**Document:** Statistical Analysis Plan
**Document Date:** March 5, 2020

**Official Study Title:** A Pilot Pragmatic RCT of a Hospital-based Precision Pharmacotherapy Smoking Cessation Program
**NCT#:** NCT04897607

**Statistical Analysis Plan**

**Specific Aim 1:** *The proposed trial will be acceptable to underserved smokers as measured by the proportions and demographic characteristics of patients who enroll (H1.1), accept pharmacotherapy (H1.2), and complete follow-up (H1.3).*

Descriptive statistics and 95% confidence intervals will be used to summarize the feasibility metrics, namely the numbers and proportions of patients who: 1) were approached, 2) deemed eligible, 3) enrolled, 4) accepted pharmacotherapy, and 5) completed follow-up. To gain a sense of whether study participants may be considered representative of the larger population of ChristianaCare smokers as measured by race and area-level measures of SES, chi-square tests and Wilcoxon rank tests will be conducted. Race is routinely collected for all admitted patients and will permit a comparison between trial participants and the larger population of ChristianaCare smokers. However, no individual-level measures of SES are routinely collected for admitted patients and therefore will not allow for a comparison between trial participants and the larger population. Therefore, census tract measures of poverty (e.g. employment status, income, and education) based on participant residence will be used as a proxy for individual-level SES. The residential addresses for the larger population of ChristianaCare smokers has been previously geocoded and linked to census tract poverty measures,[48] which will be used to compare the proportions of participants in this trial who reside in each census tract strata.

**Specific Aim 2:** *Patients assigned to precision care will more readily accept pharmacotherapy (H2.1), achieve greater treatment matching (H2.2), and demonstrate improved abstinence rates (H2.3).*

Three sets of logistic regression models will be used to compare precision pharmacotherapy vs. standard care for each of the binary effectiveness outcome measures: acceptance of pharmacotherapy, treatment matching, and abstinence. Models will adjust for demographics and other covariates, including age, race/ethnicity, nicotine dependence, and indicators of SES (employment status, income, and education).

**Exploratory Aim:** *Precision pharmacotherapy will improve patient outcome expectancies related to medication effectiveness and safety/side effects, which will be associated with greater use of pharmacotherapy (H3.1) and abstinence (H3.2). Higher rates of treatment matching in precision care will mitigate the reductions in abstinence rates for low-SES/racial minority smokers compared to standard care (H3.3).*

Mediation analyses. Two sets of logistic regression models will be used to evaluate whether patient outcome expectancies mediate the relationship between treatment assignment (precision vs. standard) and the outcome measures use of pharmacotherapy and abstinence. In the first step for each model, treatment condition will be used to predict the outcome measures, adjusting for the same covariates used above. In the second step, patient outcome expectancies will be used to predict the outcome measures, again adjusting for covariates. If both treatment condition and treatment expectancies are significantly associated with outcome measures, a third step will include both predictors to formally test for partial or complete mediation by assessing whether the inclusion of patient outcome expectancies reduces or eliminates the effect for treatment assignment.

Moderation analyses. A series of logistic regression models will be used to evaluate whether greater treatment matching mitigates (i.e., moderates) the lower rates of abstinence typically seen among low-SES/racial minority patients in usual care. The model will include the predictors of treatment matching (dummy coded as yes/no based on whether the participant used the medication matched to their nicotine metabolism rate: NRT for slower metabolizers, varenicline for faster metabolizers), measures of SES (e.g., years of education), and the product of these predictors. If the product, or interaction term, significantly predicts abstinence, that would provide evidence that treatment matching has differential impacts based on the SES of the participant. Post hoc analyses will be employed to describe the nature of the interaction. A

similar, albeit multilevel approach will be used to test for interaction between area-level variables (e.g., census tract poverty levels, tobacco outlet density) and treatment matching.