Multisite RCT of STEP-Home: A Transdiagnostic Skill-based Community Reintegration Workshop

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Study Title: Multisite RCT of STEP-Home: A transdiagnostic skill-based reintegration workshop

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STUDY PROTOCOL

1. Rationale

(a) Statement of the Problem: Post-9/11 Veterans who served in OEF/OIF face many challenges as they re-enter civilian life after structured military careers. Yet, underutilization and resistance to mental health treatment remains a significant problem [3-5]. Recent investigations of community reintegration problems among returning Veterans found that half of combat Veterans who use Veterans Administration (VA) services reported difficulty in readjusting to civilian life, including difficulty in social functioning, productivity in work and school settings, community involvement, and self-care domains [6, 7]. High rates of marital, family, and cohabitation discord were reported, with 75% reporting a family conflict in the last week [8]. At least one-third reported divorce, dangerous driving and risky behaviors, increased substance use, and impulsivity and anger control problems since deployment. Almost all Veterans expressed interest in receiving services to help readjust to civilian life, and receiving reintegration services at a VA facility was reported as the preferred way to receive help. Mental health and anger problems are often cited as driving Veterans' difficulties readjusting to civilian life. Anger is becoming more widely recognized for its involvement in the psychological adjustment problems of post-9/11 Veterans [9]. Research has shown that anger directly influences treatment outcome [10]. In fact, history of untreated PTSD and aggression have been demonstrated to be pervasive among post-9/11 Veterans who die by suicide in the months before death [11]. Veterans with probable PTSD report more reintegration and anger problems, and greater interest in services than Veterans without [6]. Reintegration and anger problems continue for years post-combat and may not resolve without intervention [7].

*In February 2023, we received approval for a 1-year cost extension to continue this study for one additional year; the study end date is now 3/31/24 instead of 3/31/23. Any relevant changes to the study protocol resulting from this timeline extension are outlined below, where appropriate.

Phase 1: Years 1 and 2
We will initiate the study at the Boston VAMC and develop Standard Operating Procedures for the addition of site 2 in Phase 2.

Phase 2: Years 3, 4, and 5
We will initiate the study at the second site, the Houston VAMC, in Year 3. We have obtained IRB approval to initiate site 2 from the Houston VA (see attached documentation of approval by Michael E. DeBakey Medical Center IRB). Given the transition to telehealth workshops, we now plan to initiate recruitment only for Veterans through site 2 (Houston) during Years 3, 4, and 5.

In-person workshops may be initiated at site 2 (with appropriate IRB approvals) in the future.

(b) Hypotheses & Aims

Primary Aim 1. Examine treatment effects of STEP-Home on primary outcomes relative to Present Centered Group Therapy (PCGT):
Hypothesis 1A. Participants randomized into the STEP-Home intervention will show improvement on reintegration, readjustment, and anger post-intervention (expressed by lower scores; less difficulty).
Military to Civilian Questionnaire (M2CQ), Post-Deployment Readjustment Inventory (PDRI), and State-Trait Anger Expression Inventory (STAXI-2) scores post-intervention (T4) < baseline (T1)

Hypothesis 1B. Participants randomized into STEP-Home will show greater improvement in primary outcomes as compared to PCGT.
Change scores baseline (T1) to post-intervention (T4) STEP-Home > PCGT change scores

Post-intervention (T4) primary outcome scores STEP-Home < PCGT primary outcome scores (T4)

Primary Aim 2. Examine maintenance of treatment effects on primary outcomes:
Hypothesis 2: Treatment effects will be maintained at follow up in both groups.
Differential treatment effect of STEP-Home over PCGT post-intervention (T4) will be maintained at follow up (T5)

Exploratory Aim 1. Explore treatment effects of STEP-Home on measures of mental health, functional and vocational status and cognitive secondary outcomes targeted indirectly in the workshop.

Exploratory Aim 2. Acquisition of core skills (problem solving, emotional regulation, attention training) will mediate the effect of treatment on primary outcomes post-intervention and at follow up.

2. Background and Significance

(a) Background: The unique and challenging needs of post-9/11 Veterans necessitate the development of novel, empirically validated, skill-based, integrative interventions for civilian reintegration that are cost-effective and can be easily implemented across the VA system. Returning Veterans face high rates of reintegration difficulties that continue for years post-deployment and may not resolve without intervention [6]. We have described this cohort as "multi-morbid" [36]. Attempting to care for such complicated patients with single modality treatments has had limited success [29-31, 37, 38] and integrated transdiagnostic treatments for this cohort are quite limited [39-41]. Those that do exist are designed for Veterans meeting multiple clinical diagnoses and may not be appropriate for the broad range of Veterans STEP-Home is designed to help. We are not aware of any skills-based program that seeks to help all Veterans (with or without clinical diagnoses) reintegrate into civilian life. Research on TBI in post-9/11 Veterans [42, 43] underscores the need for programs that utilize an interdisciplinary approach to reintegration. Programs designed to address challenges of Veterans as they reintegrate in vocational environments, particularly integrative approaches, are greatly needed [44]. The STEP-Home intervention provides such a program. STEP-Home includes focused cognitive and emotional regulation skills training and is informed by the most recent research with returning Veterans and available programs focused on reintegration in VA and military settings (e.g., Battlemind training [45]).

(b) Significance: In this proposal, we extend our previous SPiRE feasibility and preliminary effectiveness study to examine STEP-Home efficacy in a RCT design. This novel therapy will target the specific needs of a broad range of underserved post-9/11 Veterans. It is designed to foster reintegration by facilitating meaningful improvement in the functional skills most central to community participation: emotional regulation (ER), problem solving (PS), and attention functioning (AT). The skills trained in the STEP-Home workshop are novel in their collective use and have not been systematically applied to a Veteran population prior to our SPiRE study. STEP-Home will equip Veterans with skills to improve daily function, reduce anger and irritability, and assist reintegration to civilian life through return to work, family, and community, while simultaneously providing psychoeducation to promote future engagement in VA care.

The innovative nature of the STEP-Home intervention is founded in the fact that it is: (a) an adaptation of an established and efficacious intervention [2, 46, 47] now applied to post-9/11 Veterans; (b) nonstigmatizing (not "therapy" but a "skills workshop" to boost acceptance, adherence and retention); (c) transdiagnostic (open to all post-9/11 Veterans with self-reported reintegration difficulties; Veterans often have multiple mental health diagnoses, but it is not required for enrollment); (d) integrative (focus on the whole person rather than specific and often stigmatizing mental and physical health conditions); (e) comprised of Veteran-specific content to teach participants cognitive behavioral skills needed for successful reintegration (which led to greater acceptability in feasibility study); (f) targets anger and irritability, particularly during interactions with civilians; (g) emphasizes psychoeducation (including other available treatment options for common mental health conditions); and (h) challenges beliefs/barriers to mental health care to increase openness to future treatment and greater mental health treatment utilization. Many Veterans who participated in the development phases of this workshop have gone on to trauma or other focused therapies, or taken on vocational (work/school/volunteer) roles after STEP-Home.

We have demonstrated that the STEP-Home workshop is feasible and results in pre-post change in core skill acquisition that we demonstrated to be directly associated with post-workshop improvement in reintegration status in our SPiRE study. Given the many comorbidities of this cohort, our innovative treatment addresses multiple aspects of mental health, cognitive, and emotional function simultaneously and bolsters reintegration in a short-term group to maximize cost-effectiveness while maintaining quality of care [48].

(c) Relevance to Veterans Health: The successful completion of the aims proposed has the potential to significantly improve skills to foster civilian reintegration in post-9/11Veterans. Furthermore, the STEP-Home SPiRE feasibility study demonstrated that the workshop also serves as a gateway for Veterans who are hesitant to participate in traditional mental health treatments to promote openness and engagement in additional, critically needed, VA services. Given the high rate of treatment resistance in this cohort, developing acceptable interventions that promote treatment engagement and retention, and open the door to future VA care, is necessary to improve functional status and to reduce long-term healthcare costs of untreated mental health illnesses.

3. Work Accomplished

Data from our successful SPiRE feasibility and preliminary effectiveness study [10] has demonstrated: (1) STEP-Home was acceptable in this Veteran cohort; and (2) the change in treatment related skill acquisition was associated with improved community reintegration status (as measured by the Military to Civilian Questionnaire; M2CQ) post-workshop. Critically, the dropout rate for the STEP-Home workshop was less than half that observed in standard psychological treatment for PTSD in post-9/11 Veterans [11]. Data also demonstrated that STEP-Home functions as a gateway by increasing engagement in both vocational activities and critically needed mental health treatments at VA for Veterans hesitant to seek help. STEP-Home offers a much needed, palatable, and minimally stigmatizing intervention for post-9/11 Veterans struggling with reintegration difficulties that is feasible, acceptable, and has shown preliminary effectiveness.

4. Work Proposed

(a) Study Objectives: There are two major experimental objectives to this project: (1) To examine treatment effects of STEP-Home on primary outcomes relative to Present Centered Group Therapy (PCGT); (2) To examine maintenance of treatment effects on primary outcomes; and two exploratory aims: (1) To examine treatment effects on secondary outcomes targeted indirectly in the workshop; (2) To determine if acquisition of core skills or “key ingredients” mediates primary outcomes. In February 2023, we received approval for a 1-year cost extension to continue this study for one additional year; the study end date is now 3/31/24 instead of 3/31/23. Therefore, the objectives listed above will be accomplished across a 5-year timeline, instead of the original 4-year timeline.

(b) Study Design (**Phase 1):** We will conduct a randomized control trial (RCT) of STEP-Home at the VA Boston Healthcare System, Jamaica Plain campus and the Michael E. DeBakey Medical Center in Houston. With the 1-year study extension approved in February 2023, our funded aims have been updated to enroll 144 Veterans in Boston (original enrollment number was 112 in Boston) and 96 in Houston for a total of 240 participants. In order to achieve this, given drop out, we will recruit 300 Veterans overall, when accounting for participants at both sites.

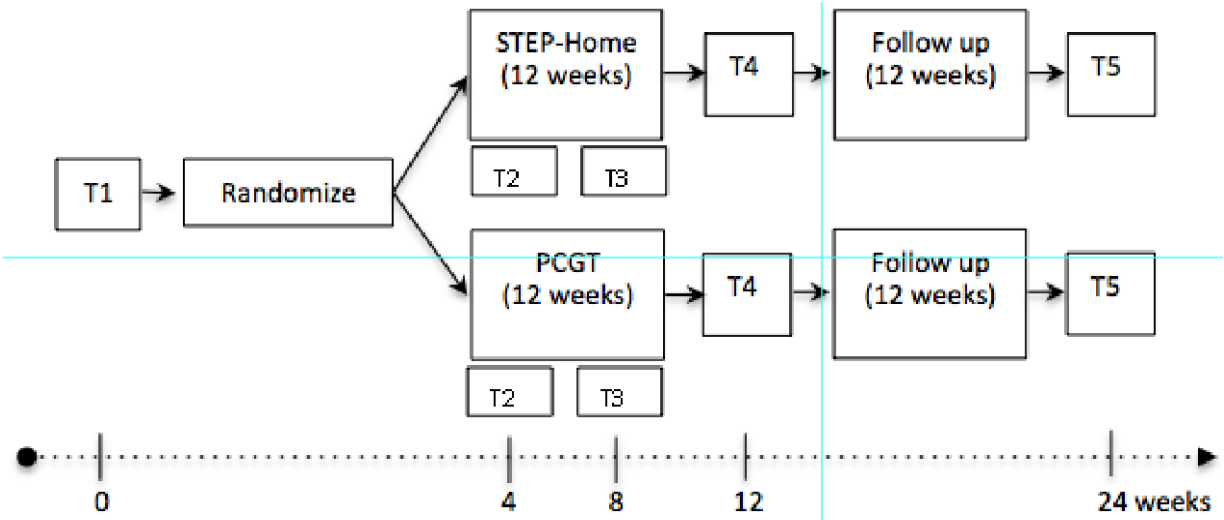
Recruitment will be conducted in Boston (Years 1-5) and Houston (Years 3-5). Beginning in Year 3, Houston TRACTS/STEP-Home staff will assist in recruitment and referrals. The Houston site will assist with any clinical and/or safety concerns for Houston Veterans under the leadership of site PI, Ricardo Jorge, MD, a licensed psychiatrist with ample experience in this arena in coordination with Boston and study PI, Catherine Fortier. All study procedures across both sites will be reviewed by our Data Safety Monitoring Board and reported to local IRBs at both sites.

Participants will be randomly assigned to receive one of the two group interventions: STEP-Home or PCGT, and each intervention will meet one time a week for 12 weeks. We will use statistical software to conduct cluster randomization to assign veterans to the intervention group. We do not plan to use matching or stratified

randomization to balance the interventions on patient characteristics (e.g. age, prevalence of traumatic brain injury and psychiatric conditions, etc.) since we do not have any a priori reason to expect that such factors will significantly influence our primary outcomes. We will assess any patient characteristics as possible confounders in our analyses if they differ across groups (see Analytic Plan below). Given the group treatment modality for both conditions, it will be necessary to accrue participants for a cohort before randomization and treatment can begin. Each cohort will include a minimum of 8 and a maximum of 20 participants who will be randomized to either STEP-Home (n=4-10 Veterans per treatment group) or PCGT (n=4-10 Veterans per active control). The treatment group and active control group will be matched in size (n's equal at randomization) and populated based on recruitment success. The goal will be to recruit 16 Veterans and randomize to two groups of 8. However, if recruitment is slow, the smallest randomization pool allowed will be 8 (4 Veterans assigned to each group). If recruitment is ahead of pace, the largest randomization pool allowed will be 20 (10 Veterans assigned to each group).

When a cohort large enough is available, randomization into STEP-Home or PCGT will occur and participation in the study begins (i.e., Time 1; T1: Pre), during which we will consent, administer the baseline assessments, randomly assign to either the STEP-Home or the PCGT arm, and schedule the treatment sessions. All participants will be assessed at the following 5 outcome points: Screening, at randomization (T1: Assessment), during treatment 4-week skills check (T2: Brief Skills Check), during treatment 8-week skills check (T3: Brief Skills Check), post-intervention (T4: Assessment), and at 3-months follow up (T5: Assessment). Assessments and skills checks are all self-report; therefore, blinded assessors are not required. Participants who decide to leave the program early will be asked to complete all assessments via secure Qualtrics link sent in MyHealtheVet or via postal mail service according to the RCT timeline following the intent-to-treat format, but will not be required to do so. Veterans will participate in their assigned treatment arm 1 day/week for approximately 2 hours. Replicating our SPiRE feasibility and preliminary effectiveness study [1], staff members will work in pairs when running groups. These same two staff members will offer to meet individually with Veterans before or after group approximately 4 to 6 times/workshop; it will be the Veterans' choice whether they participate in these individual meetings.

Assessments (T1, T4, and T5) may be done in person or online (see Data Security Section for description of Qualtrics online data entry). Brief Skills Checks (T2 & T3) may also be done in person or online.



Randomization Figure. T1 = Baseline Assessment; T2 = 4-week Skills check; T3 = 8-week Skills check; T4 = 12-week Post-Intervention Assessment; T5 = 24-week Follow-up Assessment.

- Assessments = T1, T4, and T5; Reimbursement = $20
- Brief Skills Checks = T2 & T3; Reimbursement = $0

(c) Human Studies:

Participants and Recruitment: All possible participants recruited for this study will be Veterans. Participants will be referred from three primary sources: 1) Clinical services; 2) TRACTS; (3) Community partners, other VA clinical services, and advertisements.
1) Clinical services: VA Boston Healthcare System (VABHS) clinics often include: Center for Returning Veterans, Polytrauma, Primary Care, Neuropsychology, Psychology, Neurology, Psychiatry, and PTSD Clinics (Behavioral Health and Women's Division). IRB-approved study brochures will be placed in clinics, and staff members working in these clinics will share approved recruitment materials for STEP-Home and refer Veterans who may be appropriate for the trial.
2) TRACTS: Current/former TRACTS participants at TRACTS Boston may be told about STEP-Home by TRACTS study staff. Additionally, a recruitment letter will be sent to former TRACTS participants to explain the study to them and give them STEP-Home study staff contact information should they wish to learn more about participating.
3) Other recruitment sources may include existing community partners (e.g., schools, Veteran Outreach coordinator David Hencke), VA outpatient clinics/Vet Centers/CBOCS, advertisements, social media (e.g., Facebook), and our website (www.stephome.hms.harvard.edu). Any new advertisements will be reviewed by IRB before implementation. Additionally, given the possiblility that STEP-Home workshops may be conducted via telehealth methods and advertisements may reach Veterans outside of Massachusetts, we intend to make STEP-Home available to Veterans nationwide.
4) Recruitment at the Houston site will be under the direction of Houston site PI, Ricard Jorge, and will be overseen by their IRB.
5)) The Veterans Affairs/Department of Defense Identity Repository (VADIR), a VA database containing military personnel information from the DOD. We will receive quarterly updates from VADIR; the VADIR transfer server (vaausvdrxfr20.aac.va.gov) automatically pushes the quarterly file to our study server, via secure transfer behind the VA firewall.

Each month, we will send recruitment letters to a random sample of up to 1000 newly separated Veterans received from VADIR. Specifically, this means that our first month of recruitment will involve sending recruitment letters to up to 1000 randomly selected Veterans who separated from service during the three months prior. The next month, we will exclude Veterans who already received a letter from us and extract another group of up to 1000 Veterans from the larger pool of eligible Veterans who separated from service during the three months prior (which will comprise any Veterans who are still within the window of eligibility and were not selected the previous month as well as any Veterans who are newly separated in the month between recruitment waves). This process will continue until our enrollment target is met. The recruitment letter will briefly describe the study and invite them to contact the study team if they are interested in learning more about participating. They will also have the option of sending back an "opt out" postcard in a pre-paid envelope if they do not wish to be contacted again.

Potential Veterans identified through VADIR will initially be contacted by the STEP-Home study via a written outreach letter (sent via USPS mail or email). If the Veteran does not reply to STEP-Home's initial outreach, STEP-Home staff will make up to two attempts to contact the Veteran by phone, and the phone outreach attempts will begin at least 1 week after the written outreach letter was sent.

Inclusion Criteria: Participants will be (1) Post-9/11 Veterans who report some reintegration, readjustment, or anger difficulty – i.e., Veterans who report "some difficulty" (Likert rating) on at least one of the primary measures: M2CQ; PDRI; STAXI-2; (2) 18-75 years old; (3) English-speaking (sessions will be conducted in English); and (4) Agreeing to participate (i.e., completion of ICF/HIPAA).

Exclusion Criteria: Participants will be *excluded* for (1) schizophreniform disorder/active psychosis; (2) bipolar disorder; (3) active suicidality/homicidality requiring crisis intervention; (4) other severe psychiatric disorders prohibiting appropriate group participation; (5) neurological diagnosis prohibiting appropriate group participation (excluding TBI); (6) current substance dependence; (7) *current participation in any other form of active behavioral therapy at the time of enrollment (e.g., Cognitive Processing Therapy, cognitive rehabilitation for mTBI, or other psychotherapy).

**For any potential participants who are currently participating actively in another treatment, they will be invited to participate in the next available cohort after their current treatment is complete.*

Enrolled STEP-Home participants will be instructed not to schedule initiation of another behavioral therapy until the 12-week intervention is complete. Importantly, Veterans will be allowed and encouraged to initiate any other treatment at the conclusion of STEP-Home or PCGT, even during the 12-week follow up. If another form of intervention is pursued during the actual 12-week intervention despite instruction to wait, we will allow participants to remain enrolled and track that information for use in statistical analyses similar to the 12-week post-intervention follow up period. We will, however, seek replacement participants for those who do this so that our statistical power is not diluted. Any necessary treatment for psychiatric crisis will also be allowed and tracked. Treatment enrollment and health utilization data will be collected at T1, T4, and T5 via self-report format and via CPRS chart review (please see Secondary Outcome Measures and Baseline Characteristics, protocol page 7). Psychotropic medication (and related visits) will be allowed if stable.

Note: If Veterans enrolled in STEP-Home express active suicidality/homicidality requiring crisis intervention, study staff will follow typical VA procedures including contacting Suicide Prevention Program and/or referring to Urgent Care. STEP-Home will not be seeing patients during off hours at the VA. The lead investigator (Fortier) and lead therapist (Kenna) are licensed psychologists. Appropriate safeguards will be in place if screening procedures, assessments, or intervention sessions cause any psychological distress or a psychiatric emergency emerges among participants. Staff will provide appropriate referrals and assess risk. If a psychiatric emergency is reported by a participant in the context of the study, the site PI, or in case of her unavailability, a Co-I (Dr. Kenna) will contact the disclosing participant by phone, assess for risk and safety, and provide the participant with appropriate referrals. We will utilize access to local and national mental health resources available through the VA, including the suicide prevention hotline, risk assessments through Mental Health during regular business hours (Psychiatry Urgent Care), or the Psychiatrist on call during off hours. All potential collaborators on these research activities will have completed comprehensive training in the areas of research ethics, protection of human subjects, and suicide prevention. They will also have completed all VA required trainings pertinent to cyber security, VHA privacy policy (HIPAA), research data security and privacy, ethical principles of human subjects' protection, etc., as required by local IRBs.

Informed Consent Process: The informed consent process will take place prior to participation in the study either by mail, online via VA-approved technologies, or in quiet designated testing space with the Project Coordinator and/or other trained study staff members. If informed consent takes place online, the process is done individually for each participant with one study staff member; the consent process will never take place in a group format with more than one participant at a time. During the informed consent process, participants are informed that at any point in time, they are welcome to ask questions or bring up any issues that may concern them. They can tell the research assistants, project coordinator, and/or the investigator. If the investigator is not immediately available, the research assistants and project coordinator will relay the participant's question or concern to the investigator as soon as she is available. Participants are also given the investigator's phone number, and they are welcome to call her at any time during or after their study participation is completed.

If consent takes place via mail or online:

- Consent forms will be mailed via postal mail or sent via MyHealtheVet.

Consent forms will be reviewed with study staff and verbal consent will be obtained online on VA-approved technologies at the Pre-Visit (online questionnaire session), which is conducted in a private, individual session with one participant at a time. The participant will then be asked to sign the consent on camera via approved online platform and either: return signed document by mail (USPS); fax the signed document; taking a digital image and sending it via Azure RMS encrypted email;by study staff obtaining a screen capture of the signature page; or by electronic/digitial signature. For the option of electronic/digital signature, this can be done by a signature made on a touch device or computer mouse, or through the use of DocuSign software.

Payment: Participants will be reimbursed $20 for participation in assessments at Weeks 1, and 12. For the follow-up assessment at week 24, participants will be reimbursed $40. There is no compensation for the skills-checks at weeks 4 and 8. Maximum total payment for assessments will therefore be $80. Participants will also

be reimbursed up to $120 for travel to/from the workshops over the 12 weeks. Participants will receive $10/workshop for each workshop attended, regardless of distance/time traveled. Total maximum payment is therefore $200. Payment may be in the form of a check, debit card, or electronic direct deposit.

October 2022 protocol update: If a participant signed a previous version of the consent form when direct deposit was not an option, we will contact them at the time of their next scheduled assessments and give them the option of re-signing the newer consent form so they can receive payment via direct deposit, if they so choose.

Methods and Materials:

Group Treatment Modalities

(1) Treatment Group = STEP-Home. This group will meet for ~1.5 - 2 hours a week for 12 weeks. The core skills of Emotional Regulation (ER) (45-minutes) and Problem Solving (PS) (45-minutes) are introduced and then integrated throughout all Veteran-specific content modules for practice and repetition for 12 weeks. Attention Training (AT) augments PS and ER core skills and is interspersed throughout group and individual sessions. Additional 30-minute individual skill building and goal setting sessions (see STEP-Home Manual and [1] for additional information) may occur approximately 4 - 6 times over the 12 weeks (based on individual Veteran needs). All Veterans will be offered individual skill building sessions. We have observed in past STEP-Home groups that not all Veterans chose to take advantage of these sessions, but they will be offered to all of the participants. Advisors support practice of PS/ER/AT strategies.

***Core Skills**:*

Problem-Solving (PS): Participants receive 12 45-minute sessions of group PS using the five-step approach to PS [56;57]. An acronym (SWAPS) has been developed based on these steps to help participants remember them: Step 1: Stop! Is there a problem? Step 2: What is the problem? Step 3: Alternatives and options Step 4: Pick and Plan Step 5: Satisfied? Veterans learn the approach using a variety of Veteran-centric examples with repetition in multiple contexts allowing the process to become habitual or rote.

Emotional Regulation (ER): Participants receive 12 45-minute sessions of group ER drawing on the principles outlined by D'Zurilla et al. [58; 59] and their application to TBI by Rath [60]. Cognitive behavioral techniques adapted to the unique cognitive needs of Veterans will be used [60, 61]. Emotions inevitably affect (positively or negatively) PS; therefore, ER is crucial to effective PS and anger/impulse control. To maximize generalization, ER will be contextualized by focusing on real-life Veteran problems. Group members are encouraged to share a problem that they have experienced and apply ER to that problem. As Veterans become more aware and adept at this process, they are taught to identify new, healthy alternative behaviors.

Attention Training (AT): AT is based on Attention Process Training (APT-II) [62] and Sohlberg et al.'s [63] model of attention. Attention is made up of two categories: simple attention (focused and sustained attention) and complex attention (selective, alternating, and divided attention). We use these principles to guide remediation of attentional impairments through the application of individually tailored feedback including compensatory and generalization strategies. Group discussions are focused on how individual attentional difficulties can be related to symptoms of PTSD, TBI, and/or other conditions.

***Veteran-specific Content* (see [1] and STEP-Home Manual for more information)**: Veteran-specific content is introduced and used for PS/ER/AT skills training throughout the 12-week workshop (Figure 4). The skills training that Veterans receive is fully contextualized into the content areas. We have found that Veterans typically demonstrate difficulty adjusting from military to civilian contexts based on fundamental differences in the structure of these contexts. Similar to Battlemind training [45], we use Veteran-specific content areas to demonstrate that the habitual skills needed to survive in combat may cause problems if not adapted to the civilian world. Psychoeducation in the various content areas is provided and group leaders elicit examples from Veteran participants in the content areas to practice PS/ER/AT in group. Content domains are described in

detail in the STEP-Home Manual and include: Vocational, Community Reintegration, Psychoeducation & Destigmatization (gateway to VA care), Substance Misuse, Anger Management, Veteran-to-Veteran Support, Family/Support System Involvement.

(2) Comparison Group = PCGT. A nonspecific comparison design [64] was selected to allow greater certainty that STEP-Home treatment effectiveness is due to specific aspects of the key ingredients of the experimental therapy (STEP-Home) and not merely to nonspecific therapeutic factors. PCGT was initially developed by Schnurr et al. [65] to include all elements of effective PTSD treatment that are not specifically trauma-focused. PCGT is a credible and clinically acceptable treatment often used as a control condition in PTSD trials with notably low drop out rates [65-67]. It is a nonspecific and supportive intervention to control for the nonspecific benefits of the group experience (e.g., therapist contact, instillation of hope, expectation of improvement). PCGT is fully manualized for group delivery and can be easily matched to STEP-Home as an active control arm (e.g., [65-67]). It will focus on identifying and discussing current life stressors that contribute to reintegration difficulties, psychoeducation, and promotion of wellness and physical health. Similar to the STEP-Home group, PCGT will contain homework assignments, involving monitoring diaries of stressful situations and when symptoms cause impairment in social and occupational functioning, and will also meet for ~1.5 - 2 hours a week for 12 weeks. Staff members will also offer to meet individually with Veterans enrolled in PCGT before or after group approximately 4 - 6 times over the 12 weeks. PCGT and individual sessions will not include the components that form the key ingredients or core skills of STEP-Home: CBT-based active PS, ER, or AT. Rather, PCGT employs Yalom's [68, 69] model of group therapy with a "here-and-now" focus and emphasizes the process of interpersonal learning, group cohesion, and group support. Although focus of group discussions will often be on group members' current problems, active CBT-based directive PS techniques used in STEP-Home will not be employed in the PCGT control condition. Content for group discussions will mimic STEP-Home topics including: Vocational, Community Reintegration, Psychoeducation & Destigmatization (gateway to VA care), Substance Misuse, Anger Management, Veteran-to-Veteran Support, and Family/Support System Involvement.

Outcome Measures

All measures used (except those developed for STEP-Home during the feasibility study) are commercially available, have evidence of psychometric soundness or responsiveness to the interventions proposed, and have been used in previous intervention studies of populations with PTSD and TBI. Assessments do not require blinding because all outcomes are self-report. The time points at which the different outcome measures will be administered are shown in the Table below that follows the listing of outcome measures.

(1) Primary Outcome Measures

The primary outcome measures may include the following assessments:

- Military to Civilian Questionnaire (M2C-Q): A 16-item measure of post-deployment community reintegration in post-9/11 Veterans that assesses six domains (interpersonal relationships, productivity at work, school or home, community participation, self-care, leisure, and perceived meaning of life).
- Post-Deployment Readjustment Inventory (PDRI): A 36-item measure of readjustment in post-9/11 Veterans with six subscales (career challenges, social difficulties, intimate relationship problems, health concerns, concerns about deployment, and PTSD symptoms).
- State-Trait Anger Expression Inventory (STAXI-2): A 57-item widely used measure to assess state anger, trait anger, and anger expression with three subscales (trait anger, anger expression, and anger control).

Core Skills Measures

The core skills measures may include the following assessments:

- Problem Solving Inventory (PSI): Measure of PS Confidence, Approach-Avoidance Style and Personal Control.
- Difficulties in Emotion Regulation Scale (DERS): Measure to assess multiple aspects of emotion dysregulation
- Attention-Related Cognitive Errors Scale (ARCES): Measure of everyday performance failures arising from brief failures of sustained attention.

(2) Secondary Outcome Measures
The secondary outcome measures may include the following assessments:

Mental Health
- PTSD Checklist for DSM-5 (PCL-5): A 20-item measure of PTSD updated for DSM-5.
- Depression Anxiety and Stress Scale (DASS-21): A 21-item measure of current depression, anxiety, and stress.
- Neurobehavioral Symptoms Inventory (NSI): A 22-item measure of current post-concussive symptoms.

Functional/Vocational
- World Health Organization Disability Assessment Schedule-2.0 (WHODAS-2.0): Measures functional states in six domains (understanding and communicating, getting around, self care, getting along with people, life activities (work/school), and participation in society).
- Satisfaction with Life Scale (SWLS): A 5-item measure of satisfaction with life.
- Treatment/Activities Survey: Assesses engagement in treatment, school, work, and life activities.
- Barriers to Employment Success Inventory (BESI): A measure of obstacles to employment in five areas (Personal/Financial, Emotional/Physical, Career Decision-Making and Planning, Job-Seeking Knowledge, and Training/Educaiton).
- Average # hours worked: Number of hours/month in the month before STEP-Home and in each month of the intervention, WLC, and post-treatment monitoring.

Cognitive
- Frontal Systems Behavior Scale (FrSBe): Measures apathy, disinhibition, and executive dysfunction.

Baseline Characteristics (captured via self-report measures and/or CPRS chart review)
- Demographics
- Deployment data
- Active problems/diagnoses
- Medication list
- Health utilization data
- WTAR

(3) Treatment Adherence and Program Satisfaction Measures

Feasibility/Adherence
- Supervisor Adherence: Supervisor Assessment of Therapist Adherence to Content
- Therapist Adherence: Therapist Self-Assessment of Adherence to Content
- Fidelity to Content: Participants rate fidelity to content
- Program Satisfaction: Participants rate interest, pace of delivery, and relevance of workshop goals with global and specific satisfaction ratings
- Participant Skills Self-Rating: Knowledge of core skills/key therapeutic ingredients
- Connectedness to VA services measure: Participants rate perceptions of engagement to treatment and VA

Therapist adherence to each intervention (STEP-Home and PCGT) will be rated by a supervisor. Therapists will be informed of these adherence ratings during training. Treatment adherence is an essential element of RCT design and these ratings will be required for all therapists.

Table 9. Assessment by Domain Domain	Screening	T1 Baseline 0 weeks	T2 Skills check 4 weeks	T3 Skills check 8 weeks	T4 Post-Intervention 12 weeks	T5 Follow up 24 weeks
Baseline Characteristics						
Demographics	X					
Deployment data	X					
Active problems/diagnoses	X	X			X	X
Medication list	X	X			X	X
Health utilization data	X	X			X	X
WTAR	X					
Primary Outcomes						
M2CQ	X	X			X	X
PDRI	X	X			X	X
STAXI-2	X	X			X	X
Core Skills/Key Ingredients						
PSI		X	X	X	X	X
DERS		X	X	X	X	X
ARCES		X	X	X	X	X
Secondary Outcomes						
Mental Health						
PCL		X			X	X
DASS-21		X			X	X
NSI		X			X	X
Functional/Vocational						
WHODAS-2.0		X			X	X
SWLS		X			X	X
Treatment/Activities Survey						
BESI		X			X	X
Average hours worked		X			X	X
Cognitive Outcome						
FrSBe		X			X	X
Feasibility & Program Satisfaction		X	X	X	X	X

Analytic Plan & Power Analysis

** Analytic Plan & Power calculations may include references to the full study sample, including Phase 2 recruitment at site 2 (Houston).*

**The February 2023 project modification/1-year extension requested funds to complete Cohort 19 (ongoing at the time of the project modification request) and enroll one additional cohort (Cohort 20) to ensure sufficient power for Aim 1 (Hypotheses 1A, 1B) and Aim 2, and to support final data analysis and manuscript submission in the last 6 months of the 1-year cost extension (October 2023 – March 2024). Of note, the study's Aims, listed below, remain unchanged with the project modification. The only changes involve an increase in our targeted enrollment number, to ensure sufficient power, as enrollment and measures completion rates to date are slighty under our original goals.

Data Management. Data entered in the database will be verified and quality assurance procedures will be followed; Human Subjects (*Accuracy/ Integrity of Data*); Data management plan ("09_VA_DMAP").

For continuous variables, the mean, median, standard deviation, minimum, maximum, interquartile range, and sample size for each intervention group will be reported at each time point. For categorical variables the frequency distribution will be reported for each treatment group.

Baseline Comparability. While no substantial differences between intervention groups are anticipated given randomization, we will use summary statistics, graphical techniques such as boxplots, and univariate analyses to compare baseline characteristics of groups. Pre-intervention values will be compared between

STEP-Home and PCGT groups using t-tests and chi-squared tests, as appropriate, to determine if the groups are balanced with respect to baseline characteristics. This comparison will allow us to identify potential confounders and moderators to be included in multivariate analyses. Clinical covariates include: age; education; diagnosis of TBI history; PTSD, mood disorder, anxiety, substance use, chronic pain, sleep quality.

Statistical Methods by Research Aims. The primary analysis for each aim will use an intent-to-treat (ITT) approach (i.e., all randomized subjects will be used in the analysis). ITT is optimal since it provides the least biased estimate of the treatment effect and the randomization balances STEP-Home and PCGT groups on known and unknown baseline confounders. This approach is appropriate for the proposed study given an anticipated low attrition rate of ~17% (based on attrition rates observed in our SPiRE study and Mt. Sinai's STEP RCT). We will implement quality assurance procedures to minimize protocol deviations and ensure correct treatment assignment according to the randomization. As a sensitivity analysis, we will conduct a per-protocol analysis in the subset of participants who complete an adequate amount of treatment (≥80% of weekly sessions). We will assess the assumptions of homogeneity of variance and normality of residuals for each regression model and apply an appropriate transformation of the outcome if needed. We will address missing data, under the assumption of missing at random, using multiple imputation. Any subject characteristics associated with both the treatment group and primary outcome measure will be adjusted for in the final statistical model as specified in each aim.

Aim 1. Examine treatment effects of STEP-Home on primary outcomes relative to PCGT:

Hypothesis 1A. Participants randomized into the STEP-Home intervention will show improvement on reintegration, readjustment, and anger post-intervention (expressed by lower scores; less difficulty).

Military to Civilian Questionnaire (M2CQ), Post-Deployment Readjustment Inventory (PDRI), and State-Trait Anger Expression Inventory (STAXI-2) scores post-intervention (T4) < baseline (T1)

Statistical Methods: Paired t-tests will evaluate the difference between pre- (T1) and post-scores (T4), with a separate analysis for each primary outcome.

Hypothesis 1B. Participants randomized into STEP-Home will show greater improvement in primary outcomes as compared to PCGT.

1B.1: Change scores baseline (T1) to post-intervention (T4) STEP-Home > PCGT

1B.2: Post-intervention (T4) primary outcome scores STEP-Home < PCGT

Statistical Methods: Mixed models (PROC MIXED in SAS) will evaluate pre-post differences, with a separate model for each primary outcome. The Satterwaite option will be used to account for the clustering of subjects within cohorts (identified in Section 6.2) and calculate degrees of freedom accounting for any missing data. Group (STEP-Home/PCGT) will be the between-subjects factor and time-point (T1/T4) will be the within-subjects factor. We hypothesize that there will be a significant interaction between group and time-point, with a larger improvement between pre- (T1) and post-scores (T4) in STEP-Home than PCGT. While we do not anticipate a significant interaction by cohort or site, we will evaluate the 4-way interaction and all 2-way and 3-way interactions for time-point, group, cohort, and site. The model will be rerun removing any non-significant interactions. Linear regression will be used to evaluate the difference in post-intervention (T4) by group. The final mixed and regression models for each outcome will adjust for any identified confounders.

Aim 2. Examine maintenance of treatment effects on primary outcomes:

Hypothesis 2: Treatment effects will be maintained at follow up in both groups.

Differential treatment effect of STEP-Home over PCGT T4 will be maintained at T5

Statistical Methods: Mixed models, as described under Hypothesis 1B. We hypothesize that there will not be a significant interaction between group and time-point but the main effect of group will remain significant. Since subjects may initiate behavioral therapy post-intervention, we will conduct a secondary analysis to evaluate the impact of additional psychotherapy on the treatment effects. We will stratify by group and post-intervention therapy status (therapy/no therapy) and examine paired t-tests within each of the 4 strata.

Exploratory Aim 1. Explore treatment effects of STEP-Home on measures of mental health, functional and vocational status and cognitive secondary outcomes targeted indirectly in the workshop.

Statistical Methods: Paired t-tests and mixed models, as described in Primary Aims 1 and 2.

Exploratory Aim 2. Acquisition of core skills (problem solving, emotional regulation, attention training) will mediate the effect of treatment on the primary outcomes post-intervention and follow up.

Veterans demonstrating greater acquisition of core skills will evidence greater improvement in reintegration, readjustment, and anger post-intervention (T4) and at follow up (T5).

Statistical Methods: Exploratory mediation analyses will evaluate the potential causal pathway between treatment allocation and each primary outcome, with the core skills as mediators, using the SAS *mediation*

macro developed by Valeri and VanderWeele [88]. We will run separate mediation analyses for each primary outcome and with each core skill (PS, ER, AT) as the mediator. We will evaluate acquisition of skills at two separate times during intervention (T2 and T3) as mediating the effect of treatment on post-intervention (T4). We will also examine skill acquisition at post-intervention (T4) as mediating the effect of treatment at follow up (T5). The mediation analysis will fit two models: (1) linear regression with the primary outcome as the dependent variable, group as the independent variable, and the mediator as a covariate and (2) linear regression with the mediator as the dependent variable and group as the independent variable. Both models adjust for any identified group-outcome and mediator-outcome confounders. The direct and indirect (mediating) effects are calculated from the beta coefficients of these two models and the 95% confidence intervals calculated using bootstrap (1000 replications). We will conduct a secondary analysis to evaluate the impact of any behavioral therapy initiated post-intervention for the post-intervention mediation analysis (i.e. core skills mediating effect T4 - T5), stratifying by post-intervention therapy status (therapy/no therapy).

Power Analysis. Power calculations are made for the full study, including Phase 2 recruitment at site 2 (Houston). Power calculations were conducted on the primary aims (Aims 1 and 2) to observe an effect of Cohen's *d*=0.44 or larger at one-tailed p<.05 and ≥80% power. We selected a one-tailed p-value because all primary hypotheses were stated *a priori* as one-sided. We anticipated a small to medium effect size based on the Cohen's *d*=0.44 observed in the subset of our SPiRE feasibility study (n=35) who reported at least some difficulty on M2CQ, WHODAS, or Impulsive Aggression Scale (IAS). While we did not specifically collect pilot data on the PDRI or STAXI-2, we assume the effect size will be at least as strong as *d*=0.44 observed on the proxy measures (WHODAS and IAS) since the PDRI and STAXI-2 are more sensitive and specific to post-9/11 Veterans. We further applied a conservative attrition rate of 20%, based on the attrition observed in our SPiRE feasibility study [1] and in Mt. Sinai's STEP RCT [2]. The univariate paired t-tests evaluating the improvement (Hypothesis 1A) and post-intervention maintenance (Hypothesis 2) of primary outcomes scores within the intervention groups required a total sample size of 83 after accounting for attrition. For Hypotheses 1B, the sample size was further adjusted to account for the clustering of subjects within the randomization cohort by applying an inflation of variance factor [71,89]. We used an interclass correlation of *r*=0.04 as observed in a similarly designed group therapy RCT [65]. For the univariate post-intervention and change score analyses, we would need a total sample size of 208 after accounting for clustering and attrition. Thus, a total sample size of 208 is sufficient to power both primary aims.

Potential Risks

Potential Risks: Overall, this study poses low risks to the subjects. There is an extensive literature, which describes experimental techniques similar to those used in the proposed study, which indicates that these paradigms pose limited risks to subjects. No deception is involved in any of the examinations or interventions, and subjects are fully debriefed before leaving the study. During the self-report questionnaires, outcome measurement, and the intervention, subjects may become anxious or fatigued. Some people may become mildly uncomfortable about being asked about their medical, psychological, or vocational history. While the psychological interventions can be associated with emotional distress, every effort will be made by the study staff to make the process as comfortable as possible; distressed participants will be followed up with to determine if further treatment is needed. Subjects will be made aware throughout the workshop that they are free to discontinue their participation at any time.

STEP-Home & PCGT Intervention/Workshop: Previous research shows that cognitive behavioral interventions are effective at decreasing psychological and cognitive complaints. The cognitive intervention Short Term Executive Plus (STEP), selected by this proposal, is currently considered to be an effective form of cognitive behavioral therapy for TBI and has been demonstrated to adapt well and be tolerable to the OEF/OIF participant group in our previous SPiRE award. Present Centered Group Therapy (PCGT), selected for the active control arm for this proposal, is considered to be an effective alternative supportive treatment for PTSD for those unable to tolerate trauma-focused interventions. We are mindful that discussing psychological symptoms, vocational issues, and life stressors can sometimes increase anxiety.

Adequacy of Protection Against Risks

Recruitment and Informed Consent: Recruitment and consent procedures follow VA and HIPAA regulations. In keeping with the human studies regulations of the institutions involved, before participating in testing, participants will have the nature of the experimental design explained to them. The non-clinical (research-based intervention) nature of the testing will be made clear. Participants will be given relevant consent forms to review and sign. The form(s) will be reviewed point-by-point with the potential subject by one of the research staff members before the subject's signature is requested.

Protection Against Risk:
Questionnaires: Participants will be informed that if they do not wish to answer specific questions or wish to terminate the session, they will be able to do so.
Intervention/Workshop: Participants distressed by any increase in symptoms during STEP-Home or PCGT will be asked to notify the researchers so that additional support can be provided. It is also possible that STEP-Home and/or PCGT will not help improve symptoms. A licensed psychologist or psychiatrist will be available during all group and individual sessions. If a participant becomes a safety risk to him/herself or others during participation in this study, he/she will be referred to a psychiatric emergency room for further evaluation. All STEP-Home and PCGT sessions will be conducted during regular VA hours to ensure that Urgent Care Services are available if required.

Confidentiality: All copies of records and behavioral outcomes will be stripped of identifying information and then coded. The codes will be kept in a locked safe or a password-protected database in an encrypted computer behind the VA firewall. Only key laboratory personnel will know the code. All computer files or printed data used for analysis will also be de-identified. Participants' confidentiality will be protected by never associating a subject's name with results in any published or otherwise publicly presented report.

Data Safety Monitoring Board (DSMB)

STEP-Home established a Data Safety Monitoring Board (DSMB) and standard operating procedures (SOP) of the DSMB in early 2020. The DSMB is comprised of individuals from outside of our research laboratory (TRACTS) with expertise in the patient population and disorders being studied in this trial (e.g., Veterans, PTSD, TBI), the conduct and methodology of clinical trials, and biostatistics/epidemiology; the DSMB members are Suzanne Pineles, Brian Smith, and Jennifer Wachen, all of whom are VA Boston staff.

Items reviewed by the DSMB include the following:

- -Adverse events (AE) and unanticipated problems (UP)
- -Data quality and completeness
- -Performance of individual centers/sites (e.g., Boston –Years 1 - 5 and Houston – Years 3 - 5)
- -Compliance with recruitment and retention goals
- -Protocol adherence
- -External factors that may influence study ethics or patient safety

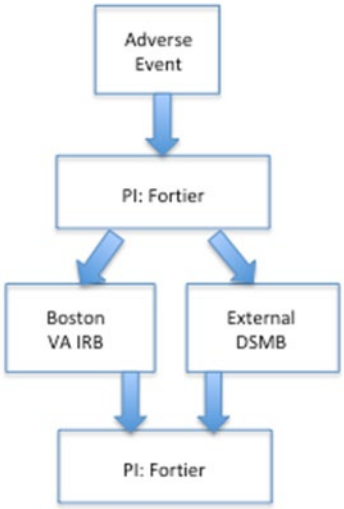
DSMB will also review all AE's and UP's within 5 working days from learning of the event/problem. Below please find a schematic that illustrates AE reporting procedures.

To date (March 1, 2023), the DSMB has held meetings on the following dates:
March 3, 2020
March 22, 2021
March 21, 2022
The fourth annual DSMB meeting will be held in the spring of 2023.
Reports from each of these annual meetings have been submitted to and acknowledged by IRB.

Adverse Event Reporting

The study PI and staff will promptly notify the IRB and DSMB of any adverse events or unanticipated problems; the required forms will be submitted no later than 5 working days from learning of the event/problem. All severe adverse events will be reported to the IRB consistent with VA's requirements. If a determination about

continued subject participation cannot be made according to the criteria defined above for adverse event reporting by the PI, then the adverse event report will be faxed to the chair of the Data and Safety Monitoring Board (DSMB), who will make a decision along with members of the Board.



Potential Benefits of the Proposed Research to the Participants and to Others

This study is being performed to advance medical knowledge. While it is expected that most participants may experience some clinical benefit from participation in the treatment, we cannot guarantee any direct benefit will accrue to study participants. However, given that this study will evaluate the effects of a known standard clinical therapy, the known risks are reasonable in relation to the general knowledge and potential clinical benefit for Veterans that will be gained to ultimately help others. Although direct clinical benefit to the participants remains theoretical, participants have often enjoyed participating in medical research in general in the past and have enjoyed the opportunity for contact with other post-9/11 Veterans and research staff members.

Importance of the Knowledge to be Gained

Identifying and treating specific factors that contribute to community reintegration difficulties after serving our country in a warzone is of utmost importance in providing adequate care to our Veterans. The identified risks noted in this study are reasonable in relation to the general knowledge that will be gained and that may ultimately help many Veterans.

Data Security

All outcomes are psychometrically sound, widely used instruments. The manual and therapist training workshops will be created for consistent administration, inter-therapist reliability, and adherence to the STEP-Home and PCGT interventions in this proposed study. Training includes direct observation, audiotaping, and participation in weekly supervision and treatment adherence meetings.

All questionnaires will be completed using Qualtrics on a VA-approved iPad or a VA laptop, or non-VA, non-networked computer. Qualtrics is a platform used to administer surveys/questionnaires by organizations and researchers nationwide, including VA medical centers, and has secure transmission services that meet all federal requirements. If questionnaires are completed off-site, non-VA, non-networked computers will be used using the secure Qualtrics link sent in MyHealtheVet or via postal mail service. Qualtrics has a secure offline app to use for data collection; the data collected are transferred to the Qualtrics secure server using a VA OIT issued encryped wireless hotspot. Data collected on VA and non-VA devices will be transmitted with research codes only. No personally identifiable data will be transmitted. Access to data will be limited to authorized study personnel via login to a secure site. The information collected in Qualtrics will have a backup copy stored on the Qualtrics server. The statistician manages the data entry and monitors the quality assurance

procedures developed at TRACTS. Additionally, the statistician uses statistical software (SAS) for additional quality assurance and creates the final analytic database used for analyses. There is an exisiting contract between TRACTS and Qualtrics that this STEP-Home study will also be able to use.

The link between the research code and the participant's identity will be stored in a separate file maintained on a separate secure, password-protected VA computer drive or in a locked file in a locked room accessible only to authorized research staff. All paper records will be stored in a locked filing cabinet behind a locked door. The signed informed consent form and HIPAA authorization form will be stored in a separate location from the participant study data. All locked cabinets are only accessible by approved study staff. The key is kept in a safe behind a locked door, with only a limited number of staff with access to the safe. These staff will verify the staff member requesting access to the locked cabinet are currently on the study protocol and will maintain a log of each access request.

All electronic databases related to the study will be stored on double-password protected servers behind a firewall. The TRACTS computer system is accessed via desktop computers situated in TRACTS offices in VA Boston Healthcare System that conform to all VA OIT directives. The desktop computers require authentication for access and these computers are assigned to authorized staff only. User accounts are promptly disabled and deleted for unauthorized staff who are no longer affiliated with projects for which access to the server is necessary. Access to the data server will be gained only through request of the PI to the network systems administrator, and with the consent of the TRACTS Director. Access may only occur through PCs requiring unique user identification code and an individually unique password. User identification codes limit access to specific directories and files. The accounts and passwords comply with existing VA policies and procedures for computer access. Only approved VA personnel assigned to be on the study who are research credentialed and are up to date with all the required VA training will be allowed to be on the study. All study personnel must be approved by the VABHS IRB and R&D committee to be on the study team.

In the event that the users of the data covered by this agreement loses confidential or Privacy-protected data, or the data is stolen or removed from designated locations, or used or disclosed for purposes other than outlined in this agreement, the custodian must report the incident immediately upon discovery of the incident to the ISO, Privacy Officer, and to the employee's/other user's immediate supervisor. Senior management should be informed immediately by the supervisor, who will further inform those in the chain of command. Incidents internal to VA must be reported to the VA-SOC within one hour of the report of the incident. The incidents should be reported to the VA-SOC via the Information Security Officer (ISO) or designee, and entered into the Privacy Violation Tracking System (PVTS) by the Privacy Officer. In turn VA at the department-level will report to the US-CERT the information regarding the incident reported to the VA-SOC and in PVTS within the hour timeframe. A distribution list (VHA REPORTS TO US-CERT) has been established for use by the facility ISO in reporting all incidents involving personally identifiable information via Exchange, and includes the key VHA representatives that need to be notified as well as the VA-SOC Manager and key VA-SOC representatives.

When study personnel are no longer part of the research team, they will be removed from the IRB list of study staff and will not have access to data files.

Data will be destroyed at the end of the study in accordance with VA data destruction policies.

5. Resources

Research Space

This study will be conducted within the scientific environment and infrastructure of the ***Translational Research Center for TBI and Stress Related Disorders (TRACTS) National Research Center (Boston and Houston sites).***

Clinical (at *VABHS, Boston MA*): The following documents our approximately 2200 square feet of laboratory space available at the Geriatric Research, Education, and Clinical Center (GRECC) and the Translational

Research Center for TBI and Stress Disorders (TRACTS) at the VA Boston Healthcare System, Jamaica Plain Campus, which is the primary location where the work proposed will take place. This space includes behavioral and medical testing rooms, computer laboratories, and workrooms. The space currently consists of four testing rooms that can be used for individual sessions. One of these testing rooms is connected to an office/instrumentation room by a two way mirror to enable observation. Another laboratory room is fully equipped for medical examinations and phlebotomy. A conference room is available within the VA Boston Healthcare System for use for Group Intervention sessions.

Computers: Both Macintosh and PC platforms are available to STEP-Home for word processing, statistical analysis, image processing, and bibliography management. A document scanner, inkjet and laser printers, photo and slide scanner, video camera, and all necessary software for statistical, graphical and word processing are available. The clinical laboratory hosts a local area network with 30 advanced Macintosh and Linux based computing systems with peripherals for printing, scanning, faxing and other operations. The laboratory hosts an extensive software library to support most aspects of psychological research including task design, paradigm presentation, statistical analysis, and MRI data processing. Additional software for manuscript preparation includes the Microsoft Office and Adobe Master software suites. The computing network is connected via four layer 3 Netgear managed gigabit switches, allowing for rapid access to shared network resources that include three servers with dual quad core Intel Xeon processors, 15 TB's of dedicated RAID storage, an Exabyte 48 slot tape back up system, and several high volume production level printers.

Offices: TRACTS has office space at the VA Boston Healthcare System, a data processing laboratory for research assistants, students, and postdoctoral fellows, as well as the MRI suite that houses the MRI scanner, patient/participant waiting room, and additional supportive facilities.

PRIVACY, CONFIDENTIALITY AND INFORMATION SECURITY IN RESEARCH INFORMATION

Q2. All information will be protected in accordance with the VA Boston, and HIPAA regulations. Information about subjects or families will not leave the institution in any form that would identify individual subjects or families. Data will be transmitted only in pooled form and/or subjects identified by code. All information will be kept in locked cabinets accessible only to study staff and on password and security protected network computers. Original electronic VA data will be backed up regularly and stored behind the VA firewall. Data will be securely transmitted using VA approved methods. We will use FIPS 140-2 validated encryption. Suspected information security and privacy incidents will be reported to the Information Security and Privacy Officers and Research Administration.

Q3. All data will be coded and subjects will not be identified by PHI in any publications or presentations.

Q4. Individually identifiable health information is necessary to participate in this study. This information will be accessible to the Principal Investigator (PI) and study staff. Participants will not have access to their own research related health records. The authorization to use participants' information will not expire, but revocation of authorization is possible. Information collected for the purpose of this research study will be kept confidential as required by law. The results of this study may be published for scientific purposes, but individual records will not be revealed unless required by law. All information will be protected in accordance with the VA Boston, and HIPAA regulations. Information about subjects or families will not leave the institution in any form that would identify individual subjects or families. This policy is also detailed in the IRB approved consent form.

Q5-Q15. Please see Authorization for Use and Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research form (HIPAA Authorization).

Q16-Q20. Please see Application for Waiver of HIPAA Authorization for Research Purposes.

Q21-22. N/A

Q24. Software packages including FSL and SPSS will be used in this study and are currently available for study use.

Q25. Questionnaires and teleforms may be completed on paper or on an iPad that is non-networked at the time of test administration using Qualtrics. Qualtrics is a platform used to administer surveys/questionnaires by organizations and researchers nationwide, including VA medical centers. The questionnaire and teleform data collected by Qualtrics will be coded and not include the patient's name, social security number, phone, address, or DOB. The key to the code is stored in a separate file behind the VA firewall. The information collected in Qualtrics is temporarily stored by the Qualtrics server and then transferred and stored behind the VA firewall. Once given an IRB number, we will establish a specific folder on the secure VA network to store the data (i.e. \\VHAVHSNAS21\TRACTS\IRB # 2354). Qualtrics uses very high standards to protect the data. Qualtrics has secure transmission services that meet all federal requirements. Access to data is limited to authorized study personnel via login to a secure site. The original data on the Qualtrics server will be deleted after it is transferred to the VA server.

Q26. Data will be collected directly from participants before being securely stored. All information will be kept in locked cabinets accessible only to study staff and on password and security protected network computers. Relevant data (clinical information) may be imported from databases noted in the protocol. Data will be transmitted only in pooled form and/or data will be coded. Data will be securely transmitted using VA approved methods. We will use FIPS 140-2 validated encryption.

Q27. Paper forms containing identifiable data are separated from the study data and kept in a locked file cabinet in an office that is locked when not occupied. Study staff maintain the only list linking subject identifiers to subject numbers. Electronic data are stored on an encrypted password protected server.

Q28. Data will not be stored on a PC hard drive.

Q29. All mobile/portable devices and media will be protected with VA approved FIPS 140-2 compliant technology. Laptops are secured in locked offices when not in use. Mobile storage devices will not contain the only copy of research information.

Q30. Paper files will be stored in locked areas and cabinets in the TRACTS offices (11th floor C- and D-wings (D11-132, D11-89, D11-86, A11-1A, C11-13, C11-13A, C11-11, C11-35), Jamaica Plain Campus, accessible only to study staff. Laptops are secured in locked offices when not in use. Electronic data are to be stored on the secure research drive of a VA network server. These servers are located on the 3rd floor Server Room (JP campus).

Q31. Data will not be removed from the VA protected environment at any time.

Q32. N/A

Q33. Data will be transmitted only in pooled form and/or subjects identified by a code. Data will be securely transmitted using VA approved methods. We will use FIPS 140-2 validated encryption.

Q34. Mobile storage devices will not contain the only copy of research information. Original electronic VA data will be backed up regularly and stored behind VA firewall.

Q35. In the unlikely scenario that sensitive research data must be shipped off-site, it will be encrypted with FIPS 140-2 validated encryption if it is electronic and will be sent via delivery service with a chain of custody.

Q36. N/A

Q37. Data will be kept indefinitely or until the law allows their destruction in accordance with the VA Record Control Schedule (www1.va.gov/VHAPUBLICATIONS/RCS10/rcs10-1.pdf). Records will be destroyed, when allowed, in the following manner).

- Paper records will be shredded
- Electronic records will be destroyed in a manner in which they cannot be retrieved.
- Digital images (photographs, x-rays, scans, video/audio recordings, etc) will be destroyed in a manner in which they cannot be retrieved.
- Audio/visual recordings on tape and/or printed photographs will be shredded.

Q38. Once study team members are no longer a part of the research team, their access to data and research materials will be terminated.

Q39. Suspected information security and privacy incidents will be reported within one hour to the Information Security and Privacy Officers and Research Administration.

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