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Statistical Analysis Plan for clinicaltrials.gov

Official Title: Digital Mental Health Intervention for Nonsuicidal Self-Injury in Young Adults

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Statistical Design and Power: Feasibility RCT

Aim 2. Feasibility. The primary aim of this study will be to pilot feasibility for a larger trial. Feasibility will be determined by 1) meeting our recruitment and enrollment goals (90 participants); 2) obtaining 80% of follow-up self-report data over 16 weeks, and 3) having an dropout rate of <30% in one or more of the digital mental health intervention (DMHI) conditions, which is in line with previous Digital Mental Health Intervention RCTs,[1] and would indicate strong engagement worthy of future research. The following analysis plan will also be piloted.

Aim 2a. Evaluate the effectiveness of the DMHI in reducing the primary outcome (frequency of NSSI behavior and urges using the ABASI checklist and ABUSI), secondary outcomes (suicidal ideation, depression, anxiety, and borderline personality disorder symptom severity using the DSI-SS, PHQ-9, GAD-7, and BEST), and psychological targets (emotional, cognitive, and behavioral regulation, and self-efficacy using the DERS, DAS-SF, CB-RSS, SEASA) relative to a psychoeducation control. We will use separate generalized linear models (GLM; one model per outcome or target) with link functions depending on the distribution of each construct (e.g., log link for count outcomes, identity link for normally distributed outcomes) to determine if there are overall group differences over time between either of the interventions relative to the control.[2,3] We will examine an interactive effect of the groups over time, and main effects, should there be no evidence of an interactive effect. With repeated measures over time within subject, we anticipate using an autoregressive correlation structure for all models. Secondary analyses of outcomes will control for basic static factors such as demographics (i.e., age and gender). As we expect this feasibility trial will be underpowered to test these hypotheses, least square means and 95% Confidence intervals of each randomization group will be plotted over time for each outcome.

***Controlling for missing data and bias*.** Should more than 5% of the outcome data be missing, we will examine the data for potential informative 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 PROC MIANALYZE.

***Aim 2b*. Evaluate the effect of coaching on engagement targets (number of app launches, time from first to last use) and all primary and secondary outcomes.** We will use the same GLM methodology as Aim 2a for the first primary outcomes (ABASI & ABUSI) and secondary outcomes, comparing coached and self-guided intervention arms. The engagement targets (number of app launches and engagement duration, defined as time from first to last use) will be compared using either an ANOVA or a Kruskal-Wallis test, depending on the observed distribution. As we anticipate that there will not have ample power to test these hypotheses, we will again present least square means and 95% confidence intervals for these outcomes by coached or self-guided DMHIs and follow-up time.

Aim 3. Experimental therapeutics modeling will explore if engagement targets (subjective and objective engagement) and psychological targets mediate significant effects for distress observed in Aims 2a (treatment vs. control) or 2b (coached vs. self-guided). These models are depicted in the Figure. A separate model will be run for each of the comparisons articulated in the two aims, for each of the outcomes. The expansion of the experimental therapeutics model to include targets of objective and subjective engagement is critical to understanding the mechanisms by which DMHIs work.[4] We emphasize that these mediational analyses are only exploratory, and serve primarily as pilots to inform the design of our experimental therapeutics aim for a subsequent, fully powered trial.

The mediational analyses will use GLM mediational models to examine that the intervention impacts primary and secondary outcomes via psychological targets, including emotional, cognitive, and behavioral regulation, and self-efficacy. Mediation will be tested using methods by Iacobucci.[5] Our models will test if patient characteristics and target engagement mediate the relationship between intervention and outcomes. Multiple models will need to be fit, increasing the possibility of an inflated type I error. To prevent this, we will implement a false discovery rate (FDR) control using methods by Benjamini-Hochberg[6] although as these are pilot studies, we

will test these models at a FDR of 10%. Depending on the distribution of the variables under consideration, we will fit linear or logistic regression models to estimate regression parameters a (messaging and the relationship to potential mediators) and b (mediator relationships to the outcome). Iacobucci shows that a normally distributed test statistic can be constructed from standardized regression parameters Za=a/SEa such that Z(mediation)=Za*Zb/ (sqrt(Za2+Zb2 + 1)) can be used to test for mediation.

Sample size considerations.

Because the primary objective of this phase of the research is to evaluate the feasibility of developing and piloting methods for a larger randomized, controlled clinical trial, the sample size (n=90) is selected to give us adequate experience to develop study procedures. The sample size is not powered for hypothesis testing. However, a power calculation was run to determine the effect size that this trial will be powered to detect. Because general linear mixed model analyses do not easily lend themselves to power calculations, as they are dependent on estimates of covariance coefficients, the effect size estimate was examined for an independent t-test at a two-sided type I error rate of 5%. With 30 participants randomized to each treatment group, we will have 80% power to detect an effect size of 0.65 between the control and interventions.

References

1. Linardon J, Cuijpers P, Carlbring P, Messer M, Fuller-Tyszkiewicz M. The efficacy of app-supported smartphone interventions for mental health problems: a meta-analysis of randomized controlled trials. *World Psychiatry.* 2019;18(3):325-336.
2. Hedeker D, Gibbons RD. *Longitudinal Data Analysis.* New York: Wiley; 2006.
3. Hedeker D, Gibbons RD. A random-effects ordinal regression model for multilevel analysis. *Biometrics.* 1994;50:933-944.
4. Graham AK, Lattie EG, Mohr DC. Experimental Therapeutics for Digital Mental Health. *JAMA Psychiatry.* 2019.
5. Iacobucci D. Mediation analysis and categorical variables: The final frontier. *Journal of Consumer Psychology.* 2012;22:582-594.
6. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society, Series B.* 1995;57(1):289-300.