

The Impact of CBT-I on Cannabis Cessation Outcomes

Dr. Kimberly Babson, P.I.

NCT02102230

Study Protocol (last approved modifications)

06/29/2015

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Approval Period: 03/27/2015 - 03/11/2016

Modification
<p>1. Summarize your proposed changes.</p> <p>We would like to propose the following three changes to the current protocol.</p> <ol style="list-style-type: none"> 1. We would like to modify the study inclusion criteria to remove the requirement that individuals be motivated to quit cannabis at study baseline. This modification does not fundamentally alter the conceptual foundation of the study, the study design, hypothesis testing, or statistical power. We expect that individuals' motivation to use cannabis as a sleep aid will decrease following receipt of the interventions (relative to the control), leading to a reduction or cessation of cannabis use, consistent with existing hypotheses. We believe that this proposed modification will also increase ecological validity of the study, as a finding of a significant effect for CBT-I would allow for implementation of the intervention among all cannabis using individuals, regardless of initial desire to quit. 2. We would like to replace the overnight polysomnography-based sleep apnea assessment with a structured clinical interview for sleep apnea. Specifically, we propose to use the STOP-Bang (Chung et al., 2008) to screen for sleep apnea, within the context of the baseline assessment. Inclusion criteria will be modified from an AHI > 15 to a score on the STOP-Bang \geq 5. 3. Staff personnel have been updated. <p>We request an expedited review of the proposed modifications as risk to participants is actually decreased (i.e., replacement of overnight sleep assessment with structured interview).</p>
<p>2. Indicate Level of Risk</p> <p>Decrease</p>
<p>3. Update the Conflict of Interest (COI) section if any changes in COI have been made since the last protocol submission.</p> <p>N Is there a change in the conflicting interest status for any existing personnel on this protocol?</p>

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CITI Training current				Y

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CITI Training current				Y

Co-Protocol Director		
Name	Degree (program/year if student)	Title

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CITI Training current				Y

Participant Population(s) Checklist

Yes/No

- Children (under 18) N
- Pregnant Women and Fetuses N
- Neonates (0 - 28 days) N
- Abortuses N
- Impaired Decision Making Capacity N
- Cancer Subjects N
- Laboratory Personnel N
- Healthy Volunteers N
- Students N
- Employees N
- Prisoners N
- Other (i.e., any population that is not specified above) Y

Study Location(s) Checklist

Yes/No

- Stanford University
 - Clinical & Translational Research Unit (CTRU)
 - Stanford Hospital and Clinics
 - Lucile Packard Children's Hospital (LPCH)
 - VAPAHCS (Specify PI at VA) Y
- Kimberly Babson
- Other (Click ADD to specify details)

General Checklist

Multi-site

Yes/No

- Is this a multi-site study? A multi-site study is generally a study that involves one or more medical or research institutions in which one site takes a lead role.(e.g., multi-site clinical trial) N

Collaborating Institution(s)

Yes/No

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- Are there any collaborating institution(s)? A collaborating institution is generally an institution that collaborates equally on a research endeavor with one or more institutions. N

Cancer Institute

Yes/No

- Cancer-Related Studies (studies with cancer endpoints), Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Specimens (e.g., blood, tissue, cells, body fluids with a scientific hypothesis stated in the protocol). N

Drug /Device

Yes/No

- Investigational drugs, biologics, reagents, or chemicals? N
- Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)? N
- Investigational Device / Commercial Device used off-label? N
- IDE Exempt Device (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) Y
- Protocol involves studying potentially addicting drugs? N

Clinical Trials

Yes/No

- Click "yes" to confirm that you have accessed the website and read the clinicaltrials.gov reporting requirements provided. Y
- This study will be registered on clinicaltrials.gov? Y

Tissues and Specimens

Yes/No

- Human blood, cells, tissues, or body fluids (tissues)? N
- Tissues to be stored for future research projects? N
- Tissues to be sent out of this institution as part of a research agreement? For guidelines, please see <http://stanford.edu/group/ICO/researcher/reMTA.html>
<http://stanford.edu/group/ICO/researcher/reMTA.html> N

Biosafety (APB)

Yes/No

- Are you submitting a Human Gene Transfer investigation using biological agent or recombinant DNA vector? If yes, please complete and attach the Gene Transfer Protocol N

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Application Supplemental Questions to section 16 of the eProtocol application.

- Are you submitting a Human study using biohazardous/infectious agents? If yes, refer to the <http://www.stanford.edu/dept/EHS/prod/researchlab/bio/index.html> Administrative Panel on BioSafety website prior to performing studies. N
- Are you submitting a Human study using samples from subjects that contain biohazardous/infectious agents? If yes, refer to the <https://ehsappprd1.stanford.edu/eprbio/> Administrative Panel on BioSafety website prior to performing studies. N

Human Embryos or Stem Cells

Yes/No

- Human Embryos or gametes? N
- Human Stem Cells (including hESC, iPSC, cancer stem cells, progenitor cells). N

Veterans Affairs (VA)

Yes/No

- The research recruits participants at the Veterans Affairs Palo Alto Health Care System(VAPAHCS). Y
- The research involves the use of VAPAHCS non-public information to identify or contact human research participants or prospective subjects or to use such data for research purposes. Y
- The research is sponsored (i.e., funded) by VAPAHCS. Y
- The research is conducted by or under the direction of any employee or agent of VAPAHCS (full- time, part-time, intermittent, consultant, without compensation (WOC), on-station fee-basis, on- station contract, or on-station sharing agreement basis) in connection with her/his VAPAHCS responsibilities. Y
- The research is conducted using any property or facility of VAPAHCS. Y

Equipment

Yes/No

- Use of Patient related equipment? If Yes, equipment must meet the standards established by Hospital Instrumentation and Electrical Safety Committee (650-725-5000) N
- Medical equipment used for human patients/subjects also used on animals? N
- Radioisotopes/radiation-producing machines, even if standard of care? http://www.stanford.edu/dept/EHS/prod/researchlab/radlaser/Human_use_guide.pdf More Info N

Payment

Yes/No

- Subjects will be paid for participation? See payment considerations. Y

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Funding	Yes/No
• Training Grant?	Y
• Program Project Grant?	N
• Federally Sponsored Project?	N
• Industry Sponsored Clinical Trial?	N

Funding

Funding - Grants/Contracts	
Funding Administered By: VA	SPO # (if available):
Grant # (if available): CX001023	Funded By (include pending): VA
Principal Investigator: Kimberly Babson	
Grant/Contract Title if different from Protocol Title:	
Y	For Federal projects, are contents of this protocol the same as described in Federal proposal application?
N	Is this a Multiple Project Protocol (MPP)?
N	Is this protocol under a MPP?

Funding - Fellowships

Gift Funding

Dept. Funding

Other Funding

Resources:

- a) **Qualified staff.**

Please state and justify the number and qualifications of your study staff.

We have a diverse and highly qualified staff with expertise in the specific duties that they will perform in the research project. This includes expertise in statistics and assessment methodology, clinical psychology, human subjects research, project management, and interview assessment of vulnerable community-based populations, as proven by clinical and scientific training or previous experience.

- b) **Training.**

Describe the training you will provide to ensure that all persons assisting with the research are

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informed about the protocol and their research-related duties and functions.

All members of the study team have been involved in the development of the protocol, and we will have team meetings both prior to study start and periodically during the study period to assure that all staff understand their role in the study and the functions that they must perform. Additionally, Dr. Babson will meet with all staff weekly to discuss research related duties and progress

c) Facilities.

Please describe and justify.

Evaluation and groups will be conducted within the National Center for PTSD on the Menlo Park campus. This facility includes a secure servers where data will be stored and maintained by VA IRMS. We have secure phone and computer resources to conduct the study.

d) Sufficient time.

Explain whether you will have sufficient time to conduct and complete the research. Include how much time is required.

We will have sufficient time to conduct and complete the research. All study team members have devoted sufficient time to the project to complete the tasks required of them. We will require 5 years to complete the study, with the majority of the time intensive work being conducted by the PI.

e) Access to target population.

Explain and justify whether you will have access to a population that will allow recruitment of the required number of participants.

We will have access to over 700 qualified patients at VAPAHCS and hope to recruit approximately 168 participants. As the study involves only completion of questionnaires, home-based actigraphy sleep assessments, and a behavioral intervention group, with participants being reimbursed of their time, we should have no difficulty recruiting 168 participants.

f) Access to resources if needed as a consequence of the research.

State whether you have medical or psychological resources available that participants might require as a consequence of the research when applicable. Please describe these resources.

The study consists of questionnaires, home-based actigraphy sleep assessments, and a 6-session behavioral intervention. We have multiple clinical psychologists on the study staff who will be available to assist should any problems occur in conjunction with the study.

g) Lead Investigator or Coordinating Institution in Multi-site Study.

Please explain (i) your role in coordinating the studies, (ii) procedures for routine communication with other sites, (iii) documentation of routine communications with other sites, (iv) planned management of communication of adverse outcomes, unexpected problems involving risk to participants or others, protocol modifications or interim findings.

1. Purpose

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a) In layperson's language state the purpose of the study in 3-5 sentences.

The proposed study will employ a novel, multi-method approach to investigate the efficacy of group-based cognitive behavioral therapy for insomnia (CBT-I), and the incremental benefit provided by an adjunctive sleep mobile app, in improving cannabis outcomes among 168 cannabis dependent Veterans.

b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.

Information from this study can be directly applied to improve SUD treatment among Veterans by targeting sleep disturbances in order to reduce rates of lapse/relapse and improve outcomes. Improved outcomes from SUD treatment can help reduce recidivism, allowing for resources to be allocated to new incidences of SUDs, and reduce wait times to receive services. Finally, these data can be used to influence policy, with the ultimate goal of increasing the efficacy, and value of SUD treatment.

c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)

The purpose of the study is to test the efficacy of a behavioral sleep intervention (with mobile app) among individuals with cannabis use disorder.

2. Study Procedures

a) Please SUMMARIZE the research procedures, screening through closeout, which the human subject will undergo. Refer to sections in the protocol attached in section 16, BUT do not copy the clinical protocol. Be clear on what is to be done for research and what is part of standard of care.

The proposed study will employ a between subjects prospective design to follow 168 Veterans with CUD and co-occurring insomnia over the course of six months while individuals complete a treatment/placebo group within the context of outpatient addiction treatment at the Menlo Park division of the VA Palo Alto Health Care System. Overall, this design will involve assessments during the following times: baseline (prior to the intervention), over the course of the intervention, upon completion of the treatment/placebo group conducted during week 6 (completion of the sleep [or placebo] intervention), and three follow-up assessments conducted 2-weeks, 4-weeks, and 6-months post-treatment. Veterans will be recruited through the outpatient substance abuse treatment program within the Menlo Park Division of the VA Palo Alto Health Care System and through fliers placed throughout the community. Interested participants will complete a brief phone-based screening with a trained research assistant to assess for initial inclusionary/exclusionary criteria. Eligible individuals will then be scheduled for a baseline assessment once enough individuals have been recruited to comprise three groups for the treatment/placebo group portion. Baseline assessments will consist of structured clinical interviews, questionnaires, and a urine toxicology to assess for the presence/absence of marijuana. Eligible participants will then be randomly assigned to one of three conditions: (1) CBT-I with adjunctive sleep mobile app (CBT-I-MA); (2) CBT-I only (CBT-I); or (3) Placebo-control(PC). The treatment/placebo groups will occur weekly for six consecutive weeks. During this time, substance use (including

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cannabis) and sleep will be monitored. Upon completion of the treatment/placebo group (week 6), individuals will complete self-report questionnaires and a home-based actigraphy sleep assessment. Follow-up assessment will then occur Two-weeks, 4-weeks, and 6-months post-treatment (follow-up assessments). Participants will complete home-based sleep assessments (actigraphy) and the same self-report and interview-based questionnaires that were administered during baseline as well as a urine toxicology to assess for the presence/absence of marijuana. Assessments will be completed in person. Baseline and 6-month follow-up interviews and questionnaires will take 3 hours to complete, while 2-week and 4-week post-treatment follow-up appointments will take 1 hour. Home-based sleep assessments will occur overnight for the length of each individual's typical sleep cycle (approximately 8 hours).

b) Explain how the above research procedures are the least risky that can be performed consistent with sound research design.

The primary risk of the current study involves confidentiality of data. Here, we have taken data security precautions that reduce this risk, including keeping all data on a secure server with study data separated from participant contact information. To reduce clinical risk, we have experienced clinical staff on the project, including clinical psychologists who are experts in and experienced with assessment of patients for substance use disorders and sleep disorders within the context of the VA. They will be available to assist if any clinical issues arise during the patient interview.

c) State if deception will be used. If so, provide the rationale and describe debriefing procedures. Since you will not be fully informing the participant in your consent process and form, complete an alteration of consent (in section 13). Submit a debriefing script (in section 16).

Deception is not used in this protocol.

d) State if audio or video recording will occur. Describe what will become of the recording after use, e.g., shown at scientific meetings, erased. Describe the final disposition of the recordings.

Interviews will be audio-taped and the reliability of a random selection of 20% will be determined and checked for accuracy by Dr. Babson. Audiotapes will be maintained in compliance with VA guidelines, and stored in locked cabinets during the study itself.

e) Describe alternative procedures or courses of treatment, if any, that might be advantageous to the participant. Describe potential risks and benefits associated with these. Any standard treatment that is being withheld must be disclosed in the consent process and form. (i.e. standard-of-care drug, different interventional procedure, no procedure or treatment, palliative care, other research studies).

The alternative is not to participate in the study. As there is no formal intervention component to the current study, there is no alternative treatment course for those who do, versus those who do not, participate in the study. All participants will have access to substance use treatment within VA, consistent with treatment guidelines.

f) Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

The outpatient SUD treatment program is currently available at the VA Palo Alto. Thus, patients can utilize it at any time. The VAPAHCS also offers cognitive behavioral therapy for insomnia which can be accessed by veterans.

g) Study Endpoint. What are the guidelines or end points by which you can evaluate the different treatments (i.e. study drug, device, procedure) during the study? If one proves to be clearly more effective than another (or others) during the course of a study, will the study be terminated before the projected total participant population has been enrolled? When will the study end if no important differences are detected?

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N/A.

3. Background

a) Describe past experimental and/or clinical findings leading to the formulation of the study.

The Prevalence of cannabis use disorder (CUD) has been steadily increasing within the Veteran Health Administration (VHA), along with the related significant physical, cognitive, and psychological sequelae. Even in patients with a strong motivation to quit and the presence of empirically-supported interventions (Roffman & Stephens, 2006), Veterans who receive treatment for CUD have high rates of lapse (63% by 6-months post-treatment) and relapse (71% within 6-months post-treatment; Moore et al., 2003). Thus, identifying strategies to improve response to CUD treatment is in the interest of all VHA stakeholders.

Disturbed sleep is common among individuals with CUD and has been shown to result in increased rates of lapse/relapse to cannabis (Babson et al., 2012). In fact, 48%-77% of individuals making a cannabis cessation attempt report lapsing/relapsing specifically to manage poor sleep (Copersino et al., 2000; Levin et al., 2010). Therefore, when individuals with poor sleep attempt to quit using cannabis, not only is their coping mechanism removed, but they are also likely to experience withdrawal-related sleep difficulties, increasing risk for lapse/relapse. Providing a behavioral sleep intervention within the context of CUD treatment, has the potential to improve these cessation outcomes.

Cognitive behavioral therapy for insomnia (CBT-I) is a well-established first-line treatment for insomnia. While CBT-I is being disseminated throughout VHA, it is rarely received by Veterans with substance use disorders (SUDs) and, among those that do receive it, it is almost always delivered following a cessation attempt. While CBT-I has been shown to be an effective treatment for improving sleep among individuals with insomnia and co-occurring conditions, including SUDs, there has yet to be an investigation of the impact of providing CBT-I prior to CUD treatment with the goal of improving cessation outcomes. In addition, the development of an adjunct behavioral intervention delivered via mobile app technology within VA holds great promise to bolster CBT-I outcomes, however, such an approach has yet to be evaluated.

b) Describe any animal experimentation and findings leading to the formulation of the study.

N/A

4. Radioisotopes or Radiation Machines

**a) List all standard of care procedures using ionizing radiation (radiation dose received by a subject that is considered part of their normal medical care). List all research procedures using ionizing radiation (procedures performed due to participation in this study that is not considered part of their normal medical care). List each potential procedure in the sequence that it would normally occur during the entire study. http://www.stanford.edu/dept/EHS/prod/researchlab/radlaser/Human_use_guide.pdf
More Info**

Identify Week/Month of study	Name of Exam	Identify if SOC or Research
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b) For research radioisotope projects, provide the following radiation-related information:

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Identify the radionuclide (s) and chemical form (s).

For the typical subject, provide the total number of times the radioisotope and activity will be administered (mCi) and the route of administration.

If not FDA approved provide dosimetry information and reference the source documents (package insert, MIRD calculation, peer reviewed literature).

- c) For research radiation machine projects, provide the following diagnostic procedures:

For well-established radiographic procedures describe the exam.

For the typical subject, identify the total number of times each will be performed on a single research subject.

For each radiographic procedure, provide the setup and technique sufficient to permit research subject dose modeling. The chief technologist can usually provide this information.

For radiographic procedures not well-established, provide FDA status of the machine, and information sufficient to permit research subject dose modeling.

- d) For research radiation machine projects, provide the following therapeutic procedures:

For a well-established therapeutic procedure, identify the area treated, dose per fraction and number of fractions. State whether the therapeutic procedure is being performed as a normal part of clinical management for the research participants's medical condition or whether it is being performed because the research participant is participating in this project.

For a therapeutic procedure that is not well-established, provide FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions.

5. Devices

- a) Please list in the table below all Investigational Devices (including Commercial Devices used off-label) to be used on participants.
- b) Please list in the table below all IDE Exempt Devices (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) to be used on participants.

5.1 Device Name: CBT-I mobile app

Describe the device to be used.

CBT-I mobile application for smartphone

Manufacturer

IDE Exemption

Y This is a legally marketed device being used in accordance with its labeling.

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6. Drugs, Reagents, or Chemicals

- a) Please list in the table below all investigational drugs, reagents or chemicals to be administered to participants.
- b) Please list in the table below all commercial drugs, reagents or chemicals to be administered to participants.

7. Medical Equipment for Human Subjects and Laboratory Animals

If medical equipment used for human patients/participants is also used on animals, describe such equipment and disinfection procedures.

N/A.

8. Participant Population

- a) State the following: (i) the number of participants expected to be enrolled at Stanford-affiliated site(s); (ii) the total number of participants expected to enroll at all sites; (iii) the type of participants (i.e. students, patients with certain cancer, patients with certain cardiac condition) and the reasons for using such participants.

In this study, we focus on a sample of 168 male and female cannabis dependent adult veterans with sleep disturbances. These subjects will be used because we are testing the impact of a behavioral sleep program (with mobile app) on cannabis use.

- b) State the age range, gender, and ethnic background of the participant population being recruited.

Subjects will range in age from 18-90, with most subjects in the 35-65 age range that is currently overrepresented in VA programs. We expect over 90% of participants will be male. We also expect a diverse representation of ethnic backgrounds, in proportion to the ethnic breakdown at the participating VA health care system. The program director estimates that the outpatient population treated at the clinic is 60% black, 20% white, 10% Hispanic and 10% other races.

- c) State the number and rationale for involvement of potentially vulnerable subjects in the study (including children, pregnant women, economically and educationally disadvantaged, decisionally impaired, homeless people, employees and students). Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects and the additional safeguards that have been included in the protocol to protect their rights and welfare.

Vulnerable subjects will be included in so far as they are representative of the patient population receiving treatment for substance use disorders at the VA Palo Alto outpatient SUD clinic. We know that persons with substance use disorders are more likely to be economically and educationally disadvantaged, decisionally impaired or homeless than other patient populations. Depending on the criteria set for defining someone disadvantaged or impaired, anywhere from a few to the majority of our subjects may be considered vulnerable. Because we are aiming to identify factors that contribute to cannabis relapse among individuals seeking outpatient treatment for SUD, it is important that we include a representative sample of patients in outpatient substance use disorder treatment. As many patients with substance use disorders could be considered vulnerable, we must include vulnerable subjects in this research study. Otherwise we risk

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collecting non-generalizable data that when used in clinical practice could do harm to the vulnerable patient population that was excluded from the study. Risks will be minimized by providing small amounts of monetary compensation at each time point, assuring no coercion in terms of study recruitment/enrollment, and immediately addressing any concerns that a subject has if he/she were to become upset during the course of the study.

- d) If women, minorities, or children are not included, a clear compelling rationale must be provided (e.g., disease does not occur in children, drug or device would interfere with normal growth and development, etc.).**

Children are not included because veterans cannot be under age 18, and we are recruiting from a clinic that treats only veterans.

- e) State the number, if any, of participants who are laboratory personnel, employees, and/or students. They should render the same written informed consent. If payment is allowed, they should also receive it. Please see Stanford University policy.**

It is highly unlikely that laboratory personnel, employees and students will be included in the study. If they are included they will be recruited in the same manner as other subjects and will complete the same written informed consent and receive the same compensation as other subjects.

- f) State the number, if any, of participants who are healthy volunteers. Provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which participants may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to the volunteers and the additional safeguards that have been included in the protocol to protect their rights and welfare.**

No healthy volunteers will be involved. All subjects will have a substance use disorder.

- g) How will you identify participants for recruitment? (E.g., by: chart review; referral from treating physician; response to ad). Attach recruitment materials in Section #16 (Attachments). All Final or revised recruitment materials, flyers, etc. must be submitted to the IRB for review and approval before use. You may not contact potential participants prior to IRB approval. See Advertisements: Appropriate Language for Recruitment Material.**

We will implement a multi-pronged recruitment process.

(1) We will advertise the study to each Veteran presenting to the outpatient SUD treatment center at VAPAHCS. In addition, staff within the outpatient SUD treatment center will provide study and contact information to patients beginning the program. In order to ensure enrollment of individuals with comorbid insomnia, we will also advertise within the outpatient SUD treatment center with flyers that specifically mention insomnia symptoms.

(2) We will recruit through flyers and presentations throughout the VAPAHCS including community based outpatient clinics.

(3) We will recruit (through flyers and presentations) in community locations where veterans congregate (this may include but is not limited to VFW's and local colleges with veterans programs).

(4) Advertisements will be placed in local newspapers. TV and radio advertisements will be placed.

(5) Recruitment through social media will be used including but not limited to recruitment through Facebook ads, Twitter, and Craigslist.

(6) We will recruit through veterans programs within local colleges and universities including San Jose

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State University (point of contact San Jose State University: Annabel Prins and Damien Bramlet).

(7) We will provide staff within veterans programs forms which they will distribute to individuals within their program. The forms will inquire if individuals are interested in hearing more about potential options for participating in research. They will be asked to check yes or no regarding their interest and provide their name and contact information. Study staff will collect the forms from the staff once/week and will contact those individuals indicating they were interested in research participation. This form can be found in section 16.

Patients interested in the study will contact the research laboratory to complete a brief phone screening for initial eligibility criteria and schedule a baseline appointment.

h) Inclusion and Exclusion Criteria.

Identify inclusion criteria.

To be included in the current study individuals must (1) be a Veteran 18 years or older; (2) meet DSM-5 diagnostic criteria for cannabis use disorder; and (3) meet DSM-5 diagnostic criteria for insomnia.

Identify exclusion criteria.

Individuals will be excluded based on evidence of the following: (1) inability to provide fully-informed written consent to participate; (2) history of, or current, psychotic symptoms or bipolar disorder; (3) current pregnancy; (4) sleep apnea as indicated by a score ≥ 5 on the STOP-Bang assessment; and (5) active suicidal/homicidal intent.

i) Describe your screening procedures, including how qualifying laboratory values will be obtained. If you are collecting personal health information prior to enrollment (e.g., telephone screening), please request a waiver of authorization for recruitment (in section 15).

Participants calling the laboratory with interest in the study will be briefly screened over the telephone to determine if they are likely to be study eligible. Likely eligible participants will be enrolled in the study and assessed for presence of cannabis use disorder, using the structured clinical interview for DSM-5, and insomnia (using the insomnia severity index). Participants who are positive for cannabis use disorder and insomnia, will be included in the study. Participants who are negative for cannabis use disorder or insomnia, will end study participation at this point.

j) Describe how you will be cognizant of other protocols in which participants might be enrolled. Please explain if participants will be enrolled in more than one study.

Participants will be asked if they are participating in any other research studies at the start of the consent process. If they are, then the principal investigator of the other study will be contacted to determine if the studies potentially interact with or confound one another or if the studies could overburden or put a participant at extra risk. If there is any possibility of complications, the participant will not be allowed to participate in this study until his participation in the other study is completed.

k) Payment. Explain the amount and schedule of payment, if any, that will be paid for participation in the study. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of participants and that they do not constitute undue pressure on participants to volunteer for the research study. Include provisions for prorating payment. See payment considerations

To reduce attrition rates, a weighted compensation schedule will be employed as follows: Baseline assessment (\$50 VA canteen voucher), post-treatment/placebo group (6-weeks) (\$50 VA canteen voucher), 2-weeks post-treatment (\$25 VA canteen voucher), 4-weeks post-treatment (\$25 VA canteen voucher), and 6-months post-treatment (\$25 VA canteen voucher), with a \$60 (VA canteen voucher) bonus for individuals

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that completed all time points. Overall, the rate of compensation was determined based on \$19/hour of daytime assessment. Compensation will be provided in the form of VA canteen vouchers.

l) Costs. Please explain any costs that will be charged to the participant.

There are no costs for participating in this study.

m) Estimate the probable duration of the entire study. Also estimate the total time per participant for: (i) screening of participant; (ii) active participation in study; (iii) analysis of participant data.

The entire study will take 5 years to complete. Total time per participant is expected to be as follows: Baseline and 6-month follow-up interviews and questionnaires will take three hours to complete, while 2-week and 4-week post-treatment follow-up appointments will take 1 hour. The behavioral group intervention is comprised of 1 hour groups on 6 occasions (i.e., 6 hours). Home-based sleep assessments (actigraphy) will occur overnight for the length of each individual's typical sleep cycle (approximately 8 hours).

9. Risks

- a) For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data on risk, a statement to this effect should be included. (In describing these risks in the consent form to the participant it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.)

Investigational devices.

N/A.

Investigational drugs. Information about risks can often be found in the Investigator's brochure.

N/A.

Commercially available drugs, reagents or chemicals. Information about risks can often be found in the package insert.

N/A.

Procedures to be performed. Include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).

N/A.

Radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and associated risks.

N/A.

Physical well-being.

There is virtually no risk to physical well-being from participation in this study.

Psychological well-being.

There is a small risk that participants may find the assessments distressing. However, because the assessments will be conducted by a clinical psychologist, it is likely that any distress can be minimized and alleviated promptly. Changes in subjects' anxiety will be monitored throughout the study and each participant will receive information, including telephone numbers, regarding VA mental health treatment services at the start of the study.

Economic well-being.

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The main risk to participants is data confidentiality, as the study will collect information about substance use, which may involve illegal behaviors, and psychological health. Breach of confidentiality could lead to negative economic consequences, such as loss of a job or imprisonment.

Social well-being.

The main risk to participants is data confidentiality, as the study will collect information about substance use, which may involve illegal behaviors, and psychological health. Breach of confidentiality could lead to negative social consequences, such as disapproval or social stigma associated with knowledge of participant mental health disorders or behaviors.

Overall evaluation of Risk.

Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

- b) If you are conducting international research, describe the qualifications/preparations that enable you to both estimate and minimize risks to participants. Also complete the 'Hyperlink to http://humansubjects.stanford.edu/research/documents/intl_rsch_APP-11.doc' International Research Form and attach it in the Attachments section. If not applicable, enter N/A.**

N/A.

- c) Describe the planned procedures for protecting against and minimizing all potential risks. Include the means for monitoring to detect hazards to the participant (and/or to a potential fetus if applicable). Include steps to minimize risks to the confidentiality of identifiable information.**

The main risk to participants is data confidentiality, as the study will collect information about substance use, which may involve illegal behaviors, and psychological health. To protect participants we will code all participant data and will store the data separately from participant identifying and contact information. These datasets will be linked only by a study ID. The crosswalk between the study ID and participant identifiers will be stored separate from participant data in a password protected file within a password protected folder on our secure server system. The mobile app does not store participant responses and therefore information will not be obtained from the app. To protect participants from feeling uncomfortable during the interview, participants will be told that they are free to not answer a question if they desire. Additionally, interviews will be completed by a clinical psychologist.

- d) Explain the point at which the experiment will terminate. If appropriate, include the standards for the termination of the participation of the individual participant Also discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the participants.**

This study does not include a medical intervention. However, if a participant becomes upset, agitated or psychotic during the interview or questionnaire session, the session will be terminated and the clinical psychologist will assess the participant.

- e) Data Safety and Monitoring Plan (DSMP). See guidance on Data Safety and Monitoring.**

A Data and Safety Monitoring Plan (DSMP) is required for studies that present Medium or High risk to participants. (See Overall Evaluation of Risk above). If Low Risk, a DSMP may not be necessary. Multi-site Phase III clinical trials funded by NIH require the DSM Plan to have a Data Safety Monitoring Board or Committee (DSMC or DSMB). The FDA recommends that all multi-site clinical trials that involve interventions that have potential for greater than minimal risk to study participants also have a DSMB or DSMC.

The role of the DSMC or DSMB is to ensure the safety of participants by analyzing pooled data from all sites, and to oversee the validity and integrity of the data. Depending on the degree of risk and the

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complexity of the protocol, monitoring may be performed by an independent committee, a board (DSMC/DSMB), a sponsor's Data Safety Committee (DSC), a Medical Monitor, a sponsor's safety officer, or by the Protocol Director (PD).

Describe the following:

What type of data and/or events will be reviewed under the monitoring plan, e.g. adverse events, protocol deviations, aggregate data?

The following will be monitored by the DMC: 1. Progress towards study endpoint 2. AEs, SAEs, SUSARs

Identify who will be responsible for Data and Safety Monitoring for this study, e.g. Stanford Cancer Institute DSMC, an independent monitoring committee, the sponsor, Stanford investigators independent of the study, the PD, or other person(s).

Clinical Science Research and Development, Central Data Monitoring Committee, Hines CSPCC, VA Hines Hospital, Hines, IL 60141

Provide the scope and composition of the monitoring board, committee, or safety monitor, e.g., information about each member's relevant experience or area of expertise. If the Monitor is the Stanford Cancer Center DSMC or the PD, enter N/A.

The DMC is comprised of MD's, PhD's, and RNs ranging in expertise including statistics, clinical psychology, and rehabilitation.

Confirm that you will report Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), or Unanticipated Problems (UPs) to the person or committee monitoring the study in accordance with Sponsor requirements and FDA regulations.

In compliance with IRB and DMC protocol, the chairs of the IRB and DMC will be informed of the occurrence of an SAE, UP, or unanticipated AE within 48 hours. Consistent with protocol, anticipated AE's will not be reported immediately, but will be included in all yearly data safety reports submitted to the DMC.

If applicable, how frequently will the Monitoring Committee meet? Will the Monitoring Committee provide written recommendations about continuing the study to the Sponsor and IRB?

The DMC will meet one time yearly and will provide written recommendations.

Specify triggers or stopping rules that will dictate when the study will end, or when some action is required. If you specified this in Section 2g [Study Endpoints], earlier in this application enter 'See 2g'.

The study will come to an end at the end of scheduled data collection unless earlier termination is indicated by the DMC.

Indicate to whom the data and safety monitoring person, board, or committee will disseminate the outcome of the review(s), e.g., to the IRB, the study sponsor, the investigator, or other officials, as appropriate.

The investigator.

Select One:

The Protocol Director will be the only monitoring entity for this study.

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Y This protocol will utilize a board, committee, or safety monitor as identified in question #2 above.

10. Benefits

- a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc.

The participants will not immediately benefit. However, the information gathered in this study will be used to develop improved substance abuse treatments for future individuals at risk for relapse to cannabis.

11. Privacy and Confidentiality

Privacy Protections

- a) Describe how the conditions under which interactions will occur are adequate to protect the privacy interests of participants (e.g., privacy of physical setting for interviews or data collection, protections for follow-up interactions such as telephone, email and mail communications).

We will protect participant privacy by conducting all interviews in private offices or on private phone lines at the Menlo Park division of VA Palo Alto. All interviews will be conducted by research team members trained in privacy and confidentiality procedures. Participants will be instructed to complete the mobile app exercises in the privacy of their home.

Confidentiality Protections

- b) Specify PHI (Protected Health Information). PHI is health information linked to HIPAA identifiers (see above). List BOTH health information AND HIPAA identifiers. If you are using STRIDE, use the Clinical Data Work Sheet to ensure that your request will match your IRB-approved protocol. Be consistent with information entered in section 15a.

We will collect and record identifiable information when the participant is screened and recruited. We will need name and phone number to allow us to schedule participant interviews. In addition, the following PHI will be obtained:

- Medical history information
- Sleep assessment results (actigraphy)
- Survey/Questionnaire responses
- Psychological test results
- Drug abuse information
- Alcoholism or alcohol use information
- Audiotapes

- c) You are required to comply with University Policy that states that ALL electronic devices: computers (laptops and desktops; OFFICE or HOME); smart phones; tablets; external hard disks, USB drives, etc. that may hold identifiable participant data will be password protected, backed up, and encrypted. See <http://med.stanford.edu/datasecurity/> for more information on the Data Security Policy and links to encrypt your devices.

Provide any additional information on ALL data security measures you are taking. You must use secure databases such as RedCap <https://clinicalinformatics.stanford.edu/services/redcap.html>. If you are unsure of the security of the system, check with your Department IT representative. Please see

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<http://med.stanford.edu/irt/security/> for more information on IRT Information Security Services and http://www.stanford.edu/group/security/securecomputing/mobile_devices.html for more information for securing mobile computing devices. Additionally, any PHI data on paper must be secured in an locked environment.

By checking this box, You affirm the aforementioned. Y

Study data will be stored at the VA National Center for PTSD. Interview data will be collected either on paper forms or directly into electronic databases. Paper forms will be stored in locked file cabinets in locked offices at the VA National Center for PTSD. Electronic databases will be kept on the VA National Center for PTSD's fire-walled, automatically backed-up, password-protected, secure server. Data will be labeled with a unique study ID. Code linking the study ID to participants will be kept separate from study data in a locked file cabinet in a locked office. No information is stored on the mobile app.

- d) Describe how data or specimens will be labeled (e.g. name, medical record number, study number, linked coding system) or de-identified. If you are de-identifying data or specimens, who will be responsible for the de-identification? If x-rays or other digital images are used, explain how and by whom the images will be de-identified.**

The PI will code participant information by a research ID and names will not be used to identify the participants in team discussions. Codes linking the study ID with identifiable participant information will be kept in a locked file cabinet separate from data files. We will maintain a cross-walk between participant identifiers and participant codes in a separate password protected folder on a secure server at the NCPTSD. The PI will maintain the key to this code and he will have access to this cross-walk.

- e) Indicate who will have access to the data or specimens (e.g., research team, sponsors, consultants) and describe levels of access control (e.g., restricted access for certain persons or groups, access to linked data or specimens).**

Only the members of the study team will have access to the study databases. The databases will be coded, but we will maintain a cross-walk between participant identifiers and participant codes in a separate password protected folder on a secure server at NCPTSD. The PI will maintain the key to this code and have access to this cross-walk.

- f) If data or specimens will be coded, describe the method in which they will be coded so that study participants' identities cannot be readily ascertained from the code.**

Participant information will be coded by a research ID and names will not be used to identify the participants in team discussions. Codes linking the study ID with identifiable participant information will be kept in a locked file cabinet separate from data files. All study data will be kept on a secure, fire-walled server at the National Center for PTSD in password protected files.

- g) If data or specimens will be coded, indicate who will maintain the key to the code and describe how it will be protected against unauthorized access.**

As mentioned above, the databases will be coded, but we will maintain a cross-walk between participant identifiers and participant codes in a separate password protected folder on a secure server at the National Center for PTSD. The PI will maintain the key to this code and he will have access to this cross-walk.

- h) If you will be sharing data with others, describe how data will be transferred (e.g., courier, mail) or transmitted (e.g., file transfer software, file sharing, email). If transmitted via electronic networks, describe how you will secure the data while in transit. See**

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<http://www.stanford.edu/group/security/securecomputing/>
<http://www.stanford.edu/group/security/securecomputing/>. Additionally, if you will be using or sharing PHI see http://hipaa.stanford.edu/policy_security.html http://hipaa.stanford.edu/policy_security.html.

We will not disclose PHI or other identifiable information to anyone outside of the study team.

- i) **How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected (e.g. conscious of oral and written communications, conducting insurance billing, and maintaining paper and electronic data)?**

The staff will be trained in confidentiality procedures using multiple methods:

- 1) formal coursework provided by the VA
- 2) through practice sessions at the start of the study, led by the PI
- 3) through day to day reinforcement during study team interactions and observation of investigators by the PI.

12. Potential Conflict of Interest

The investigators listed below are required to disclose any financial interests that reasonably appear to be related to this protocol. An email has been sent to them by OPACS (Outside Professional Activities Certification System), and each must respond Yes or No to the financial interest question in the email. If No, they're done. If Yes, they go directly to the OPACS dashboard and file their disclosure. Investigators who do not receive an email from OPACS must go directly to the OPACS dashboard and fill out information there.

You will be unable to submit this protocol until the Financial Interest disclosure is completed by all investigators.

This protocol will not be approved until all investigators who have responded YES to Financial Interests have submitted their OPACS disclosure and OPACS review has been completed by the COI Manager.

Contact <https://helpsu.stanford.edu/helpsu/3.0/helpsu-form?pcat=OPACS> OPACS HelpSU for any issues with OPACS.

Note: If any changes to disclosures are made while this page is open, simply reload the page to see current information.

Investigators	Role	Email	Has Financial Interest?	Date Financial Interest Answered	Date OPACS Disclosure Submitted	Date OPACS Review Completed
Kimberly Babson	PD	kimberly.babson@va.gov	N	01/28/2015	N/A	N/A

13. Consent Background

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13.1 Consent consent form

Check if VA related Y

a) Describe the informed consent process. Include the following.

- i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)**
- ii) When and where will consent be obtained?**
- iii) How much time will be devoted to consent discussion?**
- iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?**
- v) What steps are you taking to minimize the possibility of coercion and undue influence?**
- vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.**

Consent will be obtained by the PI or her research staff. The study will be described to participants expressing interest and the participant will be scheduled to come to the Menlo Park division of the VA Palo Alto. During this visit, the study will be explained in depth and the study team member will go over all elements of the consent with the patient. The patient will be given a copy of the consent and given time to read it and ask questions. The study team member will ask the potential participants questions to insure that they understand the procedures and risks. We expect the consent process will generally take about 15 minutes, however, potential participants will be given as much time as they need to decide whether or not to participate. To minimize the possibility of coercion and undue influence, patients will be given as much time as they like to think about participating, will be allowed to take the consent forms home to think about their participation, and a study team member will discuss participation with them to make sure that they understand that participation will not alter their clinical care. No children will be participating in this study of veterans.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See /hrpp/Chapter12.html#ch12_2 HRPP Chapter12.2 for guidance.

The participant will be asked questions about the procedures and risks, and only when they can accurately describe them will they be able to consent. We are only recruiting veterans, and all veterans must understand English or they could not work in the military. Participants with a hearing impairment will be given the documents to read, and discussion of the consent will be conducted on a computer in the interview room where the study team member can type questions into a MS Word document and allow the potential participant to answer or type in questions of their own.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent, (iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

If potential participants cannot explain the study procedures and risks back to the study team member, they will be considered not competent to participate and not allowed to participate in the study.

Additional VA questions:

i) List the people to whom you have formally delegated responsibility to obtain informed consent, and state whether they have the appropriate training to perform this activity.

Kimberly Babson or her research staff will have responsibility to obtain informed consent and have been trained in human subjects protection and the informed consent procedures.

ii) Will legally effective informed consent be obtained from the participant or the participant's legally authorized representative (LAR) or both? If LAR, is it clear who can serve as LAR?

Consent will be obtained from the participant alone.

iii) Will the circumstances of the consent process minimize the possibility of coercion or undue influence and provide the prospective participant or their representative sufficient opportunity to consider whether to participate?

The circumstances of the consent process should be minimally coercive and the participant will be given

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time during the explanation to ask questions, will be provided the consent forms to look at for as long as they want, and will be given a phone number where they can reach study team members who can answer additional questions they may have. They can consider participating for as long as they like and are under no pressure to make an immediate decision.

iv) **Will the circumstances of the consent process minimize the possibility of coercion or undue influence?**

Yes, a witness to the participant's signature will sign and date the consent document and a copy of the signed and dated consent document will be given to the person signing the consent document.

v) **Will the information being communicated to the participant or the representative during the consent process exclude any exculpatory language through which the participant or the representative is made to waive or appear to waive the participant's legal rights, or release or appear to release the investigator, the sponsor, the institution, or its agent from liability for negligence (e.g. I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research)?**

No.

vi) **Please confirm the following:**

- a. A witness to the participant's signature or the participant's legally authorized representative's signature will sign and date the consent document.
- b. If the sponsor or the IRB requires a witness to the consenting process in addition to the witness to the participant's signature and if the same person is needed to serve both capacities, a note to that effect is placed under the witness's signature line.
- c. A copy of the signed and dated consent document will be given to the person signing the consent document.
- d. The consent form is on the VA Form 10-1086.

13.2 Waiver of Documentation Telephone Screen

Check if VA related Y

a) **Describe the informed consent process. Include the following.**

- i) **Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)**
- ii) **When and where will consent be obtained?**
- iii) **How much time will be devoted to consent discussion?**
- iv) **Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?**
- v) **What steps are you taking to minimize the possibility of coercion and undue influence?**
- vi) **If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.**

During the telephone screening individuals will go through a list of questions. Individuals will be instructed that they may choose not to answer these questions. They may also choose to stop participating in interview at any time. Individuals will be instructed that the information they provide during the interview will be kept as confidential as possible as required by law. Individuals will be instructed that they may refuse to answer the questions or stop answering them at any time, there will be no penalty, and they will not lose any benefits to which you otherwise would be entitled. The risk to taking part in this interview is very small. The screening interview is not designed to ask you for sensitive personal information, but it is possible that some people may feel uncomfortable answering these questions with a person they do not know. Individuals will be instructed that if they qualify to take part in the study and are interested in taking part, then I will record your name and information; this will be kept confidential, but there is a small risk that people outside of the research team or VA Hospital could learn this information. If individuals are eligible and interested in participating, they will be informed that consent will be obtained during the initial in-person appointment. To minimize the possibility of coercion and undue influence, patients will be given as much time as they like to think about participating, and a study team member will discuss participation with them to make sure that they understand that participation will not alter their clinical care. No children will be participating in this study of veterans.

b) **What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See /hrpp/Chapter12.html#ch12_2 HRPP Chapter12.2 for guidance.**

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Consent will not be obtained during the initial telephone screening. However, individuals will be told that the information they provide during the interview will be kept as confidential as possible as required by law. Individuals will be instructed that they may refuse to answer the questions or stop answering them at any time, there will be no penalty, and they will not lose any benefits to which you otherwise would be entitled. Consent will then be obtained during the initial in-person assessment session. We are only recruiting veterans, and all veterans must understand English or they could not work in the military. Participants with a hearing impairment will have to opt to complete the telephone screening in person during which time they will be given the documents to read, and discussion of the consent will be conducted on a computer in the interview room where the study team member can type questions into a MS Word document and allow the potential participant to answer or type in questions of their own.

- c) **What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent, (iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.**

If potential participants cannot explain the study procedures and risks back to the study team member, they will be considered not competent to participate and not allowed to participate in the study.

Additional VA questions:

- i) **List the people to whom you have formally delegated responsibility to obtain informed consent, and state whether they have the appropriate training to perform this activity.**

Kimberly Babson or her research staff will complete the telephone screening during which time formal consent will not be obtained. Consent will be obtained during the first in-lab appointment. During this time, Dr. Babson or her research staff will have the responsibility to obtain informed consent and have been trained in human subjects protection and the informed consent procedures.

- ii) **Will legally effective informed consent be obtained from the participant or the participant's legally authorized representative (LAR) or both? If LAR, is it clear who can serve as LAR?**

Consent will be obtained from the participant alone during the first in-lab session. Consent will not be obtained for the telephone screening.

- iii) **Will the circumstances of the consent process minimize the possibility of coercion or undue influence and provide the prospective participant or their representative sufficient opportunity to consider whether to participate?**

Consent will not be obtained during the telephone screening. However, individuals will be instructed that they may choose not to answer these questions. They may also choose to stop participating in interview at any time. Individuals will be instructed that the information they provide during the interview will be kept as confidential as possible as required by law.

- iv) **Will the circumstances of the consent process minimize the possibility of coercion or undue influence?**

Consent will not be obtained during the telephone screening.

- v) **Will the information being communicated to the participant or the representative during the consent process exclude any exculpatory language through which the participant or the representative is made to waive or appear to waive the participant's legal rights, or release or appear to release the investigator, the sponsor, the institution, or its agent from liability for negligence (e.g. I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research)?**

No.

- vi) **Please confirm the following:**

- A witness to the participant's signature or the participant's legally authorized representative's signature will sign and date the consent document.**
- If the sponsor or the IRB requires a witness to the consenting process in addition to the witness to the participant's signature and if the same person is needed to serve both capacities, a note to that effect is placed under the witness's signature line.**
- A copy of the signed and dated consent document will be given to the person signing the consent document.**

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d. The consent form is on the VA Form 10-1086.

Select one of the following regulatory criteria for a waiver of documentation (signature) and provide a protocol-specific justification:

- 1) 45 CFR 46.117(c)(1). For research that is not subject to FDA regulation, the only record linking the participants and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality; each participant will be asked whether he/she wants documentation linking the participant with the research, and the participant's wishes govern.
- 2) Y 45 CFR 46.117(c)(2). For research that is not subject to FDA regulation, presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.
- 3) 21 CFR 56.109(c)(1). For research that is subject to FDA regulation, presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

Rationale for above selection:

Information from the phone interview will only be retained if the potential subject is eligible and interested in participating. They will then complete a written consent form upon their first appointment with the research team.

14. Assent Background (less than 18 years of age)

15. HIPAA Background

15.1 Waiver of Authorization for waiver of authorization to recruit

Recruitment

- a) Describe the protected health information (PHI) needed to conduct screening or recruitment. PHI is health information linked to HIPAA identifiers (see section 11). List BOTH health information AND HIPAA identifiers. If you are using STRIDE, use the Clinical Data Work Sheet to ensure that your request will match your IRB-approved protocol. Be consistent with information entered in section 11b.

Participant names, phone numbers and addresses will be needed for screening. Participants will also be briefly screened over the phone during the recruitment process. This screening will involve questions about sleep and psychological symptoms.

- b) Please Answer:
 - Y Do you certify that the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals?
 - Y Do you certify that the research could not practically be conducted with out the waiver?
 - Y Do you certify that you have adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted?

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Y Do you certify that the research could not practically be conducted with out access to and use of the protected health information?

c) Please describe an adequate plan to protect any identifiers from improper use and disclosure.

All identifiers will be stored in a locked file cabinet at the National Center for PTSD. The PI will code participant information by a research ID and names will not be used to identify the participants in team discussions. Codes linking the study ID with identifiable participant information will be kept in a locked file cabinet separate from data files. We will maintain a cross-walk between participant identifiers and participant codes in a separate password protected folder on a secure server at the National Center for PTSD. The PI will maintain the key to this code and he will have access to this cross-walk.

d) Please describe an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Research records will be maintained and then disposed of consistent with VA record retention policies.

16. Attachments

Attachment Name	Attached Date	Attached By	Submitted Date
Funded Grant Proposal	02/04/2014	kbabson	
VA required questions	02/04/2014	kbabson	
Appointment Reminder	02/04/2014	kbabson	
Demographics	02/11/2014	kbabson	
SCID	02/11/2014	kbabson	
Fear of Sleep	02/11/2014	kbabson	
Epworth Sleepiness Scale	02/11/2014	kbabson	
PSQI	02/11/2014	kbabson	
PSQI addendum	02/11/2014	kbabson	
DBAS	02/11/2014	kbabson	
ISI	02/11/2014	kbabson	
sleep diary	02/11/2014	kbabson	
Berlin	02/11/2014	kbabson	
Fagerstrom	02/11/2014	kbabson	
MEQ	02/11/2014	kbabson	
MCQ	02/11/2014	kbabson	
MSE	02/11/2014	kbabson	

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CUDIT	02/11/2014	kbabson	
AUDIT	02/11/2014	kbabson	
CMMQ	02/11/2014	kbabson	
MSHQ	02/11/2014	kbabson	
TLFB alc	02/11/2014	kbabson	
TLFB mj	02/11/2014	kbabson	
TLFB cigs	02/11/2014	kbabson	
PMI	02/11/2014	kbabson	
MWC	02/11/2014	kbabson	
UPPS	02/11/2014	kbabson	
EMQ	02/11/2014	kbabson	
DQ	02/11/2014	kbabson	
EA	02/11/2014	kbabson	
DERS	02/11/2014	kbabson	
PCL/LES	02/11/2014	kbabson	
DT	02/11/2014	kbabson	
ASI	02/11/2014	kbabson	
IDAS	02/11/2014	kbabson	
PANAS	02/11/2014	kbabson	
IPF	02/11/2014	kbabson	
TEF	02/11/2014	kbabson	
BABAS	02/11/2014	kbabson	
IPAQ	02/11/2014	kbabson	
KIMS	02/11/2014	kbabson	
SDS	02/11/2014	kbabson	
DPSS-R	02/11/2014	kbabson	
CEQ	02/11/2014	kbabson	
TEQ	06/17/2014	kbabson	
MAUM	08/14/2014	kbabson	

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PBN DMC Babson acceptance memo 6-19-14	08/14/2014	kbabson	
CoC_Final	08/14/2014	kbabson	
Marijuana Ladder	12/19/2014	kbabson	
recruitment sheet	03/05/2015	kbabson	
social media script	03/24/2015	kbabson	
Flyers	03/24/2015	kbabson	
Apnea Assessment	03/24/2015	kbabson	

Obligations

The Protocol Director agrees to:

- Adhere to principles of http://humansubjects.stanford.edu/research/documents/eval_study_designGUI03017.pdf sound scientific research designed to yield valid results
- Conduct the study according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and be trained in Human Research protection, ethical principles, regulations, policies and procedures
- Ensure all research personnel are adequately trained and supervised
- Ensure that the rights and welfare of participants are protected including privacy and confidentiality of data
- Ensure that, when de-identified materials are obtained for research purposes, no attempt will be made to re-identify them.
- Disclose to the appropriate entities any potential conflict of interest
- Report promptly any new information, modification, or http://humansubjects.stanford.edu/research/documents/Events-Info-Report-to-IRB_GUI03P13.pdf unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

VA Protocol Directors also certify that:

- All unanticipated internal or local SAEs, whether related or unrelated to the research, will be/have been reported to the IRB
- All subjects entered onto the master list of subjects for the study will sign/have signed an informed consent form prior to undergoing any study interactions or interventions, unless granted a waiver by the IRB.

Any change in the research protocol must be submitted to the IRB for review prior to the implementation of such change. Any complications in participants or evidence of increase in the original estimate of risk should be reported at once to the IRB before continuing with the project. Inasmuch as the Institutional Review Board (IRB) includes faculty, staff, legal counsel, public members, and students, protocols should be written in language that can be understood by all Panel members. The investigators must inform the participants of

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any significant new knowledge obtained during the course of the research.

IRB approval of any project is for a maximum period of one year. For continuing projects and activities, it is the responsibility of the investigator(s) to resubmit the project to the IRB for review and re-approval prior to the end of the approval period. A Notice to Renew Protocol is sent to the Protocol Director 7 weeks prior to the expiration date of the protocol.

Department Chair must approve faculty and staff research that is not part of a sponsored project. VA applicants must have Division Chief or Ward Supervisor approval. E-mail the Department Chair approval to IRBCoordinator@lists.stanford.edu.

All data including signed consent form documents must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, or other entities. (Policy on Retention of and Access to Research Data, Research Policy Handbook,
<http://doresearch.stanford.edu/policies/research-policy-handbook/conduct-research/retention-and-access-research-data>)

PLEASE NOTE: List all items (verbatim) that you want to be reflected in your approval letter (e.g., Amendment, Investigator's Brochure, consent form(s), advertisement, etc.) in the box below. Include number and date when appropriate.

Y By checking this box, I verify that I, as the Protocol Director (PD) responsible for this research protocol, have read and agree to abide by the above obligations, or that I have been delegated authority by the PD to certify that the PD has read and agrees to abide by the above obligations.

Comments

Comment Title	Comments / Responses	Response Necessary
NEW: 03/12/2014		
Cycle: 1		
1	<p>The General Checklist under VA states this is not funded by the VA. However the funding section states this is funded by the VA. Please clarify and revise for consistency.</p> <p>Also, is this a training grant? It seems more appropriate to check the federal funding box in the General Checklist under Funding.</p> <p>This is a VA CSR&D Training grant. I have clarified in the General checklist under VA, that this is a VA funded training grant. This is now consistent with the Funding section.</p>	Y
2	<p>Please explain what are you going to do with the videotapes in the consent form. Will they be destroyed, kept locked, etc.?</p> <p>Videotapes will not be used in the current study. We have clarified this within the HIPAA authorization. However, audiotapes will be used. We have now included the following within the consent form:</p> <p>"All audiotaped interviews will be kept locked within a file cabinet behind a locked door during, and after, study completion. Audiotapes will only be</p>	Y

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Comment Title	Comments / Responses	Response Necessary
	used to ensure researcher compliance with the conduct of the interviews. Research records, including audiotapes, will be maintained and then disposed of consistent with VA record retention policies."	
3	<p>Please add the following text to the consent form: I give consent to be videotaped during this study: Please initial: ___ Yes ___ No</p> <p>Videotapes will not be used in the current study (this is clarified in the HIPAA authorization). However, audiotapes will be used. We have now included the following in the consent form:</p> <p>I give consent to be audiotaped during this study: Please initial ___ Yes ___ No</p>	Y
4	<p>For VA studies, the HIPAA Authorization must be written in at least 14 point font</p> <p>The font for the HIPAA authorization has been revised to 14 point font consistent with VA guidelines.</p>	Y
5	<p>In the HIPAA Authorization please include the protocol title and protocol director in the header.</p> <p>The protocol title and protocol director have been added to the header of the HIPAA authorization form</p>	Y
6	<p>The IRB does not review VA contracts. Please remove Behavioral Contract to Return iPods in section 16.</p> <p>The behavioral contract to return iPods has been removed from section 16.</p>	Y
7	<p>Please see the guidance regarding payment of research participants, and justify the payment you are providing based on the 4 listed categories. See: http://humansubjects.stanford.edu/research/documents/payment_ethical_considerations_GUI03039</p> <p>Consistent with this recommendation we have included the following in the consent form:</p> <p>"Overall, compensation for time and inconvenience for completing study procedures can result in a total compensation of \$235 for completion of all portions. This is consistent with a compensation rate of \$13/hour for daytime procedures."</p> <p>*Of note, the number of hours involved in the study was calculated as follows:</p> <ul style="list-style-type: none"> - Baseline (3 hours) - 6 hourly group sessions (6 hours) - post-treatment assessment (3 hours) - 3 follow-up appointments (2 hours/appointment = 6 hours) <p>Total hours: 18; this does not include the time required for the overnight sleep assessments.</p>	Y
8	<p>Question 11(b) requires that you specify the PHI to be used in this study. This information should be consistent with the HIPAA Authorization</p>	Y

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	<p>disclosure in the paragraph 'What Personal Information Will Be Used or Disclosed?' Please revise the protocol and/or HIPAA Authorization so that these two are consistent. Content in these sections should be limited to the least amount of information needed to accomplish the purpose of the research.</p> <p>We have now specified the PHI to be used within the study in question 11 (b). The HIPAA Authorization has also been updated. Both sections are consistent with the PHI that will be used. We have included the least amount of information needed to accomplish the research.</p>	
9	<p>Why will this study take 5 years. What are the associated factors?</p> <p>This study will be conducted over 5 years as it is expected that it will take this amount of time to enroll the target sample size, complete all follow-up assessments, and complete the data analysis and write-up of the findings.</p> <p>Overall, this is a 5-year study; however, an individual's participation will only occur over 6-months. Therefore an individual will not be actively participating during the entire 5-year period. We have clarified within the consent form that the total study will take place over 5 years, however, an individual's participation will only occur over 6-months.</p>	Y
10	<p>If pregnancy is not grounds for being withdrawn from the study, it is suggested you remove it from the consent form as one of the reasons - it currently says "pregnancy, if applicable"</p> <p>Pregnancy is grounds for being withdrawn from the study as this is a study exclusion criteria. We have maintained this within the consent form, but have removed the statement "if applicable."</p>	Y
11	<p>As the staff do not have any consultative or financial relationships this section can be removed from the consent form (page 6). The requirement is to list such relationships, not the absence of such.</p> <p>The consultative or financial relationships section has been removed from the consent as requested.</p>	Y
12	<p>The consent form includes the statement: May we contact you (by phone or mail) about future research studies that may be of interest to you? ___ Yes ___ No.</p> <p>VA policy requires the maintenance of the list of names be covered by an IRB and R&DC approved "database" protocol.</p> <p>Thus, to the extent you wish to retain the names of participant for potential contact for future studies, confirm you will submit a separate database protocol after this study closes to maintain the list of names. Otherwise remove this statement from the consent form.</p> <p>This statement has been removed from the consent form.</p>	Y
13	<p>According to the consent and application form only audiotaping will be performed. If that is the case, remove reference in the HIPAA text of using videotaping and other images in this study. The information listed in the HIPAA should be limited to only what is needed to conduct the study.</p>	Y

**PROTOCOL
 APPLICATION FORM
 Human Subjects Research
 Stanford University**

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Comment Title	Comments / Responses	Response Necessary
	Only audiotaping will be included in the current study. We have removed reference to using videotaping within the HIPAA Authorization.	
14	As the HIPAA text follows the consent information in the single document attached in section 13, please delete the duplicate (assuming it is a duplicate) document attached in section 15. A duplicate HIPAA document was attached in section 15. This has been removed.	Y
15	Please repond to comments by noon, Tuesday, March 11. Thank you. N/A	N
REVISION: 09/10/2014		
16	You have attached a DMC Report in section 16. However, section 9(e) states the Protocol Director will be the only monitoring entity for this study. Please clarify and update section 9(e). A VA DMC has been assigned to monitor the project. This has been updated in section 9 (e).	Y
17	Please update the flyer to be consistent with the updated payment section. The recruitment flyer has been updated to reflect the updated payment section (i.e., compensation in the form of VA canteen vouchers)	Y
18	Please revise your flyer to include: 'For general information about participants rights, contact 1-866-680-2906.' The recruitment flyer has been updated to include the following statement: "For general information about participants rights, contact 1-866-680-2906."	Y
19	What is a VA canteen voucher? A VA canteen voucher is a VA gift card that can be used within any VA store.	Y
20	Since the CBT-I is a mobile app that provide or facilitates supplemental clinical care by helping participants manage their health in their daily environment, this needs to be listed in section 5(b) under IDE Exempt. Please check "yes" to the "IDE Exempt Device" question in the General Checklist section and add the CBT-I mobile app to section 5(b). For additional information: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ConnectedHealth/MobileMedicalApplications/ucm255978.h Section 5b has been revised consistent with the above recommendations.	Y
RENEWAL: 03/11/2015		
21	Returned for editing per PD request on 2/12/15. Thank you for returning the protocol for editing. The edits made included the addition of a minor amendment to increase recruitment strategies. This change have been described in question 6 of the continuing review form.	Y
Cycle: 2		
22	Please confirm that you will set up your Facebook page so that the security	Y

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Comment Title	Comments / Responses	Response Necessary
	<p>settings do not allow participants or others from the public to post on the wall. They should only be able to send messages via Facebook. This is so that they are not posting private information or PHI on the publicly viewed wall.</p> <p>Advertisements made through Facebook will be done using the VA Facebook page. The VA Facebook page is set up so the security settings do not allow participants or other individuals to post on the wall. Therefore private information or PHI will not be available on a publicly viewed wall.</p>	
23	<p>Please attach any social media ads used in facebook, twitter, etc., newspaper ads, tv and radio advertisements and verify that they conform to recruitment guidance's found at: http://humansubjects.stanford.edu/research/documents/GuidanceAdvertisements.pdf</p> <p>We have now attached the content of our media ads in section 16. We confirm that the content of the ads is consistent with the guidelines found at: http://humansubjects.stanford.edu/research/documents/GuidanceAdvertisements.pdf</p>	Y
Cycle: 3		
24	<p>Please revise your flyer to include: 'For general information about participants rights, contact 1-866-680-2906.'</p> <p>We have added the above statement to our advertisements and flyers. These have been modified and attached in section 16.</p>	Y
Cycle: 4		
25	<p>Returned for editing per PD request on 3/05/15.</p> <p>Thank you for the opportunity to add an additional modification to the protocol. The following modifications have been made.</p> <ol style="list-style-type: none"> 1. A modification to the recruitment strategy to include veteran recruitment through veterans programs within local colleges and universities including San Jose State University. 2. A modification to our recruitment strategy to add a new form which will allow us to gather names and phone numbers of veterans interested in participating in research. This form will be handed out by staff within veterans programs. They would then be collected once/week by study staff and those interested in hearing about research opportunities will be contacted. A draft of the form has been added to section 16. In addition this change has been made to section 8G. 3. A modification to our current phone screener has been made to include question related to the following: veteran status, diagnosis of sleep apnea, screening question for mania and psychosis, and medication changes in the past 2 weeks. The phone screener has been updated and attached in section 13. 	Y