ADOLESCENT MEDICINE TRIALS NETWORK FOR HIV/AIDS INTERVENTIONS
U19HD089875

Statistical Analysis Plan
Comparative effectiveness trial of a clinic-based delivery of the Young Men's Health Project (YMHP) targeting HIV risk reduction and substance use among young men who have sex with men (YMSM)

ATN *Scale It Up* U19: 145 YMHP

ClinicalTrials.gov NCT03577301

Sponsors: National Institute of Child Health and Human Development; National Institute on Drug Abuse

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1.0 DATA MANAGEMENT AND ANALYSIS PLAN

1.1 Data Management and Data Quality

The *SIU* MC will be handling data management for the randomized controlled trials in a standard manner including scale scores, composites, syntax, etc. in order to facilitate rapid analyses by the AC. Data will be entered directly by participants through Qualtrics using systems established by the REC. Data dictated by participants who request assistance completing surveys may also be entered by the site RA. The database, data structure, and data quality will be routinely reviewed by the REC with support from the AC. Where indicated, we will use full-information maximum likelihood estimation to account for missing data under missing at random assumptions.

1.2 Quantitative Analysis Plan

The primary hypothesis is that receipt of YMHP (regardless of delivery format) will be associated with greater improvements in sexual health management (as measured by decreased STIs, CAS and increased PrEP uptake/adherence) as well as greater reductions in substance use, compared with youth who receive the standard of care (individual HIV testing) only. Our secondary hypothesis is that youth who elect to receive YMHP remotely will report more barriers to accessing health care compared to those who elect to receive the intervention in clinic. In addition, we hypothesize that remote-based YMHP will demonstrate greater improvements in sexual health management (as measured by decreased STIs, CAS, and increased PrEP uptake/adherence) as well as reductions in substance use, compared to clinic-based YMHP, among YMSM who do report barriers to health care access. In contrast, it is hypothesized that clinic-based YMHP will demonstrate greater improvements in sexual health management and reduced substance use among YMSM who do not report barriers to health care access. Self-management model analysis is described in the AC.

The AC will test the effect of clinic-based versus remote delivery on STI rates, alcohol and drug use behavior, CAS, and PrEP uptake through multi-level growth mixture modeling (GMM). A separate model will be run for each outcome. Each model will be a 2-level model in which individuals (Level I) are nested in clinics (Level II). This approach controls for the non-independence of individuals within clinics. Because three SRVs provide extremely limited predictive power at Level II, no site covariates are included in the model. (The models are empty at Level II).

In a GMM, a latent growth curve with an intercept and linear slope factor is specified. Latent class analysis is applied to these 2 growth components (intercept and slope) to identify groups of individuals who share trajectories. For example, with regard to drug or alcohol use, “immediate and sustained responders” may have the lowest post-intervention intercept and a flat slope. Meanwhile, “non-responders” might have the highest post-intervention intercept and a flat slope. In contrast, “delayed responders” might have a high post-intervention intercept but a significant negative slope, indicating reductions in missed medication over the follow up period.

If modeling results indicate that discrete classes are not present, we will proceed with analyses in which the growth factors (intercept and slope) are predicted directly by intervention condition (and demographic factors found to be associated with condition after randomization or with attrition over follow up). GMMs can subsequently incorporate predictors of class membership. These analyses can be conceptualized as a multi-nominal logistic regression with the latent trajectory-class membership constituting the outcome. The predictors

of primary interest will be intervention condition, the presence of any barriers to health care access, and the interaction between condition and barriers to access. We will include as covariates any demographic variables that were associated with condition after randomization or with attrition over the follow up period.

1.2.1 Power Analysis

First, we analyzed power assuming independence of participant observations (assuming that the nesting of people-within-clinic was irrelevant). With regard to STIs, we utilized the "repeated measures" module of PASS 13.0 to examine power to detect odds ratio differences in a repeated measures design. Specifying compound symmetry, we allowed ρ to vary between .2 and .5. Assuming the prevalence of STIs in the remote-based condition varies between .05 and .15, the proposed design (N = 270) has power .80 to detect an odds ratio of .20 to .50. Similarly, with regard to the odds of PrEP uptake, allowing the rate of uptake in the remote-based condition to vary between .05 and .20 and allowing ρ to vary between .4 and .7, the proposed design has power of .80 to detect an odds ratio of 1.9 to 2.3. With regard to number of alcohol and drug use days, we utilized the *Tests for Two Poisson Means* module in PASS 13.0. Based data from our previous studies, we allowed the rate of heavy drinking in the phone-based condition to vary between 7 and 9 days during a 30-day assessment. The study is adequately powered to detect a 3% reduction in number of heavy drinking days in the clinic-based condition at any single follow up point. Allowing the rate of drug use in the remote-based condition to vary between 3 and 5 days during a 30 day assessment period, the study is adequately powered to detect a 4% reduction in drug use in the clinic-based condition. A similar analysis was conducted with respect to CAS. Based on our previous research, we allowed the rate of CAS in the phone-based condition to vary between 2 and 4 acts in a 30 day assessment period. The study is powered to detect a difference as small as 5% between the remote and clinic-based YMHP conditions. The nesting of individuals within SRVs has the potential to reduce power because substantial variability in outcome across SRVs can obscure level II treatment effects [70, 71]. The design effect can be used to tailor power analyses calculated under assumptions of independence. In the case of a Level I predictor with a fixed effect which is uncorrelated with other covariates in the model, the design effect is equal to the $1 - \rho$, where ρ is the intra-class correlation or the percentage of variance accounted for by variability between SRVs [71]. In previous intervention trials conducted within the ATN [72], between clinic site variability in HIV related outcomes did not differ significantly from zero. Based on the characteristics of ATN clinics, we anticipate a similar absence of variability across clinics, suggesting that the design effect would result in a negligible reduction in power. Finally, a sample size of 270 is sufficient to detect a moderation effect with an $f2$ of .02. Cohen [73] designates this as a small effect, however recent work has characterized an effect of this size as moderate to large as applied to moderation [74].

1.2.2 Equivalency Checks

The AC will ensure that randomization is stratified by city and the presence of any barriers to healthcare access. Further, they will monitor randomization to ensure that condition is not associated with characteristics that would require adjustment in proposed analyses. To assess differential attrition, we will utilize a multilevel modeling approach (to account for the nesting of participants within clinic/city) to assess for condition, time, and condition × time interaction effects in the proportion of completed assessments across the length of follow-up. Any evidence of differential attrition will be examined to determine whether there are baseline demographics, behavioral, or biological predictors that are associated with such differences in attrition. These effects will be adjusted for in subsequent analyses.

1.2.3 Equivalency Tests

A series of bivariate analyses will be conducted to examine between condition differences at baseline and evaluate

the success of randomization procedures. We will utilize chi square tests of independence, t-tests, ANOVA and Spearman's rho correlations as appropriate to examine whether intervention conditions differed significantly with respect to key demographic variables and outcome variables at baseline. In the event that significant baseline differences are observed, these demographic factors will be incorporated into subsequent outcome analyses.