residual AHI and mask leaks. Studies show that use of

PAP within the first week predicts long-term use.[16-17] As a result, we will begin to address potential concerns before PAP equipment is provided to the participant, and in most instances, PAP therapy will be initiated at Session 3. In some cases, the PAP equipment may be provided at a different point in treatment to accommodate patient needs and preferences. We chose this approach based on our preliminary data that women with SA often feel unprepared to begin PAP therapy, which can create initial resistance.

- **Control program (Table 4)**

This 6-week program will "control for" added social contact of participation and align with usual care for SA at our VA. The interventionist will not provide individualized recommendations, but will give accurate, non-directive, information about SA, sleep hygiene and sleep across the lifespan. We have used such control programs in prior trials, and participants report they are credible, but we have found no effect on sleep quality or other outcomes.[1] We plan to provide PAP equipment at Session 3. The control program interventionist will log into the Encore Anywhere system and verify the PAP machine is transmitting data, but this data will not be used during intervention sessions as it is in the ABC-SA program. If data transmission has not occurred within one week of PAP initiation, the interventionist will address this during session 4. The frequency of PAP adherence monitoring in the control group will be 1 week and 1 month after PAP initiation, consistent with American Thoracic Society recommendations.[18]

- **PAP devices**

We have purchased the same types of PAP devices that are provided by the SDC. The PAP device will be provided to the participant by an experienced research respiratory therapist following the protocols of the SDC. Participants will be instructed on the set-up, use, and maintenance of the PAP. Participants will be given the opportunity to choose between several different masks and will practice using the PAP in the presence of the respiratory therapist. These procedures are all standard practice in the SDC for patients who are prescribed PAP equipment.

Remote PAP telemonitoring using Encore Anywhere, which is used by the SDC and by our research group (Alessi, project #0015), will be used to objectively monitor PAP use and adherence, as well as mask leaks, and AHI. Each PAP machine will be equipped with a modem that transmits daily PAP usage data to a secure server maintained by the manufacturer (Phillips Respironics, Inc.). The data are accessed through the Encore Anywhere website.

In addition, each PAP contains an internal SD (data storage) card that contains PAP usage data. In instances when the modem data are incomplete, the SD card data will be imported into the study's database on the Encore Anywhere website. The SD card data will be compared to the modem data to ensure that there are complete data for the entire 12-month follow-up period. The temporary removal of the SD card from the PAP machine will not impact the therapeutic benefits of PAP use nor its function. In a study conducted by our research group (Alessi, project #0015), we found subtle variation in the modem PAP use data across time, which was addressed by having an SD card download available at various timepoint in the study. SD card downloads at 3, 6, 9 and 12 months will insure the accuracy and completeness of the PAP use data.
Both methods allow collection of PAP usage data with no additional burden to participants. We will use monthly PAP use as an outcome measurement.

All participants will continue to receive usual care from the SDC, including periodic telephone contact to monitor PAP adherence and follow-up physician visits. Participants will continue to be followed by the clinic at the conclusion of the study.

- **Intervention process measures (ABC-SA and control)**

Participants in both study groups will complete the following questionnaires at the end of the first treatment and final (sixth) treatment sessions. We have selected this approach since some measures cannot be completed until the individual has a basic understanding of the treatment program she will receive.

Acceptance and Action Questionnaire-II (AAQ-II):[19] The AAQ-II is a 7-item questionnaire to assess experiential avoidance as conceptualized in ACT (higher scores suggest more avoidance). The AAQ-II has acceptable psychometric properties. In a recent study of 376 adults with depression or anxiety symptoms,

using a unidimensional item response theory (IRT) model, the AAQ-II was found to be a unidimensional measure of experiential avoidance with satisfactory reliability. Key variable: AAQ-II total score.

Dysfunctional Beliefs and Attitudes about Sleep – 10 item (DBAS-10):[20] The DBAS-10 is an abbreviated version of the original 28-item DBAS examining beliefs about the immediate and long-term negative consequences of insomnia as well as beliefs about the need for control over insomnia. This 10-item version has been shown to be well correlated (r=0.83) with the full scale and sensitive to cognitive changes resulting from cognitive-behavioral therapy for insomnia. Key variables: DBAS total score.

Sleep Hygiene Index (SHI):[21] The 13-item sleep hygiene index is based on diagnostic criteria for inadequate sleep hygiene, and has superior reliability compared to other (typically longer) sleep hygiene questionnaires (Chronbach's α=0.66). This measure will be used to identify sleep hygiene related behaviors, including the use of alcohol, caffeine and tobacco within 4 hours of bedtime. Key variable: SHI total score.

Credibility/expectancy questionnaire (CEQ):[22] The CEQ is a 6-item questionnaire used both at the beginning and end of treatment. This questionnaire will be administered at the end of the first treatment session and again at the end of the final treatment session in both groups. Since this measure cannot be used until the individual understands the type of treatment she will receive, it will not be assessed until after session 1 when information about the treatment is available. The post-treatment items will be administered at the end of the final treatment session as well (session 6). Differences in scores between the groups will be explored. Key variable: CEQ total scores at the beginning and end of treatment.

Treatment sessions will also be audio recorded and one of the study investigators will listen to and rate sessions using a Fidelity Monitoring Form to assess adherence to the intervention content and competency of the study interventionist.

COVID-19 amendment for intervention /control sessions

Randomized participants will be mailed the session materials for all 5 weeks of the intervention/control conditions prior to the first session. They will also be provided with postage-paid return envelopes to mail the sleep diaries and process measure questionnaires to the research office. Interventionists will meet weekly with participants via video platform. The content of the sessions will be identical to the in-person sessions and the interventionist will follow the same protocols as described above. PAP devices will be mailed to participants following session 2. (GLAHS Sleep Medicine clinics are currently mailing PAP devices to patients and providing set-up instructions using VVC.)

Table 4: Weekly Components and Topics in ABC-SA and Control Programs

	ABC-SA Program		Control Program	
Week	**Title**	**Components/Topics**	**Title**	**Components/Topics**
Week 1	*Don't* take out the trash: Understanding SA and PAP	· Metaphor: Trash can for unwanted feelings · What is SA? · How does PAP work? How will it impact my sleep? · What is important to me/how can PAP fit into my life? · De-fusion from thoughts about PAP · Sleep education/healthy sleep habits · Introduce sleep dairy	Understanding sleep	General information about sleep in adults; sleep stages, circadian rhythms
Week 2	Putting the day to rest: Getting ready for PAP	· Metaphor: Wearing glasses · Sleep apnea and relationships with others · Review homework/sleep diary · Develop sleep schedule with specific bedtime/rise time. · Develop bedtime routine · Preparing for PAP: take steps to get ready	What is sleep apnea?	General information about sleep apnea; Basics of PAP use (usual care)
Week 3	**PAP therapy begins**			
	Going swimming: Getting started with PAP	· Metaphor: Jumping into cold water · Review homework/sleep diary · Practice with equipment and mask · Adjustment of sleep schedule · Revise bedtime routine to include PAP setup · How will PAP use fit into your life? · Introduce sleep diary with PAP use monitoring	What is PAP?	Basic information about sleep disordered breathing; introduction to PAP equipment
Week 4	What was it like to try something new?	· Metaphor: Tasting new foods · Review homework/sleep diary, review PAP usage data · Troubleshoot equipment challenges · Informed choices about PAP use: moods and feelings · Adjust bedtime/rise time (if indicated)	Good sleep hygiene I	Sleep hygiene: sleep environment considerations
Week 5	What have I noticed?	· Metaphor: Pause button · Review homework/sleep diary, PAP usage data · Troubleshooting techniques · Adjust bedtime/rise time (if indicated) · Review "how will PAP fit into my life" from week 1 and adjust if needed.	Good sleep hygiene II	Sleep hygiene: diet, exercise, nicotine, alcohol, and caffeine
Week 6	How can I use PAP over the long run?	· Metaphor: sailing · Review homework/sleep diary, PAP remote monitoring data · Long-term planning for PAP use: preempt problems · Maintaining good sleep quality over the long-term · Implement sleep schedule	Age related changes	Sleep changes with age in women; sleep architecture; menopause and sleep
Week 8	Telephone follow-up	· Answer questions about sleep or PAP use		

Follow-up assessments
We will encourage participants to complete assessments even if they elect not to complete the intervention. All follow-up assessments will be conducted by research staff who are blinded to group assignment.

- **Post-treatment assessment**

The post-treatment assessment will begin on the same day that the participant completes session 6 of either the ABC-SA or control program. At the end of session 6, a participant will be provided with an actigraph to wear at home for 1 week and a sleep diary to complete during that time period. When the participant returns the actigraph and sleep diary after 1 week, she will be administered the same questionnaires included in the Part 2 and Part 3 baseline assessment (with the exception of the SCID) (Table 6). Participants who complete the 3-month follow-up will receive $75 for their travel and time.

- **Three-month follow-up (main outcome time point)**

Three months after session 6 is completed, participants will be scheduled to complete the three-month follow-up assessment. This assessment will include 2 visits to the study site. At visit 1, Part 2 questionnaires will be completed, and the participant will be provided with an actigraph to wear at home for 1 week while completing a sleep dairy. At visit 2, the participant will complete Part 3 questionnaires. We selected the 3-month follow-up time frame as it strikes a balance between the desire to evaluate longer-term effects of the program while considering that lengthy follow-up intervals may decrease our ability to contact women for re-assessment. Participants who complete the 3-month follow-up will receive $75 for their travel and time. After the 3-month follow-up assessment is completed, participants may request to receive the education program that they did not receive.

COVID-19 amendment for follow-up data collection
In lieu of in-person visits, we will administer the baseline questionnaires via a VA approved video telehealth platform or by telephone. Participants will receive and return the wrist actigraph and sleep diary either by mail or by meeting research staff in a VA parking lot or in the lobby of Building 25. If devices are mailed, we will use UPS and will provide participants with a return box and a pre-paid label.

- **12-month PAP monitoring**

We will make efforts to collect PAP usage data for 12-months following the date of PAP initiation for all participants. To achieve this, we will monitor the modem data monthly. If usage data are missing, a research assistant will contact the participant to troubleshoot. At the 3-month follow-up, participants will be asked to bring their PAP with them to the appointment and the PAP SD card data will be imported into the study's database on the Encore Anywhere website. In addition, we may contact participants by telephone at 6, 9, and 12-months after receipt of the PAP when modem data are missing. We may ask the participant to mail (or deliver) the PAP SD memory card to the research office so the information can be downloaded. The SD card will be mailed back to the participant after the data are imported.

- **Follow-up for Missed Appointments**

Participants who miss a study appointment will be telephoned by research staff on the day of the missed appointment. If the participant does not return the call within 10 days of the missed appointment, a letter will be sent that encourages the participant to contact the research office (see Missed Appointment Letter).

If a participant has not returned an actigraph or Watch-PAT device, the letter will also include a paragraph about the importance of returning the device. If the participant does not return the device after 10 days from the date of the first letter, a second letter will be sent that explains that failure to return the device requires staff to submit a missing equipment report to VA police (see Failure to Return Device Letter).

Participant payments
Enrolled participants will receive up to $250 cash over the course of the study and up to $75 in VA Canteen Service coupons. For the baseline assessment, participants will receive $25 for the overnight sleep apnea monitoring, $50 for answering questionnaires, and $25 for wearing the wrist actigraph. For each of the two follow-up assessments, participants will receive $25 for wearing the wrist actigraph and $50 for answering the

questionnaires. As an incentive to mail the SD cards at 6, 9, and 12-month follow-ups, participants will be give $25 in VA Canteen Service coupons.

Description of data collection instruments and devices listed in Table 5

Measures were chosen to maximize reliability and validity and allow for inclusion of constructs likely to increase our understanding of study findings. Instruments will be scored using published/standard procedures. Our team has experience with all proposed measures and techniques. We have processes in place to minimize missing data.

Demographics: Age, gender, race/ethnicity, marital status, living situation, income, education, employment, menopausal status, and smoking history will be collected to describe the sample and gather information on potentially relevant variables for subgroup analyses.

Medical conditions/symptoms:

Self-Administered Cormobidity Questionnaire[23] measures the frequency and severity of 14 medical conditions. Respondents indicate whether they receive treatment for the condition and whether the condition limits activities. A higher score indicates greater medical comorbidity. We will add 32 other common medical and psychiatric conditions in women Veterans to the questionnaire.

Table 5: Measures at each data collection timepoint

	Baseline	Post-treat.	3 mo F/U	12 mo F/U
Part 1				
Demographics questions	✓			
Self-Administered Comorbidity Questionnaire + 32 additional items	✓			
WatchPAT overnight home sleep monitoring	✓			
Mini-Mental State Examination (MMSE)	✓			
Part 2				
Mini-International Neuropsychiatric Interview (MINI)	✓			
PTSD Checklist for DSM-5 (PCL-5)	✓	✓	✓	
Patient Health Questionnaire - GAD-7	✓	✓	✓	
Anxiety Sensitivity Index -3 (ASI-3)	✓	✓	✓	
Restless Legs Syndrome (RLS) questionnaire	✓	✓	✓	
Epworth Sleepiness Scale (ESS)	✓	✓	✓	
Brief Pain Inventory	✓	✓	✓	
Nighttime urination questions	✓	✓	✓	
Wrist actigraph (7 days)	✓	✓	✓	
Sleep diary	✓	✓	✓	
Part 3				
Insomnia Severity Index	✓	✓	✓	
Pittsburgh Sleep Quality Index	✓	✓	✓	
DSM-5 diagnostic criteria questions	✓	✓	✓	
Disturbing Dream/Nightmare Severity Index (DDNSI)	✓	✓	✓	
Glasgow Sleep Effort Scale	✓	✓	✓	
WHO-QOL BREF	✓	✓	✓	
European Quality of Life Scale (EQ-5D)	✓	✓	✓	
Calgary Sleep Apnea Quality of Life Index (SAQLI)		✓	✓	
PHQ-9	✓	✓	✓	
Flinders Fatigue Scale (FFS)	✓	✓	✓	
Perceived Stress Scale (PSS)	✓	✓	✓	

Medications taken during week wearing actigraph	✓	✓	✓	
Healthcare utilization questionnaire	✓	✓	✓	
Remote telemonitoring of nightly PAP use		✓	✓	✓
PAP use data		✓	✓	✓
Everyday Discrimination Scale		✓		
Major Experiences of Discrimination Scale		✓		

The Brief Pain Inventory (BPI) -Short Form:[24] is a 9-item version of the BPI which measures pain severity, treatments, and daily interference over the past week. The BPI has been validated and is sensitive to changes over time.

Nightttime urination, including number of times participant gets up to urinate, and a rating of how bothersome getting up at night is, will be asked at each assessment timepoint.

Medications will be abstracted from medical records and participants will be queried about use of over-the-counter, herbal and non-VA prescription medications. Sleep medication use will be tracked within the daily sleep diary at baseline, post-treatment and 3-month follow-up. Medication data will be coded by drug class, focusing on psychotropic medications that may affect sleep, and summarized categorically (i.e., use/non-use). We will look at sedating medications taken at bedtime, including hypnotics, sedating antidepressants, sedating antipsychotics and antihistamines.

Psychiatric conditions/symptoms/quality of life:

The Mini-Mental State Examination (MMSE) will be used to measure baseline cognitive status in participants aged 65 years and older. This scale assesses orientation, registration, attention/ calculation, recall, language and construction, and has standard instructions. MMSE responses will be used in evaluating appropriateness for randomization.

The Mini-International Neuropsychiatric Interview (MINI)[25] is a standardized structure interview for diagnosing DSM-5 lifetime and current Axis I mental disorders. The MINI will be administered by trained clinicians (Drs. Martin, McGowan). Women will not be excluded due to presence of mental health conditions; however, this will be considered an important descriptive variable and will be used for conducting sub-group analyses of patients with specific comorbidities.

The PTSD Check List for DSM-5 (PCL-5)[26] is a standardized assessment for PTSD, based on DSM-5. A Life Events Checklist will be used to identify traumas experienced by women Veterans, and the most distressing event will be used for completion of the PCL.

The Generalized Anxiety Disorder-7 (GAD-7)[27] will be used to assess anxiety symptoms.

The Patient Health Questionnaire-9 (PHQ-9)[28] is a 9-item depression module in the PHQ, which is part of the Primary Care Evaluation of Mental Disorders (PRIME-MD) suite of evaluation tools. The PHQ-9 is widely used to screen for depression across VA.

The Perceived Stress Scale (PSS)[28a] is a global measure of stress. The 14-item scale measures how unpredictable, uncontrollable and overloaded respondents feel about stressful situations in the previous month. Responses are chosen from a 5-point Likert scale.

The WHOQOL-BREF[29] is a 26-item version of the WHOQOL-100, and is frequently used as a quality of life outcome measure in clinical trials. The questionnaire includes four domains: physical health, psychological health, social relationships and environment. It also includes one question on overall quality of life and one on general health.

The European Quality of Life Scale (EQ-5D)[29a] is a measure of health-related quality of life that can be used in a wide range of health conditions and treatments. It contains 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

The Calgary Sleep Apnea Quality of Life Index (SAQLI)[29b] is a 35-item questionnaire that evaluates 4 domains of quality of life associated with sleep apnea: daily functioning, social interactions, emotional functioning, symptoms, and treatment-related symptoms (for individuals using PAP therapy).

The Anxiety Sensitivity Index-3 (ASI-3)[36] is an 18-item questionnaire that measures fear of anxiety-related sensations based on beliefs about their harmful consequences. The ASI-3 has 3 6-item subscales that measure physical, cognitive, and social concerns.

Everyday Discrimination Scale: is a 9-item measure of daily discrimination as it relates to gender or race/ethnicity, assessed from "never" to "almost every day." A total score is computed by summing all items.
(Williams, D.R., Yu, Y., Jackson, J.S., and Anderson, N.B. "Racial Differences in Physical and Mental Health: Socioeconomic Status, Stress, and Discrimination." Journal of Health Psychology. 1997; 2(3):335-351.

Major Experiences of Discrimination Scale: is a 9-item measure assessing the last time a person experienced discrimination ranging from "past week" to "one year ago" and frequency of experiences of discrimination over the person's lifetime (total number).
(Williams, D.R., González, H.M., Williams, S., Mohammed, S.A., Moomal, H, Stein, D.J. "Perceived Discrimination, Race and Health in South Africa: Findings from the South Africa Stress and Health Study." Social Science and Medicine, 2008; 67: 441-452.)

Medical record review:
A structured medical record review will be performed at baseline and at the 3-month follow-up assessment to obtain information on health history and utilization of VA healthcare services, including outpatient visits in the 90 day period prior to study enrollment, and inpatient stays in the prior year. Problem list diagnoses and prescribed medications will be abstracted to inform randomization eligibility decisions (at baseline) and gather descriptive data about participants at 3-month follow-up.

Sleep Measures:
We will use unattended home sleep apnea testing (HSAT) to assess SA. In the past, SA was largely diagnosed with overnight laboratory polysomnography (PSG); however, this method has several limitations including cost and inconvenience. As an alternative to PSG, there are commercially-available devices to assess SA in the home. Although there are limitations to HSAT, VA has been an early adopter of HSAT. Our experience with women Veterans suggests that attended laboratory PSG, which entails observation by a (usually male) technician during sleep, is a significant barrier to SA diagnosis. Some women would also incur additional burden due to overnight childcare needs during laboratory PSG. HSAT is also less expensive, enabling us to study a larger group of women.

We will use the WatchPAT system (Itamar Medical, Caesarea, Israel) HSAT, because of its validity, reliability, ease of use, comfort, and low cost. This wrist-mounted system has an embedded actigraph to estimate sleep, fingertip sensors for measuring peripheral arterial tone (PAT) and pulse oximetry, and a reusable snoring/body position sensor. The system measures respiratory disturbances based on PAT (a reflection of autonomic nervous system changes) and pulse oximetry during sleep. Compared to laboratory PSG, studies have demonstrated a correlation of r=.85-.96 for respiratory disturbance index (RDI) and AHI.

Participants will review a brief video describing the WatchPAT device, the opportunity to practice with the WatchPAT sensors and to ask questions. They will be given an instruction booklet and a 24-hour toll-free company-supported advice line to call if difficulties arise overnight.

The 4-item Restless Legs Syndrome (RLS) questionnaire[30] will be used to identify significant RLS as well.

The Pittsburgh Sleep Quality Index (PSQI)[31] assesses sleep quality and disturbances over the past month. The PSQI is sensitive for distinguishing normal and abnormal sleepers and has good test-retest reliability. We will use the 3-factor scoring, which has been shown to have superior psychometric properties.

The Insomnia Severity Index (ISI)[32] is a 7-item instrument using Likert-type scales to measure severity of insomnia symptoms. The ISI correlates well with scores on the PSQI (r=.67), and with sleep diary measures (r's=.32-.91).[31]

The Epworth Sleepiness Scale (ESS)[31a] An 8-item questionnaire measuring level of daytime sleepiness, based on likelihood of dozing off or falling asleep in specific situations (e.g., reading, watching television).

The Disturbing Dream/Nightmare Severity Index (DDNSI)[31b] is a 5-item index that measures severity and intensity of nightmares on a 0-4 Likert-type scale. A score greater than 10 may indicate the presence of a nightmare disorder.

The Glasgow Sleep Effort Scale[31c] is a 7-item scale that measures perceived effort to fall asleep over the past week.

The Flinders Fatigue Scale (FFS)[33] is a 7-item scale used to measure general symptoms of fatigue. The FSS is sensitive to change after sleep-related interventions and will be used as an outcome measure.

Four of the DSM-5 diagnostic criteria questions that address length of time having sleep problems and adequate opportunity and circumstances to sleep will be asked.

Participants will complete daily sleep diaries based on the American Academy of Sleep Medicine Consensus Sleep Diary, which we adapted using a cognitive interviewing process with women Veterans, at baseline, post-treatment and at the 3-month follow-up. PSQI, ISI and sleep diaries will be used as measures of subjective sleep quality.

Wrist actigraphy will be used to objectively measure sleep. Participants will wear an actigraph (Actiwatch 2, Minimitter/Respironics, Bend, OR) on the non-dominant wrist for one week. The actigraph is a small watch-sized device useful in longitudinal, naturalistic assessment of sleep patterns.[34,35] Actigraphs contain accelerometers which measure movement. In general, movements below an established threshold is interpreted as sleep while high activity is interpreted as wakefulness. Commercially available software uses validated algorithms to determine minute-by-minute sleep vs. wake. Actigraphy has been validated in numerous studies, and evidence-based guidelines direct use of this technology. Agreement between wrist actigraphy and PSG in young and older people is .89-.95. We have developed highly standardized research procedures and protocols for use and scoring of actigraphy, and we have trained, experienced members of our research team to apply these protocols. In our work with women Veterans, actigraphy has been well-tolerated, with less than 2% missing data. We will analyze actigraphy data defining "night" and "day" based on sleep diary-reported bedtimes and rising times.

Potential Risks:

None of the procedures within this study are high risk; however, there are a number of minor risks, which will be minimized to the extent possible.

Sleep monitoring devices: The known risks associated with wearing the sleep monitoring devices are minimal. The sleep apnea sensors worn for one night and the sleep watch worn for 8 days may be annoying or uncomfortable. Rarely, they may cause skin irritation or an allergy. We have extensive experience using wrist actigraphy and the WatchPat system, and have chosen these devices because they are well-tolerated by participants. They are also substantially less burdensome than other objective methods of recording sleep (i.e., requiring the participant to spend a night in a sleep laboratory). Research staff will review carefully with participants potential skin problems associated with wearing the wrist actigraph and the WatchPat. Participants will be told to remove the device if they have any significant discomfort or any evidence of skin injury. Participants will have access to a research staff person 24 hours a day, in case they have questions or concerns about the equipment. In addition, the company which makes the WatchPAT device has a 24-hour advice line that also provides troubleshooting support. Our monitoring devices are checked regularly to insure safe and proper operation. The PI will be notified immediately of any significant discomfort experienced by study participants.

Questionnaires: Some participants may find completion of the questionnaires tedious or tiring, or may find other mental discomfort in answering some items. To lessen the risk of mental discomfort among participants, research staff will be trained to recognize discomfort in participants, and they will be trained to remind participants of the voluntary nature of the research and that they may refuse any portion of the study.

Sleep apnea education program: Participants may find that coming to the 6 education sessions is tiring or inconvenient. In addition, adjustments to the participant's sleep habits may result in some initial daytime sleepiness. The education sessions will be scheduled at times that are convenient for participants and will only last 45 minutes or less. Conducting the session over the telephone will be offered for participants who have unexpected difficulties in coming to the VA. Participants will be advised that they may experience daytime sleepiness as a temporary result of their modified sleep schedule (e.g., reduced daytime napping and maintaining a regular bedtime and wake up time) and it will likely resolve within one week.

Safety Monitoring Plan:

Since this study does not include any investigational drugs or devices, and carries only minimal risks, we will not have a formal safety monitoring board as required for FDA studies. However, we have developed a procedure for monitoring and reporting any study-related adverse events among the women who we meet face-to-face.

Step 1: If a participant reports a study-related adverse event, research staff will report this to the Principal Investigator (Dr. Martin) as soon as possible (always within 24 hours). When Dr. Martin is unavailable, Dr. Alessi (study co-investigator) will be contacted.
Step 2: If indicated, Dr. Martin will speak with the participant to determine the severity and likely cause of the concern. If medical examination is needed, the participant will be advised to go to the VA outpatient clinic and their VA primary care provider will be notified (by phone or by medical record research notes).
Step 3: Dr. Martin will report the event to the IRB and will make a determination whether study protocols should be modified for that participant, whether the participant should be withdrawn from the study, or whether the study protocols should be modified overall.
Step 4: All concerns reported by research staff will be documented, whether or not they appear to be study-related, and will be reviewed monthly by Drs. Martin and Alessi.
In the event that a participant expresses a serious medical or psychiatric concern, research staff will immediately contact Dr. Martin or Dr. Alessi, or if they are unavailable, will escort the participant to the Emergency Room (or outpatient clinic), or dial 911. All research staff are trained annually on participant safety issues, have the phone numbers of the Veterans Crisis Line, and have access to clinicians to assist with urgent safety concerns should they arise.

Sample size estimates

We anticipate sending 2,000 recruitment letters over the course of the study. Based on recent experience with similar methods, we expect 20% (n=400) will "opt out" of being contacted, 15% (n=300) will not be reachable by phone, and 20% (400) will refuse telephone screening. Based on these estimates, 900 women will be screened by phone. We estimate that 80% of women will meet criteria for the study (n=720) and approximately 40% of these women will be enrolled into the study (n=300). Given that women will be identified as having one or more SA risk factors, we anticipate that 45% (n=130) will have SA after objective testing. We expect that an additional 20% will not meet the final set of study inclusion criteria for randomization (described below) or will refuse further participation after completion of baseline. This will leave a total of 104 women potentially appropriate for randomization. To address the study aims a total of 90 women will need to be randomized. If we are unable to meet enrollment or randomization targets using these criteria, we will expand our list of SA risk factors extracted from the CDW (e.g., heart disease, depression).

Data management and analysis

Each participant will be assigned a unique ID which will be entered into electronic files and used on study forms. Using existing protocols, we will secure paper records and electronic data files in compliance with VA data security policies. All data will be coded by the data manager, then entered into databases using procedures established in prior work to minimize errors. Datasets will be cleaned by screening for out-of-range values, and comparing a random sample of 10% of entered data to original data forms. Double entry procedures will be used on a second, 10% random sample of cases in each dataset, with additional training and review of data if errors are identified. Cleaned data will be scored and aggregated, then data will be merged into one main database for analyses. Analyses will be preceded by a thorough inspection of data, scrutinizing for out of range values, implausible values, and outliers. Statistical assumptions for all tests will be assessed (e.g., for example, linearity and homogeneity of regression for the ANCOVA analyses).

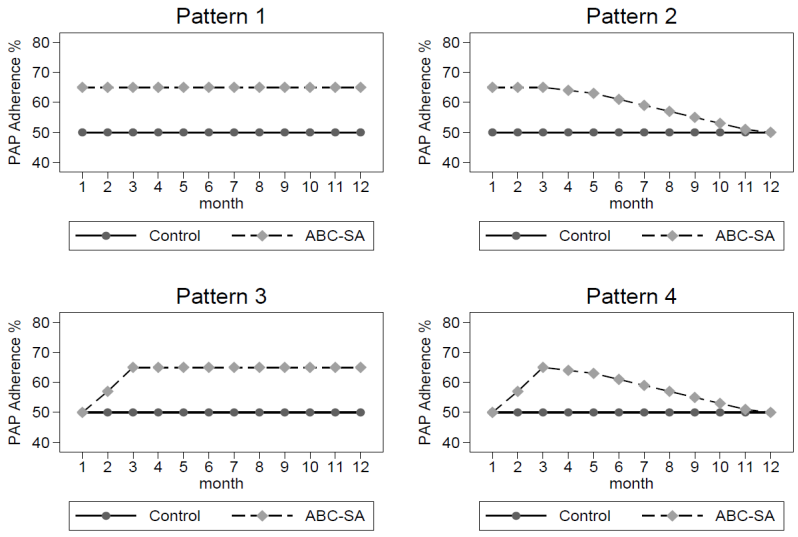
Study Design Considerations: Study design and analysis will follow CONSORT guidelines. Participants will be randomly assigned to ABC-SA or control, and adequacy of randomization will be assessed by comparing groups on baseline measures. We will follow intention-to-treat (ITT) principles. We will collect follow-up data from all randomized patients whether or not they complete the intervention to which they are assigned. Since PAP adherence data will be gathered remotely using tele-monitoring technologies (PAP machines transmit data to a cloud-based server), complete data (including confirmed non-use) is expected for each person for all 12 months. In a previous study, PAP adherence data or confirmed non-use has been obtained in 100% of participants. Based on our recent work with women Veterans, we anticipate 20% of participants will have missing or incomplete data at the 3-month follow-up. To improve retention, participants will be offered compensation for follow-up assessments, regardless of whether they complete the intervention. While we do not anticipate differential attrition, we will compare completion rates between groups and we will compare baseline characteristics between those with complete vs. incomplete follow-up data to test for systematic attrition. To preserve the equivalency formed by randomization (and since ITT analysis requires complete

data), missing data will be imputed using multiple imputation. Sensitivity analyses will be performed comparing the ITT results (with imputation) to results for those with complete data only. For outcomes other than PAP adherence, we have allowed for 20% missing data in sample size computations [N=72 (36/group) at 3-months follow-up]. Significance tests will use two-tailed tests and alpha=.05. Power analyses are computed using two-tailed tests, alpha=.05, and power=80%. When assessing power, Cohen's d is used to describe the size of an effect, which can be detected for the specified sample size and power. For tests comparing two groups, Cohen's d=of .20 is described as small, .50 as medium, and .80 as a large effect.

Aim 1 Data analysis/sample size calculations: Aim 1 examines effects of ABC-SA on PAP adherence. We will compute the proportion of nights (out of 30 nights) with ≥4 hours of PAP use per month. PAP adherence will be computed for the first 30 days (month 1), and for each subsequent 30-day period (months 2-12). The proportion of nights a patient uses PAP ≥4 hours will be computed by summing nightly scores (1=PAP use ≥4 hours; 0=PAP <4 hours) and dividing by the number of nights (i.e., 30). Denoting $\hat{p}_{ij}$ as the proportion of nights for person *j* in month *i*, the sampling distribution of $\hat{p}_{ij}$ will have an expected value of p_i (the true proportion who use PAP in the population in month *i*) and the SD of this sampling distribution is sqrt($N*p_i*(1-p_i)$). Based on the central limit theorem, the sampling distribution of these monthly proportions, $\hat{p}_i$ is expected to be normal, justifying use of normal theory statistics for analysis of monthly adherence.

Data analysis: For Hypotheses 1a and 1b, mixed-effects models will be used to compare monthly PAP adherence for ABC-SA vs. control. When applied to longitudinal designs, mixed-effects models permit specification of a wide variety of residual covariance structures. PAP adherence will be analyzed using a 2X12 factorial mixed-effects model with a fixed intercept.[78] Treatment group will be the 2-level between subjects factor and time (months) will be a 12 level categorical repeated measures factor. This approach will allow us to examine potential non-linear trends, which would not be apparent if time were treated as a continuous variable. The Bayesian Information Criteria (BIC) will be used to identify and select the best fitting residual covariance structure. Using the mixed-effects model, the difference in adherence rates between the ABC-SA and control groups will be assessed and tested at each month. To understand the nature of the treatment effects, we will dissect the "time by treatment" interaction into a series of tests of the simple effect of the treatment effect at each month. **Figure 2** illustrates four possible patterns of results. Consistently significant treatment effects is consistent with Pattern 1. Significant treatment effects in early months, followed by non-significant effects in later months is consistent with Pattern 2. Non-significant treatment effects in early months, followed by significant treatment effects in the remaining months is consistent with Pattern 3. Lastly, finding significant treatment effects in the middle months, but not early and later months is consistent with Pattern 4.

Figure 2: Possible patterns of results illuminated by the proposed



Power Analysis: Power was computed assuming complete data (N=90; 45/group). Analyses focus on the treatment effect (ABC-SA vs. control) in terms of the proportion of nights with PAP use >4 hours per month; thus, the power analysis shows the power to detect differences in the proportion of nights of PAP use >4 hours per month between ABC-SA and control groups. The SD of this proportion is conservatively estimated as SD=.091 [computed as sqrt(.5*(1-.5)/30)=.0913]. Given this SD, alpha=.05 and power=.80, the study can detect a difference in the average proportion of nights of PAP use ≥4 hours as small as 5.5% between ABC-SA and control for a given month. In interpreting the results, we will focus on larger, more clinically-important effects. This study will have ample power to detect clinically meaningful effects. The power to detect a 7.5% difference in adherence rates between groups would be .97. The power to detect a 20% difference would exceed .99. We would consider a difference of 10-15% to be clinically significant, and an effect >15% to be of substantial clinical importance. Results will be interpreted with these benchmarks in mind.

Aim 2 Data analysis/Sample Size Calculation: Aim 2 compares outcome measures that we expect to improve with improved PAP adherence. Outcomes tested are objectively measured (Aim 2a) and self-reported

(Aim 2b) sleep quality. The sample size for these analysis is expected to be N=72 (n=36 per group), accounting for 20% missing data from the 90 randomized participants.

Data Analysis. Hypotheses 2a and 2b will be tested using ANCOVA models where the outcome at 3 months is the DV, the treatment group assignment (ABC-SA vs. control) is the IV, and the covariate is the outcome variable measured at baseline. Compared to a "split-plot ANOVA" or analysis of change scores, this strategy offers greater statistical power and better controls for possible baseline differences.

Power Analysis. The detectable effect size with ANCOVA varies as a function of the pretest-posttest correlation. We used data from a prior RCT[1] to estimate the expected correlation and 95% CI. Baseline to 6-month correlations for the four outcomes were: actigraphy sleep efficiency (r=.71, 95%CI=[.62,.79]); PSQI (r=.48, 95%CI=[.35,.60]); ISI (r=.39, 95%CI=[.24,.52]); self-reported sleep efficiency (r=.49, 95%CI=[.35,.61]). Using the lower confidence limits (LCLs), we computed the detectable effect size (Cohen's d), then multiplied the Cohen's d by the SD of each outcome to yield the detectable effect in the natural units of the outcome, i.e. the study has sufficient power to detect a difference in PSQI of 2.1 points. The study can detect effects from d=.51 to .641 (**Table 6**).

Table 6. Power Analysis Results for Aim 2

Outcome	Pretest/Posttest Correlation (LCL)	Detectable Effect Size (Cohen's d)	Detectable Effect (Natural Units)
Actigraphy SE	r=.62	d=.52	3.3%
PSQI	r=.35	d=.62	2.1
ISI	r=.24	d=.64	3.4
Reported SE	r=.35	d=.62	9.6%

SE=sleep efficiency

Exploratory Aim 3 Data Analysis: As with Aim 2, ANCOVA models compare ABC-SA vs. control for each outcome (quality of life, depression, fatigue) at 3-months with baseline values as covariates.

Power Analysis. Using the same approach as Aim 2, correlations (and 95% CI) between baseline and 6-month measures of outcomes were: SF12-Physical (r=.65, 95% CI=[.55,.74]), SF-12 mental (r=.58, 95% CI=[.46,.68]), and PHQ9 (r=.48, 95% CI=[.34,.59]). The LCL for these values were used to compute the detectable effect sizes for two-tailed tests, alpha=.05, and 80% power (**Table 7**) Cohen's d was multiplied by the SD to convert the effect into units of the outcome. Detectable effects range from d=.55-62. We will have sufficient power to detect medium or larger effects for these exploratory outcomes.

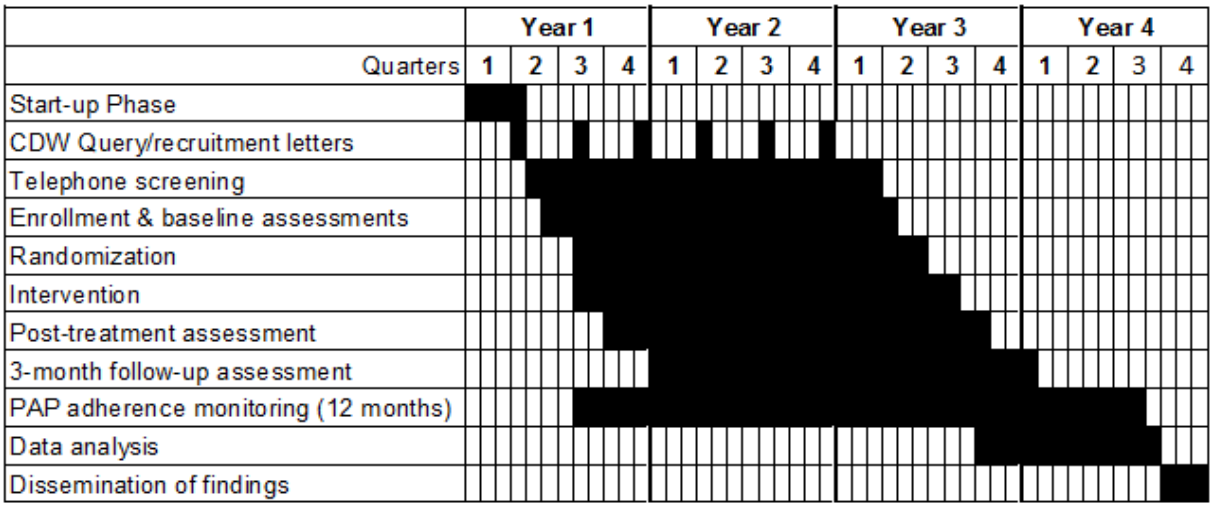
Table 7. Power Analysis Results for Aim 3

Outcome	Pret/Posttest Correlation (LCL)	Detectable Effect Size (Cohen's d)	Detectable Effect (Natural Units)
SF12-Physical	r=.55	d=.552	5.9
SF-12 Mental	r=.46	d=.590	5.6
PHQ9	r=.34	d=.621	2.7

Secondary analyses for Aims 1 and 2: In addition to the main analyses we will explore potential predictors of treatment outcomes within the ABC-SA group. We will do this by testing for associations between baseline measures (e.g. demographics, psychiatric symptoms) and PAP use (Aim 1) and sleep variables (Aim 2). If multiple factors are identified, multiple regression models will be used to evaluate the impact of potential predictors of treatment success.]

PROJECT MANAGEMENT PLAN

Project Timeline: The proposed project will be carried out over a 4-year period (see GANTT):



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