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Protocol

- **Use the section headings to write the Protocol, inserting the appropriate material in each. If a section is not applicable, leave heading in and insert N/A.**
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1. Abstract

Alcohol use disorders (AUDs) are prevalent among Veterans and result in significant physical and psychological burden. Among those who receive treatment for AUDs, 1 in 3 relapses to problematic drinking within one year of treatment. Thus, additional strategies are needed to enhance alcohol treatment outcomes. One promising approach involves providing concurrent treatment for a common complaint – difficulty falling or staying asleep. Up to 74% of Veterans seeking treatment for AUD report co-occurring symptoms of insomnia. Given the negative impact of insomnia on attention and emotion regulation, insomnia symptoms may decrease patients' abilities to attend to alcohol treatment and manage negative emotions that lead to craving and relapse. Moreover, approximately 50% of individuals with AUDs report using alcohol to help them sleep, making relapse more likely for those with no other tools or skills to help them sleep. Indeed, sleep disturbance has been identified as a risk factor for relapse among individuals in alcohol treatment. Thus, effective treatment of sleep problems may enhance alcohol treatment. Cognitive Behavioral Therapy for Insomnia (CBT-I) has been effective in reducing insomnia severity in individuals with AUDs; however, no investigations have examined the efficacy of CBT-I delivered concurrently with AUD treatment to determine its impact on treatment outcomes. This R21 aims to examine the feasibility, acceptability, and initial efficacy of a CBT-I supplement to outpatient alcohol treatment. A randomized pilot trial with 80 Veterans who meet diagnostic criteria for AUD and Insomnia Disorder will be conducted. Participants will be randomly assigned to receive Cognitive Behavioral Therapy for Insomnia (CBT-I) or minimal treatment (sleep hygiene handout only; SH) in addition to alcohol treatment as usual. Outcomes will be assessed at the end of the active intervention period (6 weeks) and 6 weeks post-intervention. Outcomes of interest include recruitment/retention rates, treatment satisfaction, insomnia severity, use of alcohol as a sleep aid, percentage of heavy-drinking days, and alcohol-related problems. Analyses will focus on size of treatment effects. This study will provide initial evidence that treatment of insomnia not only improves sleep but also allows participants to derive greater benefit from outpatient alcohol treatment.

2. Objectives (include all primary and secondary objectives)

(1) To test the feasibility and acceptability of a CBT-I supplement to outpatient alcohol treatment.
(2) To evaluate the initial efficacy of the CBT-I supplement on alcohol use outcomes.

3. Background

Up to 74% of Veterans seeking treatment for alcohol use disorder (AUD) report symptoms of insomnia.[1,2] These symptoms represent a **barrier to alcohol treatment** for three distinct reasons. First **(1)**, approximately 50% of individuals with alcohol use disorders report using alcohol to help them sleep;[3-5] thus, those without alternative sleep aids may relapse to drinking if insomnia persists. Insomnia symptoms have also been associated with significant deficits in **(2)** attention/working memory[6,7] and **(3)** emotion regulation.[8-11] Because cognitive-behavioral alcohol therapies (CBT) capitalize on individuals' use of these abilities to identify and adapt to the stimuli that lead to alcohol use, CBT-based treatments may have limited effectiveness for patients

with insomnia. This combination of factors – continued insomnia and limited cognitive/emotional capacity to respond to treatment – may explain in part why insomnia symptoms precipitate relapse[12] among the 1 in 3 individuals who relapse to problematic drinking within one year of alcohol treatment.[13,14]

Cognitive Behavioral Therapy (CBT-I) is the first line of treatment for insomnia. It has been associated with moderate to large improvements in insomnia outcomes, with effects maintained 24 months after treatment.[15] It has been effective in reducing insomnia severity and sleep complaints among U.S. military Veterans, including those with comorbid PTSD and depression.[16-18] It has also been effective in reducing symptoms of insomnia – but not subsequent rates of relapse – among alcohol dependent individuals with 1+ months of sobriety.[19-21] However, **no research has examined the impact of CBT-I among individuals actively engaged in alcohol treatment**. Improving sleep is expected to enhance the efficacy of alcohol treatment among Veterans by enhancing their abilities to attend to treatment, regulate their emotions, and initiate sleep without alcohol.

Consistent with PA-18-202, the proposed R21 aims to examine the feasibility, acceptability, and initial efficacy of a CBT-I supplement to outpatient alcohol treatment. The **primary objective** of this study is to enhance alcohol treatment to account for the unique needs of Veterans with sleep disorders. We propose a 6-week randomized trial, in which 80 Veterans will be randomly assigned to receive Cognitive Behavioral Therapy for Insomnia (CBT-I) or minimal treatment (sleep hygiene only; SH) in addition to treatment as usual. Individuals participating in the Addictions Treatment Program at the Truman VA will be eligible to participate if they meet DSM-5 criteria for AUD and the episodic criterion (≥1mo) for Insomnia Disorder. Participants will complete assessments at baseline, post-treatment, and 6-week follow-up. We propose the following specific aims:

Aim 1: To test the feasibility and acceptability of CBT-I delivered concurrently with alcohol treatment. Recruitment (anticipated enrollment of at least 2 Veterans per month) and retention rates (goal ≥70% complete 6/6 treatment sessions) will indicate feasibility of the intervention. Treatment satisfaction (average score ≥ 3, indicating 'mostly satisfied') will serve as an indicator of acceptability. Retention and satisfaction will be measured separately for insomnia and alcohol treatments.

Aim 2: To evaluate the initial efficacy of CBT-I on insomnia and alcohol use outcomes. We hypothesize that Veterans receiving CBT-I will demonstrate greater improvements in insomnia severity, sleep efficiency, use of alcohol as a sleep aid, percentage of heavy-drinking days, and alcohol-related problems post-treatment and at 6-week follow-up.

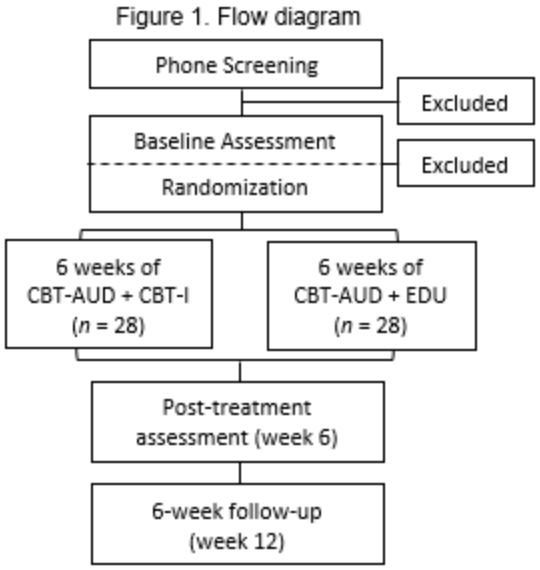
Aim 3 (exploratory): To examine proximal intervention outcomes. We hypothesize that Veterans receiving CBT-I will demonstrate greater post-treatment improvements in attention (vigilance), working memory, treatment-related learning, negative affect, and emotion regulation.

4. Study Procedures

This study will examine the feasibility, acceptability, and initial efficacy of Cognitive Behavioral Therapy for Insomnia (CBT-I) delivered concurrently with CBT for AUD using a randomized, parallel, two-group design (see Figure 1). Eighty Veterans will be randomly assigned to either **CBT-I** or a sleep hygiene education control (**SH**). All outcomes will be assessed at baseline, post-treatment, and 6-week follow-up. This design will allow us to test the feasibility and acceptability of CBT-I among those in treatment for AUD (**Aim 1**); evaluate the initial efficacy of CBT-I in improving insomnia and alcohol-related outcomes (**Aim 2**); and examine CBT-I effects on attention, working memory, learning, negative affect, and emotion regulation, which may be examined as mediators in a subsequent trial (**Aim 3**).

Study site. Participants will be recruited through the Addictions Treatment Program at the Harry S. Truman Memorial Veterans Hospital (Truman VA) in Columbia, MO. We will recruit 115 participants over 20 months (see Table 2) to obtain a final sample of at least 80 participants.

Participants. Patients in the Addictions Treatment Program at the Truman VA will be **included** if they meet DSM-5 criteria for Alcohol Use Disorder and the episodic criterion (≥1mo) for Insomnia Disorder. Criteria for AUD include 2+ symptoms in the past 12 months that result in distress or impairment related to alcohol use (e.g., using more than intended, unsuccessful attempts to cut down). Criteria for insomnia include difficulty (>30min) falling asleep, staying asleep, or waking up too early on 3+ nights per week despite adequate opportunity and circumstances for sleep; and daytime impairment in mood, cognitive, social, or occupational activities.[22] Participants will be **excluded** if they are unable to provide informed consent, demonstrate cognitive impairment, report continuous sobriety for more than 2 months at baseline assessment, report a manic episode or seizure (contraindications for sleep restriction)[23] in the past year, have a severe psychiatric disorder that requires immediate clinical attention (e.g., psychosis, suicidal ideation with intent and plan), or began a new sleep medication in the past 6 weeks. Consistent with standard practice, those who endorse symptoms of sleep-related breathing disorders (≥2/8 symptoms on the STOP-BANG[24]), restless leg syndrome, periodic limb movement disorder, or narcolepsy will be referred for overnight polysomnography.



Recruitment and initial screening. Patients in the Addictions Treatment Program (ATP) at the Truman VA will be recruited via flyers and provider referral. All residential patients at the ATP will receive a flyer about the study and complete a brief (9-item) screener for the study as part of the intake process. Providers will share the de-identified results of the screener with PI Miller. If participants are interested in the study, they may contact the research team directly. However, to decrease burden on both providers and participants, providers will also have the option of providing the research team with contact information for patients who may be eligible and interested. The research team will then reach out to the patient directly to assess their interest in participating. Research staff will reach out to potential participants three times by phone. Research staff will also attend the beginning of treatment groups/meetings in order to inform individuals about the study and answer any questions they may have. PI Miller will participate in weekly behavioral health team meetings to facilitate the screening and recruitment process (i.e., reminding them about the study, updating them on recruitment progress, and answering any questions).

Phone screening. A research assistant (RA) will share more details about the study and conduct a brief eligibility screen (~15min) with the potential participant in person or over the phone (see Table 1). Those who screen eligible will be scheduled for baseline.

Baseline assessment. Participants will provide written informed consent prior to completion of baseline (see Table 1). In the case of remote baseline assessments, an RA will walk the participant through an electronic version of the written consent form, which they will be asked to sign electronically via the Qualtrics platform. The RA will then print and sign the electronic version of the participant's consent. The baseline evaluation will involve assessment of substance use and sleep disorders and full eligibility criteria using the Mini International Neuropsychiatric Interview (MINI) 7.0.2. Consistent with standard practice, those who endorse symptoms of sleep-related breathing disorders, restless legs syndrome, periodic limb movement disorder, or narcolepsy will be referred for polysomnography. Given the prevalence of sleep apnea in this population, individuals who meet all eligibility criteria but report symptoms of sleep apnea will complete one night of holter monitoring (using an Evo Holter Recorder, SpaceLabs Healthcare) at home in their own beds to rule out for sleep apnea.

Eligible participants will complete baseline assessment measures and will be randomly assigned to either the CBT-I or SH condition. Participants in both conditions will be oriented to the prospective sleep diary, which

they will be asked to complete every morning for the next 6 weeks. The RA will provide all participants with a general handout on sleep hygiene (from the National Sleep Foundation website) and answer any questions they may have about the guidelines.

To confirm diagnosis of insomnia, all eligible participants will complete one week of daily sleep diaries (between baseline and treatment session 1), which will be collected electronically and time-stamped each morning using the Qualtrics data management system. Participants who have not completed the diary each morning by noon will receive a reminder text or phone call from study staff. Sleep diaries measure sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency, and sleep quality. In this study, sleep diaries will also assess use of sleep medication and use of alcohol/other drugs (yes/no) to help with sleep. Sleep medication variables will include name, dosage, and time taken and will be converted to lowest recommended dosage units for data analysis.[25] Participants who are unable to complete the daily sleep diaries by computer or phone will be provided with pen-and-paper surveys to fill out each day by hand.

Follow-up. Follow-up assessments (see Table 1) will be administered in person by the RA, who will be blind to participant condition. Upon completion of the study, SH participants will be offered a referral for CBT-I, which is available with trained providers at the VA.

Remote appointments. If needed, treatment and follow-up appointments may be completed remotely using Zoom Pro or the VA's Video Connect service. Using their VA email from the VA laptops, research staff would send the participant a link to launch the session. Participants wanting to use their iPhone or iPad for the session would have to download the VA Video Connect application onto their device. On all other devices (e.g., PCs, laptops, Android devices), the participant will simply open the email and click the link to launch the secure video session. This service uses encryption to ensure that sessions are private and secure and is designed for Veterans in rural areas with limited access to healthcare facilities.

Table 1. *Assessment, therapy, and payment schedule*

Week	Assmt	CBT-I	Paymt	Bonus
1	BL		10	
2		S1	20	10
3		S2		
4		S3		
5		S4		
6		S5		
7	Post-tx	(S6)	40	
8				10
9				
10				
11				
12	1mo		50	
13				10

Note. 1mo = 1 month. Assmt = assessment. BL = baseline. Bonus = bonus payment for completion of all 7 daily surveys. Paymt = standard payment. Tx = treatment.

Retention strategies. To enhance follow-up rates, participants will receive:

- Up to $40 for baseline (~2hr): $10 for completing the assessment, $10 for completing all seven daily surveys, and $20 for returning the actiwatch.
- Up to $50 for the post-treatment assessment (~1hr): $40 for completing the assessment and $10 for completing all seven daily surveys
- Up to $60 for the 6-week follow-up (~1hr): $50 for completing the assessment and $10 for completing all seven daily surveys

Participants will also receive reminder texts/calls, have access to free parking, and receive treatment at no cost.

Cognitive Behavioral Therapy for Insomnia (CBT-I). CBT-I will be delivered individually, in person, in five weekly one-hour sessions. A sixth week of treatment will be included – and scheduled for the same date as the post-treatment assessment – if the participant and research team agree that it would be beneficial (e.g., if a participant has difficulty grasping cognitive therapy concepts). Study therapists will follow the 2014 CBT-I in Veterans manual developed by leading researchers in the behavioral sleep medicine field (see Table 3).[23] Intervention components include (1) sleep hygiene: limiting naps; avoiding caffeine, tobacco, alcohol, and rich/heavy foods before bedtime; exercising; establishing a bedtime routine; and creating a comfortable sleep

environment; (2) sleep restriction: limiting time in bed in order to improve sleep efficiency, or the percentage of time in bed that is actually spent sleeping; time in bed will be titrated each week based on sleep efficiency; (3) stimulus control: strengthening association between bedroom and sleep to decrease conditioned arousal; (4) relaxation: diaphragmatic breathing, progressive muscle relaxation, and visual imagery to reduce arousal; and (5) cognitive therapy: identifying and challenging thoughts that interfere with sleep.

Sleep hygiene (SH). All participants will receive a one-page handout on sleep hygiene. This is the only intervention that participants assigned to the SH condition will receive and is consistent with what may be expected as standard care in a doctor's visit with a primary care physician.

Table 2. Survey Instruments and Schedule of Administration

Use	Construct	Measure(s)	Cut-score		
Screen	**Insomnia severity**, past 2 weeks	Insomnia Severity Index (Morin et al., 2011)	≤ 9 excluded at phone screen		
	Sleep apnea, past month	STOP questionnaire (Chung et al., 2008)	≥ 3 excluded at phone screen		
Use	**Construct**	**Measure(s)**	**BL**	**Post**	**6wk**
Cov	**Demographics**	See instruments	X		
	Other drug use, past 6 weeks	Drug Use Screening Inventory	X	X	X
	Use of sleep medication	Daily Sleep Diary (Carney et al., 2012)	X	X	X
Aim 1	**Recruitment**	Completion of ≥ 1 session of CBT-I		X	
	Retention	Completion of 6/6 sessions of CBT-I		X	
	Treatment satisfaction, measured separately for CBT-I and CBT-AUD	Client Satisfaction Questionnaire (Larsen et al., 1979)		X	
Aim 2	**% abstinent days**, past 6 weeks **% heavy-drinking days** (≥4/5 drinks/day for women/men)	Timeline Follow-back (TLFB) for alcohol (Sobell & Sobell, 1996)	X	X	X
	Alcohol problems, past 6 weeks	Short Inventory of Problems (Miller et al., 1995)	X	X	X
	Use of alcohol or other drugs to help with sleep, past 6 weeks	Daily Sleep Diary (Carney et al., 2012)	X	X	X
	Insomnia severity, past 2 weeks	Insomnia Severity Index (Morin et al., 2011)	X	X	X
	Total wake time, average past week	Daily Sleep Diary (Carney et al., 2012)	X	X	X
	Sleep quality, average past week	Daily Sleep Diary (Carney et al., 2012)	X	X	X
	Dysfunctional beliefs, past month	Dysfunctional Beliefs about Sleep Scale	X	X	X
Aim 3	**Treatment-related learning**	Project SAVE Alcohol Quiz Project SAVE Alcohol Vignette	X	X	X
	Executive functioning	Psychomotor Vigilance Task (Dinges et al., 1985) *N*-back Task (Schmiedek et al., 2014) Monetary Choice Questionnaire UPPS Measure of Impulsivity Cognitive Failures Questionnaire	X	X	X
	Negative affect, past week	Positive and Negative Affect Schedule	X	X	X
	Emotion regulation, past 30 days	Brief Difficulties in Emotion Regulation Scale (Bjureberg et al., 2016)	X	X	X
	Alcohol craving, past week	Penn Alcohol Craving Scale	X	X	X
	Mental health symptoms	PTSD Checklist for DSM-5 Patient Health Questionnaire-9 for depression GAD-7 measure of anxiety Satisfaction with Life Scale	X	X	X

Note. BL=baseline. Cov = potential covariates. Post = post treatment. Wk = week.

Blinding. PI Miller will not be blinded to block size or participant assignment because she will inform study therapists of participant assignment to conditions. However, PI Miller and study therapists will be blinded to assessment outcomes, and the assessment RA will be blinded to participant condition.

Treatment integrity. Treatment integrity will be assured in three steps. (1) Delivery. The study therapist will receive training in use of the treatment manual via audio-recorded mock therapy sessions. PI Miller and co-I McCrae, both of whom are licensed clinical psychologists, will evaluate audiotapes of mock sessions and provide corrective feedback. All intervention sessions will be audio-recorded, given participant permission. PI Miller and co-I McCrae will review session audiotapes for ongoing training and supervision. PI Miller will score five randomly selected tapes to assess treatment fidelity using a checklist of treatment elements. Descriptive analyses will be used to determine the proportion of intended treatment elements covered in intervention sessions. (2) Comprehension. Participants will be provided with a workbook detailing treatment instructions, rationale, and handouts and encouraged to ask questions. (3) Enactment. Workbooks will contain written instructions on home assignments, and therapists will encourage assignment completion.

Early termination. All participants will receive sleep hygiene recommendations immediately following baseline assessment, so every participant who attends baseline will receive some form of treatment for insomnia. However, participants may decide to stop participating in the study at any time without penalty. If they decide to withdraw their participation, therapy will be terminated. This will be discussed as part of the informed consent process.

5. Inclusion/Exclusion Criteria

Eligibility criteria include (a) participation in the Addictions Treatment Program at the Truman VA, (b) DSM-5 criteria for moderate to severe Alcohol Use Disorder, (c) alcohol use in the past 2 months at baseline, and (d) the DSM-5 episodic criterion (duration at least 1 month) for Insomnia Disorder.

Participants will be excluded if they are unable to provide informed consent, demonstrate cognitive impairment (Mini Mental Status Exam score <26), report a manic episode or seizure in the past year (contraindications for CBT-I),[23] have a severe psychiatric disorder that requires immediate clinical attention (e.g., psychosis, suicidal ideation with intent and plan), or began a sleep medication in the past 6 weeks. Consistent with standard practice, those who endorse symptoms of sleep-related breathing disorders (≥2/8 symptoms on the STOP-BANG[24]), restless leg syndrome, periodic limb movement disorder, or narcolepsy will be referred for polysomnography.

6. Drugs/ Substances/Devices

N/A

7. Study Statistics

Outcome measures. Outcome measures are listed in Table 1 above. Primary outcomes include recruitment, retention, and treatment satisfaction (Aim 1) as well as insomnia severity, total wake time, sleep quality, percent days abstinent, percent heavy-drinking days, alcohol problems, and use of alcohol or other drugs as a sleep aid (Aim 2). Secondary (Aim 3) outcomes include treatment-related learning, executive function (attention, working memory, delayed discounting, impulsivity), negative affect, emotion regulation, craving, and mental health symptoms (PTSD, depression, anxiety, life satisfaction).

Aim 1 analyses. Recruitment (goal ≥4pts/mo) and retention rates (≥70% complete 5/5 sessions) will indicate feasibility of the intervention. Treatment satisfaction (average score ≥3, indicating 'good' quality) will serve as an indicator of acceptability. Recruitment, retention, and satisfaction will be measured separately for insomnia and alcohol treatments. We do not expect group differences in recruitment. Descriptive statistics, chi-square, and t-tests will be used to determine between-group differences in retention and satisfaction.

Aims 2-3 analyses. Cohen's *d* (adjusted for baseline scores) and 95% CIs will be used to examine the magnitude of between-group differences at post-treatment and 6-week follow-up. We will use HLM to compare conditions at post-treatment and 6 weeks. We chose HLM over other statistical approaches (e.g., ANOVA) because it requires fewer assumptions, has superior ability to handle missing data, and will yield greater

statistical power. In each model, the Level 1 variable will be time. Level 2 portions of the model will include the effect of condition. Hypotheses will be tested by regressing condition on the Level 1 intercept and time effect. Analyses will be intent-to-treat. We will examine whether attrition is associated with any baseline variables and control for such variables when necessary.

Power analysis. Post-hoc power analyses conducted in G*Power 3.0.10 indicate that 80 participants will provide strong power ($1 - \beta = .99$) to detect within-between interactions of moderate magnitude ($f = .25$).

Early stopping rules. PI Miller will monitor adherence to the study protocol and adverse events on an ongoing basis and discuss these issues with the research team during weekly meetings. All serious and unexpected adverse events will be reported to the IRB within 24 hours of receipt of information. Other adverse or potentially adverse events will be monitored and reported at annual continuing reviews. After discussion with the IRB, we will discontinue the trial if there is (a) compelling evidence from this or another study of a serious adverse effect of CBT-I that has potential to override potential benefit, (b) compelling evidence from this or another study of a significant beneficial effect of CBT-I, such that continued denial to other groups would be unethical, or (c) low probability of addressing study aims within a feasible time frame.

8. Risks

We believe the risks associated with completing assessments and participating in the intervention are minimal. Potential risks include: temporary daytime fatigue (due to restriction of time in bed), subjective discomfort from answering questionnaires, coercion, and the possibility of a breach of confidentiality. Because the sleep restriction component of CBT-I places individuals with a history of mania at risk for additional manic episodes, the treatment will be modified for these individuals. Participants will not incur financial risk. There are no other known iatrogenic effects of CBT-I or completion of sleep diaries. However, if any emerge, they will be addressed immediately by research and/or clinical staff.

The following safeguards will be implemented to protect participants from risks related to study participation:

Temporary fatigue. Participants will be informed as part of the consent process that restricting their time in bed may increase daytime fatigue for the first few weeks of treatment (although this will be temporary, as time in bed will be expanded as sleep efficiency improves). Consistent with standard insomnia treatment procedures, time in bed will never be restricted to less than 5 hours in order to avoid impaired vigilance and significant daytime sleepiness. Participants will also be provided with recommendations on ways to increase alertness and counter daytime fatigue (e.g., staying active, engaging in social activities).

Discomfort. Participants will be informed of the types of questions that they will be asked to answer as part of the informed consent process, and they will have the opportunity to skip questionnaire items or discontinue participation in the study at any time without penalty. Referrals will be provided to participants during the consent and throughout the study, in the event that participants report experiencing distress.

Coercion. Participants will be provided with modest compensation for their participation in the study (up to $150 for 3 assessments and 3 complete weeks of daily sleep surveys). We believe these compensation rates are commensurate with the time and effort involved in these tasks, and the amounts are consistent with compensation provided for other clinical studies with Veterans. Participants are free to discontinue at any time and will receive compensation for any and all assessments that they complete.

Confidentiality. Study data will be handled only by research staff and will be used strictly for research purposes. All research staff will be trained in responsible research conduct and the handling of private and confidential information. Identifying information will not be recorded in computerized or paper-and-pencil assessments; rather, assessment instruments and related study data will be identified and tracked using a unique study identification number. The database containing identification numbers and contact information will be stored separately from study data and will be used to link baseline, post-treatment, and 6-week follow-up assessments. This database will be stored on a password-protected computer accessible only to research staff and will be destroyed immediately upon completion of the study. Study computers will also be stored in a locked office accessible only to research staff (PI Miller's laboratory space in the Department of Psychiatry). Identifying information (names and dates) will appear only on consent forms, payment receipts, and the contact

information form. All paper forms containing identifying information will be kept in a locked filing cabinet in Toni Maraldo's office (C201E) at the VA, separate from any data; and only research staff will have access to these filing cabinets. Audiotaped sessions, which will be used in fidelity coding, will not be labeled with identifying information and will be deleted permanently once fidelity coding is complete. Data collected using computer software will be stored electronically and identified by unique study number only. No personally identifying information will be included in the data. A password will be required to access data that are stored electronically, and only personnel involved with the project will have access to the electronic data. The computer-administered surveys provide an additional layer of confidentiality protection relative to paper and pencil surveys where staff would see a participant's data as they were entering or storing it.

Participants will be informed verbally and in writing during the consent process that mandatory reporting laws will be followed. Subjects who indicate danger to themselves or others will be escorted to the emergency room.

Given the sensitive nature of information being collected, all data will be protected by a Certificate of Confidentiality and identified using unique ID numbers assigned to participants specifically for this project. Names and identifying information required for follow-up reminders will always be kept separate from research data and will not be used as study data. Computerized survey data will be stored electronically on the secure VA server. Digital audio recordings of sessions, which will be used to determine treatment fidelity, will be stored on password-protected computers to which only project staff will have access. All research staff will be trained in procedures for maintaining data and participant confidentiality. Study personnel will no longer have access to the study data when they are no longer part of the research team. Data will not be removed from the VA.

Protocol modifications for individuals with a history of mania or bipolar disorder. Because the sleep restriction component of CBT-I places individuals with a history of mania at risk for additional manic episodes, the treatment will be modified for these individuals (see Section 4 above) and individuals with a recent (past year) history of mania will be excluded.

Data safety and monitoring plan. PI Miller will monitor procedures to ensure that they conform to the approved protocol. Specifically, she will monitor (a) the progress of the research, including participant recruitment and retention and assessments of data quality; (b) adverse events and procedures for making determinations that there may be a change to the benefit-to-risk ratio of research participation; and (c) procedures to protect participant privacy and confidentiality. She will monitor all serious, unexpected, and other adverse or potentially adverse events. Serious adverse events include those resulting in death, inpatient hospitalization, a threat to life, persistent or significant disability or incapacity, congenital anomalies/birth defects, or serious health risk. Unexpected adverse events are those that were unforeseen based on the anticipated potential risks outlined in the study protocol and informed consent. Other adverse or potentially adverse events include those that may be causally related to study participation and lead to participant distress or drop-out.

PI Miller will monitor data quality and adverse events on an ongoing basis. All serious and unexpected adverse events will be reported to the IRB within 24 hours of receipt of information. Other adverse or potentially adverse events will be monitored and reported at annual continuing reviews.

9. Benefits

Participants in the CBT-I and SH conditions may benefit from the sleep-related information provided. Participants may also appreciate the opportunity to engage in research that may help others benefit from treatment. Beyond these potential benefits to subjects, this research is expected to inform future research and clinical efforts to treat insomnia and reduce the consequences associated with alcohol use among Veterans. As noted above, we believe the risks of this research to participants are minimal and the overall benefits of this research to subjects and society outweigh these risks.

10. Payment and Remuneration

To enhance follow-up rates, participants will receive up to $40 for completion of the baseline assessment ($10 for the in-person assessment, $10 for completing all seven daily surveys, and $20 for returning the actiwatch), up to $50 for the post-treatment assessment ($40 for assessment, $10 for all daily surveys), and up to $60 for the

6-week follow-up ($50 for assessment, $10 for all daily surveys), with the potential to earn up to $150. Participants will also receive reminder texts/calls, have access to free parking, and receive treatment at no cost. Participants who choose not to complete an assessment will not receive payment for that assessment; however, they will be invited to participate in any subsequent assessments (e.g., if they decline the post-treatment assessment, they will still be invited to complete follow-up).

11. Costs
Participants will be expected to travel to the VA for assessment and therapy appointments. It is unlikely that the expense of this travel will be a burden to participants, as the VA is easily accessible by foot, car, and public transportation. However, participants will be expected to cover the cost of these expenses. Participants will not be charged for other study procedures or for treatment.

12. Data Use
PI Miller will use all project data to oversee project management, treatment, and data analysis. Co-I McCrae will access audio data to provide clinical supervision (i.e., feedback on treatment integrity). Co-I Maddoux will access outcome data for data analysis.

13. Software
The computer program Inquisit will be required for assessments of executive functioning. Funds for Inquisit were included in the NIH application budget; thus, the PI will provide funds for this software. Participants' performance on executive functioning tasks will be saved on the computer's hard drive. However, these data will be tracked using unique participant identification numbers, rather than identifying information. All data will be transferred to the VA secure server as soon as possible.

SPSS will be required for data analysis. The PI was informed that SPSS is available through VINCI.

All software will be approved through the One VA Technical Reference Model for installation and use on the VA network.

14. Web applications
All eligible participants will also complete sleep diaries, which will be collected electronically and time-stamped each morning using the Qualtrics data management system. As a company, Qualtrics is familiar with the nature of academic research and the importance of confidentiality, and their data handling procedures meet strict privacy standards (https://www.qualtrics.com/privacy-statement/). All data will be identified using unique participant IDs. The Qualtrics data centers utilize many security measures. Qualtrics' database access is restricted and requires authorization. All computer equipment (servers, SANs, switches, routers, etc.) is redundant and is located in secure, environmentally controlled data centers with 24/7 monitoring. Web traffic does not directly access the database and database requests are reversed proxy via an application server to the database. All information is secured via industry standard firewalls and stringent IT security policies and procedures. Qualtrics utilizes industry standard web application firewalls and DDOS protection. Qualtrics also leverages panel partners who are meticulous in their multiple levels of security, which include redundant data centers, secure servers, encryption which includes one-way encryption, numeric IDs, secure .NET platforms, security clearance, industry standard firewalls, 24/7 monitoring of data centers, confidentiality agreements, and physical, electronic, and managerial procedures. While Qualtrics typically tracks IP addresses as part of its protocol, our research project will opt out of IP address tracking to ensure the survey responses remain confidential. Once downloaded, the data will be stored securely on the VA's network server.

The VA's Video Connect service will be used for remote appointments, if necessary. This service uses encryption to ensure that sessions are private and secure and is designed for Veterans in rural areas with limited access to healthcare facilities. Additionally, Zoom Pro will be an alternate videoconferencing resource for remote appointments. This service has end-to-end encryption and password-protected meetings. Data from these sessions will not be recorded or downloaded

15. References

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