Appendix F

Engage Study Final Statistical Analysis Plan

ClinicalTrials.gov trial number NCT03656874

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1. Study Objectives

Primary Objective
Aim 1: Assess the impact of tobacco CDS on the frequency of provider-delivered brief smoking interventions or referral to a quitline for smoking cessation treatment.

Hypothesis 1.1 (Objective 1): Smokers seen in dental clinics using CDS will be more likely to report that their provider delivered a brief smoking intervention or referral to a quitline for smoking cessation at their index encounter than smokers seen in clinics without CDS.

Secondary Objectives
Aim 2: Assess the impact of tobacco CDS on smokers' cessation and reduction actions.

Hypothesis 2.1 (Objective 2): Smokers seen in dental clinics using CDS will be more likely to report contacting a quitline, setting a quit date, developing a plan to quit or starting nicotine replacement or other medication to help quit within 7 days of their index encounter than smokers seen in clinics without CDS.

Hypothesis 2.2 (Objective 3): Smokers seen in dental clinics using CDS will be more likely to report quitting smoking, or reducing their smoking within

2. Study Design

The study is a 2-group, parallel arm, cluster (clinic)-randomized controlled trial with primary and secondary outcomes assessed post-intervention through patient surveys. The study is conducted in two settings: predoctoral dental schools and private-practice clinics participating in the National Dental PBRN.

3. Randomization

Within the predoctoral and dental hygiene clinics, 14 clinic modules will be randomized to study arm (CDS or control) using covariate-based constrained randomization. The balancing covariates selected were school site (location A or B), number of consented dental students in each module, percentage of students in their third year of dental school, and number of patients seen within each module. All consented student providers and their patients will be allocated to the study arm to which their clinic is assigned.

Within private practice clinics up to 22 clinics will be randomized to study arm using covariate adaptive randomization. Balancing covariates include factors that are measurable across all clinics in the recruitment pool and include proportion of public pay patients (<50% versus >50%), the number of active patients (<2500 versus >2500 patients), and count of clinics previously allocated to each study arm. Clinics will be randomized by the study statistician as they became eligible for the study.

4. Primary and Secondary Study Endpoints

Primary Objective

Aim 1 - Receipt of a brief smoking intervention or referral to a quitline (H1, Objective 1): The dependent variable for H1 (Objective 1) is a binary indicator of whether the patient reported that their provider 1) delivered a brief smoking intervention: the provider discussed a) developing a quit plan, or b) setting a quit date, or c) using medications to help patients quit or d) discussed strategies for quitting, or 2) referral to a quitline: a) provided information about how to contact a tobacco quitline, or b) arranged for the patient to be contacted by the tobacco quit line, for smoking cessation at the index dental visit. This composite variable is satisfied if the patient reports that any of the intervention activities or referral was delivered. This information is obtained from the phone survey of patients within 1-7 days of their index dental visit.

Secondary Objectives

Aim 2 – Smoker's cessation actions, within one week of visit (H2.1, Objective 2): The dependent variable for H2.1 (Objective 2) is a binary indicator of whether the patient reported that they contacted a smoking cessation quitline, set a quit date, developed a plan to quit, or starting nicotine replacement or other medication to help quit. The CDS is designed to provide a more tailored and targeted message that may lead to more tobacco cessation actions by the smoker. This composite variable is satisfied if the patient reports that they have done any of these actions within the 1-7 day period between the index dental visit and date of the first patient survey. This information is obtained from the phone survey of patients within 1-7 days of their index dental visit.

Aim 2 - Smoker's cessation actions, six months after the visit (H2.2, (Objective 3): The dependent variable for H2.2 (Objective 3) is a binary indicator of whether the patient reported that they quit smoking (stopped smoking for more than one day because they were trying to stop smoking), or reduced their smoking use (50% reduction in amount smoked at 6 months compared to baseline). This composite variable is satisfied if the patient reports that they have done any of these actions within the 6 month +/- 1 week period between the index dental visit and date of the second patient survey. This information is obtained from the phone survey of patients 6 months after the index dental visit.

5. Study Populations

The intent to treat population consists of all patients who had a dental encounter at a previously randomized dental school clinic module or private practice clinic, and who consented to study participation.

The modified intent to treat population consists of all patients who had a dental encounter at a previously randomized dental school clinic module or private practice clinic, who consented to study participation, and completed a survey within 1-7 days of the index dental encounter.

The follow-up modified intent to treat population consists of all patients who had a dental encounter at a previously randomized dental school clinic module or private practice clinic, who consented to study participation, completed a survey within 1-7 days of the index dental encounter, and completed a survey at 6 months after the index dental visit.

6. Analysis Plan

Because of the numerous differences in the dental school and private practice settings and the interest in testing generalizability of the intervention in both settings, all analyses are conducted separately within each setting.

Analysis plan for Objective 1 (primary) and Objectives 2,3 (secondary)

Hypothesis 1.1 (Objective 1) posits that patients seen at clinics randomly assigned to the tobacco CDS intervention will be more likely to report that their provider offered a brief smoking intervention or referral to a tobacco cessation quitline than patients seen at clinics with CDS. Hypothesis 2.1 (Objective 2) posits that patients seen at clinics randomly

assigned to the tobacco CDS intervention rather than control clinics will be more likely to report that they have engaged in short-term activities towards cessation of contacting a quitline, setting a quit date, starting nicotine replacement or other medications to quit, or developing a quit plan. Hypothesis 2.2 (Objective 3) posits that patients seen at clinics randomly assigned to the tobacco CDS intervention will be more likely to report that they have engaged in cessation activities of quitting smoking for one day or longer or reducing smoking use.

The design specifies that clinics are the unit of randomization and the outcome varies at the level of the patient. To accommodate this data structure, generalized linear mixed model regression with a logit link and binomial error distribution, and R-side random effect for clinic will be used to test the effect of the intervention on the binary endpoints of Objectives, 1, 2, 3. Because the count of private practice clinics having completed patient surveys is limited, and the mean number of completed patient surveys per randomized unit (dental school module or private practice clinic) is also limited, the analyses for Objectives 1, 2, 3 are simplified. Fixed effects for the analysis of each composite endpoint will include only a fixed effect for clinic-level study arm. And no stratification, covariate adjustment, or heterogeneity of treatment effect analysis will be conducted. Objectives 1 and 2 will be based on the modified intent to treat population and Objective 3 will be based on the follow-up modified intent to treat population.

6. Handling of missing data

Endpoints for Objectives 1-3 are binary indicators from patient surveys. Since the only patients consented for the study are those who complete a baseline survey, missing data for individual composite endpoints for Objectives 1 and 2 is rare and the analysis for Objectives 1 and 2 will use pairwise deletion. Small sample sizes prevent the use of other approaches (e.g., multiple imputation) for handling missing data. As such, the analysis of Objective 3 utilizing 6-month survey data will also utilize pairwise deletion and will remove from analysis those patients who do not complete the 6-month survey or those who do not complete the constituent survey items for the Objective 3 composite.