ACT for Life: a Brief Intervention for Maximizing Recovery After Suicidal Crises

NCT02751983

Protocol and Statistical Analysis Plan

October 22, 2019

For questions concerning this protocol or for information about the resulting publication please e-mail Sean Barnes at Sean.Barnes2@va.gov. A manuscript based on this work is currently under review. The protocol reflects the most recent IRB approved protocol and has been edited to focus on aspects of the protocol directly relevant to NCT02751983

The following pilot study aims are designed to determine the feasibility of a future randomized clinical trial to evaluate the efficacy of a novel application of Acceptance and Commitment Therapy (ACT) in a larger sample of Veterans hospitalized due to suicide risk. By design, the proposed study is not powered to determine the efficacy of the intervention. That objective will be addressed in a subsequent trial. However, each aim is a necessary precursor to an anticipated efficacy study.[1] As recommended by Thabane et al.,[2] a priori criteria for feasibility outcomes have been specified. Using a two arm, randomized controlled design, we will:

Aim 1: Determine the acceptability of ACT for Life. Acceptability refers to the suitability of the intervention from the perspective of the clinical population of interest.[3] To determine if participants find the intervention to be acceptable, defined as ≥ 70% of participants scoring ≥ 24 on the Client Satisfaction Questionnaire (CSQ),[4] we will examine the percentage of participants obtaining CSQ scores ≥ 24. Responses on the Narrative Evaluation of Intervention Interview (NEII),[5] a qualitative interview, and Reasons for Termination[6] scale will be used to identify potential areas for modification to the intervention.

Aim 2: Determine the feasibility of the study design and research procedures. This will be accomplished by examining the following outcomes: a) number of patients approached who are eligible for the study and the number who enroll in the study. Feasibility is defined as ≥ 50% eligible and (of these) ≥ 30% willing to participate in the proposed time frame. b) providers' adherence to the treatment protocol (i.e., clinicians' ability to deliver the intervention as intended in a routine inpatient setting) will be examined using the treatment fidelity checklist, with ≤ 15% of deviations for each clinician across participants considered acceptable fidelity. c) participant completion of intervention modules will be measured by examining the percentage of patients randomized to ACT who complete the treatment per protocol. This is crucial to ensuring that patients receive an adequate dose of the intervention. A minimum of 70% completing the entire intervention will be considered feasible. d) percentage of participants lost to follow up (LTFU) across both groups. This will be measured by examining the percentage of participants across both groups who fail to complete the three-month follow-up visit, with ≤ 30% LTFU in each group considered feasible. This will inform the target sample size and retention strategies for the subsequent study.

Aim 3: Characterize participants' functional outcomes and self-directed violence at baseline, one-month and three-months post-discharge. This aim will provide variability estimates on: (a) progress towards living consistently with self-defined values (assessed by the Valued Living Questionnaire[7]) and engagement in a range of functional behaviors, (assessed by the Inventory of Psychosocial Functioning, Outcome Questionnaire 45.2, and select PROMIS modules[8]), (b) objective treatment engagement based on medical record review, and (d) self-directed violence

as assessed by the Columbia-Suicide Severity Rating Scale[9] and medical record review. Variability estimates can then be used to inform selection of outcome measure(s) and the sample size for a subsequent efficacy trial.

A. Outcome Measure(s):

Aim One Measures: Acceptability. The ***Client Satisfaction Questionnaire*** (CSQ-8)[4] is a self-report measure that will be used to assess patients' satisfaction with ACT for Life. (*Duration:* 5 minutes; *Administration:* Post-Treatment). The ***Narrative Evaluation of Intervention Interview* (NEII)**[5] is a 16-item semi-structured interview assessing each participants' perspective of the impact of the intervention, helpful and unhelpful components, and comparison to other interventions. This yields rich information regarding how the intervention can be modified to better meet patients' needs (*Duration:* 15 minutes; *Administration:* Post-Treatment). Participants who withdraw from treatment, but agree to remain in the study will also complete the ***Reasons for Termination (Client and Therapist versions;* RT-C/RT-T)**[6] scale, which assess the impact of 19 common reasons why patients terminate therapy. Study clinicians will also complete the RT-T (*Duration:* 5 minutes; *Administration:* Following withdrawal from treatment).

Aim Two Measures: Feasibility. A ***treatment fidelity checklist*** was developed for the current study to monitor clinician adherence to the treatment manual after each recorded session. (Audio recorders will be FIPS compliant.) It was modeled off of fidelity checklists included in trials of other cognitive behavioral therapies and incorporates treatment competency items from an ACT fidelity measure used in the ACT for Depressed Veterans roll out. (Please note that this checklist is for internal use only/is not given to participants and therefore is not included in the measures submitted with this application.)

Aim Three Measures: Characterize Treatment Outcomes. The following measures will be included as candidate outcome measures for a future efficacy trial, and be administered at baseline, one-month, and three-month assessment sessions. The ***Valued Living Questionnaire (VLQ)***[7] is a self-report measure that assesses participants' life values as well as the perceived consistency with which they have been living according to their values. Participants rate the importance of ten domains of living (e.g., friendship). Then participants rate how consistently they have lived with the valued behavioral pattern within each domain over the past week. (*Duration:* 10 minutes). The ***Inventory of Psychosocial Functioning (IPF)***[10,11] assesses impairment within the last 30 days across a spectrum of psychosocial domains (e.g., work, socializing etc.). The 80-item self-report measure was developed and validated in a sample of Veterans. The scale does not require respondents to make attributions regarding the cause of impairments and is therefore ideal for transdiagnostic assessment of functioning (*Duration:* 15

minutes). The ***Outcome Questionnaire-45.2 (OQ-45)*** is a 45-item self-report scale that assesses symptom distress, interpersonal relationships, and social role (functioning in the workplace, school, and home) for the past week. It was designed for repeated measurement of client progress in therapy (*Duration*: 5 minutes). The ***PROMIS Global Short Form v1.1***[12] is a ten-item self-report measure assessing multiple domains of health. The scale yields two subscales: Global Physical Health and Global Mental Health (*Duration:* 5 minutes). The ***PROMIS Short Form v2.0- Satisfaction with Social Roles and Activities 8a***[13] is an eight-item self-report measure that assesses satisfaction with respondents' ability to perform various social activities (*Duration:* 5 minutes). The ***Columbia Suicide-Severity Rating Scale (C-SSRS)***[9] is a clinician-administered interview that assesses suicidal ideation and attempts. The C-SSRS assesses severity of suicidal ideation and behavior (*Duration:* 15 minutes).

B. Description of Population to be Enrolled:

Participants will consist of all eligible and willing Veterans who meet the following eligibility criteria

Inclusion Criteria: 1) Eligible for VHA care [Medical Record Review]**,** 2) Age 18-89 [Medical Record Review]**,** 3) Currently hospitalized due to suicide risk [Medical Record Review]**,** and 4) Willing to be randomized and participate in the two conditions (i.e., treatment and control) [Asked by study team member during recruitment. Reiterated during the consent process].

Exclusion Criteria: 1) Inability to provide informed consent [Pre-consent Questions]**,** 2) Inability to complete study measures (e.g., due to significant acute intoxication/withdrawal symptoms, mania, psychosis, aggression, catatonia, cognitive impairment) [Medical Record Review, Consultation with treatment team, Experimenter or Study Therapist Observation], or 3) membership in vulnerable population [e.g., pregnant women, prisoners, etc. see p.4 of Application for protocol review; Medical Record Review, Consultation with treatment team, Pre-consent Questions, Experimenter or Study Therapist Observation].

C. Study Design and Research Methods

Design: We are proposing a two arm, randomized, controlled pilot study to assess *the feasibility of a future randomized clinical trial evaluating the efficacy of ACT for Life*. Veterans psychiatrically hospitalized at the Denver VA Medical Center (Denver VAMC) who are eligible and interested in participating in the study will be randomized to: (1) enhanced care as usual (E-CARE) or (2) E-CARE plus ACT for Life (referred to as the ACT group).

Description of Treatment Conditions. ***Enhanced Care as Usual (E-CARE).*** Group therapy and medication management are the primary treatment modalities. About 25% of patients also receive individual psychotherapy. We are referring to this group as "enhanced" treatment as usual because, in addition to standard care, all participants will complete the assessment sessions and the VLQ, which will cause participants to reflect on their values and the consistency of their behavior with their values. The assessment alone has the potential to beneficially impact the participants.[14] ***ACT for Life.*** Act for Life is a 3-6 session individual therapy applying Acceptance and Commitment Therapy to promote functional recovery from suicidal crises and prevent future suicidal behavior. (Please contact the study PI, Sean Barnes, at Sean.Barnes2@va.gov for reference to a manuscript describing the treatment protocol in more detail.)

Measures:

The following measures were selected based on their content validity and other psychometric properties. **Descriptive Measure.** The ***Rocky Mountain MIRECC Demographics Form*** will be used to assess demographic variables such as age, sex, and ethnicity, as well as variables related to education, employment, housing, and military history (*Duration:* 5 minutes; *Administration:* Baseline assessment).

Safety Monitoring Measure. The ***University of Washington Risk Assessment Protocol (UWRAP)***[15] is a structured clinical interview that evaluates participants' acute emotional state prior to the study and capacity to complete the study procedures. At the end of the study, the UWRAP debriefing protocol will be initiated. Members of the research team will evaluate responses and access additional assistance as necessary (*Duration:* 10 minutes; *Administration:* All Assessments).

Aim One Measures: Acceptability. The ***Client Satisfaction Questionnaire*** (CSQ-8)[4] is a self-report measure that will be used to assess patients' satisfaction with ACT for Life. (*Duration:* 5 minutes; *Administration:* Post-Treatment). The ***Narrative Evaluation of Intervention Interview*** **(NEII)**[5] is a 16-item semi-structured interview assessing each participants' perspective of the impact of the intervention, helpful and unhelpful components, and comparison to other interventions. This yields rich information regarding how the intervention can be modified to better meet patients' needs (*Duration:* 15 minutes; *Administration:* Post-Treatment). Participants who withdraw from treatment, but agree to remain in the study will also complete the ***Reasons for Termination (Client and Therapist versions;*** **RT-C/RT-T)**[6] scale, which assess the impact of 19 common reasons why patients terminate therapy. Study clinicians will also complete the RT-T (*Duration:* 5 minutes; *Administration:* Following withdrawal from treatment).

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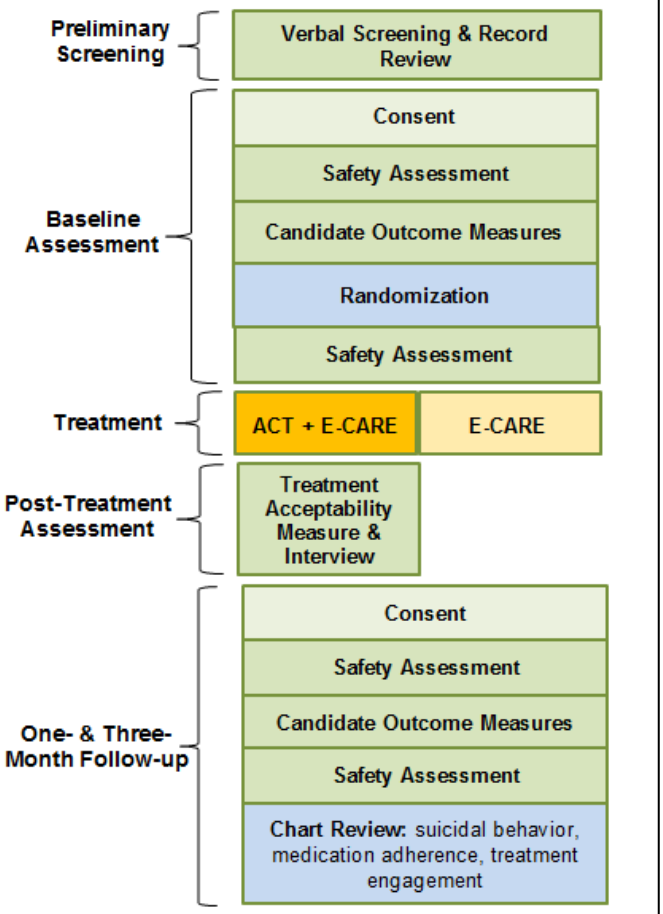
Figure 1. Research Procedures



(*Duration:* 5 minutes). The ***PROMIS Short Form v2.0- Satisfaction with Social Roles and Activities 8a***[13] is an eight-item self-report measure that assesses satisfaction with respondents' ability to perform various social activities (*Duration:* 5 minutes). The ***Columbia Suicide-Severity Rating Scale (C-SSRS)***[9] is a clinician-administered interview that assesses suicidal ideation and attempts. The C-SSRS assesses severity of suicidal ideation and behavior (*Duration:* 15 minutes).

Procedures:

Recruitment and Preliminary Screening. Participants will be recruited from the Denver VA Medical Center's psychiatric inpatient unit. Potential participants will be told about the study by a member of their treatment team. The PI and Co-Is are treatment providers on the inpatient unit and will have a treatment relationship with potential participants. They will work in conjunction with the other inpatient treatment providers to identify potentially eligible participants. A waiver of consent and HIPAA are being requested so that the study team can review medical records of potential participants to determine whether they are likely to be eligible for the study. Apart from gauging Veterans' interest in participation, it will be possible to assess all inclusion and exclusion criteria based on chart review and verbal consultation with other treatment team members. If it is determined, in consultation with other treatment providers, that a Veteran is likely to be eligible for study participation, the PI or a Co-I will tell them about the study and see if they are interested in participating. If the Veteran is interested in participating, they will be scheduled for their baseline assessment session.

Baseline Assessment Session and Randomization. After passing the consent questions and providing documented consent (see Informed Consent section below for more details), participants will complete the safety measure (UWRAP), demographics form, and then candidate outcome measures (VLQ, IPF, OQ-45, PROMIS, C-SSRS). The study assessor and participants will be blind to condition. At the end of the session, participants will be randomized to ACT or E-CARE. Group assignment will be predetermined by the study statistician using block randomization (random block sizes), and concealed in a sealed envelope. The baseline assessment session is expected to last roughly one and a half hours. Participants will be compensated $20. ***Treatment Participation.*** Participants randomized to ACT will complete ACT for Life while hospitalized. Depending on participants' anticipated length of stay and clinical needs they will receive approximately three hours of treatment delivered in about three to four sessions. No compensation will be provided for treatment participation. ***Post-treatment Assessment Session.*** A study assessor will meet with participants in the ACT condition and administer the UWRAP and treatment acceptability measures (CSQ-8, NEII, and RT-C if appropriate). The post-treatment assessment session is expected to last roughly 30 minutes. Participants will be compensated $10. ***One-Month and Three-Month Follow-ups.*** A different assessor, still blind to condition, will administer the one- and three-month follow-up measures (UWRAP, VLQ, IPF, OQ-45, PROMIS, C-SSRS). These assessment session are expected to last roughly one hour each. Participants will be compensated $20 for each assessment. [This was

later increased to $50 per session.] If participation in post-treatment or follow-up sessions is limited by lack of funds to travel to the Denver VAMC, participants may be provided with additional mileage reimbursement at the government rate or funds to pay for public transportation.

Enrollment:

Informed Consent. Participation will be voluntary, and potential participants will have ample time to review the informed consent with trained staff and to ask questions about the study. Authorization to collect protected health information (PHI) will also be obtained (HIPAA authorization). Research staff will assess patients' ability to provide informed consent, based on whether they can adequately respond to the following questions about the study:

1) *What are you being asked to do?*
2) *Finish this sentence - The purpose of this study is to find out…*
3) *True or False: After beginning this study, you can decide not to continue at any time, without penalty.*
4) *What should you do if you have questions about this study?*
5) *Who should you call if you feel you have been harmed in this study?*
6) *What are the risks of participating in this study?*
7) *What are the benefits of participating in this study?*

Veterans who cannot adequately answer these questions will be excluded from participating. Veterans who provide informed consent and HIPAA authorization will receive signed and dated copies of the informed consent and HIPAA forms.

Adverse Events

Significant adverse events are not expected. For the purposes of this study, adverse events are defined as any newly identified medical diagnoses noted by medical personnel, or symptoms reported by the participant, which are *directly related to participation in the study and occur during the administration of testing/treatment or appear shortly thereafter*. Participants will be instructed to contact the principal investigator if they believe they have potentially experienced an adverse event. Any adverse event will be reported to COMIRB by the PI in keeping with COMIRB regulations

Data Analysis Plan

Analyses will be descriptive in nature, although variability and precision estimates (95% confidence intervals [CIs]) will be provided for acceptability and feasibility summary statistics. Results will be presented across participants and individually for each group. **Sample Size.**

Arean and Kraemer recommend 20-30 participants per condition for a "dress rehearsal for the clinical trial" (p. 95).[16] We will enroll 35 participants per condition to account for attrition.

Aim 1: Acceptability. To examine whether participants find ACT for Life acceptable (i.e., ≥ 70% of participants with CSQ ≥ 24), we will compute the proportion of participants who found the intervention acceptable. If fewer than 70% of participants find it acceptable, we will turn to the qualitative data collected with the NEII and RT-T/C to determine areas for improvement. To examine acceptability qualitatively, we will employ qualitative description and analyze NEII responses using qualitative content analysis.[17,18]

Aim 2: Feasibility. a) Participant recruitment rates. Recruitment rates will be monitored to determine the feasibility of recruiting enough participants for a future efficacy trial. The proportion of eligible patients will be reported as the number of patients who meet criteria for inclusion in the study out of all of the patients who are admitted to the unit during the study period. This proportion will be compared to the *a priori* ≥ 50% eligible criterion for feasibility. Similarly, the proportion of eligible and willing patients out of all eligible patients will be compared to the *a priori* feasibility criterion of ≥ 30% of eligible patients willing to participate. **b) Treatment Fidelity.** To examine whether ACT for Life can be delivered as intended (≤ 15% of deviations for each clinician across participants on the treatment fidelity checklist), the proportion of sessions in which each clinician achieved acceptable fidelity out of all of the clinician's sessions will be reported for all clinicians. If treatment fidelity is less than desired, qualitative review of the fidelity checklists will be used to identify areas of difficulty and inform clinician training procedures and revisions to the treatment manual. **c) Participant completion of intervention.** The proportion of participants randomized to the ACT condition who completed all three modules of the intervention out of all participants randomized to the ACT condition will be computed and compared to the *a priori* ≥ 70% criterion. If fewer than 70% of participants were able to complete the intervention, the clinicians will identify barriers (e.g., too much treatment content, participant fatigue, early hospital discharge, etc.) and review reasons for any instances of treatment discontinuation (assessed by RT-C/T). These factors will inform revisions to the treatment manual and implementation procedures. **d) Participant completion of study procedures.** The proportion of participants not completing the three-month follow-up (i.e., participants LTFU) across both groups relative to all participants enrolled in the study will be calculated and compared to the *a priori* ≤ 30% LTFU feasibility criterion. If greater than 30% of participants are LTFU, the study team will review known causes of attrition (e.g., participant relocation, unable to contact, etc.) and integrate additional participant retention measures for future studies (e.g., increased compensation, more frequent reminders, travel assistance) and adjust target enrollment numbers to ensure adequate power to test the efficacy of the intervention.

Aim 3: Characterize functional outcomes and self-harm behaviors. We will provide descriptive statistics, including estimates of variability, for each of the candidate outcome measure at baseline and one-month and three-month follow-up assessments. Statistics will be reported across participants and separately for each group. **(a) Valued Living.** "Progress living consistently with self-defined values" will be operationalized as change in each participant's VLQ consistency score between the baseline and follow-up assessment. **(b) Engagement in Functional Behaviors.** Progress in functional engagement will be reported as the change in IPF, OQ-45, and PROMIS measures between baseline and follow-up assessment. **(c) Objective treatment engagement.** Engagement in outpatient mental health treatment will be determined using medical record review and reported categorically as the proportion of participants having attended at least one individual mental health appointment, out of all participants. **(d) Suicide attempts.** Suicide attempts will be reported based on a combination of self-report (C-SSRS) and medical record review. When both sources of data are available they will be compared for consistency, any discrepancies will be clarified. If one source of data is missing, the other will be used to determine whether any suicide attempts occurred during the follow-up period. The proportion of participants who attempted suicide will be reported. Descriptive data on suicidal ideation and planning will also be reported. Finally, the magnitude of missing data will be calculated for all outcome measures to help inform selection of outcome(s) for an efficacy trial.

D. References

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