COVID-19 Treatment Cascade Optimization Study

NCT05305443

Statistical Analysis Plan

3/30/2022

Statistical Analysis Plan

Data analysis: Aim 1. We will estimate the (1) differences in the effects of first-stage interventions (NS vs brochure), (2) differences in the effects of second-stage interventions (BC vs NS among those who complete testing and referral vs CD among testing decliners), and (3) differences in the effects of selected adaptive interventions on acceptance of testing and adherence to IL recommendations. For differences between NS and brochure, cross-tabulations of the interventions with each outcome will be generated, and crude odds ratios comparing the two will be calculated. For the effects of second-stage and third-stage interventions, we will perform a similar analysis as that for the first-stage interventions but on corresponding subsets as indicated in the specific comparison groups. The estimation of effects of embedded adaptive interventions will use weighted and replicated estimation techniques. Under these procedures, the data set will be restructured wherein an individual's outcome will be replicated in the data set depending on the number of adaptive interventions consistent with this outcome. Since randomization at both stages is based on equal probabilities, weighing is not necessary. The restructuring of the data set as described allows the utilization of standard statistical software for parameter estimation and hypothesis testing. A generalized linear model using logistic regression will be performed where estimation of model parameters will be done using generalized estimating equations due to the presence of replicated subjects. We will then use tests of contrasts to compare selected adaptive interventions. The analysis of the adaptive interventions will be done using PROC GENMOD in SAS. To adjust for baseline characteristics and test for their moderating effects, we will incorporate these terms and their interactions with first-stage, second-stage, and adaptive interventions in their respective models. Only the baseline characteristics will be used for adjustment, as outcomes of the first-stage intervention are biased if incorporated into this model. Odds ratios, 95% CI, and Wald's test for the effect of interventions and covariates will be obtained from these results. Sex/gender and race/ ethnicity will be among these covariates that we will consider for adjustment and moderation analysis.

Interim analyses

An interim analysis will be conducted bi-monthly by study analysts once data collection starts. This will include the development of syntax to clean the data (e.g., missingness analysis, identification of data entry errors, recoding variables). The key variables will be reviewed. Descriptive data will be presented to PIs and members of the NCCB. The NCCB will review preliminary findings presented by the PIs on a bi- monthly basis to address any potential adverse reactions that may occur and any safety concerns that may arise. If any participants are found to be unresponsive to the intervention, or getting worse during the course of the study, an NCCB sub-committee will discuss the case and the participant may be terminated from the study and referred to relevant services in the community. The PIs will meet weekly with the study staff to review the study protocol adherence and address any potential problems. The PIs will also have weekly supervision meetings with intervention facilitators to review the results from fidelity ratings and address any potential deviance from interventions.

Methods for additional analyses (e.g., subgroup analyses)

Aim 2: To identify other predictors of these outcomes, we will include these variables as covariates using logistic regression analysis. We will model probabilities of testing behavior (completed vs testing decliners) and adherence to IL recommendations as functions of the first-stage intervention and other covariates in the logistic regression analysis.

Qualitative component analysis: Critical dialog sessions and in-depth interviews will be digitally audio-recorded and transcribed. Data will be entered into Atlas ti, a qualitative data processing program. Analysis rooted in phenomenology and grounded theory will include continuous coding, comparison, and recoding to yield categories and connect experiences and themes. The analysis will focus on participant reports about their experiences with the intervention, barriers to testing and adherence to IL recommendations, and suggestions on how to address these barriers.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data

We will perform an intent-to-treat analysis of the data. Subjects will be groups according to how they are randomized. The multiple imputation strategy described will be adapted. This uses a time-ordered nested conditional imputation strategy with multiple imputation of missing values. In this approach, the fully conditional specification (FCS) imputation framework wherein a separate model for each variable is fitted will be applied. We will consider the time ordering of the data. For example, observed baseline variables will be used to impute for missing data from the first-stage results. Then, the imputed and observed values of the first-stage results will be used in conjunction with baseline variables to impute missing values for the second-stage results. We will examine the distribution of missing data according to intervention groups, covariates (e.g., demo-graphic characteristics, adherence, reason for discontinuation), outcome variables, and time. We will determine whether the missing data pattern is not inconsistent with the missing-at-random (MAR) mechanism. We will also check whether the amount of missingness is monotonic over time. The r software packages mice and pan will be used for imputation.