# Comparing Group Therapies for Veterans with Depression and PTSD

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**Study Title**: **Comparing Group Therapies for Veterans with Depression and PTSD**

## RESEARCH DESIGN AND METHODS

| **TIMELINE** Year / Quarter **Milestones** | Y1 Q1 | 2 | 3 | 4 | Y2 Q1 | 2 | 3 | 4 | Y3 Q1 | 2 | 3 | 4 | Y4 Q1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hiring and Training of Project Staff | ■ | ■ | | | | | | | | | | | | | | |
| IRB Approval and Renewal | ■ | | | | ■ | | | | ■ | | | | ■ | | | |
| Recruitment /Randomize /Follow-Up | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | |
| Fidelity and Reliability Checks | | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | |
| Data Entry /Cleaning /Analysis | | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | |
| Manuscript /Presentation Preparation | | | | | | | | | ■ | | | | | | ■ | ■ |
| Final Report / Dissemination | | | | | | | | | | | | | | | ■ | ■ |

**RCT of G-TBT**

Objective

To examine efficacy of G-TBT on improving quality of life, psychological well-being, and social reintegration of Veterans with PTSD, MDD, and related conditions compared to G-DSTs using a non-inferiority design. Patient satisfaction, access, and predictors of feasibility (attendance and discontinuation) also will be assessed.

Recruitment Strategy and Feasibility of Recruitment

Veterans will be recruited through the Primary Care Mental Health Integration, General Outpatient Mental Health, and CBT Clinic programs at the Ralph H. Johnson VAMC and local affiliated VA community-based outpatient clinics (e.g., Trident, Goose Creek, and Beaufort). IRB-approved study flyers will be distributed through each clinic/setting. Within these programs, all Veterans reporting symptoms of depression and anxiety meet with a mental health staff member to complete a clinical interview and self-report measures. If Veterans endorse symptoms consistent with a depressive/anxiety disorder, interest in participating in research will be assessed and, if agreeable, the Veteran will be referred to project staff. All referred Veterans will be called by project staff to discuss the project, confirm initial interest, and schedule the initial research assessment. Research assessments may be completed either in-person or via VA-approved telehealth technologies, based upon the preference of the participant. If the Veteran selects telehealth for the initial research assessment, the consent/HIPAA forms, a self-address and stamped envelope, and instructions for the telehealth research appointment will be mailed to the Veteran prior to the appointment. The research assessment will be completed with the project staff to first complete consent documentation and then assess inclusion/exclusion criteria (with a targeted sample of 326 VAMC patients), including a semi-structured clinical interview and self-report questionnaires focused on quality of life, social integration, and psychiatric symptoms (described later). Participants who meet inclusion/exclusion criteria will be randomized into a study condition and will be assigned to a project therapist. Because most VAMC patients who meet study criteria likely will present with multiple depressive/anxiety disorders (Brown et al., 2001), principal diagnosis, or the most impairing of the diagnosable disorders, will be used to inform randomization. Principal diagnosis will be determined via diagnostic severity scores in the Anxiety Disorders Interview Schedule-5 (ADIS-5) (Brown, 2014). To balance diagnoses across the two conditions, a stratified random assignment based on principal diagnosis will be used (MDD and PTSD) (Gros, 2015). Based on referrals to the PI's CDA, it is expected that at least 45% of the recruited Veterans will have served in OEF/OIF and $\geq$50% will be representative of minority groups. During the consent process, staff will explain the purpose of the research, nature of the interventions, potential benefits and risks, the voluntary nature of participation, and the data collection procedures. If the Veteran agreed to consent, they will be asked to sign the consent form. If the consent is completed via telehealth, staff will ask participants to hold up the signed forms to the camera so that the staff may take a screen shot of the signature. These images will be capture on a VA furnished device and stored on the secure VA research network. Participants will then be asked to mail back the completed, signed consent form in the return envelope provided.

Eligibility Criteria

**Inclusion criteria:** 1) participants must be clearly competent to provide informed consent for research participation, 2) participants must meet DSM-5 criteria for either MDD or PTSD, and 3) participants must be 18 - 80 years of age. **Exclusion criteria involve:** 1) recent history (≤ 2 months) of psychiatric hospitalization or a suicide attempt and/or suicidal ideation with acute intent as documented in their medical record or reported during clinical interview, 2) current diagnosis of substance use disorder as documented in their medical record or reported in clinical interview, 3) acute, severe illness or medical condition that likely will require hospitalization and/or otherwise interfere with study procedures as documented in their medical record (e.g., active chemotherapy/radiation treatment for cancer), 4) recent start of new psychiatric medication (≤ 4 weeks), 5) diagnosis of traumatic brain injury (TBI) in their medical record and/or endorsement of screener questionnaire (McAllister et al., 2016), or 6) diagnosis of schizophrenia, psychotic symptoms, and/or bipolar disorder as documented in their medical record or reported in clinical interview. Additional comorbid psychiatric diagnoses that were not listed as exclusion criteria are permitted as long as they are considered secondary to the principal diagnosis of MDD or PTSD as determined by the diagnostic interview. Of note, if participants request changes to their psychiatric medications at any time during the treatment, a medication consult will be completed with a prescriber in VA Mental Health. Any changes in medications and/or initiation of non-study psychotherapy will be recorded for inclusion in the analyses as a possible covariate. Ineligible Veterans will be referred for non-study-related treatments within mental health at the RHJ VAMC.

Procedures

Eligible VAMC patients will be randomized into one of two treatment conditions: G-TBT or G-DSTs. Both treatment conditions will include 12 weekly 90-minute group sessions. Both treatment conditions will be delivered either in-person and via VA-approved telehealth technologies, based upon the preference of the participant and the group schedule. The general format of sessions will involve: 1) brief check-in; 2) review of materials from previous sessions; 3) review of homework assignments; 4) overview of new materials and in-session exercises; and 5) assignment of homework for next session. Attendance and homework completion will be recorded.

Randomization Procedures

Participants will be randomly assigned (1:1) to one of the two study arms (n = 163 per arm) using a permuted block randomization procedure. Randomization will be stratified by principal diagnostic group (or most impairing disorder between MDD and PTSD if both disorders are present, based upon ADIS disorder-specific interference and distress severity scores) and block size will be varied to minimize the likelihood of unmasking. If both disorders evidence identical severity scores (highly unlikely), participants will be asked which of the two disorders is more impairing/significant for randomization purposes. After determining eligibility and completing consent and baseline assessment materials, enrolled participants will be assigned to treatment conditions by the Research Coordinator/Therapist using a computer-generated randomization scheme. Once a participant is randomized, they will be included in the intent-to-treat analysis. The Research Coordinator/Therapist, and the statistical analyst in charge of randomization (Dr. Allan) will be the only research team members aware of the randomization assignment. Randomization will occur at the participant level. As such, we will take the following steps to minimize contamination between the two arms of the study: 1) only one member of a household will be eligible for enrollment; and 2) other VA providers will be informed of their patients' participation in the study, but will be blinded to the treatment condition.

Group Transdiagnostic Behavior Therapy

TBT was developed as a streamlined protocol to address transdiagnostic avoidance via the use of four different types of exposure techniques (situational/in-vivo, physical/interoceptive, thought/imaginal, and [positive] emotional/behavioral activation). From the transdiagnostic avoidance perspective, the four exposure practices are matched to the type(s) of avoidance experienced by patients based upon their cluster of symptoms/disorders. For example, a patient with PTSD would receive situational and imaginal exposures to address their symptoms, whereas a patient with comorbid PTSD and MDD would receive situational, imaginal, and positive emotional exposures. Per protocol, the first six sessions of TBT are designed to educate on, prepare for, and practice the four different types of exposure techniques. The next five sessions are focused on practicing and refining exposure practices as participants work through their lists of avoided situations/sensation/thoughts. The final session reviews treatment progress and relapse prevention strategies.

Although this specific G-TBT protocol has not been tested in Veterans to date, it mirrors the individual protocol tested in multiple Veteran samples as well as the G-TBT protocol tested in civilians that have been shown to be effective across studies.

G-DSTs Control Condition Matching and Assignment

To provide an evidence-based comparison for the G-TBT condition, G-DSTs will be used that are matched to the participant's principal diagnosis (Gros et al., 2018). G-DSTs will include groups for the most common principal diagnoses that have VA-approved protocols and training programs, including PTSD (Cognitive Processing Therapy for PTSD) and MDD (CBT-Depression). Each of these G-DSTs have published manuals for administration and have received extensive support in the literature (Bieling et al., 2006). Participants randomized to a G-DST group will be matched to the G-DST based on the diagnostic severity scores in the ADIS-5.

Treatment groups (G-TBT, Group CBT-Depression, Group Cognitive Processing Therapy for PTSD) will require at least 6 participants and maximum of 12 participants to begin. Upon randomization, participants will be notified of the group assignment and expected wait period for the group to begin. Wait periods (in days) will be recorded as an indicator of access to treatment across groups. Based on data from Dr. Gros's CDA, it expected that it may take between 4-8 weeks to fill the three treatment groups; however, groups will begin as soon as the required number is reached. This group scheduling/wait-time is consistent with successful group therapy programs in the community (Gros et al., 2018).

Treatment Training and Fidelity

Training workshops (3 days each) will be provided for each of the three treatment protocols, consistent with the standard VA rollout for DSTs. Although less time may be needed for the TBT training (Gros et al., 2017), all three workshops will be standardized in duration to control for potential training differences. Established trainers/experts will be recruited to provide each of the trainings. Trainings will be supported by weekly supervision on the three protocols co-led by VA staff psychologists well-versed in the study therapies for the duration of the study, with additional supervision sessions provided as needed. Backup clinical supervision will be provided by Drs. Gros (PI) and Szafranski (Co-Investigator; also trained in all three treatments). Each course of therapy groups will be led by one of the project therapists in a rotating fashion.

Consistent with other well-designed treatment outcome studies, all treatment sessions will be audio recorded with 20% of sessions randomly selected for review for treatment integrity and fidelity. These integrity and fidelity reviews will focus on evaluating the match between the treatment manuals and the material covered in session (e.g., treatment components introduced/reviewed, in session exercise, and homework assigned). To evaluate adherence, treatment-specific rating forms will be used to determine if the therapist appropriately covered the content of each session. External experts will be recruited to rate the recordings independently, with feedback provided to the therapists throughout the duration of the study to maintain/improve treatment delivery.

Safety Measures for Suicidal Ideation or Intent

All assessment and treatment providers will be trained and supervised by the Principal Investigator, who is a licensed psychologist (and with backup supervision coverage from Dr. Szafranski, licensed psychologist). At intake, participants identified by clinical interview with suicidal ideation and acute intent will be excluded from the study and immediately offered emergency psychiatric care at the VAMC. During the duration of the study, the Principal Investigator (or covering Co-Investigator) will immediately contact the participant and assess suicide risk when any instance of suicide risk is identified (preferably before the participant leaves the appointment). If suicidal ideation is present but not intent, the participant will be retained in the study and reassessed for suicide risk by the investigators in one week. In cases of acute suicidal intent, state law requires immediate hospitalization and these guidelines will be followed.

Assessment of Quality of Life, Psychological Well-Being, Social Reintegration, Psychiatric Symptomatology, and Treatment Satisfaction

The battery of self-report questionnaires and a diagnostic interview will be completed pre-, mid-, and post-treatment and at the 6-month follow-up to track participants' progression through treatment and maintenance. The mid-treatment assessment will include the self-report questionnaires only (no diagnostic interview). Following the initial assessment at pre-treatment, all assessment sessions will be completed either in-person and via VA-approved telehealth technologies, based upon the preference of the participant. These time points for the assessments are consistent with CBT research with Veterans with depressive/anxiety disorders, as well as with the PI's CDA. Participants will be compensated $40 for pre-treatment, $60 for mid-treatment, $80 for post-treatment, and $120 for 6-month follow-up for completion of assessment procedures for a total of $300 for the entire study. To reduce the likelihood of missing data, all assessments will be scheduled separately from normal treatment sessions. Assessments of quality of life, social reintegration, and general symptoms of the depressive/anxiety disorders, rather than multiple disorder-specific questionnaires, were chosen due to the

transdiagnostic approach and related research aims of the proposed study. In addition, participants will be asked to voluntarily solicit a friend or family member to complete a collateral report on a measure of functioning (IIRS). Procedures for adapting and analyzing the collateral report will follow previously published investigations of self-other assessments by the study team (Gros et al., 2010; Simms et al., 2010). All assessments will be completed by the Project Research Recruiter and Assessor. Additional training will be required prior to administration of the diagnostic interview (ADIS-5). The assessor will be required to observe the PI administer the ADIS-5 twice and then administer the ADIS-5 twice themselves under the direct observation of the PI. The assessor will be blinded to treatment condition and supervised by the PI. ADIS-5 assessments will be recorded to investigate inter-rater reliability of diagnoses, with 20% of recordings being re-assessed by an external ADIS-trained assessor after the participant has completed all study procedures, with feedback provided to the assessor throughout the duration of the study to improve reliability. In addition to the four assessment points, select measures (PHQ-9 and PCL-5) will be administered every other treatment session to monitor safety and treatment progress.

**Albany Panic and Phobia Questionnaire (APPQ).** The APPQ is a 27-item self-report measure that assesses agoraphobia, social anxiety, and interoceptive avoidance (Rapee et al., 1994/1995). Each subscale has been shown to have good internal consistency ($\alpha s > .85$) and temporal stability ($rs > .87$) (Brown et al., 2005).

**Anxiety Disorder Interview Schedule-5 (ADIS-5).** The ADIS-5 is a semi-structured interview designed to assess a wide range of Axis I disorders (Brown, 2014). The ADIS-5 assesses current and past diagnoses with DSM diagnostic criteria, severity scores, and lists of feared and avoided situations for the anxiety disorders. The ADIS-5 has demonstrated excellent inter-rater reliability and validity of depressive/anxiety disorder diagnoses.

**Anxiety Sensitivity Index 3 (ASI-3).** The ASI-3 is an 18-item self-report measure of AS. This scale was developed to provide a more stable measure of the three most widely recognized AS subfactors (cognitive, social and physical concerns) than the previous ASIs provided (Taylor et al., 2007). The measure has shown good psychometric properties (Taylor et al., 2007). The ASI-3 will be utilized to assess level of overall AS.

**Attentional Control Scale - Straightforward (ACS-S).** The ACS-S is a 20-item scale that measures the voluntary attentional focusing and attentional shifting related to anterior system functioning. The scale measures a general capacity for attentional control with subfactors related to the abilities: to focus attention, to shift attention between tasks, and to flexibly control thought. The ACS is internally consistent (Derryberry & Reed, 2002).

**Community Reintegration of Servicemembers (CRIS).** The CRIS is a 151-item self-report measure that assesses participation and community reintegration in Veterans (Resnik et al., 2011). The CRIS includes three subscales for extent of participation, satisfaction with participation, and perceived limitations. The CRIS has demonstrated excellent psychometric properties across studies (Resnik et al., 2011; 2012). In addition, a computerized adaptive version of the CRIS has been developed that reduces the items and related time commitment by 66% (Resnik et al., 2012), and will be used in the proposed study.

**Craig Handicap Assessment and Reporting Technique (CHART).** The CHART is a 27-item self-report measure that assesses long-term rehabilitation outcomes (Whiteneck et al., 1992). As recommended in previous studies, only the social integration (6-items) and occupational functioning (7-items) subscales will be investigated. Both subscales have demonstrated high test-retest reliability, good agreement between ratings, and convergent validity with other reports of functioning (Whiteneck et al., 1992).

**Depression Anxiety Stress Scales 21-Item Version (DASS).** The DASS is a 21-item measure with three subscales designed to assess dysphoric mood, fear and autonomic arousal, and tension and agitation (Lovibond & Lovibond, 1995). The reliability and validity of the subscales have been supported in the literature (Antony et al., 1998). The DASS scales also have demonstrated excellent convergence with similar measures of depression and anxiety and high internal consistency (Antony et al., 1998).

**Illness Intrusiveness Rating Scale (IIRS).** The IIRS is a 13-item questionnaire that assesses the extent to which a disease interferes with important domains of life, including health, diet, work, and several others (Devin et al., 1983). The IIRS has been shown to have strong psychometric properties in the previous literature in participants with physical and/or emotional health concerns (Devins, 2010), and has been used in previous TBT studies (Gros, 2014; Gros et al., 2017; 2018).

**Intolerance of Uncertainty Scale Short Form (IUS-12).** The IUS-12 is a 12-items scale for measuring trait intolerance of uncertainty (Carleton, Norton, & Asmundson, 2007). In other words, it is used for assessing the degree to which individuals are able to tolerate the uncertainty of ambiguous situations, the cognitive and behavioral responses to uncertainty, perceived implications of uncertainty, and attempts to control the future.

**Medical Outcomes Study Social Support Survey Form (MOSSS).** The MOSSS is a widely used 19-item self-report measure designed to assess social support. Responses are given on a 6-point scale ranging from 1-6 with greater scores indicating greater support. The MOSSS has been shown to be an accurate measure of social support in veteran samples with mental health issues (Jakupcak et al, 2011).

**Perseverative Thinking Questionnaire (PTQ).** The PTQ is a 15-item measure of repetitive negative thinking (Ehring et al. 2011). Perseverative thinking is repetitive, negative thoughts that persist intrusive to the point of being seen as unproductive to the individual. The thought process and the individual seeing the thoughts as dysfunctional can also characterize this thinking. Items are measured on a 5-point Likert-type scale of Never (0) to Almost Always (4). These 15 questions address repetitiveness, intrusiveness, difficulty to disengage, unproductiveness, and capturing mental capacity. Studies have shown that the PTQ hold convergent validity, predictive validity, internal consistency, and test-retest reliability.

**PHQ-9.** The PHQ-9 is a 9-item depression scale derived from the *Patient Health Questionnaire* to assess the symptoms and diagnosis of depression (Kroenke et al., 2001). The PHQ-9 has been shown to have good reliability as well as validity in clinical samples (Kroenke et al., 2001). In addition, the PHQ-9 has been incorporated into standard screenings at the VA.

**PTSD Checklist 5 (PCL-5).** The PCL-5 is a 20-item self-report measure that assesses DSM-5 criteria PTSD symptoms (Weathers et al., 2013). Previous versions of the PCL have been shown to have excellent internal consistency and excellent test-retest reliability in veterans (Orsillo et al., 2001). In addition, the PCL-5 has been incorporated into standard assessment for PTSD at the VA.

**Satisfaction with Therapy and Therapist Scale – Revised (STTS-R).** The STTS-R assesses patients' level of satisfaction with their therapeutic experiences (Oei & Green, 2008). The STTS-R contains 12 items that represent two subscales: satisfaction with therapy and satisfaction with therapist. The measure has been investigated in a large sample of patients receiving group CBT for depressive/anxiety disorders. The two subscales have demonstrated excellent internal consistency and high positive correlations with indicators of successful group CBT outcomes (Oei & Green, 2008).

**State-Trait Inventory for Cognitive and Somatic Anxiety – Trait Version (STICSA-Trait).** The STICSA-Trait is a 21-item measure that assesses trait cognitive and somatic anxiety (Gros et al., 2007; Ree et al., 2008). The cognitive and somatic subscales have been supported in the literature and both subscales have high internal consistency (Gros et al., 2007). In addition, the STICSA-Trait scale was found to remain stable over repeated administrations during several stress manipulations.

**Structured Assessment for Evaluation of TBI (SAFE-TBT).** The SAFE-TBI was designed to identify the level of evidence for exposure to mild TBI (McAllister et al., 2016). The SAFE-TBI includes a definition of mild TBI as well as three multi-part screening questions, regarding: 1) exposed to, screened for, or put on restricted duty due to any head or brain injury from six examples (e.g., blast or explosion); 2) associated symptoms that occurred immediately after the head or brain injury (e.g., duration of loss of consciousness, feeling dazed or confused, amnesia); and 3) memory loss of events just before or after the injury. The SAFE-TBI has demonstrated moderate levels of agreement for inter-rater and test-retest reliabilities (McAllister et al., 2016). In addition, the SAFE-TBI demonstrated reasonable convergent validity with more extensive measures of TBI.

**Veterans Short-Form Health Survey (V/SF-36).** The V/SF-36 is a 36-item measure designed to assess functional health, well-being, and quality of life in Veterans, and can be scored to produce two primary subscales for physical health and mental health (Kazis, 2000). The V/SF-36 was adapted from the original SF-36, which has received extensive support in the literature (Ware & Sherbourne, 1992).

**2a.3b. Data Entry and Management**

All data collected for this study will be specifically collected for research purposes and will not be used for any other purpose. The study database will be maintained in a VA network shared drive with access limited to

authorized members of the research team. Other authorized persons, such as regulatory authorities, also may have access to these records. Regarding security, data will be stored on VA computers that require secure login, on a secure VAMC server, behind the VAMC firewall, and access is logged. All privacy obligations under the Health Insurance Portability and Accountability Act (HIPAA) will be met. Participant information always will be treated as confidential.

Our software (logical) security policy has three main components: 1) VAMC standard antiviral protection; 2) password policies; and 3) additional level of firewall protection. The National VA maintains firewall protection. The backup schedule at the RHJ VAMC consists of fully-verified daily backups.

All data will be entered into an SPSS database. The SPSS database will be created by the PI, statistical analyst (Dr. Allan), and project staff will be responsible for all data entry. Data quality and consistency checks (e.g., data range checks) will be integrated as part of the data entry procedure. Data quality will be monitored and assured in several ways: 1) as reported; and 2) as entered into the study database. For the former, all hardcopy data forms will be visually inspected by project staff prior to data entry. Furthermore, a manual comparison of randomly selected data hardcopy forms with data output generated from the SPSS database will be performed with consistency.

**2a.3c. Data Monitoring Board**
Both an internal Data Safety and Monitoring Committee (DSMC) and a Data Safety and Monitoring Board (DSMB) will be assembled.

The internal DSMC will consist of the PI (Gros) and co-investigators on the proposal. The functions of the DSMC will include: 1) providing scientific oversight; 2) reviewing all adverse effects or complications related to the study; 3) monitoring enrollment; 4) reviewing summary reports relating to compliance with protocol requirements; and 5) providing advice on resource allocation. The DSMC will meet at least quarterly (online or via conference line) and as necessary. The recommendations of the DSMC will be reviewed and the PI will take appropriate corrective actions as needed and also will be forwarded to the DSMB for review.

In addition to the internal DSMC, a DSMB will be established. The DSMB will be made up of professionals with appropriate expertise, who are willing to participate, and who do not have any conflicts of interest. The DSMB will include: 1) two experts in the area of transdiagnostic psychotherapy, 2) a biostatistician with expertise in the conduct of clinical trials, and 3) two members with expertise in the treatment of Veterans. The DSMB will meet annually. The DSMB will perform the following activities: 1) review the research protocol and plans for data and safety monitoring; 2) evaluate the progress of the intervention, including periodic assessments of data quality and timeliness, participant recruitment, enrollment, and retention, participant risk versus benefit, integrity of the intervention, and other factors that can affect study outcome; 3) consider factors external to the study when interpreting the data, such as scientific or clinical developments that may impact the safety of study participants or the ethics of the study; 4) make recommendations to the internal DSMC, local VA R&D, and MUSC IRB for continuation or termination of the trial; and, 5) protect the confidentiality of study data and monitoring.

The DSMB will have the authority to temporarily or permanently discontinue the trial if it perceives that harm is occurring due to the intervention. The DSMB will meet with the internal DSMC yearly to review adverse event reports, patient complaints if any, and enrollment rates. Data will be provided at these meetings by the investigators on key variables that may indicate harm (e.g., changes in self-report scores). The DSMB biostatistician will evaluate the confidentiality and integrity of the database and the procedures for recording and storing confidential files. The DSMB also will review the elements of the plan to manage emergencies.

**Sample Size Determination for Proposed Analyses**
For all study outcomes, Veterans will be randomly assigned (1:1) to the G-TBT and G-DST conditions. To reduce potential Type I errors, the primary outcomes of interest for Primary Aim 1 will be patient-reported IIRS, PCL, and DASS depression scores. The power analysis was calculated to be powered at 90% with a Bonferroni-corrected 1-tailed $\alpha = .0008$ (.025/3 primary outcomes) to detect non-inferiority for G-TBT in comparison to the G-DSTs. Meta-analyses of group CBT for depression (McDermut, Miller, & Brown, 2001) and Group treatment for PTSD (Haagen et al., 2015; Sloan et al., 2013) found effect size estimates ranging from 0.56 (PTSD; Sloan et al., 2013) to 1.03 (depression; McDermut et al., 2001). In Veterans, Haagen et al. (2015) reported a Hedges g of 0.63. Thus, we conducted our power analysis with a conservative expected d of 0.60. Using procedures recommended by Chow, Shao, and Wang (2017) for non-inferiority designs, which utilize the pre-specified non-inferiority margin

(here prespecified as Δ d = 0) and the estimated effect in the active comparison treatment (d = 0.60), we determined that 152 participants (76 per cell) would be needed. However, this does not account for the group clustering effect.
Following Schnurr et al. (2001), we adjusted the sample size to account for potential group effects. Based on the intraclass coefficient (.025) found in the pilot G-TBT trial (Gros et al., 2018), an estimated 174 participants would be needed to adjust for potential clustering effects if groups average 8 participants. We adjusted the sample size upward 37% to adjust for potential discontinuation and 27% based on observed missing data for telehealth assessments, resulting in a final sample size of 326 participants (163 per cell).

**Analysis Plan – Treatment Outcome Symptomatology and Feasibility (Primary Aims 1-2)**

Preliminary Descriptive Analyses
Univariate descriptive statistics and frequency distributions will be calculated as appropriate for all relevant variables to identify potential departures from distributional assumptions of proposed analyses. If necessary, appropriate data transformations will be applied, or alternative analysis procedures (e.g., nonparametric) will be used. Baseline values for demographic, quality of life, social integration, and symptom variables will be described via frequency distributions for categorical variables, measures of central tendency (mean, median), and variability for the total sample and within race groups. The baseline variables will be compared between intervention conditions using t-tests (or Wilcoxon rank sum tests) for continuous outcomes and chi-square (or Fisher's Exact Test) for categorical variables.

Missing Data
The full intent-to-treat (ITT) analysis set will comprise all randomized participants. Missing data in the full analysis set will occur if participants discontinue treatment prior to the end of the study or do not complete an outcome measure. Participants will not be discontinued from the study because of non-adherence and all will remain in the study unless consent is withdrawn or if there are concerns regarding participant safety. Missing data for the ITT analysis set will be imputed using multiple imputation (MI) methods, which are superior to most alternative missing data approaches even when data is missing completely at random (MCAR) or missing at random (MAR; Schafer & Graham, 2002; Enders, 2010). Although the use of MI will result in the least biased parameters, regardless of data missingness, several approaches will be undertaken to better understand the exact mechanisms for missing data. Little's (1988) MCAR test will be applied to all final models to determine whether data can be considered MCAR. Further, the results of analyses using study completers and protocol adherers (completer and per-protocol analyses) will be compared with results using the ITT analysis set to test sensitivity of study conclusions to study discontinuations and protocol non-adherence. Baseline differences also will be explored between treatment completers and those that discontinue. If baseline differences are detected, these covariates will then be included in the final model as auxiliary variables to improve the plausibility of assuming data is MAR (Collins et al., 2001; Enders, 2010; Graham, 2003;). Finally, discontinuation proportion will be used as one of the outcome measures of intervention feasibility.

Non-Inferiority Analyses (Primary Aim 1)
The continuous measures of quality of life, psychological well-being, and social reintegration are CHART (disability), CRIS and CHART (social reintegration), IIRS and V/SF-36 (quality of life and impairment), APPQ (agoraphobia, social anxiety, and interoceptive avoidance), DASS (depression, anxiety, and stress), ADIS-5 (disorder dimensional severity scales), PCL-5 (PTSD), and STICSA-Trait (cognitive and somatic anxiety). Although multiple variables will be examined, the primary outcomes of interest will be IIRS, PCL-5, and DASS depression scores. All other analyses will be conducted in an exploratory fashion to inform future studies. Parameter estimates to calculate the effect size difference will be arrived at using three-level (measurement occasions nested within participants nested within assigned treatment group) generalized mixed-effects regression models (MRM). MRM is a method of repeated measures analyses that allows for modeling of continuous and categorical independent and dependent variables and for appropriate modeling of covariance structures when observations are correlated across time and/or across group. This analytic approach fully captures variability in outcomes across multiple follow-up assessments and accounts for any potential effect of the group to which a participant is assigned and is thus preferred over methods that collapse data over time. We will calculate between-group treatment differences as the d, based on the effect of treatment condition on the intercept parameter when the model is centered on post-intervention and on the effect of treatment condition on the intercept parameter when the model is centered on month 6. We prespecified the non-inferiority margin (d) to be 0 (indicating we expected G-TBT to be at least equivalent to G-DST) and the one-sided CI for our three primary analyses at α = .0008. In the primary analyses of outcome variables, we will covary for the baseline value

of the variable of interest. We will also include the linear effect of time as well as a time by condition interaction effect to determine whether treatment differences (or lack thereof) were stable from post-intervention through the follow-up. Additional covariates (e.g. age, number of psychiatric comorbidities, race, sex, combat theatre, and number of treatment sessions) will be added to the model to adjust for putative confounding variables. Effect size CIs that do not contain 0 provide evidence in support of noninferiority for G-TBT.

Feasibility and Acceptability Analyses (Primary Aim 2)

Measures of feasibility and acceptability are discontinuation proportions (discontinuation y/n), proportion of sessions attended, proportion of homework assignments completed, wait-time from baseline to start of the group treatment (access, measured in days), and patient satisfaction scores on the STTS-R. Frequency distributions describing the participants' reasons for noncompliance and discontinuation of participation will be developed. Because feasibility and acceptability analyses involve changes from baseline to post-intervention only and several of the outcomes are categorical, the generalized linear mixed model (GLMM) framework will be used to compare G-TBT to G-DST on treatment satisfaction, retention (discontinuation), and treatment adherence (% missed sessions, % homework completion). Discontinuation proportions (dichotomous outcome), % of missed visits, and % homework completion will be compared between the intervention groups using GLMM, with logistic/binomial regression analyses as special cases for dichotomous and percentage outcomes; access and STTS-R will be modeled as a continuous outcome using an appropriate link function. We also will model the longitudinal profile of adherence as a dichotomous outcome at each visit (e.g. attended/did not attend a given session). This will allow us to evaluate the trends in session attendance and to determine if the trends differ by intervention (e.g. whether the probability of missing visits is less/greater at earlier or later time points).