Analysis plan:

Data Analysis: Analyses will be performed using SPSS version 22 to run diagnostics (tests for normality, multicollinearity, heteroscedasticity) to assess violations of analytic assumptions, univariate statistics, bivariate tests, and multivariate linear regression. Because study retention may be influenced by preconditions, t-tests or Wilcoxon test will be used to compare intervention group and control group on all T1 variables. T- tests can be used for normal distribution while Wilcoxon test can be used in skewed distribution. Implications of significant differences will be discussed. Based on the intent to treat approach, missing T2 data will be imputed to retain all participants in analyses. We will include all participants who provide informed consent and engage in the T1 assessment, regardless of what portion of the assigned treatment or control protocol is completed. Data will be imputed using multiple imputation for participants who fail to complete the T2 (posttest) assessment. **Sensitivity analyses** will explore the implications of the imputation methods employed (e.g., multiple imputation, propensity score matching). Post- recruitment attrition (loss of potential participants who were recruited but failed to engage in any assessments or part of the treatment or control protocol) will be explored in all discussion and implications of study findings. The following series of regressions will assess study hypotheses.

Hypothesis 1: Exposure to mhealth intervention will result in significant improvement in PrEP adherence compared to the control group. We will firstly examine the distribution of all variables and their correlations. Where two similar variables are correlated at $r>0.4$, 1 variable will be selected for inclusion in regression models to avoid collinearity (see Patel et al., 2016). We will employ multivariate linear regression to estimate the association between the intervention and PrEP adherence. In order to compare the difference of PrEP adherence (after 12 weeks) between intervention group and control group, the first regression model will only include the dichotomous treatment variable (intervention group versus control). Based on the first model, the second regression model will add three confounders (three demographic variables: age, education, and income) to compare the gaps after controlling for age, education and income level. Based on the second model, besides the 3 confounders, the third regression model will add an interaction term, the dichotomous treatment variable and the dichotomous intervention variable (before the intervention vs after) and their interaction. The coefficient of the interaction term will be the difference between the increase in intervention group and the increase in control group.

Hypothesis 2: The impact of intervention on the primary outcome will be mediated through key factors, i.e. increased PrEP self-efficacy, increased PrEP knowledge, increased intention to follow PrEP guidelines, and reduced stress burden. To test

the mediation effect, the following three regressions will be conducted. First, we will set PrEP adherence as the dependent variable, demographic variables and dichotomous treatment variable and other independent variables as the independent variables. Second, we will set PrEP adherence as the dependent variable, and each of the four mediators as the independent variable. Third, we will set the dichotomous treatment variable as the dependent variable and each of the four mediators as the independent variables. The coefficients of the three regressions will show the mediation effects. Time on PrEP will be examined as a potential moderating variable, including the potential for moderated mediation in which mediators may become significant only at certain levels of the time since starting PrEP. Results will be interpreted via the standard interpretation of a sequence of regression models (Aneshensel, 2002; Baron & Kenny, 1986) to determine whether these variables mediate or partially mediate intervention effects, and the extent to which time on PrEP moderates these relationships.

Measures. Both baseline (T1) and 12-week follow up (T2) data will be collected on the following key measures: Primary outcome measure: The primary outcome compares differences between (T1) and (T2) for the key measure of interest: PrEP adherence: Our Phase 1 open-ended data revealed participants' general discomfort with blood tests and needles. Thus, we will not seek PrEP blood levels in Phase 2 to measure adherence as doing so would likely pose a barrier to recruitment and retention. Instead, we will use Wilson's simple 3-item self-report adherence measure which showed good psychometric characteristics and good construct validity when compared with an electronic drug monitoring standard, for both HIV and non-HIV medications, and has been validated with culturally-diverse patient groups, including MSM (Fowler et al., 2014; Wilson et al., 2014; 2016). The items include: 1) In the last 30 days, on how many days did you miss at least one dose of any of PrEP (write in # of days) 2) In the last 30 days, how good a job did you do at taking your PrEP in the way you were supposed to? (6-point Likert) 3) In the last 30 days, how often did you take your PrEP in the way you were supposed to? (6-point Likert). Note: We will also examine self-report app adherence data. App adherence data can only be collected via the app as yes or no responses to pill reminders, and thus cannot serve as pre-intervention baseline. We will, however, compare app adherence data from weeks 1 and 12.

Consideration of Relevant Biological Variables: We will only include culturally-diverse young adult males who have sex with other males in our study as they are disproportionately represented among groups at increased risk for HIV. Moreover, males account for 95.3% of all PrEP users (Huang et al., 2018).

Mediating Variables: We propose four mediating variables: PrEP self-efficacy, intention to follow PrEP guidelines, PrEP knowledge and stress burden. To measure PrEP treatment self-efficacy, we will use the **Adherence Self-Efficacy Scale** (ASES) (Johnson et al., 2007). It is a 12-item scale of patients' confidence to carry out

important HIV treatment-related behaviors, most of which overlap with PrEP behaviors (Kogelman, personal communication, 2019), including taking medication in face of barriers (e.g., How confident are you that you can stick to your medication when your daily routine is disrupted?). Dr. Kogelman made slight modifications to the ASES for use with PrEP. We include **intention to follow guidelines** as a mediator because we believe that intending to follow guidelines reflects greater "patient activation" (see Hibbard & Greene, 2013), which is associated with better medication adherence. Furthermore, showing up for 3-month testing, in itself, increases patients' interactions with providers, which can also positively impact adherence (see Chen et al., 2013).

Because there were no measures for **intention to follow PrEP guidelines**, Drs. Weitzman and Kogelman created a 5-item measure informed by a 2-item measure of safe sex intentions developed by Fischer et al. (1998) for use with MSM. A sample item from the new measure includes: While I'm on PrEP, I intend to be tested for HIV and STDs every 3 months (5-point LIkert ranging from very untrue to very true). There are also no PrEP knowledge measures. Therefore, Drs. Weitzman and Kogelman created a **6-item multiple-choice instrument** with face validity based on the Truvada patient education booklet and CDC guidelines. Content covers PrEP knowledge (medication purpose, side effects, concomitant condom use, HIV testing), all of which will be covered in educational texts.

Sample item: If you take PrEP, you should use condoms: a) every time you have anal intercourse b) most times you have anal intercourse c) only if you have anal intercourse with a HIV+ partner d) you don't need to use condoms if you are on PrEP (correct answer: a). Because our Phase 2 study is twice the length of Phase 1, participants will receive twice as many PrEP education texts. Thus, we still expect to see PrEP knowledge improvement in Phase 2, despite lack of change in Phase 1.

Perceived stress burden will be included as a potential mediating variable for two reasons: First, the intervention targets stress burden via supportive texts and an online community. Second, reductions in perceived stress can facilitate medication adherence (Stewart et al., 2005). Stress burden will be assessed using the 10-item **Perceived Stress Scale** (Cohen et al., 1983), which has been validated with a wide-range of patient and non-patient groups (e.g. Chiu et al., 2016; Perera et al., 2017). We will analyze psychometric properties and construct validity on the two new measures (intention to follow guidelines and PrEP knowledge) as a part of our Phase 2 analyses.

Moderating Variable. Length of time on PrEP (in months) will be included as a moderator as it seems possible that the greater the length of time on PrEP, the more likely a participant has developed personal strategies to support adherence or have supports (family members, friends, healthcare providers) in his social environment that help with adherence.

Demographic and Control Variables. T1 assessments will also gather a number of demographic indicators, including age, years of education, income and, as mentioned above, length of time on PrEP. Income will be coded categorically from 1 to 7 in relation to the federal poverty level federal poverty level: <100% (1), 100%-149% (2),

150%-199% (3), 200%-249% (4), 250%-299% (5),
300%-349% (6), 350%-399% (7), and ≥ 400%.

Randomization: Participants will be randomly assigned to intervention or control group via the randomizer function on Qualtrics software. **Sample size:** We will aim to recruit and gain consent from 110 participants (55 each for intervention and control arms). **Power analysis:** Based on our Phase 1 pretest results, an a priori power analysis for a multiple regression with 4 predictors of PrEP adherence was conducted to determine a sample size with a power of at least 90% with a two-sided alpha level of .05. The desired minimum sample size was 92 participants (Rosner, 2010). In the event of 20% attrition, we added 20% additional participants to the sample, and set 110 as the total sample size. Therefore, even if the study encounters diminished recruitment or greater post-recruitment attrition, it should still be possible to detect moderate effects.