Study Protocol

Improving Veteran Adherence to Treatment for PTSD Through Partnering with Families

Funding Agency: VA HSR&D

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Tool Revision History

Version number 1
Version date: December 5, 2016
Initial protocol version first submitted to CIRB for project PI/SC.

Version number 2
Version date: May 9, 2017
Summary of revisions made: Final project PI/SC submission to CIRB after reviewer response and feedback.

Version number 3
Version date: November 6, 2017
Summary of revisions made: Amendment 1; Added an option that an off-team staff member or referring provider can provide a Veteran with a study brochure and ask the Veteran if he/she wants to be called about the research study. Study staff can be notified via CPRS consult or encrypted email. Staff will then contact Veteran within 48 hours of referral.

Version number 4
Version date: December 1, 2017
Summary of revisions made: Amendment 2; Updated our study procedures to administer Baseline and Posttest diagnostic structured clinical interviews to up to ten IC cases.

Version number 5
Version date: January 16, 2018
Summary of revisions made: Amendment 3; 1) Requiring Veterans and SPs to complete a baseline survey assessment before they can be randomized to a study arm. Failure to complete the baseline survey will result in study ineligibility. 2) Defined treatment dropout. Participants missing more than 6 consecutive weeks of treatment sessions will be considered treatment dropouts. These participants will then be referred to the clinic for treatment outside of the study. 3) Risk issues disclosed by participants to study staff will be forwarded to treating clinician with Co-I/PI as back up. 4) Added 3 month follow-up survey. 5) The posttreatment assessment will be given 16 weeks after the Veteran completes session 1 (versus 16 weeks after baseline assessment as specified in the prior IRB proposal). 6) Modify/update the measures and items used in our baseline, weekly, and posttest survey questionnaires for the RCT phase. 7) Changed that participants are given their first weekly survey at week 2. 8) Revised the schedule of when weekly assessments were given. For the RCT phase, Veterans and SPs will be given surveys during weeks 2, 4, 5, 6, 8, 10 and 12 of treatment and will be compensated $10 for completing each survey. Veteran assessments on Weeks 2 and 8 will be comparative longer (i.e., about twice as long), so payments will be $20 for these assessments. 9) Modify the incentive amounts given to participants for completing the baseline and posttest surveys. We increased posttreatment survey compensation to $40 and baseline to $20. 10) Added brochures for Veterans and SPs.

Version number 6
Version date: February 21, 2018
Summary of revisions made: Amendment 4; 1) Eliminate psychiatric medication stability as an eligibility criterion for patients entering the study. Patients were excluded if they have had a change in psychotropic medication in the 1 month prior to treatment. We dropped this exclusion criterion. 2) Modify our informed consent forms and support person information sheets to eliminate the statement “We will also obtain a Certificate of Confidentiality, which helps researchers protect the privacy of participants by protecting them from requirements to comply with legal proceedings, such as court orders and subpoenas.

Version number 7
Version date: May 1, 2018
Summary of revisions made: Amendment 5; 1) Added an exclusion criteria-- inability to participate in treatment due to a medical condition (not mental health-related). 2) Communicate the diagnostic clinical assessment results of ineligible subjects back to the treatment team (non-study clinical staff) for purposes of patient

treatment planning and continuity of care. This will be proposed to participants during informed consent, and patients will have the ability to decline this request. 3) Added the ability to recruit participants from CBOCs and offer to provide the treatment within the study by telemedicine. The telemedicine option would use VA approved electronic communication methods and information technology to provide Prolonged Exposure therapy to patients by study clinicians. 4) Defining the Posttreatment assessments in the protocol. For RCT phase, structured clinical interviews will take place at Baseline (week 0) and posttest (within 4 weeks of final session). Self reports/surveys will take place at Baseline (during week 0) and at posttreatment (during final session). For drop out Veteran participants, posttest surveys will be completed 16 weeks post-session 1 and the posttreatment clinical assessment will be done within 4 weeks of that posttest survey. For late treatment completers (i.e., treatment takes more than 16 weeks), all posttest surveys and post clinical interviews will be delayed but will be done no later than 24 weeks post-session 1.

Version number 8
Version date: September 25, 2018
Summary of revisions made: Amendment 7; 1) Added a letter that will be sent in the mail with Veteran and support person weekly surveys reminding them to complete the survey and mail back to the VA. 2) Added a final contact letter that will be sent as one final outreach to Veterans who had expressed interest in study participation. 3) Added a VA telehealth video-to-home option for study treatment allowing participants to receive Prolonged Exposure therapy in their own homes. 4) Submitted a waiver of documentation of informed consent to conduct informed consent verbally over the phone with Veteran participants. 5) Altered the intimate partner violence questionnaire for better precision in assessment. 6) Replaced the PC-PTSD-5 measure with the PCL for support person's when initially screened for PTSD. 7) Now allow subjects with an 'initiation of a new active psychotherapy in the past 2 months' AND 'a successful completion of PE in the last 6 months' to enter the study. 8) Added the ability to use MyHealtheVet secure messaging technology in our study communications with participants. 9) Added the ability to provide childcare costs during therapy visits for participants in the study.

Version number 9
Version date: May 24, 2019
Summary of revisions made: Amendment 8; 1) Added letters that will be sent in the mail with Veteran and support person post-treatment and 3 month follow-up surveys reminding them to complete the survey and mail back to the VA. There will be 3 separate survey package mailings in an effort to optimize response rates. 2) Added a postcard reminder that will be sent in the mail to remind participants to complete their posttreatment and 3 month follow-up surveys that were sent to them prior. 3) Added a reminder letter for clinical assessments. 4) Modifed the incentive amounts given to participants for completing the posttest surveys, the 3 month follow-up surveys, the post clinical assessment, and the qualitative interview. 5) Changed the IPV eligibility criteria. If a Veteran participant is the victim of relationship violence (rather than the primary aggressor), they will be permitted to select an alternative SP on a case-by-case basis. Our prior criteria deemed participants ineligible for any indication of moderate IPV within the screening and baseline survey responses. We would like to modify the criteria to permit Veteran victims to remain eligible, based on Investigator determination.

Version number 10
Version date: November 5, 2019
Summary of revisions made: Amendment 9; 1) Increased the number of approved enrolled participants for the study. 2) Added more versions of study brochures. 3) Increase incentives for baseline surveys. 4) Changed the language in our recruitment letters to Veterans. Currently, our proactive recruitment letter states, "We have your contact information because you were recently seen at the Minneapolis VA Health Care System for trauma or military-related concerns." We would like to modify that statement to say "We are reaching out to Veterans who receive care at the SITE VA." 5) Modifed our recruitment scripts and consent documents for better clarity. 6) Added letters that will be sent in the mail with Veteran and support person 2nd and 3rd baselines surveys reminding them to complete the survey and mail back to the VA. We also are requesting to add a reminder postcard. 7) Begin reviewing PCL-5 scores, when available, to screen out Veterans without significant PTSD symptoms prior to completing structured clinical interviews. A Veteran must have a PCL

score of at least 28 or higher to move forward in the study. If the Veteran's PCL score is less than 28, they will be ineligible to continue. This change is to ensure that Veteran participants are a good fit for a trauma focused therapy.

Version number 11
Version date: January 7, 2020
Summary of revisions made: Amendment 10; 1) Modifed our baseline assessment protocol to require participants to retake the baseline survey and baseline clinical interview if their therapy start date would occur 2 months after their baseline data was collected. 2) Added a letter to be sent in the mail with baseline surveys that need to be retaken by participants.

Version number 12
Version date: March 4, 2020
Summary of revisions made: Amendment 11; 1) Change inclusion/exclusion criteria to reflect: Excluding Veterans who are homicidal or suicidal in the last 30 days and excluding Veterans with a past history of multiple psychiatric hospitalizations and/or a psychiatric hospitalization in the last 30 days. 2) If a participant completes their survey before consent, this will not be immediately reportable to CIRB. Instead, staff will document this occurance in a spreadsheet to be given to CIRB at continuing review. Staff will then be required to get consent from the participant within 30 days of receiving the baseline survey. If consent is not obtained within the 30 day window, the deviation is immediately reportable to CIRB and staff will complete a protocol deviation.

Version number 13
Version date: April 1, 2020
Summary of revisions made: Amendment 12; 1) Changes to risk: All surveys will be screened upon receipt by study staff. If a psychiatric emergency is reported on surveys (i.e., expression of risk for suicide or homicide), a number of steps will be taken. The patient's treating clinician will be notified and the disclosing participant will be contacted by phone, assessed for risk and safety, and provided with appropriate referrals. We anticipate in this population of participants that indications of suicidality and homicidality are chronic, common, and known to the clinician team. Specifically, study staff will check the final item of the PHQ-9 on all returned surveys. Staff will also read any text written into the survey for any concerns that the participant may be at risk to harm themselves or others or may be at risk to be harmed by someone else. In cases of low severity (subject endorsed "1" on PHQ-9), study staff will immediately notify the treating clinician and indicate that they can follow-up with the patient as clinically indicated. For more severe cases (subject endorsed a "2" or "3" on PHQ-9), a trained staff member will immediately reach out to the participant and assess them for risk and safety and provide them with appropriate resources. Staff will then notify the patient's treating clinician to inform them of the situation. 2) Modified the letters sent in the mail with study surveys to state "If you would like to discuss any of your survey responses further with a study staff member, please call." 3) Added a more precise item to more accurately identify those who need outreach after study surveys, which would help optimize the amount of outreach effort done by site PIs (when no VA MH provider is assigned or available). Add the two questions used in CSP 591 (comparative effectiveness trial comparing two psychotherapies for PTSD) to assess suicidal ideation; adapted from the Linehan BRTC SI screen.

Version number 14
Version date: June 8, 2020
Summary of revisions made: Amendment 13; 1) Added use of Qualtrics FedRAMP electronic survey for study surveys. 2) Added correspondence with study participants using email usage. 3) Added correspondence with study participants using VA cell phone, personal cell phone, or Doximity when study staff are teleworking. 4) Added use of alternative forms of VVC (formats approved by the VA). 5) Requiring patients be seen via telehealth when in-person treatment isn't available.

Version number 15
Version date: August 26, 2020

Summary of revisions made: Amendment 15; added follow-up emails to provide participants with the online survey link and personal code, and revised follow-up letters to include survey URL and code.

Version number 16
Version date: September 7, 2021
Summary of revisions made: Amendment 16; adding information regarding teleform surveys being mailed from Atlanta site to main site in Mpls MN.

Abstract

Impacts. This study aims to improve Veterans' adherence to evidence-based treatment for PTSD, through increasing family support for treatment. Improving retention rates in evidence-based PTSD treatment will positively impact Veterans' health and well-being, lower the cost of treating PTSD, and decrease long-term demand for PTSD services. If effective, this approach could help resolve national calls for routine inclusion of family involvement in PTSD treatment. Once demonstrated for PTSD, these strategies could be utilized for other conditions and problems relevant to Veteran populations (e.g., suicide prevention, TBI rehabilitation) and stimulate shifts across practice and policy to better routine and evidence-based involvement of families in care.

Background. PTSD occurs in as many as 1 in 5 combat Veterans and is associated with a host of negative, long-term consequences to the individual, their families, and society at large. Evidence-based psychotherapies, such as Prolonged Exposure (PE), result in clinically significant symptom relief for many. Yet, adherence to these treatments (i.e., session attendance and homework compliance), which is vital to ensuring recovery, can be poor. Engaging families in Veterans' treatment may provide a powerful method for promoting EBP adherence. Our data indicate that 70% of Veterans express some interest in involving their family in their care for PTSD; yet, only 17% of providers have had any contact with Veterans' families. The objective of the proposed study is to evaluate the effectiveness of improving family support as a tool to improve Veterans' EBP adherence. This research agenda directly addresses two VA HSR&D priorities: 1) innovative mental health care; 2) improving the quality of life for Veterans and their caregivers. The work aligns with the VHA Blueprint for Excellence and Strategic Plan through meeting the unique needs of military-service disabled Veterans, providing a novel treatment approach, and emphasizing patient- and family-centered care.

Objectives/Aims.
Aim 1: To improve Veterans' adherence to PE through engaging families in care.
Aim 2: To improve the clinical outcomes of Veterans receiving PE through engaging families in care.
Aim 3: To examine barriers/facilitators of implementing family support for PE.
Exploratory Aim: To identify mechanisms underlying adherence differences between treatment conditions.

Methods. We are proposing a practical randomized controlled trial to compare Veteran adherence, and to PE with and without family attendance at PE's educational sessions, with the ultimate goal to improve Veterans' clinical outcomes. For Aim 3, we will use a concurrent process evaluation to identify potential implementation facilitators and barriers to family involvement in PE within VA. Participants will include Veterans with clinically significant symptoms of PTSD within VA across three sites, plus a family member or friend of the Veteran. Aim 1 outcome variables include session attendance and homework compliance. Aim 2 outcomes include PTSD symptom severity, depression, quality of life, and relationship functioning, measured over the course of treatment. Key social influences (Exploratory Aim) will be assessed through brief weekly self-reports.

List of Abbreviations

BSI	Brief Symptom Inventory
BFT	Behavioral Family Therapy
CAPS-5	Clinician-Administered PTSD Scale for DSM-5
CCDOR	Center for Chronic Disease Outcomes Research
CDA	Health Services Research and Development Career Development Award
CEQ-PTSD	Credibility/Expectancy Questionnaire, adapted for EBPs for PTSD
Co-I	Co-Investigator
Co-PI	Co-Principal Investigator
CPRS	Computerized Patient Record System
CPT	Cognitive Processing Therapy
CSQ-9	Client Evaluation of Services Questionnaire
CTS-2	Conflicts Tactics Scale-2
SF CTS-2	Short Form of the Conflicts Tactics Scale-2
EBP	Evidence Based Psychotherapy
FES	Family Environment Scale
HSR&D	Health Services Research and Development
IC	Intensive Coaching
IIR	Investigator-Initiated Research
IRB	Institutional Review Board
MI	Motivational Interviewing
OCD	Obsessive Compulsive Disorder
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OMHS	Office of Mental Health Services
PCL	Posttraumatic Stress Disorder Checklist (DSM-IV)
PCL-5	Posttraumatic Stress Disorder Checklist (DSM-5)
PE	Prolonged Exposure
PHQ-9	Patient Health Questionnaire
PI	Principal Investigator
PTSD	Posttraumatic Stress Disorder
QRI	Quality of Relationships Inventory
RCT	Randomized Controlled Trial
REACH	Reaching out to Educate and Assist Caring, Healthy Families
RTAP	rapid Turn-around Analytic aPproach
RRP	Rapid Response Project
SCID-5-CT	Clinical Trials Version of the Structured Clinical Interview for DSM-5
SORTS	Significant Others' Responses to Trauma Scale
SP	Support Person
VA	Veterans Affairs
VAHCS	Veterans Affairs Health Care System
VA-CRAFT	Community Reinforcement and Training for Veterans with substance use and
VHA	Veterans Health Administration
VISN	Veterans Integrated Service Network
WHOQOL	World Health Organization - Quality of Life, Brief

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2.0 Introduction

Post-traumatic stress disorder (PTSD) occurs in as many as 1 in 5 combat Veterans[15-17] and is associated with a host of negative, long-term consequences, including high rates of suicide and traumatic death.[47;48] Trauma-focused cognitive-behavioral therapies for PTSD, like Prolonged Exposure Therapy (PE), result in significant improvement for many patients.[22] While these proven psychotherapies have been disseminated in VA, poor adherence interferes with treatment response.[49;23] Previous reviews of treatment completion in randomized controlled trials find that one in five patients dropout from active, change-focused treatments for PTSD, including PE and Cognitive Processing Therapy (CPT).[26] Rates of PE/CPT drop out are even higher

among Veterans,[27-29;50;51] with estimates across studies converging around 35%.[27-29] Importantly, those with the greatest need for PTSD treatment are likely at the highest risk for premature termination.[23] Similar problems with tolerating treatment are found among cognitive behavioral therapies, broadly.[26] Consequently, adherence, in and of itself, was identified as a top priority for real-world use of Evidence-Based Practices (EBPs) by the World Health Organization, Institute of Medicine, and the US Surgeon General.[22;32-34]

PE addresses PTSD through confronting trauma memories to reduce fear, facilitate emotional processing, and promote new learning.[52] Disrupting entrenched patterns of avoiding trauma reminders requires persistence by Veterans, through daily trauma exposure exercises at home. While these exercises require considerable Veteran commitment, they are similar to those of other demonstrated, effective, cognitive-behavioral therapies,[53] and psychotherapies with homework are associated with better treatment outcomes.[25;54] Meta-analysis indicates 24% more patients will improve just from adding homework to a given psychotherapy.[54] Across multiple meta-analyses, compliance with these assignments predicts treatment response.[24;25;53;56;57] Additionally, adherence to more challenging homework assignments, like exposure exercises, predicts treatment response better than adherence to less difficult exercises (i.e., readings, self-monitoring).[55] Ultimately, the key for optimizing Veterans' gains from PE likely lies with efforts to maximize Veterans' engagement, through consistent attendance and homework compliance.

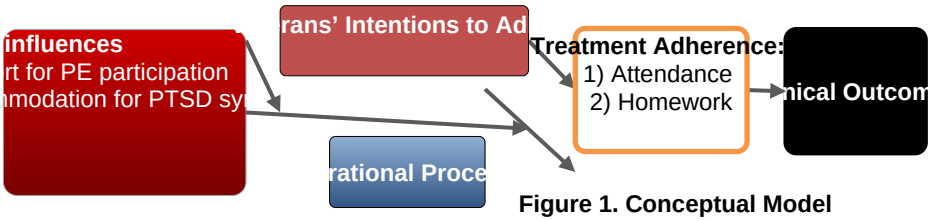


Figure 1. Conceptual Model Underlying Partner Supported PE

Optimizing adherence through improving family support for treatment provides one novel approach to this problem. Despite research demonstrating poor social support among Veterans with PTSD,[58] many Veterans with PTSD who seek treatment are living with an intimate partner[59] or have a close relationship with a non-romantic support person (a family member or close friend). These relationships play a critical role in influencing Veterans' treatment seeking.[60;61] Many Veterans are also highly motivated to involve support persons (SPs; intimate partners, blood-relatives, close friends) in their PTSD care.[62] For over a decade, national calls have persisted in their appeals for routine family involvement in PTSD treatment.[35-37;63] Devising systematic methods to engage SPs in EBPs for PTSD is responsive to this demand. Generally, family involved psychotherapies result in comparable or better outcomes than patient-only treatments for depression, substance use, bipolar disorder, schizophrenia, and panic disorder with agoraphobia.[64-66] For substance use, treatments that include families lead to consistently better outcomes and retention of gains than individually-oriented treatments.[65] Treatment adherence is infrequently a target of family involved interventions. However, better medication adherence has been found for family versus individual-only treatment for patients with bipolar disorder[67] and depression.[68] Relevant to PTSD treatment, recent data is particularly encouraging that supports a couple therapy for PTSD, using cognitive-behavioral techniques, similar to individually-oriented CPT.[39] Consistent with proposed strategies, VA PE trainings currently recommend encouraging Veterans to talk to their families about their treatment. These suggestions are informal, optional for providers, and untested. Engaging with families aligns with good clinical practice within PE but is in need of systematic evaluation. Of note, while increasing family support for adherence may be viable for both CPT and PE, this strategy may not look or work the same in both treatments. We began with PE as Veterans may find it more challenging, given some evidence drop out may be worse for PE than CPT.[51]

2.1. Conceptual Framework: Social Factors Affect Treatment Adherence

Drawing upon the Theory of Planned Behavior,[69] we propose that Veterans' adherence to PE (attendance and homework compliance) is predicted by Veterans' attitudes towards adherence, Veterans' perceptions of control over adherence (self-efficacy), and social norms promoting or discouraging PE participation (key social influences). Each of these factors can improve adherence by strengthening Veterans' behavioral intentions to

complete tasks or attend sessions. While the PE treatment protocol explicitly addresses Veterans' attitudes and self-efficacy through education, it does not explicitly address social influences.

Social influences are critical.[70] Prior qualitative and quantitative work by our team demonstrates SPs facilitate entry into mental health care for Veterans with PTSD, and highlights social influences are a central but underdeveloped predictor of adherence behavior.[60;61;71] Dr. Spoont (Co-I) and colleagues found the odds of initiating mental health care were 50% higher among Veterans with PTSD who were encouraged to seek help by friends and family (N=7,645).[61] Social influences within the Theory of Planned Behavior are most effective as predictors of behavioral intentions when defined by both what SPs believe Veterans should do (r = .44), such as beliefs supporting PE participation (See Figure 1), and what SPs *actually* do (r = .46), such as efforts, even well-intentioned, to accommodate for Veterans' symptoms of PTSD.[70] Accommodation refers to changes in SP behavior to prevent or reduce a Veteran's PTSD-related distress,[72] such as helping a Veteran avoid stressful trauma reminders and undermining PE participation. These behaviors can be interpreted as unspoken SP beliefs that approaching trauma reminders is dangerous, the Veteran cannot tolerate PE, or PE is not worth the Veteran's efforts. Accommodation predicts poor response to treatment for substance use (i.e., enabling behaviors)[73] and anxiety disorders.[10] Meta-analysis of family inclusive treatments for OCD found that interventions that focused on accommodative behaviors resulted in better treatment response.[10;11]

The Theory of Planned Behavior has been criticized for a focus on 'rational' decision making at the expense of non-rational processes, such as implicit cognitions (cognitive short cuts, like 'anxiety is bad'), immediate influences (including social network members), and emotional reactions.[74;75] Patients make day-to-day decisions about adherence that are influenced by non-rational processes.[74] PE providers have 1-2 formal sessions per week with Veterans; they are limited in their ability to address non-rational processes between sessions. Through altering social influences, we may mitigate negative influences of non-rational processes on decision making through helping SPs provide appropriate support when Veterans discuss feelings about the treatment or its tasks, increasing the frequency at which SPs encourage Veterans to persist in PE, and contributing to an environment that broadly supports change in Veterans' day-to-day lives. Ultimately, through optimal Veteran engagement in PE, we hope to maximize the gains that Veterans can achieve in treatment.

2.2 Strategies for Family Supported PE

2.2A. Structure of Standard PE.

The PE treatment protocol includes education, imaginal exposure (repeatedly imagining and describing a trauma memory to the provider), in vivo exposure homework (exposure to trauma reminders in real life), and listening to audio recordings of Veterans' trauma accounts between sessions (imaginal exposure homework).[52] The first sessions are largely educational. Imaginal exposure begins in Session 3. Due to the volume of material provided in Session 2, in VA care, it is frequently divided into two sessions: 2a (education on PTSD and avoidance; detailed rationale for in vivo exposure) and 2b (building a hierarchy of situations to approach at home; see Figure 2).

2.2B. Overview of Family Supported PE.

SPs will attend PE Sessions 1, 2a, and 2b; receive two check-in telephone calls; and be invited to elective in-person check-ins if indicated (see below). Dividing Session 2 into 2a and 2b allows for more time to discuss the content outlined below. Strategies for how to engage with families are drawn from existing evidence-based approaches. The goals for family engagement are to 1) educate SPs about how avoidance maintains PTSD, 2) facilitate discussion of how SPs encourage/discourage PE participation (accommodation), and 3) develop a plan, tailored to the Veteran-SP dyad, for how SPs will help Veterans participate (support plans). The VHA Blueprint for Excellence emphasizes patient-centered care,[40] which is both flexible and tailored.[44] Flexibility is essential to implementation of family involved treatments,[76] and to improving the clinical relevance of interventions.[1;4] Consequently, inclusion/exclusion criteria only require Veterans bring a SP to Session 1 (if randomized), and discuss further SP attendance with their provider.

2.2C. Description of Strategies.

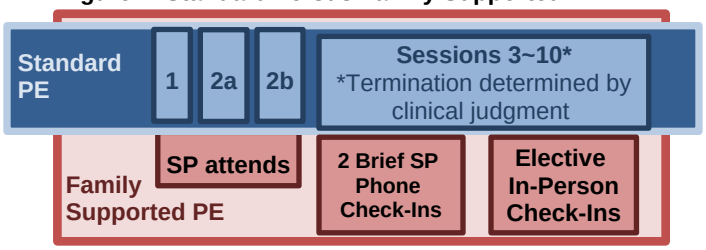
Simply by attending Sessions 1-2b, SPs will take part in essential education about PE and how it works. This education is used to motivate Veterans to engage in PE. We anticipate it will also motivate SPs, improving their support for Veterans' PE participation. We will use existing, evidence-based strategies drawn from Behavioral Family Therapy for substance use (BFT)[65] to frame a discussion of accommodation for symptoms (enabling substance use within BFT). BFT will also be used to facilitate effective communication when creating the SP's support plan, including encouraging "I feel" statements, active-listening, and role playing solutions to anticipated barriers to the plan. Our approach to generating the support plan will be guided by Motivational Interviewing, a well-established, patient-centered counseling method for exploring attitudes about, planning for, and initiating behavior change.[77-80] This will assist providers in avoiding confrontation and emphasizing collaboration, using reflection and open-ended questions. The support plan will include practical steps and preparation for barriers to success. In Session 1, to encourage continued SP attendance, we will use MI strategies to elicit and explore the dyad's reasons for further SP attendance and create a broad SP support plan, should Session 1 be the only family attended session. Follow-up telephone check-ins with SPs will trouble-shoot problems with their support plan and provide encouragement. If problems with the support plan cannot be addressed in these brief telephone calls, additional 30-60 minute, in-person, check-ins will be offered at the provider's discretion to address these problems, consistent with how this intervention would be delivered in good clinical care.

2.3. SIGNIFICANCE

The influence of a successful course of PTSD treatment on a Veteran's life is considerable. In addition to reducing symptoms of PTSD and associated mental health problems (e.g., depression), successful PTSD treatment improves social functioning and reduces, and may even reverse, the negative physical health effects associated with PTSD.[46;84] Increasing the number of Veterans successfully treated will improve treatment access for others and reduce the cost of PTSD.[45] Given VA's investment in PE, increasing the numbers of Veterans who complete and fully benefit from this therapy is of high priority to Office of Mental Health Services (OMHS) and the National Center for PTSD. Improving PE adherence will likely require mobilizing all resources to ensure success, including the critical and underutilized resources within Veterans' families. Despite congressional legislation and national mandates within VA/DoD for family involvement in PTSD care,[35-38] there are no proven strategies for how to effectively include family in traditional individual (i.e., one-on-one) EBPs for PTSD. Clinical programs are unlikely to answer to these national calls without evidence and clear guidelines. Addressing this misalignment between VA guidelines and realized practice is of high importance to our National Center for PTSD and OMHS partners.

Our proposal is responsive to two HSR&D priority areas: Mental and behavioral health and Caregiving.

Figure 2. Standard versus Family Supported PE



Concordant with the mental and behavioral health priority area, this proposal will support work refining EBPs for PTSD to promote higher rates of recovery and family support for treatment. Consistent with priorities to improve the quality of life for Veterans and their Caregivers, we anticipate that family supported PE may enhance family adjustment. Our approach to engaging with families is consistent with Caregivers' preferences for involvement in care, identified in our prior work. The proposed work is also highly aligned with the VHA Blueprint for Excellence and Strategic Plan through its focus on meeting the unique needs of military service disabled Veterans (i.e., PTSD), improving patient health outcomes and functional status through patient-centered care, and investigating novel approaches to treatment for health issues unique to Veterans.[40;41]

Lastly, this project will contribute to the broader scientific literature regarding methods of speeding the translation of science to clinical care. This delay is due, in part, to a traditional developmental approach that emphasizes incremental, delimited steps from efficacy to implementation, and research designs that prioritize internal validity (minimizing threats to causal inference) over external validity (generalizability and clinical

applicability).[1;4;43;85;86] Blending effectiveness, efficacy, and implementation research is part of the solution.[1;42;85] We have built flexibility into our treatment protocol, emphasized external validity, and incorporated patient preferences (for how to involve families). We will also generate information on barriers and facilitators of family supported PE and implementation strategies.[42] Our design integrates recommendations for patient-centeredness within the actual design of clinical trials through broad recruitment and inclusion, meaningful outcomes, effective comparator treatments (i.e., standard PE).[87] If our approach to engaging families proves effective, next steps will include evaluating methods for implementing family involvement in PE that increase effective family support and Veteran adherence, while minimizing costs. This proposal will provide the initial test of a model of family engagement that can be translated to other problems faced by Veterans, including suicide prevention, Traumatic Brain Injury (TBI) rehabilitation, and pain management, contributing to a broader evolution towards evidence-based, family-inclusive care.

3.0 Objectives

The objective of the proposed study is to evaluate the effectiveness of family support as a tool to improve Veterans' EBP adherence. We are proposing a randomized practical clinical trial employing an effectiveness-implementation Hybrid 1 design.[42] This design will focus on external validity, flexibility, and liberal inclusiveness of the patient population.[1;4;43;44] We will also identify potential facilitators and barriers of involving family in PE within VA. Our central hypothesis is that when families support Veterans' PE participation through attending PE's educational sessions (family supported PE), adherence will improve over PE as delivered in routine care.

Aim 1: To improve Veterans' adherence to PE through engaging families in care.
We hypothesize that when families support Veterans' PE participation through attending PE's initial educational sessions, Veterans' attendance to PE (H1a) and homework compliance (H1b) will improve, compared to PE as typically delivered.

Aim 2: To improve the clinical outcomes of Veterans receiving PE in routine care through engaging families in Veterans' treatment.
We hypothesize that family supported PE will be more effective than standard PE in reducing PTSD severity and comorbid problems (depression, quality of life, relationship functioning) from pre-to-posttreatment.

Aim 3: To examine barriers/facilitators of implementing family supported PE through a mixed-method, multi-stakeholder process evaluation[100] with patients, providers, and mental health leadership.

***Exploratory Aim*: To identify mechanisms underlying differences in adherence between treatment conditions.**
We will explore if differences in adherence between family supported PE and standard PE are mediated by changes in key social influence variables, including family perceptions of treatment credibility, family support for Veterans' PE participation, and families' accommodation for PTSD symptoms.

4.0 Resources and Personnel

4.1. Research Sites

1. Center for Chronic Disease Outcomes Research, Minneapolis VA, Minneapolis, MN. Activities that take place at this site include the following:
    a. Data extraction
    b. Recruitment, obtaining informed consent, and data collection, including interviews by trained staff, who are the study coordinator and study manager
    c. Intervention administration/delivery
    d. Data analysis
2. Ann Arbor VA
    a. Recruitment, obtaining informed consent, and data collection, including interviews by trained staff, who are the study coordinator
    b. Intervention administration/delivery
    c. Data analysis
3. Atlanta VA
    a. Recruitment, obtaining informed consent, and data collection, including interviews by trained staff, who are the study coordinator
    b. Intervention administration/delivery
    c. Data analysis
4. VA Greater Los Angeles Healthcare System
    a. Intervention training, supervision, and fidelity coding
    b. No data collection, but site investigators will have access to PHI
5. Phoenix VA Health Care System
    a. Intervention training, supervision, and fidelity coding
    No data collection, but site investigators will have access to PHI

4.2. Principal Investigator.

Laura Meis, PhD, LP

a. Will have access to protected health information

b. Will be involved in recruiting subjects; obtaining informed consent; supervising and administering interview procedures/conduct of interviews, training and supervising providers in intervention delivery, and performing data analysis

4.3. Co-Investigators.

1. Shannon Marie Kehle-Forbes, PhD; Shannon.kehle-forbes@va.gov, 612-467-4772; VA employee Minneapolis VAHCS
    a. Role: Co-Investigator; She will serve on the Implementation/Dissemination, Trial, and Qualitative Subgroups. She will be involved in supervising and conducting interviews; and performing data analysis and manuscript writing
    b. Will have access to protected health information
2. David Nelson, PhD; dave.nelson@va.gov, 612-467-2775; VA employee Minneapolis VAHCS
    a. *Role:* Lead Statistician
    b. Will be involved in performing data analysis and participate in manuscript writing
    c. Will have access to protected health information
3. Melissa Anderson Polusny, PhD; Melissa.polusny@va.gov, 612-467-3965; VA employee Minneapolis VAHCS

a. Role: Co-Investigator; She will serve on the Intervention, Trial, and Assessment Subgroups. Will be involved in training and supervising providers in intervention delivery as well as fidelity coding, performing data analysis, and manuscript writing
b. Will have access to protected health information

4. Michele Spoont, PhD; Michele.spoont@va.gov, 612-467-1428; VA employee Minneapolis VAHCS
   a. Role: Co-Investigator; She will serve on the Assessment and Qualitative Subgroups. Will be involved in supervising and administering interview procedures/conduct of interviews, performing data analysis, and manuscript writing
   b. Will have access to protected health information
5. Afsoon Eftekhari, PhD; afsoon.eftekhari@va.gov, (650) 493-5000 x22393, VA employee Palo Alto VAMC
   a. She will serve on the Intervention and Implementation/Dissemination Subgroups and lead efforts to identify dissemination channels and facilitate dissemination of study findings
   b. Will NOT have access to protected health information
6. Carl E. Isenhart, MBA, PsyD; carl.isenhart@va.gov, (602) 277-5551 x6394, VA employee Phoenix, AZ VHA
   a. Role: Co-Investigator; He will serve on the Intervention and Trial Subgroups. Will be involved in training and supervising providers in intervention delivery as well as fidelity coding and manuscript writing
   b. Will have access to protected health information
7. Shirley M. Glynn, PhD; Shirley.glynn@va.gov, 310-268-3939; VA employee Los Angeles VHAGLA
   a. Role: Co-Investigator; She will serve on the Intervention, Trial, and Implementation/Dissemination Subgroups. She will be involved in training and supervising providers in intervention delivery as well as fidelity coding, performing data analysis, and manuscript writing
   b. Will have access to protected health information
8. Millie C. Astin, PhD; millie.astin@va.gov, (404) 321-6111 x205176; VA employee Atlanta VAMC
   a. Role: Site Principal Investigator; She will oversee study activities at the Atlanta VAMC and participate in the Trial Subgroup.
   b. Will have access to protected health information
9. Erin Smith, PhD; erin.smith3@va.gov, 734-845-5645; VA employee Ann Arbor VHA
   a. Role: Site Principal Investigator; She will oversee study activities at the Ann Arbor VAMC and participate in the Trial Subgroup.
   b. Will have access to protected health information
10. Katherine Porter, PhD; Katherine.porter2@va.gov, 734-845-5335; VA employee Ann Arbor VHA
    a. Role: Site Co-Principal Investigator; She will oversee study activities at the Ann Arbor VAMC and participate in the Trial Subgroup.
    b. Will have access to protected health information

4.4. Collaborators.

1. Michelle D. Sherman, PhD; Sherman@umn.edu, 612-302-8200; Professor, Department of Family Medicine and Community Health, University of Minnesota
   a. Role: Consultant; In year 1, she will review and provide feedback on drafts of recruitment materials, the provider treatment manual, and training materials. During the course of the trial, she will continue to consult on recruitment and on issues that arise with the treatment protocol during therapist consultation calls (no identifying information will be provided or discussed). She will also participate in quarterly all-team meetings to facilitate collaboration and

communication. This will require 25 hours of effort for each year of the project and 12 hours during the final year.

b. Will NOT have access to protected health information

4.5. Study Personnel.

1. Erin Linden, MPH; erin.linden@va.gov; 612-467-5790; VA employee Minneapolis VAHCS
    a. Role: Project Manager; She will oversee and manage project activities at all sites
    b. Will be involved in recruiting subjects; obtaining informed consent; supervising and administering interviews and surveys, fidelity coding, data collection and supervising these processes across sites
    c. Will have access to protected health information
2. Taylor Oakley, MA; taylor.oakley@va.gov, 612-467-7966; VA employee Minneapolis VAHCS
    a. Role: Research Assitant; She will recruit subjects; obtain informed consent; administer interviews and surveys, fidelity coding, and data collection
    b. She will also administer surveys and interviews to participants at other sites by mail and telephone
    c. Will have access to protected health information
3. Ann Bangerter, BS; ann.bangerter@va.gov, 612-467-1384; VA employee Minneapolis VAHCS
    a. Role: programmer
    b. Will have access to protected health information
    c. Will not have contact with research participants
4. Emily Hagel Campbell, MS; emilyhagelcampbell.@va.gov, 612-725-2000 x7451; VA employee Minneapolis VAHCS
    a. Role: statistician
    b. Will not have access to protected health information
    c. Will not have contact with research participants
    d. Will be involved in performing data analysis of de-identified quantitative data
5. Andrea Cutting, MS; andrea.cutting@va.gov, 612-467-1881; VA employee Minneapolis VAHCS
    a. Role: programmer
    b. Will have access to protected health information
    c. Will not have contact with research participants
6. Sean Nugent, BA; sean.nugent@va.gov, 612-467-3906; VA employee Minneapolis VAHCS
    a. Role: programmer
    b. Will have access to protected health information
    c. Will not have contact with research participants

5.0 Study Procedures

5.1 Study Design

This is a 3.5 year study. We will employ a two-group (standard PE vs family supported PE), three-site, practical randomized controlled trial, using a Type 1 Hybrid design with 156 Veterans and 156 of their nominated Support Persons (78 Veterans/78 SPs in standard-of-care PE with no family involvement in treatment and 78 Veterans/78 SPs in family supported PE).[42] We will also conduct semi-structured interviews via telephone for up to 8 study therapists per site (N = 12-24) and 2 members of mental health leadership at each site (N = 6) for Secondary Aim 2 (process evaluation).

Practical RCTs use conditions mirroring clinical practice and are intended to directly inform care with generalizable answers to important but simple questions.[4] They rely on randomization and include limited use of elaborate quality assurances, as these efforts cannot be sustained in clinical care.[4;43;88] A Hybrid 1 design tests an intervention while assessing its potential for real-world implementation.[42] We will use liberal inclusion/ exclusion criteria, designed to mirror clinical practice. In the first six months, we will hire and train staff, obtain supplies, and finalize procedures. We will refine intervention and provider training materials and train study providers. We will begin study recruitment and treatment delivery, which will proceed until our N is achieved, which we anticipate will be in Year 3. In the final year, we will obtain remaining posttreatment assessments and analyze data. During Year 4, we will also prepare manuscripts and disseminate findings.

Table 1. Abbreviated Timeline of Major Tasks

	Y1				Y2				Y3				Y4	
Activity **Quarter**	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Hire and train staff	X	X												
Refine intervention/training materials	X	X												
Refine Recruitment Materials	X	X												
Provider Training	X	X												
Recruitment/Baseline Assessments		X	X	X	X	X	X	X	X	X	X			
Treatment Administration		X	X	X	X	X	X	X	X	X	X	X		
Posttreatment Assessments				X	X	X	X	X	X	X	X	X	X	
Provider/ Leadership Interviews											X	X	X	
Create and finalize dataset											X	X	X	X
Qualitative Analyses									X	X	X	X	X	X
Quantitative Analysis											X	X	X	X
Manuscripts and dissemination													X	X

5.1A. Randomization and Intervention Delivery.

Provider skill may differ, and randomizing providers to only one condition risks imbalance in skill of delivery across conditions. At the same time, when the providers are involved in both conditions, provider learning may diffuse into both conditions (i.e., skills for improving family support for PE influencing standard PE delivery). We anticipate the risk of the latter is limited as the treatment condition under study involves including families in care, which are excluded from the standard PE arm. Consequently, providers will deliver both interventions. We will use block randomization within providers and within site, employing a completely randomized repeated measure block design (3 sites, 4 providers per site, 13 patients per provider). Randomization will be conducted by the study programmer, using blocks generated by the statistician. Participants will be informed of their randomization when they are contacted to schedule their first treatment session (after consenting and finalizing eligibility – discussed further below). Fidelity coding of session tapes will examine diffusion of family supported PE skills into standard PE. Veterans living 50 or more miles from the facility will be eligible for travel pay. Dyads with children will also be offered compensation for childcare, if necessary. Participants will be allowed $10 an hour for childcare payments (e.g. 2 hour session plus 1 hour travel time equates to $30 for childcare per session). Afterhours appointments will also be available at each study site.

5.1B. Providers and Training.

VA PE providers will provide the treatment. Across all sites, there are approximately 57 trained PE providers. Seventeen have expressed a desire to participate. All providers will attend a 2 day training in-person at the Minneapolis VA. Training will cover basic information on working with families, including confidentiality, managing conflict, and managing reports of relationship violence. It will provide instruction on educating families about accommodation, and facilitating constructive family communication through “I feel” statements,

active-listening, and role plays, using BFT approaches. Lastly, it will use tips from Motivational Interviewing for eliciting SP encouragement for PE participation, creating a tailored plan for SPs to support PE, and assisting SPs in follow-up telephone calls. The training team is highly seasoned in educating providers in these methods. The training will be video-taped for use in training future providers (e.g., due to provider attrition during the course of the study).

5.1C. Standard PE.

Providers will deliver PE consistent with the standard of care, with a flexible end date as they typically would in routine practice and will divide Session 2 into 2a and 2b. VA PE trainings encourage extending the therapy as needed, routinely resulting in a range of 8 to 15 sessions. Posttreatment assessments will be scheduled to coincide with when Veterans complete treatment to allow for this flexible end date. If participants are still in treatment at 16 weeks post-session 1, the posttreatment assessment will be delayed to allow them to get through as much of the treatment as possible prior to assessment. If the Veteran never attends session 1, their posttreatment will be scheduled 16 post-first missed appointment for session 1.

Family attendance will not be solicited by providers in standard PE. If a SP contacts a provider, the provider will proceed as he/she would in his/her routine practice, consistent with our design emphasis on real-world care. Quantity and quality of provider-SP contact will be measured by weekly provider report. We anticipate risk for cross-over effects from SPs reaching out to providers is minimal as considerable effort is required by SPs to gain access to Veterans' providers (i.e., Veterans must request and sign a Release of Information). Additionally, while we did not capture who initiated the provider-SP contacts reported among 17% of SPs within Project HomeFront, qualitative interviews suggest these contacts are typically initiated by providers. In qualitative interviews, SPs were enthusiastic about being involved in Veterans' care, but few SPs had considered reaching out to Veterans' providers.

Table 2. Content Added for Family Supported PE

PE#	Task
1	• Eliciting benefits of further SP attendance • Brief discussion of how SPs can help in PE
2a	• Brainstorm how SPs encourage/discourage PE adherence and approaching trauma-reminders
2b	• Develop SP's plan for supporting adherence • Anticipate barriers to success; role play solutions
3, 5	• SP telephone check-ins for trouble-shooting support plan with longer in-person check-ins when indicated

5.1D. Family Supported PE (Table 2).

Providers will deliver the 10 session PE protocol as they typically would with additional material outlined session by session below. As discussed above, they will divide session 2 into 2a and 2b (11 total sessions delivered over an 11-16 week period). If the dyad is randomized to include their family in treatment sessions, SPs will attend the first session with the Veteran and be encouraged to attend both session 2a and 2b (see Table 2). Each session attended by a family member will include the following content. We will ask Veterans in self-reports prior to session 1 about their preference for having their SP present for their Session 1 trauma discussion with their providers (i.e., trauma interview). This preference will be honored to promote early retention and keep the intervention Veteran-centered.

Session 1: The last twenty minutes of Session 1 will involve a) eliciting how further SP attendance could be of benefit the dyad, using Motivational Interviewing tips, b) discussion of how the SP can support PE participation should this the only family session, c) and discussion of the benefits of talking further about trauma with loved ones, using Motivational Interviewing strategies.

Session 2a*:* We will devote fifteen minutes to discussing how SPs naturally encourage or discourage Veterans to approach trauma reminders and participate in treatment. Session 2b: Thirty minutes will be devoted to a) create a tailored plan for SPs to support Veterans' PE participation*,* including planning trauma disclosure to family when indicated or desired and b) problem-solving barriers to the success of the SPs' support plan. Telephone check-ins*:* Following Session 2b, SPs will have two 15 minute telephone check-ins to make support plan adjustments. Call 1 will occur after the first *in vivo* exposures (Session 3), and Call 2 will occur two weeks later. If telephone check-ins reveal a) the family support plan is not going well, b) unresolved ambivalence about the treatment, or c) requests for more assistance in supporting Veterans' care, providers can add dyadic session(s), consistent with how this intervention would likely be delivered in good clinical practice. These sessions will discuss progress and the support plan. They can also be used to plan and facilitate trauma

disclosure if clinically indicated and desirable. Dyads expressing additional family or SP needs (e.g. mental health), will be provided site-specific referrals, including services for SPs, children, parenting training, and family/couple counseling as indicated.

After finishing treatment in both study conditions, Veterans will be referred back to their VA mental health care team in order to determine if they have any remaining mental health treatment needs. If they do not already have an established primary mental health care team or provider, they will be referred to the mental health care team at their VA facility to establish care and evaluate any remaining mental health treatment needs.

5.1E. Delivery by Telemedicine

We will recruit participants from CBOCs and offer to provide Prolonged Exposure treatment within the study using telemedicine. The telemedicine option would use VA approved electronic communication methods and information technology to provide Prolonged Exposure therapy to patients by study clinicians. This option would greatly benefit participants. Psychotherapy, including Prolonged Exposure (PE), is currently widely available within VA by telemedicine to improve Veteran access to care. The major benefit of telemedicine is that it eliminates travel that may be disruptive or costly to patients. Many individuals in need of specialized PTSD services live in geographically remote regions. Additionally, individuals needing mental health services may have physical limitations or disabilities. Providing Prolonged Exposure therapy to these individuals solely in medical centers can impose a tremendous financial, travel, or personal burden. Allowing a telemental health option for PE therapy will ease these burdens by making services more accessible to patients.

Our study sites have robust telemedicine programs that provide PE by telemedicine. Study sites will follow all procedures and regulations that are currently in place at their VA hospital and surrounding CBOCs to ensure services provided to Veterans are safe and accurate. Additionally, all practitioners treating patients using telemedicine will be qualified to deliver the level of consultation, care, and treatment involved.

5.1F. Defining Drop Outs

Participants could, without notice, stop coming to treatment, and then contact their providers several months later to request to re-initiate treatment. This could lead to vastly different periods of time that some participants are in treatment (watering down treatment effects and potentially artificially influencing study findings) and could also pose administrative problems if they would be unable to complete posttreatment or follow-up assessment during the period of funding for the project. Additionally, at some point such a break in treatment would become long enough such that starting treatment again would be equivalent to starting treatment over (e.g., like a new course of care). Consequently, any unanticipated break in treatment for longer than 6 consecutive weeks will trigger an official 'end' to their treatment period. Participants will remain in the study protocol (i.e., receive all study assessments and not removed from the study). They will be assessed at 16 weeks post session 1 for their posttreatment survey and interview. If they request to re-enter care, they will be referred to the clinic to intiate a new course of care with the clinic, outside of the study.

5.1G. Provider Monitoring and Fidelity Assessment.

Provider monitoring will mirror practices for potential future implementation and necessary for promoting good clinical practice (versus for a traditional efficacy trial). As study team members, providers will be trained in how to deliver the treatment consistent with the treatment protocol as an extension of how the PI would deliver it. To ensure the treatment is delivered properly, providers will have weekly consultation calls with study investigators, including the PI (Meis, Polusny, Isenhart, Glynn). These meetings will include discussion of issues that arise with implementing the treatment protocol as intended. Providers will also record session attendance, rate subjects on homework compliance, and track out-of-session contact between providers and family members. Unlike an efficacy trial, providers will not be provided fidelity scores from reviewed sessions, as this unfeasible for large scale implementation. However, provider fidelity and competence in intervention strategies will be coded from audiotapes of sessions for use as covariates in study

analyses. Ten percent of providers' sessions where content varies between PE and family supported PE (1, 2a, 2b) will be randomly selected and coded using a fidelity checklist. Fidelity checklists will also evaluate potential contamination of family supported PE skills into standard PE. Study staff will be trained by Dr. Meis and Isenhart using checklists developed by the intervention team. Twenty-percent of sessions coded will be coded by a second expert coder (Dr. Isenhart), and reliability evaluated. If reliability is lower than benchmarks (i.e., kappa > .79), additional training of coders will ensue. Tapes will be re-coded and a new set of 20% will be coded by Dr. Isenhart until thresholds are achieved.

5.1H. Provider/Leadership Interviews.

Study therapists and 2 members of mental health leadership at each site will be invited to participate in semi-structured interviews conducted via telephone for Secondary Aim 2 (process evaluation). Clinic leadership at each site was consulted in the development of these study procedures for the grant application that we were awarded to support this project. They will be reminded by email a few months before formal recruitment efforts begin. Therapist interviews will last approximately 50 minutes and leadership interviews will last approximately 30 minutes. The interviews will be recorded and transcribed.

5.1I. Human Subjects Involvement and Characteristics.

5.1I.1. Overview. There are 4 groups of participants in this study: Veterans, their support persons (SPs), their providers, and mental health leadership.

Veterans and SPs

Intensive Coaching Phase. Prior to initiating treatment for randomized treatment cases, providers will deliver family-supported PE for up to 2 dyads (Veteran and his/her SP), with intensive coaching and feedback by the investigative team (Intensive Coaching Phase). A study investigator will review the audio recording of each session delivered that is unique to family-supported PE (Sessions 1-2b) and provide feedback for each session. Providers will also have access to participants self-reports for patient-centered feedback on their progress in the intervention.

Intensive Coaching participants are not randomized, so their data cannot be used for the RCT. Consequently, they will be assessed at fewer time points (i.e., only 3 administrations of weekly assessments) and procedures used to establish inclusion/exclusion criteria will rely on less burdensome processes (chart review and self-reports), consistent with how inclusion/exclusion would likely be evaluated if this intervention was delivered in routine clinical care (see below for greater detail). We aim to enroll up 96 participants for this phase (48 Veterans and 48 SPs among on up to 24 providers, due to potential provider attrition).

Randomized Controlled Trial (RCT) Phase. For the RCT phase, we will aim to enroll 225 Veterans and 225 of their SPs (with the goal of randomizing 156 dyads or 312 participants). Veterans can be of any age and combat era and either self-referred (e.g., individuals who reach out to study team members about participating after hearing about the study) or provider-referred (e.g., seeking evidence based psychotherapies through the PTSD Clinical Teams at the Minneapolis, Ann Arbor, and Atlanta VAs). They will be randomly assigned to either Prolonged Exposure (PE) for PTSD, as delivered within routine clinical care or family supported PE. Related to potential risk, we will not include Veterans' who are actively suicidal or homicidal with an intent and/ or plan, who have experienced an episode of psychosis or mania in the past 3 months, who have had a severe substance use disorder in the past 3 months, or who report moderate relationship violence (by either Veteran or SP support, during the screening process).

Providers will deliver the 10 session PE protocol as they typically would and will divide session 2 into 2a and 2b (11 total sessions delivered over an 11-16 week period). If the dyad is randomized to include their family in treatment sessions, SPs will attend the first session with the Veteran (up to session 3), two 15 minute telephone check-ins with providers. If telephone check-ins reveal a) that the family support plan is not going well, b) unresolved ambivalence about the treatment, or c) preferences for greater assistance to the SP in how to support the Veteran's care, the provider can elect to add dyadic session(s) to discuss these issues, consistent with how this intervention is likely to be delivered in real-world care if their 15 minute check-ins prove insufficient. These sessions will discuss progress and the support plan using skills from prior sessions. Dyads expressing additional family needs or support for SPs' mental health will be provided site-specific referrals, including services for SPs, children, parent skills training, and family or couple counseling as indicated. Study assessments are described below under 'Data Sources.'

Providers

Providers will be members of the research team and included in the IRB as study staff (to be added in future amendments). After providers have completed their role in delivering the treatment, they will be invited to participate in semi-structured interviews conducted via telephone for Secondary Aim 2 (process evaluation). Therapist interviews will last approximately 50 minutes and leadership interviews will last approximately 30 minutes. The interviews will be recorded, transcribed, and coded. Therapist interviews will last approximately 50 minutes. The interviews will be recorded, transcribed, and coded.

Mental Health Leadership

Two members of mental health leadership at each site will be invited to participate in semi-structured interviews conducted via telephone for Secondary Aim 2 (process evaluation). and leadership interviews will last approximately 30 minutes. The interviews will be recorded, transcribed, and coded.

5.1I.2. Data Sources. Sources of data are depicted in Table 3.

Veterans and SPs

Intensive Coaching Phase. Inclusion/exclusion will be assessed through a combination of chart review and reports on paper-and-pencil measures described in more depth in subsequent sections. Paper-and-pencil self-report measures at Baseline and Posttreatment for Veterans will assess treatment satisfaction, quality of life, family functioning, therapist-to-SP contact and demographics. Paper-and-pencil self-report measures at Baseline and Posttreatment for SPs will assess similar domains, as well as SP distress. Weekly assessments will measure social influences on treatment experiences (Veterans and SPs), PTSD symptom severity (Veterans only), and provider-SP contact (SP only). Paper-and-pencil questionnaires for this phase of the research will be given by participants directly to the providers as it will be used for feedback to providers on how treatment is progressing during the treatment sessions where SPs attend. Consequently, weekly paper-and-pencil assessments will only be completed for the first 3 weeks of treatment. At posttreatment, some Veterans (N < 11) will also complete Exit Interviews (a posttreatment discussion of likes and dislikes about including family in PE).

In order to finalize and solidify all processes before beginning the RCT phase of the study, we will administer Baseline and Posttest diagnostic structured clinical interviews to up to ten IC cases. This process allows clinical interview administrators to acclimate to the interview procedures and to prepare for the RCT phase. Before beginning treatment, participants may be asked to participate in the structured clinical interview that will assess his/her PTSD symptoms. We will also ask some participants (N < 13 Veterans and 13 SPs) to complete “cognitive interviews” about the forms we will admininster to RCT participants. In Cognitive Interviews, participants are asked to think-aloud about their reactions to study questions and surveys to improve their format and clarity. This will allow us to insure forms are easy to respond to, items and instructions are clear, and the length of instruments is not too long to be burdensome. The participants can decline these interviews without effecting their eligibility in the study. If the participant chooses to participate in any of these interviews, they will be compensated for their time.

RCT phase. Broadly, structured clinical interviews with Veterans will assess inclusion/exclusion criteria (Baseline only), symptoms of PTSD (Baseline and Posttreatment), and a posttreatment discussion of likes and dislikes about including family in PE (exit interviews as discussed for IC participants; family supported PE participants only). Paper-and-pencil self-report measures at Baseline, Weekly During Treatment, and Posttreatment will mirror those used for the IC Phase.. Veterans and SPs will be given weekly surveys during weeks 2, 4, 5, 6, 8, 10 and 12 of treatment. We will also send Veterans and SPs a follow-up survey 3 months after the posttreatment assessment.

This study will not collect any biological specimens.

Providers

Providers will complete patient ratings on treatment adherence (homework compliance), treatment attendance, and report on any out-of-session contact with SPs. After completing their treatment cases for the study, providers will be invited to participate in an Exit Interview to assist with understanding the barriers and facilitators of implementing family supported PE in routine practice.

MH Leadership

Table 3. Data Sources

Participant	N	Baseline	Weekly During Treatment	Posttreatment
IC Veterans	10	Optional Structured Interview and Cognitive Interview	Paper-and-pencil measures (3 weeks only)	Optional Structured Interview, Exit Interview, and Cognitive Interview
	96	Paper-and-pencil measures		Paper-and-pencil measures
IC SPs	96			
RCT Veterans	225	Structured Interview	Paper-and-pencil measures	Structured Interview and Exit Interview
	225	Paper-and-pencil measures		Paper-and-pencil measures
RCT SPs	225	Paper-and-pencil measures	Paper-and-pencil measures	Paper-and-pencil measures
Provider	12-18	--	Provider report of subject homework compliance	Qualitative Interview
Leadership	6	--	--	Qualitative Interview

5.1I.3. Inclusion of Women and Minorities. Women and minorities will be represented in our study sample. Any patient who enters the Minneapolis, Ann Arbor, or Atlanta outpatient PCT clinics during the study period and meets inclusion criteria will be eligible for participation regardless of gender or race.

5.1I.4. Inclusion of Children. All study subjects are expected to be 18 years of age or older.

5.1J. Potential Risks.

5.1J.1. Veterans and Support Persons (SPs)

- All Veterans will receive Prolonged Exposure, one of the most extensively studied and efficacious treatments for PTSD, which is likely to improve Veterans' well-being. At the same time, benefit cannot be guaranteed. Questions about how Veterans and SPs are doing and discussion of symptoms or painful memories during the course of treatment can cause emotional discomfort. Additionally, asking the Veteran and his/her loved one to discuss their relationship could cause emotional discomfort and alter their relationship. Participants can refuse to answer any question(s) and discontinue participation at any time. The risks are no greater than those encountered in routine clinical care.
- Participants may feel uncomfortable about being audio taped.
- While unlikely, participation may result in a loss of privacy. This would occur if someone not associated with the study heard one of the participant's audio tapes or saw participants' data. All data is labeled with a study ID number, which can only be linked to participant names by a few study staff. The link between study ID numbers and names will be kept in a secure, password protected location behind the VA firewall. Additionally, a breach of confidentiality could occur if your information is required to report child or elder abuse or required to prevent you from hurting yourself or someone else.
- There are no anticipated physical risks in this study.
- Economic risks include potential loss of wages, transportation costs associated with traveling to and participating in the research intervention, and child care, when necessary.

5.1J.2. Providers

- Providers may feel uncomfortable about being audio taped.
- There is also the possibility they may be uncomfortable answering some of the questions in exit interviews. They are free to skip any questions they wish not to answer, or withdraw from the study at any time.
- There is a risk that participation may result in a loss of privacy. This would occur if someone not associated with the study heard one of the participant's audio tapes or saw participants' data. All data is labeled with a study ID number, which can only be linked to participant names by a few study staff. The link between study ID numbers and names will be kept in a secure, password protected location behind the VA firewall.

- We do not anticipate that any sensitive information pertaining to provider's personal histories or experiences will be discussed or disclosed in interviews.
- While unlikely, a loss of privacy could also occur if someone not associated with the study heard one of the participant's audio tapes or saw participants' data. All data is labeled with a study ID number, which can only be linked to participant names by a few study staff. The link between study ID numbers and names will be kept in a secure, password protected location behind the VA firewall.

5.1J.3. Mental health Leadership

- Participants may feel uncomfortable about being audio taped.
- While unlikely, participation may result in a loss of privacy. This would occur if someone not associated with the study heard one of the participant's audio tapes or saw participants' data. All data is labeled with a study ID number, which can only be linked to participant names by a few study staff. The link between study ID numbers and names will be kept in a secure, password protected location behind the VA firewall.

5.1K. Protection Against Risk

5.1K.1. Social and Psychological Appropriate safeguards will be in place if surveys, screening interviews, interviews, or therapy sessions cause any psychological distress or a psychiatric emergency emerges among participants. Importantly, this protocol establishes the minimal thresholds for staff to use when interviewing and intervening with participants at risk for a psychiatric emergencies. Sites may elect to use more stringent approaches to assessment when those approaches are preferred by their site PI or R&D committees.

Each of the lead investigators at each site are licensed clinical psychologists (Minneapolis: Meis; Ann Arbor: Smith; Atlanta: Astin). The PI has expertise in assessing and managing risk for IPV, including within a clinical trial, and will closely train and supervise study staff in assessing and managing risk for IPV. Dr. Meis worked at a domestic violence center for 4 years. During her tenure there, she served as a therapist for IPV perpetrators and victims. She also served as the project coordinator for a randomized controlled trial of two therapies for male IPV perpetrators (randomized to group or individual therapy). For this work, she was responsible for establishing safety protocols, training and supervising others in the implementation of these safety protocols, and training and supervising others in telephone administration of IPV screening instruments (i.e., CTS-2).

All staff with contact with study participants will be trained on how to recognize, assess, and intervene, in a manner appropriate to their training backgrounds, in the case of a psychiatric emergency. They will be trained and supervised by an on-site team member who is a licensed clinical psychologist (PI, Co-I, or site PI). Staff will be trained with direct instruction and role plays, using the structured protocol depicted in Figure 1. The protocol is described in further depth below. Training will take place prior to initiating contact with any potential participants and again on an as-needed basis for staff added to the project in the future.

All potential collaborators and study therapists 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, good clinical practice, and suicide prevention. In addition, Dr. Meis's graduate coursework included a three-credit course on ethics.

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 facility's Emergency Room during off hours. In the unusual event of an on-site psychiatric emergency involving a participant who is not a Veteran, including threats of or acute risk for IPV, the participant will be triaged within VA facilities. If indicated based on psychiatric evaluation, non-Veterans will be transferred for appropriate care in community. Once stabilized, they will be eligible to enter or re-enter the study.

<u>Suicide Management Protocol</u>

Non-clinical study staff conduct screening and consenting with participants. Consequently, these staff should be prepared should a veteran or his/her support person express distress or thoughts indicating potential risk for a psychiatric emergency. Research staff's obligation is to minimize risk to participants by eliminating immediate danger (Wendler & Grady, 2000). Short, straight-forward, interview instruments are ideally suited for staff, with any training background, to take an algorithmic approach to participants who may pose an imminent danger to themselves and warrant emergency intervention.

Our protocol parallels that utilized by other investigators at the hub site (i.e., Schertz et al., in preparation). We will employ their algorithm, which includes four phases: (1) Activation, (2) Decision Making, (3) Action, and (4) Documention (Figure 1). *Activation* is the phase during which concerning risk-related statements are identified (purple boxes in Figure 1). This leads staff to enter the *Decision Making* phase. Decision making includes a series of structured questions with clear decision rules. The flow chart in Figure 1 accounts for the multiple scenarios in which suicidal ideation and behavior may have been encountered within our study. We anticipate that in some circumstances depression or suicidal ideation and behavior will be suspected by research staff but not explicitly endorsed. In this case, staff will initiate the First Tier (2a) of the Decision Making phase (pink boxes in Figure 1), which will use a modification of the Patient Health Questionnaire-2 to assess depression and thoughts of self-harm (Kroenke, Spitzer, & Williams, 2003). When suicidal ideation and behavior is directly endorsed, staff will enter the Second Tier of the Decision Making phase (2b; blue boxes in Figure 1), which will utilize the Columbia-Suicide Severity Rating Scale (C-SSRS) Adult Screener for Primary Care to assign what action staff should preform (Figure 2; Posner et al., 2011). This concise measure includes six questions and can be administered by non-clinicians via telephone or in-person (The Columbia Lighthouse Project, 2016). The Schertz et al. (in preparation) protocol replaced the use of the double barreled final PHQ-9 item (In the past two weeks, have you been having any thoughts that you would be better off dead, or of hurting yourself?) with a modified item adapted from the Ask Suicide-Screening Questions (ASQ) "In the past two weeks, have you been having thoughts about killing yourself?") due to concerns that participants may have trouble responding to the double-barreled PHQ-9 item and that the PHQ-9 item does not directly ask about active thoughts of suicide. The ASQ item was selected due to its direct, action-oriented wording.The *Action* phase (3; green boxes in Figure 1) will use responses from the C-SSRS to stratify patients into low-concern or high-concern categories to aid immediate decisions around what response staff should provide. Staff response will be informed by proximity to the patient, if the participant has a VA MH provider, resources available at the study site, and level of concern. Responses range from providing resources for support, referral for assessment, immediate evaluation by a mental health professional, phone transfer to a crisis hotline (e.g., the National Suicide Prevention Lifeline), admission to the emergency department, to contacting 911 to coordinate a welfare visit (Draper et al., 2015). Of note, all responses involve notifying the participants' VA MH provider of this protocol, when one exists. The *Documentation* phase is described in greater detail below.

When staff interact with participants over the phone and wish to transfer a participant to the National Suicide Prevention hotline, it is possible, albeit unlikely, that the patient will decline the transfer or hang up. This refusal to be transferred does not necessarily mean the patient is immediate danger of suicide. We consulted with the hub site's Suicide Prevention Program Coordinator on how to respond in this scenario (Eric Whittenberg). Mr. Whittenberg recommended the following: (1) If the staff member is able to determine that the patient is not in immediate danger for suicide (e.g., "Are you certain you are safe today?"), then staff member should express his/her care and concern, encourage help seeking, provide the patient with the national suicide hotline number and local MH phone number(s), and respect his/her wishes not the be transferred. (2) If the staff member is concerned the participant may be in immediate danger, he/she will contact local police and intitate a well-check if the participant is unwilling to be transferred. (3) If the staff member does not have enough information to determine if the participant is in immediate danger, he/she will immediately consult with the site PI (each of whom are clinical psychologists) or another MH provider among the study staff, whomever the staff member is able to reach first. This is most likely under scenarios in which the participant hangs up on the staff member and failed to respond to the staff members efforts to call him/her back.

The final phase of our suicide management protocol is *Documentation*. Staff will report use of the suicide management protocol within the same day to the site's study coordinator and site principal investigator. For veteran participants who receive their care at that study site, use of the protocol will be documented in the

patient's electronic medical record. This will also be done for VA patients not enrolled in the study (e.g., when interactions happened during recruitment). If the participant has a VA mental health provider, this individual will be notified by co-signing the provider on the CPRS note (their MH provider, or if no MH provider their PCP) using the use the CPRS Action "Identify Additional Signers". Lastly, this will be recorded in study records as an adverse event and in an excel document for the study that documents all the steps taken in response to the participant's expressed suicidal ideation.

Figure 1. Suicide Management Protocol

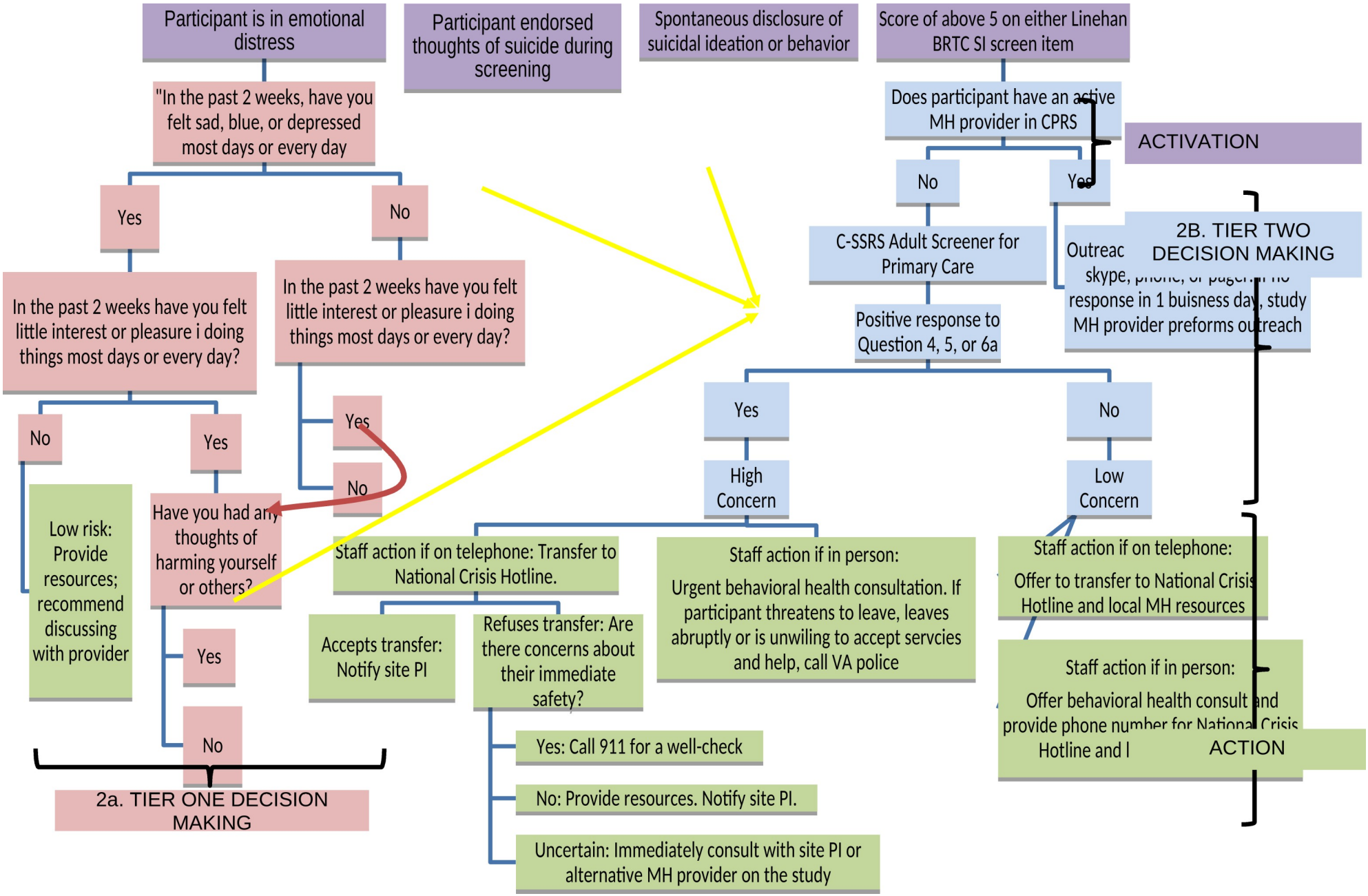
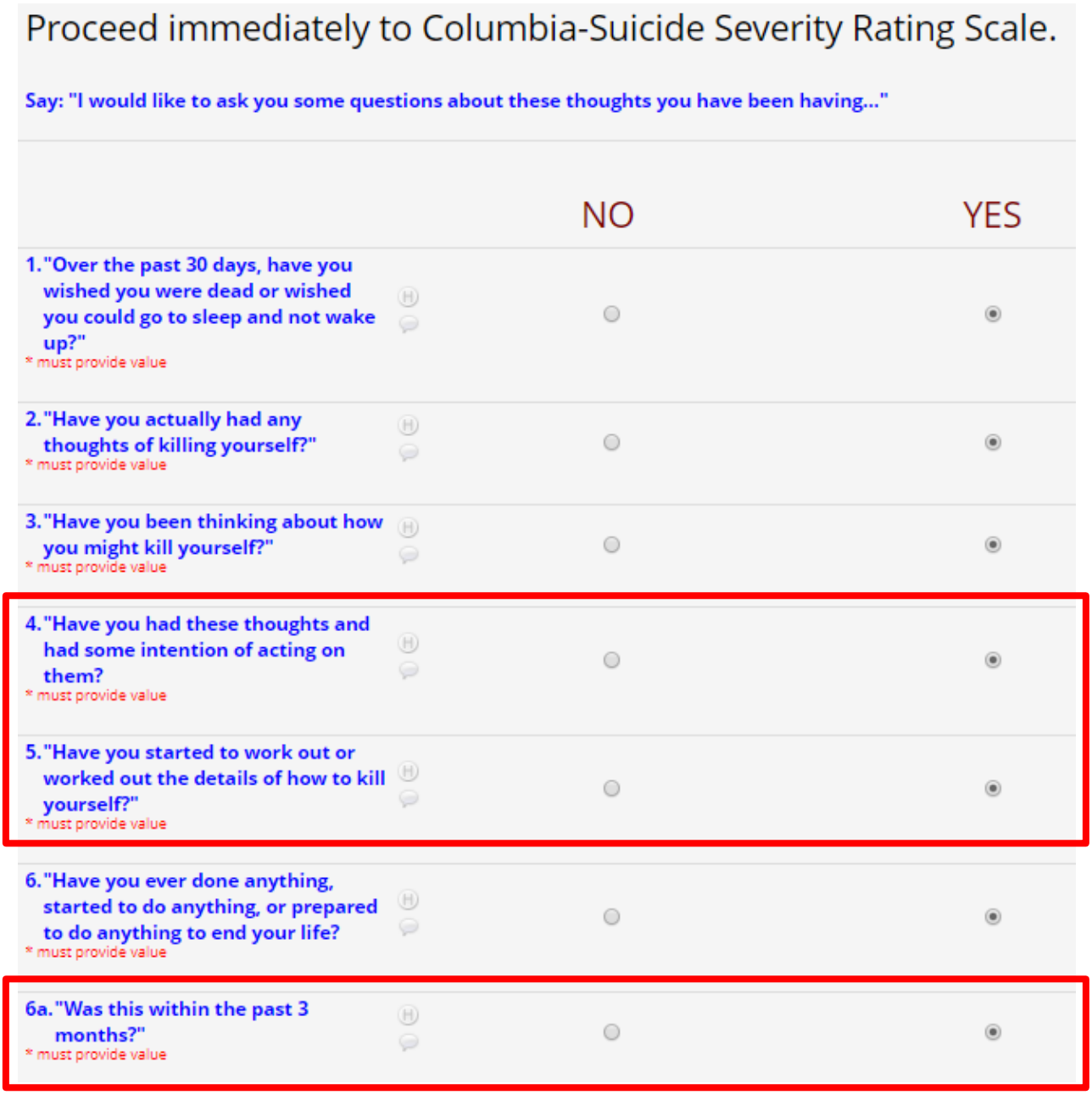

Participant is in emotional distress
Participant endorsed thoughts of suicide during screening
Spontaneous disclosure of suicidal ideation or behavior
Score of above 5 on either Linehan BRTC SI screen item
"In the past 2 weeks, have you felt sad, blue, or depressed most days or every day
Does participant have an active MH provider in CPRS
ACTIVATION
Yes
No
No
Yes
In the past 2 weeks have you felt little interest or pleasure i doing things most days or every day?
In the past 2 weeks have you felt little interest or pleasure i doing things most days or every day?
C-SSRS Adult Screener for Primary Care
2B. TIER TWO DECISION MAKING
Outreac
skype, phone, or pager. If no response in 1 buisness day, study MH provider preforms outreach
Positive response to Question 4, 5, or 6a
Yes
No
No
Yes
Yes
No
High Concern
Low Concern
Low risk: Provide resources; recommend discussing with provider
Have you had any thoughts of harming yourself or others?
Staff action if on telephone: Transfer to National Crisis Hotline.
Staff action if in person:
Urgent behavioral health consultation. If participant threatens to leave, leaves abruptly or is unwiling to accept servcies and help, call VA police
Staff action if on telephone:
Offer to transfer to National Crisis Hotline and local MH resources
Staff action if in person:
Offer behavioral health consult and provide phone number for National Crisis Hotline and l
ACTION
Yes
No
Accepts transfer: Notify site PI
Refuses transfer: Are there concerns about their immediate safety?
Yes: Call 911 for a well-check
No: Provide resources. Notify site PI.
Uncertain: Immediately consult with site PI or alternative MH provider on the study
2a. TIER ONE DECISION MAKING

Figure 2. Columbia-Suicide Severity Rating Scale (C-SSRS) Adult Screener for Primary Care (Screenshot from Screenshot of REDCap C-SSRS Measure)



Proceed immediately to Columbia-Suicide Severity Rating Scale.

Say: "I would like to ask you some questions about these thoughts you have been having..."

	NO	YES
1. "Over the past 30 days, have you wished you were dead or wished you could go to sleep and not wake up?" * must provide value	○	◉
2. "Have you actually had any thoughts of killing yourself?" * must provide value	○	◉
3. "Have you been thinking about how you might kill yourself?" * must provide value	○	◉
4. "Have you had these thoughts and had some intention of acting on them?" * must provide value	○	◉
5. "Have you started to work out or worked out the details of how to kill yourself?" * must provide value	○	◉
6. "Have you ever done anything, started to do anything, or prepared to do anything to end your life?" * must provide value	○	◉
6a. "Was this within the past 3 months?" * must provide value	○	◉

Responses of “Yes” to questions 4, 5, or 6a categorize the patient as “high-risk”

Reports of risk during Diagnostic Structured Clinical Interivews. Depression and imminent risk for suicide are assessed routinely, using the SCID, as part of our inclusion/exclusion criteria. These assessments are conducted by liscenced clinical psychologists. However, they are conducted in accordance with study inclusion/exclusion criteria, not VA specific guidelines for a suicide risk assessment. VA guidelines evolve and fluctuate and are rolled out within the MH service line for providers with VA privilegedes. Consequently, it may not be feasible for study assessors to stay abreast of the guidelines for assessing patient risk in a VA-conconcordant manner. When a participant meets the 'high-risk' criteria highlighted above (i.e., positive responses to 4, 5, or 6a), study assessors will transfer patients to the National Suicide Hotline as described above.

Reports of risk on study surveys. All surveys will be screened within 2 buisness days of receipt by study staff. This will ensure that surveys are typically screened within 48 hours of receipt by a study staff, barring holidays and weekends (e.g., staff has until Tuesday to screen a survey received on Friday). Staff will read any text written into the survey for any risk-related concerns, as well as review responses to the adapted Linehan BRTC SI screen items that directly assess suicidal ideation. Staff will be carefully trained about the importance of opening surveys promptly and entering receipt of each survey into the study tracking application. Auditing will be performed quarterly to ensure that the staff member reviewed the participants responses on Linehan BRTC SI screen items and intervened appropriately when the final item response was greater than "5".

If any psychiatric emergency is reported on surveys (i.e., expression of risk for suicide or homicide) or a response of greater than "5" on Linehan BRTC SI screen items, the participant's VA Mental Health Provider will be notified using phone, skype, and pager. If the participant does not have a VA Mental Health Provider or their VA Mental Health Provider is unavailable (we are not able to reach the provider within the same business day), a study designated MH provider would do the necessary outreach. There are a number of licensed MH providers on the study team. Some are clinically privileged and others are not clinically privileged (e.g., Research Service employees). When providers are not privileged, we propose they will utilize the C-SSRS screener as outlined in the study protocol (see "Suicide Management Protocol"). When providers are privileged, we propose they use either the C-SSRS screener protocol or a more stringent approach to suicide risk assessment that is consistent with VA guidelines.

IPV reports on surveys. Baseline, weekly, and posttreatment surveys ask about intimate partner violence (IPV). IPV reports are not routinely considered psychiatric emergencies that warrant breaching participants' confidentiality. Additionally, reaching out to all those who endorse IPV may have unintended negative consequences. Reaching out when uninvited to ask IPV vicitims to further discuss their IPV may be distressing and bring up traumatic memories. The outreach may be unwelcome, perceived as intrusive, and discourage future reporting. Discussing violence over the phone may also place the victim at risk to be overheard by the abuser, other loved ones, or children in the home. Consequently, a list of resources will be included with baseline, posttreatment, and follow-up surveys, including for IPV. Letters accompanying surveys will encourage respondants to contact study staff if they would like to discuss any of their survey responses. We will rely on participants to contact study staff if they wish to discuss their IPV experiences further. If participants are excluded due to IPV, the staff member notifiying the reporter of their exclusion will offer local and national resources for IPV.

When the IPV reporter is actively engaged in psychotherapy in our study (i.e., veterans who are actively participating in PE and loved ones are actively participating in PE2), the reporter has has an ongoing relationship with their study provider. In this circumstance, the reporter has the

reasonable expectation that the provider is reviewing their surveys and may ask them more about it. Thus, when a participant is actively engaged in psychotherapy in our study, providers will review IPV survey responses and intervene as clinically indicated, keeping the safety of the reporter of paramont concern. Providers will not breech the reporter's confidentiality unless they have the reporter's verbal permission or are concerned they must do so to prevent imminent harm.

Veterans will be considered 'actively engaged in psychotherapy in our study' when their study therapist has not officially closed their therapy case. Cases are closed when the veteran has completed their course of PE, when the veteran tells their therapist they have quit PE, or when providers have exhausted oureach attempts to a veteran who has missed a scheduled session(s). SPs in the PE2 condition are considered 'actively engaged in psychotherapy in our study' when their veteran is actively engaged in psychotherapy in our study. SPs in the Standard PE condition are never considered 'actively engaged in psychotherapy in our study.'

Managing risk from CBOCs and in-home video telehealth sessions. Due to the nature and distance between the Veteran and telemental health provider incurred in telemedicine practice, additional measures will be taken to ensure patient safety. These procedures will be in place during all telemedicine sessions:

a. Study providers will follow the guidelines detailed in the 2017 Department of Veteran Affairs National Telemental Health Supplement and the 2012 Telemental Health Suicide Prevention and Emergency Care manual.
b. Providers will use VA approved electronic communication methods
c. All study providers will follow their site's local telemental health policies and emergency procedures at each facility and clinic.
d. Providers will always adhere to established face-to-face assessment protocols.
e. Telemental health provider will have detailed contact information from the patient with particular attention to who could be contacted in the event of an emergency. All emergency contact information, local police phone numbers and local emergency room contact information should be readily retrievable during all sessions.
f. Providers will use the National Telehealth Help Desk when necessary: 1-866-651-3180.

Additional manners to manage risk from CBOCs.

a. For all telemental health sessions at CBOC locations, a CBOC staff person will be available to assist Veteran should the need arise.
b. CBOC staff will be available by telephone for the remote telemedicine study provider should they need to emergently contact an on-site VA staff.
c. If a patient becomes suicidal, homicidal, psychotic, or agitated, the Telehealth provider will ask for assistance from the CBOC staff who would help in deescalating the patient and/or initiating commitment.

Additionally, the study will abide by the requirements contained in the VHA Handbook for the credentialing of VHA practitioners who provide clinical services using telemedicine. All practitioners treating patients using telemedicine will be qualified to deliver the level of consultation, care, and treatment involved.

5.1K.2. Privacy. There is a risk that participation may result in a loss of privacy. This would occur if someone not associated with the study heard participants' session recordings or saw participants' data. In order to minimize that risk, all participant data is labeled with a study ID number, which can only be linked to names by a few study staff. The link between study ID number and names will be kept in a secure, password protected location behind the VA firewall.

Further, all hard-copies of data will be kept in a locked filing cabinet within a locked room and will only be accessible to study staff. Recordings will be initially recorded on VA encrypted digital recorders and uploaded onto network folders behind the VA firewall.

5.1K.3. Economic. Participants may choose to take time off work or may incur transportation costs as a result of participating in this study. Every effort will be taken to schedule assessments and therapy sessions at times convenient to participants to minimize loss of wages and/or cost of childcare.

5.1L. Potential Benefits of the Proposed Research to the Subject and Others

Veterans in both conditions will receive Prolonged Exposure for PTSD, one of the most effective and extensively studied treatments for PTSD, PE participation is likely to increase Veterans' well-being. Additionally, SPs may find participating in their Veterans' care helpful for their relationship with the Veteran. There are no other direct benefits to participation.

5.1L.1. Importance of Knowledge to be Gained The knowledge to be gained during the course of this study may positively impact the health and well-being of Veterans with PTSD, lower the cost of treating PTSD, and decrease long-term demand for PTSD services. The knowledge gained may lead to improving treatment adherence to PE and, ultimately, treatment response and quality of life for Veterans with PTSD. This study will lead to the development of evidence-based methods to involve family in treatments for PTSD to maximize Veterans' chances of recovery. PTSD is a debilitating mental health problem that affects Veterans' mental health, physical health, overall quality of life, and the broader functioning of their entire family. The potential risks of the research objectives to participants are minimal, and the potential benefits appear to balance any potential risks.

5.1M. Data and Safety Monitoring Plan

This project will operate under the oversight of the VA Central IRB for Protection of Human Subjects. The IRB reviews research projects which involve human subjects to ensure that two broad standards are upheld: first, that subjects are not placed at undue risk; second, that they give uncoerced, informed consent to their participation. After initial review, each approved project is re-evaluated annually. The Central IRB works with investigators to modify projects to ensure adequate protection for its subjects' welfare and right of self-determination. VA regulations require that all investigators and individuals who work on the study undergo comprehensive training annually in research integrity and protection of human subjects.

We will also report at least annually to the HSR&D Data and Safety Monitoring Board (DSMB). This will include ongoing monitoring of the progress of the study and the safety of participants performed by the PI, study coordinators, study assessors, and study providers. Further, we will log all phone calls received from any participants and carefully evaluate any concerns raised about the protocol. Reporting will cover: 1) safety of study participants (e.g., unanticipated serious adverse events), 2) study enrollment relative to expectations, 3) characteristics of study participants, and 4) retention of study participants at posttreatment evaluation.

Of note, we are not preforming any lab or other tests that could identify new health problems in specific Veterans. Also, all participants receive Prolonged Exposure, an established efficacious treatment for PTSD. Half of the RCT phase and all of the IC Phase participants will be randomized to have their families attend educational sessions. We do not expect the need to convey study findings to participants or health care providers before the end of the study.

However, if some information does arise that necessitates communication, the study team will contact participants by phone and providers via encrypted email.

5.2 Recruitment Methods

5.2A. Study Settings and Recruitment.

Data collection will take place at three sites, including the Minneapolis, Atlanta, and Ann Arbor VA Health Care Systems. All three sites deliver a high volume of PE and provide an ideal environment for this work. We approached a number of sites delivering a high-volume PE, identified from an ongoing study conducted by Drs. Kehle-Forbes and Nina Sayer. We then selected sites with a strong research culture, history of clinical trials of PTSD treatments, existing structure for recruiting and conducting trials for Veterans with PTSD, and a large number of trained PE providers (n = 57, across sites). The study will be based in the Center for Chronic Disease Outcomes Research (CCDOR). Atlanta's and Ann Arbor's Site PIs each have experience conducting RCTs with Veterans with PTSD and were actively involved in study development.

5.2B. Veteran Recruitment

Given the importance of recruitment to the success of any study, we plan to rigorously train all staff in established best-methods for recruiting for behavioral intervention trials (e.g., Leonard, Lester, Rotheram-Borus, Mattes, Gwadz, & Ferns, 2003).[106] Training will address how to handle difficult situations while maintaining boundaries, establish and maintain rapport while not antagonizing or alienating participants, and handling reports of IPV or other risk issues. Methods will include role-play of challenging situations (e.g., reluctance to continue an interview as a family member enters the room, multiple phone interruptions, and requests participants may make that are outside the scope of the interview protocol, such as an additional stipend or loan from the interviewer). It will also include regular recruitment supervision meetings where team members share successful tips from prior studies or experiences within the current study, led by study investigators and staff with backgrounds in clinical and counseling psychology (e.g., Study Manager and all site PIs). Given the importance of establishing rapport to successful participant recruitment[107] and plans for careful training and supervision, staff will be trained in the use of scripts as guides to avoid impersonal or alienating recitation of scripts. Reading scripts verbatim may interfere with establishing rapport, adaptive social norms that promote asking questions, and a safe environment for individuals share when they do not understand or have concerns about the study. See Study Materials for example scripts.

5.2B.1. Referral Sources. We will rely on three methods of identifying potentially eligible Veterans for both the IC and RCT phases of the study: 1) provider referral, 2) self-referral, and 3) identification from hospital records.

Provider Referral. Provider referral will provide our first-line recruitment source, as this will mirror how the intervention is delivered in typical clinic care. We will make announcements about the study in multiple settings and forums (e.g., announcements at team meetings, presentations at grand rounds). We will provide flyers and brochures to providers and discuss the study with them to inform them about the study. As providers and patients may prefer to discuss the study together, prior to referring the patient to our team, fliers and brochures with assist in these efforts. Providers may or may not choose to discuss the study with the Veteran first. We will then receive contact information for potentially eligible patients (i.e., those seeking PTSD care or trauma-focused treatments) by (1) providers or by (2) team-leads in specialty clinics notifying study staff as patients are referred for evidence

based PTSD treatment. Study staff will be provided with patients' contact information through secure email, verbally, or through a cosigned CPRS note that an individual is interested in trauma-focused care (with subsequent communication verbally or through secure messaging).

Self-Referral. To facilitate self-referral, we will use study fliers and brochures strategically placed in appropriate clinic locations and make announcements to inform others about the study. We will also distribute fliers and brochures, make announcements, and provide presentations to community organizations to facilitate self-referral. Individuals who are self-referred to the study will reach out to study staff to express their interest directly.

Identification from Hospital Records. If approaches self and provider referral prove insufficient to reach recruitment goals, we will identify potentially eligible Veterans who have a diagnosis of PTSD through an administrative data pull and recruit these Veterans through the mail and telephone, using the same methods employed for provider referral participants.

5.2B.2. Recruitment Processes: RCT

Provider Referral. Step 1. If the referral source chooses, they can provide Veterans with a study brochure and ask the Veteran if he/she wants to be called about the research study. This will give Veterans an opt out option. If a Veteran responds "no", clinic staff will not contact study staff members. If a Veteran responds "yes", and would like to be called regarding a research study, the provider/staff will notify study staff. Off-team individuals will not make any efforts to recruit the Veteran and will refer the Veteran to study staff with any questions. Alternatively, Veterans' who have not been asked if study staff can contact them will receive a letter in the mail and brochure about the study, informing them they will be contacted and how to decline study recruitment efforts.

Prior to intitating contact with the Veteran, study staff will review hospital records to determine the presence of any study exclusionary criteria (e.g., the patient is currently hospitalized for a psychiatric emergency or reporting active psychotic symptoms).

Step 2. Veterans will then be contacted by telephone and/or in person (i.e., within Mental Health Clinics) by a trained interviewer to discuss the study and for initial screening. In person contacts will only be conducted for Veterans who have already expressed in an interest in participating to their provider or to study staff in telephone recruitment efforts. Prior to direct recruitment, all individuals will be mailed a letter describing the study and how to opt out, as well as a study brochure.

In most cases, we expect that provider referrals will come from patients actively seeking mental health care. When a provider or off-team staff member refers a Veteran to study staff without first asking them if they would like to be called regarding a research study, we will send them a study letter and brochure and wait 7 days prior to efforts to reach them. If, upon contact, the individual has not received their study letter, we will offer to contact the individual again at a later date and to re-mail the recruitment letter. When a provider or off-team staff member refers a Veteran who has expressed an interested in being called regarding a research study, study staff will call the Veteran as soon as possible to give them information about the study and for initial screening. This eliminates a delay in getting Veterans into care, and follows the current clinic mandates regarding minimum wait times for evidence based treatment for PTSD. When Veterans referred through providers are deemed ineligible, we will notify their referring provider and refer Veterans back to their mental health care provider.

We will make up to 3 calls a week for 3 weeks, unless the Veteran declines recruitment or requests an alternative schedule (e.g., if he/she asks us to call more often to try to catch them at a time when they aren't busy or are somewhere in private). We will leave up to one

message per week, unless the Veteran requests no voicemails or requests an alternative schedule. See Materials for an example voicemail script.

Step 3. Upon contact with the Veteran, with their permission, a trained interviewer will then discuss the study and complete an initial screening, including for the presence of an eligible SP (see Table 4), willingness to include a SP in at least one session of PE, and presence of moderate intimate partner violence (SF CTS-2), and presence of symptoms of PTSD on the PC-PTSD-5 (see inclusion/exclusion criteria for further detail). When the veteran's baseline surveys are received prior to their structured clinical interview for inclusions/exclusions (described below), we will also review their PCL-5 scores for the presence of symptoms of PTSD. Veterans with a PCL of 27 or lower will be screened out and will not be scheduled for structured clinical interviews.

Level of relationship satisfaction and distress will be assessed through a single item from the Couples Satisfaction Index (CSI-1) and the Interpersonal Stressors Scale of the Life Stressors and Social Resources Inventory (see appendix with Study Materials) in order to compare differences in relationship strain between those who ultimately do and do not enroll. The study procedures (assessment data gathering, intervention, session recording) and study design (including the nature of randomization to condition) will be fully described to the participant at the time of the initial contact (and again at the time that consent is documented). See script for initial screening call in Materials. For interested and eligible Veterans, we will begin recruitment efforts for their SPs and begin or schedule the over-the-phone informed consent meeting with the Veteran to complete enrollment.

For Veterans who have expressed interest in the study (i.e., study staff spoke with them over the phone, Veteran completed screener, and/or Veteran completed informed consent), if at any time during the recruitment process study staff are unable to reach them, we will send them one final letter. The letter will inform the participant that we have been unable to reach them and that without contact within 2 weeks, we will have to close their case from our study records. The letter informs the Veteran that we will no longer attempt to contact them, and gives them the opportunity to reach out to study staff if they still have interest in participation in the study.

Self-referral and Referral through Identification from Hospital Records. Procedures will following the same general process as above with a few exceptions. For self-referrals, these individuals will be contacting study staff first, so we will immediately initiate efforts to return their calls while also sending them an introductory letter and study brochure. See Materials for Introductory Letter.

For patients identified through hospital records, the volume of mailings anticipated makes individual review of patients' records prior to their initial mailing impractical, so this component of the process will not take place prior to mailing for Veterans referred through this channel. Additionally, as these individuals are not necessarily seeking treatment, we will wait 7 days after the initial mailing before attempting to contact them by telephone.

5.2B.3. Recruitment Processes: IC Phase

Provider Referral. All participants for this phase will be identified through provider referral as described above with some exceptions. The difference between IC participants and participants for the randomized controlled trial are (1) providers will receive personalized feedback on every family-supported PE session for these cases (sessions 1, 2a, and 2b) based on review of the audio tape, (2) data will not be used at part of the RCT, since participants are not randomized. As data will not be used for the RCT, we will establish inclusion/exclusion criteria using methods consistent with how this intervention would likely be delivered in routine care (i.e., hospital record review and self-report). These methods are not based on the rigorous gold-standard assessment instruments required for the larger RCT.

Step 1. Hospital records will be reviewed to determine the presence of study exclusionary criteria (e.g., the patient is currently hospitalized for a psychiatric emergency, actively suicidal/homicidal, or reporting active psychotic symptoms, manic symptoms, or severe substance use). Providers who have consented to the study may discuss the study with patients they identify. If interested, providers will ask (1) patient's permission for study staff to call them and ask about (2) the presence of an eligible SP (see Table 4), (3) willingness to include a SP in at least one session of PE, and (4) the presence of moderate intimate partner violence (SF CTS-2; See IC Veteran Self-Report Form in Materials). These changes from the RCT are done for efficiency of recruitment and, due to the small volume of cases in the IC phase are feasible to ask of study providers for this phase of the study.Providers and staff who are not on the study team may provide Veteran patients with a study brochure and ask Veterans if they want to be called about the research study. This will give Veterans an opt out option. If a Veteran responds "no", clinic staff will not contact study staff members. If a Veteran responds "yes", and would like to be called regarding a research study, the provider/staff will notify study staff by encrypted email or through a co-signature on a clinic note in CPRS. Off-team individuals will not make any efforts to recruit the Veteran and will refer the Veteran to study staff with any questions.

If Veterans were not asked if the study could contact them prior to study referral (e.g., provider or an off-team staff did not ask them if they would be willing to be called regarding a research study), Veterans will be sent a letter and brochure describing the study, informing them they will be contacted and how to decline study recruitment efforts. Clinicians will continue to provide study staff with patients' contact information through secure email, verbally, or through a cosigned CPRS note that an individual is interested in trauma-focused care (with subsequent communication verbally or through secure messaging).

Step 2. Veterans will then be contacted by telephone and/or in person (e.g., coordinating with other medical appointments) by a trained interviewer to discuss the study. As with the RCT, for those requiring a pre-notice letter, we will wait 7 days prior to efforts to reach participants. If, upon contact, the individual has not received their study letter, we will offer to contact the individual again at a later date and to re-mail the recruitment letter. For those whose provider obtained permission for staff to contact them and who completed the brief self-report form, Veterans can begin or be scheduled for an informed consent meeting to complete final enrollment.

As with the RCT, we will make up to 3 calls a week for 3 weeks, unless the Veteran declines recruitment or requests an alternative schedule (e.g., if he/she asks us to call more often to try to catch them at a time when they aren't busy or are somewhere in private). We will leave up to one message per week, unless the Veteran requests no voicemails or requests an alternative schedule. See Materials for an example voicemail script.

Step 3. For those who have not completed initial self-reports with their providers (regarding presence of a SP and IPV), upon reaching the Veteran, with their permission, a trained interviewer will then discuss the study and complete an initial screening, including for the presence of an eligible SP (see Table 4), willingness to include a SP in at least one session of PE, and presence of moderate intimate partner violence (SF CTS-2).

The study procedures (assessment data gathering, intervention, session recording) and study design (including the nature of treatment) will be fully described to the participant at the time of the initial contact (and again at the time that consent is documented). See script for initial screening call in Materials. For interested and eligible Veterans, we will begin recruitment efforts for their SPs and begin or schedule the informed consent meeting with the Veteran to complete enrollment.

5.2C. SP Recruitment: IC and RCT Phases

After receiving Veterans' permission to contact their nominated SPs, the recruitment procedures will be similar for SPs. They will be sent a letter, a brochure describing the study, informing them they will be contacted and how to decline study recruitment efforts. This initial mailing will also include an Information Sheet including all of the components of informed consent to be discussed by telephone. They will be contacted by telephone by a trained interviewer to discuss the study, their interest, and assess the presence of moderate relationship violence on the SF-CTS and screen for PTSD, using the same schedule of contacts used for Veterans, described above. If the SP is unable to speak in private to complete the SF CTS-2 and PTSD screen (see Materials for script), we will offer mailed administration and/or schedule a time to administer the brief measure in private by telephone.

5.2D. Provider recruitment.

When it is time to recruit providers for exit interviews (after completing their treatment cases), we will email them to remind them about the interview. Providers will be able to respond to the e-mail to either opt out of contact for the study or to schedule an interview date and time. If providers do not respond to the e-mail, they will receive a follow-up e-mail and three phone calls from the study team. If we do not reach or hear back from the provider after those contacts, we will assume they are not interested in participating in the interview.

5.2E. MH Leadership recruitment.

Each of the mental health leadership members have also already been approached by the site PIs as part of establishing the feasibility of this study for the grant proposal supporting this project. They will be re-contacted through email and telephone within the 3 months prior to the interview (see 5.3C). In case of attrition, any additional providers will be recruited through email contact by the site PI, followed by a second email, if needed and three follow-up phone calls.

5.3 Inclusion/Exclusion Criteria

See Table 4. With the exception of criteria relevant to SP inclusion (criteria 3, 4, 9, & 10), inclusion/exclusion criteria reflect those consistent with PE delivery within VA. RCT phase participants must meet diagnostic criteria for PTSD or subthreshold PTSD,[91] assessed using the gold-standard Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).[3] Consistent with recommendations, subthreshold PTSD will be defined as endorsement of criteria A (trauma), F (duration), and G (impairment), with at least one symptom from each of the remaining diagnostic criteria.[92] As IC phase participants' data NOT will be part of the larger RCT, how this is assessed for IC phase participants will vary to streamline recruitment processes. It will be assessed through a positive screen for PTSD on the PTSD Checklist (PCL-5)[2] administered in paper-and-pencil questionnaires. Items 5-7 will be assessed using the Clinical Trials Version of the Structured Clinical Interview for DSM-5 (SCID-5-CT)[12] for RCT participants. For IC phase participants, Items 5 and 7 will be assessed by self-report questionnaire (PHQ-9; AUDIT; DAST) and item 6 through hospital records review. Structured clinical interview for inclusion/exclusion criteria will be administered by trained and supervised assessors blinded to condition from the hub site (Minneapolis VA).

In order to finalize and solidify all processes before beginning the RCT phase of the study, Minneapolis assessors will administer the gold-standard Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)[3] and the Clinical Trials Version of the Structured Clinical Interview for DSM-5 (SCID-5-CT)[12] to up to ten Intensive Coaching (IC) cases. This process allows clinical interview administrators to acclimate to the interview procedures and to prepare for the RCT phase.

As all structured clinical interviews will be administered by Minneapolis VA staff, most interviews will take place by telephone. Minneapolis VA participants will have the option for in-person administration.

Table 4. Inclusion/exclusion criteria

Inclusions	Measure	Exclusions	Measure
1. Enrolled in VHA care	CPRS	6. Actively suicidal/homicidal with intent and/or plan in the last 30 days; hospitalized in the last 30 days for psychiatric reasons; multiple hospitalizations for psychiatric reasons in the past year	SCID-5-CT[12]
2. Clinically significant PTSD symptoms	CAPS-5	7. Episode of mania/ psychosis in past 3 months	SCID-5-CT[12]
3. Have a SP (intimate partner, family member, or friend) with contact at least 3 times a week	Self-report item	8. Severe substance use problem in past 3 months	SCID-5-CT[12]
		9. Moderate relationship violence	IPSVS Adapted[108]
4. Will allow a SP to participate	Self-report item	10. Veteran has underlying medical condition or a planned medical procedure liklely to impair ability to engage in treatment.	
5. Willing to be seen via telehealth when in-person treatment options aren't available.		11. SP screens positive for PTSD	PCL-5
		12. Veteran and/or SP fails to complete baseline survey	

Criteria for items 3-4 will be assessed through single yes/no self-report items administered to Veterans during telephone screens or on self-reports (IC participants only). Given the emphasis on flexibility, item 4 will require the Veteran to agree to (a) allow a SP to complete study assessments, (b) bring a SP to Session 1, if randomized to family supported PE, and (c) discuss further SP attendance with his/her provider. Variability in SP attendance will be included as a covariate in analyses and examined as a predictor of adherence. Relationship violence will be assessed by telephone from both Veteran and SP-report (item 9), defined as one or more episodes of severe violence in the past year (e.g., kicked or beat up) on the IPSVS Adapted Scale[106]. We will exclude Veteran participants if he/she has an underlying medical condition or a medical procedure (item 10) planned that would greatly impair their ability to participate in a weekly psychotherapy (i.e., a severe seizure disorder making weekly attendance difficult or a planned major surgery within a month of beginning treatment). This item will be assessed during the initial phone screening. We will administer a PTSD screen (PCL-, response options adapted to a yes/no format for efficiency of delivery by telephone) to SPs by telephone and exclude SPs who screen positive for PTSD on the PCL-5. SPs and Veterans will be required to complete a baseline survey assessment before they can be randomized to a study arm. Failure to complete the baseline survey will result in study ineligibility (item 11). If a family member is determined to be ineligible due to a positive PTSD screen or failure to complete his/her baseline survey, but the Veteran is otherwise eligible, the Veteran will be contacted by telephone and given the opportunity to designate another family member for participation. The details of the reason their initial SP was ineligible will not be disclosed.

Regarding relationship violence, when the veteran reports they have been the target of moderate violence from their SP, the study team, under the supervision of the local Site PI, will determine if the violence should be the immediate focus of clinical attention. That is, (1) is the reporter is in danger of harm and, therefore, the focus of clinical attention should be on safety, or (2) would the reporter prefer to focus on IPV rather than PTSD. Importantly, each Site PI is a licensed, clinical psychologist with the appropriate training and expertise to make these

decisions. If the violence should be the focus of immediate clinical attention, then the dyad will be deemed ineligible and provided appropriate referrals. If the violence should not be the focus of clinical attention (e.g., the reporter is not in danger and does not wish to focus on IPV) the reporter may select a different loved one with which to participate in the study.

The new SP will also be screened and subject to the same inclusion/exclusion criteria, including that the new SP cannot be ineligible due to moderate IPV towards the veteran. The original SP will be deemed ineligible. The details of the reason the initial SP was ineligible will not be disclosed. The reporting dyad member(s) will be provided with resources and referrals for IPV (see IPV risk algorithm). Ineligible dyads may be re-evaluated for eligibility when this exclusionary criteria has been resolved (i.e., one year has passed without an episode of severe violence or six months without minor violence).

5.4 Informed Consent Procedures

5.4A. SP Informed Consent.

We will seek an approval of verbal informed consent over the phone and waiver of written informed consent. All contact between study staff and SPs randomized to standard PE (without family involvement) will be remote (i.e., by mail and telephone). The study poses minimal risks, waiving informed consent does not affect the well-being of participants, and decreases participant burden that would be associated with scheduling and attending an in-person appointment at the VA hospital, especially for SPs who have full time jobs and have never been to the VA hospital. Verbal consent will be obtained by telephone, pending final confirmation of Veteran's eligibility at the eligibility assessment/consent described above.

During the initial phone call with SPs, all study procedures (assessment data gathering, intervention, audiotaping) will be fully described to the participant using the Information Sheet SPs received by mail to guide the discussion. Participants will be informed of the study design (including, for RCT participants, that they will be randomized to condition and will receive notice of their condition after the Veteran signs informed consent documents and Veteran eligibility is finalized) before they decide to participate. After reviewing the study and answering all questions, for those SPs who remain interested in participating, the consenting staff will ask to audio record their consent to the study and consent to audio recording treatment sessions (if assigned to family supported PE).

If Veterans are deemed ineligible due to inclusion/exclusion criteria or lack of interest, SPs will be informed that full inclusion/exclusion criteria were not met for the Veteran and thus the dyad is no longer eligible for enrollment. Specific details on which inclusion/exclusion criteria (including level of interest in the study) will not be disclosed. The same approach will be used for SPs' who decline participation or report moderate relationship aggression (i.e., Veterans will be informed that full inclusion/exclusion criteria were not met and thus the dyad is no longer eligible for enrollment). Appropriate alternative referrals to mental health treatment, including substance use treatment or psychotherapy, or to address relationship aggression will be made as upon request and when clinically indicated (i.e., positive screens for psychosis, substance use, suicidality, homicidally, etc.).

Of note, while consent takes place after the initial phone screening, randomization (RCT phase only) does not take place until participants have met inclusion/exclusion criteria. Since we are proposing that consent procedures for SPs be the same regardless of their treatment assignment (consent by phone), we do not need to know randomization when we are recruiting and consenting SPs. Once both members of the dyad have been deemed eligible for the study,

participants will be notified of their randomization when it is time to schedule their (or the Veteran's) first treatment session.

5.4B. Veteran Informed Consent.

After completing the recruitment steps described above, Veterans will participate in informed consent procedures. Veteran participants will participate in informed consent over the telephone with a study staff member. Subjects can meet with a study staff member for in-person informed consent if they prefer. In this case, participants meeting face-to-face for informed consent will be required to sign an official informed consent form instead of having their consent recorded.

Informed consent will be obtained before obtaining any Baseline self-reports (IC and RCT) or Baseline interviews (RCT and up to 10 IC cases). As these Baseline procedures are also necessary for establishing final eligibility (RCT: SCID-5-CT and CAPS-5; IC: PCL-5, PHQ-9, AUDIT, DAST), Veterans will be notified that the baseline procedures are necessary for establishing final eligibility and they may be deemed ineligible for the study after these procedures. For IC participants, those who meet final inclusion/exclusion criteria and remain interested will proceed with treatment (family-supported PE). For RCT participants, those who meet final inclusion/exclusion criteria and remain interested will then be randomly assigned. They will receive notification of their assignment when contacted to schedule their first therapy appointment. Individuals deemed ineligible will be told by telephone and Veterans referred back to their referring providers.

When Veterans are deemed ineligible by a study assessor after completion of the Structured Clinical Interview (i.e., positive screens for psychosis, substance use, suicidality, homicidally, etc.), study staff will communicate the assessment results of these ineligible subjects back to the treatment team (non-study clinical staff) for purposes of patient treatment planning and continuity of care. Conveying a patient's assessment results to the treatment team allows patients to be referred to appropriate treatment in a timely manner, while also eliminating any inconvenient and redundant reassessments. This will be proposed to participants during informed consent, and patients will have the ability to decline this request.

The site PI at each location will be responsible for training and supervising others at their site in obtaining informed consent. All staff will have completed all necessary human subjects trainings (e.g., TMS trainings and CITI training). Those obtaining informed consent will emphasize to the individuals that participation in the study is voluntary and that they can choose not to participate in any part of the study at any time.

Veteran participants will receive all of the information contained within informed consent by mail. The mailing will contain an opt-out option for those who do not want to be contacted any further along with 1) information explaining the risks and benefits of study participation, 2) their rights as study participants and their privacy rights and 3) required elements of informed consent. This material will then be reviewed by telephone prior to participation and verbal informed consent will be obtained and recorded. When the telephone consent is obtained, they will have already had the opportunity to review study details, consider their participation, and consult with loved ones about participation. Discussing this material with a staff member over the phone will provide greater time and freedom to consider or decline study participation, prior to investing more time and energy in the study.Participants will also verbally consent to permitting the use of audio/video recordings throughout the study. All consent will be recorded and saved in study files. Staff will solicit and answer all questions, and they will also ask the participants questions to ensure participant comprehension of the informed consent document including, but not limited to, what their understanding is of the risks and benefits of participation, when

assessments will occur and what topics they will cover. The team is sensitive to the importance of the informed consent process and will make every effort to ensure that participants give their consent voluntarily and fully informed about the potential risks and benefits.

If a participant requests to have an informed consent meeting face-to-face with a study staff member, this will be permitted. Some participants may prefer to coincide other appointments at the VA with an in-person consent meeting with our study staff. In this case, participants meeting in-person for informed consent will be required to sign an official informed consent form, a Consent for Production and use of Verbal or Written Statement, Photos, Digital Images, and/or Video or Audio Recordings by VA form, and an Authorization for Use and Release of Individually Identifiable Health Information form instead of having their consent recorded.

5.4C. Retaking Baseline Assessments

For safety and risk implications, we will require Veteran and SP participants to retake the baseline survey and preclinical assessment if the therapy start date would occur 2 months after their baseline data was collected. Time gaps between baseline data and therapy start dates can occur for various reasons, including scheduling issues, provider availability, patient travel arrangements, etc. It is important that patient baseline data is as close to therapy start dates as possible, as clinical data can change over several weeks. For example, in the gap between assessment and therapy start, patients could have a serious substance use relapse or a suicide attempt that would then make it clinically inappropriate for them to begin a trauma-focused therapy, prior to addressing their more pressing concerns around establishing their safety or sobriety. Additionally, we expect many of the constructs we assess to naturally change with time (e.g., family functioning, relationship satisfaction). So, baseline assessments that are more than 2 months old at the time of therapy start may no longer truly represent the patient, support person, or family functioning at the beginning of treatment, confounding study results.

Subjects will be informed of this requirement during the informed consent process and on the information packet or informed consent form. Participants would get paid again for retaking these assessments ($40 for the baseline survey; $50 for the preclinical interview).

5.4D. Receiving Baseline Surveys Before Subject Informed Consent

If a participant completes their survey before consent, this will not be immediately reportable to CIRB. Instead, staff will document this occurance in a spreadsheet to be given to CIRB at continuing review. Staff will then be required to get consent from the participant within 30 days of receiving the baseline survey. If consent is not obtained within the 30 day window, the deviation is immediately reportable to CIRB and staff will complete a protocol deviation.

5.4E. Incentives.

IC phase: Participants will receive a $25 incentive for Baseline self-reports, $40 optional for baseline Cognitive Interviews, $50 for optional Baseline Structured Clinical Interviews (Veterans only), $5 per Weekly form, $25 for Posttreatment self-reports, $40 for optional posttreatment Cognitive Interviews, and $50 for optional Posttreatment Structured Clinical interviews (Veterans only). Veterans can earn up to $250 and $170 for SPs. Telephone administration will be offered for interviews to increase response rates.

RCT Phase: Participants will receive a $40 incentive for Baseline self-reports, $50 for Baseline interviews (Veterans only), $50 for Posttreatment self-reports, $60 for Posttreatment interviews (Veterans only), and $60 for 3-month follow-up self-reports. Veterans and SPs will be given weekly surveys during weeks 2, 4, 5, 6, 8, 10 and 12 of treatment. Participants will be

compensated $10 for completing surveys during weeks 4, 5, 6, 10 and 12. The weekly surveys during week 2 and 8 will be lengthier and more thorough, thus participants will be paid $20 for completing weekly surveys on those two weeks of treatment. Veterans can earn up to $290 and SPs' $190. Telephone administration will be offered for to increase response rates.

Up to 40 Veterans randomized to Partner Enhanced PE will be offered the opportunity to complete an over-the-phone qualitative interview. Veterans who are offered and complete the qualitative interview will be compensated $60. The incentive for the qualitative interviews will not be reflected in the total amount a Veteran can receive, because it will not be offered to all participants.

5.4F. Communicating with Participants using MyHealtheVet Secure Messaging.
We will incorporate the use of MyHealtheVet application as a study communication method with participants. My HealtheVet is an online portal created by the Department of Veterans Affairs to help Veterans in managing their health care, work with healthcare providers to reach informed decisions, and improve their overall health. My HealtheVet offers a suite of tools including access to their health records and a Secure Messaging system to communicate with their healthcare team and other VA staff. Our study will use MyHealtheVet in study communication techniques so Veteran participants who use the application can access their health records, receive email reminders about appointments, and communicate with members of the study team using Secure Messaging.

5.4G. Provider and Leadership Informed Consent.
5.4G.1. Providers. Exit interviews with providers will take place by telephone. We will request a waiver of written consent from the IRB. We will obtain oral informed consent and consent to be audio-taped, both of which will be captured on the audio-recording. Once a provider schedules an interview, an Information Sheet, covering all the elements of informed consent, will be e-mailed. At the beginning of the phone interview, we will thoroughly describe the risks and benefits and give the potential participants time to ask questions. We will take extra care to ensure that they understand that their participation is voluntary and will not affect their employment.

Providers will be allowed to ask questions prior to the interviewer beginning the audio-recording. Once the provider indicates his/her willingness to agree to the elements of informed consent and audio-recording, the interviewer will turn on the recording device and confirm the participant's consent to both the interview and the audio recording. As participants received the information sheet reviewing all the elements of informed consent document by email, they will have ample time to review the consent document. Staff will solicit and answer all questions, and they will also ask the participants questions to ensure participant comprehension of the informed consent document including, but not limited to, what their understanding is of the risks and benefits of participation and what is being asked of them.

5.4H.2. MH Leadership. We will request a waiver of written consent from the IRB. Once a member of leadership schedules an interview, a copy of the Information Sheet will be e-mailed. At the beginning of the phone interview, we will obtain oral informed consent and consent to be audio-taped. MH leadership will be allowed to ask questions prior to the interviewer starting the audio-recording. Once the provider indicates his/her willingness to agree to the elements of informed consent and audio-recording, the interviewer will turn on the recording device and confirm the participant's consent to both the interview and the audio recording.

5.5 Study Evaluations

5.5A. Quantitative Data Collection (Aim 1, Aim 2, Exploratory Aim).

Except where indicated, data collection for the IC and RCT phase is identical. Aim 1 outcome variables will be obtained from Medical Records (attendance) and Provider Report (homework compliance). Aim 2 outcomes will be obtained from Baseline (week 0) and Posttreatment (16 weeks post-session 1)) assessments of PTSD symptom severity, depression severity, quality of life, and relationship functioning. Aim 3 outcomes will be obtained from qualitative sources. Our Exploratory Aim outcomes will be obtained from Baseline, Posttreatment, and brief Weekly self-reports from Veterans and SPs. See below for measures.

5.5A.1 Aim 1. Aim 1 outcomes will be measured with methods drawn from Project HomeFront and our prior work coding session notes for PE/CPT treatment completion.[51] PE attendance will be counted from review of Medical Records. Participants will have 'completed' PE when providers record they have successfully completed PE in a final session note. Providers will also be asked to log patient attendance and indicate the dates of attended sessions, missed sessions, and cancelled/rescheduled sessions. Homework compliance will captured through patient observation by providers (Provider Report). Rating items were adapted from those used with Exposure and Response Prevention Therapy for Obsessive Compulsive Disorder (also a cognitive-behavioral exposure therapy).[93] Providers will also report on rates SP-provider contact weekly.

5.5A.2 Aim 2. Clinical outcomes for Aim 2 will be assessed through multiple forms (i.e., self-report and structured clinical interview), consistent with gold-standard methodology used in prior RCTs of PE and CPT. Baseline and posttreatment paper-and-pencil questionnaires will be completed by participants in both the RCT and IC phase of the study. Some participants in the IC phase will also receive structured interviews to allow the study team to implement all study procedures prior to beginning the RCT.IC participants will receive in-treatment assessments before sessions 2a and 2b to contribute to the intensive coaching and feedback providers receive for these early cases.

For RCT phase, structured clinical interviews will take place at Baseline (week 0) and posttest (within 4 weeks of final session). Self reports/surveys will take place at Baseline (during week 0) and at posttreatment (during final session). For drop out Veteran participants, posttest surveys will be completed 16 weeks post-session 1 and the posttreatment clinical assessment will be done within 4 weeks of that posttest survey. For late treatment completers (i.e., treatment takes more than 16 weeks), all posttest surveys and post clinical interviews will be delayed but will be done no later than 24 weeks post-session 1.

For the IC phase, weekly surveys will be given for the first 2 weeks of treatment (session 2a, and 2b). For the RCT phase, weekly surveys will be given during weeks 2, 4, 5, 6, 8, 10 and 12 of treatment. For participants, the weekly surveys during week 2 and 8 will be lengthier and more thorough. All structured interviews (CAPS-5[3] and SCID-5-CT)[12] will be administered by trained and supervised assessors who are blinded to condition. Assessors will be trained and supervised weekly by Dr. Spoont, a licensed clinical psychologist with expertise in conducting structured diagnostic clinical interviews and assessing and intervening with patients experiencing mental health crises. For mailed assessments, we will use CCDOR's well-established modified-Dillman protocol with repeated mailings and an incentive (incentive schedule described below).[6] For surveys of Veterans with PTSD, our team's response rates

have ranged from 55% to 85%. Given the short interval between assessments, we will include a telephone call reminder and an offer telephone administration to optimize response rates.[6]

5.5A.3 Exploratory Aim. Exploratory Aim outcomes (key social influences) will be measured from self-reports from both Veterans and SPs at Baseline, Posttreatment, and Weekly intervals. The frequency of measurement in necessary for examining the nature, shape, and change of key social influences week-by-week over the course of treatment. For the IC phase, the Weekly self-report for Veterans will be completed before each treatment session with a $5 incentive for each form. IC phase participants will only receive these assessments for the first 3 weeks of treatment (session 2a and 2b). For the RCT phase, Veterans and SPs will be given surveys during weeks 2, 4, 5, 6, 8, 10 and 12 of treatment. Participants will be compensated $10 for completing each survey during weeks 4, 5, 6, 10 and 12. The weekly surveys during week 2 and 8 will be lengthier and more thorough, thus participants will be paid $20 for completing weekly surveys on those two weeks of treatment. Staff will make reminder calls to Veterans to ensure these weekly surveys are completed and offer telephone administration. SP data collection will take place by mail or online, because if SPs in standard PE receive assessments with Veterans at the medical center, we may unintentionally increase the rates of SPs reaching out to providers, artificially inflating family assistance within standard PE (i.e., cross-over effects). Veteran and SP participants are required to complete their baseline assessment survey before beginning treatment, as the baseline survey is part of study eligibility criteria. Participants will be given a $40 incentive for the baseline surveys. Veteran and SP participant posttreatment assessments will be administered using CCDOR's modified-Dillman protocol, with a $50 incentive for Posttest surveys, as well as a post-card reminder, second and third survey mailing package, telephone call reminders, and an offer of telephone administration to optimize response rates.[6] For Weekly assessments, SPs from both conditions will receive a packet of self-report forms and postage paid envelopes at study enrollment (RCT only, these measures will be administered in person when SPs attend sessions in the IC phase). SPs will mail completed self-report forms to staff weekly and receive their incentive for each completed form. Study staff will make reminder calls each week to participants to complete the weekly survey. If study staff fail to reach a participant, another weekly survey will be sent along with a letter reminding him/her to complete the survey and mail back to the VA. For the few sessions that SPs in family supported PE attend, they will be offered in person administration of their weekly forms for convience. We will also send Veterans and SPs a follow-up survey 3 months after the posttreatment assessment. Participants will receive a $60 incentive for completing the 3 month follow-up survey, and we will use CCDOR's modified-Dillman protocol once again to optimize response rates. See attached Materials for study measures.

5.5A.4 Veteran/SP Measures. Unless otherwise specified, all measures have established reliability and validity (See Table 5). Aim 2: PTSD symptom severity will be assessed through Baseline, during treatment, and Posttreatment self-reports on the PTSD Checklist (PCL-5)[2] and Baseline and Posttreatment assessments using a structured clinical interview (CAPS-5; RCT only).[3] Additional clinical outcomes will include depression severity (Patient Health Questionnaire; PHQ-9),[13] quality of life (World Health Organization - Quality of Life, Brief; WHOQOL),[94] relationship functioning (Quality of Relationships Inventory, QRI),[89] and treatment satisfaction (Client Evaluation of Services Questionnaire, CSQ-8).[95] One defining principal of practical RCTs is prioritizing outcomes that are simple, clinically friendly, and typical of everyday good practice to improve the clinical relevance of findings.[4] In typical VA practice, PE response is evaluated through repeated administration of the PCL[5] or PCL-5,[2] which is simpler and quicker than a structured clinical interview. Consequently, PCL-5 scores will serve as our main

outcome for Aim 2. CAPS-5 (RCT only) scores will provide an important secondary outcome for formal diagnoses and facilitate comparison across trials.

5.5A.5 Exploratory Aim Outcomes: SPs' support for PE participation will be assessed using the Credibility/Expectancy Questionnaire, adapted for EBPs for PTSD (CEQ-PTSD)[96]. SPs' symptom accommodation will be assessed through the Significant Others' Responses to Trauma Scale (SORTS).[97] SPs' behavioral support for treatment participation will be assessed through Veteran-report on the Support Checklist, developed during Project HomeFront (α = .78; item-total correlations: 23-.70; significantly correlates with SP knowledge of and attitudes about treatment, SP contact with providers, social support, and symptom accommodation). Items assess SP behaviors in the past week that support or discourage PE attendance (e.g., help with homework).

***5.5A.6 Covariates*.** SP support for PE may better influence adherence with less SP distress, less family conflict, greater provider-SP contact, and certain demographic characteristics (e.g., gender, age, or race/ethnicity). SP distress will be assessed using the PROMIS Percieved Stress scale[98] and General Functioning scale of Family Assessment Device (FAD). Frequency of provider-SP contact will be assessed in weekly provider reports. Demographic variables such as race, gender, SP-Veteran relationship (e.g., spouse, parent, adult child), and frequency of SP-Veteran contact will also be assessed at Baseline.

5.5A.7 Qualtrics Online Surveys

Survey administration format will transition to Qualtrics FedRAMP electronic survey software accessed via the VA cloud. This transition will support data collection during the current COVID 19 directives. Our study sites have been ordered to "shelter in place" during the pandemic, making paper survey mailings unachievable. Paper surveys will still be available to those who need or request them, but we plan to use online surveys as our primary modality.

Qualtrics FedRAMP has been approved for use from the VA OIT Security standpoint (Authority to Operate or ATO). The ATO status is currently approved for 1 year and a full 3-year ATO is in the works. Qualtrics FedRAMP surveys will contain a study ID number, time of data entry and limited individually identifiable information. Within the VA firewall, the study team at the VA will create a custom- built tracking app that will track each participant's enrollment and study status. Data will be routinely extracted from Qualtrics FedRAMP in the VA cloud and stored on secure CCDOR servers, using SQL database connections. All data will be stored and utilized within secure CCDOR servers that are part of the Minneapolis VAMC network and which operate behind the VA firewall. All data is tracked using a SQL database, with a GUI-front end system that restricts access to only those with approval to study data.

Qualtrics FedRAMP surveys will contain minimal individually identifying information. The only identifying information will be information that is self-reported by the participants (e.g. name, phone, email, which is best method of contact). No sensitive data will be stored outside of the VA protected environment. Once data are transferred for data analysis, data will be maintained on password-protected VA computers in the VA environment and on secure VA servers.

Study staff will monitor the functioning of the Qualtrics FedRAMP application. Only staff affiliated with this research protocol will have access to Qualtrics FedRAMP data collected for this study.

The PI or her designee will be responsible for monitoring data storage location and transfer of data between the VA cloud and VA server.

Participants will be sent their Qualtrics survey via a generic email to their personal email address, if the patient opts in for email useage. Prior to emailing participants, we will contact them by phone to ask permission to use their email for this purpose. If the participant does not opt in for email useage, they will be given the Qualtrics survey URL verbally over-the-phone or written on the recruitment and/or follow-up letters sent to them in the mail. Participants can complete hard copies of the survey by hand if they prefer.

All emails to participants will be extremely generic and will follow VA guidelines; they will not mention details of the study in the body of the email, participant names and PHI will not be used, and only generic secure hyperlinks (connected to Qualtrics) will be used.

Study providers will also use email to contact participants, when approved by their site, using their site's approved email protocol when patient's opt in for personal email usage.

Table 6. Implementation Framework Elements Guiding Process Evaluation[100]

Element	Key Question	Data Sources
Reach	• Percentage approached who agree to participate? • Differences between participants and non-participants? • What influences willingness to participate?	• Patient Screening Database • Process Log • Exit Interviews • SP self-reports
Effectiveness	• What is the effect of the intervention?	• Study outcomes • Exit Interviews • VA Interviews
Adoption	• Greatest barriers to adoption? • Supports needed for clinics to adopt the intervention?	• Process Log • VA Interviews
Implementation	• What supports are needed to ensure consistent intervention delivery? • What tools are needed for consistent intervention delivery?	• Process Log • VA Interviews • Fidelity Monitoring • Exit interviews • SP self-reports
Maintenance	• What resources are needed to maintain the intervention? • What adaptations are needed to integrate into regular practice?	• Process Log • VA Interviews • Fidelity Monitoring

5.5B. Qualitative Data Collection (Aim 3).

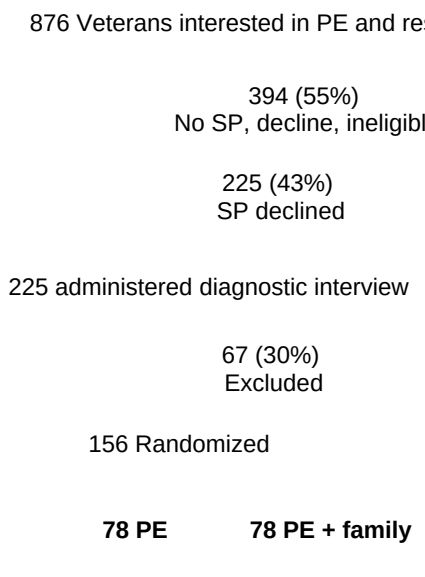
For Aim 3, we will examine the barriers/facilitators of real-world implementation and strategies to facilitate implementation through a mixed-method, multi-stakeholder process evaluation[100] with patients, providers, and mental health leadership. The RE-AIM framework will guide interview questions and assessments to evaluate Reach (factors influencing participation rate within target population), Effectiveness (impact of an intervention), Adoption (factors influencing if/how many VA hospitals would adopt the program), Implementation (factors influencing intervention integrity in real-world settings), and Maintenance (sustainability).[101]

Data collection is modeled after a prototypical Hybrid 1 study[42;100] and will take place throughout the trial. Data sources include 1) study outcomes described above, 2) a Patient Screening Database, 3) a team observational Process Log for day-to-day observations,[100] 4) post-intervention interviews with providers and leadership (VA Interviews), 5) qualitative Exit Interviews with Veterans in partner supported PE, 6) Fidelity Monitoring, and 7) SP self-reports from Posttreatment. See Table 6.

The Patient Screening Database will reflect the number of participants screened and reasons for exclusion/inclusion. The Process Log will include observations and reflections on the team's daily experience with essential activities in implementing family supported PE within the trial. The Log allows for recording comments from clinical staff and patients not readily reported in formal data collection methods.[100] Qualitative open-ended interviews will be conducted with study providers and leadership at each site (i.e., study providers, team leaders, mental health leadership), upon completion of intervention delivery. Interviews will focus on relevant RE-AIM domains and implementing family supported PE with specific Veteran subgroups (i.e., women, racial/ethnic minorities, same sex couples). Brief semi-structured Posttreatment Exit Interviews with Veterans in family supported PE will assess *1) reactions to the intervention, including experiences with trauma disclosure to SPs,* 2) how SPs influence Veterans personal treatment outcomes, and 3) recommendations for changes to improve the effectiveness of family engagement. Fidelity monitoring will evaluate the effectiveness of training, intervention integrity, and which intervention strategies proved particularly difficult/easy to master. SP self-reports and Veteran Exit Interviews will identify practical attendance barriers and solutions.

5.6 Data Analysis

Figure 3. CONSORT Diagram



5.6A. Power analysis and sample size for the RCT phase.

Based on annual rates of patients initiating EBPs for PTSD at each site, we estimate 1751 Veterans will be referred for EBPs over the recruitment period (27 months). Based on response rates for Project HomeFront, we anticipate 50% (n = 876) will be interested in research. See Figure 3 for recruitment flow. Estimates are conservative and incorporate Project HomeFront data, including that 8% will not have eligible SPs, 34% of Veterans will be unwilling to ask SPs to participate, and 20% of SPs will not be interested. To support recruitment success, we will also use study fliers and brochures strategically placed in appropriate clinic locations. We will contact patients until we reach 156 patients randomized (78 in each arm).

We expect to enroll 2 subjects per month, per site, during recruitment for a total n of 156 Veterans and 156 SPs. Session attendance serves as the primary outcome. Analyses below indicate our proposed minimum n of 156 is sufficient to detect clinically meaningful differences between standard PE and family supported PE on Aim 1 and Aim 2 outcomes. Data analysis will take place at the Minneapolis VA Health Care System. Individuals involved in data analysis (quantitative and qualitative) will include Emily Hagel Campbell and Drs. Nelson, Meis, Kehle-Forbes, Spoont, and Polusny.

5.6A1. Aim 1. Preliminary Project HomeFront data indicate the average number of sessions attended is 7.30 (*SD* = 4.45). Seventy-eight participants in each arm yields 80% power to detect a two session difference between treatment conditions. A two session improvement corresponds to an effect size of (*d* = 0.43), slightly below conventions for a moderate effect size (*d* = .50). A greater sample size could detect smaller effects, but these are unlikely to be clinically meaningful. An alternative approach is to power the study based on a minimally

clinically significant increase in rates of treatment completion (e.g., at least 10%). However, given the increased power needed to detect change in a dichotomous outcome, this would not be feasible; we would need at least 692 subjects for 80% power.

5.6A2. Aim 2 (family supported PE will lead to greater reductions in PTSD symptoms than standard PE). Power analyses are based upon our ability to detect a clinically meaningful difference between our two treatment conditions on PTSD symptom severity using the PCL.[5] A five-point difference on the PCL is the minimal threshold for determining if an individual has responded to treatment (i.e., differences not due to chance); a ten point difference is the minimal threshold for clinically relevant differences.[7] Smaller differences are unlikely be clinically meaningful. Analyses take into account our repeated measures, two-armed design and estimates of variance and auto-correlations between repeated PCL assessments from our prior work (Project HomeFront, Time 1 PCL SD = 12.16; Time 2 PCL SD = 14.8; Time 1 and Time 2 PCL, r = .61). Using a plausible range of auto-correlations (r = .50-.70) and standard deviation estimates (SD = 12.16-14.8), and assuming 20% missingness on posttreatment PCL scores (n = 124), we are sufficiently powered (80%) to detect a 4.1 to 5.8 point difference between treatment conditions on posttreatment PCL total scores (d = .34-.40). Analyses will rely on the latest version of the PCL (i.e., the PCL-5[2]). Data currently is unavailable translating clinically meaningful differences on the PCL to the PCL-5; however, preliminary work suggests the ranges described above will be similar for the PCL-5.[2]

5.6B. Data Analysis.

5.6B1. General Approach. The study is a two arm patient-level randomized superiority trial, nested within 3 sites, each with 4 providers. Analyses will consider this design structure and follow intent-to-treat methodology. First, we will examine the distribution of all study variables (data verification). Second, we will evaluate bivariate associations between condition assignment and study outcomes and covariates to determine unadjusted measures of effect and identify imbalance in baseline covariates. Due to randomization, we do not anticipate imbalances in baseline characteristics between groups, but we will adjust for any differences by including these variables as covariates. Third, we will examine the impact of missing survey items and adjust for their influence. After testing and identifying the mechanism underlying any missingness (MAR,NI), we will use the implied specific imputation methods to impute missing covariates and factors and generate five imputed data sets. Final analyses will include complete case analysis and an aggregated analysis based on the multiply imputed data.

5.6B2. Aims 1 and 2. After completing the above steps, we will test our hypothesis for Aim 1 using generalized linear mixed models. The number of sessions attended, within the assumed and appropriate fitted distribution, will be modeled with treatment and site as fixed effects and a random provider effect (clustering by provider). Analyses for Aim 2 will similarly use mixed models to examine differences between conditions on PCL-5 scores over time, modeling the treatment, time, and treatment by time effects. Secondary analyses will examine CAPS-5 scores and loss of diagnosis on the CAPS-5 (both PTSD diagnosis and subclinical PTSD diagnosis) to facilitate comparisons with existing and ongoing research on treatments for PTSD. We will also examine differences between conditions on PHQ-9, WHO-QOL, QRI, and CSQ-8 scores.

Analyses will follow the same general approach as Aim 1, with some exceptions. First, some indices are dichotomous (i.e., presence or absence of PTSD or subclinical PTSD diagnosis). Models will be fit using appropriate distribution and link functions (i.e. for binomial distribution and logit links for PTSD diagnosis; whereas mean group differences might fit a normal distribution). Second, unlike Aim 1, which relies on administrative data, Aim 2 outcomes rely on

self-report data, where some attrition is inevitable. Analyses will include examining group differences using available data, as well as analyses employing imputation as described above. To study the time-dependence of clinical outcomes, we will model the first-order transition probabilities of Markov chains (under treatment and control) with auto regressive random intercepts, random slope (provider), and fixed effects for treatment, site, sessions attended, and homework compliance. Lastly, we will explore indirect pathways from family supported PE to improved treatment outcomes through greater adherence (e.g., treatment condition ➔ session attendance ➔ PTSD symptoms), using approaches for testing indirect effects described below.

5.6B3. Aim 3. Quantitative data sources include primary and secondary study outcomes (addressed above) and Patient Screening Databases. Patient Screening Databases will be examined descriptively to answer Key Questions from Table 4. Interviews and Process Log entries will be examined using a rapid turn-around analytic approach (RTAP) for qualitative data.[102] RTAP is a team-based method that can be used to obtain rich qualitative results in a brief amount of time. Interviews will be transcribed. The first step of analysis is data reduction (an analytic approach that sorts, focuses, and organizes data).[103] Drs. Kehle-Forbes and Meis will draft, field, and revise two templated forms. One for use by staff to summarize each interview transcript and a second to organize and summarize Process Log entries. Dr. Kehle-Forbes will then train and supervise staff on use of the final template. She will transfer summary points from templates into data matrices that organize points for each RE-AIM factor by population (i.e., Veteran, provider, leadership). The Qualitative Subgroup investigators will then meet to provide their impressions of the matrix contents. We will then develop tables listing 1) barriers/facilitators to implementation of family supported PE, 2) relevant findings from qualitative interviews, 3) relevant existing literature, 4) proposed implementation strategies, and 5) literature relevant to the proposed implementation strategies. Tables will also include, the degree to which barriers/facilitators are likely amenable to change, how conclusions may vary with subgroups (e.g. gender, racial/ethnic minorities, era), and how we anticipate implementation strategies will influence intervention fidelity.[104] Dr. Kehle-Forbes will create a final memo summarizing the findings and key themes that emerged.

5.6B4. Exploratory Aim. For this Aim, we will test if differences between family supported PE and standard PE are mediated by the key social influences targeted by family supported PE (e.g., treatment condition ➔ family support for PE participation ➔ session attendance). Mediators include weekly scores on the CEQ-PTSD[96] (SP report), SORTS[97] (SP report), and Support Checklist (Veteran report). Analytic approaches will be similar to Aim 1, with social influence variables incorporated as mediators. This basic mediation model is a special case of random effects structural modelling, where each equation will have random intercept and provider terms, adjusted for site fixed effects. Indirect effects for mediators treated as single summary scores will be directly tested using bootstrapped confidence intervals[105] to avoid the often-violated assumption underlying Sobel's (1982) method that the sampling distribution of the indirect effect is normal. Analyses will also examine differences between conditions on the rate and shape of change in key social influences.

5.7 Withdrawal of Subjects

Participants can withdraw from the study at any point in time and for any reason by contacting study personnel in person, by telephone, or by mail, and requesting to withdraw. We anticipate termination of participation if:

1. The participant becomes ineligible to participate
2. The participant does not follow instructions from the researchers

3. The study is unexpectedly suspended or canceled.

6.0 Reporting

We will follow the VA Central IRB Table of Reporting Requirements for all issues that must be reported (i.e. summary of adverse events, unexpected problems and any actions or changes with respect to the protocol).

Adverse events (AE) include any untoward medical occurrence in a patient or clinical investigation subject administered an intervention and which does not necessarily have a causal relationship with this treatment. We will collect the following safety information (adverse events) that occurred within 7 days leading up to the final assessment.

1. Suicide attempts
2. Hospitalizations for mental health
3. Episodes of family violence

Therapists will be instructed to notify study staff immediately when such events occur during treatment delivery. Staff will report directly to the local site PI regarding any events. Counselors will also meet regularly by phone for case consultation with a study investigator, where the occurrence of any of these events will be further discussed and tracked. Questions regarding the occurrence of each of these three events will be included in posttreatment assessments. Data obtained from participants will be reviewed for safety concerns. In the case of problems, the staff will discuss this with the appropriate site PI.

Of note, survey reports of IPV on posttreatment and follow-up surveys will be reported when respondants endorse items consistent with severe violence. This includes the following: (1) hit my partner with a fist or something hard, (2) kicked my partner, (3) slammed my partner against something, (4) beat my partner, (5) burned my partner on purpose, (6) tried to hurt my partner by choking or suffocating him/her, or (7) used a knife or gun on my partner. Examples of serious adverse effects, according to the FDA, include death, life- threatening adverse events, suicide attempts, and hospitalization. Consequently, endorsement of items 6 or 7 will be considered a SAE. Given the population, some incidents of severe IPV are expected. Reports of severe IPV on baseline surveys are part of our exclusionary criteria (see inclusions/exclusions). Thus, severe IPV in reported in baseline surveys will not be reported as adverse events.

All site PIs are licensed clinical psychologists. Events will also be immediately communicated to the study PI, who is also a licensed clinical psychologist. The PI in turn will report any problems to the central IRB. Once learned of any SAEs, UAP, compliance issues, RCO, and/or protocol deviation from the study coordinator or local site PIs, the study PI will report these events as defined by the VA Central IRB Table of Reporting Requirements to the VA Central IRB. The study PI will complete the appropriate forms (i.e. 119 or 129) as listed on the VA Central IRB Table within 5 business day of learning of its occurrence. If there are modifications or amendments to the study the study PI will also complete the appropriate Central IRB form (i.e. 116) and wait for approval prior to implementation.

7.0 Privacy and Confidentiality

Protected Health Information will need accessed for the conduct of this study, but PHI will not be disclosed. Steps to ensure confidentiality and secure data are described below.

7.1 Confidentiality

For all participants, strict confidentiality procedures will be maintained to minimize the potential risk of loss of confidentiality. Participant privacy will be further assured by conducting interviews in a private office and by assigning arbitrary identifiers in place of individual names in the field notes. Data analysis, interpretation, and reporting will be based on these de-identified field notes and transcriptions. Since subject responses will not be linked to identifying information, participant confidentiality will be assured. The time commitment will be explained to all participants prior to their participation in the study. Every effort will be made to minimize the length of time and maximize the convenience of the interviews. Participants will be assured that participation is completely voluntary and that they have the right to stop participation, decline answering any questions, or change the course of the interviews for any reason, including potential feelings of discomfort.

7.2 Data Security

All data will be stored on the servers of the Center for Chronic Diseases Outcomes Research (CCDOR) at the Minneapolis VAHCS. CCDOR has well-established procedures to protect the privacy of research participants. Names, social security numbers, and contact information will not appear on any study materials. Instead, only unique study identification numbers randomly assigned to each unique record will be used. Only site lead investigators (Meis, Smith, Porter, Astin), project coordinators, and study programmers (when extracting data to obtain treatment adherence and compare survey responders to non-responders for the survey) will have access to an encrypted crosswalk table linking study identification numbers to identifying information. The CCDOR Statistical and Data Management (SDM) team, in partnership with IRM staff, maintain several secure servers, access to which is granted only to SDM members who have been screened and assigned appropriate security clearance to work with patient data. One common-access server contains individual project data. Access to individual project data on this server is granted only to project staff by an SDM team member, as authorized by the study investigator. Identifiers will be destroyed as quickly as possible. Audio recordings (i.e., qualitative interviews) will be stored digitally on CCDOR servers and only accessible to the principal investigator and project coordinator. Participants will be asked not to use last names or provide identifying information during recorded interviews.

CCDOR protects data collected for the purpose of conducting research projects at a level higher than that provided for clinical encounters. We use “stand-alone,” secure data servers that are accessible only to designated, security-cleared, and trained personnel and data are de-identified as quickly as is feasible. Details about CCDOR’s specific data privacy assurance procedures to be employed for this study are provided below.

7.2A. Maintaining Secure Servers.

CCDOR maintains three secure computer servers that are protected under the Minneapolis VA Windows 2000 network. All individuals with administrative access privileges to CCDOR’s servers, including IRM personnel and the CCDOR Statistical & Data Management Team, have been screened and assigned a security clearance putting them in trusted positions of the hospital with clearances to work with patient level data. These individuals and their access to the CCDOR servers is ultimately monitored and controlled by Sean Nugent, Senior Program Analyst for the CCDOR Statistical & Data Management Team. IRM’s access to the data is strictly limited to backing up server data, which prevents catastrophic loss of data. Backups are

written to tapes that are stored in a secure location accessible only to IRM personnel. CCDOR's Statistical & Data Management Team members maintain permissions, data storage, and all server applications.

7.2A.1 Organization and Access to Research Data. With the exception of one server, named the "CCDOR Server," only the CCDOR Statistical & Data Management Team has access to remaining Center servers. Data on the "CCDOR Server" are organized by projects within folders designated by each investigator. Only members of a given project have access to a specific project folder on the "CCDOR Server." Even then, access to project data is obtained through Windows authentication (i.e., user's name and password to the network). It is virtually impossible for any person without a login name and password to the VA hospital's domain network to access data on the Center's servers. Thus, all data housed on the "CCDOR Server" are extremely secure, and access by unauthorized persons highly unlikely. Data containing patient identifying information are not stored on the CCDOR Server but are stored on the servers accessible only to CCDOR Statistical & Data Management Team members who are directly involved in the project. Thus, not even the PI can link individual names to their PHI without first obtaining permission to do so from the Statistical & Data Management Team. These protections exceed the usual protections provided PHI by the VA system.

7.2A.2 Securing Confidential Research Data. Data collected for individual Center projects are often obtained through primary (e.g., surveys) or secondary (e.g., VISTA and Austin databases) sources. All extractions of secondary data collection are stored on servers accessible to the CCDOR Statistical & Data Management Team only. Secondary data used for a study are de-identified according to HIPAA criteria and provided a random study identification number. A crosswalk table is created linking the study id with the primary key of the secondary data source. These data are only accessible to those employees of the Statistical & Data Management Team who have undergone the necessary security background checks, received appropriate security clearances, and are an integral part of an IRB-approved study. Primary data that involves surveys contain only the coded study identification number to identify study participants. The paper version of these forms/surveys is kept in locked cabinets within a locked room. Data from these surveys/forms are scanned or data entered by project staff or CCDOR Statistical & Data Management Team members to a secure folder. Completed Surveys from the Ann Arbor VA site, that cannot be scanned onsite will be mailed in sealed envelopes using USPS or UPS to the attention of the Study Coordinator located at the main site in Minneapolis, MN. Additionally, teleform surveys from the Atlanta site will be mailed using FedEx with a tracking number to the attention of the Study Coordinator located at the main site in Minneapolis, MN. Upon receipt, approved study staff will upload completed surveys to the secure server where they will be accessible to the Statistics and Data Management Team. This secure folder is on a server accessible only to the CCDOR Statistical & Data Management Team members directly involved in the study. All other scanned surveys will remained in locked cabinets within a locked room at the site as described. This protects the integrity of the data as well as its confidentiality. Primary data collection involving direct data entry is performed through a custom application written by a CCDOR Statistical & Data Management Team programmer. This ensures that data is located in a secure environment and accessible to only those individuals with permission to access the data. Only individuals with a need to access the data, as vetted by the project's Principal Investigator are granted access. Even then, only the absolute minimum number of data elements is released.

7.3A. Data Used for Analysis.

For all projects conducted in CCDOR, the final quantitative data is constructed in Statistical Analysis Software (SAS) data sets. Qualitative data includes audio recordings of interviews that are transcribed and then stripped of all identifiers. De-identified transcripts are then uploaded into qualitative analysis software (NVIVO). Quantitative analyses are mostly conducted by statisticians assigned to the project or by other members of the project (e.g. Principal Investigator). Qualitative analyses are conducted by study investigators with qualitative expertise (e.g., Kehle-Forbes and study PI).

SAS data sets and qualitative transcripts will be de-identified according to HIPAA criteria, using only subjects' coded identification number as the primary key. The de-identified data set will be made accessible to those project members who are conducting analyses. Only the data elements required for the analysis under consideration are released. In summary, a separate workspace on a server accessible only to project Statistical & Data Management Team members will be created to work with administrative data. Any of the administrative data containing patient level data will be encrypted when not being used by a project programmer. All patient-identifying information will be removed from the administrative records. Upon completion of all study data, de-identified analysis data sets will be created in SAS and NVIVO that will use the subjects' coded study identification numbers as the only key.

8.0 Communication Plan

P.I. Dr. Laura Meis will meet regularly with Erin Linden, the project manager. At these meetings, Dr. Meis will check in with Ms. Linden to ensure that the following key communications occur:

1. Ensure that required local site approvals are obtained
2. Keep engaged sites informed of changes to the protocol, informed consent, and HIPAA authorization
3. Inform local sites of any Serious Adverse Events, Unanticipated Problems, or interim results that may impact conduct of the study.
4. Notify all local facility directors and LSIs when the study reaches the point that it no longer requires engagement of the local facility

The study team will also review relevant sections of the protocol periodically, so that we can make sure that the phases of the study are conducted according to the IRB-approved protocol.

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