Statistical Design and Power for Proposed Pilot Study: The Reducing Exercise Sensitivity with Exposure Training (RESET) Study

NCT Number: NCT05099926

Document Date: 1/26/2024

Statistical Design and Power for Proposed Pilot Study: The Reducing Exercise Sensitivity with Exposure Training (RESET) Study

Aim 1. Evaluate the feasibility, acceptability, and appropriateness of a home-based reducing exercise sensitivity with exposure training (RESET) intervention among acute coronary syndrome (ACS) survivors.

Aim 1 will be tested by assessing the following endpoints:
1. Proportion of participants that complete a majority (>90%) of the intervention;
2. Proportion of participants who complete the outcome assessments upon program completion;
3. Proportion of participants that had a majority (>90%) of the intervention sessions administered as intended;
4. Proportion of participants who report scores ≥4 for their final rating of the intervention's feasibility;
5. Proportion of participants who report scores ≥4 for their final rating of the intervention's acceptability;
6. Proportion of participants who report scores ≥4 for their final rating of the intervention's appropriateness.

Statistical approach for Aim 1. In addition to computing the proportions listed above, we will conduct secondary analyses regarding measures 4, 5, and 6 (see above) as follows. A one-tailed t-test will be conducted comparing the mean for each scale against the comparison value of each 5-point scale's midpoint of 3.

Sample Size and power estimates are based on Aim 1. Although some have used pilot studies to estimate effect sizes for primary outcomes, we agree with leaders in our field who argue that effect size estimates from small pilot studies are too imprecise to meaningfully inform effect size assumptions of power analyses for larger, later stage studies. Therefore, we do not provide power calculations for the effects of our intervention on adherence and behavioral health outcomes. We will, however, use estimates from these studies (e.g., standard deviations, attrition rates) to help determine an appropriate sample size for a subsequent study that is adequately powered to detect meaningful improvements in measures of exercise sensitivity and physical activity levels.

As this is a pilot study, our sample size was guided by the need to enroll enough participants who recently survived an ACS to examine the feasibility of conducting a larger stage II or III randomized clinical trial of our RESET intervention in this patient population. In particular, we will determine whether we are capable of recruiting, retaining, and assessing participants as well as implementing the desired intervention with high fidelity. If the observed proportion of eligible participants who agree to participate in the trial is 40%, 50%, or 60%, and we therefore have to approach 75, 60, or 50 patients, respectively, in order to enroll 30 patients in this pilot. This number is entirely feasible based on enrollment numbers (n=478) from our large observational trial of ACS patients with eligibility criteria that largely overlap with this pilot study.

Exploratory Aim. Assess pre- to post-intervention changes in exercise sensitivity and physical activity levels among ACS survivors completing the RESET intervention.

Exploratory Aim will be tested by assessing the following endpoints:
1. Pre-to-post program change in exercise sensitivity (measured as the within-person difference in the sum of the 18 items from the Exercise Sensitivity Questionnaire);
2. Pre-to-post program change in physical activity levels (measured as the within-person difference in an estimate of total physical activity in MET-min/week derived from the 7 item international physical activity questionnaire-short form).

Statistical approach for Exploratory Aim. We will test this exploratory aim by evaluating the change scores listed above. We hypothesize that the pattern of means will reveal a reduction in exercise sensitivity and increase in physical activity levels. As mentioned above, this Phase-I trial is not powered to test the significance of these changes, nor is there a control comparison group to test whether the effects are caused by the RESET intervention in this feasibility pilot study.

General Approach.

For descriptive statistics, categorical data will be presented as percentages and continuous data will be presented as means with standard deviations for (approximately) normally distributed measures and as

median with interquartile range for measures that are markedly 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).

Planned Interim Analyses.

Given the relatively small sample size of this study (N=30 participants) and the expected minimal risk of RESET, interim analyses will not be planned unless requested by the safety officer. Nevertheless, if concerns arise related to adverse events, then an unblinded interim analysis may be conducted, and the trial may be stopped early.