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Introduction Page 1 * Abbreviated Title: Optimizing Smoking Cessation Interventions for PLWH

*** Full Title: Optimizing smoking cessation interventions for PLWH in Nairobi, Kenya**

STATISTICAL ANALYSIS PLAN

Power Calculations: With a total of 300 participants and an estimated 20% attrition, we expect 60 participants per cell in the factorial design. This will provide a total of 120 participants per main effect condition (Drug or Psychosocial Intervention). All power analyses were conducted with a two tailed alpha of .05 and powerset to .80. With the expected sample and the anticipated retention rate, the study's 2 main effects((1) bupropion vs. placebo; (2) PSF versus SOC) are each powered to detect a Cohen's h of from .28 to .36 (small effect)98. In addition, we will be able to determine if there is a significant additive effect (i.e. whether the combination of bupropion and PSF issignificantly better than either treatment alone). For this comparison we have sufficient power to detect an effect size of h = .39 – .49 (small to medium effect). The evaluation of the exploratory interaction Aim is a possible but not necessary benefit of a factorial design that could determine whether the combination of the two treatments provides more than a simple additive effect. The interaction effect is powered to detect a Cohen's d of .9 (large effect)98. Power was calculated using the PASS software. (Version 13, Logistic Regression Procedure.) Overview of Analytic Methods: The primary study analyses will adopt an intent-to-treat strategy. Data will be screened for errors using frequency and contingency tables and univariate and bivariate plots before formal analysis. These plots and summaries will allow us to be cognizant of data distribution characteristics before building regression models. To assess indication of self-selection bias, we will compare the demographic characteristics of the participants that agreed to participate in the study to those who were approached, but were not interested in participating. Covariate Selection: We expect, due to randomization and sufficiently large sample size, that demographic, clinical characteristic, and outcome variables at baseline in the four conditions will not be significantly different. However, we will perform tests for differences (imbalances) on demographic (e.g. age, race, gender) and other potential confounder variables acrossthe four groups. Imbalances may occur in spite of the randomization procedure. If there are important variablessignificantly out of balance we will add them as covariatesin the models. In addition, all models will include covariatesindicating whether the participants are using HAART. Missing Data: Missing data can arise from active refusal and from participants who cannot be located. Attrition will be carefully monitored. We will attempt to assess all participants at follow up regardless of whether they engage with smoking cessation services during the study (intent-totreat). To assess the potential confounding effects of missing data, we will compare the baseline characteristics of participants who do and do not complete the 12- and 36-week assessments. If we find significant differences between dropouts and completers and differential attrition, we will include any potential confounding variables as covariates. If a subject failsto complete interim visits, we will attempt to re-engage him/her for the 36 week visit in order to ascertain the primary abstinence endpoint. If a subject refuses to be contacted or otherwise loses contact with the investigators, we will censor data at the point of loss and the subject will be considered non-abstinent. In addition, the investigative team will agree by consensus on a set of rulesto guide the imputation of missing data

values in the various study scales. If necessary, we will conduct a sensitivity analysis to investigate how estimates/results change over a range of several plausible assumptions regarding the missing mechanism together with multiple imputations to most accurately capture existent random variability. Multiple Comparisons: We will use the sequential Bonferonni-type procedure for dependent hypothesistests99 to control the false discovery rate (the expected (or on average) proportion of falsely rejected hypotheses) at 5%. Primary Aims: We will use separate logistic regression models(SAS, 9.3: Proc Logistic) at each post baseline time point to assessthe main effects of bupropion vs. placebo (Drug) and PSF vs. SOC (Beh) on smoking cessation. In addition, we will assess any covariatesthat were identified above. The test of the hypotheses will be the test of whether the coefficientsfor the main effects are significantly different from 0 based on the likelihood ratio test. To assessif the combination of bupropion and PSF issignificantly more effective than either of the treatments alone, we will create an indicator variable for these 3 conditions with the combined treatment as the reference. The analysis will proceed as described above. Exploratory Analyses: Other smoking outcomes: We will use a Generalized Linear Mixed Model (GLMM; Proc MIXED) to assessif the treatment conditions have a significant effect on othersmoking outcomes (e.g. number of cigarettes smoked per day) over time. Treatment conditions, time and the interaction of time with the treatment conditions will be included in the model. A random intercept will be used to account for the nonindependence of the repeated measures. An unstructured covariance matrix will be employed. Significant effects will be followed up with specific contraststatements. Mediation: We will use Proc Mixed to assess the interventions impact on possible mediating variablesfor bupropion (craving, withdrawal) and for PSF (self-efficacy, depression, loneliness, substance abuse, and dosage of the PSF intervention (number of sessions completed)). Mediators will be assessed at 12 weeks, controlling for baseline. For those variables that are significant we will conduct additional analysesto determine if change in those mediatorsisrelated to smoking cessation at 36 weeks. If all conditions are met, we will use the MacKinnon 100 approach to formally assessfor mediation ofsmoking cessation by the targets of the interventions. Moderators: We will assess possible clinical (e. g. depression,smoking severity at baseline, years smoked, etc.) and demographic moderators on smoking cessation. We use the analyses described for the primary aim to assess moderation by including these variables and their interaction with the treatment conditions to the models