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Statistical Analysis Plan for clinicaltrials.gov

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Statistical Analysis Plan

Aim 2. Feasibility

The primary aim of this study will be to evaluate the feasibility of conducting a larger SMART trial. Feasibility will be determined by:

1. meeting recruitment and enrollment goals;
2. obtaining at least 80% of follow up self-report data at primary endpoints; and
3. maintaining dropout below 30% across treatment conditions.

Descriptive statistics will be used to summarize recruitment, retention, completeness of self-report measures, and patterns of missing data. These analyses will inform the suitability of procedures for a future fully powered trial.

Aim 2a. Effectiveness of messaging interventions relative to active control

To evaluate the effects of the adaptive and randomized messaging interventions relative to the control condition, we will model trajectories of the primary outcome (psychological distress; K10) and secondary outcomes (PHQ-9, GAD-7, DSI-SS, and CB-RSS). For each outcome, we will estimate a generalized linear mixed model (GLMM) with one model per outcome, fixed effects for treatment arm, time, and the treatment by time interaction, a participant-level random intercept, an autoregressive correlation structure for repeated observations, and an identity link for normally distributed outcomes, with alternative link functions used as appropriate based on distributional properties. The primary inference will focus on the treatment by time interaction to determine whether either intervention produces a different rate of change over time compared to control. Secondary models will control for baseline demographic covariates (e.g., age, sex, race, ethnicity).

Controlling for missing data and bias. Should more than 5% of the outcome data be missing, we will examine the data for missing mechanisms and use multiple imputation rather than complete case analysis for the primary analysis to avoid bias, combining results from 5 imputed datasets using “mice”.

Aim 2b. Effectiveness of adaptive versus randomized messaging

If the treatment by time interaction indicates a significant difference between at least one messaging intervention and the control group for a given outcome ($p < .05$), as described in 2a, we will compare the adaptive and randomized messaging interventions for that outcome using the same GLMM approach, restricted to the 2 treatment arms. Outcomes will include the primary clinical outcome measure (K10) and secondary outcome measures (PHQ-9, GAD-7, DSI-SS, CB-RSS). The second primary outcome, engagement duration (time from first message received to last participant interaction), will be summarized descriptively by reporting means and standard deviations, and will be further explored using distribution-appropriate comparisons, as needed.

Aim 2c. Effectiveness of coaching for early disengagement

Participants in the intervention arms who meet predefined criteria for disengagement during the first 2 weeks will be re-randomized to receive coaching or continue without coaching. Analyses will use the same GLMM methods described in Aim 2a incorporating coaching as a covariate to explore whether coaching improves: engagement outcomes (engagement duration, response percentage, number of URL clicks), outcomes (K10, PHQ-9, GAD-7, DSI-SS, CB-RSS). Given the limited statistical power for this embedded re-randomization, results will be summarized descriptively, reporting model coefficients and confidence intervals rather than conducting formal hypothesis tests.

Aim 2d. Exploratory predictors of early disengagement

The need for coaching will be defined as meeting the disengagement criterion during the first 2 weeks. We will compare baseline demographic, clinical, and attitudinal variables between participants who do and do not meet this criterion. Continuous variables will be compared using the Wilcoxon rank sum test, and categorical variables will be compared using Pearson’s chi squared test or Fisher’s exact test when expected cell counts

are small.

In addition, exploratory predictive models such as random forests will be considered to evaluate whether combinations of baseline variables can classify participants who are likely to disengage early. These analyses are exploratory and intended to generate hypotheses for future trials.

Aim 3. Experimental therapeutics modeling
We will explore whether engagement targets (engagement) and psychological targets (coping skill use; CB-RSS) mediate treatment effects on psychological distress outcomes (K10) and secondary outcomes (PhQ-9, GAD-7, DSI-SS). Mediation analyses will be conducted only if the necessary preconditions for mediation are met (e.g., a significant effect of intervention condition(s) on the outcome (Aims 2a-2c), and a significant effect of intervention condition(s) on the proposed target (engagement or coping skill use; CB-RSS).

If these conditions are met for an outcome/target pair, we will use generalized linear models to estimate paths a (intervention to target) and b (target to outcome) using appropriate link functions based on variable distributions. Mediation will be evaluated using the Iacobucci method, which constructs a normally distributed test statistic from standardized regression coefficients. Because these analyses are exploratory and involve multiple parallel models, we will control the false discovery rate (FDR) using the Benjamini-Hochberg procedure, with an FDR threshold of 10% appropriate to pilot mediation work. If the prerequisite conditions are not met for a given mediator or outcome, mediation models for that pair will not be estimated.