STATISTICAL ANALYSIS PLAN

Written Exposure Therapy to Reduce PTSD Symptoms in Survivors of Acute Cardiovascular Events: A Pilot Randomized Trial

National Clinical Trial (NCT) Identified Number: NCT03605693

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STATISTICAL DESIGN AND POWER

Statistical Hypotheses

1. The majority (≥50%) of acutely distressed survivors of CVD events who are eligible for our RCT will agree to be enrolled into a randomized trial of Written Exposure Therapy (WET) versus usual care.
2. It is feasible to complete 30-day outcome assessments for the vast majority (≥80%) of participants.
3. A majority of intervention participants (≥6 of 10) will complete the majority (≥3 of 5) of WET sessions.

Primary Feasibility Endpoints

1. Proportion of acutely distressed CVD event survivors eligible for our RCT who agree to be enrolled into a randomized trial of WET.

Primary Efficacy Endpoint

1. PTSD Checklist - Stressor Specific (PCL-S) score [Time Frame: 1 month after hospital discharge]

This is to measure PTSD symptoms due to the index cardiovascular event. The PCL-S is self-report measure of the symptoms of PTSD. Respondents rate how much they were bothered by a symptom on a 5-point scale ranging from 1 (not at all) to 5 (extremely). The PCL-S (specific) asks about symptoms in relation to an identified stressful experience. The PCL-S aims to link symptom endorsements to the index cardiovascular event

Secondary Endpoints:

- Number of subjects completing the written exposure therapy [Time Frame: Approximately 1 month after hospital discharge]

  This is to measure the feasibility of the therapy - completion to all 5 sessions among participants assigned to the intervention group
- Adherence to cardiovascular medications [Time Frame: Approximately 1 month after hospital discharge]

  This is measured by the scoring from the voils adherence questionnaire (3-items).
- PHQ-8 score [Time Frame: Baseline, 1 month after hospital discharge]

  This is to measure change in depressive symptoms. The eight-item Patient Health Questionnaire depression scale (PHQ-8) is established as a valid diagnostic and severity measure for depressive disorders in large clinical studies. Scores range from 0 - 24 and a score of 10 or greater is consistent with at least moderate depressive symptoms.
- Short Form health survey Version 2.0 (SF-12v2) score [Time Frame: Approximately 6 months after hospital discharge]

  This is to measure quality of life. A health survey that uses 12 questions to measure functional health and well-being from the patient's point of view.

Sample Size and Power Estimates

As this is a pilot study, our sample size was guided by the need to enroll enough participants to examine the feasibility of conducting a larger scale trial of our intervention. In particular, we wanted to ensure that we were capable of recruiting, retaining, and assessing participants as well as implementing the desired intervention. Based on this goal, we estimated we needed to randomize 20 participants (10 per group) into the study. We felt that it was essential to include a randomization arm as this will give more realistic estimates of patients'

willingness to participate in a randomized experiment of this intervention being delivered in a novel context (for prevention and for those with CVD-event PTSD)—information that will be helpful for planning the larger study.

Statistical Analyses

General Approach. For descriptive statistics, categorical data will be presented as percentages and continuous data will be presented as means with standard deviations for normally distributed measures and as median with interquartile range for measures that are not normally distributed. Checks of assumptions (e.g., normality) underlying statistical procedures will be performed and corrective procedures will be applied (e.g., log transformation or nonparametric tests).

Missing Data. Our primary strategy for preventing missing data will be to invest in collecting data as completely as possible. We will carefully design our instruments and train our research coordinators to prevent/minimize dropout and collect all data completely. Data from in-person visits will be collected via iPads using an electronic data capture system (Filemaker) which will minimize loss of data and data entry costs. We will conduct weekly queries of the database to monitor for missing data.

Analysis of the Primary and Secondary Outcomes.

Primary Statistical Analyses for Feasibility Outcomes. We will use descriptive statistics to describe our participants and their outcomes; to determine the proportion of participants needed-to-screen; the proportion who complete 1-month follow-up without loss-to-follow-up; and the proportion who adhere to the WET intervention.

Statistical Approach for Efficacy Outcomes. All randomized participants will be analyzed according to the group to which they are assigned (i.e., intent-to-treat principle; ITT). All participants will be followed for 1 month.

Baseline Descriptive Statistics. Given this is a pilot feasibility design, there is no reason to compare key characteristics of patients randomized to the intervention versus control arms and assess whether the randomization happened to result in group differences.

Planned Interim Analyses. Given the relatively small sample size of this study (N=20 participants) and the expected minimal risk of written exposure therapy, interim analyses will not be planned

Subgroup Analyses. Given this is a pilot feasibility study, we will not conduct any pre-planned subgroup analyses.