Title : An RCT of a Primary Care-Based PTSD Intervention: Clinician-Supported PTSD Coach
Approval Period: **Draft**

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Continuing Review Form

1. Participant Enrollment

a. Number of participants entered (or number of specimens examined or charts reviewed) since the beginning of study. If this is a combined VA-Stanford study, in addition indicate how many of the participants (or number of VA specimens examined or VA charts reviewed) enrolled with a VA consent. If this is a multi-site study, in addition to the number of participants enrolled locally, include the number of participants enrolled study-wide.

At the VA Palo Alto HCS, we have enrolled 122 participants since the beginning of the study on May 1, 2017. Of these, 70 were eligible for randomization to study treatment conditions.

At the collaborating site, the VA Syracuse, 234 participants have been enrolled since they began recruitment on February 1, 2017. Of these, 164 were eligible for randomization to study treatment conditions.

*The original N for the entire study (i.e., across both sites) proposed for randomization to study conditions was 260. As is reflected in our DSMB report for 2019 (attached in Section 16) we reconsidered statistical power given that we had sufficient data to update assumptions we used to originally calculate power and the resultant sample size required to achieve it in the proposal. The original assumption of the standard deviation for the CAPS-5 (i.e., our primary outcome measure) was much higher (i.e., 16) than what we found in the data we had collected to date (i.e., SD = ~11). Therefore, we used this empirically-derived figure to recalculate power and the minimum required sample size needed to achieve it. Based on this, we needed to randomize at least 95 participants per condition instead of the originally proposed 130 per condition. We ultimately were able to randomize 114 to CS PTSD Coach and 118 to TAU, which will provide sufficient power to test our primary as well as our secondary outcomes.

b. Number of: males, females, others or individuals whose sex/gender are unknown or not reported.

Of the 122 enrolled at Palo Alto:
Number of Females= 7
Number of Males= 115

c. Minority status of participants entered since beginning of study.

29 African American/Black
16 Asian/Pacific American
5 Native American/Indian
10 Hispanic
17 Others
(55 Caucasian/White)
*Categories not mutually exclusive

d. Number of children (less then 18 years) entered since beginning of study.

N/A

e. Number of other potentially vulnerable subjects (if applicable) entered since the beginning of study, including prisoners, pregnant women, economically and educationally disadvantaged, decisionally impaired and homeless people.

None

2. Study Problems/Complications

a. Number of withdrawals of participants from the research (both participant and investigator initiated) since the beginning of the research study. Provide reasons for the withdrawals.

5 withdrawals
Reasons: 1 had a CAPS 5 that was zero (i.e., no PTSD symptoms); 3 started receiving mental health treatment the day before their baseline assessment, with study personnel finding out only after they completed their baseline and were deemed eligible for the study. As receipt of mental health treatment for PTSD is an exclusion criterion, these participants were withdrawn. And, 1 withdrew himself because of other medical issues and was hospitalized.

b. Number of participants lost to follow-up since the beginning of the study.

There are 11 participant lost to follow-up since the beginning of the study.

c. State if all adverse events have occurred at the expected frequency and level of severity as per study documents or provide a narrative summary of the adverse events since the last continuing review indicating whether the adverse events were expected and/or related to the study.

No adverse events were experienced by participants at our site (i.e., the VA Palo Alto). At the collaborating site, the VA Syracuse, 5 adverse events were reported (through February 2018) with all being deemed to be unrelated to study participation (please see section 16 for the most recently submitted DSMB report (for 2020)for details).

d. Have there been any unanticipated problems involving risks to participants or others (UPs) since the beginning of the study? A UP must be unexpected (including in severity or frequency), related, AND harmful. Confirm that all UPs have previously been reported to the IRB (guidance GUI-P13).

No unanticipated problems involving risks to participants or others have occurred in the past year.

e. Provide a narrative summary of all external (e.g. FDA, OHRP, sponsor) audit reports, monitoring visits, inspections, and multi-center trial reports received in the past year. Include corrective actions taken as a result of any audits, inspections, or monitoring visits.

No reports were received in the past year.
A consent audit was completed on October 11, 2019 with 94 informed consent documents and HIPAA authorization forms reviewed by the VA Research Compliance Office. No reportable findings were found in that audit.

f. Complaints about the research in the past year.

No complaints were received about the research in the past year.

g. Have there been any instances of noncompliance or deviations since the beginning of the study that have not already been addressed in 2e? Provide a summary and indicate if it has been previously reported to the IRB. Provide a corrective action plan that includes how you will ensure the noncompliance does not recur.

We had 2 issues of noncompliance, both of which were previously reported to the IRB and are summarized below.

1. Study personnel (statistician), Lingyao(Jaden)Yang mistakenly queried Veteran identifiers to create a temporary dataset for recruiting for this study (as specified in this protocol) on the VA Corporate Data Warehouse (CDW), instead of accessing these data through the study's VINCI account. This violated VA policies for Information Security and Privacy of not using operational access to the CDW for research purposes. However, the query was written with inefficient join conditions and was terminated midway by the CDW staff to protect overall shared resources on the server. The data required for the research was never obtained. Hence, Veteran identifiers were not used or disclosed in any manner. Ms. Yang's access

toboth CDW and VINCI was temporarily inactivated and was reinstated only after she completed a corrective action plan including additional VA training in proper procedures for accessing these sensitive VA data sources. (Reported to IRB on 1/8/18).

2. We accidently used an expired consent form which the participant signed (reported to the IRB on 1/19/18). We quickly recognized the mistake, consulted with the IRB, and had the participant review and sign the updated, current form. To prevent this from happening again, we removed all expired consent forms from out study materials and replaced them with updated forms, placed the updated electronic version in the consent form folder on the VA's network, and entered a calendar reminder in VA's Outlook to remind study personnel in the days before that the current consent form will be expiring (i.e., 1/8/2020) and they should begin to prepare for using the updated form.

3.Study Assessment

a. Provide a narrative summary of any interim findings from your data in the past year.

We are currently preparing the data for analysis; therefore, there are no interim findings to report at this time.

b. Provide a narrative summary of any recent relevant literature.

To our awareness, no recent relevant literature having direct bearing on this project has been published.

c. Attach Data Safety Monitoring Reports in section 16 received in the past year which have not previously been submitted to the IRB.

Attached DSMB report for 2020 in section 16.

d. Provide a narrative summary of benefits experienced by participants in the past year.

Many participants in the study have reported decreases in their PTSD symptoms after completing the PTSD Coach condition and several participants still in need of care have requested referrals for additional mental health services. Most TAU participants have completed initial assessments with a PC-MHI provider for a brief assessment of symptoms and treatment planning or referral to specialty mental health services.

e. Provide an assessment of whether the relationship of risks to potential benefits has changed.

No change.

4. Description of remainder of project:

a. N **Is the study open to enrollment?**

b. Y **Is the study permanently closed to enrollment of new participants?**

c. Y **Have all participants completed all research-related interventions?**

d. N **Are you still engaged in research-related intervention(s)? If yes, please describe.**

e. N **Do you wish to renew this study ONLY for long term follow-up?**

f. Y **Are you ONLY doing data analysis?**

5. Potential Conflict of Interest

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N **Is there a change in the conflicting interest status of this protocol?**

6. Protocol Changes

Please note that if these changes involve changes to Radiation Safety or Biosafety, the IRB will hold its approval until Radiation Safety or Biosafety forwards its approval to the IRB. Use track changes IF revising consent, assent or HIPAA.

- **Summarize all of the proposed changes to the protocol application including consent form changes.**

  None

- **Indicate Level of Risk**

  No Change

- **Describe any other changes.**

  None

Protocol Director

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Eric Roland Kuhn		Ph.D.		Clinical Assistant Professor (Affiliated) [VAPAHCS]
Department VAPAHCS, PTSD	334 PTSD MPD	**Phone** 650-493-5000 x23160		**E-mail** eric.kuhn@va.gov
CITI Training current				Y

Admin Contact

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Eric Roland Kuhn		Ph.D.		Clinical Associate Professor (Affiliated) [VAPAHCS]
Department Psych/Public Mental Health & Population Sciences	334 PTSD MPD	**Phone** 650-493-5000 x23160		**E-mail** eric.kuhn@va.gov
CITI Training current				Y

Investigator

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Department		**Phone**		**E-mail**
CITI Training current				

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Other Contact

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Prof Craig Steven Rosen		Ph.D.		Assoc Prof-Med Ctr Line
Department	5717	**Phone**		**E-mail**
Psych/Public Mental Health & Population Sciences		650-493-5000 x22812		craig.rosen@stanford.edu
CITI Training current				Y

Academic Sponsor

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Department		**Phone**		**E-mail**
CITI Training current				

Other Personnel

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Jason Owen		Ph.D., MPH		Research Clinical Psychologist
Department		**Phone**		**E-mail**
		650-493-5000 x. 23478		jason.owen@va.gov
CITI Training current				Y

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Marylene Cloitre		Ph.D.		Clinical Professor (Affiliated) [VAPAHCS]
Department		**Phone**		**E-mail**
				marylene.cloitre@va.gov
CITI Training current				Y

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Shaili Jain		M.D.		Clinical Assistant Professor (Affiliated) [VAPAHCS]
Department		**Phone**		**E-mail**
Psychiatry VA Research				sjain1@stanford.edu
CITI Training current				Y

Name		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.**
Deloras Natasha Puran		MPH, MSBH		Health Science Specialist
Department		**Phone**		**E-mail**

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Psych/Public Mental Health & Population Sciences				deloras.puran@va.gov
CITI Training current				Y

Name Mark A Greenbaum		**Degree (Program/year if student)** MA		**Position, e.g. Assistant Professor, Resident, etc.** Health Science Specialist
Department Psychiatry and Behavioral Sciences		**Phone** (650) 493-5000 ext. 22115		**E-mail** mark.greenbaum@med.va.gov
CITI Training current				Y

Name Eric Neri		**Degree (Program/year if student)**		**Position, e.g. Assistant Professor, Resident, etc.** Research Data Analyst
Department Psych/Major Laboratories and Clinical & Translational Neurosciences Incubator	5718	**Phone** (650) 723-7793		**E-mail** eneri@stanford.edu
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
• International Participants	N
Please enter the countries separated by comma	

Study Location(s) Checklist	**Yes/No**

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- Stanford University Y
- Clinical & Translational Research Unit (CTRU)
- Stanford Hospital and Clinics
- Lucile Packard Children's Hospital (LPCH)
- VAPAHCS (Specify PI at VA) Y

  Eric Kuhn, Ph.D.
- 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**

- 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. Y

Institution Name	Contact Name	Contact Phone	Contact Email	Permission?	Engaged?
Syracuse VA Medical Center	Kyle Possemato, Ph.D.	315-425-4400 x53551	kyle.possemato@va.gov	Y	Y

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

Clinical Trials **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? Y
- IDE Exempt Device (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) Y

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• Will this study be registered on# clinicaltrials.gov? (See Stanford decision tree)	Y
• Who will register for ClinicalTrials.gov? NCT#	N

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 https://sites.stanford.edu/ico/mtas	N

Biosafety (APB)	**Yes/No**
• Are you submitting a Human Gene Transfer investigation using a biological agent or recombinant DNA vector? If yes, please complete the Gene Transfer Protocol Application Supplemental Questions and upload in Attachments section.	N
• Are you submitting a Human study using biohazardous/infectious agents? If yes, refer to the Administrative Panel on BioSafety website prior to performing studies.	N
• Are you submitting a Human study using samples from subjects that are known or likely to contain biohazardous/infectious agents? If yes, refer to the 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**

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• Use of Patient related equipment? If Yes, equipment must meet the standards established by Biomedical Engineering (BME) (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/reimbursed for participation? See payment considerations.	Y

Funding	**Yes/No**
• Training Grant?	N
• Program Project Grant?	N
• Federally Sponsored Project?	Y
• https://doresearch.stanford.edu/policies/research-policy-handbook/definitions-and-types-agreements/specialized-categories-sponsored-p Industry Sponsored Clinical Trial?	N

Funding

Funding - Grants/Contracts

Funding Administered By : VA
SPO # (if available) :
Grant # (if available) : IIR-14-288
Funded By (include pending) : VA
Principal Investigator : Eric Kuhn, Ph.D. (& Possemato)

Grant/Contract Title if different from Protocol Title :

Y For Federal projects, are contents of this protocol consistent with the Federal proposal?
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.

VA Palo Alto staff will be involved with this project. Staff includes 4 clinical psychologist researchers (Drs. Kuhn, Rosen, Owen, & Cloitre), 1 physician researcher (Dr. Jain), and a full-time study coordinator (TBD) and a full-time RA (Sharfun Ghaus), who will be supervised by the PI (Dr. Kuhn). In addition, we have Lingyao (Jaden) Yang at Stanford as our biostatistician.

VA Syracuse (collaborating site)staff will also be involved in this project and have obtained and will maintain their own IRB approval for their role on the project (see Attachments for the VA Syracuse IRB approval letter).

b) Training.

Describe the training you will provide to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.

All research staff will have completed the full suite of VA and Stanford-required trainings for research personnel involved in human subject research.
Project staff will meet regularly to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.

c) Facilities.

Please describe and justify.

All research duties and functions will take place at the VAPAHCS, in primary care settings and at the National Center for PTSD or through telehealth applications (including telephone and video-conferencing technology) by study staff who have the required VA training and approval to telework from their home. VAPAHCS and the VA NCPTSD have the appropriate resources and facilities to ensure success of this study.

d) Sufficient time.

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

As a research clinical psychologist, I have sufficient time to conduct this research, which will entail 25% of my time for 4.0 years. Sufficient time has also been allocated to the Co-Is and other study staff.

The total duration of the study is anticipated to be 4 years. We expect that it will take approximately 6 months to stand up the infrastructure for the study (e.g., hire staff), 33 months to recruit the participants and deliver the intervention, and 9 months to conduct the analyses, and prepare and successfully submit a manuscript.

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.

130 Veterans with PTSD receiving care in VAPAHCS primary care will be recruited over 30 months equating to roughly 1 study enrollee per week. The PC-MHI program at VAPAHCS sees over 400 patients per year with a PTSD diagnosis.

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.

Study participants will be primary care patients receiving existing PC-MHI services from clinical staff at VAPAHCS so they will have access to all appropriate clinical resources.

We do not expect that participation in this study will result in additional need for medical or psychological resources. The mobile application being tested (PTSD Coach) includes psychoeducational materials and informational resources available to the public on VA websites (e.g., PTSD.va.gov, myhealth.va.gov) and is designed to be used as an educational and self-help tool (i.e., not as a clinical intervention by itself). If participants are acutely distressed as a result of the assessment or other study-related procedures, licensed clinical psychologists (Drs. Kuhn, Rosen, Owen, and Cloitre)will be available to assist them and connect them with their PC-MHI provider and other appropriate VA resources.

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

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

Posttraumatic Stress Disorder (PTSD) is an often severe and frequently disabling condition. It is associated with compromised health, early mortality, and substantial economic costs. PTSD is common in VA primary care patients; however, brief, effective treatments for PTSD are not available in the primary care setting. Instead, patients with PTSD are referred to mental health settings, yet many patients do not accept these referrals or do not adequately engage in such services. Thus, this project seeks to improve health care for Veterans by testing the effectiveness of a primary care-based treatment called clinician-supported PTSD Coach. In this treatment a primary care mental health clinician guides patients in using the PTSD Coach mobile app to learn about PTSD symptoms, treatment options, and strategies to cope with common PTSD-related concerns.

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

We hope to learn if Clinician-Supported PTSD Coach is an effective treatment for PTSD in VA primary care settings. If this treatment is found to be effective at reducing PTSD symptoms and increasing use of mental health care, it will provide a tremendous benefit to Veterans with PTSD seen in VA primary care.

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)

Human subjects must be used for this project as it is testing the effectiveness of a psychological intervention for patients with PTSD being treated in VA primary care settings.

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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.

Participants will be Veterans enrolled in VA Palo Alto primary care reporting ≥33 on the PTSD Checklist-5 (PCL-5). Patients will be excluded if they have symptoms that would not allow them to engage in the study (i.e., 1) gross cognitive impairment, 2) current symptoms of mania or psychosis) or have more pressing concerns needing attention first (i.e., 3) suicide attempt in the last 2 months or current suicidal intent). We will also exclude patients who 4) are already receiving MH counseling, 5) started or changed psychotropic medication for PTSD in the last 2 months prescribed outside of VA PC, and 6) prefer direct referral to MH specialty care. Patients without a smart device will be lent an iPod Touch so they can participate. All participants will be monitored for high risk behavior (e.g., excessive substance use, suicidiality) by their PC-MHI provider and by research staff at each assessment point.

For recruitment, patients screening positive for PTSD as part of standard practice or who have had an encounter in primary care in which PTSD was indicated as a diagnostic code associated with that visit, will be referred by their PCPs, PC-MHI providers, or OEF/OIF/OND case managers. Research staff will facilitate the referral process by creating a list of these patients and asking their providers to refer them to the study. Study staff will send a letter to referred Veterans that is signed by a PACT member introducing the study. Study staff will call referred patients to assess interest in participation. Interested patients will be scheduled for a baseline appointment to determine eligibility.

At the baseline appointment (which will be held in person or by phone), research staff will obtain oral informed consent and HIPAA authorization. Next self-report measures will be administered to assess eligibility. Participants will be randomized to 1) PC-MHI TAU or 2) CS PTSD Coach. Within a week of baseline (and before session 1) participants will complete the CAPS-5 by phone with an independent assessor. A post-treatment assessment (8 weeks) and two follow-up assessments (16 weeks and 24 weeks) will be conducted following baseline. These will be completed via survey link (from a no-reply email from REDCap), or by phone (based on participant preference), with the exception of the CAPS-5, which will be by phone.

There are two study conditions: 1) Clinician-Supported PTSD Coach (CS PTSD Coach) consists of four 20-30 minute sessions focused on assigning specific PTSD Coach activities. Existing PC-MHI providers will deliver CS PTSD Coach following a treatment manual. Participants can use their own smart device or borrow a study-owned iPod Touch. During the baseline session after randomization, research staff will assist in downloading the research version of the PTSD Coach app on the device. This version of PTSD Coach allows for collection of de-identified app usage data, including how much and often the app was used, date and time of use, duration of use, assessment item

responses, and which components of the app were used. Participants are assigned a unique, randomly-generated string of alpha-only characters (over 308 million possible permutations) that unlocks the app and allows for a de-identified link between the participant's mobile device and the HIPAA-compliant research server where the app data is stored. The research version of PTSD Coach does not allow for the collection of any personally-identifying information and does not contain any open text fields that would enable participants to enter personally-identifying information. Within one week, participants will complete session 1, which may be face-to-face or by phone (as will sessions 2-4), depending on patient preference and if conditions related to COVID-19 have been resolved. At the 4th session,
participants scoring ≥33 on the PCL-5 (probable PTSD), will be recommended for specialty MH treatment.
2) Control Condition: PC-MHI Treatment as Usual (PC-MHI TAU): PC-MHI TAU consists of licensed independent providers providing brief assessment and interventions to Veterans and consultation to PACT staff.

The primary outcomes include: PTSD symptom severity (CAPS-5); specialty MH visits; and patient satisfaction with their treatment (CSQ, Patient Feedback Interviews).
Measures of potential mediation, moderation, breadth, and maintenance of treatment effects will include: PTSD Coach usage data; coping self-efficacy (CSE); depressive symptoms (PHQ-9); quality of life (WHOQOL-BREF); and for PTSD severity (PCL-5) across all time points.

Participants will be paid for time spent completing assessments at a rate of approximately $20/ hour (baseline session- $30, CAPS-5- $20, post-treatment assessment- $40, 16-week follow-up- $20, 24-week follow-up- $20, and $20 bonus for completing all study procedures) and can earn up to $150. Reimbursement will be by VA check mailed to their home. Participants will not be reimbursed for intervention sessions. Payments will be pro-rated to reflect percent completion.

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

The research procedures are the least risky that can be performed consistent with sound research design. The risks associated with participating are considered minimal but include the possibility of psychological discomfort associated with answering questions about traumatic events and psychological symptoms from them. To manage the possibility of this discomfort, study personnel who are licensed clinical psychologists (Drs. Kuhn, Rosen, Owen, and Cloitre) will be available. Risks of participating in Clinician-Supported PTSD Coach and PC-MHI TAU treatment conditions are minimized by having existing licensed mental health providers in VA primary care settings administer both conditions.

Although there is a risk that participation in this protocol will produce clinical-level psychological distress, research on the assessment of PTSD in both clinical and nonclinical populations indicates that this is an infrequent occurrence. In fact, patients report a desire to be asked about past experiences and psychological

symptoms (Murdoch & Nichol, 1994). Furthermore, in studies of PTSD in patient populations (e.g., Ouimette et al., 2004, pilot for the proposed study: Possemato, Kuhn, et al., in press - attached) the majority of patients have reported high satisfaction with their participation.

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).

NA, no deception will be used.

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.

Participants will be audio recorded. This will occur during each of the four sessions of Clinician-Supported PTSD Coach to ensure the therapist is adhering to the manualized protocol. Participants will also be audio recorded during the telephone-based clinical interviews (i.e., CAPS 5) at baseline and at 8 weeks (i.e., CAPS 5 and qualitative interview). This recording will be used to ensure diagnostic accuracy and to transcribe qualitative interviews. All recordings will be erased after they have achieved their intended purpose.

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).

As a pragmatic effectiveness trial, no standard treatment will be withheld from any participants and all standard treatment will be available to all study participants.

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

NA, a primary aim of this study is to encourage participants to get the
most appropriate treatment at any time during their participation.

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?

The proposed sample size (N = 130) is based on pilot work (Possemato, Kuhn, et al., in press - attached) and power calculations to statistically evaluate the primary aims of the trial. If a study condition proves to be clearly more effective than the other, the study could be discontinued. The study will end when the full sample of 130 has been enrolled.

3. Background

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

We conducted a pilot study that investigated the feasibility and

preliminary efficacy of Clinician- Supported PTSD Coach (CS-PTSD Coach), using recruitment and procedures similar to those of the current study (Possemato, Kuhn, et al., in press - attached). Twenty PC patients with significant PTSD symptoms (PCL ≥40) were enrolled over 2 months and randomized to CS-PTSD Coach or Self-Managed (SM) PTSD Coach, which consisted of one 10-minute session to provide instructions on how to use PTSD Coach. PC-MHI providers delivered CS and SM PTSD Coach. Participants were 95% male, 65% White with an average age of 42 (SD=12). Nearly half (45%) were employed, 15% were students, and 35% were retired. Previous deployments were 50% OEF, 40% OIF/OND, 15% Gulf War I, 5% Vietnam. Ninety percent owned their own smart device. Retention was 100% in the treatment sessions and 90% (18/20) at the post-treatment assessment. Both treatments resulted in reductions in PTSD symptoms, with 7 Clinician-Supported PTSD Coach and 3 Self-Managed PTSD Coach participants reporting clinically significant improvements. Clinician-Supported PTSD Coach resulted in more specialty PTSD care use post-intervention and possibly greater reductions in PTSD symptoms.

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

NA

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. More Info

Identify Week/Month of study	Name of Exam	Identify if SOC or Research

b) For research radioisotope projects, provide the following radiation-related information:

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:

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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.

5. 1 Device Name : PTSD Coach

Describe the device to be used.

PTSD Coach is a VA mobile app that is freely available (since 2011)to the public in both the Apple App Store and Android Google Play market. It is designed to help those with PTSD symptoms self-manage their distress using information, access to support resources, CBT-based symptom coping tools, and self-assessment and monitoring of symptoms.

Manufacturer : **VA**

Risk : **Non-significant**

Y I confirm the above are true.

Rationale for the device being non-significant risk:

The PTSD Coach is a publically available mobile app that provides sound psycho-educational information about PTSD and its treatment as well as cognitive-behavioral tools to help individuals with PTSD cope with acute distress. These tools include anxiety reduction skills such as deep breathing, positive imagery, and progressive muscle relaxation. It also includes coping self-statements intended to help individuals cope with difficult situations and emotional states. PTSD Coach does not include any trauma-focused interventions (e.g., prolonged exposure).

Sponsor of Project

Indicate who is responsible for submitting safety reports to the FDA:

Y The sponsor is the STANFORD (SU, SHC, LPCH, VA) investigator.

Please read the following:

Sponsor-Investigator Research Requirements

If you would like further information on this process and/or assistance prior to submitting your protocol contact: The Stanford Center for Clinical and Translational Education and Research (Spectrum) at clinicaltrials@med.stanford.edu or for cancer research contact: ccto-regulatory@stanford.edu

Y I have read and understand the above guidance.

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate. If no, please provide an explanation. :

Y Confirm?

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 : PTSD Coach

Describe the device to be used.

VA's PTSD Coach mobile app

Manufacturer VA

IDE Exemption

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

6. Drugs, Reagents, or Chemicals and Devices

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.

NA

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.

(i)130 eligible VA Palo Alto Health Care System primary care patients
(ii) 260 eligible VA primary care patients in total in the study (the VA Syracuse site will recruit 130 or more primary care patients depending on recruitment efforts at Palo Alto).
(iii) All primary care patients will be Veterans who have screened positive for posttraumatic stress disorder (PTSD). The intervention being tested in intended to address PTSD in Veterans who are treated in VA primary care settings.

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

All participants will be 18 years old or older. Both genders will be included as will patients of all ethnic backgrounds. However, all participants will be English-speaking and English-literate to ensure proper and consistent comprehension of both written materials and instructions.

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.

As this is a pragmatic effectiveness trial, we will include as broad a swath of the VA primary care patient population as possible by limiting exclusion criteria so an unknown number of potentially vulnerable participants may participate, including pregnant women, economically and educationally disadvantaged, and homeless Veterans. We will not include children and the decisionally impaired. All participants will be involved in PC-MHI treatment with a licensed clinician.

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.).

Women and minorities will be included. Minors will not be included, as this is a study of adults.

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.

NA

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.

All participants will be VA primary care patient with PTSD symptoms.

g) How will you identify and recruit potential participants about the research study? (E.g., by: Honest Broker or other https://researchcompliance.stanford.edu/participantengagement Research Participation services; chart review; treating physician; ads). 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.

Recruitment of participants will involve 2 methods:
1) Direct in person referral from clinical staff on the patient's health care team (PACT) in the primary care setting.
2) Review of charts for patients screening positive for PTSD as part of standard practice (with approved waiver of authorization for recruitment) or who have had an primary care encounter in which PTSD was listed as being addressed in that visit. We will accomplish this by using VINCI data to generate a monthly list of all veterans enrolled in primary care within the VA Palo Alto healthcare system who screen positive on the PC-PTSD screen, which is delivered as part of standard practice, or who have had a recent encounter with PTSD listed as a reason for the visit. This list will include names, Real SSNs, address, phone number, Palo Alto provider name, PC-PTSD raw score and score date, and gender. A list of each individual primary care provider's patients who are identified will be generated and submitted to the provider requesting that they refer these patients to the study. Study staff will send an invitation letter to those patients deemed appropriate for the study by their primary care provider. This letter will be signed by a PACT member introducing the study. Study staff will call referred patients to assess their interest in participation. Interested patients will be scheduled for a baseline appointment within their PC clinic or by telephone to determine study eligibility.

h) Inclusion and Exclusion Criteria.

Identify inclusion criteria.

Participants will be Veterans enrolled in VA Palo Alto primary care reporting ≥33 on the PTSD Checklist-5 (PCL-5), which indicates significant PTSD symptoms.

Identify exclusion criteria.

Patients will be excluded if they demonstrate symptoms that would not allow them to engage in the CS PTSD Coach (i.e., 1) gross cognitive impairment, 2) current symptoms of mania or psychosis) or who have more pressing concerns needing attention first (i.e., 3) suicide attempt in the last 2 months or current suicidal intent). We will also exclude patients who 4) are already receiving psychotherapy or MH counseling, 5) started or changed psychotropic medication for PTSD in the last 2 months prescribed outside of VA PC, and 6) prefer to be directly referred to MH specialty care.

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).

We will use chart review to identify potential participants. A list of patients who have screened positive for PTSD (using the PC-PTSD screen) in primary care will be generated. A waiver of authorization for recruitment will be obtained for this approach.

During the phone screen (see attachment), potential participants will be informed about whom the study wishes to recruit, including a description of common PTSD symptoms. Potential participants will be asked if they believe they would be appropriate for the study based on whether or not they have those types of symptoms. For those who are not sure, the 4 item PC-PTSD screen will be administered.

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.

We will ask potential participants if they are enrolled in any other research studies that would conflict with their participation in this one. Participants may be enrolled in studies unrelated to this one.

k) Payment/reimbursement. Explain the amount and schedule of payment or reimbursement, 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

Participants will be reimbursed for time spent completing study measures. They will not be reimbursed for attending treatment sessions. They can earn up $150. Payments will be pro-rated: if the participant completes half of an assessment he/she will be paid half of the amount for that session. The proposed payments are reasonable and would not constitute undue pressure to participate. The payment schedule below reflects a rate of approximately $20/hour for participation.

Baseline session- $30
Baseline phone interview- $20
8 week follow-up- $20
8 week phone assessment- $20
16 week follow-up- $20
24 week follow-up- $20
Bonus for completing all assessments (and returning a study-owned iPod Touch, if borrowed)- $20

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

No cost will be charged to participants for their involvement in the 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.

Each participant's total time involvement in the study will be approximately 6 months and involve roughly 6.5 hours of assessments.

The total duration of the study is 4 years. We expect it will take 6 months to hire and train study staff, 33 months to recruit and run participants, and 9 months to complete data entry, analyses, and disseminate results.

9. Risks

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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.)

The risks of the Investigational devices.

NA

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

NA

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

NA

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

NA

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

NA

The risks of the Physical well-being.

There is no foreseeable risk of physical harm from participation.

The risks of the Psychological well-being.

Participation is not expected to put participants at risk of psychological harm.

The risks of the Economic well-being.

There is no cost to participation.

The risks of the Social well-being.

There is no foreseeable risk of social harm.

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. Provide an explanation as to why the research must be completed at this location and complete the [LINKFORINTERNATIONALREASEARCHFORM] International Research Form. If not applicable, enter N/A.

NA

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.

At the baseline assessment, procedures for maintaining confidentiality will be stated to allay concerns about reports of emotional/uncomfortable material. To minimize risks to the confidentiality of identifiable information, we will protect against breaches of confidentiality by coding participant data with an identification number and keeping the master list linking names and numbers in a separate cabinet or password protected e-file behind the VA firewall. Only project staff will have access to the master list. Computer data files will be protected by passwords. No individuals will be identified by name or any other personally identifiable information when presenting data in lectures, seminars, professional presentations, or papers. Participants will use their study ID number when completing self-report measures or will complete

measures using REDCap (*please see below for a complete description of REDCap's security features) surveys. Participants will be provided with the research version of PTSD Coach. This version of PTSD Coach allows for collection of de-identified app usage data, including how much and often the app was used, date and time of use, duration of use, assessment item responses, and which components of the app were used. Participants are assigned a unique, randomly-generated string of alpha-only characters (over 308 million possible permutations) that unlocks the app and allows for a de-identified link between the participant's mobile device and the HIPAA-compliant research server where the app data is stored. The research version of PTSD Coach does not allow for the collection of any personally-identifying information and does not contain any open text fields that would enable participants to enter personally-identifying information. As participants complete the study procedures, their app usage data will be saved to a secure VA server. Only the research staff listed on this protocol will have access to the linking codes that will link the app usage data with the self-report and clinical interview data.

It will be emphasized throughout the protocol that participation is voluntary and may be stopped at any time. Participants will be told that stopping their participation will not adversely affect the care they receive at the VA. They will also be notified that they can choose to be referred to behavioral health services as an alternative to their participation in the research. In addition, resources (e.g., referrals, educational materials on PTSD) will be provided upon request.

During the completion of an assessment, a participant may disclose that they intend to harm themselves or someone else. In our experience it is more common for participants to report suicidal ideation without intent to harm themselves. In this case, research staff will further assess suicidal ideation, consult with the clinical back-up, and help connect the participant to any VA, Vet Center, or community behavioral health services that can provide treatment. If participants report suicidal or homicidal concerns during an intervention session, the clinicians will follow the policies just described and also any of the internal clinic policies of their VA primary care clinic, including involving other treatment providers in care and increasing the intensity of contact with the participant through use of a suicide prevention coordinator. In cases of imminent risk and child/elder abuse, mandated reporting and referrals to appropriate mental health services will take place. If participants report significantly worsening symptoms of PTSD, the PI will contact them to further assess their symptoms and whether this could be an adverse reaction to the protocol. Additional clinical resources, as described above, will be offered. Participants will be withdrawn from the protocol if it is determined to be an adverse reaction or if more intensive treatment services are indicated. All participants will be reminded that participation is voluntary and they can stop at any time. The PTSD Coach app also has resources built into it to allow participants to seek help on their own. These include hotlines and treatment centers to call.

*Description of REDCap
Study data will be collected and managed using REDCap (Research Electronic Data Capture). REDCap is a secure, web application designed to support data capture for research studies. It provides user-friendly, web-based case report forms, real-time data entry validation (e.g. for data types and range checks), audit trails and de-identified data export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). The system was developed by a multi-institutional consortium which includes Stanford University and was initiated at Vanderbilt University. The database is hosted at the Stanford University School of Medicine secure data center. The system is protected by Secure Socket Layer (SSL) encryption and a strong web based authentication system. Data collection is customized for each study or clinical trial based on a study-specific data dictionary defined by the research team with guidance from the Stanford Center for Clinical Informatics REDCap administrator.

REDCap is a secure, HIPAA compliant electronic REsearch Data Capture system originally developed at Vanderbilt that is now widely used by academic medical centers across the U.S. to store clinical research data (see www.project-redcap.org for more info). The implementation of this system at Stanford University School of Medicine (SoM) has the following security and HIPAA compliance features:
• User authentication handled by integration with the campus Kerberos server via WebAuth, such that user passwords are never stored locally and password strength is enforced by central campus IT infrastructure
• User authorization handled by the built-in REDCap role based security machinery, which permits very

fine grained access control to all aspects of the system
• Comprehensive logging of all activity permits accurate and detailed reconstruction of how each user interacted with the system at all times
• Sophisticated data integrity and data cleansing features ensure high quality data capture
• All communications from client browser to web application server are routed through the SoM BIG-IP network security appliance which enforces SSL for all trans-intranet communications
• All administrative features have been sequestered in the Stanford implementation to a separate virtual machine, access to which is only available using two-factor authentication
• Both host based firewalls and institutional firewalls safeguard not only the application server but also the database server and file system used to store the data. The database server is on a separate, non-routable network from the web/application server for additional security
• Production and development each have their own parallel, equally secure systems, to further safeguard production data
• Hourly filesystem snapshots ensure against the possibility of data loss or corruption
• All data is backed-up daily and regularly stored off site in encrypted formats

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.

Recruitment will terminate when the goal of enrolling 130 participants has been met and they have completed all study procedures.

Participants will be informed that study personnel may choose to discontinue their participation at any time if it is deemed necessary (e.g., participant evidences psychotic symptoms).

In the unlikely event of a clinical emergency during an assessment, the research staff will have a specific protocol to follow regarding emergency care (e.g., walking the patient to the emergency room, calling VA police if the patient needs to be escorted, contacting the facilities suicide prevention coordinator, connecting the participant to the Veterans Crisis Line) and will contact clinical back-up that is part of the study staff (Drs. Kuhn, Rosen, Owen, and Cloitre).

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 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 PIs will train all project staff to recognize and report any adverse events immediately to the site PI. Adverse events involving human subjects include physical injuries, worsened physical or mental health, suicidal ideation, panic attacks, and depression. Other adverse events may also include the inadvertent disclosure by research staff of confidential research information to other persons. The PIs will provide an annual summary report of all adverse events to the IRB as part of the annual review and to the

Federal Agency as part of the annual Progress Report. Serious Adverse Events (SAE) may include: deaths, hospitalization, and all life threatening or disabling/incapacitating events among research subjects. SAEs must be reported to the PI immediately and the PI will report them to the IRB within 3 days. If necessary, the event will first be reported to the Federal Agency by telephone followed by a written report within 3 days.

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).

The PIs will jointly oversee all data and safety monitoring functions to ensure the safety of participants and the validity and integrity of the data obtained in the study. The PIs and project coordinators will meet weekly to track study progress and review these monitoring procedures. The PIs, along with this investigative team, will regularly oversee all aspects of the study, including participant recruitment, informed consent, data collection, data management and data analysis procedures, as well as regularly assess the risk/benefit ratio associated with participation in the study. A Data Safety Monitoring Board (DSMB) is assigned to funded projects by VA HSR&D.

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.

TBD by VA HSR&D (the funder)(see attached letter).

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.

We will report all 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.

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?

On an annual basis, the PIs and study staff will provide a report to the DSMB that includes data on enrollment, baseline and follow-up clinical data, protocol compliance, data quality, adverse events, and protocol deviations. The DSMB will meet, discuss the report, and give a written report to the PIs, which will be shared with the IRBs. The PIs will also call a special meeting of the DSMB if any patient safety issues arise beyond what is expected in the protocol.

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'.

If the PIs determine that there is sufficient evidence of an adverse event to necessitate suspension of data collection, further IRB review, modification of the protocol or other changes, the PIs will immediately discuss the recommendation with the Chairpersons of the IRBs and reach a determination whether to suspend data collection or to stop the study from proceeding and also consult with the DSMB. Resumption shall be based on the concurrence of the PIs, DSMB, and the Chairpersons of the IRBs. The Federal Agency will receive a written report within three days of any such suspension and/or resumption of data collection.

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 DSMB will disseminate the outcome of their reviews to the IRB, the study sponsor (if required), and the investigators.

Select One:

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

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.

We cannot promise that participants will personally receive any benefit from participating in this study. All participants will be receiving treatment from a VA PC-MHI clinician which is intended to address PTSD symptoms. It is hoped that the study will produce important knowledge about the benefits of including a mobile app for PTSD along with clinician support to address a gap in primary care PTSD treatment. If successful, the experimental treatment could be implemented nationally across VA primary care settings.

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).

For phone communication, study staff will call from private offices from the VA Palo Alto campus and from the VA Syracuse (for the blind assessor, see protocol) or through telehealth applications (including telephone and video-conferencing technology) by study staff who have the required VA training and approval to telework from their home. Email will not be used to correspond with participants. The exception to this is that links to REDCap surveys will be sent to participants through the REDCap system using a no-reply email account (i.e., participants cannot reply to the emails with the survey links). Mail communication will use sealed envelopes devoid of any disclosing information (e.g., study purpose) on the exterior.

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 STARR, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol. Be consistent with information entered in section 15a.

Prospective participants' medical charts will be reviewed to ascertain study eligibility (with a Waiver of HIPAA Authorization for Recruitment). These charts will be evaluated for a positive PTSD screen (PC-PTSD) and whether or not the patient is or will be receiving mental health treatment outside of VA primary care.

If a prospective participant has screened positive for PTSD and is not and will not (i.e., no referral or appointment) be receiving mental health treatment outside of VA primary care, their name, address, and telephone number will be collected from the chart.

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Information from the participants'VA administrative data will be extracted regarding date and types of mental health visits they have attended. Information about any new or existing mental health diagnoses (including alcohol or substance use conditions) will be extracted from the progress notes of these visits. Information about the nature of the mental health treatment received (e.g., psychotherapy, medications) will also be collected.

The study will collect information about participants' demographic characteristics (e.g., age, race, ethnicity). Participants' voice will also be audio recorded (during each of the four sessions of Clinician-Supported PTSD Coach and during the telephone-based clinical interviews). Finally, IIHI will also be collected during the study using self-report questionnaires and interviews.

Finally, participants' email address and survey data will be collected and stored using Stanford University School of Medicine's REDCap system (see 9. Risks, c).

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 https://researchcompliance.stanford.edu/panels/hs/redcap RedCap. If you are unsure of the security of the system, check with your Department IT representative. Please see 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

All study data will be stored separately from informed consent documents, contact information, and referral-related PHI. All hard copy will be stored in locked cabinets in a locked office. All digital data will reside on a FISMA-II compliant VA server (vhapalmpncptsd1) and survey data will be collected and stored in Stanford University School of Medicine's REDCap system.

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.

All research data will be identified by subject codes (3-digit) maintained by the study coordinator.

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 listed study personnel will have access to the data.

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.

All data will be identified by subject codes (3-digit) maintained by

the study coordinator.

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.

Participant IDs will be maintained by the study coordinator and be stored on a FISMA-II compliant VA server.

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 http://www.stanford.edu/group/security/securecomputing/ http://www.stanford.edu/group/security/securecomputing/. Additionally, if you will be using or sharing PHI see https://uit.stanford.edu/security/hipaa https://uit.stanford.edu/security/hipaa.

All data will be stored a on FISMA-II compliant VA server. Sharing of de-identified data with collaborating site with occur by allowing access to this VA server.

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)?

Study staff will by necessity complete the CITI training and an extensive set of VA data security and privacy trainings, yearly.

12. Potential Conflict of Interest

Investigators are required to disclose any financial interests that " https://researchcompliance.stanford.edu/eprotocol-coi" target="_blank" reasonably appear to be related/li to this protocol.

Financial Interest Tasks

Investigators	Role	Potential COI?	Date Financial Interest Answered	Date OPACS Disclosure Submitted	COI Review Determination
Eric Roland Kuhn	PD	N	11/12/2021		N/A
Prof Craig Steven Rosen	OC	N	11/16/2021		N/A

13. Consent Background

13. 1 Waiver of Documentation Consent for CS PTSD Coach RCT

Title : An RCT of a Primary Care-Based PTSD Intervention: Clinician-Supported PTSD Coach
Approval Period: **Draft**

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.

(i) Study research staff (RA or Study Coordinator) will obtain oral consent. (ii) Consent will be obtained by phone or in person at the VA Palo Alto. (iii) Consent is expected to take up to 15 minutes. (iv) This amount of time should be adequate for potential participants to consider whether or not to participate. If a potential participant needs more time, research staff will accommodate. (v) Potential participants will be informed that their decision to not participate will not affect their VA care. Research staff not involved in their ongoing care will obtain consent. (vi) NA.

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 Chapter12.2 for guidance.

Potential participants will be required to be able to speak English. We will make accommodations for individuals who may have disabilities that would require alternative or additional modalities of communication to ensure they understand the information contained in the consent form.

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.

Participants will be referred to the study by their primary care providers who are knowledgeable about the study, including that those with gross cognitive impairment are not eligible. If gross cognitive impairment is apparent during the consent process, they will not be eligible for 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.

At this point, 2 individuals on the study team would be responsible for consenting participants. The are study research coordinators: Sharfun Ghaus & Deloras Puran.

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?

Yes, oral informed consent will be obtained from the participant. All participants must be able to provide consent for screening so will not be obtained from LARS.

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 informed consenting process will minimize the possibility of coercion or undue influence and will provide the prospective participant sufficient opportunity to consider whether to participate. This will be done by having only research staff consent participants (not clinician's involved in their care), providing adequate discussion and time to consider consenting, and informing prospective participants that their participation is voluntary and their decision to not participate will not affect their VA care.

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

Yes.

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)?

Yes.

Title : An RCT of a Primary Care-Based PTSD Intervention: Clinician-Supported PTSD Coach
Approval Period: **Draft**

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.**

Select ALL applicable regulatory criteria for a Waiver of Documentation and provide a protocol-specific justification:

1)		**45 CFR 46.117(c)(1)(i)., that 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 (or legally authorized representative) will be asked whether he/she wants documentation linking the participant with the research, and the participant's wishes govern.**
2)		**45 CFR 46.117(c)(1)(ii)., that the research 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)		**45 CFR 46.117(c)(1)(iii)., if participants or legally authorized representatives (LAR) are members of a distinct cultural group in which signing forms is not the norm, the research presents no more than minimal risk and there is an appropriate alternative mechanism for documenting that informed consent was obtained.**
4)	Y	**21 CFR 56.109(c)(1)., 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:

This study uses routine behavioral health assessments and interventions that are typically used in VA. The novel aspect of this study is that it combines two routine interventions (i.e., VA primary care mental health & the publicly available PTSD Coach app) into one intervention (i.e., Clinician-Supported PTSD Coach).

13. 2 Waiver of Documentation Telephone screen script 2017

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.**

(i) Research staff (RA or Study Coordinator) knowledgeable about the study will conduct the screen. (ii) Consent will be obtained by phone or in person at the VA Palo Alto. (iii) The phone screen is expected to take up to 10 minutes. (iv) This amount of time should be adequate for potential participants to consider whether or not to participate. If a potential participant needs more time, research staff will accommodate. (v) Potential participants will be informed that their decision to not participate will not affect their VA care. Research staff not involved in their ongoing care will obtain consent. (vi) NA

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 Chapter12.2 for guidance.

Potential participants will be required to be able to speak English. We will make accommodations for individuals who may have disabilities that would require alternative or additional modalities of communication to ensure they understand the information contained in the phone screen.

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.

Participants will referred to the study by their primary care providers who are knowledgeable about the study, including that those with gross cognitive impairment are not eligible. If gross cognitive impairment is apparent during the phone screen, they will not be eligible for 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.

i) At this point, 3 individuals on the study team would be responsible for phone screeing. These include: The study PI: Eric Kuhn; the study research coordinator: Sharfun Ghaus; the study research assistant: TBD.

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?

ii) Yes, informed consent to phone screening will be obtained from the participant. All participants must be able to provide consent for screening so will not be obtained from LARs.

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?

iii) The phone screening process will minimize the possibility of coercion or undue influence and will provide the prospective participant sufficient opportunity to consider whether to participate. This will be done by having only research staff screen potential participants (not clinician's involved in their care), providing adequate discussion and time to consider participating, and informing prospective participants that their participation is voluntary and their decision to not participate will not affect their VA care.

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

Yes

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)?

Yes

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.**

Select ALL applicable regulatory criteria for a Waiver of Documentation and provide a protocol-specific justification:

1) 45 CFR 46.117(c)(1)(i)., that 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 (or legally authorized representative) will be asked whether he/she wants documentation linking the participant with the research, and the participant's wishes govern.

2) 45 CFR 46.117(c)(1)(ii)., that the research 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) 45 CFR 46.117(c)(1)(iii)., if participants or legally authorized representatives (LAR) are members of a distinct cultural group in which signing forms is not the norm, the research presents no more than minimal risk and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

4) Y **21 CFR 56.109(c)(1)., 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:

We will be telephone screening potential participants for eligibility prior to a more thorough in person assessment that will be completed following informed consent.

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

15. HIPAA Background

15. 1 Waiver of Authorization for Recruitment

waiver of authorization for recruitment

a) **Describe the protected health information (PHI) needed to conduct screening or recruitment. PHI is health information linked to HIPAA identifiers. List BOTH health information AND HIPAA identifiers. If you are using STARR, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol.**

Patient names, postal address information, telephone numbers, PC-PTSD scores, SSNs, and mental health treatment history. The waiver will allow us to receive referrals from primary care staff for patients who may be eligible for this study. It will also allow us to facilitate these referrals by creating a list of patients who screen positive on the PC-PTSD on a monthly basis and then ask their providers if they will refer these patients to the study. Without the waiver, we would not be able to recruit the number of participants necessary to do the study. Without access to their medical information, we would not know who to recruit or have a way to contact the patients.

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?**

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.**

Identifiers will be stored on a secure VA server (vhapalmpncptsd1/Shared Research). Only research staff will have access to this information. This information is only used for recruitment purposes.

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.**

Identifiers will be maintained through the duration of the research study and then destroyed consistent with VA policy.

Title : An RCT of a Primary Care-Based PTSD Intervention: Clinician-Supported PTSD Coach
Approval Period: **Draft**

15. 2 Waiver of Authorization hipaa authorization

a) **Describe the Protected Health Information (PHI) needed to conduct the research. PHI is health information linked to HIPAA identifiers. List BOTH health information AND HIPAA identifiers. If you are using STRIDE, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol.**

Information from the participants'VA administrative data will be extracted regarding date and types of mental health visits they have attended. Information about any new or existing mental health diagnoses (including alcohol or substance use conditions) will be extracted from the progress notes of these visits. Information about the nature of the mental health treatment received (e.g., psychotherapy, medications) will also be collected. The study will collect information about participants' demographic characteristics (e.g., age, race, ethnicity). Participants' voice will also be audio recorded (during each of the four sessions of Clinician-Supported PTSD Coach and during the telephone-based clinical interviews). Finally, IIHI will also be collected during the study using self-report questionnaires and interviews. Finally, participants' email address and survey data will be collected using Stanford University School of Medicine's REDCap system (see 9. Risks, c).

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?**

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.**

Identifiers will be stored on a secure VA server. Only research staff will have access to this information. This information is only used for recruitment purposes.

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.**

Identifiers will be maintained through the duration of the research study and then destroyed with VA policy.

16. Attachments

Attachment Name	Attached Date	Attached By	Submitted Date
VA HSR&D Grant Protocol	11/18/2015	ekuhn	
VA Required Questions	11/25/2015	ekuhn	
Study Measure Part 1	11/25/2015	ekuhn	
Study Measures Part 2	11/25/2015	ekuhn	
Recruitment Letter	11/25/2015	ekuhn	
Letter from Funder about DSMB	11/30/2015	ekuhn	
Possemato, Kuhn et al., in	11/30/2015	ekuhn	

press			
Modified Demograpics Form	03/10/2017	ekuhn	
Collaborating Site IRB Approval Letter	06/20/2017	ekuhn	
Recruitment Letter Revised	07/17/2017	ekuhn	
HIPAA Waiver Request Form	09/14/2017	ekuhn	
VINCI Information for IRBs	09/14/2017	ekuhn	
KuhnRequestSSN 9-19-2017 signed	09/19/2017	sghaus	
DSMB Annual Report FY16	12/08/2017	ekuhn	
DSMB 2017-2018	12/07/2018	ekuhn	
DSMB Feb-Dec 2018	11/25/2019	ekuhn	
Information for at-home intervention-assessment	03/27/2020	ekuhn	
COVID Stressors Survey	05/15/2020	ekuhn	
DSMB Jan-Dec 2019	11/10/2020	ekuhn	
DSMB Jan-Dec 2020	11/12/2021	ekuhn	

Obligations

The Protocol Director agrees to:

- Adhere to principles of 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 Stanford 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 unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

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

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.

https://stanfordmedicine.box.com/shared/static/qbsi8u8h47qsotxhdpuzz50xlrqa0sgo.pdf Report promptly any new information, complaints, possibly serious and/or continuing noncompliance, or unanticipated problems involving risks to participants or others.

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)

APPROVAL LETTER/NOTICE NOTE: List all items (verbatim) that you want to be included in your approval letter (e.g., Amendment date, Investigator's Brochure version, consent form(s) version(s), advertisement name, etc.) in the box below.

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.