Adapting Treatment Delivery to Improve Retention in Evidence-Based PTSD Treatment (CDA 21-191)

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PROTOCOL TITLE: Adapting Treatment Delivery to Improve Retention in Evidence-Based PTSD Treatment

PRINCIPAL INVESTIGATOR: Stephanie Wells, PhD

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Purpose

The purpose of this study is to improve the delivery of evidence-based psychotherapies (EBPs) for posttraumatic stress disorder (PTSD) in VA by examining an alternative method to delivery VA PTSD EBPs: massed treatment delivery (i.e., more frequent delivery of therapy sessions to be completed in a shorter period of time, typically PTSD EBPs delivered at least three days a week and completed in approximately month). Massed treatment delivery has shown promising results outside of VA to increase PTSD EBP completion rates with similar clinical benefit as non-massed treatment (Foa et al, 2018). Completion rates are associated with better clinical outcomes (Myers et al., 2019), which can positively impact Veterans' mental health and functioning. Therefore, there is substantial benefit of the current project which aims to examine the feasibility and acceptability of massed treatment delivery for PTSD EBPs in VA PTSD outpatient clinics.

Background and Significance

PTSD has a Significant Impact on Veterans and Effective Treatment is Available. Posttraumatic stress disorder (PTSD) affects between 23-31% of Veterans (Fulton et al., 2015; Weiss et al., 1992) and is associated with worse depression, substance use, suicidal ideation, physical health, quality of life, and functioning. Veterans Affairs (VA)/Department of Defense (DOD) Clinical Practice Guidelines (VA/DOD Clinical Practice Guidelines, 2023) recommend Prolonged Exposure Therapy (PE) and Cognitive Processing Therapy (CPT) as effective first-line treatments with strong evidence to reduce PTSD symptoms in Veterans. Due to their effectiveness, VA has required that Veterans have access to PE and CPT (Dept of VA, 2012) and has trained a large number of clinicians in these treatments (Karlin et al, 2010).

Treatment Completion in PTSD EBPs is Low and Associated with Worse Clinical Outcomes. In a national sample of 265,566 Veterans with PTSD, 60% who started an evidence-based psychotherapy (EBP) did not complete treatment (Maguen et al., 2019). A meta-analysis found that 42% of Veterans dropped out of treatment in routine clinical care compared to 28% in randomized clinical trials (RCTs), suggesting Veterans in clinical settings are at higher risk of dropout than trial participants (Goetter et al., 2015). An adequate dose of treatment (i.e., 8 sessions; Ready et al., 2018; Holder

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et al., 2020) is associated with better treatment response (Holmes et al., 2019). However, dropout typically occurs early in therapy (e.g., prior to session 5), preventing an adequate treatment dose, and is associated with worse clinical outcomes and greater healthcare utilization (e.g., Myers et al., 2019). Further, completer samples in PTSD EBP RCTs demonstrate greater symptom change than intent-to-treat samples, which include individuals who dropped out (Schnurr et al., 2007). Increased completion may improve clinical outcomes and reduce subsequent healthcare utilization (Tuerk et al., 2013).

Between-session Psychological Variables Contribute to Veterans' Drop out from PTSD EBPs. Quantitative studies predicting dropout based on Veterans' demographic characteristics have largely yielded inconsistent or non-significant findings (Sciarrino et al., 2021) with the exception of younger age, which is consistently associated with higher risk of dropout (e.g., Garcia et al., 2011; Kehle-Forbes et al., 2016; Jeffreys et al., 2014). Qualitative studies have found that addressable psychological variables including avoidance symptoms, perceived symptom worsening, and low self-efficacy to tolerate treatment-related distress contributed to dropout (Hundt et al., 2018; Doran et al., 2019). Given the aforementioned reasons for dropout, adapting *how* we *deliver* treatment may enable therapists to intervene quickly on psychological variables contributing to dropout to increase completion.

Prior Attempts to Improve Completion have had Limited Success. Studies have examined Veteran-focused adjunctive or preparatory interventions to improve PTSD treatment completion, but the majority of studies have not examined PTSD EBPs specifically and only found modest effects (Murphy et al., 2009; Seal et al., 2012; Rosen et al., 2017; Mott et al., 2014). Two naturalistic studies (Dedert et al., 2020; DeViva et al., 2017) found that treatment readiness groups (i.e., groups designed to prepare patients for PTSD EBPs) did not improve PTSD EBP completion (Dedert et al., 2020; Deviva et al., 2017). Treatment readiness groups did not improve completion rates in either study. Another study on telephone care increased session attendance compared to usual care (Rosen et al., 2017) however, only a minority of Veterans in telephone care management (10-27%) completed an adequate dose of PTSD treatment. Taken together, these studies suggest that Veteran-facing, adjunctive interventions for PTSD EBPs have modest effects, at best, on session attendance and little effect on improving treatment completion rates. Novel strategies are needed – *adapting how VA delivers* existing PTSD EBPs may be more effective than augmenting existing treatments in increasing treatment completion.

Massed Treatment: Adapting the Frequency of PTSD EBP Delivery. PTSD EBPs were designed to be delivered once weekly for 3 months, but studies have found the average number of days between sessions to be up to 11 days (Youn et al., 2019). This is problematic because less frequent sessions over longer periods of time are associated with diminished PTSD symptom change and greater likelihood of dropout (Gutner et al., 2016; Fleming et al., 2020). An alternative delivery method is to use massed treatment delivery, which is defined as treatment that is delivered at least three

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days a week or more and completed within a month, unless additional sessions are warranted, which may extend the overall length of treatment (Held et al., 2019). Massed PTSD treatments may decrease missed sessions and dropout because there is less time between sessions for interference from Veterans' PTSD-related avoidance (i.e., putting off therapy sessions) and demotivation related to concerns that their PTSD symptoms are worsening or not improving (Sherrill et al., 2020). More frequently scheduled sessions reduces the time between sessions where Veterans could engage in between-session avoidance behaviors and perceive symptom exacerbations. The increased session frequency enables Veterans to quickly receive support and corrective feedback from therapists who can encourage continuation in treatment. Due to the faster rate of recovery during massed EBPs, concerns about symptom worsening that can trigger dropout may dissipate more quickly due to faster signs of improvement (Sherrill et al., 2020).

A number of primarily uncontrolled non-VHA studies have examined the use of massed treatment to deliver PTSD EBPs. Initial research provides encouraging evidence for their impact on completion. A meta-analysis of 11 studies found that massed treatments have large effect sizes for PTSD symptom reduction and only 6% of individuals dropped out of massed treatment (Sciarrino et al., 2020). This dropout rate is up to *six times lower* than dropout rates in standard delivery of PTSD EBPs (18-36%; Goetter et al., 2015; Imel et al., 2013). To date, three RCTs have tested massed treatments, two of which were included in the aforementioned review. These studies found massed treatments to result in similarly large reductions in PTSD symptoms compared to non-massed treatments. Although dropout findings were mixed across the three trials, massed treatments had the benefit of achieving faster symptom reductions, which could result in improved quality of life more quickly. No RCT to date has been conducted with Veterans, which is important due to higher dropout rates in Veterans compared to civilians (Varker et al., 2021) and unique context factors within the VA Health Care System. Overall, observational data from uncontrolled studies in clinical settings are strong, but data from RCTs conducted research environments are conflicting and inconclusive. Existing RCTs have focused on patient-level outcomes rather than also examining provider-level (e.g., satisfaction, perceived appropriateness) and systems-level outcomes (e.g., reach of the intervention). Understanding stakeholders' (e.g., providers, administrators) preferences, perceived implementation barriers and facilitators, and their experiences with massed treatment is critical. It is critical to have evidence from an RCT in Veterans that incorporates implementation considerations from the beginning.

Benefits of the Proposed Project to VA. The VA has invested significant operational resources to implement PTSD EBPs (Karlin et al., 2010) and these are endorsed in the 2023 VA/DOD Clinical Practice Guidelines (VA/DOD Clinical Practice Guidelines, 2023) so it is critical to conduct rigorous research that maximizes the full potential of PTSD EBPs to improve Veterans' PTSD and well-being. The existing preliminary research from primarily uncontrolled trials suggests that massed PTSD treatments have the potential to increase completion rates, which is associated with

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better clinical outcomes and lower mental healthcare utilization (Myers et al., 2019; Tuerk et al., 2016). If massed treatments increase session attendance, it may lower cancellation and no-show rates for clinics. Increasing the variety of effective delivery formats (e.g., massed, weekly) may increase patient-centered care by being able to offer Veterans with more choices for how to receive care. Identifying additional effective ways of delivering PTSD treatments also increases the options providers can offer to Veterans to facilitate patient-centered care. Addressing Veterans' PTSD and mental health is a top priority for the VHA, which is reflected in Strategy 2.2.2 in the Strategic Plan for fiscal year 2018-2024 and the Annual Performance Plan and Report.

Design

This project will include a pragmatic pilot feasibility and acceptability randomized controlled trial (RCT; Aim 2a). A summative evaluation with Veterans (Aim 2b) will be conducted to elicit input from Veterans' about their experiences with treatment, satisfaction, and suggestions for refinement. A summative evaluation with providers will also be conducted (Aim 2c) about their experiences with treatment, perceived satisfaction and acceptability, as well as suggestions for refinement. The summative evaluations with Veterans and providers will help with the interpretation of satisfaction measures, reasons for dropout, and areas for future refinement of the massed treatment delivery.

Specific Aims:

Aim 2a. Conduct a pilot pragmatic RCT (n = ≤ 30 Veterans) to examine the feasibility and acceptability of massed EBP PTSD treatments, specifically cognitive processing therapy (CPT) and prolonged exposure therapy (PE), (EBP-massed; i.e., CPT and PE delivered at least three days a week) compared to PTSD EBPs (CPT and PE) delivered through usual care (EBP-TAU; i.e., how PTSD EBPs are routinely offered, which is typically about once a week) in an outpatient PTSD clinic. In addition, we will gather preliminary data on satisfaction, completion rates, session attendance, and PTSD, depression, and functioning outcomes.

Aim 2b: Conduct a summative evaluation via qualitative interviews with Veterans in the pilot trial (*n*= up to 30) to contextualize the quantitative findings and further refine the massed PTSD EBP program.

Aim 2c. Conduct a summative evaluation via self-report questionnaires and qualitative interviews with providers (*n*= up to 15) who delivered massed treatment to contextualize the quantitative findings and further refine the massed PTSD EBP program.

Study Procedures Aims 2a and 2b: Pilot Trial and Summative Evaluation with Veterans.

Aims 2a and 2b include the following research assessment visits: A baseline assessment, post-treatment follow-up, which also includes a qualitative interview, and a 3-month follow-up. The therapy offered in this study will be conducted through the

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Durham VA PTSD Clinic (also known as Durham Trauma Recovery Program) and be delivered by providers and/or supervised trainees in the clinic. Treatment type [e.g., CPT, PE] and modality (e.g., in-person, telehealth) will be determined via usual care processes although study staff may discuss these with Veterans and communicate with the clinic providers, as needed.

Study Visits.

Veterans will complete a preliminary phone screen (see Recruitment section for more information; see Appendix 1 for phone screen). Following consent (see Informed Consent section below), Veterans will complete a baseline assessment to determine eligibility. If eligible, Veterans will be randomized to the EBP-massed or EBP-TAU condition. Veterans will then be scheduled to begin their selected PTSD therapy (e.g. CPT or PE) delivered by providers in the Durham VA PTSD clinic at the frequency in which they were randomized to (e.g., EBP-massed or EBP-TAU). The therapy delivered as a part of this study will be conducted by clinic providers trained in CPT and/or PE and the therapies offered in this study (i.e., CPT or PE) are recommended in the VA/DOD PTSD Clinical Practice Guidelines and are routinely offered in VA to Veterans with PTSD. Following therapy, Veterans will be asked to complete a post-treatment assessment, which will also include a qualitative interview, and a 3-month follow-up assessment as a part of the study. We estimate that the baseline, post-treatment, and 3-month follow-up assessments will take approximately two to three hours of time. The qualitative interview will be approximately an hour.

At the baseline assessment, Veterans will complete clinician-administered interviews and self-report measures. At the post-treatment assessment, Veterans will complete clinician-administered interviews and self-report measures. Additionally, as a part of the post-treatment process, Veterans will also be invited to partake in an approximately 60-minute semi-structured qualitative interview about their experiences with treatment (see Appendix 2 for the Veteran Interview Guide). Autotranscription through VA Microsoft Teams and study staff will transcribe the interviews. At the 3-month follow-up assessment, Veterans will complete clinician-administered interviews and self-report measures. See Study Measures section for more information.

Study visits will occur via a VA telehealth approved platform (e.g., VA Teams, VA Webex, VA Video Connect), in-person, or telephone, depending on preference and availability. Providers delivering the therapy in the Durham VA PTSD Clinic will follow local clinic procedures for delivering therapy via local approved platforms or in-person. At baseline, post-treatment, and 3-month follow-up visits, the clinician-administered interviews will be recorded for quality assurance purposes. Assessments will be recorded using VA approved recording methods (e.g., VA Microsoft Teams, VA Webex, VA Powerpoint, voice recorder app). The qualitative interview conducted at the post-treatment assessment will also be recorded and autotranscribed using VA approved recording methods (e.g., VA Microsoft Teams, VA Powerpoint, VA Webex, voice recorder app). Study staff will also assist with transcription, as needed. If any participant refuses to be recorded, they will still be able to participate, and the interviewer will take notes.

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Study staff may collect study data through a variety of methods depending upon patient preference, availability, and to reduce burden on clinic providers including but not limited to: mail, telephone, encrypted email with Veterans and/or VA providers, BHL Touch which is routinely used in VA mental health clinics to administer self-report measures, paper and pencil questionnaires, MyHealtheVet, chart review and extraction from the CPRS or JLV record or My Mental Health Assistant, communication with a clinic provider, VA RedCap (e.g., staff entry intro RedCap or emailing surveys to providers or Veterans from RedCap), or VA Qualtrics. Study staff may provide appointment reminders or follow up messages and calls for missed appointments through telephone, MyHealtheVet, or encrypted email. If staff are unable to reach a Veteran in the study, a letter may be sent to help re-initiate contact (see Appendix 3 for Lost to Contact letter).

Veterans' involvement in the study will last approximately 12 months on average but may last up to 18 months depending on scheduling and length of treatment. This will allow time to complete treatment and engage in a 3-month follow-up, and allow time for potential cancellations. To randomize up to 30 people, we will consent up to 175 Veterans for eligibility.

Recruitment

The proposed two-arm pilot RCT is aimed at demonstrating the feasibility and acceptability of EBP-massed compared to EBP-TAU. For the purposes of screening, recruiting, and determining eligibility, information will be obtained through written or verbal communication with the prospective participant and/or identifiable private information will be obtained by accessing CPRS or JLV medical records, Corporate Data Warehouse (DART Request), communication with providers, or VA clinic lists, or the Traumatic Stress and Health Laboratory's "Contact Database" IRB #1080." Veterans will be recruited from the Durham VA PTSD clinic and other relevant Durham VA Health Care System clinics and providers. As additional means of recruitment, Veterans may also be recruited through other relevant VA clinic lists of patients, the Traumatic Stress and Health Laboratory's "Contact Database" IRB #1080, IRB-approved flyers (see Appendix 4) and/or brochures (see Appendix 5) in VA hospitals and clinics, as well as in community settings.

As a part of standard clinic procedures, Veterans will partake in a collaborative treatment planning conversation with a VA clinician in the clinics. For this study, we are examining the feasibility and acceptability of massed PTSD EBPs (e.g., CPT and PE) delivered in an individual format. Therefore, Veterans who select individual CPT or PE in their preferred modality (e.g., in-person, telehealth, or a hybrid of both) may be informed about the study by clinic staff. If a Veteran is interested in the study, clinic staff may inform the study staff about the Veteran's interest through any of the following methods: co-signing them on a CPRS or JLV note, placing a CPRS or JLV consult, sending an encrypted email with the Veteran's information, sending a VA Teams message with the Veteran's information, or providing the Veteran with the study staff's contact information. If referred by a VA clinician or VA clinic staff, study staff will contact the Veteran via telephone, mail, MyHealtheVet, or encrypted email to inform them about the study.

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If potentially eligible Veterans are identified via any method other than referral from clinician following Veteran permission (e.g., identified from VA clinic lists, the contact database IRB #1080, or a DART request using data from the Corporate Data Warehouse) a letter will be sent to the Veteran and given 7 days to opt out (see Appendix 6 for Veteran Recruitment Letter). If the Veteran does not opt out in 7 days, study staff will call the Veteran to inform them about the study, MyHealtheVet, or send an encrypted email to attempt to contact them about the study. Veterans may also self-refer to the study (e.g., through brochures, flyers). Given that the therapy provided in this study is being delivered by Durham VA PTSD clinic providers, Veterans may be referred to the VA clinics, as needed, for any treatment planning discussions to determine appropriateness of PTSD treatment and which treatment the Veteran would engage in.

Participants and Selection of Subjects.

Randomized participants will be up to 30 adult Veterans who have PTSD. Table 1 summaries the study inclusion/exclusion criteria.

Table 1. Veteran Inclusion and Exclusion Criteria.

Participants will meet the following inclusion criteria:	**Participants who meet any of the of the exclusion criteria will be excluded:**
Veterans aged 18 years or older	High acute suicide risk, which is assessed by the suicide risk screen and/or clinician judgment
Meets criteria for current PTSD as determined by the Clinician Administered PTSD Scale for DSM-5	Active manic symptoms that would likely interfere with treatment as assessed by chart review and/or clinician judgment
Willingness to be randomized to either condition (e.g., EBP-massed or EBP-TAU)	Active psychotic symptoms that would likely interfere with treatment as assessed by chart review and/or clinician judgment
Decision to receive CPT or PE in a treatment planning session with a Durham Trauma Recovery Program clinic provider	Currently in a concurrent trauma-focused evidence-based treatment for PTSD (e.g., CPT, WET, EMDR, PE)
Ability to provide informed consent	

Informed Consent.

After being eligible on the phone screen and expressing interest in the study, the informed consent process will be conducted either in person, remotely through a VA approved telehealth platform (e.g., VA VVC, VA Webex, Microsoft Teams) or via the telephone. Informed consent will be provided either in written form or via VA Docusign. Study staff will enter a note into CPRS to document the consent process. Study staff will allow Veterans to ask questions and answer them. Participants will be given the chance to thoroughly read the consent prior to participation. Participants will also be given a

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copy of the signed informed consent form and phone numbers to call if they have additional questions about the consent form or the research, if they have any problems during the study, or if they have questions about participating in research studies in general. No study procedures will begin until informed consent has been obtained. See Appendix 7 for the Veteran Informed Consent.

Study Measures and Outcomes.

Veterans will complete the measures in the table below as a part of this study (See Appendix 8 for Study Measures for Veterans).

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Table 2. Study Outcomes and Study Measures for Veterans

Measure	Time (min)	Baseline	Weekly Tx	Post-Tx	3 Month Follow-up
Feasibility and Acceptability Measures					
Acceptability of Intervention (AIM)	1			X	
Client Satisfaction Questionnaire-8 (CSQ-8)	2			X	
Clinical and Functioning Measures					
Life Events Checklist for DSM (LEC-5)	60	X			
Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)	60	X		X+	X
PTSD Checklist for DSM-5 (PCL-5)	5	X	X[1]	X+	X
Pain, Enjoyment of Life, General Activity Scale (PEG)	1	X		X	X
PHQ-9	3	X	X[1]	X+	X
Posttraumatic Cognitions Inventory-9 (PTCI-9)	3	X		X	X
Brief Inventory of Psychosocial Functioning (B-IPF)	3	X		X+	X
WHO-QOL BREF	5	X		X+	X
Demographics & Secondary Measures					
Demographics Measure	3	X			
Credibility and Expectancy Questionnaire (CEQ)	3	X			
Trauma Coping Self-Efficacy (CSE-Trauma)	3	X		X	X
Everyday Discrimination Scale	3	X			
AUDIT-c	1	X			
DUDIT-c	1	X			
Suicide Risk Screen^	10	X		X*	X*

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[1] Clinic providers routinely administer these measures to Veterans during therapy. These measures will be collected by the VA clinic providers as a part of their routine care. ^ See Appendix 9 for Suicide Risk Screen * Will administer Suicide Risk Screen at post-treatment and 3 month follow-up as indicated (see Safety Concerns section for more information). + These measures should be modified to assess for past week in the instructions.

Additionally, as a part of examining feasibility of massed treatment for this study, study staff will monitor participant recruitment, treatment completion, study retention, feasibility of assessment, randomization feasibility, and study withdrawals.

Study staff may also collect data about other important study outcomes through chart review or communication with the clinic therapy providers through requesting information via encrypted email, CPRS, JLV, and My Mental Health Assistant, MyHealtheVet, VA RedCap, Qualtrics, or other aforementioned data collection methods stated above in the protocol about out therapy outcomes, such as but not limited to: 1) Treatment completion status (e.g., completer or dropout); 2) Number of therapy sessions attended; 3) Fidelity to the frequency of the intervention (e.g., EBP-massed or EBP-TAU); 4) Modality for each therapy session (e.g., telehealth or in-person). Clinic providers also routinely complete as a part of routine care information about Veteran's homework completion and fidelity to the treatment interventions during therapy in their VA clinical notes. Therefore, study staff may conduct a chart review for this information that is often in clinical notes or have providers provide information about this through a self-report checklist or communication with the clinic staff.

Treatment fidelity to the CPT and PE protocols will be monitored. Clinic providers also routinely self-report treatment fidelity when entering notes into CPRS or JLV. Clinicians delivering the therapy will be asked to complete a fidelity checklist for PE or CPT or enter information into clinical notes about fidelity and also homework collection, which is routine. Self-report fidelity checklists have been shown to effective in rating fidelity and yield similar results to tape review fidelity (Wiltsey-Stirman et al., 2021).

Fidelity to the delivery of the EBP-massed and EBP-TAU conditions (e.g., fidelity to session frequency), will be determined by examining the number of CPT and PE sessions attended each week while in the episode of care for the study for each Veteran through CPRS or JLV chart review.

Study Costs & Participant Payments. There are no costs associated with the study unless the Veteran has copayments for services provided through the Durham VA clinics where the therapy will be provided for the study. For the pilot RCT, Veterans will be paid $50 each for completing the assessments that are a part of the baseline, post-treatment, and 3-month follow-up assessments. Veterans will be paid $50 for the qualitative interview that is also included in the post-treatment process for the summative evaluation.

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Randomization. This is a two-arm pilot RCT comparing massed PTSD delivery (EBP-massed) to PTSD treatment delivered treatment as usual (EBP-TAU). Eligible Veterans will participate in the treatment type (e.g., CPT or PE) and delivery modality (e.g., in-person, telehealth, or hybrid) that they select with a clinician as a part of routine care and that is clinically indicated. They will then be randomized to receive this treatment in one of two conditions: 1) Massed PTSD delivery (EBP-massed; i.e., treatment intended to be delivered at least three days a week) or 2) PTSD EBP Treatment as usual (EBP-TAU; PTSD EBPs as they are typically delivered, which is usually once per week). Randomization will be stratified by treatment type (i.e., CPT or PE).

Study Interventions.

Veterans in both arms of the study (i.e., EBP-massed or EBP-TAU) will receive either individual CPT or PE, which will be decided upon with a clinician in the clinic, typically the PTSD clinic. These treatments are routinely provided within VA to Veterans with PTSD and are recommended in the VA/DOD Clinical Practice Guidelines for PTSD. Consistent with routine care, CPT & PE will be delivered in the modality agreed upon between the clinician and their provider (e.g., telehealth, in-person, or hybrid) given that several studies have found PTSD treatments delivered over telehealth are as effective as in-person care (e.g., Acierno et al., 2017; Morland et al., 2014; Liu et al., 2020) but Veterans may discuss this with the study team and the study team communicate with the providers as needed. These treatments will be delivered by Durham VA licensed independent providers (LIP) or trainees (e.g., postdoctoral fellows, interns) supervised by an LIP who are trained in CPT or PE and work in the Durham PTSD clinic. The PI of this project is also an LIP and trained in CPT and PE. Veterans will be randomized to receive the above agreed upon interventions in either the EBP-massed or EBP-TAU format.

Veterans randomized to the EBP-massed group will be intended to attend therapy at least three times per week. Veterans in the EBP-TAU group will be intended to attend treatment as usual, which is typically once a week.

While the frequency of care will be determined by randomization (EBP-massed vs. EBP-TAU), the PTSD treatment provided will be decided upon with the clinician in the clinic and will be treatments recommended by VA/DOD Clinical Practice Guidelines. As such, the therapy visits will be classified as clinical visits in the medical record and entered by clinic providers as a part of their routine care.

Risk/Benefit Assessment.

Aims 2a and 2b are determined to be no more than minimal risk due to receiving a routine care intervention (e.g., CPT or PE), which are recommended in the VA/DOD Clinical Practice Guidelines. The experimental aspect of the study (e.g., massed vs. TAU) is also not expected to be above minimal risk as it is just adjusting the frequency of scheduling of evidence-based treatments. Additional study procedures are also determined to be no more than minimal risk.

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Potential Risks

Some of the questions asked, such as about mental health symptoms or trauma history, may concern sensitive issues. Being asked some of these questions may cause psychological distress or discomfort. These procedures will be conducted by trained research personnel or clinic staff who have received education on the protection of study participants and are trained to handle any minor discomfort elicited by the questions. All Veterans in the study will receive PTSD treatments recommended in the VA/DOD Clinical Practice Guidelines as a part of routine care. However, benefit cannot be guaranteed. Discussions during the course of therapy with their clinic provider may cause temporary emotional discomfort. The therapy will be delivered by existing VA therapists or supervised trainees (e.g., postdoctoral fellows) with expertise in the treatment of PTSD. The PI is also a licensed clinical psychologist who is trained in CPT and PE. These risks are no greater than in routine care.

While research staff will keep study-related information including recordings as confidential as possible, complete confidentiality cannot be guaranteed. All data is labeled with a study ID number, which can only be linked to participant names by study staff. The link between study ID numbers and names will be kept in a secure, location behind the VA firewall that only study staff have access to. Additionally, a breach of confidentiality could occur if the Veterans information is required to prevent them from hurting themselves or others. Organizations may view and/or copy research records for regulatory purposes, quality assurance, and data analyses including IRBs' and Research & Development Committees. These are no anticipated physical risks in this study. Economic risks include potential loss of wages due to time spent in research activities, transportation costs associate with traveling to and participating in the research intervention (although virtual care is offered), and any insurance copays for psychotherapy appointments. Participants will be compensated for their time to complete the baseline, post-treatment, and follow-up visits, and the qualitative interview to off-set these economic risks.

Adequacy of Protection from Risk

Regarding risks of psychological distress, no participant will be required to answer any question that causes discomfort. All participants will be reminded that participation in research is voluntary and that whether they choose to participate in research or not will have no impact on current or future medical care at VA or non-VA facilities. All enrolled study participants will be able to withdraw from the study at any time or decline to answer any questions without jeopardizing their health care or future participation in research (participants will have the option to be referred for non-study care). Distress that may arise during study treatment as a part of routine care (e.g., CPT or PE) will be managed by the clinicians delivering therapy in the clinic as per site clinical protocols; all providers delivering CPT and PE to study participants are existing VA therapists or supervised VA trainees (e.g., postdoctoral fellows) with expertise in treating Veterans with PTSD.

All study staff will be trained by Dr. Wells to recognize and respond to psychological distress that occurs at research visits (e.g., baseline, post-treatment, 3-month follow-up, and the qualitative interview) as outlined in the protocol (see Suicide

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Risk & Homicide Protocols below). Dr. Wells is a licensed clinical psychologist with expertise in the treatment of Veterans with PTSD and suicide risk management.

As stated above, only study staff will have access to study data, which will be stored behind a VA secure firewall.

Safety Concerns.

The treatments offered as a part of the study (e.g., CPT & PE) have been demonstrated to reduce suicidal ideation (Skayton et al., 2019) and are not associated with increased risk of self-harm or suicide. However, Veterans with PTSD are at higher risk of suicide than the general population, as such, study staff will employ stringent safety procedures during research visits (e.g., baseline, post-treatment, qualitative interviews, and 3 month follow-up).

Study staff will be informed that participants should be asked to identify an emergency contact for the participant to be used only in emergencies (e.g., medical crisis, high risk suicidal ideation). Trained study staff will administer a suicide risk screen (see Appendix 9 for Suicide Risk Screen) and homicide risk screen at baseline (see Appendix 10 Homicide Risk Screen). If suicidal ideation is endorsed, trained study staff will help determine the level of risk based on the Suicide Risk Screen and utilize the lab's internal Psychiatric Emergency SOP (see Appendix 11 for Psychiatric Emergency SOP) to guide how to respond and intervene depending on the level of risk.

At the post-treatment and follow-up visits, trained study staff will administer the Suicide Risk Screen if acute indicators of SI are present during the visit. The Psychiatric Emergency SOP will be used to help guide how to respond and intervene depending on the level of risk. Similar suicide risk protocols have been used in prior studies successfully at the Durham VA. Study staff may inform the Veteran that the PI or another licensed clinician may contact the Veteran if necessary to ensure participant safety. The study PI is a licensed psychologist, and she or another licensed provider will be available to help manage suicide or homicide risk, as needed. In cases of imminent suicidality (or homicidality) which are not anticipated, we will utilize psychiatric emergency services, which may include, but is not limited to the following: seek guidance from the Psychiatric Emergency Clinic on best strategies for management and follow-up, self-presentation at the VA's emergency room with the help of an emergency contact, calling 911, a warm handoff to 988, or calling local police for a wellness check or to inform them of imminent serious risk to another person. Study staff may send copies of safety plans to Veterans, as needed, through mail, encrypted email, MyHealtheVet, or other VA approved platforms.

If suicidal (or homicidal) risk arises during weekly treatment in the study, the clinician providing CPT and PE in the clinic will address this following local clinic procedures as this care is being delivered through the Durham PTSD Clinic in a routine care setting.

Aim 2c Procedures: Summative Evaluation with Providers.

Study Visit & Recruitment

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After clinic providers finish providing therapy to Veterans in the study through the Durham PTSD Clinic, providers will be invited to participate in a semi-structured interview (see Appendix 12 for provider interview guide) and complete self-report questionnaires to assess feasibility of massed PTSD treatments (see Appendix 13 for Study Measures for Providers), which may be collected via paper and pencil, encrypted email, VA RedCap surveys, VA Microsoft Teams, VA Qualtrics, or when meeting with the provider. This visit will be conducted either in-person, remotely through a VA approved telehealth platform (e.g., VA Microsoft Teams or VA Webex), or through phone. Qualitative interviews will be recorded and autotranscribed using VA approved recording software (e.g., VA Microsoft Teams, VA voice recorder) for later data analysis purposes. Study staff will assist with transcription, as needed. This visit will last approximately 60 minutes. Providers will be invited through email (see Provider Recruitment Email in Appendix 14), referred by word of mouth, and/or Teams and/or study staff may present about this opportunity at local meetings.

Participants and Selection of Subjects. Participants will be up to 15 providers who delivered treatment to Veterans in the pilot trial.

Table 3. Inclusion/Exclusion for Providers in the Summative Evaluation.

Inclusion	**Exclusion**
Provided CPT or PE to Veterans who were in the pilot trial	

Informed Consent. A waiver of documentation of informed consent is requested for Aim 2c, which will involve a semi-structured interview with providers and completion of self-report questionnaires. Providers will complete the informed consent process remotely to reduce provider burden as many providers work remote or hybrid schedules but in-person consent may be accommodated when possible, if requested. Study staff will schedule a brief phone call or videoconferencing session with the provider or administrator to review the consent script which includes the purpose of the study, procedures, and risks and benefits of participation and give participants the opportunity to ask questions (see Appendix 15 for Provider Informed Consent Script). We will take care to ensure that they understand their participation is voluntary and will not affect their employment. After reviewing the study and answering all questions, for those who remain interested in participation, the consenting staff elicit verbal consent from the provider. For those who want additional time to consider participation, a follow-up appointment will be scheduled to complete the informed consent process. Providers will be given a copy of the consent script, if requested. A study spreadsheet stored on a secure drive behind the VA firewall will track consenting, including provider or administrator's name, date of consent, if verbal consent was provided, and person who

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obtained the consent. This will be kept here: R:\
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Study Costs and Compensation
There are no costs for the providers to participate in the study. Providers are unable to compensated for their participation.

Risk/Benefit Assessment & Protection from Risk
Providers may be uncomfortable answering some of the questions in interviews, although the interviews are not anticipated to include sensitive information related to the interviewee's personal life. Providers and administrators will be informed that they are free to skip any questions they wish not to answer or withdraw from the study at any time. Providers may be uncomfortable being audio-recorded. There is a risk that participation may result in a loss of confidentiality. This would occur if someone not associated with the study heard one of the participant's audio tapes or saw participants' data. To protect participant privacy, we will store recordings behind the VA firewall on the shared drive. All data will be 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 location in the study folder, behind the VA firewall. There are no anticipated physical or economic risks for this study.

Study Measures and Procedures

Table 4. Measures For Providers to Complete During Summative Evaluation (see Appendix 13 for Provider measures).

Measures	Time to complete
Demographics questionnaire	2 min
Feasibility of Intervention Measure (FIM)	1 min
Acceptability of Intervention Measure (AIM)	1 min
Intervention Appropriateness Measure (IAM)	1 min
Perceived Characteristics of Intervention Scale (PCIS)	5 min
Provider Satisfaction Item	1 min

Adverse Events for Aims 2a, 2b, and 2c

All adverse events will be reported per Durham VAMC requirements. All Serious, Unanticipated and Related adverse events will be reported to IRB within 5 business

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days of hearing of the event. All other adverse events will be reported at continuing review.

Expected study-related adverse events:
The PTSD psychotherapies (e.g., CPT & PE) provided in this study are recommended in the VA PTSD Clinical Practice Guidelines and involve talking about, thinking about, and confronting memories and behaviors related to Veterans' past traumatic events. It is expected that this may cause psychological distress among patients, although this distress is typically temporary, and should not pose a serious risk. The distress experienced from these interventions as a part of this study should not exceed distress that occurs in routine care as these interventions are recommended in VA PTSD Clinical Practice Guidelines and widely offered throughout VA.

During the research assessment process, Veterans will be asked about their past traumatic event(s) and other current difficulties (e.g., depression). This may cause psychological distress among patients, however, it is expected to be temporary and should not pose a serious risk.

Providers may be uncomfortable answering questions, which could cause temporary distress, but should not pose a serious risk and they can decline to answer any questions.

Expected adverse events resulting from the underlying condition of the population:

The course of PTSD is often characterized by fluctuations in symptoms, particularly based on reminders of traumatic experiences. Thus, it is possible that significant exacerbations of PTSD symptoms will occur during the course of treatment or during the study. Exacerbations of co-occurring conditions, such as depression, alcohol or substance use or dissociation, are also possible. As has been demonstrated previously, when significant exacerbation of symptoms during psychotherapeutic treatment of PTSD occurs, it has minimal or no impact on rates of attrition or improvement (Larsen et al., 2016; Larsen et al., 2022). There is no reason to believe that such exacerbations would be made more likely by virtue of participating in one of these interventions than they would if they did not partake in one of these interventions.

Data and Safety Monitoring
The PI and study staff will be responsible for data safety and monitoring. The PI will meet regularly with the study staff to discuss study progress and will be available for study questions or concerns. Regular meetings between the PI and study staff will allow for discussions such as but limited to ongoing progress reports, including the number of participants currently involved in the study, attrition rates, and scheduled data collection from participants, as well as notification and review of any AEs. Safety monitoring for AEs will be conducted in real time by the PI and/or study staff. There will be multiple ongoing mechanisms for monitoring and reporting AEs: 1) ongoing participant contact via study personnel 2) weekly meetings between the PIs and study personnel 3)

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information obtained in the electronic medical record. The following information about adverse events will be collected and tracked in an AE database: 1) Description of the event; 2) the onset and outcome (e.g., resolution of the AE), 3) an assessment of the severity (use existing grading scales whenever possible), 4) an assessment of the relationship of the event to the study (definitely, probably, possibly or not related), and 5) action taken (e.g., none, referral to physician, start or increase concomitant medication). The PI will determine the severity of the event, will assign attribution to the event, and study staff will monitor the event until its resolution but no longer than the end of study involvement. Study-related serious adverse events (SAEs) for participants in this project are not expected, but should they occur, will be reported the Durham VA Health Care System Institutional Review Board in accordance with local human protections program guidelines. Any protocol deviations, adverse events, breaches of confidentiality, or unanticipated or unexpected problems will be reported to the IRB, as well as other offices (research compliance, information security, privacy), as appropriate and detailed as per IRB and research compliance regulation.

Withdrawal of Participants

Participants may voluntarily withdraw from participation in the study at any time. The PI may withdraw participants due to inability, or unwillingness, to complete study procedures or attend appointments. In the event of any clinical or psychiatric emergency that in the opinion of the PI, in collaboration with the Veterans' treatment team, would take precedence over the ongoing treatment of PTSD (e.g., marked increase in suicidal ideation/intent), the participant would be withdrawn from the study. The participant would continue to have access to VA mental health treatment at their study site.

Participants who withdraw from or terminate CPT or PE prior to completion will continue to be enrolled in the study and invited to complete the post-treatment, 3-month follow-up, and qualitative interview unless they also choose to formally withdraw from the entire study and at that point would be considered a study withdrawal.

Data Analysis and Statistical Considerations

Aim 2a. Analyses will be conducted on an intent-to-treat basis, with participants analyzed in the arm to which they were randomized. To examine the feasibility and acceptability of our trial, we will compare between arms, the rates for each of the primary outcome measures (e.g., retention, completion), at each of the measurement time periods. We will also calculate descriptive statistics (e.g., mean/median and distribution) of clinical and secondary outcome measures and compare between arms. When appropriate, we will also compare changes from baseline to estimate effects with confidences intervals around them to reflect the limited power of the pilot trial design.

Aims 2b and 2c.

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The qualitative interviews will be primarily used to inform the refinement of the massed treatment program and to determine the training process and content for providers and for subsequent publications and presentations. Analyses will be conducted separately for each stakeholder group (i.e., Veterans and Providers). Rapid qualitative analysis[51,52] will be used, as needed, to quickly gather feedback. If rapid analysis is used, the qualitative team will analyze interview data using Hamilton's approach to rapid qualitative analysis (Hamilton & Finley, 2019). Interview transcripts and structured interviewer notes will be reviewed, edited for clarity, and then summarized into a matrix guided by the theoretical frameworks and interview questions. Further analyses will consist of iterative memo development and matrix analyses (Averill, 2002) to elucidate common and contrasting experiences and identify themes. Transcripts, and audio recordings as necessary, will be reviewed for accuracy of findings and to extract quotations. At each step, the qualitative team will meet regularly to review subsets of the analyses, and any analytic disagreements will be resolved through discussion and consensus. The analytic plan will be modified, if needed, based on the data and study needs. Additional thematic analyses will also be utilized for an in-depth exploration of relevant themes. NVivo or Atlas.ti may be used for qualitative data analysis and coding.

Mixed Methods Data Analysis for Aims 2a, 2b, and 2c. An explanatory sequential mixed-methods design (QUANT → qual) will be used to contextualize the quantitative findings from the pilot RCT to increase our understanding of feasibility, acceptability, explain quantitative findings (e.g., satisfaction), and understand reasons for dropout. We will also examine convergence between the quantitative and qualitative findings (e.g., the same conclusions from quantitative and qualitative data, such as high satisfaction with the intervention). We will use expansion to use the qualitative data to explain the quantitative data. For example, if dropout rates are lower (quantitative) among massed treatment compared to the standard of care, we will identify reasons to explain this difference in the qualitative interviews. We can also enhance our understanding of clinicians and Veterans' satisfaction with massed treatment; for example, if clinicians rate a low score on the PCIS for massed treatment (quantitative) we may identify aspects of the intervention that they were unsatisfied with through the qualitative interviews (qualitative). Providers' will provide feedback about implementation issues and potential facilitators, which could inform refinement to the intervention or future implementation strategies.

Privacy, Confidentiality, and Information Security

1. **Lists of Data Reviewed and/or Collected for Screening/Recruitment and Conduction of Study:**

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The Personal Health Information that will be obtained, used, and/or shared for this study includes:

Identifier(s)	**Source(s) of Health Information**
☒ Names	☒ Medical history & physical exam information
☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, and zip code. Describe: Street, address, city, zip code	☒ Photographs, videotapes, audiotapes, or digital or other images
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, visit or treatment dates, etc.; and all ages over 89, Describe: Birthdate, mental health visit and consult dates, admission and discharge dates	☐ Biologic specimens (e.g., blood, tissue, urine, saliva). Describe:
☒ Telephone numbers	☒ Progress notes
☐ Fax numbers	☐ Diagnostic / Laboratory test results
☒ Electronic mail addresses	☐ Operative reports
☒ Social Security Numbers	☐ Imaging (x-ray, CT, MRI, etc.)
☐ Medical record numbers	☐ Discharge summaries
☐ Health plan beneficiary numbers	☒ Survey / Questionnaire responses
☒ Account numbers	☐ Billing records
☐ Certificate and/or license numbers	☐ HIV testing or infection records
☐ Vehicle identifiers and serial numbers, including license plate numbers	☐ Sickle cell anemia information
☐ Device identifiers and serial numbers	☒ Alcoholism or alcohol use information
☐ Web Universal Resource Locators (URLs)	☒ Drug abuse information
☐ Internet Protocol (IP) address numbers	☒ Mental health (not psychotherapy) notes
☐ Biometric identifiers, including finger & voice prints	☒ Psychological test results
☐ Full-face photographic images and any comparable images	☐ Genetic testing

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Identifier(s)	Source(s) of Health Information
☒ Any other unique identifying number, characteristic, or code, describe : Study ID number **Note: This is not the unique code assigned to otherwise de-identified health information for re-identification purposes.*	☒ Other, describe: Audiorecordings of interviews with Veterans and qualitative interviews with Veterans and providers

2. Data and/or Specimen Acquisition:

Data for this study will be collected through (*check all that apply*):

☒ Prospective data and/or specimen collection obtained from participants. Provide description of processes: Data will be obtained through self-report questionnaires, clinician-administered interviews, qualitative interviews, BHL Touch which is routinely used by providers in routine care, and medical record review, which could include the use of JLV, My Mental Health Assistant, as well.

☒ Retrospective data collection and/or specimens obtained from medical chart review/data access. Describe how data will be obtained (e.g., fileman, CDW, etc.): In accordance with a Waiver or Alteration of HIPAA Authorization to screen and recruit Veterans, names, addresses, telephone numbers, emails, social security numbers, recent mental health appointments & associated progress notes, and diagnostic information of potential participants will be obtained from the VA's Regional Data Warehouse or medical record.

☐ Retrospective data collection and/or specimens obtained from an IRB-approved data and/or specimen repository. Indicate the repository source including name, VA location, and IRB number:

Note: for data and/or specimens obtained from a VA approved data repository, a Data Use Agreement (DUA) must be executed prior to obtaining data and/or specimens. See VHA Handbook 1200.12 for further information.

3. Level of Data:

The following level(s) of data will be acquired/maintained for this study (*check all that apply*):

☒ Identifiable—Data contains direct identifiers.
☒ Coded—Data linked to a specific by a code rather than a direct identifier for re-identification purposes. Only someone possessing the key to the code can link the data to a particular participant.
☐ De-Identified (all 18 HIPAA identifiers removed

☐ Verified Statistically
OR
☐ Verified by Absence or Removal of 18 HIPAA identifiers
☐ Limited Data Set
☐ Other: Describe:

4. Location of Data and/or Specimens, and Data Retention Plan:

A. Data and/or Specimen Location:

Data will be stored electronically in R:\Adapting_Treatment_Wells_IRB_1787108 and in VA Docusign, VA RedCap, Qualtrics, NVIvo, and Atlas.ti.

Data that will be stored electronically include name, address, phone number, email, social security number, amount of study payment earned, date of visits, self-report and clinician administered interview data, qualitative interviews, audio recordings of qualitative interviews and clinician-administered assessments, transcripts from qualitative interviews, recruitment information, information about recent mental health visits, consents, the study database that links the PHI with the study identification number.

Paper records of data include informed consents that were not completed via DocuSign, questionnaires that subjects completed by hand (instead of electronically; no identifiable data included), clinician administered interviews done in-person, notes from qualitative interviews done in person, and will be stored in a locked file cabinet in a locked room (outside Room 741) of the Legacy building that only study staff can access.

☒ Data will be also be placed at the VA Informatics and Computing Interface (VINCI; http://vaww.vinci.med.va.gov/vincicentral/VINCIWorkspace.aspx). The VA Informatics and Computing Infrastructure is a partnership between the VA Office of Information Technology and the Veterans' Health Administration Office of Research and Development. Researchers and operations staff can use VINCI to access data and statistical analysis tools in a virtual working environment through a certified VHA network computer using the VA Intranet or Virtual Private Network (VPN).

B. Data Retention Plan

☒ Research records will be maintained and destroyed according to the National Archives and Records Administration, Records Schedule Number: DAA-0015-2015-0004. Records destruction, when authorized, will be accomplished using the then current requirements for the secure disposal of paper and electronic records. Currently,

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destruction of research records (see DAA-0015-2015-0004, section 7.6 “Research Investigator Files” for materials included in research records) is scheduled for 6 years after the cut-off (the cut-off is the completion of the research project) and may be retained longer if required by other federal agencies. Records will not be destroyed without pre-notification to the facility records manager. .

☐ Other data retention plan, describe:

5. Data Access and Data Recipients:

Only members of our DVAMC research team will have access to identifiers and coded data. Coded data with direct identifiers removed (i.e., name, address, telephone numbers, SSN, DOB) will be placed at \\ vhadurhsmcifs01.v06.med.va.gov\ R:\Adapting_Treatment_Wells_IRB_1787108

All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up-to-date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one’s password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins).

Access to study data will be removed for all study personnel when they are no longer part of the research team.

6. Data and/or Specimen Transportation and/or Transmission for all data and/or specimens involved in the study:

I. ☐ Data and/or specimens will not be transported or transmitted outside of Durham VAMC environment.

II. ☒ Data and/or specimens will be transported BETWEEN sites that are under the auspices of the Durham VA Medical Center. If a Veteran requests to meet in-person for study assessment data collection, then study staff will collect data at

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the VA-leased space at 3022 Croasdaile Drive, Durham, NC at the VISN-6 MIRECC or at building 5 (VA research building). These data will then be transported in a locked briefcase from this building to the VA HSR&D at Legacy Tower and stored in a locked file cabinet in a locked room (outside Room 741) of the Legacy building that only study staff can access.

III. ☐ Data and/or specimens will be transmitted to other VA sites using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted disk (encryption is optional).

☐ Data are coded or contain identifiers and thus will be sent

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional).

☐ Specimens are coded or contain identifiers and thus will be sent via VA-authorized carrier with tracking.

☐ Other, describe:

IV. ☐ Data and/or specimens will be transported to non-VA/VHA sites (e.g., academic affiliates, laboratories, etc.) using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted CD.

☐ Data are coded or contain identifiers and thus will be sent using VA—approved carrier with tracking.

☐ Data are coded or identified and will be sent using Azure RMS encryption via a VA email account.

☐ Data are coded or identified and will be uploaded to sponsor website using electronic case report form (eCRF) <

☐ Other, describe:

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B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional) or will be hand-delivered by research study personnel. Specify method of delivery:

☐ Specimens are coded and thus will be sent via VA-approved carrier with tracking or will be hand-delivered by research study personnel. Specify method of delivery:

In accordance with the HIPAA and the Privacy Act, for any coded or identifiable data or specimens released from the Durham VAMC (with the exception of Limited Data Sets), an Accounting of Disclosure (AOD) will be maintained (e.g., in a database or spreadsheet) that includes the participant's name, date of the disclosure, description of the nature of the Individually Identifiable Information (III) disclosed, purpose of each disclosure, and the name and address of the person/agency to whom the disclosure was made.

C. ☒ Local DVAMC memorandum "Authorization to Use, Process, Store, or Transmit VA Sensitive Information Outside VA Owned or Managed Facilities" has been pre-filled out for each study team member who may transport the data and/or specimens off-site. This (these) forms are included with the IRB materials. .

D. ☒ Containers (e.g., briefcase, bin) are labeled with the following notice (label placed on the outside of container) in accordance with VHA Directive 6609:

NOTICE!!!

Access to these records is limited to: AUTHORIZED PERSONS ONLY. Information may not be disclosed from this file unless permitted by all applicable legal authorities, which may include the Privacy Act; 38 U.S.C. §§ 5701, 5705, 7332; the Health Insurance Portability and Accountability Act; and regulations implementing those provisions, at 38 C.F.R. §§ 1.460 – 1.599 and 45 C.F.R. Parts 160 and 164. Anyone who discloses information in violation of the above provisions may subject to civil and criminal penalties.

V. ☒ We will communicate with veterans enrolled as participants in this research study through MyHealtheVet.

7. Risk Mitigation Strategies:

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☐ Data are fully de-identified (stripped of HIPAA 18 and study ID/code) before being shared outside of Durham VAMC.

☐ Specimens are fully de-identified (stripped of HIPAA 18 and study ID/code before being shared outside of Durham VAMC.

☒ Data or specimens are coded and the code is not related to, or derived from, information about the individual and that code is not otherwise capable of being translated as to the identify the individual. Only someone possessing the key to code can link the data to a particular participant.

☐ Other, specify:

8. Suspected Loss of VA Information:

Should any incident such as theft or loss of data, unauthorized access of sensitive data or non-compliance with security controls occur it will be immediately reported according to VA policy. All incidents regarding information security/privacy incidents will be reported to the ISO and PO within 1 hour of acknowledgement of issue and done so using the VHADUR Research Events Report e-mail group (VHADURResearchEventReport@va.gov).

9. Reporting of Results:

☒ Reporting of results, such as in scientific papers and presentations, will never identify individual subjects. Data will be presented in aggregate and individual-level data will not be published.

☐ Other results reporting plan, describe:

10. Future Use of Data:

☐ Data will be retained for future use. This is described elsewhere in the protocol and is noted in the HIPAA authorization.

☐ Future Use of data is optional (i.e., not required by the research subject).

☐ Future Use of data is required for participation in the study.

☒ No future use of data is currently planned.

11. Use of Mail Merge Technology

☒ Mail merge programs will be used to generate letters and/or address labels for mailings to potential or already enrolled research subjects. The study team is aware

that to reduce risk of mail merge related privacy incidents, use of mail merge programs requires a 25% accuracy check to verify that (potential) research subject name and mailing address are properly "matched". If discrepancies are found, a 100% accuracy check is required before letters may be mailed.

12. Use of Non-Standard Software

☐ I do NOT intend to use any new specialized software (i.e. Software that's not already approved OR installed) in this study.

☐ I intend to use specialized software that has not already been installed and it has been approved for use by the VA Technical Reference Model (TRM) Group.
(Note: All new software must be approved by TRM before it can be installed on VA systems.)

☒ I intend to use previously installed software on my VA computer.

We intend to use previously installed, TRM-approved qualitative data analysis software (QDAS; e.g., NVivo, Atlas.TI) for the purposes of qualitative data management, analysis, visualization, and reporting. VA approved software will be used to enter participant data, questionnaires, and study tracking, such VA RedCap or Qualtrics

Use of Cloud Computing Services

☐ Cloud computing services will NOT be used in this study.

☒ Cloud computing services WILL be used in this study as described below and have been approved nationally by the VA Chief Information Officer (CIO). (Note: ONLY cloud computing services that have been approved nationally may be used.)

VA RedCap or VA Qualtrics may be used in this study. NVivo and Atlas.ti.

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Appendix A: Expedited Review of Research

The categories of research that may be reviewed by the IRB through the expedited review procedure include research activities that present no more than minimal risk to human subjects **AND** involve procedures listed in one or more of the specific categories listed below.

The expedited review procedure is not to be used when identification of the subjects or their responses would reasonably place them at risk of criminal or civil liability; be damaging to the subjects' financial standing, employability, insurability, or reputation; or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review.

EXPEDITE CATEGORIES
1-Drugs and Devices: One of the following must be met: (1) The research is on drugs for which an IND application is not required. (2) The research is on medical devices for which an investigational device exemption (IDE) application is not required; or the medical device is cleared or approved for marketing, and the medical device is being used in accordance with its cleared or approved labeling.
2-Blood Samples: Collected by finger / heel / ear stick or venipuncture: (1) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 milliliters (ml) in an 8-week period, and collection may not occur more frequently than two times per week; or (2) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kilogram (kg) in an 8-week period, and collection may not occur more frequently than two times per week.
3-Noninvasive Collection of Biological Specimens: Collected prospectively for research purposes by noninvasive means: (1) Hair and nail clippings in a non-disfiguring manner. (2) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction. (3) Permanent teeth if routine patient care indicates a need for extraction. (4) Excreta and external secretions (including sweat). (5) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue. (6) Placenta removed at delivery. (7) Amniotic fluid obtained at the time of rupture of the membrane prior to, or during, labor.

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EXPEDITE CATEGORIES
(8) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques. (9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings. (10) Sputum collected after saline mist nebulization.
4-Noninvasive Collection of Data: Data must be collected through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. (1) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy. (2) Weighing the subject. (3) Testing sensory acuity. (4) Magnetic resonance imaging (MRI). (5) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography. (6) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing, where appropriate, given the age, weight, and health of the individual.
5-Collected Material: Research involves: (1) Materials (data, documents, records, or specimens) that have been collected for any purpose, including previous research; or (2) Materials (data, documents, records, or specimens) that will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).
6-Collection of Data From Voice, Video, or Photographs: Research involves collection of data from voice, video, or photographs.
7-Group Characteristics, Surveys, Interviews, and Quality Assurance: Research must be on individual or group characteristics or behavior (including, but not limited to: research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior), or will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. ***NOTE****: Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(2) and (b)(3)). This listing refers only to research that is not exempt.*

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