Statistical Design and Power for Proposed Pilot Study: Family-Authored ICU Diaries to Reduce Fear in Patients Experiencing a Cardiac Arrest (FAID Fear)

NCT Number: NCT05144477

Document Date: 2/26/2021

Statistical Design and Power for Proposed Pilot Study: Family-Authored ICU Diaries to Reduce Fear in Patients Experiencing a Cardiac Arrest (FAID Fear): A Pilot Intervention Study

Aim 1: *Enroll 15 partners of cardiac arrest (CA) patients and surviving patients to* **(a)** *pilot recruitment procedures,* **(b)** *estimate retention, and* **(c)** *assess acceptability of study procedures for both family members and patients in the intervention condition.*

Aim 1 will be tested by assessing the following measures:

OUTCOME MEASURES

1) Proportion of eligible *partners* of cardiac arrest (CA) patients whom we approach who enroll in the pilot study.

2) Proportion of enrolled *partners* who complete the pilot study outcome assessments one month following either the death of the patient or patient discharge from the ICU.

3) Proportion of *partners* that adhere to the diary intervention (complete ≥2 diary entries/week).

4) Proportion of *partners* that agree that the intervention was acceptable using the mean of the 4-item Acceptability of Intervention Measure (score ≥ 4; 1 = *completely disagree*, 5 = *completely agree*).

5) Proportion of *partners* that agree that the intervention was feasible using the mean of the 4-item Intervention Feasibility Measure (score ≥ 4; 1 = *completely disagree*, 5 = *completely agree*).

6) Proportion of *partners* that agree that the intervention was appropriate for reducing cardiac anxiety about the patient's heart using the mean of the 4-item Intervention Appropriateness Measure (score ≥ 4; 1 = *completely disagree*, 5 = *completely agree*).

7) Proportion of eligible *CA patients* whom we approach who ultimately agree to participate in the pilot study.

8) Proportion of enrolled *CA patients* who complete the outcome assessments one month following discharge from the ICU.

Statistical approach for Aim 1. We will compute the proportions listed above, including 95% confidence intervals.

Sample size and power estimates are based on Aim 1. Although some have used pilot studies to estimates effect sizes on 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 fear-based mechanisms or behavioral outcomes. We will, however, use estimates from these studies (e.g., standard deviations, attrition rates) to help determine appropriate sample sizes for a subsequent study that is powered to detect meaningful reductions in measures of cardiac anxiety.

As this is a pilot study, our sample size was guided by the need to enroll enough participants – cohabiting partners of patients who recently survived CA – to examine the feasibility of conducting a larger stage II or III randomized clinical trial of our FAID-Fear intervention in this population. In particular, we will determine whether we are capable of recruiting, retaining, and assessing participants, and of implementing the proposed intervention with good compliance. 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 38, 30, and 25 partners, respectively, in order to enroll 15 partners. We will compute a 95% confidence interval around this recruitment rate. Furthermore, our planned recruitment number is feasible. The large observational trial of CA patients that will provide the infrastructure for the present study has enrolled 114 participants within a two-year period – with patient eligibility criteria that would exclude otherwise eligible partners from this study. In terms of retention, based on our prior successes, we expect retention rates of ~90%. A sample size of $N = 15$ partners results in a 95% confidence interval of this estimate equal to 75% – 100%, providing sufficient precision for study planning. We will additionally estimate proportion and 95% confidence interval for the number of CA patients who also enroll in the study and the number who are retained. Note that all above measures assessed in *partners* are considered primary, and all *patient* measures are secondary.

Aim 2: *Obtain an estimate of the association of intervention v. control with* **(i)** *partner and patient fear (operationalized as cardiac anxiety about the patients' cardiac condition) at hospital discharge and* **(ii)** *partner*

and patient posttraumatic stress symptoms (PTSS) 30 days post-discharge. Obtain an estimate of the longitudinal association between partner fear during ICU stay with patient fear at discharge and patient and partner posttraumatic stress symptoms (PTSS) at 30 days post-discharge.

Aim 2 will be tested by assessing the following measures:

9) Intervention v. control difference in *partners'* cardiac anxiety about the patients' heart at discharge, measured as the mean of the 8-item fear subscale of the Cardiac Anxiety Questionnaire.

10) Intervention v. control difference in *CA patients*' cardiac anxiety about the patients' heart at discharge, measured as the mean of the 8-item fear subscale of the Cardiac Anxiety Questionnaire.

11) Intervention v. control difference in *partners'* posttraumatic stress symptoms in relation to the patients' cardiac arrest at one month post-discharge, measured as the sum of the 20-item Posttraumatic Stress Disorder Checklist.

12) Intervention v. control difference in *CA patients'* posttraumatic stress symptoms in relation to the patients' cardiac arrest at one month post-discharge, measured as the sum of the 20-item Posttraumatic Stress Disorder Checklist.

13) Correlation between *partners'* cardiac anxiety about the patients' heart at discharge and *CA patients'* cardiac anxiety about the patients' heart at discharge

14) Correlation between *partners'* cardiac anxiety about the patients' heart at discharge and *CA patients'* posttraumatic stress symptoms in relation to the patients' cardiac arrest at one month post-discharge

Statistical approach for Aim 2. We will compute **(2a)** the mean difference in cardiac anxiety and PTSS between intervention and control conditions and **(2b)** the correlation between partner cardiac anxiety during ICU stay with patient cardiac anxiety at discharge and patient and partner PTSS at 30 days. For each, the estimate – 1 standard error will be used for sample size calculations when planning the larger study to account for uncertainty in small samples. As mentioned above, this Phase-I feasibility trial is not powered to test the significance of these intervention v. control differences, or these patient-partner associations.

Exploratory Aims: **(1)** *Obtain an estimate of the association of intervention v. control with partner and patient aversive cognitions towards exercise at hospital discharge.* **(2)** *Test feasibility of objective monitoring of patient physical activity during the first 30 days post-discharge.*

15) Intervention v. control difference in *partners'* aversive cognitions towards patients' exercise at discharge, assessed using the mean of the 5-item avoidance subscale of the Cardiac Anxiety Questionnaire.

16) Intervention v. control difference in *CA patients'* aversive cognitions towards patients' exercise at discharge, assessed using the mean of the 5-item avoidance subscale of the Cardiac Anxiety Questionnaire.

17) Proportion of patients who wear the FitBit ≥10 hours for ≥4 days/week.

Statistical approach for Exploratory Aims. We will compute the mean difference in partner and patient aversive cognitions towards exercise at hospital discharge in intervention v. control conditions, and also the estimate – 1 standard error. We will compute the estimate – 1 standard error for FitBit wear time (days, hours).

Planned Interim Analyses. Given the relatively small sample size for this pilot (N = 15 participants) and the expected minimal risk, interim analyses are not planned. If concerns arise related to adverse events, as outlined in the data safety monitoring plan, then an unblinded interim analysis may be conducted, and the trial may be stopped prematurely.