Using factorial design to examine efficacies of technology-based augmentations for improving treatment adherence and skills utilization in a self-help CBT program for binge eating (CONQUER)

9/1/2022

NCT Number

STATISTICAL DESIGN AND POWER

Descriptive statistics and exploratory graphing for all variables at all time points will be examined. We will compare baseline characteristics between treatment conditions using ANOVA for continuous variables and a chi-square test for categorical variables. Baseline variables that differ by treatment condition will be considered for use as covariates in the analyses described below. Patterns of missing data will be examined. Likelihood-based estimation methods and multiple imputation models will be used to handle missing data.[1, 2] If the missingness mechanism is related to the missing outcome itself, we will use sensitivity analyses to explore how robust our findings are with respect to a range of assumptions regarding missing data.

Primary Aim 1. To test target engagement of each intervention factor, we will model the pattern of change in treatment adherence and skills utilization separately over time using multilevel models (PROC MIXED in SAS).[3] The first level will model individual participant's treatment adherence (or skills utilization) over time with baseline as time 0. At the second level, the individual intercept and slope will be entered as outcomes with each intervention factor as a predictor. We will examine each of the two intervention factors separately. The cross-level interaction between time and the intervention factor will be used to determine the effect of the intervention component on the pattern of change in the treatment targets.

Primary Aim 2. To assess feasibility and acceptability (primary aim 2), we will assess feasibility estimate (a) recruitment success (n=76) and (b) retention (>75% through all assessments), and (c) satisfaction via Likert (≥"high") and coded interview ratings utilized in our team's previous clinical trials and other studies.[4-7]

Primary Aim 3. To examine the independent efficacy of the two intervention factors, we will model the pattern of change in binge eating frequency over time using mixed-effect models.[3, 8] This approach will allow us to account for the nested structure of the data, with assessment nested within participants nested within conditions. Covariance structure for the repeated measures will be determined based on the Akakie Information Criteria (AIC) and Bayesian Information Criteria (BIC). The cross-level interaction between time and the intervention factor (e.g., JITAIs ON vs. OFF) will be used to determine the effect of the intervention factor on the pattern of change in binge eating frequency. Both intervention factors will be examined separately. Similarly, we will model the pattern of change in EDE global scores over time using generalized mixed-effect models. The cross-level interaction between time and the intervention component will be used to examine the effect of the intervention factor on change in EDE global scores. In addition, statistical contrasts will be performed for both intervention factors on primary outcomes at post-treatment and 3-month follow-up.

Primary Aim 4. To test target validation of each intervention factor, we will test whether temporally precedent change in treatment adherence and skills utilization mediates the effect of each of the two intervention factors on primary outcomes. In particular, we will use the mediation model outlined by Preacher and Hayes to examine whether increases in treatment adherence and skills utilization by each factor from baseline to mid-treatment are associated with improvements in post-treatment outcomes and increases at post-treatment are associated with improvements in outcomes at 3-month follow-up.[9, 10] The bias-corrected bootstrap test will be applied to test the joint significance of the indirect pathways, which expands on Baron and Kenny's methods by providing additional guidelines and techniques that allow for the most robust and accurate interpretation of these mediating effects.[11, 12]

Exploratory Aim. To explore the component interaction effects, higher-order interaction terms (e.g., three-way interaction between Advanced Digital Data Sharing, JITAIs and time) will be added to the mixed-effect models and the generalized mixed-effect models outlined in primary aim 1. Due to the model complexity and limited statistical power for this aim, effect sizes will be relied upon for interpretation.

Power Analysis

The study's data will consist of repeated assessments over time within randomized individuals within conditions. Therefore, power calculations are dependent on both an expected effect size of the intervention factors as well as the clustering of the data, resulting in a mixed-effect model structure. We conducted power analysis using the method described by Raudenbush and implemented with the software Optimal Design.[13-15] For target engagement, effect sizes are estimated from a meta-analysis evaluating 11 clinical trials of self-help CBTs augmented with technology-based intervention factors for transdiagnostic binge eating showed large effect size improvements in treatment adherence (defined as accessing treatment resources and adherence to treatment prescription) (d = 0.78).[16] A sample size of 76 would be necessary for 80% power to detect a large effect of condition with alpha of 0.05 and three assessment points, assuming the ratio of the variability of level-1 coefficient to the variability of level-1 residual is one. For independent efficacy of intervention factors analysis, effect sizes are estimated from a systematic review and meta-regression evaluating 50 clinical trials of self-help CBTs for transdiagnostic binge eating showed large effect size improvements in change in binge eating frequency (d = 0.78 for change in binge eating frequency) and change in EDE global scores (d = 0.70 for EDE global).[17] For change in binge eating frequency, a sample size of 64 is required for 80% power with the significant level of 0.05 and four assessment points to detect a medium to large effect (d = 0.78), assuming the ratio of the variability of level-1 coefficient to the variability of level-1 residual is at least one. While allowing for up to 15% attrition, the study is adequately powered for binge eating frequency with the proposed sample size of 76. For change in EDE global scores, a sample size of 78 is needed to achieve 80% power with the significant level of 0.05, four assessment points, and a small to medium effect (d = 0.70). Due to the pilot nature of an R34 mechanism, we will compute and rely on the estimates of effect size and their confidence interval for the efficacy of intervention factors on change in EDE global scores. The estimates of these quantities are useful in the design of a future larger scale randomized controlled trial. For target validation analyses (regressions), tests of mediation will utilize bias-corrected bootstrapping, which demonstrates the best balance of statistical power and type I error.[18] Fritz and MacKinnon documented sample size requirements to guarantee 80% power at the significance level of 0.05 for regression-based mediation models.[19] Under the assumption of a medium effect size for the intervention factor on the mediator and a medium effect size for the mediator on binge eating frequency controlled for intervention, the required sample size is 71 to achieve 80% power in mediation models.[19] Hence, the proposed sample size of 76 is adequately powered to examine mediation on EDE global scores. For change in EDE global scores, we will be underpowered and rely on effect sizes to interpret findings.