Statistical Analysis Plan

NCT05740098

April 1, 2023

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Condition Assignment/Randomization

The study consists of a baseline assessment, 12 weeks of exposure to the treatment conditions, and follow-up visits at 24 and 48 weeks following their quit dates. Participants will be randomly assigned to one of the three study conditions (Best Practices [BP], Best Practices plus Financial Incentives [BP+FI], Best Practices plus Financial Incentives plus Nicotine Replacement Therapy [BP+FI+NRT]), with randomization conducted using a covariate-adaptive randomization scheme. Covariates considered in the randomization scheme include the age of the child who will participate in the trial with Mother (< 6 years of age versus 6-11 years of age), number of cigarettes/day (CPD) smoked by the mother (≤ 20 CPD versus > 20 CPD), mother's level of education (< high school versus high school diploma or higher), maternal use of e-cigarettes (yes versus no), number of smokers in the home (mother only versus at least one other smoker), type of insurance (Medicaid versus private insurance) and recruitment site. Randomization was conducted separately for mothers based on the presence or absence of opioid use disorder (OUD).

Sample Size

Sample size was determined based on having sufficient power to detect differences between treatment conditions corresponding to our first specific aim on point prevalence abstinence differences at the 12-week end-of-treatment assessment and the 24-week follow-up assessment. Our completed trials on smoking cessation among pregnant women provide relevant information for estimating sample size for the proposed study (Higgins et al., 2022). Across three trials, biochemically-verified, 7-day point-prevalence abstinence in the contingent and non-contingent incentive conditions at the end-of-pregnancy were 35% in the contingent conditions and ranged from 9-23% in the non-contingent control conditions. We estimate that the BP+FI and BP+FI+NRT conditions will produce ≥ 35% abstinence rates and the BP condition will produce 15% abstinence rates. The proposed trial sample size of 240 trial participants (80/condition) will result in estimated power of 0.95 using alpha = 0.05 for detecting differences among the treatment conditions (i.e., 40% vs. 15%) at 12-week end-of-treatment assessment. Power is estimated to be 0.80 to detect a 15% (i.e., 20% vs. 5%) difference between treatment conditions at the 24-week follow-up assessment. For the second specific aim relating to the objective measure of secondhand smoke exposure (SHSe) in children, power is estimated to be 0.80 using alpha = 0.05 to detect treatment differences of approximately 35% with respect to the mean decrease in urine cotinine levels from baseline and > 0.80 in comparisons by maternal smoking status. This computation is based on variability estimates from Hovell et al. (2009) which corresponds to a log transformed analysis and geometric means. This assumes moderate correlation (r = 0.50) between cotinine levels within subjects across assessment times. If our average baseline levels are similar to theirs, this relative difference translates to an absolute mean difference of approximately 4.2 ng/ml between treatment conditions and larger effects in comparisons by maternal smoking status. For the logistic regression analyses corresponding to the secondary aim on behavioral economic predictors, power is estimated to be 0.80 using alpha = 0.05 for detecting explanatory variables that have odds ratios ranging from 2.0 to 2.5 per one

SD change from their mean assuming total model R^2 ranging from 0.20 to 0.40. This exact estimate is dependent on the total number of predictors and the overall R^2 of the model with lower detectable OR's associated with smaller overall R^2.

Study Populations

Intention-to-Treat Population

Participants will be randomized to study conditions after the completion of the intake assessment. For data analyses, the full analysis population will include participants completing the randomization process, which included successfully completing the intake assessment and being randomized to a treatment condition. Participants will be analyzed based upon the condition to which they were assigned, regardless of protocol violations and/or compliance to condition assignment. Our primary results will be based on this intention-to-treat population (i.e., randomized to a condition and received the specified treatment) (Armitage, 1983). Participants missing assessment visits and/or lost-to-follow-up will be assumed to be smokers for these analyses.

Statistical Analysis

Baseline Characteristics

Baseline characteristics will be summarized by treatment condition (BP, BP+FI, BP+FI+NRT) to identify any group imbalances post-randomization. Continuous variables will be summarized by mean and standard deviation and compared by one-way ANOVA, with variable transformations conducted as necessary to improve the normality of the distributions. Categorical variables will be summarized by frequencies and percentages and compared using the Chi-square test.

Primary Endpoint Analysis

The primary endpoints are maternal 7-day point-prevalence smoking abstinence at the 12- and 24-week assessments. Comparison of point-prevalence abstinence among treatment conditions across all periodic assessments will be analyzed using a mixed model repeated measures for categorical data based on generalized estimating equations utilizing a logistic link function (SAS PROC GENMOD, SAS Institute, Cary, NC). Covariates of interest that will be identified, based on characteristics that differ significantly across study conditions and are predictive of outcome, will be included in the model. Data analysis for child SHSe will be based on child urine cotinine levels, assessed at 6-, 12-, 24-, and 48-week assessments. Comparison of treatment conditions will use a mixed-model repeated-measures analysis (SAS PROC MIXED, SAS Institute, Cary, NC), with baseline urine cotinine levels included as a covariate. As noted for the point-prevalence abstinence rates, covariates of interest will be identified based on characteristics that differ significantly across study conditions and are predictive of outcome. In addition, models will include potential confounders (Collins et al., 2020). Analysis of variance will be used to compare SHSe levels by maternal smoking status at the follow-up assessments, controlling for baseline levels. Additional covariates include those characteristics included in the prior analyses.

Secondary Endpoint Analysis

Group comparisons on continuous abstinence from quit date to 24-week assessments will be assessed using a 3x2 contingency table with a Chi-square test. A significant overall Chi-square test will be followed with pairwise tests. Logistic regression will be used to examine the association between baseline temporal discounting, measured by the Kirby delay discounting task, and other measures of price sensitivity, measured by the Cigarette Purchase Task (CPT), with subsequent abstinence at follow-up assessments (6-, 12-, 24- and 48-week assessments). Baseline delayed discounting will be expressed as the logarithm of each participant's estimated parameter k. Measures from the CPT will be transformed as necessary. Models will include treatment condition and the interaction of treatment condition with k or the CPT measures.

Missing Data

We will treat missing data on maternal smoking status as if the woman is a smoker. The comparison of groups across time on child urine cotinine is based on maximum likelihood estimation which allows the use of all available data for cases with incomplete urine cotinine data.

Reporting Conventions

P-values greater than or equal to 0.001 will be reported to 3 decimals places; those less than 0.001 will be reported as <0.001.

References

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Collins, B.N., Nair, U.S., DiSantis, K.I., Hovell, M.F., Davis, S.M., Rodriguez, D., Audrain McGovern, J., 2020. Long-term results from the "FRESH" RCT: Sustained reduction of children's tobacco smoke exposure. Am J Prev Med. January; 58(1): 21-30. doi: 10.1016/j.amepre.2019.08.021.