

## Study Measurements

### Evaluation of Primary Endpoint: Smoking Cessation

Long-term smoking cessation is the primary endpoint of the proposed study. We propose to assess smoking cessation by self-report, exhaled carbon monoxide, and by salivary cotinine. All baseline assessments and follow-ups will be obtained at the clinic.

The primary measure of smoking cessation will be both point prevalent and self-reported prolonged abstinence. The major advantage of point prevalence estimates is that they are widely reported in the literature and can be verified biochemically. However, point prevalence abstinence does not account for slips and lapses that might occur between follow-up periods. Prolonged abstinence, on the other hand, which is abstinence sustained after a two-week grace period, accounts for these lapses but cannot be verified biochemically, and ultimately, must be assessed via self-reports. However, self-reports tend to be accurate, and misreporting rates are generally very low (Velicer et al., 1992). Relapse is defined as smoking on 7 consecutive days or smoking at least once each week on two consecutive weeks (Hughes et al., 2001). The latter defines participants who smoke regularly after the quit date, but less than on a daily basis (e.g. social smoking). We also will measure continuous abstinence (i.e., not smoking, not even a puff since target quit date) at 6, 12, and 24 months after randomization. The number of days quit prior to relapse and current smoking rate will be assessed for participants who are not abstinent at end of treatment. Smoking status and rate will be assessed at 6-, 12-, and 24-month follow-ups.

As indicated above, biochemical markers will serve as the primary outcome measure for any inconsistent findings between self-report and CO. We will use existing standardized protocols used in many previous studies.

Carbon monoxide: Exhaled carbon monoxide will be used to assess adherence with smoking cessation and will be used as a tool for reinforcement of cessation behavior. Expired carbon monoxide will be taken on all subjects at baseline and follow-ups. This procedure involves having the subject hold his/her breath for 10 seconds and then exhale into a disposable tube attached to a small machine that indicates carbon monoxide levels in parts-per-million. This is a safe, non-invasive procedure.

Salivary Cotinine: We also plan to use more specific biochemical markers with a longer half-life for smoking cessation validation. Cotinine is a specific major metabolite of nicotine that can be detected in body fluids for 48 to 72 hours. The specificity and relatively long half-life make cotinine the biologic marker of choice for quantifying exposure to nicotine and tobacco products. Cotinine can be measured in a variety of body fluids such as blood, urine, and saliva (Etzel, 1990; Haley et al., 1983; Watt et al., 1990). We have chosen to measure salivary cotinine as this is a noninvasive collection method. Cotinine measurement is considered the best biomarker for smoking cessation (Benowitz et al., 2001), especially when NRT is not currently being used. All biochemical assessments will occur several weeks after NRT is discontinued to provide

sufficient time for “wash out” in order not to confuse NRT use with smoking. Saliva cotinine will be obtained on all subjects who report abstinence but have CO levels >10 ppm. Participants reporting abstinence, but having saliva cotinine levels at 15 ng/ml or above will be treated as smokers in the analyses. Cotinine is stable in unrefrigerated saliva and saliva collected via mail even up to 12 days (Foulds et al., 1994; Greeley et al., 1992).

### **Other Study Measurements**

Fagerstrom Test of Nicotine Dependence (FTND): We plan to use the Fagerstrom Test for Nicotine Dependence (Heatherton et al., 1991) to assess nicotine dependence in all participants. This instrument has been widely tested and used in smoking cessation studies. We plan to compare level of nicotine dependence as measured by the FTND with smoking cessation rates.

Stages of Change: We also will use Prochaska and DiClemente’s stages of change model to assess readiness to initiate behavioral change in the participants at the screening visit and at each follow-up (Prochaska et al., 1983, 1993). We plan to use stage of change in the analysis as a potential confounder for smoking cessation. However, since participants will be volunteers, we anticipate that the overwhelming majority of these subjects will be in the Action stage at entry into the study. Readiness to quit will be re-assessed at all follow-ups (prior to initiation of a new step) to assess changes in this attribute over time.

Depressive Symptomatology: Depressive symptoms and how they may interact with treatment outcome will be assessed using the Center for Epidemiological Studies – Depressed Mood Scale (CES-D; Radloff, 1977). The CES-D is a well-validated and frequently used self-report measure of depressive symptoms. Participants are asked to report their level of agreement with each of 20-items on a four-point, Likert-type scale. The CES-D has been found to have good internal consistency and concurrent validity, and has been shown to be appropriate for use in populations with a broad range of demographic characteristics (Radloff, 1977).

Other Important Measures: We intend to collect basic demographic information (age, height/weight, gender, ethnicity, occupation, income, education) on factors that may relate to our primary outcomes. We will also monitor participant and physician adherence, medication side effects, and adverse events during the study on all participants. In addition, we will monitor, at the follow-ups, use of any other product (or programs) that may have influenced their cessation rates. We will monitor, for example, additional patch or gum use or use of nicotine nasal spray, inhaler, or lozenge. Use of anti-depressants (e.g., nortriptyline) to aid cessation efforts will also be assessed, as will participation in behavioral stop-smoking programs (e.g., Smoke Enders). Based on our current work, we expect that the use of these post-intervention products will be low and not vary by condition. Because these can affect cessation rates, we will carefully track them and adjust our cessation rates if necessary.

### Process Endpoints

The proposed project will also assess physician adherence in the delivery of the smoking cessation intervention. This will be accomplished as in our other primary care trials. That is, after seeing the physician, the participant will complete a brief questionnaire that inquires about the information the health care provider was to deliver. In addition, the health educator will also complete a checklist of the information provided to the patient. These data will be analyzed for level of agreement.