Official Title: Improving Sleep and Functioning in Veterans with Posttraumatic Stress Disorder

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Study Protocol with Statistical Analysis Plan

Scientific Background: Sleep disturbance is the most commonly endorsed symptom among Veterans with PTSD[1], and obstructive sleep apnea (OSA; 47%) and insomnia (26%) are the most common diagnoses among Veterans with any sleep disorder.[2] The first-line treatment for OSA is positive airway pressure (PAP), which forces air into the airway while the patient is asleep to prevent upper airway collapse. PAP use results in reductions in daytime sleepiness and improvements in functioning and quality of life.[3-5] Among those with PTSD, PAP use is associated with reduction in overall PTSD symptom severity.[6-8] However, PAP adherence rates are notably low among those with PTSD.[9,10] In addition, PAP use alone may not be sufficient in resolving quality of life/sleep-related functioning among those with PTSD, likely due to the comorbid insomnia that many patients experience. Both the American College of Physicians and American Academy of Sleep Medicine's guidelines for the management of chronic insomnia recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for insomnia as a first-line intervention.[11,12] In spite of frequent comorbidity, little is known about the outcome of CBT-I in those with sleep apnea because they are usually excluded from trials. Furthermore, insomnia itself is associated with PAP non-adherence.[13] By offering a behavioral intervention that reduces insomnia and addresses PAP adherence at the initiation of care for sleep apnea, Veterans may have greater success in adhering to treatment and realizing symptom and functional improvement. Furthermore, there is no integrated approach to treating Veterans with OSA and insomnia concurrently, but rather only through a piecemeal sequence, which is often uncoordinated between different treatment clinics and across a prolonged timeline. The proposed project allows for the evaluation of a treatment that addresses sleep apnea and insomnia in tandem and within the context of PTSD.

Objective: **Aim 1: Conduct a pilot RCT comparing AIR (*n* = 40) with sleep education (control condition; *n* = 40) for Veterans with OSA, insomnia, and PTSD. Hypothesis 1a**: Veterans receiving AIR will demonstrate improved quality of life (WHOQOL-BREF; primary outcome) and functioning (FOSQ-10; secondary outcome) compared with control at post-treatment and follow-up assessments. **Hypothesis 1b**: Veterans receiving AIR will demonstrate greater reduction in symptoms of insomnia (ISI and actigraphy) and PTSD (CAPS-5), and greater adherence to PAP (device data capture) compared with control at post-treatment and follow-up.

Aim 2: Evaluate the feasibility and acceptability of AIR. Participants will complete a Feasibility and Acceptability Questionnaire (FAQ) and follow-up interview based on their questionnaire responses. Topics will include content of treatment as well as experience completing the treatment delivered via telehealth. Examination of treatment dropout and attendance at other PAP-related appointments will also be monitored to determine whether the treatment facilitated increased engagement in care. **Hypothesis 2a:** Veterans receiving AIR will report at least moderate agreement with items on the FAQ. **Hypothesis 2b:** There will be lower dropout in the AIR condition compared with control. **Hypothesis 2c:** There will be greater engagement in apnea care in the AIR condition compared with control

Aim 3 (*Exploratory*): Evaluate moderators of treatment outcome. I will evaluate the data for trends indicating potential moderators of treatment outcomes, such as sleep apnea severity or concurrent medication use.

Design: First, I will conduct a randomized controlled trial of AIR and a sleep education control condition. The primary outcome will be quality of life. Next, I will solicit Veteran feedback to assess the feasibility and acceptability of AIR and evaluate measures of engagement in care. Finally, I will identify moderators of treatment outcome, which may help target Veterans for whom the treatment needs further refinement.

Methods:

Recruitment Procedures. After Veterans receive a referral for sleep apnea testing, research staff will send a letter inviting them to participate in the research study and notifying them that they will be contacted by study staff if we do not hear from them within 2 weeks opting-out. Veterans will have the option to opt-out via phone or email information provided in the letter. Veterans may also be contacted via invitation letter at the point of sleep apnea diagnosis and/or after review of PAP data demonstrating non-adherence to PAP. If a Veteran returns an interest in research form as part of their sleep apnea testing questionnaire packet and indicates they are interested in research, study staff may reach out via phone. Additionally, VA healthcare providers may refer their patients to the study if Veteran agrees to be contacted by research staff. This verbal consent to contact will be documented in the medical record. VA providers will refer patients through secure methods of notification, such as encrypted email, alert in medical record, and/or through a phone call. If VA healthcare providers give the Veteran approved informational brochure or flyer, the Veteran may also directly contact study staff. Veterans may also be identified as potential study participants via chart review prior to other VA appointments, such as appointments in PTSD clinic, to allow for identification of Veterans who may be eligible but are either not yet connected to VA sleep care or were previously connected but no longer engage in sleep care.

Data Collection Procedures.

Screening. Veterans will become eligible for initial screening following referral for sleep apnea testing. Sleep apnea testing is routine clinical care. The Research Assistant will contact potential participants to complete a phone screening. For those interested, the RA will obtain verbal consent to screen the potential participant for initial eligibility and inform participants that questions may address traumatic experiences and reactions. The screening questions will consist of basic contact information, insomnia symptoms, and PTSD symptoms. The screening will also establish any recent or upcoming changes to PTSD or sleep treatment aside from potential treatment for sleep apnea via the Sleep Clinic, as well as screen for exclusion criteria of recent substance use disorder, psychosis or manic episode within last 5 years, acute suicidality requiring alternate treatment, night shift or rotating shift work, lack of stable housing, and pregnancy. *This is solely for research purposes.

If the Veteran's sleep study took place in 2018 or earlier, we will obtain their weight at time of sleep apnea testing from the medical record and ask the Veteran their current weight. We will also ask them if they currently snore loudly, feel fatigued during the day, have been recently observed to stop breathing while they sleep, and have a history of hypertension. We will then send this information to a SFVA Sleep Medicine provider via encrypted email who will determine if this Veteran would benefit from an updated sleep apnea test and/or other clinical care prior to enrollment in this study. This will facilitate routine clinical care.

Consent. Potential participants deemed initially eligible via phone screen will be invited to attend a consent appointment via phone or video. Prior to the appointment, the consent document will be sent via mail, Secure Messaging on MyHealtheVet (if the Veteran has a printer) or email. The RA will review the consent document with the Veteran and emphasize that participation in the study is voluntary and the Veteran's choice to participate or not will not affect their eligibility for standard care in VA. The Veteran will sign a written consent form and return to study staff.

Clinical interview. Trained clinical interviewers will conduct the CAPS-5 interview to establish PTSD diagnosis and SCID-5 interview to establish insomnia diagnosis. This will take place over phone or video. The SCID-5 will also be used to rule out diagnostic exclusion criteria and establish comorbid mental health conditions for data analytic purposes. A brief medication interview will be conducted to obtain information about recent and current medication use. Interviews will be audio-recorded and reviewed by the Stress and Health Research Program's clinical assessment supervisor *This is solely for research purposes.

Baseline prospective sleep data. Once eligibility is established, the Veteran will be shown how to complete a sleep diary. He or she will then record one week of baseline sleep data. Research staff will email the Veteran a link to enter sleep diary data via Qualtrics. The Veteran's PAP setup appointment (if needed) and treatment schedule will be planned. *This is for research purposes; however, please note that completing a sleep diary is also part of routine care.

Actigraphy. The actigraph is a device worn on the risk to measure time asleep vs. awake. A subset of participants will be asked to wear the actigraph. The information will be used solely for research purposes. It is not part of the treatment.

Baseline appointment. The Veteran will complete pre-treatment measures. He or she will be randomized to either AIR or SE. * Many of the pre-treatment measures are completed as part of routine care, but some are added for research purposes.

Randomization procedure. A block-randomization procedure will be used to assign participants to AIR or SE in a 1:1 ratio. Block sizes will be a random permutation of 4 and 6. Statistical consultant [REDACTED] will produce the computer-generated list. Each therapist will have his or her own randomization list. The randomization to treatment is for research purposes.

Weekly assessment. At the start of each treatment appointment, the Veteran will complete two self-report questionnaires assessing sleep (ISI and ESS). The Veteran's PAP adherence data and actigraphy data will also be downloaded or requested verbally. A copy of the Veteran's sleep diary will be obtained. At his or her final treatment appointment, the Veteran will be asked to complete a sleep diary to submit at the Post-Treatment

Assessment appointment. In addition, at weeks 1, 3 and 5, the Veteran will complete the primary and secondary functioning outcome measures (WHOQOL-BREF and FOSQ-10.) *Completion of ISI and ESS, sleep diary data, and PAP adherence are part of routine care and will also be used for research purposes. The additional WHOQOL-BREF AND FOSQ-10 at weeks 1, 3 and 5 are for research purposes.

Post-Treatment Assessment. One week following his or her final treatment appointment, the Veteran will attend the post-treatment assessment appointment via phone or video. He or she will turn in the sleep diary with data from the preceding week. He or she will turn in the actigraphy device. The Veteran will complete post-treatment questionnaires. A trained, blinded clinical interviewer will repeat the CAPS-5 interview (current symptoms only) and SCID-5 (insomnia portion only) and inquire about medication changes. The Veteran will complete a brief feedback interview about their treatment experience with study staff. The Veteran's PAP adherence data will be downloaded or provided verbally. *This is for research purposes.

3-Month Follow-Up Assessment. Veterans will complete the 3-month follow-up questionnaires. PAP adherence data will be downloaded or provided verbally. If the Veteran's PAP device does not have a functional modem, the study team will arrange for the Veteran to provide their SD card for data download. The data will be uploaded to the appropriate clinical data monitoring system and the SD card will be returned to the Veteran. Veterans' charts will be checked to track PAP follow-up appointment attendance, if applicable. Veterans will be sent a sleep diary to complete the week prior to this appointment and will submit it at this appointment. *This is for research purposes. However, review of PAP adherence data at 3-month follow-up is also part of routine care in the Sleep Clinic.

Intervention Descriptions

Apnea and Insomnia Relief (AIR). This treatment will be offered over six sessions. All six appointments will be conducted via telehealth and will last 60 minutes. The main components of the AIR protocol are (a) psychoeducation, (b) motivational interviewing, (c) PAP adherence strategies, and (d) cognitive behavioral therapy for insomnia. All of these components are based in established strategies from other behavioral interventions but have not been evaluated in a combined protocol. The table beneath this description provides for a session-by-session overview of the treatment.

Psychoeducation. Education about insomnia, sleep apnea, and PTSD is primarily provided in the first session, though it is interwoven into subsequent sessions based on each Veteran's needs. Sleep apnea education involves review of what sleep apnea is, how the severity of sleep apnea is measured (AHI), and understanding what his or her own AHI means (e.g., "I stop breathing 25 times each hour.") Veterans identify how sleep apnea affects functioning and quality of life, including nighttime symptoms, daytime symptoms, and impact of physical health. Veterans then learn about how PAP helps sleep apnea. Insomnia education involves definition of insomnia; in particular, early, middle, and late insomnia are defined, and the Veteran identifies which type(s) of insomnia he or she is experiencing. An emphasis is placed on how sleep apnea affects quality of sleep, while

insomnia may impact quantity of sleep. A brief review of PTSD symptoms, particularly sleep-related symptoms, is integrated into this component.

Motivational interviewing. Strategies to increase motivation for treatment will be employed throughout treatment as needed, but motivational interviewing is a particularly strong focus in the first session. The therapist will help the Veteran identify benefits to engaging treatment, both in the short-term and long-term. Veterans will be guided through specifying goals for treatment. They will also identify potential barriers to treatment as well as solutions to these barriers.

PAP adherence strategies. The Veteran will typically receive their PAP on the same day as their first treatment session. When the Veteran receives his or her PAP device, a certified sleep technician and/or respiratory therapist trained in sleep instructs the Veteran in the device's use and care. At the first AIR appointment, the therapist reviews with the Veteran how he or she can check his or her progress on the device itself. The therapist and Veteran work together to identify problems with and barriers to PAP use each week. This may include physical problems that require a return visit to the sleep technician (e.g., mask air leak from poor fit), and the therapist will prompt the Veteran to arrange an appointment. Another barrier that may be addressed is difficulty remembering to put the mask on before bed; the therapist will assist the Veteran in setting up reminders to facilitate PAP use. Should the Veteran experience anxiety, claustrophobia, or general discomfort (not stemming from a physical issue requiring further assessment by the sleep technician) related to PAP, which is not uncommon with PTSD or anxiety, the therapist will guide the Veteran though PAP desensitization. PAP desensitization will also be advised if the Veteran is removing the mask in the middle of the night.

PAP desensitization. PAP desensitization is a type of graded exposure that is used to acclimate Veterans to PAP. This is indicated in the case of Veterans who have increased difficulty falling asleep or back asleep with the mask on, experience anxiety or claustrophobia when using PAP, or who those who remove PAP (either consciously or unconsciously) while asleep. The Veteran will use their PAP (with mask and machine on) while awake. He or she will engage in another activity, such as listening to music or watching TV, rather than focusing on his or her breathing. By acclimating to the sensation of the PAP device while awake, the Veteran will become more comfortable using the device at night and will be more likely to tolerate it overnight. The therapist first explains the rationale for PAP desensitization to the Veteran. For Veterans with anxiety or claustrophobia caused by PAP, the therapist will introduce the Veterans to a rating scale to indicate their level of discomfort so that reductions in anxiety can be tracked. The therapist will also discuss coping strategies the Veteran can use while engaging in desensitization. The therapist will guide the Veteran through an in-session desensitization practice. Should the Veteran experience anxiety, the therapist will coach the Veteran through using coping skills and observing his or her anxiety levels decrease over the course of exposure. The therapist will then work with the Veteran to generate a plan for engaging in desensitization at home. It is recommended that the Veteran complete desensitization for 30 minutes daily.

Cognitive Behavioral Therapy for Insomnia (CBT-I). CBT-I is an established behavioral treatment for insomnia. Its main components are sleep restriction therapy and stimulus

control. Secondary components include sleep hygiene, cognitive strategies, and relaxation techniques.

Sleep restriction therapy. Typically, people with insomnia spend much more time in bed than they spend asleep. This means that they are sleeping inefficiently (i.e., their sleep is not consolidated.) The goal of sleep restriction therapy is to help the Veteran achieve consolidated sleep; rather than sleeping in several small chunks throughout the night, he or she instead falls asleep quickly and stays asleep. Using data from sleep diaries, the Veteran's average sleep ability is calculated (how much time the Veteran actually sleeps during the night). The Veteran's sleep opportunity (time in bed) is then matched to their sleep ability to limit their time in bed to how much sleep they are currently able to produce. (Note: a Veteran's sleep opportunity is not set to lower than five hours for safety reasons.) Over the course of treatment, the Veteran's bed time is moved 15 minutes earlier or later depending on how his or her sleep efficiency has been over the past week. Thus, the first step is consolidating the Veteran's sleep, and then we slowly expand the Veteran's sleep opportunity to help him or her learn to generate more sleep. A key part of sleep restriction therapy is having a consistent wake time to help the Veteran generate sleep drive over the course of the day. The therapist works with the Veteran to generate strategies to cut down on going to bed early, sleeping in late, and/or napping – all of which reduce the Veteran's sleep drive.

Stimulus control. Stimulus control is a behavioral strategy based in the concept of classical conditioning. As Veterans spend time in bed while awake, they build an association between the bed (i.e., BED = AWAKE.) This association can be perpetuated by engaging in activities in bed other than sleep or sex, such as watching television, using one's cell phone, or engaging in worry or rumination. Instead of BED = AWAKE, stimulus control promotes the association between BED = ASLEEP. This is accomplished by (a) using the bed for only sleep and sex, (b) moving other activities once done in bed to other locations, (c) only going to bed when feeling sleepy, (d) getting out of bed if unable to fall asleep or back sleep after 15-20 minutes, and (e) refraining from sleep in locations other than the bed. The therapist helps the Veteran implement these strategies.

Additional treatment components. Though the main components of CBT-I are sleep restriction therapy and stimulus control, later sessions cover additional material. The therapist helps the Veteran identify elements of sleep hygiene that may be improved, such as making the bedroom environment more comfortable or reducing caffeine intake in the afternoon and evenings. Another secondary element of CBT-I is a discussion of cognitions that may perpetuate insomnia. This includes attentional bias towards cues for sleepiness during the day and belief in several myths about sleep (e.g., 8 hours is everyone's ideal amount of sleep.) Though not a major focus of treatment, the therapist also introduces the Veteran to basic relaxation strategies that may be incorporated into the Veteran's bedtime ritual.

Apnea and Insomnia Relief (AIR) session content

Session	Content
1	Psychoeducation about sleep apnea, insomnia, and PTSD; assessing/increasing motivation and identifying goals for treatment; learning to complete sleep diary
2	Continued motivational interviewing; Reviewing PAP experience; introducing PAP desensitization (in-session and at home) if needed; reviewing sleep diary; learning about sleep restriction
3	Reviewing PAP experience; continuing PAP desensitization; reviewing sleep diary; introducing stimulus control; continued motivational interviewing, if needed
4	Reviewing PAP experience; continuing PAP desensitization; reviewing sleep diary; sleep hygiene; continued motivational interviewing, if needed
5	Reviewing PAP experience; continuing PAP desensitization; reviewing sleep diary; cognitions about sleep; relaxation strategies; continued motivational interviewing, if needed
6	Reviewing PAP experience, continuing PAP desensitization; reviewing sleep diary; reviewing progress and relapse prevention

Sleep Education Control (SE). The control treatment will also be offered over 6 sessions via telehealth, to match time with the attention provided in the AIR condition. The protocol is an adaptation of the non-directive sleep education control condition in a study of CBT for insomnia among older adults at the Greater Los Angeles Healthcare System. Topics covered include the sleep cycle, sleep across the lifespan, sleep and the mind, evening activities and the sleep environment, and daytime activities and sleep. The table beneath this description provides for a session-by-session overview of the treatment.

Sleep Education Control session content

Session	Content
1	Purpose of sleep, the sleep cycle/stages of sleep
2	Review of personal sleep history, sleep across the lifespan, aging and sleep
3	Consequences of poor sleep, stress and poor sleep, relaxation exercise
4	Healthy sleep environment: falling asleep (temperature, light, noise)
5	The body and sleep (physical exercise, diet)
6	Reviewing past sessions' content, most important tips to remember

Feasibility and Acceptability. Aim 2 of this study is to assess the acceptability and feasibility of AIR in Veterans with PTSD, insomnia, and OSA. We will assess feasibility and acceptability using a combination of Veteran self-report (questionnaire and interview) and behavioral metrics. The results of these inquiries will guide changes to treatment that must occur prior to the full-scale RCT that will be proposed in a VA Merit Review application.
Questionnaires. As described above, Veterans will complete the Feasibility and Acceptability self-report questionnaire at the post-treatment assessment (see Appendix 4). The items include questions specifically about the content of the intervention as well as use of telehealth. We will evaluate descriptive statistics for each item. On a group level, any item with less than moderate agreement (4.0 on 5.0 scale) will be identified as an element requiring further retooling in future work. Veterans will also complete the CSQ-8, a more global assessment of treatment satisfaction, to evaluate treatment satisfaction and assess differences between Veterans receiving AIR and Veterans receiving SE. *This is for research purposes.
Interview. After completing the self-report questionnaires, the Veteran will meet with the Research Assistant to participate in an approximately 20-minute interview to obtain further information about his or her responses on the Feasibility and Acceptability Questionnaire. The RA will follow up about any items rated less than 4.0 on the Feasibility and Acceptability questionnaire. The RA will also probe for more information on the Veteran's experience in the telehealth sessions, including any aspects that were particularly positive or negative, and any problems encountered. *This is for research purposes.
Dropout. An important aspect of feasibility and acceptability is behavioral: whether Veterans attend and complete treatment. We will examine whether there are differences in completion between AIR and SE. If there is higher dropout in the AIR condition, we will need to make thoughtful adjustments to the protocol prior to the full-scale RCT proposal based on Veterans' feedback about treatment. We will also examine when dropout does occur. If most dropout should occur immediately after randomization (as has been our experience in previous trials), we will be less concerned about the acceptability of treatment than if most dropout occurs later once treatment is initiated. *This is for research purposes.
Engagement in follow-up care. Veterans with new PAP setups in the Sleep Clinic are scheduled for a return visit with a sleep technician or nurse practitioner approximately three months following receipt of PAP. This visit is important to ensure optimal treatment and address any barriers to adherence and follow-up care in the case of non-adherence. If PAP is not going to be used, other treatments may be indicated (such as oral appliance or surgery), but if the Veteran does not attend this appointment, he or she is lost to follow-up and will go untreated. We will assess for differences between AIR and SE in attending this follow-up appointment. This analysis will only be applicable to Veterans with new PAP setups that occurred during this participation in this study. *This is for research purposes.

Statistical Analysis Plan: Baseline characteristics of both groups (demographic, diagnostic, and pre-treatment levels of outcome measures) will be described using appropriate summary statistics. We will examine the distributions of outcome measures for outliers and evaluate the need to transform data. Identification of potential outliers will prompt review of data to evaluate for data entry errors; analyses including and excluding

outliers will be conducted to evaluate influence on outcomes. Primary analyses will be unadjusted intent-to-treat analyses, with all subjects randomized to a treatment condition included. We will use linear mixed models, which are robust to data missing at random, to accommodate missing data due to dropout. Demographic and other baseline variables that show large group imbalances despite randomization will likewise be entered as covariates in a secondary sensitivity analysis, but will not be included in the primary analyses. Substantial differences in inferences supported by the primary and secondary analyses would indicate a potential problem of randomization failure, and would warrant caution in interpreting results of the primary analyses

Hypothesis Testing.

Hypothesis 1a: Veterans receiving AIR will demonstrate improved quality of life (WHOQOL-BREF; primary outcome) and functioning (FOSQ-10; secondary outcome) compared with control at post-treatment and follow-up assessments.

Analyses. The WHOQOL-BREF psychological domain score will be considered the primary outcome of the study, whereas the FOSQ-10 is a secondary measure of functioning. Both the WHOQOL-BREF and FOSQ-10 are administered at pre-treatment, week 3, week 5, post-treatment, and 3-month follow-up. Separate analyses will be conducted for each measure. A linear mixed model will be estimated for each score with subjects entered as a random effect and treatment group and time entered as fixed effects. Pre-treatment scores will be entered as a covariate, and time (week 3, week 5, post-treatment, and follow-up) will be entered as a categorical predictor to accommodate non-linear changes over time. The hypothesis will be tested by the significance of the group differences in baseline-adjusted post-treatment scores. The baseline-adjusted group difference at post-treatment will be divided by the standard deviation of baseline scores to calculate the standardized effect size. Durability of effects at 3 months will be tested by examining group differences in baseline-adjusted follow-up scores.

Hypothesis 1b: Veterans receiving AIR will demonstrate greater reduction in symptoms of insomnia (ISI and actigraphy) and PTSD (CAPS), and greater adherence to PAP (device data capture) compared with control at post-treatment and follow-up assessment.

Analyses for insomnia: The ISI is administered several times over the course of treatment: pre-treatment, sessions 1-6, and post-treatment. A linear mixed model will be estimated for each score with subjects entered as a random effect and treatment group entered as a fixed effect. Pre-treatment score will be entered as a covariate. Time (sessions 1-6 and post-treatment) will be modeled linearly and non-linearly, with the choice of functional form governed by likelihood ratio tests and BIC criteria. The choice of whether to include a random effect for time will be determined by choosing the best fitting model according to the likelihood ratio test. All modeling choices will be made before examining any significance tests. The hypothesis will be tested by the significance of the group difference in baseline-adjusted marginal means (least squares means) at post-treatment derived from the full model. The difference in marginal means at post-treatment will be divided by the pre-treatment standard deviation to calculate the standardized effect size. These analyses will be repeated with the insomnia variables of interest derived from actigraphy

(TST and WASO), with data grouped by week. The primary variable for this analysis will be TST.

Analyses for PTSD: The CAPS is administered at pre- and post-treatment. The primary analysis examining the CAPS will be based on the CAPS total score. A linear mixed model will be estimated for CAPS total score with subjects entered as a random effect and treatment group and time point entered as fixed effects. The hypothesis will be tested by the significance of the group by time interaction. The baseline-adjusted group difference at post-treatment will be used to calculate the effect size.

Analyses for PAP adherence: PAP adherence will be measured via device data capture. The primary metric used to measure this will be average hours of PAP use in the past 7 days. This will be measured starting at session 1 and will continue through post-treatment, and again for 1 week at follow-up. A linear mixed model as described above for the ISI will be estimated for PAP adherence. The hypothesis will be tested by the significance of the group difference in marginal means at post-treatment derived from the full model. The difference in marginal means at post-treatment will be divided by the pre-treatment standard deviation to calculate the standardized effect size. Durability of effects at 3 months will be tested by comparing model-adjusted marginal effects for the two groups at follow-up. Effect size of treatment at 3 months will be calculated from the marginal effect of group at follow-up divided by the standard deviation of week 1 adherence scores.

Hypothesis 2a: Veterans receiving the behavioral sleep treatment will report at least moderate agreement with items on the Feasibility and Acceptability Questionnaire.

Analyses: Descriptive statistics will be calculated for each item of the Feasibility and Acceptability questionnaire, provided in the Appendix. The mean response to each item will be the primary metric for evaluation of this hypothesis. A mean in the range of 4.0 to 5.0 will be considered acceptable.

Hypothesis 2b: There will be lower dropout in the AIR condition compared with the SE condition.

Analyses: We will conduct a chi-square analysis to compare dropout in the two conditions (completed all six sessions vs. not).

Hypothesis 2c: There will be greater engagement in apnea care in the AIR condition compared with the SE condition.

Analyses: We will conduct a chi-square analysis to compare how many Veterans attend their first PAP follow-up appointment with a sleep technician or sleep NP in the two conditions.

Exploratory Analyses.

Evaluation of moderators of treatment outcome: We will evaluate the data for potential moderators of treatment outcomes. This will facilitate adjustments to the protocol prior to a large-scale RCT.

Analyses: We will evaluate interactions between subject characteristics and treatment effects to generate hypotheses for informing future work. This exploratory process is necessary because the sample size in the proposed project is insufficiently powered for multiple formal subgroup analyses. In these exploratory analyses, the focus will be on estimated effect sizes rather than statistical significance. These will be calculated based on interaction terms in the models described under Hypothesis 1a above. The primary

moderators of interest are: AHI, concurrent use of sedative-hypnotic medication, baseline PAP self-efficacy (SEMSA), baseline daytime sleepiness (ESS), and baseline sleep quality (PSQI). We will also examine demographic variables and comorbid medical or psychiatric conditions

Secondary treatment outcomes: Veterans receiving the behavioral sleep treatment will demonstrate greater increase in sleep efficiency (sleep diary), greater reduction in daytime sleepiness (ESS), greater reduction in PTSD symptom severity (PCL-5), greater improvement in sleep quality (PSQI), and greater improvement in self-efficacy in using PAP (SEMSA) compared with control at post-treatment and follow-up assessment.

Analyses: SEF will be the primary variable of interest derived from sleep diaries. The ESS is administered at pre-treatment, sessions 1-6, and post-treatment. The PCL-5, SEMSA, and PSQI are completed at baseline and post-treatment. Separate linear mixed models as described for primary hypotheses 1a and 1b will be estimated for each measure, with each secondary outcome hypothesis tested by the significance of the group difference in baseline-adjusted marginal mean scores post-treatment. Standardized effect sizes will be calculated as the marginal post-treatment group differences divided by pre-treatment standard deviations.

Evaluation of global treatment satisfaction: We will examine CSQ-8 total scores for evidence of treatment satisfaction. We will evaluate the data for group differences in treatment satisfaction.

Analyses: Descriptive statistics will be calculated for the total score on the CSQ-8. An average total score in the range of 24-32 will be considered acceptable. We will conduct a t-test to compare CSQ-8 total scores in the two conditions.

Evaluating association between improved sleep and change in functioning: We will evaluate the relationship between improvement in insomnia and functioning and PAP adherence and functioning.

Analyses: We will estimate subject-specific treatment effects on the ISI and WHOQOL-BREF from the mixed models described above, and calculate the Pearson correlation coefficient to assess the relationship between improvement on these two outcomes. We will add PAP adherence as a predictor to the mixed models for WHOQOL-BREF and ISI to test whether changes in functioning or insomnia differ by level of PAP adherence (less than 1 hour nightly, between 1 and 4 hours, greater than 4 hours.)

CBT-I outcomes among Veterans with uncontrolled OSA: We will evaluate group differences in insomnia outcomes among the subset of Veterans who do not adhere to PAP during treatment. This will provide data about the efficacy of CBT-I among those with untreated sleep apnea, which is a gap in the literature.

Analyses: We will repeat the analyses described above for the ISI and actigraphy outcome measures (hypothesis 1b), in the sample limited to Veterans who are not adherent to PAP.

References:

1. Roszell DK, McFall ME, & Malas KL. (1991). Frequency of symptoms and concurrent psychiatric disorder in Vietnam veterans with chronic PTSD. Psychiat Serv, 42, 293-296.
2. Alexander M, Ray MA, Hébert JR, et al. (2016). The national veteran sleep disorder study: descriptive epidemiology and secular trends, 2000–2010. Sleep, 39, 1399-1410.

3. Engleman HM, Martin SE, Douglas NJ, et al. (1994). Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet, 343, 572-575.
4. Engleman HM, Cheshire KE, Deary IJ, et al. (1993). Daytime sleepiness, cognitive performance and mood after continuous positive airway pressure for the sleep apnoea/hypopnoea syndrome. Thorax, 48, 911-914.
5. Ballester E, Badia JR, Hernandez L, et al. (1999). Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med, 159,495-501.
6. Krakow B, Lowry C, Germain A, et al. (2000). A retrospective study on improvements in nightmares and post-traumatic stress disorder following treatment for co-morbid sleep-disordered breathing. J Psychosom Res, 49, 291-298.
7. Tamanna S, Parker, JD Lyons J, et al. (2014). The effect of continuous positive air pressure (CPAP) on nightmares in patients with posttraumatic stress disorder (PTSD) and obstructive sleep apnea (OSA). J Clin Sleep Med, 10, 631.
8. El-Solh AA, Vermont L, Homish GG, et al. (2017). The effect of continuous positive airway pressure on post-traumatic stress disorder symptoms in veterans with post-traumatic stress disorder and obstructivesleep apnea: a prospective study. Sleep Med, 33, 145-150.
9. El-Solh AA, Ayyar L, Akinnusi M, et al. (2010). Positive airway pressure adherence in veterans with posttraumatic stress disorder. Sleep, 33, 1495-1500.
10. Collen JF, Lettieri CJ, & Hoffman M. (2012). The impact of posttraumatic stress disorder on CPAP adherence in patients with obstructive sleep apnea. J Clin Sleep Med, 8, 667.
11. Schutte-Rodin S, Broch L, Buysse D, et al. (2008). Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med, 4, 487.
12.Qaseem A, Kansagara D, Forciea MA, et al. (2016). Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians Management of Chronic Insomnia Disorder in Adults. Ann Intern Med, 165, 125-133.
13. Wickwire EM, Smith MT, Birnbaum S, et al. (2010). Sleep maintenance insomnia complaints predict poor CPAP adherence: a clinical case series. Sleep Med, 11, 772-776