Document: Statistical Analysis Plan

Official Study Title: Digital Community to Improve Health in Rural Areas

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Statistical Analysis Plan – AG C-RCT

The statistical analyses will examine the intervention effect (i.e., experimental versus control) on the primary, secondary, and tertiary outcomes, with the covariate of individuals' drug use status (i.e., PWUD versus PWNUD) (see Table 1). The primary analyses will be conducted using the intention-to-treat (ITT) method. That is, all participants who completed the baseline measure will be included in the analyses by replacing missing data by carrying forward the last observation. We will perform multi-level modeling with clustered cohorts and report the intra-class correlations (ICC) of the cohort (i.e., group). In these models, we will specify 16 models with four sets of random effects models (i.e., random intercept only, random slope only, random intercepts and slopes without their correlations, and random intercepts and slopes with their correlations) and select the best one based on model-fit indices (i.e., AIC, BIC, and the likelihood ratio test).

The primary outcome is a composite score summing six yes/no behaviors promoted in the intervention: (a) HIV testing, (b) HCV testing, (c) HIV prevention, (d) requesting Naloxone before the assessment time point (i.e., the requests made at the immediate follow-up are counted for the 3-month follow-up), (e) carrying Naloxone, and (f) making or rebuilding at least one social connection. The assessment of HIV prevention depends on each participant's sexual risk and drug injection risk and includes PrEP use, use of condoms during sex, use of syringe service programs, and disinfecting injection equipment. Specifically, individuals engaging in sexual behaviors receive a score of 1 if they report using condoms during sexual encounters or using PrEP. Likewise, individuals at risk of drug injection receive a score of 1 if they report using PrEP, using syringe service programs, or disinfecting their injection equipment. For participants

who neither engage in sexual behaviors nor are at risk of drug injection, an HIV prevention score of 1 is recorded. The primary outcome is treated as a continuous variable, ranging from 0 to 6.

For the secondary and tertiary outcomes (see Table 1), we will specify a binomial family for the analysis of binary data. For outcomes about change, such as substance use frequency, baseline responses will be subtracted from those obtained at the follow-up assessments (i.e., T1 – T0). We will impose no alpha correction/adjustment for multiple outcome comparisons because we have no conjunction hypotheses and these outcomes are not the primary outcome.

The design of the study allows for the assessment of the total effect of the Zoom sessions, GROV app, and HIV/HCV testing and Narcan kit availability. Therefore, that test is possible only for the immediate follow-up and will be conducted in an initial outcome paper that examines the efficacy of this multi-level program.

The 3-month and 6-month follow-ups provide an idea of the impact of the intervention when all participants have the option of receiving HIV/HCV testing and Narcan kits and also permit an examination of the durability of the effects. Therefore, these outcomes will be reported in a second paper.

We will carry out the following sensitivity analyses: (a) modified ITT analyses (i.e., including only those experimental participants who attended at least one session); (b) per-protocol analyses (i.e., including only data from participants who completed all three Zoom sessions originally allocated); and (c) analyses including relevant baseline measures, GROV activities, intervention process evaluation, fidelity assessment, and HIV/HCV testing and Narcan kit shipment schedules as covariates to assess the robustness of the results. The sensitivity analyses described here are not exhaustive, and new analyses can be added based on the research

team's decision (e.g., replacing the request data with the delivery/shipment data in the composite score).

We will also carry out process analyses by examining the content of the sessions with ChatGPT 4.0 (or later versions) and testing if these variables, as well as the number of sessions attended and GROV use, correlate with the study outcomes in the intervention group.

Table 1.

C-RCT Outcomes

Primary Outcome	Secondary Outcomes	Tertiary Outcomes
Sum of Yes to (a) self-testing for HIV, (b) self-testing for HCV, (c) HIV prevention, (d) requesting Naloxone, (e) carrying Naloxone, and (f) making at least one social connection (new or reestablished).	HIV and HCV testing	Seeking substance use or mental health treatment or recovery services (i.e., attending a 12-step group or another abstinence-based program, attending a substance use treatment program that uses medications, and/or attending a faith-based substance use group and being referred to healthcare and mental health/substance use recovery)
	HIV prevention behaviors (i.e., PrEP use, use of condoms during sex, use of syringe service programs, and disinfecting injection equipment)	Interacting positively with people who use substances during and outside the sessions and drug stigma
	Requesting Naloxone (Narcan)	Substance use without a prescription or more than prescribed (with baseline level at 3 and 6 months)
	Carrying Naloxone (Narcan)	Injection substance use (with baseline level at 3 and 6 months)
	Making social connections (new or reestablished)	Seeking treatment for HIV and HCV if participant is seropositive