Harnessing social network support to improve retention in care and viral suppression among young Black men in Chicago and Alabama: A hybrid type I effectiveness-implementation trial of Project nGage

January 30, 2023

PROJECT NGAGE RANDOMIZED CONTROLLED TRIAL

STATISTICAL ANALYSIS PLAN

The statistical plan and the aim specific analyses are described below. Analysis of qualitative implementation data is described in full in the research strategy (see Research Strategy and References Cited).

Aim 1 Analysis. The primary analysis will involve an intent-to-treat comparison of our primary outcomes after 12 months between the 300 individuals randomized to nGage and the 300 individuals randomized to TAU (Aim 1a). These comparisons will be performed using generalized linear models (MVP) and marginal regression models (longitudinal data). For example, regressing quarterly visit status (missed vs. completed) on treatment group using a marginal logistic model will permit us to estimate the overall difference between groups in the likelihood of missing a visit. Covariates such as recruitment site and length of time in care will be included to increase power and reduce bias in the estimated treatment effect. The models will be fit using the Generalized Estimating Equations (GEE) approach assuming either an exchangeable or autoregressive correlation among observations within the same individual. This modeling strategy will also permit us to explore whether the effectiveness of the intervention changes over time (by including an interaction term between treatment group and time) and/or how it is associated with time-varying covariates such as continued participation by the SC. To determine if continuing the intervention after 12 months provides additional benefit, we shall refit the models among the subset of men originally assigned to nGage (Aim 1b). A binary covariate distinguishing between the 12–24 month visits among the group randomized to Sustained nGage and those in the remaining group will be used to estimate the benefit of continuing nGage. This second analysis is formally equivalent to that for a pre-post study in which the pre-randomization observations (i.e., the visits from 0–12 months) are included as responses in the model; as with such models, we shall constrain the expected group means to be equal from 0–12 months as justified by the randomization, increasing power for comparison between groups.

Aim 2 Analysis. The purpose of these analyses will be to determine whether there is evidence of a difference in the intervention effect between Chicago and AL (Aim 2a), and to evaluate the role of theoretically important moderators (Aim 2b) and mediators (Aim 2c) of the intervention effect. Aims 2a-2b will be accomplished by estimating and testing appropriate interaction terms between treatment group and site (2a) and between treatment group and potential moderators (2b). We will report results both with and without post-hoc tests, e.g., Bonferroni correction, Holm-modified Bonferroni. Analyses for Aim 2c will be performed using the counterfactual approach to mediation analysis which permits estimation of direct and indirect effects in nonlinear models, with multiple mediators, and in longitudinal models with time-varying mediators.

Attrition and Item-Nonresponse. Because MVP and VS will be extracted from EMR data, we will have little (if any) missing data for this measure. For other measures, every effort will be made to obtain complete data. Nevertheless, some missing data due to attrition and item non-response is inevitable. To avoid potential bias and/or loss of power due to casewise deletion, we will use Multiple Imputation to impute missing values. The rich set of background, clinical, network, and psychosocial data we collect will help to justify the Missing At Random (conditional on the observed data) assumption required by Multiple Imputation.

Power Considerations. The proposed sample size of 600 will provide excellent power to detect differences between nGage and TAU in our primary outcomes (Aim 1a). For example, if we assume that MVP in the TAU group is 0.50, that each subject has just three scheduled visits during the first 12 months, and that the within-participant correlation between visits is 0.60 (all conservative assumptions), then we shall have approximately 90% power to detect a reduction in MVP among the nGage group to 0.39 (OR 0.63). This is consistent with our experiences in prior studies and with interventions of this type. For Aim 1b, we will have good power due to the availability of baseline observations obtained during the first 12 months. Specifically, if we assume that 30 of the 300 participants (10%) initially randomized to nGage drop out prior to re-randomization and that the MVP among those randomized to Sustained nGage is 0.35, then we shall have approximately 82% power to detect an increase in MVP among the non-sustained group back up to 0.44 (OR 1.4). This is based on a simulation assuming just three scheduled visits from 12–24 months and a correlation between visits of 0.60; while assuming a higher correlation would reduce the amount of information in each additional visit, it would also increase the value of incorporating the 0–12 month observations.

Six-hundred randomized participants will also provide good power for the analyses in Aim 2. For example, for the mediation analyses, assume conservatively that we have a single binary outcome (for simplicity) with overall proportion 0.5, a binary treatment variable with 0.5 assigned to each group (by design), and a continuous mediator. We further assume an overall treatment effect of 1.8 (OR), an effect of the mediator conditional on treatment of 1.3 (OR) per one SD increase, and a correlation between treatment group and the mediator of 0.25, corresponding to a proportion of treatment effect explained (PTE) of just 22%. Under these assumptions, we shall have approximately 87% power for testing the null hypothesis of no mediation effect. For moderation analyses with a continuous moderator, we shall have approximately 84% power to detect a change in the effect of the intervention from 1.2 (OR at the mean of the moderator) to 2.1 (OR at one SD above the mean of the moderator). Finally, we shall have approximately 85% power to detect a difference in the effect of the intervention between sites of 1.3 (OR at one site) versus 3.5 (OR at the other site). These calculations assume a binary outcome for simplicity, however the actual power will be greater for our planned longitudinal analyses.