Provider Supported Self-Help Cognitive Behavioral Therapy for Insomnia (Tele-Self CBTI)

NCT03727438

Protocol and Statistical Analysis plan

Contingent approval 10/13/22, full approval 11/10/22

PROTOCOL TITLE: Tele-Self CBTI Trial

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A. Purpose

The proposed study is a randomized controlled trial comparing Tele-Self CBTI to Health Education Control for improved insomnia severity among treatment-seeking Veterans with Insomnia. In this 2-arm trial, 200 participants will be randomized in a 1:1 ratio to Tele-Self CBTI or a Health Education Control condition. Veterans will be identified using electronic health records and telephone interviews. Outcomes will be assessed at 3 time points: baseline, 8 weeks, and 6 months after baseline. Participants in both arms will continue to receive usual medical care. Each assessment period involves a) 2 weeks of home-based sleep assessment (diary and actigraphy), and b) completion of telephone interview. Following completion of a home-based sleep assessment period, a questionnaire-based assessment will be conducted by phone.

B. Background and Significance

Insomnia is one of the most common complaints among service-members and Veterans of recent military conflicts. When Veterans of the Iraq and Afghanistan conflicts were asked what services they would be most likely to use if offered by the VA, “help with sleep” was endorsed more frequently than any other service[1]. Accordingly, insomnia diagnoses increased 19-fold among military service members from 2000 to 2009[2]. Insomnia has been shown to play a causal role in depression, anxiety, suicidality, disability due to a mental health disorder, hypertension, obesity, metabolic syndrome, diabetes, and all-cause mortality[3-8]. Thus, insomnia is a risk factor for the most common conditions seen in patients utilizing the VA healthcare system.

Cognitive-Behavioral Therapy for Insomnia (CBTI) produces both short-term and sustained resolution of insomnia with fewer adverse side effects than pharmacotherapy[9,10], and CBTI can be effectively delivered using a range of treatment modalities[11,12]. But access to behavioral sleep medicine expertise within the VA is very limited[13], and recent efforts to disseminate CBTI across the VA will have only limited reach. Innovation is essential to simultaneously increasing Veteran access to CBTI while minimizing increased provider resources. Self-management and telehealth are viable options for achieving these goals. Our team has conducted qualitative research with Veterans to derive their attitudes and preferences for self-management of insomnia. Our findings suggest that Veterans would engage with provider-supported self-management strategies for insomnia, including CBTI via e-Health and telehealth approaches.

Considering the high prevalence of sleep difficulties among Veterans (>50%), the mental health risks of poor sleep (e.g., anxiety, depression, and suicide), and Veterans’ desire for assistance with sleep, addressing Veterans’ sleep difficulties should be a central goal of VA efforts to achieve Veteran-centered care. The objectives of the proposed research are aligned with the following HSR&D High Priority Research domains: Healthcare Access-using telehealth to increase rural Veteran access to care; and Mental and Behavioral Health-testing new models of care to improve access, cost and outcomes. Since CBTI has demonstrated efficacy for

reducing suicidal ideation in Veterans, the proposed research is also responsive to an ORD-wide priority area: suicide prevention. Treatment of insomnia in Veterans has the potential to improve outcomes across virtually all life domains, including mental health, physical health, psychosocial functioning, and quality of life. A provider-supported self-management strategy for insomnia can bridge the gap between unavailable resources and high demand for services.

Aim 1: To test the effect of Tele-Self CBTI on insomnia severity in Veterans with insomnia.
Hypothesis 1: Relative to Health Education, participants randomized to Tele-Self CBTI will have greater improvements in insomnia severity, as measured by the Insomnia Severity Index (ISI) at 8 weeks.
Aim 2: To test the effect of Tele-Self CBTI on subjective and objectively assessed sleep, fatigue, depression symptoms, and sleep quality of life (QOL).
Hypothesis 2: Relative to Health Education, participants randomized to receive Tele-Self CBTI will have greater improvements in subjective sleep (per diary on sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency (SE), and objective sleep (per actigraphy WASO, total sleep time (TST), and SE), fatigue, depression symptoms, and sleep QOL at 8 weeks. *Aim 3*: To inform future efforts, we will use qualitative research methods to examine nurse and clinic administrator perspectives on implementing and disseminating Tele-Self CBTI.

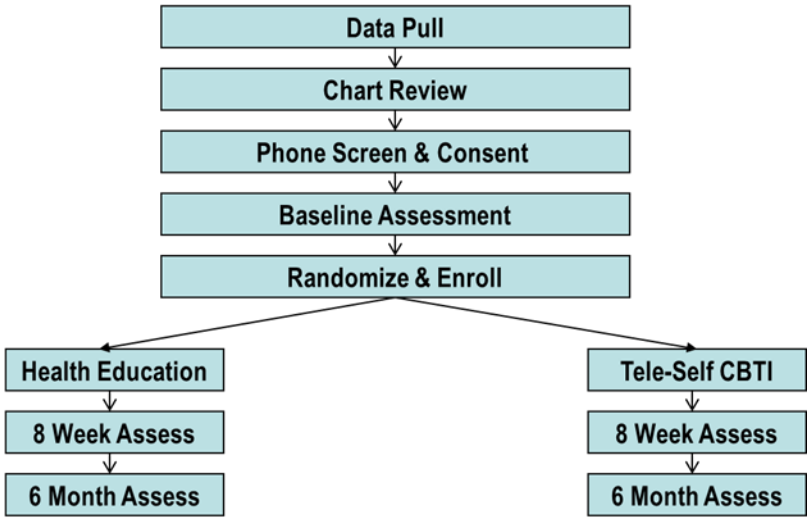

Figure 1

C. Randomized Controlled Trial (Aims 1 and 2)

C.1 Study Design

The proposed study is a randomized controlled trial comparing Tele-Self CBTI to Health Education Control for improved insomnia severity among treatment-seeking Veterans with Insomnia (Figure 1). In this 2-arm trial, 200 participants will be randomized in a 1:1 ratio to Tele-Self CBTI or a Health Education Control condition. Veterans who are: a) prescribed sleep medications; b) diagnosed with insomnia; or c) referred for clinic based CBTI (but not yet treated) will be identified using electronic health records (EHR) and telephone interviews. Outcomes will be assessed at 3 time points: baseline, 8 weeks, and 6 months after baseline. These time points were selected to assess the immediate (8 weeks) effects of Tele-Self CBTI, and to determine if Tele-Self CBTI results in sustained improvements (6 months). Participants in both arms will continue to receive usual medical care. Each assessment period involves a) 2 weeks of home-based sleep assessment (diary and actigraphy), and b) completion of self-report

questionnaires. Following completion of a home-based sleep assessment period, a questionnaire-based assessment will be conducted by phone by a research assistant blinded to treatment condition. Study participants will be asked to return actigraphy devices (as well as any paper forms) at the end of each assessment period via prelabeled UPS envelopes dropped off at a UPS location.

C.2 Study Population

The target population for this trial is treatment-seeking Veterans with Insomnia from the Durham Veteran's Affairs Healthcare System. Because few VA PCPs routinely document insomnia in the medical record[79], identifying patients with insomnia in the EHR is challenging. Prescribed sleep medications are the most common PCP response to an insomnia complaint, although some patients are referred for CBTI. Consistent with the larger literature, we found no difference between Veterans prescribed sleep medications and those who were not prescribed sleep medications in terms of improvements in insomnia severity (f=.15, p=.70) following participation in group based CBTI at the Durham VAMC[80]. Thus, we have defined treatment-seeking Veterans with Insomnia as those who are: a) prescribed sleep medications; b) diagnosed with insomnia; or c) referred for clinic-based CBTI (but not yet treated).

Table 1. Eligibility Criteria Assessment: Methods and Measures

Eligibility Criteria	Assessment Method
Level 1 (L1)-Data Pull and Chart Review	
Inclusion	
≥ 18 years of age	EHR data pull
Insomnia Diagnosis OR prescribed sleep medications OR referred for CBTI	EHR data pull & record review
Exclusion	
Psychotic DO; Bipolar DO; Substance Use; Alcohol Abuse	EHR data pull
Dementia; Cognitive Impairment; Epilepsy; Seizure DO	EHR data pull
Severe OSA with treatment non-adherence	EHR record review
Unstable housing and/or no/unreliable telephone	EHR record review
Unstable Co-morbid Sleep DO; and current or prior participation in CBTI	EHR record review
No current/prior CBTI participation	EHR record review
Nursing Home Residence	EHR record review
Level 2 (L2)-Phone Screening, Consent & Enrollment	
Inclusion	
Insomnia Disorder diagnostic criteria are met per ICSD-3	DSISD Insomnia DO Module[6]
Insomnia Severity Index score of ≥10	ISI[7]
Exclusion	
Severe OSA with treatment non-adherence (when unclear from EHR review)	Phone Screening
Unstable housing and/or no/unreliable telephone (when unclear from EHR review)	Phone Screening
Excessive daytime sleepiness	Epworth Sleepiness >15
Nighttime or Rotating Shift Work w/in the last year	Phone Screening
Confirm no current/prior CBTI participation	Phone Screening
Severe Depression and Suicidality	PHQ-8 >19 and/or SI
Current Recreational Drug Use	Drug Use Screener endorsed
Nursing Home Residence (to complement information from EHR chart review)	Phone Screening

EHR=electronic health record; DO=Disorder; ICSD-3= International Classification of Sleep Disorders; ISI=Insomnia Severity Index; OSA=Obstructive Sleep Apnea; PHQ=Patient Health Questionnaire; SI=Suicidal

Ideation.

C.3 Participant Selection and Recruitment

We plan to recruit Veterans using both CPRS record review and recruitment from the following clinics: Sleep Medicine Clinic; Behavioral Sleep Medicine Clinic; OEF/OIF/OND Clinic; Mental Health Clinics and Primary Care. We may utilize 1 or more of the following approaches to screen and recruit Veterans into the study:

Approach 1-EHR Recruitment

We will recruit treatment-seeking Veterans with Insomnia from the Durham VA Healthcare System using the criteria in Table 1. In Step 1, we will extract data from the EHR. Potentially eligible Veterans will be randomly selected from the data pull for chart review to identify those meeting Level 1 (L1) inclusion/exclusion criteria.

Veterans identified as eligible at Level 1 (L1 in Table 1) will receive a letter and Study Information sheet describing the study and offering the option to opt out of future study contacts. Those not opting out will receive a phone call to assess interest in the study. Interested Veterans will be screened for Level 2 (L2) criteria by phone (Veterans meeting these criteria and providing verbal informed consent will be invited to participate in the study. Veterans who are excluded from the study will be offered tailored interventions for insomnia through our Behavioral Sleep Medicine clinic and/or referred to our medical sleep clinic for additional assessment or treatment, as needed.

Approach 2-Provider-Assisted Recruitment

Approach 2 involves healthcare provider assistance with recruitment. Clinicians in clinics throughout the medical center will be provided information about study eligibility and basic procedures (see provider email content) as well as a flyer they can provide to patients. Clinicians will be asked to refer potentially eligible veterans. Clinicians have reported that Veterans often indicate that they prefer that their names and contact information be provided directly to study staff. We'd like to make it easy for interested Veterans to get involved in research, while protecting the privacy of those Veterans who are not interested in research. Towards that end, we would like to allow a clinician to refer a participant directly to our study. Dr. Ulmer will send providers an email message to simultaneously recruit for two studies involving insomnia treatment; this study and a small pilot study (Path to Better Sleep Pilot Study) being conducted by Dr. Ulmer (see provider email content). Dr. Ulmer will attach a flyer to the recruitment email that clinicians may provide to interested Veterans. As indicated in the email message, providers who identify interested and potentially eligible Veterans can refer their patients to the study by adding the study PI or study staff as a co-signer to a CPRS note wherein the clinician has documented the Veteran's wish to be contacted about study participation. Dr. Ulmer will record in an excel file located here (\\v06.med.va.gov\DUR\HSRD\Insomnia_Self_CBTI_Trial_IRB_2147\Data\Databases\Tracking Database\Physician Referrals) the name of patients meeting initial eligibility criteria (i.e., diagnosed with insomnia, prescribed sleep medications, and/or referred to the BSM clinic for insomnia treatment). Research staff will then follow the recruitment procedures described in Approach 1 above, beginning with chart review. In addition to the recruitment process described above, research staff may offer presentations at clinic staff meetings to inform providers about the study and provide guidance on the referral process.

Other recruitment procedures will be conducted within the Behavioral Sleep Medicine (BSM) clinic. Dr. Ulmer (study PI) may identify potentially eligible patients during the conduct of

her clinical work in the Behavioral Sleep Medicine (BSM) clinic; specifically, those who have been referred to the BSM Clinic and/or patients awaiting the availability of a provider to begin treatment. This will be accomplished by reviewing the chart of patients who have been referred to the BSM clinic with an insomnia complaint, and reviewing the BSM Clinic electronic waiting list/s. Dr. Ulmer will record in an excel file located here (R:\Insomnia_Self_CBTI_Trial_IRB_2147\Data\Databases\Tracking Database\Physician Referrals) the name of patients meeting initial eligibility criteria (i.e., diagnosed with insomnia, prescribed sleep medications, and/or referred to the BSM clinic for insomnia treatment). Research staff will then follow the recruitment procedures described in Approach 1 above, beginning with chart review.

Approach 3-Flyer Posting and Brochure Placement

Approach 3 involves placement of recruitment flyers in the VA approved research recruitment bulletin boards located throughout the hospital and CBOC clinics. We have also created a brochure about the study that may be distributed in clinics.

Exclusion criteria: 1) Severe Obstructive Sleep Apnea with treatment non-adherence; 2) unstable co-morbid sleep disorder determined via chart review (e.g., rule out for Narcolepsy, rule out for Shift Work Disorder); 3) current or prior participation in CBTI; 4) excessive daytime sleepiness; 5) nighttime or rotating shift work within the last year; 6) psychotic disorder diagnosis; 7) bipolar disorder diagnosis; 8) recreational substance use/abuse; 9) current alcohol abuse; 10) severe depression or suicidality; 11) dementia diagnosis; 12) cognitive impairment; 13) epilepsy or seizure disorder 14) lack of proficiency in the English language; 15) hearing impairment that impedes telehealth intervention; or lack of stable housing and/or no access to a telephone.

Rationale for Inclusion/Exclusion Criteria:

Insomnia Disorder: To be eligible for this study, patients must meet diagnostic criteria for Insomnia Disorder (in accordance with the International Classification of Sleep Disorders-3 (ICSD-3) diagnostic criteria-e.g., at least 3 months of insomnia symptoms; daytime consequences of insomnia symptoms; and is not better explained by another condition). Since patients are often reticent to discuss insomnia with their providers until they have struggled with insomnia for some time, most treatment-seeking patients are likely to meet Insomnia Disorder diagnostic criteria. Still, by ensuring that diagnostic criteria are met we will exclude individuals: 1) with acute sleep difficulties that may resolve without intervention; 2) whose sleep complaints are the result of self-imposed sleep restriction (inadequate opportunity for sleep); and those whose symptoms are not at a frequency/severity which adversely impacts daytime functioning.

Excessive Daytime Sleepiness and Severe Untreated Sleep Apnea: Sleep restriction, an essential element of CBTI, is contraindicated in those with extreme daytime sleepiness. Since extreme sleepiness is common among those with severe untreated sleep apnea, they are not appropriate candidates for CBTI because they are unlikely to benefit from CBTI and need sleep apnea intervention (i.e., Positive Airway Pressure or other).

Rotating or Night Shift Work: Promoting a consistent sleep-wake schedule is a central treatment target of CBTI. As such, there is no empirical base supporting the use of CBTI among those engaged in Shift Work. Similarly, those engaged in night shift work are typically unable to entrain a consistent sleep schedule due to shifting back to a more typical sleep schedule, on weekends or when not working, to facilitate social interactions. As such, they are unlikely to benefit from standard CBTI without adjunctive circadian interventions. Thus, they will be excluded from participation.

Unstable Co-Morbid Sleep Disorders and Psychiatric Conditions: We are excluding those who are engaged in a process of being worked up for identification/diagnosis of sleep disorders and/or psychiatric disorders because our ability to determine eligibility criteria is hindered by the uncertainty of their condition, and the possibility that we might enroll someone who is later determined to be ineligible for the study.

Psychotic Disorder and Cognitive Impairment: Individuals with these conditions will be excluded due to concerns regarding their ability to complete sleep diaries and to fully engage with treatment.

Bipolar Disorder: Sleep restriction can promote manic episodes in those with Bipolar Disorder. Thus, an essential element of CBTI (sleep restriction therapy) is contraindicated for this population.

Current Abuse of Alcohol and Recreational Drugs: Individuals engaged in substance abuse are excluded because they are unlikely to benefit from CBTI while using/abusing substances known to interfere with sleep.

Nursing Home Residence: Veterans living in nursing homes have little control of their sleep environment, which is an essential element of treatment. CBTI in these settings must be modified considerably.

Outside of Catchment area: Veterans living outside of the Durham VAMC catchment will be excluded because information in CPRS will not be adequate to screen for inclusion/exclusion criteria.

PCP Assignment: Patients without a Primary Care Physician assignment will be excluded because information in CPRS will not be adequate to screen for inclusion/exclusion criteria.

Unstable Housing: Veterans who do not have access to stable housing and/or a reliable telephone will be excluded because they may have an irregular sleep schedule or environment that would make controlling their sleep environment difficult in order to be adherent in treatment. A reliable phone is needed to complete this telephone-based study.

Veterans identified as eligible at Level 1 (L1 in Table 1) will receive a letter and Information Sheet describing the study and offering the option to opt out of future study contacts. Those not opting out will receive a phone call to assess interest in the study. Interested Veterans will be screened for Level 2 (L2) criteria by phone (See Appendix 2a-2f). Veterans meeting these criteria and providing verbal informed consent will be invited to participate in the study. For veterans who are excluded from the study but interested in further treatment for their sleep, the PI will place a clinic note to their PCP or MH provider and/or refer them to the Behavioral Sleep Medicine clinic for additional assessment or treatment, as needed.

C.4 Consent Process

We are requesting a Waiver of Informed Consent and HIPAA Authorization to identify and contact potentially eligible Veterans using the processes described above. We are also requesting a Waiver of Written Informed Consent as this would be the only document connecting patients to this study. By using these approaches that involve both record reviews and pre-screening via telephone, we limit the degree to which ineligible Veterans are required to travel to the VA to determine their study eligibility. We believe that asking these questions presents only minimal risk to potential study participants while simultaneously reducing the burden of traveling to the VA to assess eligibility. All potential participants found to be eligible for the study, and expressing desire to enroll in the study, will first provide their verbal consent prior to collection of baseline measures.

C.5 Randomization

Following completion of the baseline assessment, study participants will be randomized to either Tele-Self CBTI or HEC in a 1:1 ratio, resulting in 100 participants in each condition. To assure equivalency across conditions on important variables, randomization will be stratified by Insomnia Severity Index score (≤20/>20: based on findings for Veterans in the VA CBTI National Dissemination and presence/absence of a mental health disorder.

C.6 Participant Compensation

Since study participants will experience some inconvenience to participate in this study, they will be compensated in the amount of $58 for each of 3 assessment periods. Study participants will receive an additional $3 per day (up to $42 for the 2-week period) for completion of sleep diaries. In sum, study participants may receive up to $100 for each 2-week assessment period, for a total of $300 for completion of all study procedures. As noted above, each assessment period involves tracking sleep and wearing the actigraphy device at home for a period of 2 weeks and completing questionnaires by telephone.

Payment occurs in the form of a check to be mailed to the study participant or electronic funds transfer within 6 to 8 weeks of completion of each study period. Participants not completing the entire study will not be compensated for incomplete study periods. The study participant's name, SSN and address will be provided on the Subject Payment Form, in addition to information regarding the amount of compensation and study information. Table 2 below outlines the Study Timeline, Table 3 outlines the assessment measures employed and timing thereof, and Table 4 outlines the contacts with study participants, the purpose of each contact, and the time commitment required on the part of participants. These timelines are considered to represent the study design and schedule we hope to achieve. However, in some cases we may be unable to contact Veterans in strict accordance with this schedule. Study participants who are non-responsive to study staff such that the timing of their involvement varies considerably from other study participants would be withdrawn from the study. In addition to the contacts outlined in Table 4, participants may also receive phone calls to remind them to complete their daily sleep diary. This is discussed in greater detail below.

C.7 Study Timeline: The study timeline is summarized in Table 2.

Table 2.

Study Activity (Months)	**Yr 1**				**Yr 2**				**Yr 3**				**Yr 4**	
	1	2	3	4	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**
Study Start-Up														
Hire and Train Staff (0-6)	●	●												
Create/ test tracking databases (0-6)	●	●												
Study Conduct														
Aims 1 & 2: Recruitment (6-30)			●	●	●	●	●	●	●	●				
Aims 1 & 2: Intervention (7-32)			●	●	●	●	●	●	●	●	●			
Aims 1 & 2: 8 Week Follow-Up (8-33)			●	●	●	●	●	●	●	●	●			
Aims 1 & 2: 6 Month Follow-Up (12-37)					●	●	●	●	●	●	●	●	●	
Aim 3: Recruitment and Qualitative Data Collection										●	●	●	●	
Evaluation & Dissemination														
Aims 1 & 2 & 3 Analyses (35-40)												●	●	●

C.8 Measures

Screening Measures: The following screening measures will be used to assess eligibility.

Insomnia Diagnosis: The Duke Structured Interview for Sleep Disorders (DSISD)[81] is a structured clinical interview for screening and diagnosing sleep disorders and is being revised to concord with newer diagnostic nosologies (DSM-V)[14] and the ICSD-3[82]. The DSISD Insomnia Disorder module will be administered to ensure that Insomnia Disorder diagnostic criteria are met. *Insomnia Severity Index (ISI)[97]:* The ISI is recommended as the standard for self-reported insomnia symptoms, with a score of 10 or more to indicate active insomnia symptoms[96,]

Contraindicated Hypersomnia Disorders: The Epworth Sleepiness Scale (ESS)[84] will be used to exclude those with occult obstructive sleep apnea (OSA) and those for whom sleep restriction therapy would be contraindicated due to either untreated sleep apnea or hypersomnia in the absence of apnea. The ESS is an 8-item measure assessing one's self-rated typical sleep propensity in daily life and is sensitive for daytime sleepiness across a range of settings and research paradigms[86]. An ESS score of >15 indicates the possibility of undiagnosed or untreated sleep apnea or narcolepsy and will be used to exclude potential study participants[84].

Severe Depression: We will use the Patient Health Questionnaire-8[87] to screen Veterans for severe depression. The validity of the PHQ-8 was established using data from the 2006 Behavioral Risk Factor Surveillance Survey[87]. Veterans scoring in the severe depression range (>19) will be ineligible for the study but may become eligible at a later date if symptoms decline. Dr. Ulmer will ensure that medical providers of Veterans scoring in the severe depression range are aware of their mental health status. Veterans endorsing suicidality will be managed in accordance with the Suicide Safety Plan

Substance Use/Abuse: We will define alcohol abuse as documentation in the medical record of current alcohol abuse. Those with the two most recent AUDIT-C administrations documented in the medical record and scored as negative will be eligible for the study. The AUDIT-C[88], a well-validated 3-item screener for alcohol abuse used in VA[89] and primary care settings[90], to screen out those who are actively abusing alcohol. We will use the clinical scoring criteria for men and women respectively. We will use a single item to screen out those engaged in recreational drug use[91]. This item was found to be highly sensitive (100%) and moderately specific (73.5%) for detecting those with a drug use disorder and had good sensitivity (81.8%) and specificity (72.5%) for laboratory-based evaluation of drug use[91].

Table 3. Assessment Measures

	Items	Timing		
		BL	8 weeks	6 months
Background-EHR Data				
VA Sleep & Psychotropic Medications	n/a	●		
Medical Conditions	n/a	●		
Mental Health Conditions	n/a	●		
Background-Self Report				
Demographic Characteristics	18	●		
Medical Conditions	up to 16	●		
Primary Outcome				
Insomnia Symptom Severity: ISI	7	●	●	●
Secondary Outcomes				
Actigraphy (WASO, TST and SE)	n/a	●	●	●
Sleep Diary (SOL, WASO and SE)	8	●	●	●
Fatigue: Multidimensional Fatigue Inventory	20	●	●	●
Depression: PHQ-8	8	●	●	●
Chronotype: MEQ	19	●	●	●
Trauma-related Sleep Disturbances (PSQI Addendum)	10	●	●	●
International Physical Activity Questionnaire	11	●	●	●

Glasgow Sleep Impact Index	7	●	●	●
Insomnia Treatment Knowledge Questionnaire	10	●	●	●
Ask if participant has accessed CBTI Coach and/or Path to Better Sleep	2		●	●

Outcome Measures

Outcome measures will be collected by phone by the project's research assistant (RA) at baseline, 8 weeks, and 6 months. Copies of self-report outcome measures are listed below.

Insomnia Severity Index (ISI)[97]***:*** The ISI is recommended as the standard for self-reported insomnia symptoms[96] and will be used as our primary outcome measure. The ISI is a 7-item questionnaire providing a global measure of perceived insomnia severity. Each item is rated on a 5-point Likert scale and the total score ranges from 0-28. The following guidelines are recommended for interpreting the total score: 0-7 (no clinical insomnia), 8-14 (sub threshold insomnia), 15-21 (insomnia of moderate severity), and 22-28 (severe insomnia). In clinical samples, a cut off score of 10 was shown to have the greatest sensitivity and specificity for correctly identifying study participants meeting criteria for insomnia diagnosis[98]. The ISI has adequate psychometric properties and has been validated against diary and polysomnographic measures of sleep[97].

Sleep Diaries: We will use the Consensus Sleep Diary (CSD)[99] to assess the impact of Tele-Self CBTI on sleep onset latency (SOL); wake after sleep onset (WASO); and sleep efficiency (SE). The Consensus Sleep Diary is the result of an effort to standardize sleep diary data collection across sleep research projects. The CSD was developed by an expert panel with an eye towards optimal wording, content, and format. Collection of sleep diary data using a time-restricted approach (i.e., participant has < 24 hours to record entry) is more valid than paper diaries wherein study participants can record data from memory. However, remote collection of sleep diaries data is challenging in the VA due to concerns about secure transfer of research data across the VA firewall. We will be collecting data using an Interactive Voice Response (IVR) system wherein Veterans record sleep data by responding to phone-based questions using a telephone keypad was successfully used in our pilot study and is configured for this purpose. Participants not reporting diary data will receive a reminder call to complete diaries and troubleshoot any reporting difficulties. Participants will also be provided with a paper copy of the diary for use in the unlikely event of technical difficulties with the IVR reporting system, and a pre-addressed UPS envelope for returning the watch and completed paper sleep diaries to study staff. Diary data will be averaged across each 2-week assessment period to determine diary-based SOL, WASO and SE.

Wrist Actigraphy: We will use Actiwatch® (Respironics, Inc.) wristwatch style actigraphy watches for collecting objective sleep data as used in several prior studies. Actiwatches contain a calibrated accelerometer that samples, digitizes, and stores movement activity. When interfaced with a computer and Actiware software at the VA research site, a scoring algorithm provides estimates of various sleep parameters. Wrist actigraphy is recommended for assessing treatment response in adults with insomnia following intervention[96]. The Actiwatch Spectrum Plus device is proposed and includes sensors for light and "off the wrist" which increase scoring accuracy. We will average data across each two-week assessment period to determine actigraphy-based WASO, Total Sleep Time (TST) and SE.

Instructions for Home Data Collections: The cover letters and instructions regarding use of the Actiwatch and Sleep Diary and timelines for the study will be provided to each patient with each delivery of the Actiwatch device.

Daytime Consequences of Insomnia: As recommended for insomnia research[96], we will assess fatigue, mood, and quality of life to evaluate the impact of Tele-Self CBTI on adverse

daytime consequences of insomnia. The Multidimensional Fatigue Inventory (MFI)[100] is a 20-item measure wherein the responder indicates, using a 5-point Likert scale, the extent to which each statement applies to their situation over the previous day). The MFI assesses 5 dimensions of fatigue, including: general fatigue; mental fatigue; physical fatigue; reduced activity; and reduced motivation. The PHQ-8 described above, will be used as our depression measure.

Morningness-Eveningness Questionnaire: The Morningness-Eveningness Questionnaire (MEQ) was the first self-report measure developed for the assessment of chronotype and continues to be the most widely used measure for this purpose. The MEQ has established psychometric properties[101]. We will use an updated version of the MEQ[10] having rephrased questions that better conform to contemporary language. In addition, the revised MEQ utilizes a discrete item response set in lieu of the original visual response scales, allowing respondents to calculate their own score. MEQ scores range from 16 to 86, with lower scores indicating greater eveningness and higher scores indicating greater morningness. Total scores are used to categorize respondents into 5 categories, as follows: definitely morning; moderately morning; neither type; moderately evening; and definitely evening.

Trauma-Associated Sleep Disturbances: The Pittsburgh Sleep Questionnaire Addendum will be used to assess PTSD-related sleep quality and has acceptable psychometric properties.

International Physical Activity Questionnaire: The International Physical Activity Questionnaire is an 11- item questionnaire that assesses the respondent's physical activity over the previous week. This measure been widely implemented and has been used in the Veteran population.

Glasgow Sleep Impact Index: We will be using a 7-item modified version of the Glasgow Sleep Impact Index that excludes questions meant for clinical use only. This index is the only measure available that is specifically designed to assess sleep-related quality of life impairment.

Insomnia Treatment Knowledge Questionnaire: The Insomnia Treatment Knowledge Questionnaire was developed for the pilot study and will be used to assess participant comprehension of treatment components. In the pilot study, participants in the intervention condition reported higher scores (better understanding of concepts) at post-intervention relative to those in the control condition.

The study coordinator will inform patients of randomization arm at the end of the baseline. The various time points have windows in which the assessment period should be completed in. Participants may start the baseline assessment up to a month after consent. The 8-week assessment can start as soon as 6 weeks after starting the intervention period (if all nurse phone calls are completed) to no later than 8 weeks after intervention period has started. Participants have a 5-week window to start and complete baseline and 8-week assessment activities. Participants have a 6-week window to begin and complete 6-month assessment activities.

Covariate and Other Measures*:* Due to their established association with sleep, the following variables will be evaluated as potential covariates and included in analyses as appropriate: age; gender; body mass index (BMI); co-morbid medical conditions; co-morbid mental health conditions; smoking status and pack years; anxiolytic/hypnotic usage; and other medications. Self-report information about demographic characteristics and current medical and mental health conditions will be collected at baseline. During the 8 week and 6-month Assessments, we will ask participants in the Tele-Self CBTI condition if they have sought or received treatment for their sleep complaints beyond what was offered in this study.

C.9 Missing Data: Because the main predictors of interest are collected at baseline, we do not anticipate much missing data in these variables. We do, however, anticipate some missing values in the longitudinal outcomes owing to dropout or, rarely, patients not completing the sleep diaries or returning Actiwatches. Although we did not lose any Actiwatches in our pilot study, participants did not return 2 of 162 devices (1%) in a past trial4. If the missing values are related to other measured patient factors, such as age, comorbidities, or employment status (as we have seen in previous studies), then multiple imputation (MI) provides a framework for incorporating information from these auxiliary variables while still preserving a parsimonious main treatment effect mode. This framework is described as a significant advantage in recommendations from the Panel on Handling Missing Data in Clinical Trials. Depending on the type and scope of missing data for other longitudinal variables, as a sensitivity analysis, MI will be conducted via the SAS procedure PROC MI or the SAS macro IVEware. A general linear model for each outcome variable will then be applied to each of the imputed datasets, and estimates combined using Rubin's rules as implemented in PROC MIANALYZE.

Table 4. Contacts with Participants

STUDY CONTACTS			
Week#	**Purpose of Contact**	**Measures**	**Time Commitment/Contact Modality**
0	TELEPHONE-BASED SCREENING	Shift Work Question Drug Use Screener Prior participation in CBTI Question DSISD Epworth Sleepiness Scale Insomnia Severity Index PHQ-8	30 minutes/phone call
0	CONSENT AND ENROLL		20 minutes/telephone
2	BASELINE ASSESSMENT o Participant calls IVR sleep diary system daily for 2 weeks o At end of 2 weeks, participant completes baseline questionnaires by phone o Following questionnaire completion, participant is randomized and informed of assigned treatment arm by phone	Adverse Events Demographic and Service Information Comorbidity Questionnaire Insomnia Severity Index (ISI) Multi-Dimensional Fatigue Inventory (MFI) Morning Eveningness Questionnaire (MEQ) Pittsburgh Sleep Quality Index (PSQI) Glasgow Insomnia Index IPAQ short phone (physical activity) Insomnia Treatment Knowledge Questionnaire Sleep Medication Question COVID questions	5 minutes daily/IVR 40-50 minutes/phone call
3-8	INTERVENTION ARM Interventionist calls with participant to support treatment engagement and adherence.	Intervention Adherence Questions	6 nurse contacts @ 20 mins/call
3-8	HEALTH EDUCATION ARM Interventionist calls with participant to ensure equivalent contact time across arms.		6 nurse contacts @ 20 mins/call

STUDY CONTACTS			
Week#	**Purpose of Contact**	**Measures**	**Time Commitment/Contact Modality**
9-10	8 WEEK ASSESSMENT o Participant calls IVR sleep diary system daily for 2 weeks o At end of 2 weeks, participant completes 8-week assessment questionnaires by phone	Adverse Events query Insomnia Severity Index (ISI) Multi-Dimensional Fatigue Inventory (MFI) Morning Eveningness Questionnaire PSQI addendum Glasgow Insomnia Index IPAQ short phone Insomnia Treatment Knowledge Questionnaire PHQ-8 COVID questions Sleep medication and Other Treatment for your Sleep Complaint Intervention arm only: Treatment Acceptability/use	5 minutes daily/IVR <50 minutes/telephone
27-28	6 MONTH ASSESSMENT o Participant calls IVR sleep diary system daily for 2 weeks o At end of 2 weeks, participant completes 6-month assessment questionnaires by phone	Adverse Events query Insomnia Severity Index (ISI) Multi-Dimensional Fatigue Inventory (MFI) Morning Eveningness Questionnaire PSQI addendum Glasgow Insomnia Index IPAQ short phone Insomnia Treatment Knowledge Questionnaire PHQ-8 COVID questions Sleep medication and Other Treatment for your Sleep Complaint	5 minutes daily/IVR <50 minutes/telephone

Study Interventions

Tele-Self CBTI*:* The nurse interventionists will make an introductory call and set up a weekly call appointment time. As noted above, Tele-Self CBTI is comprised of two treatment components: 1) Self-management via our workbook entitled, "Improve your Sleep: A Self-Guided Approach for Veterans with Insomnia" with Session Guides; and 2) telephone-based nurse support. Our Tele-Self CBTI workbook includes the following typical CBTI treatment components: Sleep Restriction; Stimulus Control; Cognitive Therapy; Relaxation; and Sleep Hygiene Education[93]. We will deliver Tele-Self CBTI across 6 weekly telephone contacts of 20 minutes or less. Table 5 describes the treatment modules and content of each telephone session, and the relative timing of treatment components.

Table 5. CBTI Treatment Components and Sessions

Module: Content	Veteran Workbook Readings	Nurse Support	Sleep Diary
Weekly		**Weekly**	**Daily**
1: Sleep Education; Sleep Diary Instructions	Session 1 (page 5)	X	X
2: Sleep Restriction Therapy	Session 2 (page 15)	X	X
3: Stimulus Control	Session 3 (page 19)	X	X
4: Sleep Hygiene; Cognitive Therapy 1	Session 4 (page 31)	X	X
5: Relaxation; Cognitive Therapy 2	Session 5 (page 39)	X	X
6: Relapse Prevention	Session 6 (page 51)	X	X

Health Education Control (HEC)*:* To assess the impact of provider phone contacts on outcomes, patients randomized to HEC will receive 6 weekly phone calls from a study nurse. Consistent with phone contacts in the intervention arm, HEC phone contacts will last no more than 20 minutes and will match as closely as possible call duration with Tele-Self CBTI participants. Sleep-focused content will be prohibited during HEC calls. Health education scripts in HEC were used in a previous trial[94] and address a range of health topics (i.e., colorectal and skin cancer, healthy backs, medication management, heart healthy foods, lower sodium diets and how to prevent heart problems. At the end of the study, HEC participants will be offered either face to face group-based treatment or Tele-Self CBTI treatment through our Durham VA Behavioral Sleep Medicine Clinic.

Provider Training and Treatment Fidelity*:* Dr. Ulmer will train the research nurses to provide Tele-Self CBTI using an approach informed by the VA CBTI dissemination training model. This approach will ensure the research nurses have a thorough understanding of all CBTI treatment components. Training case sessions will be recorded and evaluated for treatment fidelity using the Yale Adherence and Competence Scale (YACS)[95]. The research nurse will also be trained in emergency procedures for addressing suicidal ideation (SI) or homicidal ideation (HI) revealed during telephone sessions, including assistance from the Veterans Crisis Line.

D. Qualitative Study (Aim 3)

We will conduct qualitative interviews with providers and administrators in order to gain information on barriers to implementation of self-management CBT-I the primary care setting.

D.1 Study Design

We will conduct focus groups and/or individual interviews with nurses and administrators from the Durham VAHCS to participate in this qualitative component of our research/study. Each participant will participate in an interview or focus group using a script to elicit responses.

D.2 Study Population

The target population will be employees of the Durham VAHCS who work as a nurse or administrator. Local union nurse representatives will be notified per proper procedures/protocols prior to contacting potential nurse participants. Although supervisors may provide a list of nurses by clinics, they will not be involved in the conduct of any other research activities. Supervisors will not be notified of identifiable, individual level employee participation or provided individual level data. Nurse employment will not be impacted by participation status. Participation is voluntary and confidential. Steps will be taken to protect the identity of the respondents. The identity of the respondents will be kept confidential by the research team and identifiers will be kept separate from the coded data. Results will be reported in aggregate and individual quotes when used will not be identifiable.

D.3 Participant Selection

We plan to conduct focus groups and/or individual interviews with up to approximately 20-30 nurses and up to approximately 5 clinic administrators from the Durham VAHCS. We may recruit and enroll/consent more than the above numbers to reach our targets (up to 50 nurses and up to 10 administrators). Potential participants will be purposefully sampled based on criteria such as site type (i.e., CBOC and hospital) or location (i.e., rural and urban), with a randomly generated priority order for contact if necessary by sites (based on number of nurses at each site) or all nurses at that site if numbers are small.

D.4 Subject Recruitment

Approach #1 – Email Recruitment

Step 1: A list of nurses at the Durham VAHCS Primary Care and Sleep Clinics will be obtained by emailing and/or calling the facility's Nurse Management Leaders and/or Clinic Managers to identify the appropriate healthcare providers. We will provide an overview of the study during our initial contact with these individuals. We will also obtain and confirm the email group name for nurses within each clinic for use in step 2 of the recruitment process. Multiple emails and/or phone calls may be made to collect the nurse email list and confirm the email group name/s.

Step 2: Using the email group names provided by clinic managers or their staff, we will send an introductory email to Durham VAHCS Nurses identified in Step 1. This introductory email will provide nurses with study information about the study in addition to explaining a procedure for opting out of future contacts. Nurses who do not want to receive subsequent contacts about the study will be instructed to "opt out" by calling and/or emailing the principal investigator or study coordinator.

Step 3: Nurses will then be selected for receipt of recruitment email from the email group lists obtained in Step 1, with those who opted out in Step 2 being excluded. Administrators will be selected based upon their role in the system – we will endeavor to obtain a range of perspectives about potential barriers and facilitators to implementing Tele-Self CBTI in clinical care. Selected nurses and administrators will receive a personalized email and/or phone call wherein they will be asked if they would like to participate in the proposed study. Multiple emails and/or phone calls may be made to reach the potential participant. We may also use MS Teams to communicate and possibly schedule the interview/focus group. Potential participants will not officially "opt in" to complete the interview until they are contacted by phone or in person and provide verbal consent to participate in the study. If the study staff receives no response after multiple attempts, we will assume the nurse/administrator is not interested in participating in the study.

Approach #2: Staff Meeting Recruitment Durham VAHCS

Step 1: A phone call will be made to each clinic lead to schedule a presentation during a regularly scheduled staff meeting. During the meeting we will provide an overview of the study and answer any questions.

Step 2: During the presentation, nurses and administrators who are interested in participating will be provided with the contact information of the PI and study staff for purposes of reaching out to express their interest in participating in the study or to receive additional information. This will help keep participation anonymous among the clinic staff.

Approach #3 –Email Recruitment VISN 6 Primary Care (if necessary following Approaches #1 and #2)

Step 1: Study staff will send an email to the VISN 6 primary care ACOSs (excluding the Durham VA) and their administrative assistants if available to introduce them to the study and ask them if we may contact their various clinic nurse managers to discuss recruitment within their clinics. We may use email group names that are provided by the nurse managers or use a list of nurses obtained from them to send direct emails to nurses. If an ACOS does not want their facility to participate we will not attempt to contact any nurse or administrator for this study at that facility. Non-responding ACOSs will be contacted by phone to obtain this information. More than one phone call may be made to reach the non-responding ACOSs.

Step 2: Once nurse email groups or individual nurse lists are obtained the study staff will continue to follow steps 2 and 3 from Approach #1.

Potential participants will be purposefully sampled based on criteria such as site type (i.e., CBOC and hospital) or location (i.e., rural and urban), with a randomly generated priority order for contact if necessary by sites (based on number of nurses and as described in more detail below), to be contacted by email, phone, and MS Teams to discuss participation in the study and be scheduled for the interview.

D.5 Consent Process

We request a waiver of documented informed consent. An information sheet will be emailed to the potential participant. This aim of the study will be fully explained prior to initiating any study procedures, and verbal consent will be required for study participation. Since most nurses/administrators will only be available to engage in the study interview by phone, verbal consent with phone or MS teams interview is the most feasible option for this research. Furthermore, there are no anticipated physical, psychological, legal, social, genetic, or economic risks associated with this research study.

The nurse/administrator's email address or telephone number used during the recruitment process will not be retained with study data collected during the interviews. All the study data collected during the demographic survey and semi-scripted interview will be given a Study ID number.

Study participants will be verbally informed that the research interview will be recorded via MS Teams for later analysis and will be used for purposes pertaining only to this research study. They can also end the interview at any time without penalty. When the audio recording is turned on the study staff conducting the interview will obtain verbal assent for the recording. This assent process will be captured on the recording prior to recording the interview. The participant can decline questions they don't want to answer. When the recording is transcribed any names or other identifiers will be removed.

D.6 Participant Compensation

Consistent with VA policy, VA employees will not receive compensation for study participation.

D.7 Measures

A focus group interview guide has been created to guide qualitative interviews. The interviews will be recorded, transcribed, and coded, which is described in further detail in data analysis.

E. Data Management (Aims 1-3)

Study tracking data will be securely stored in a SQL server database created for this project. Members of the study team will be granted role-based permissions to connect to the database to enter, view, and update data using a Microsoft Windows tracking application created and supported by the Durham HSR&D software development team. We have used this tracking software for multiple prior studies. Because many processes for identification, enrollment, and follow-up of participants are similar to prior studies, we can easily customize the database and software to meet the specific needs of the proposed project. The database allows us to track: the status of each patient (eligible, enrolled, refused, etc.), results of medical record reviews, results of screening interviews, and all tasks due for each participant (e.g., follow-up assessments). We are also able to randomize participants within this database, as the randomization sequence and necessary stratification variables can be imported. Customized reports allow the research team to identify daily tasks in need of completion, as well as flow charts to monitor overall study progress. Screening and outcome measures (except for the sleep diary and actigraphy data) will be defined and entered using REDCap™, a web-based survey tool also running on a secure server behind the VA firewall. The REDCap software is a web-based survey tool running on HSR&D computer systems operated by VA OI&T personnel on behalf of HSR&D. At no time will the email function in REDCap be used for this project. Only data can be entered into this web-based survey tool. The data is stored on the servers at HSR&D and the coordinators and master statistician will have access to the raw data. The

tracking database is in the study folder at the location identified above. The study tracking database containing Study ID, full names, full SSN, addresses, phone numbers, and eligibility (yes/no), mailed recruitment letter (yes/no), and phone screened (yes/no), treated in clinic (yes/no) and will be protected using passwords and study group policies. Staff also have created a couple excel datasheets stored only in the study folder for use during active recruitment in order to track Actiwatches which contain subject ID, Actiwatch number and log in/out dates, and an excel sheet for asking study-related questions to the PI. In addition, an excel sheet in the protected study folder will be used to store contact information of potential qualitative participants as well as record contacts and participation status (date of consent, refusal, etc.). Consent and demographic data will be collected via REDCap using a subject ID. Data will be accessible to only personnel on current staff listing who need to contact subjects, such as the project coordinators, research assistants, and PI. Once a study staff member is removed from the staff list their privileges will be revoked and they will no longer have access to the study folder or study cabinet.

The tracking database, REDCap survey results, sleep diary and actigraphy datasets will respectively use IVR and Actiware software and be linked via participant study identifier for analyses. The Actiwatch, as well as any paper sleep diaries which have subject ID on them will be mailed back via UPS carrier. The watch contains subject ID, initials, and actigraphy (motion) data for the most recent participant. Actigraph data can only be accessed/downloaded via specialized licensed software located on the project coordinator or RA computer. Statistical analysis will be perfumed using Actigraph data will be analyzed by Actiware software that comes with the device, (Phillips Respironics, Andover MA), SAS, (SAS Institute, Cary, NC) and qualitative data will be organized using AtlasTi (Scientific Software Development, Berlin, GmbH).

E.1 Data Summary (Aims 1 & 2): Descriptive statistics, including graphical displays, will be used to summarize all study variables, both overall and by intervention group. Evidence of imbalance in baseline characteristics will be noted and discussed as to whether they are clinically significant. As recommended by Committee for Proprietary Medicinal Products[108] guidelines, we will consider sensitivity analyses adjusting for these baseline characteristics to ensure that an observed intervention effect is not due to baseline imbalance. Trajectory plots and frequency distributions will be used to explore longitudinal outcomes. We do not anticipate substantial deviations from symmetric, normal distributions for the study outcome variables. Additionally, correlation patterns over time, both overall and by intervention group, will be examined via scatter plots. The main conclusions drawn from this trial will be based on the pre-specified primary and secondary hypotheses outlined below and will be tested with two-sided p-values at the standard 0.05 level. All statistical analyses will be performed using the SAS software package (Cary, NC); the Durham HSR&D Center of Innovation maintains the current SAS release on the Durham VA hospital servers.

E.2 Intent to Treat Analyses (Aims 1 & 2): All primary and secondary analyses focus on the effect of the intervention compared to control. We, therefore, plan to use the intent-to-treat assumption for all analyses; participants will be analyzed as part of the group to which they are randomized, regardless of intervention adherence.

Hypothesis 1: Relative to Health Education, participants randomized to receive Tele-Self CBTI will have greater improvements in insomnia severity, as measured by the Insomnia Severity Index (ISI), at 8 weeks. The ISI is a continuous measure wherein lower scores indicate less severe insomnia symptoms. A general linear model will be used to estimate changes in ISI over time and test the primary hypothesis. Because of the small number of time points, we will apply

an unstructured covariance matrix to take into account the within-patient correlation between repeated measures over time. The predictors in the model will include a dummy coded time effect and an indicator variable for Tele-Self CBTI interacting with the time effect. The mean structure of the model will have the form: Y = β 0 + β 1*6wk + β 2*(month6) + β 3*(Tele-Self CBTI*6wk)+ β4*(Tele-Self CBTI*month6) + β 5*(age) + β 6*(baseline ISI), and model parameters will be estimated using the SAS procedure MIXED (Cary, NC). Note that this model is a constrained intercept model, which assumes a common baseline mean[109]. We will formally evaluate the intervention effect by testing that β 3 differs from zero and report the mean difference and corresponding 95% confidence interval. A mean difference significantly less than zero provides evidence that Tele-Self CBTI patients have greater improvements in ISI at 8 weeks. The model will also include centered, stratification variables of age (≤50/>50 years), baseline ISI (≤20/>20), *mental health disorder status (presence/absence), psychotropic medication (use/non-use) and sleep medication (use/non-use)* as recommended in the CPMP guidelines[108].

Hypothesis 2: Relative to Health Education, participants randomized to receive Tele-Self CBTI will have greater improvements in subjective sleep (per diary SOL, WASO, and SE), objective sleep (per actigraphy WASO, TST, and SE), fatigue, depression symptoms, and QOL at 8 *weeks*. As described above, sleep parameters (both diary and actigraphy) are recorded daily during each of the three 2-week assessment periods. Daily values will be averaged across each 2-week period, resulting in three repeated continuous outcomes for each of the sleep parameters, including baseline, 8 weeks, and 6 months. Treatment group differences at 8 weeks and 6 months for these subjective and objective sleep measures will be tested via the same general linear model as specified above for the primary hypothesis. Similarly, the fatigue, depression symptoms and QOL outcomes will also be analyzed with a general linear model as specified above for the primary hypothesis. Again, PROC MIXED will be used to estimate and test the appropriate model parameters, and the mean difference and corresponding 95% confidence intervals will be reported.

E.3 Sample Size Considerations (Aims 1 & 2): Our sample size estimates are based on the Hypothesis 1 primary outcome – Insomnia Severity Index. Because this is a longitudinal study with repeated measurements on each subject, mean change is estimated with increased precision. In sample size calculations, the increase in precision can take into account the correlation between repeated measures. With Tele-Self CBTI, we anticipate seeing smaller effects than might be seen with in-person CBTI. Additionally, our comparison group receives more than usual care, again leading to smaller effects. In a recent meta-analysis, the effect of CBTI on ISI yielded large Hedge's g effect sizes of 0.98. Conservatively, we then base our sample size estimates on an effect size of 0.5; this translates into a relative mean improvement on the ISI of at least 2.8. Assuming a baseline SD of 5.8, a repeated-measures correlation of 0.6 (both quantities estimated from previous studies[37,52,54,114], and a type-I error of 5%, we will need to have 73 patients in each arm to detect a relative mean improvement of 3 on the ISI with 90% power. To account for dropout and possible deviations from our assumptions, we plan to enroll and randomize 100 patients in each arm (total sample size n=200). With this sample size, we will also have adequate power to examine our secondary outcomes. For example, previous studies of SE show a baseline SD of 12.5 and repeated-measures correlation of 0.7. With our projected sample size, we will have 90% power to detect a relative improvement in SE of at least 6.2. The repeated-measures design option in PASS[115] was used for all calculations.

E.4 Data Analysis (Aim 3)

Focus groups will be comprised of 8-10 nurses, and the exact number of focus groups will be dictated by thematic saturation[102]. Individual nurse interviews will be conducted as needed to explore in greater depth concepts discussed in focus groups and/or due to scheduling. Individual interviews will be conducted with Administrators to obtain their perspective on the barriers/facilitators to consider when implementing Tele-Self CBTI. Focus groups and individual interviews will be conducted by a trained qualitative specialist using a moderator guide developed by Drs. Ulmer and King (Appendices). The moderator guide was developed in accordance with Weiner's Theory of Organizational Readiness for Change (ORC), which refers to the extent to which organizational members are prepared to make changes in organizational policies/practices necessary to support innovation (change commitment) and their perceived ability to do so (change efficacy). Attributes impacting ORC include change valence (perceived value of the innovation) and information about perceived task demands, resource availability, and situational context (e.g., competing demands). Dr. King has previously utilized ORC to understand implementation of programs by VA facilities[103], including implementation of lung cancer screening[104], currently funded QUERI/HSR&D projects (Spreading Healthcare Access, Activities, Research and Knowledge Partnered Research Initiative) and an implementation evaluation of tele dermatology on Veterans' access to dermatology. Participants will also complete a questionnaire to characterize sample demographics and work history (e.g., tenure as nurse and with VA). Focus groups will be approximately 1 hour and individual interviews will be approximately 20-30 minutes. *Focus groups and interviews will be conducted, recorded, and transcribed using the functionalities of MS Teams (REFERENCE: Research Cybersecurity FAQ - Applications (sharepoint.com)). Recordings and transcripts will be downloaded and saved to the study folder, which is on a secure server behind the VA firewall. Recordings and transcripts will be deleted once saved to the study folder.* A structured notetaking form/template for each focus group and interview will be used to organize and compile qualitative data. Rapid qualitative analysis will be used to analyze notes, supplemented with the recordings/transcripts. Matrix techniques will be used to facilitate data analysis and presentation. We will develop a table based on the guide and organized by question/domain. Data extracted and summarized from notes and recordings/transcripts will be used to populate the table for each focus group/interview and summarized across, supported by illustrative, exemplar quotes, and consolidated into matrices to identify and describe aspects of organizational readiness for change, for example.[105]

F. Handling of Unexpected and Adverse Events

F.1 Risk/Benefit Assessment

This study involves a low risk cognitive-behavioral intervention. There are no investigational drugs or devices being tested in this study. The risks of this intervention are no greater than those incurred during a standard clinical intervention for insomnia. The main risk of study participation is the possibility of becoming upset when answering personally probing questions on the study questionnaires, or during engagement in the intervention. Participants will have the option of refusing to answer distressing questions or withdrawing from the study at any time without adversely affecting their ongoing care. Hence, the risks of such discomfort are mitigated by the options offered to participants. The PI will report any serious, unexpected, and study-related adverse event or unanticipated problem to the patient's provider and local IRB according to the institution's requirements (5 business days). The IRB will review all adverse events during continuing review, which will likely occur annually. All adverse events will be reported in the annual report to the VAMC IRB.

The Qualitative study involves interviews that will be approximately 20-30 minutes or

focus groups will be approximately 1 hour. Risks of discomfort is assessed to be low. Participants are informed they can refuse to answer questions or drop out at any point of participation.

F.2 Adverse Events

While we do not anticipate adverse events related to study activities, all adverse events that do occur will be reported per Durham VAMC requirements. All Serious, Unanticipated and Related adverse events will be reported to IRB within 5 business days of hearing of the event. All other adverse events will be reported at continuing review.

F.3 Safety Plan for Suicidal Ideation

During study screening and each assessment period, a Research Assistant (RA) will administer the Patient Health Questionnaire (PHQ-8) to assess depression. If patients endorse suicidal ideation or express clinical warning signs of elevated risk of self-harm (e.g., severe depression), study staff will gather more information from the participant, including information about suicidal plan, means, intent, and history of suicidal behavior, by administering a structured screener, the P4 Screener, to assess the potential for suicide risk .

Patients with greater than minimal risk as assessed by the P4 will be excluded from the study, but not dropped from study participation if already enrolled, and offered a warm hand off to the VA Crisis Line in accordance with the approach suggested by the VA Crisis Line (see VA Veterans Experience website-document entitled Veteran In Crisis Handout.pdf). If they decline the warm hand off to the crisis line, the participant will be informed that a study clinician may contact him/her to talk more about his/her suicidal ideation. The study coordinator will obtain current contact information for the participant and inform Dr. Ulmer or Dr. Beckham, study clinicians who are trained in suicide assessment, who will contact the participant as necessary to ensure participant safety.

At their professional discretion, Drs. Ulmer or Beckham will contact and assess the patient over the phone and take appropriate action. Assessment will include evaluation of suicidal plan, intent, means, history of suicidal behavior, and other relevant clinical information. If the patient is deemed to be at moderate to high risk of suicide, Drs. Ulmer or Beckham will provide education to the patient regarding resources at VA and in the community for psychiatric emergency care. Patients will be urged to seek acute mental health care, and where possible, Drs. Ulmer or Beckham will help establish a follow-up plan for this care.

If the patient is deemed to be at imminent risk for suicide, he/she will be asked to come to his/her local ER or VA ED immediately. If he/she is unwilling or unable to go to the nearest ER or ED, Drs. Ulmer or Beckham will follow DVAMC policy for contacting local authorities for assistance in securing and transporting the patient to a hospital/mental health facility where he/she will receive appropriate help. When possible, Drs. Ulmer or Beckham will remain in contact with the patient until local authorities have secured the patient. Following the contact, Drs. Ulmer or Beckham will document the incident in CPRS and will notify via CPRS the patient's VA primary care physician and/or mental health provider.

F.4 Withdrawal of Participants

Veterans self-reporting current suicidal ideation at any time during the study protocol (both screening and study procedures) may be excluded/withdrawn from the study if the Principal Investigator deems that their continued involvement in the study could adversely impact the patient.

F.5 Data and Safety Monitoring

Coded data with direct identifiers removed (i.e., name, address, telephone numbers, SSN, DOB) will be placed at VINCI. We will be using REDCap a VA Intranet Web application

approved by VA and run by VA VIReC. The REDCap software is web-based but participants will be interviewed over the phone and data will be entered by study staff behind the VA's firewall. The data are housed on a VA Informatics & Computing Infrastructure (VINCI) Server. Data from the Actigraph device will be downloaded to tour local server behind the VA firewall at \v06.med.va.gov\DUR\HSRD \Insomnia_Self_CBTI_Trial_IRB_2147 HSR&D servers are located in a secured area at 508 Fulton St., Room FG104-1, Durham, NC 27705. All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up to date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins). Access to study data will be removed for all study personnel when they are no longer part of the research team.

This is a minimal risk intervention for insomnia and we do not anticipate any safety issues related to the intervention. Patient activity will be monitored for Serious adverse events during the intervention period by intervention nurses.

Screening, baseline, and outcomes data will be collected via telephone at baseline, after the intervention (week 6) and at the 6-month follow-up. Suicidality will be assessed across the same timepoints, as part of the PHQ-8. The Suicide Safety plan will be implemented for patients endorsing suicidality during completion of the PHQ-8 at any point in study conduct, as discussed above.

Any Serious Adverse events will be filed using IRB paperwork and filed in study binder which will be stored in a locked cabinet.

Privacy, Confidentiality, and Information Security

1. Lists of Data Reviewed and/or Collected for Screening/Recruitment and Conduction of Study:

The Personal Health Information that will be obtained, used, and/or shared for this study includes:

Identifier(s)	Source(s) of Health Information
☒ Names	☒ Medical history & physical exam information
☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, and zip code. Describe: Home address including house number, street, city, state, zip code and PO Box number.	☒ Photographs, videotapes, audiotapes, or digital or other images. Audio recordings of participants' intervention calls. MS Teams audio recordings of qualitative interviews/focus groups.
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, visit or treatment dates, etc.; and all ages over 89, Describe: Date of birth; Date of enrollment, date of phone-based Sleep Diary entries, date of follow-up surveys, dates of primary care and specialty visits.	☐ Biologic specimens (e.g., blood, tissue, urine, saliva). Describe:
☒ Telephone numbers	☒ Progress notes
☐ Fax numbers	☐ Diagnostic / Laboratory test results
☒ Electronic mail addresses (qualitative participant emails)	☐ Operative reports
☒ Social Security Numbers	☐ Imaging (x-ray, CT, MRI, etc.)
☒ Medical record numbers	☐ Discharge summaries
☐ Health plan beneficiary numbers	☒ Survey / Questionnaire responses
☐ Account numbers	☐ Billing records
☐ Certificate and/or license numbers	☐ HIV testing or infection records
☐ Vehicle identifiers and serial numbers, including license plate numbers	☐ Sickle cell anemia information
☒ Device identifiers and serial numbers	☒ Alcoholism or alcohol use information
☐ Web Universal Resource Locators (URLs)	☒ Drug abuse information
☐ Internet Protocol (IP) address numbers	☒ Mental health (not psychotherapy) notes
☐ Biometric identifiers, including finger & voice prints	☐ Psychological test results
☐ Full-face photographic images and any comparable images	☐ Genetic testing
☒ Any other unique identifying number, linked study ID, characteristic, or code, describe: Demographic data, study ID	☒ Other, describe: Actigraph device data

2. Data and/or Specimen Acquisition:

Data for this study will be collected through (*check all that apply*):

☒ Prospective data and/or specimen collection obtained from participants. Provide description of processes: Initial screening information will be gathered through a medical record chart review and phone screening process. The phone screening process may also occur in person if the veteran was identified as potentially eligible and interested during a BSM clinic appointment such as a sleep orientation session. General study data will be obtained through telephone-based interviews and completed questionnaires/surveys. Actigraphy data will be collected via a device worn by the patient, which is described above in greater detail. Sleep diary information will be collected using an IVR system or on paper sleep diary. HSR&D IT staff has developed a process for extracting data from the IVR system into an excel file. This file resides in a folder located behind the VA firewall.

Additional study data may be obtained during the intervention phase when the interventionist is working with the participant over the phone. Any important information related to the study will be saved in the electronic study folder. Qualitative study data are collected by recording interviews, transcribing, and then coding data, which will be connected to the subject by subject ID.

☐ Retrospective data collection and/or specimens obtained from medical chart review/data access. Describe how data will be obtained (e.g., fileman, CDW, etc.):

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☐ Retrospective data collection and/or specimens obtained from an IRB-approved data and/or specimen repository. Indicate the repository source including name, VA location, and IRB number: .

Note: for data and/or specimens obtained from a VA approved data repository, a Data Use Agreement (DUA) must be executed prior to obtaining data and/or specimens. See VHA Handbook 1200.12 for further information.

3. Level of Data:

The following level(s) of data will be acquired/maintained for this study (*check all that apply*):

☒ Identified (e.g., names, addresses or other identifiers included)
☒ Coded (direct and/or all identifiers removed, but study code/ID included)
☐ De-Identified (all HIPAA 18 and study ID/code removed):
- ☐ Verified Statistically

OR

- ☐ Verified by Absence or Removal of HIPAA 18 and study ID

☐ Limited Data Set
☐ Other: Describe:

4. Location of Data and/or Specimens, and Data Retention Plan:

A. Data Location: Data will be stored electronically, in the study folder at \\v06.med.va.gov\DUR\HSRD\Insomnia_Self_CBTI_Trial_IRB_2147. Initial REDCAP survey data are housed on a VA Informatics & Computing Infrastructure (VINCI) Server. The IVR phone surveys are collected through the IVR reporting system that saves to an HSR&D server. Electronically stored data will include chart reviews, questionnaires, actigraphy data, and IVR reported sleep diaries. If the IVR phone system goes down, as backup, participants should record sleep diaries on paper. That information is then entered electronically, and the paper forms are stored in VA locked filing cabinets. Recording of intervention phone calls will be done utilizing VA approved software installed and configured by VA OI&T personnel after sanctuary exemptions have been obtained. Currently this is done using Sparky. Once Sparky is no longer allowed, we will transition to Audacity, WebEx, or another application having RMS approval. The data will continue to be saved on a restricted study folder on the R drive. VA laptops used to collect study data will use FIPS 140-2 validated encryption. The audio recordings and/or transcripts will be mainly used for study staff training purposes. During the verbal consent participants can opt in or opt out of being recorded. For those who agree to be recorded, at each nurse call the nurse will obtain assent by asking the Veteran to confirm they agree to be recorded during the phone session. This assent will be captured on the recording.

☒ Data will also be placed at the VA Informatics and Computing Interface (VINCI; http://vaww.vinci.med.va.gov/vincicentral/VINCIWorkspace.aspx). The VA Informatics and Computing Infrastructure is a partnership between the VA Office of Information Technology and the Veterans' Health Administration Office of Research and Development. Researchers and operations staff can use VINCI to access data and statistical analysis tools in a virtual working environment through a certified VHA network computer using the VA Intranet or Virtual Private Network (VPN).

B. Data Retention Plan

☒ Research records will be maintained and destroyed according to the National Archives and Records Administration, Records Schedule Number: DAA-0015-2015-0004. Records destruction, when authorized, will be accomplished using the then current requirements for the secure disposal of paper and electronic records. Currently, destruction of research records (see DAA-0015-2015-0004, section 7.6 "Research Investigator Files" for materials included in research records) is scheduled for 6 years after the cut-off (the cut-off is the completion of the research project) and may be retained longer if required by other federal agencies. Records will not be destroyed without pre-notification to the facility records manager.

☐ Other data retention plan, describe:

5. Data Access and Data Recipients

Only members of our DVAMC research team will have access to identifiers and coded data that is located behind the VA firewall on our local server (see address above) and on the VINCI server. Coded data with direct identifiers removed (i.e., name, address, telephone numbers, SSN, DOB) will be placed at VINCI for the purpose of analysis. With the exception of Dr. King only coded data will be shared with Co-Investigators and the Scientific Advisory Board.

All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up to date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins). Access to study data will be removed for all study personnel when they are no longer part of the research team.

6. Data and/or Specimen Transportation and/or Transmission for all data and/or specimens involved in the study:

I. ☐ Data and/or specimens will not be transported or transmitted outside of Durham VAMC environment.

II. ☐ Data and/or specimens will be transported BETWEEN sites that are under the auspices of the Durham VA Medical Center.

III. ☒ Data and/or specimens will be transmitted to other VA sites using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted disk (encryption is optional).

☐ Data are coded or contain identifiers and thus will be sent

☒ Other, describe: Limited amount of PHI (such as task lists with study IDs) will be transported outside of the Durham VAMC environment. Those staff who will transport any PHI will complete a VASI form. Staff work in office and remotely with VA laptops. Electronic study data and information are retained within the VA environment.

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional).

☐ Specimens are coded or contain identifiers and thus will be sent via VA-authorized carrier with tracking.

☐ Other, describe:

IV. ☐ Data and/or specimens will be transported to non-VA/VHA sites (e.g., academic affiliates, laboratories, etc.) using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted CD.

☐ Data are coded or contain identifiers and thus will be sent via <chose method of transfer such as FIPS 140-2 encrypted CD or FIPS 140-2 encrypted hard drive/flash drive> using VA—approved carrier with tracking.

☐ Data are coded or identified and will be uploaded to sponsor website using electronic case report form (eCRF) <insert information including sponsor name and URL and the encryption the site uses.>

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional) or will be hand-delivered by research study personnel. Specify method of delivery:

☐ Specimens are coded and thus will be sent via VA-approved carrier with tracking or will be hand-delivered by research study personnel. Specify method of delivery:

In accordance with the HIPAA and the Privacy Act, for any coded or identifiable data or specimens released from the Durham VAMC (with the exception of Limited Data Sets), an Accounting of Disclosure (AOD) will be maintained (e.g., in a database or spreadsheet) that includes the participant's name, date of the disclosure, description of the nature of the Individually Identifiable Information (III) disclosed, purpose of each disclosure, and the name and address of the person/agency to whom the disclosure was made.

C. ☒ Local DVAMC memorandum "Authorization to Use, Process, Store, or Transmit VA Sensitive Information Outside VA Owned or Managed Facilities" has

been pre-filled out for each study team member who may transport the data and/or specimens off-site. These forms are included with the IRB materials.

D. ☒

Containers (e.g., briefcase, bin) are labeled with the following notice (label placed on the outside of container) in accordance with VHA Directive 6609:

NOTICE!!!

Access to these records is limited to: AUTHORIZED PERSONS ONLY. Information may not be disclosed from this file unless permitted by all applicable legal authorities, which may include the Privacy Act; 38 U.S.C. §§ 5701, 5705, 7332; the Health Insurance Portability and Accountability Act; and regulations implementing those provisions, at 38 C.F.R. §§ 1.460 – 1.599 and 45 C.F.R. Parts 160 and 164. Anyone who discloses information in violation of the above provisions may subject to civil and criminal penalties.

7. Risk Mitigation Strategies:

☐ Data are fully de-identified (stripped of HIPAA 18 and study ID/code) before being shared outside of Durham VAMC.

☐ Specimens are fully de-identified (stripped of HIPAA 18 and study ID/code before being shared outside of Durham VAMC.

☒ Direct identifiers will be maintained separately from data and or specimens by using a code to "identify" subjects. In a separate database (i.e., a "linking" or "cross-walk" database) this code will be linked to identifying subject information.

To mitigate the risk of unauthorized access, data will be stored behind the VA firewall with password protected access. The PI, individuals study coordinators and statistician will bear responsibility for overseeing the privacy and security of the data.

☐ Other, specify:

8. Suspected Loss of VA Information:

Should any incident such as theft or loss of data, unauthorized access of sensitive data or non-compliance with security controls occur it will be immediately reported according to VA policy. All incidents regarding information security/privacy incidents will be reported to the ISO and PO within 1 hour of acknowledgement of issue and done so using the VHADUR Research Events Report e-mail group (VHADURResearchEventReport@va.gov).

9. Reporting of Results:

☒ Reporting of results, such as in scientific papers and presentations, will never identify individual subjects. For the quantitative aspects of the trial, Data will be presented in aggregate and individual-level data will not be published

In order for this research to have an impact, stakeholders, and those in position to effect change based on study findings, will be informed of the study findings. We also anticipate presenting the findings of this study at professional conferences with a focus on Sleep. The annual meetings for the following professional organizations are likely venues for these presentations: the HSR&D Annual Meeting; and the annual meetings of the American Academy of Sleep Medicine. Further, we are likely to produce several manuscripts describing the outcomes of the study. We expect manuscript preparation to begin following completion of the study.

☐ Other results reporting plan, describe:

10. Future Use of Data:

☐ Data will be retained for future use. This is described elsewhere in the protocol and is noted in the HIPAA authorization.

☐ Future Use of data is optional (i.e., not required by the research subject).

☐ Future Use of data is required for participation in the study.

☒ No future use of data is currently planned.

11. Use of Mail Merge Technology

☒ Mail merge programs will be used to generate letters and/or address labels for mailings to potential or already enrolled research subjects. The study team is aware that to reduce risk of mail merge related privacy incidents, use of mail merge programs requires a 25% accuracy check to verify that (potential) research subject name and mailing address are properly "matched". If discrepancies are found, a 100% accuracy check is required before letters may be mailed.

12. Use of Non-Standard Software

☒ I do NOT intend to use any new specialized software (i.e., Software that's not already approved OR installed) in this study.

☐ I intend to use specialized software that has not already been installed and it has been approved for use by the VA Technical Reference Model (TRM) Group.
(Note: All new software must be approved by TRM before it can be installed on VA systems.)

☐ I intend to use previously installed software on my VA computer.

13. Use of Cloud Computing Services

☒ Cloud computing services will NOT be used in this study.

☐ Cloud computing services WILL be used in this study as described below and have been approved nationally by the VA Chief Information Officer (CIO). (Note: ONLY cloud computing services that have been approved nationally may be used.)

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