NCT04567680

Acceptance and Commitment Therapy to Improve Social Support for Veterans With PTSD

Study Protocol with Statistical Analysis Plan

January 9, 2026

This project evaluated the efficacy of *Acceptance and Commitment Therapy to Improve Social Support for Veterans with PTSD* (ACT-SS). The goal of this treatment is to assist Veterans with PTSD to improve their social relationships, community integration, and quality of life. This goal will be accomplished by providing Veterans with PTSD with more adaptive coping skills (i.e., acceptance and mindfulness, focus on values-based living) to interact with others, develop and maintain relationships, and help manage PTSD-related distress. The primary aim of this research study is to conduct a three-site randomized controlled trial of ACT-SS (*n*=75) vs. Present-Centered Therapy (PCT; *n*=75).

The objectives of this project were to:

Aim 1 (Primary Outcome): Evaluate whether ACT-SS is more efficacious than PCT in improving social support and social relationships (MOS Social Support Survey and Social Adjustment Scale) for Veterans with PTSD at the end of treatment, 3-month follow-up, and 6-month follow-up.

- **Hypothesis 1:** Veterans in ACT-SS will have significantly better improvement in social support and social relationships than PCT at the end of treatment and at the 3- and 6-month follow-up periods.

Aim 2 (Secondary Outcome): Test whether ACT-SS is more efficacious than PCT in improving quality of life (Quality of Life, Enjoyment, and Satisfaction Questionnaire) for Veterans with PTSD at the end of treatment and at the 3- and 6-month follow-up periods.

- **Hypothesis 2:** Veterans in ACT-SS will have significantly better improvement in quality of life than PCT at the end of treatment and at the 3- and 6-month follow-up periods.

Aim 3 (Secondary Outcome): Assess whether ACT-SS is more efficacious than PCT in improving PTSD symptoms (CAPS and PCL-5) at the end of treatment and at the 3- and 6-month follow-up periods.

- **Hypothesis 3:** Veterans in ACT-SS will have significantly greater improvement in PTSD symptoms than PCT at the end of treatment and at the 3- and 6-month follow-up periods.

The project was conducted at the VA Bedford Healthcare System in Bedford, MA, the VA Denver Healthcare System in Aurora, CO, and the VA Connecticut Healthcare System in West Haven, CT.

Multi-Site Design - Site Coordination and Standardization Across Sites: The success of the proposed study is dependent on the coordination of both proposed trial sites to assure adherence to study procedures and protocol and for adequate recruitment of the study sample. *The Bedford Site Project Coordinator was the overall trial manager.* The key responsibilities for the trial manager were to 1) have the lead role in planning, coordinating, and completing the project, 2) maintain communication with the VA Denver and VA Connecticut sites, 3) organize and motivate staff from the three sites, and 4) assist with managing the trial budget. The lead site drafted a trial management plan that will include the objectives of the study, timeframe and study milestones, and describe the tasks that needed to be completed. The trial management plan also had information on project initiation, project execution, project monitoring, data analysis, and project reporting. We created standardized data collection forms for both sites during the study start-up period (first five months) to ensure a high quality of data collection. We had a virtual kickoff meeting for the study, where all project staff met and reviewed the study rationale and overview, eligibility, recruitment and screening procedures, research procedures, how to handle adverse events, assessments, the interventions, data collection and study randomization procedures, and the communication plan. In addition, a weekly teleconference led by Dr. Kelly (Bedford VAMC) was attended by investigators and study staff from each site. The purpose of these calls was to monitor screening for both phases of the study, assure fidelity to the diagnostic interview and screening assessments, monitor engagement in treatment and post-treatment follow-up, monitor the security and quality of data collection, address barriers to recruitment, and monitor ongoing psychiatric symptoms and treatment. Emergent issues related to screening, eligibility, the interventions, research methods, and data collection were discussed by phone or email as they arise, in order to maintain standardization of research procedures across sites.

Research Methods

Research Design: We conducted a two-arm randomized controlled trial that compares ACT-SS to PCT with Veterans with PTSD. To balance baseline variables between the two conditions, following enrollment we will randomize with stratification based on PTSD severity. Social functioning and PTSD outcomes were measured at baseline, end of treatment, 3-months, and 6-months post-treatment.

Inclusion/exclusion criteria. *Inclusion Criteria:* 1) Current DSM-5 PTSD diagnosis, 2) Minimum score of

31 on the PCL-5, 3) Clinically significant difficulties in interpersonal relationships, 4) Competent to provide written informed consent, 5) Ages 18 and older, 6) If being treated with psychoactive medication, no change in drugs or dose for the past 2 months, and 7) Willingness to be audio-taped. We included Veterans with co-morbid mental health disorders, including mood disorders, with some exceptions (see exclusion criteria). *Exclusion Criteria:* 1) Any current or lifetime DSM-5 psychotic disorder, 2) Current or recent (within 1 month of study entry) DSM-5 substance use disorder, 3) Cognitive impairment that would interfere with study participation, 4) Current manic episode, 5) Recent clinically significant suicidality (past 3 months), 6) Moderate to severe domestic violence (measured by the Conflict Tactics Scale-2), and 7) Current PTSD psychotherapy.

Recruitment. Initial recruitment was aimed at 150 Veterans (see inclusion/exclusion criteria in Human Subjects section). Subjects were recruited from the VA Bedford Healthcare System in Bedford, MA, the VA Denver Healthcare System in Aurora, CO, and the VA Connecticut Healthcare System in West Haven, CT, which has excellent access to study participants. To increase recruitment, we advertised the study on popular websites, flyers around the hospital, VHA-affiliated clinics, community programs, and Vet Centers, and letters and presentations to healthcare professionals. We also found success in using targeted mailings to recruit for research studies.

Screening Procedures. Eligible participants were scheduled for an in-person assessment with study staff, who confirmed study eligibility and obtained informed consent. A highly trained and supervised RA conducted clinician-rated assessments, and subjects completed self-report measures (see below). A detailed inclusion/exclusion criteria checklist was used by study staff to help determine whether Veterans were eligible for the study. When individuals did not qualify for or choose not to participate in the study, reasons were documented and mental health resources were provided.

Treatment Procedures. Veterans with a DSM-5 diagnosis of PTSD were randomized to ACT-SS or PCT. Treatment conditions were balanced on PTSD symptom severity. Veterans randomized to either ACT-SS or PCT received 12, 50-minute weekly sessions of individual treatment.

ACT Treatment Components. The following nine components are emphasized in ACT-SS: *1) Identifying Problems with Social Avoidance:* Participants identify efforts to avoid interpersonal experiences. Discussions focus on how avoidance is problematic for developing and maintaining relationships. *2) Triggers for Avoidance*: Negative thoughts and emotions that lead to poor functioning and low quality of life are identified (e.g., worry over rejection, not being able to trust others, anger, feelings of being unworthy), and Veterans practice acceptance and mindfulness to manage these experiences. *3) Acceptance:* Veterans are encouraged to accept interpersonal situations that trigger concerns with mindful acceptance rather than avoid them. *4) Mindfulness*: Participants engage in mindfulness exercises in order to practice nonjudgmental acceptance of their thoughts about others and negative emotions (e.g., leaves on a stream exercise, mindfulness of anger). *5) Self-Compassion*: Veterans are encouraged to view themselves with more compassion, and practice self-compassion exercises (e.g., view themselves as a child who needs compassion). *6) Valued Living*: Participants clarify their values and goals (i.e., building relationships, work achievement, community participation), and identify barriers that prevent them from achieving life goals. *7) Willingness Exercises (Exposure)*: Participants develop hierarchies for interpersonal triggers and avoided social experiences and practice mindful acceptance during scheduled willingness exercises. *8) Cognitive Defusion*: Participants learn that they are not their anxieties or fears, and they mindfully observe and accept these internal experiences. *9) Committed Action*: Participants identify life goals and increase activities to improve social functioning, quality of life, and social reintegration. Participants commit to achieving valued goals (see Table 1 for an overview of ACT-SS manual content).

ACT-SS procedures. Participants received 12 weekly 50-minute individual counseling sessions. Session 1 is devoted to an explanation of the treatment rationale and identifying interpersonal triggers. Sessions 2-6 focus on mindfulness, cognitive defusion, and acceptance of PTSD symptoms, anxiety over interacting with others, and acceptance of other negative thoughts and emotions. Sessions 7-11 focus on self-compassion, relating to others, values, anger, and forgiveness, with a large emphasis on committed action and

Table 1. ACT-SS Manual Content

Major Content Areas of ACT-SS	
Identifying Problems with Social Avoidance	Veterans are asked to identify efforts to avoid interpersonal experiences and how this is problematic for developing and maintaining relationships
Identifying Triggers	Interpersonal triggers are identified, with an emphasis on how PTSD-related triggers and symptoms are related to interpersonal conflict and avoidance.

Acceptance and Mindfulness	Veterans participate in mindfulness exercises in order to practice nonjudgmental acceptance of interpersonal experiences and PTSD symptoms that interfere with interpersonal interactions (e.g., irritability and feelings of detachment).
Valued Living	Veterans clarify their values and goals (i.e., reasons for changing patterns in interpersonal experiences), and identify barriers (thoughts, feelings, sensations associated with PTSD) that prevent them from achieving these goals.
Cognitive Defusion	Veterans learn that partners, family members, and peers are not threats to their safety and to mindfully observe anxieties about social interactions.
Willingness Exercises	Veterans create exposure hierarchies for social interactions and face them with mindful acceptance to become more comfortable with these experiences.
Committed Action	Veterans will incorporate more social activities in their lives and opportunities to interact with others that are consistent with valued goals. Veterans will commit to spending more time with important social supports and develop new relationships.
Specific Content Areas to Address for Veterans with PTSD in ACT-SS	
Social Isolation	Goals focus on being willing to engage in social interactions and increasing community involvement, while accepting PTSD-related symptoms.
Building Healthy Relationships	Ask Veterans to be present, validate the other person, be compassionate, share valued activities, and practice connection.
Anger	Veterans learn to be more mindful of anger and to choose to act according to their values.
Trust	Veterans balance values around trust with values around self-protection and practice mindful trusting - be aware of the person's behavior and provide trust when it is earned.

exposure hierarchies for social anxiety and avoidance. In the termination phase (sessions 11-12), therapy focuses on termination, planning for the future, as well as reviewing progress and gains in treatment.

Control Condition. We have replaced the original control condition for our pilot ACT-SS studies (Person-Centered Therapy) with Present-Centered Therapy (PCT) as we believe it is important in this fully-powered RCT to compare ACT-SS to the gold standard comparison condition for PTSD-related interventions. The goal of PCT treatment is to focus on the Veteran's current life and help the Veteran to connect their PTSD symptoms to their present life situation and areas they want to work on. The treatment: 1) helps Veterans to alter present maladaptive patterns and behaviors, 2) provides psychoeducation regarding the impact of trauma on the client's life, and 3) teaches about the use of problem-solving strategies that focus on current life issues. PCT is a clinically realistic comparison since it addresses the problems presented by many Veterans who seek PTSD care from VHA [3]. **PCT was delivered in 12 50-minute sessions, matched to the length and frequency of ACT-SS sessions.**

Assessments. A broad range of reliable and valid measures were used in the study (see Table 2). On average, the complete baseline battery took 2 hours to complete (diagnostic interview and assessments); post-treatment and follow-up assessments required ~1 hour. Measures were administered at the same intervals as indicated above.

Diagnostic Measures: The *Clinician Administered PTSD Scale (CAPS-5)* is a structured interview that was used to diagnose PTSD and to obtain data (pre and post treatment, follow-up) on the frequency and severity of PTSD symptoms. The CAPS-5 is the gold standard for assessing PTSD. It has excellent psychometric properties and diagnostic efficiency [61]. The CAPS for DSM-5 uses only a single 5-point ordinal rating scale to measure symptom severity. CAPS-5 scores range from 0 to 80 with higher scores indicating greater PTSD symptom severity [62].

The *Structured Clinical Interview for DSM-5 (SCID-5)* was used for diagnosing mental health disorders other than PTSD [63]. The SCID is a widely used structured interview that is used to diagnose mental health disorders. Studies show that the SCID yields highly reliable diagnosis for mental health disorders [64].

Intimate Partner Violence: *The Conflicts Tactics Scale 2 (CTS-2)* is the most widely used method for identifying and measuring intimate partner violence [65]. This measure was used to exclude potential participants based on presence of intimate partner violence.

Social Adjustment and Interpersonal Functioning: The *Social Adjustment Scale-Self Report (SAS-SR)* [66] is a 54-item measure of current social functioning in 6 domains: Work; Social and Leisure; Extended Family; Primary Relationship; Parental; and Family Unit. The social and leisure scale is the primary measure of change in social functioning for this study. An Overall Adjustment scale provides a total score (α = .74-.85; test-retest *r*'s = .78-.80). The SAS-SR is sensitive to change and has good convergent and discriminant validity.

Social Support: The *MOS Social Support Survey* is a 19-item multidimensional, self-administered survey of social support for individuals with chronic conditions [67]. It includes four functional support scales, including

emotional/informational, tangible, affectionate, and positive social interaction.

Loneliness: The *UCLA Loneliness Scale – Short Form* [68] is an 8-item scale designed to measure one's subjective feelings of loneliness as well as feelings of social isolation. Participants rate each item on a scale from 1 (Never) to 4 (Often). The measure has high internal consistency and test-retest reliability.

Quality of Life: The *Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)* [69, 70] is a commonly used self-report measure to assess quality of life in several domains: general activities, physical health, subjective feelings, leisure time activities, social relationships, work, and household duties.

PTSD Symptoms: The *PCL-5* is a 20-item self-report measure of PTSD symptoms [71-73], selected for its dimensional sensitivity, with higher scores reflecting greater PTSD severity.

Clinical Global Impressions: *Clinical Global Impressions Scale (CGI)* is a 3-item observer-rated global rating scale that will be completed by both subjects and the IE that measures illness severity and improvement, and is frequently used in both clinical and research settings [74].

Table 2: Assessment Measures by Occasion

Measure	Rater	Self		Week 0	Weeks 4 and 8	Week 12 (End of Treatment)	3- and 6-month Follow-Ups
Demographics	X			X			
Diagnostic							
CAPS	X			X		X	X
SCID-5	X			X			
Intimate Partner Violence							
CTS-2		X		X			
Social Adjustment and Support							
SAS-SR		X		X	X	X	X
MOS-Social Support		X		X	X	X	X
Loneliness		X		X	X	X	X
Quality of Life							
Q-LES-Q		X		X		X	X
PTSD Symptoms							
PCL	X			X	X	X	X
Clinical Global Impressions						X	X
CGI	X	X		X	X	X	X
Process							
AAQ-II		X		X	X	X	X
MPFI		X		X	X	X	X
Treatment Satisfaction							
CSQ-8		X				X	
Therapeutic Alliance							
WAI-S		X			X	X	
Suicidal Ideation and Behavior							
C-SSRS	X			X		X	X

Process Measures: Experiential avoidance was measured with the *Acceptance and Action Questionnaire-II (AAQ-II)* [24], a widely-used 7-item self-report measure of emotional avoidance and inaction. The AAQ-II has good reliability and validity, with scores concurrently, longitudinally, and incrementally associated with and predictive of a range of outcomes including mental health outcomes and work absence rates.The *Multidimensional Psychological Flexibility Inventory (MPFI)* [75] is a 30-item self-report measure that assesses psychological flexibility. The MPFI is conceptually grounded in the ACT Hexaflex model (see Figure 2 above), and assesses six dimensions of flexibility (i.e., present moment awareness, self as context, acceptance, contact with values, committed action, cognitive defusion), six dimensions of inflexibility (cognitive fusion, self as context, inaction, lack of contact with values, lack of contact with the present moment, experiential avoidance), and 2 global composite dimensions. The MFPI is sensitive to clinical change [76]. The MFPI scales have demonstrated excellent internal consistencies across several subpopulations [76].

Patient Satisfaction with Treatment: *Client Satisfaction Questionnaire-8 (CSQ-8)* [77]: This 8-item scale yields a total score that reflects global satisfaction with and perceived quality of mental health services as well as the degree to which treatment was effective. This scale has been used in mental health and other health centers and has acceptable internal consistency (Cronbach's α=.83-.93) [78].

Therapeutic Alliance: *Working Alliance Inventory-Short Form (WAI-S)* [79]*:* This 12-item scale was administered to obtain both an early and a late alliance assessment. It has acceptable internal consistency

(Cronbach's α=.83-.98) [79] and predictive validity related to therapy outcome [79-81].

Suicidal Ideation and Behavior: *Columbia Suicide Severity Rating Scale (CSSRS)* [82]*:* The CSSRS is a state-of-the-art suicide measure that assesses the severity of suicidal ideation for both lifetime and current (i.e., the last 30 days) time frames. Severity of suicidal ideation is rated on a 6-point scale ranging from no suicidal ideation (0) to active suicidal ideation with specific plan and intent (5). Additionally, the measure assesses lifetime and current suicide attempts. The CSSRS demonstrates good internal consistency [83]. The CSSRS was used for monitoring of clinical stability.

Sample size determination. We used Mixed Effects Modeling to test for a time by intervention interaction. We have based our power analysis and sample size estimation on our primary outcome of interest, the Social Adjustment Scale-Self-Report. Using our preliminary data as a guide, we expect the correlation between time points to be approximately 0.5. For a desired power of 0.80, a Type I error rate of 0.05, and linear increasing effect sizes of 0, .3, and .6, we estimate that we will need 104 participants [84-86]. We have used more conservative effect size estimates compared to the results of our preliminary study because the reliability of effect sizes is susceptible to small sample sizes [87, 88], and we did not wish to be left with an underpowered study. We also expect potential dropout rate of 20% and plan on conducting multiple tests. Therefore, we planned on enrolling a total of 150 participants for this study.

Statistical Analysis Plan

Data analyses will be organized around the specific aims and hypotheses; however, in general, we will first perform descriptive statistics and graph our data to better understand its nature and structure. Next, we will perform bivariate analyses (Chi-square tests for categorical variables and Welch's t test for continuous variables) to investigate differences in demographic, psychiatric, and psychosocial variables between the two conditions to ensure randomization was successful. For the primary longitudinal analyses, we will adopt an intent-to-treat approach and will include all available data on subjects who started treatment. Because each specific aim will involve investigating the effect of condition and other possible covariates on an outcome over time, we will begin each longitudinal analysis by first testing an unconditional means and an unconditional growth model to ensure enough variance is available to be explained by our predictor and independent variables before we undergo our model building and hypothesis testing [92]. A significance level of 0.05 will be used for the main hypotheses and a Bonferroni correction will be applied for any post-hoc tests and secondary analyses. All analyses will be performed using SAS or Mplus (for Exploratory Aim 4) software.

The same fundamental procedures will be used for fitting all repeated measures models in this proposal. We will test study hypotheses on repeatedly measured quantitative outcomes, using Mixed-Effects Models, which will allow for different numbers of observations per subject, use of all available data, and are unaffected by randomly missing data. In addition, the use of repeated mixed effects models, which preserve all available data, will in general also improve power [93]. We will presume a linear trend across time unless otherwise indicated by graphical review of our data. Models will include a condition by time interaction and will adjust for significant and/or substantive demographic and clinical variables (e.g., site). We will confirm the normality assumption of the residuals for each outcome. The model will be reduced in a backwards-elimination fashion, removing covariate variables that are non-significant and unimportant confounders. A significant interaction term in the final model will imply a significant difference in trajectories between the conditions, in which case predicted means or mean frequency of use and rates will be presented separately for each time point. Post hoc analyses may involve testing pairwise comparisons across conditions at specific time points or testing hypotheses around specific types of trajectories based upon observation of the adjusted least square means or predicted probabilities by condition and time. We will also calculate standard effect sizes (Cohen's d) by dividing the estimated treatment effects by the pooled SD at follow-up. In addition, we will conduct sensitivity analyses for the main outcomes, examining the robustness of the results to different assumptions regarding data. For example, we will investigate whether previous PTSD treatment experience contributed to the outcomes. We will determine whether previous treatment measured dichotomously (yes/no), type of previous treatment, and/or amount of treatment may impact study results.

Aim 1: Evaluate whether ACT-SS is more efficacious than PCT in improving social support and social relationships (MOS-Social and SAS-SR) at the end of treatment, 3-month follow-up, and 6-month follow-up. Hypothesis 1: Veterans in ACT-SS will have significantly better improvement in social support and social relationships than PCT at the end of treatment and at the 3- and 6-month follow-up periods.

To test this hypothesis, we will fit linear mixed models for each outcome variable with the between-subject factor of treatment, ACT-SS vs. PCT, the within-subject factor of time and the interaction between two factors.

Several different correlation structures will be considered for repeated measures within individuals, and the best fitting structure based on Akaike Information Criterion (AIC) selected. Significant treatment by time interaction, with significant differences at follow-up on social functioning measures (MOS-Social and SAS-SR), will be considered supportive of our hypotheses.

Aim 2: Test whether ACT-SS is more efficacious than PCT in improving quality of life (Q-LES-Q) for Veterans with PTSD at the end of treatment and at the 3- and 6-month follow-up periods.

Hypothesis 2: Veterans in ACT-SS will have significantly better mental health functioning and quality of life than participants treated with PCT at the end of treatment and at the 3- and 6-month follow-up periods.

To test this hypothesis, we will use the same analysis approach as for Specific Aim 1 but with the Q-LES-Q score as the outcome variable. The correlation structure will be selected based on the AIC. Significant group by time effect, with greater decrease from baseline to follow-up in the ACT-SS group compared to the PCT control group, will be considered supportive of the hypothesis.

Aim 3: Assess whether ACT-SS is more efficacious than PCT in improving PTSD symptoms (CAPS and PCL-5) at the end of treatment and at the 3- and 6-month follow-up periods.

Hypothesis 3: Veterans in ACT-SS will have significantly greater improvement in PTSD symptoms than PCT at the end of treatment and at the 3- and 6-month follow-up periods.

To test this hypothesis, we will use the same analysis approach as for Specific Aims 1 and 2 but with CAPS and PCL scores as the outcome variable. The correlation structure will be selected based on the AIC. Significant group by time effect, with greater decrease from baseline to follow-up in the ACT-SS group compared to the PCT control group, will be considered supportive of the hypothesis.

Exploratory Aim 4: Explore whether social functioning treatment outcomes in the ACT-SS group (but not the comparison group, PCT) are mediated by experiential avoidance and psychological flexibility (Multidimensional Psychological Flexibility Inventory), psychological measures that are central to the theoretical model underlying ACT.

Based upon our previous work [28], we hypothesize that the ACT group's (but not the comparison group's) social functioning outcomes will be mediated by experiential avoidance and psychological flexibility. We will conduct all mediation analyses using the structural equation modelling package Mplus Version 7.2 or later. Our mediation analysis strategy will be similar to that proposed by Baron and Kenny [94]—i.e., we will test for ACT-SS intervention effects on the outcome (Social Adjustment Scale-Self-Report) and the proposed mediators (Experiential Avoidance, Psychological Flexibility), then fit a full model to estimate the direct and indirect effects of the intervention on the outcome—but with statistical models that account for the repeated measures of both mediator and outcome (i.e., a parallel process model) [95], while considering the confounding of the effect of mediator on outcome is probable [96] and allowing for the measurement error of the mediator and outcome [97]. We will assess the proportion of the intention-to-treat effect of the ACT-SS intervention attributed to its effect on experiential avoidance. All statistical testing will be two-tailed. Level of experiential avoidance and psychological flexibility (Multidimensional Psychological Flexibility Inventory) will be assumed to be the mediators and Social Adjustment Scale-Self-Report the outcome—primarily motivated by preliminary findings and the fact that the development of the intervention was to target experiential avoidance and psychological flexibility as the mechanisms of change. We will estimate the parameters of the chosen model by testing the underlying validity of the model.