ADOLESCENT MEDICINE TRIALS NETWORK FOR HIV/AIDS INTERVENTIONS

Statistical Analysis Plan

Enhancing Sexual Safety: Couples' Communication and HIV Testing Among YMSM: ATN 156

NCT04289116

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1.0 DATA MANAGEMENT AND ANALYSIS PLAN

1.1 Data Management and Data Quality

We will utilize Scale It Up's existing infrastructure to collect and store data. We have discussed issues of data management and storage with representatives of SIU-Management Core (MC) and Dr. Starks is directly involved with the discussion of related issues with the SIU-AC. We will collaborate with the SIU's existing Study Monitoring Committee (SMC) and follow all SIU-wide procedures, including obtaining and maintaining approval of study procedures from the relevant Institutional Review Board (IRB). On a weekly basis, project staff will meet to review procedures being employed to ensure that all IRB-approved procedures are being followed. Any adverse events will be reported to PLs Feldstein Ewing and Starks, who will then immediately contact the SIU IRB to inform the committee of the adverse event. The PLs will then submit a detailed description and written report of the event following established procedures.

1.2 Quantitative Analysis Plan

The primary hypothesis is that due to developing skills in self-management and assertive communication, inclusion of adjunct components will be associated with clinically significant decreases in HIV transmission risk behavior (TRB) as compared to partnered YMSM who receive CHTC (only). Secondarily, we propose that these intervention effects will be mediated by assertive communication skills. As stated above, we focus on four behavioral indicators of TRB. At the individual-level, we examine: (1) number of CAS acts with a casual partner in the absence of PrEP and (2) any positive chlamydia or gonorrhea diagnoses in the absence of PrEP. At the couple-level, we will examine (3) any sex in the absence of PrEP with a primary partner who reports CAS with a casual partner; and (4) any sex in the absence of PrEP with a primary partner who receives a positive chlamydia or gonorrhea diagnosis. Any missing data and additional covariates will be informed by attrition analyses prior to primary analyses.

1.2.1 Analytic Plan

All primary outcome variables will be tested in the context of a multilevel growth model, which accounts for the nesting of individuals within couples. In order to capture within-individual change over time, we will utilize a latent growth curve approach to modeling follow-up data. At the individual level (Level I), models will include an intercept and linear slope component to represent the initial value and change over time in each participant's outcome. We will explore the inclusion of quadratic components as indicated by model fit. Mplus provides the flexibility to accommodate count and dichotomous outcomes. Growth factors will then be regressed on intervention condition at the couple level (Level II) and the effect of the intervention will be evaluated by examining the regression coefficient (and associated *p* value) associated with intervention condition for each of these factors.

Secondary analyses of individually reported self-management and dyadic functioning as potential mediators of the intervention's effect on TRB will specify growth factors for self-management, dyadic functioning, and communication skill scores during the follow-up period. In this manner, growth factors for the outcome can be regressed on growth factors for the putative mediator. Intervention effects (a couple-level predictor) will be determined by examining regression coefficients associated with intervention in the prediction of growth factors for both

the outcome of interest and mediator. For significant direct effects, indirect pat from intervention communication will be tested using bootstrapping tests of mediation. Where outcome distributions prevent bootstrapping, we will utilize a model constraint approach to evaluate significance of indirect effects. The product of constituent direct effects is constrained as zero. The overall model fit under this constraint is compared to one where the constraint is not specified. A statistically significant reduction in fit associated with constraint represents evidence that indirect effects differ from zero[53].

1.2.2 Power Analysis

Consistent with the intervention development goals of Phase 2, we are not powered to detect significant between-condition differences in primary outcomes for that phase. Power analyses for Phase 3 were conducted based on our preliminary pilot data extracted from a similar study (R34 DA036419; PI Starks) testing adjunct CHTC components in emerging adult gay male couples aged 18-29 years. Preliminary results from the 3 month wave of data collection (the most distal available with sufficient data to estimate effects at the time of protocol paper submission) suggested that viewing ACT videos prior to CHTC was associated with a 56% decrease in the odds of CAS with a casual partner (relative to CHTC alone) among HIV negative participants not on PrEP. Of particular relevance to our mediation hypotheses, viewing ACT videos prior to CHTC was associated with a 5 to 6 point decrease in avoidant communication as measured by the Communication Patterns Questionnaire (CPQ) [54]. In turn, CPQ avoidant communication scores had a significant positive association with CAS with casual partners among HIV negative men not on PrEP (expB = 1.06, $p < .01$). Separately, our previous study of brief MI interventions with YMSM suggest it is associated with as much as an 83% reduction in the odds of CAS with a casual partner [55] compared to an attention-matched psychoeducation control condition.

These preliminary effect sizes were utilized as parameters in power analyses using a Monte Carlo simulation approach in Mplus (version 7.3)[53]. This approach provides a direct estimation of power while modeling both the multilevel structure of data (individuals are nested within couples) and the longitudinal design of the study (each individual provides data at 3 follow-up points). The program generates random samples from the specified population and, within each sample, examines the significance of freed parameters. Power is defined as the proportion of simulated samples in which the freed parameter has a p value of less than .05. All models specified a random seed and used 10,000 sample replications. Power analyses conducted based on these preliminary effect sizes suggests that $n = 144$ couples ($n = 288$ individuals), anticipating a minimum of $n = 232$ individuals retained at 6 months, is adequate to achieve power > .80 for all hypothesized direct effects as well as indirect pathways.

1.2.2 Equivalency Tests

We will follow standard procedures in cleaning data and examining initial distributional properties (means, standard deviations, medians, skew, kurtosis) in addition to graphical summaries (boxplots and density plots). Subsequently, we will evaluate the success of randomization by testing between-condition differences with respect to demographic covariates and primary outcomes reported at baseline. Note, because participants are nested within dyads, these analyses will utilize the Generalized Estimating Equation (GEE) module within SPSS to

control for the non-independence of observations and specify outcome distributions that are appropriately matched to the variables of interest.

Finally, we will conduct an analysis of attrition to determine if dropout at each follow-up time-point is associated with (1) demographic variables assessed at baseline and/or (2) drug use or TRB outcomes assessed at baseline. At each wave, we will utilize GEE models to evaluate whether those participants retained at the given wave differ significantly with respect to demographic or baseline outcome values compared to those who were not retained. As with the analyses of randomization success, the use of GEE permits analyses to control for the nesting of participants within couples and specify outcome distributions that are matched to variables of interest. Factors which are observed covary significantly with attrition will be incorporated as covariates in outcome analyses. Mplus has a variety of options for handling partial attrition including full-information maximum likelihood estimation [56]. Non-random and consequential missingness can also be modeled directly through the addition of latent variables which account for the probability of missingness at any time point. Where indicated, we will explore the use of these procedures in the analyses described below.