Effect of Banning Menthol Flavored Cigarettes on Smoking Cessation

NCT02342327

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The following is a summary of protocol changes approved by the IRB for study "Effect of Banning Menthol Flavored Cigarettes on Smoking Cessation" (#1406M51364). The originally submitted and approved protocol follows this summary.

09-18-2014

1. Modification of the Tobacco Use History (smoking intake) questionnaire
   Rationale: To get a more thorough understanding of subjects' current tobacco use
2. Distribution of transit tokens to subjects that use public transportation to study visits
   Rationale: To increase likelihood of attendance at visits for subjects who rely on public transportation

11-25-2014

1. Collection of subject height and weight
   Rationale: To calculate BMI in order to get a better description of the study population

02-25-2016

1. Change to the inclusion criteria regarding amount of cigarettes smoked per day by lowering the required average number of cigarettes from 8 to 5
   Rationale: To keep consistent with the inclusion criteria now commonly used in smoking studies

08-16-2016

1. Use of an information session to disseminate study information in a group setting
   Rationale: To better utilize resources for screening potential subjects who are then more likely to attend a subsequent visit

11-17-2016

1. Addition of the Cigarette Evaluation Questionnaire
   Rationale: To collect data about how smokers perceive menthol and non-menthol cigarettes over time

09-08-2017

1. Increase in the number of subjects approved for enrollment from 200 to 250
   Rationale: To meet the study goal of having at least 120 subjects complete the study

Project Summary:

With the passage of the Family Smoking Prevention and Tobacco Control Act, the United States Food and Drug Administration (FDA) acquired broad ability to regulate tobacco products. One of the areas over which the FDA gained regulatory authority is the use of flavorants in cigarettes. Effective September 2009 the FDA banned cigarettes flavored with fruit or candy but menthol was specifically excluded from this ban as the FDA examines the role of menthol in initiation, maintenance and health risks associated with use of such products. A critical piece of information that is currently not available regarding the consequences of a menthol ban is how such a ban would affect current smokers of menthol cigarettes. Our preliminary data demonstrates that if menthol cigarettes are not available, most African American menthol smokers would switch to non-menthol cigarettes. Others have demonstrated that African Americans have more difficulty with cessation of menthol cigarettes relative to non-menthol cigarettes. It is currently not known if by switching to non-menthol cigarettes prior to a cessation attempt, menthol cigarettes smokers would experience greater cessation success than they would if attempting to quit without first switching. The aim of the proposed study is to determine the likely effects of a menthol ban on smoking cessation success. We hypothesize that switching to non-menthol cigarettes before a quit attempt (as menthol smokers are likely to do in the event of a ban) will improve cessation success, increase motivation and self-efficacy to quit and will enhance support for a ban on menthol cigarettes. In order to pursue this aim, we will enroll 140 smokers of menthol cigarettes who will be randomized to either continue smoking their usual brand cigarettes for four weeks or switch to non-menthol cigarettes for four weeks prior to a smoking cessation attempt. Smokers will be evaluated at a screening visit, a baseline visit, 3 pre-cessation visits and 7 post-cessation visits occurring over a 26 week evaluation period. Time to smoking lapse, tobacco and nicotine product use, motivation and self-efficacy to quit smoking, severity of craving and withdrawal symptoms and support for a ban on menthol cigarettes will be assessed. Data will be analyzed to determine if there are differences between groups in measures of interest.

Significance and innovation of the proposed research:

Background and Significance:

a) Introduction: With the passage of the Family Smoking Prevention and Tobacco Control Act (FSPTCA), the United States Food and Drug Administration (FDA) acquired broad ability to regulate tobacco products. One of the areas over which the FDA gained regulatory authority is use of flavorants in cigarettes. Effective September 2009, the FDA banned cigarettes flavored with fruit or candy in response to evidence that such flavoring encourages experimentation by young people and leads to regular use and ultimately addiction (1). Menthol was specifically excluded from this ban as the FDA examines the role of menthol in initiation, maintenance and health risks associated with use of such products (1).

As required by the FSPTCA, the Tobacco Products Scientific Advisory Committee (TPSAC) in March, 2011 submitted a report to the FDA reviewing the impact of the use of menthol cigarettes to public health and provided the overall recommendation that "Removal of menthol cigarettes from the marketplace would benefit public health in the United States" (2). This recommendation was based on data suggesting that 1) the availability of menthol cigarettes increases experimentation and regular smoking, 2) the availability of menthol cigarettes increases the likelihood of addiction and degree of addiction in youth smokers and 3) in African Americans the availability of menthol cigarettes results in lower likelihood of smoking cessation success. It was therefore concluded that eliminating menthol cigarettes would result in fewer youth initiating smoking and greater success among African Americans in successfully quitting smoking. Based on two models simulating menthol cigarette elimination, TPSAC estimated that over 17,000 excess deaths in the US population (and over 4,000 in the African American community) would be prevented and over 2.2 million fewer individuals would initiate smoking through 2020 if menthol cigarettes were not available (2, 3).

b) Smoking Cessation Success from Menthol vs. Non-Menthol Cigarettes: The TPSAC report reviewed 27 studies to determine if smoking cessation is more difficult for those smoking menthol vs. non-menthol cigarettes. Twelve of these showed a detrimental effect of smoking menthol cigarettes

with only two showing a better outcome among menthol smokers (the remaining found no effect). The TPSAC report further narrowed these studies to evaluate those that met more rigorous criteria such as comparing cessation rates among racial / ethnic groups (due to possible differences in response to menthol), studies that had sufficient sample sizes, that were broadly representative of a general population of smokers and that had appropriate criteria for cessation. Among the eleven studies meeting the more rigorous criteria, seven found menthol to be associated with a lower level of cessation particularly among African American smokers. This led to the conclusion that "there is sufficient evidence based on national surveys to show that non-white smokers, particularly African American, of menthol cigarettes compared to non-menthol cigarettes experience more difficulty with cessation. The data in whites is mixed." The TPSAC report also concluded that menthol cigarette smoking leads to less responsiveness to medications (2). Among the studies published after submission of the TPSAC report, one found lower quit rates among menthol users in a secondary analysis of a trial of naltrexone augmentation of nicotine replacement (4), one found that prepartum menthol use was associated with significantly lower odds of maintaining postpartum smoking abstinence in white women with near significance (p=0.08) in African American women (5), another not showing an overall effect of menthol use on nicotine patch assisted short term smoking cessation rates (6) and a study finding no difference in quit rates between menthol and non-menthol users among those calling the Minnesota quit line (7). The data as a whole therefore suggest that menthol cigarettes are detrimental to the smoking cessation attempt in African Americans (i.e. the group most likely to smoke menthol cigarettes). No studies however have attempted to switch menthol smokers to non-menthol cigarettes prior to a smoking cessation attempt so as to potentially improve cessation rates.

c) Preliminary data - Switching menthol smokers to non-menthol cigarettes: In an open-label study, 31 African American menthol cigarettes smokers (smoking $\geq$ 8 cigarettes per day) completed a study in which they were asked to abstain from smoking menthol cigarettes for a 4 week period. Subjects were seen at a screening visit, a baseline visit and 1 week, 2 weeks and 4 weeks after stopping smoking menthol cigarettes. Subjects were given no specific instructions regarding how to cope with the inability to smoke menthol cigarettes (as would be the case if a menthol ban were enacted). All subjects reported switching to non-menthol cigarettes with three subjects making a smoking cessation attempt during the 4 week period. At the conclusion of the study, subjects were asked to rate on a 10 point scale how difficult it was to quit menthol cigarettes (1=easy; 10=hard) and the extent to which they were supportive of banning menthol cigarettes (1=not supportive; 10= very supportive). Subjects indicated that quitting menthol cigarettes was difficult (average score = 7.2); nonetheless motivation to quit increased slightly during the period (5.3 at baseline vs. 6.3 at week 4, p=0.03). Based on a preliminary analysis, upon switching to non-menthol cigarettes, participants smoked slightly fewer cigarettes over the 4 week period (12.0 cigarettes per day during the week prior to baseline vs. 10.6 during week 4, p=0.14) and had lower exhaled carbon monoxide concentrations relative to baseline (16.0 ppm at baseline vs. 13.2 ppm at week 4, p=0.05). At the conclusion of the study, subjects were generally supportive of banning menthol (average score = 7.1). These data suggest that a simulated ban on menthol likely did not result in any greater harm than continued menthol cigarette smoking (i.e. smoking did not increase and motivation to quit was not reduced). Furthermore, after experiencing a simulated menthol ban, menthol smokers were supportive of banning menthol cigarettes. The pilot study did not assess if there was in fact benefit, as would be the case if switching to non-menthol cigarettes resulted in increased subsequent smoking cessation rates. Such an outcome would be consistent with research studies finding that cessation rates are generally higher for African American non-menthol smokers relative to African American menthol smokers.

There is little additional data regarding the effects of switching menthol smokers to non-menthol cigarettes. In a study by Strasser et al, menthol smokers progressed through three study periods in which they smoked usual brand cigarettes for 5 days (period 1), followed by Camel Crush cigarettes with instructions to crush the pellet and release the menthol for 15 days (period 2), followed by Camel Crush cigarettes with instruction not to crush the pellet (period 3, i.e. non-menthol cigarettes) (8). Differences in several subjective measures were found among periods with significant increases

between period 2 and 3 in a rating of “worse taste”, significant decrease between periods 1 and 3 in a rating of “too mild” (i.e. non-menthol cigarettes were less mild), a significant increase in bad aftertaste between periods 3 and both periods 1 and 2 and significantly less pleasant smell in period 3 than period 2. On a number of subjective measures associated with taste and flavor, this study therefore found non-menthol cigarettes to not be rated as highly as menthol cigarettes. On most objective measures such as cigarettes smoked per day, carbon monoxide boost, nicotine and cotinine concentrations there were no differences between period 2 and period 3. This is consistent with our data demonstrating relatively small differences in objective smoking measures upon switching to non-menthol cigarettes yet smokers nonetheless reporting that this switch was difficult. Other studies comparing menthol and non-menthol cigarettes in the same subjects have typically had participants inhale smoke from only a few cigarettes of each kind in a laboratory setting rather than having smokers switch from menthol to non-menthol cigarettes for a prolonged period of time and are therefore less relevant in determining if switching to non-menthol cigarettes could facilitate cessation (for example, references (9-12)).

In summary, our preliminary data suggest that if menthol cigarettes are not available, most African American menthol smokers would switch to non-menthol cigarettes. Others have demonstrated that African Americans have more difficulty with cessation of menthol cigarettes relative to non-menthol cigarettes. It is currently not known if switching African American menthol smokers to non-menthol cigarettes would result in higher subsequent smoking cessation rates than would occur if they attempted to quit smoking without first switching. This gap in knowledge is of critical importance since demonstrating that switching menthol cigarette smokers to non-menthol cigarettes is a step towards successful cessation would strongly strengthen the rationale for banning menthol flavoring in cigarettes.

b) Interest in banning menthol cigarettes: Menthol cigarettes are used at particularly high rates among minority populations, adolescents and young adults. For example although menthol smokers account for between 28% and 34% of all US cigarette smokers, over 80% of African American smokers and over 40% of adolescents smokers report menthol cigarettes as their usual choice (2). Among Hispanics smokers, almost 30% of males and over 40% of females report smoking menthol cigarettes (2). A ban on menthol would therefore affect many smokers but would have a disproportionate effect on African American smokers.

There is support among smokers for a menthol ban with rates of those favoring the ban higher in African Americans than in Caucasians. A nationally representative cross-sectional sample contacted by telephone found that 53% of whites and 68% of African Americans supported a ban on menthol cigarettes (13). Another survey found that overall 20% supported a ban on menthol cigarettes (with an additional 52% not expressing a strong opinion) with the level of support higher among Hispanics (36%) and African Americans (29%) (14). As reported previously, our preliminary study found high levels of support for banning menthol cigarettes even after finding it difficult to abstain from menthol cigarettes over a four week period. We did not determine support for a smoking ban prior to menthol smokers switching to non-menthol cigarettes and it may be that their ability to switch to non-menthol cigarettes (despite the difficulty in doing so) resulted in greater support for a menthol ban. The proposed study would determine if support for a ban does in fact increase when menthol smokers switch to non-menthol cigarettes. This is important data that needs to be collected in that it may suggest that support for a ban on menthol cigarettes would increase after its enactment.

Although surveys of menthol smokers suggest that a substantial number would attempt to quit if menthol cigarettes were unavailable (2, 14, 15), our preliminary data found that relatively few in fact made a cessation attempt (only 3 out of 31 subjects). However, our study was not recruiting smokers specifically interested in cessation. It is not known at this time if among those interested in cessation, switching to non-menthol cigarettes (as our preliminary data suggests menthol smokers would do in the event of a menthol ban) would result in greater cessation success. Clearly, if smoking cessation success rates were to increase following a menthol ban, the health effect of such a policy would be favorable. However, since it is not known if this would occur, research is needed to obtain data on the

consequences of a ban on menthol cigarettes in order to ensure that banning menthol cigarettes would not undermine smoking cessation rates.

Innovation: Although much research has been conducted on the epidemiology and health effects of menthol cigarettes and studies have compared cessation rates among those who prefer menthol vs. non-menthol cigarettes, there is currently little information regarding how smokers of menthol cigarettes would adjust their tobacco use if their preferred cigarettes were no longer available. It seems likely that studies comparing quit rates in those who naturally prefer menthol vs. naturally prefer non-menthol cigarettes may underestimate the beneficial effect of menthol smokers first switching to non-menthol cigarettes prior to a cessation attempt since they would be switching to a non-preferred product and therefore perhaps more likely to quit tobacco use completely. Obtaining data determining if this is indeed the case is critical considering that over 25% of all smokers and over 80% of African American smokers are currently using menthol cigarettes. Our proposed study in which African American menthol cigarettes smokers will switch to non-menthol cigarettes prior to a cessation attempt is innovative in that it attempts to approximate what is likely to happen to smoking cessation success rates were the FDA to ban menthol cigarettes.

Specific Aims/Study Objectives:

In follow-up to our previous study demonstrating that when African American menthol smokers were asked to abstain from menthol cigarettes, they switched to non-menthol cigarettes, were generally supportive of a ban on menthol and experienced an increase in motivation to quit smoking, we are proposing a follow up study to determine if switching to non-menthol cigarettes is an effective first step to cessation. We propose to study the following specific aim:

Determine the impact of a ban on menthol cigarettes on smoking cessation success rates in African American menthol smokers

We hypothesize that a) switching to non-menthol cigarettes before a quit attempt will improve cessation success. We further hypothesize that switching to non-menthol cigarettes prior to cessation will b) increase motivation and self-efficacy to quit and c) enhance support for a ban on menthol cigarettes. We anticipate that no greater harm will result from the elimination of menthol cigarettes.

Research Design and Methods:

Sampling Plan

Design Overview: This study will randomize 140 African American menthol cigarette smokers to receive either menthol cigarettes (i.e. continue smoking menthol cigarettes) or non-menthol cigarettes for a four week period. At the conclusion of the four week period, participants will attempt to quit smoking all cigarettes and will return for follow-up over a 6 month period. Tobacco use, nicotine use, motivation and self-efficacy to quit, nicotine craving and withdrawal measures and support for a ban on menthol cigarettes will be assessed during the study period. Urine cotinine concentrations will be measured at each visit. The primary outcome in this study is time from cessation to the first smoking lapse.

Subjects: In order to be eligible for this study, subjects must: 1) be African American (based on self-identification); 2) smoke primarily menthol cigarettes (greater than 80% of cigarettes smoked are menthol); 3) be between the ages of 18 and 64; 4) Smoke on average, at least 8 cigarettes per day for a period longer than 1 year and 5) express an interest in quitting smoking (rate themselves $\geq$ 7 on a 10 point scale assessing motivation to quit smoking). Subjects will be excluded if they have: 1) A current unstable medical / psychiatric condition as determined by self-report; 2) Substance abuse within six months of beginning the study based on self-report; 3) Regularly use any form of nicotine or tobacco other than cigarettes or 4) Are pregnant or breast feeding based on self-report (subjects will

be given a urine pregnancy test at the screening visit with pregnancy later in the study and breast feeding based on self-report).

As the risks associated with the study procedures are small, all medical assessments are based on self-report (except for a urine pregnancy test at screening).

Recruitment will be limited to African American smokers for several reasons. Menthol cigarette use is particularly prevalent in the African American community with 80% of African Americans reporting menthol cigarettes as their usual choice (2). Additionally, data suggest that greater difficulty in cessation of menthol cigarettes (vs. non-menthol cigarettes) may be limited to African Americans (2) and therefore methods to improve cessation rates from menthol cigarettes are particularly relevant to this population. Since our preliminary study suggests that few menthol smokers spontaneously attempt to quit when asked to abstain from menthol cigarettes, we will only enroll those interested in smoking cessation.

African American menthol smokers will be recruited via the use of flyers and advertisements in local newspapers and neighborhood newspapers with a high African American readership or on internet resources such as Craigslist. If additional advertisement becomes necessary, radio or television advertisements may be utilized. Our research team has considerable experience recruiting smokers and we have determined which advertisement strategies are most effective.

Implementation Plan

Overview: Each subject will attend a screening visit to determine if they are eligible for the study. If subjects are eligible, they will be randomized to either the 'menthol' or 'non-menthol' group. Subjects will continue smoking in their normal manner for one week after the screening visit to gather information on their baseline smoking patterns after which they will attend a baseline visit. Week 0 will be considered their quit date, therefore the baseline visit will be week -4 (i.e. 4 weeks before their target quit date). Additional visits will be scheduled at week -3, week -2 and week 0 (i.e. 1, 2 and 4 weeks subsequent to the baseline visit). Follow up visits will occur at weeks 1, 2, 4, 6, 8, 12 and 26. The procedures occurring during each of these visits are described below.

Screening Visit: All subjects will undergo a screening visit prior to enrollment at which written informed consent will be obtained and eligibility will be verified. Medical and psychiatric history will be obtained via subject report. Baseline questionnaires assessing smoking history and nicotine dependence will be administered. Exhaled carbon monoxide (CO) will be measured to confirm that they are smokers (CO $\geq$ 8 ppm) with a NicCheck performed (with a cut-off of $\geq$5) for those who state that they smoke $\geq$ 8 cigarettes per day but for whom CO is less than 8 ppm (e.g. they didn't smoke that morning, they are coming from a smoke free work environment, etc.). Subjects that qualify and are interested in participating will be asked to maintain a smoking diary for the duration of the study and will be scheduled for the baseline visit.

Baseline and Pre-Quit Visits: Smoking behavior subsequent to the screening visit will be determined as will subjects' level of craving, withdrawal, perceived health risk, motivation and self-efficacy to quit smoking and support for a menthol ban. At the baseline visit subjects will be told their randomization and given appropriate product (i.e. menthol or non-menthol cigarettes, based on randomization) at no cost to them for a total of 4 weeks. Subjects will be given a quantity of cigarettes equivalent to approximately 120% of their average daily use based on smoking diaries collected at the baseline visit or at pre-quit visits up to a maximum of approximately 1.5 packs per day. Since cigarettes packs generally contain 20 cigarettes, these percentages are approximations subject to rounding. This amount is chosen in case smoking increases as a result of switching to non- menthol and to allow for flexibility in scheduling subjects for subsequent visits (i.e. if a visit is delayed by several days, subjects will still have product). Subjects will be asked to smoke only study product for the 4 week period following the baseline visit. They will be given no specific instructions regarding using medicinal nicotine (i.e. nicotine patch, gum) or the use of e-cigarettes but will be asked to record any instances

of using any nicotine or tobacco product. If subjects ask specifically about e-cigarettes, they will be told they can be used as long as they report their use at the next visit. Since e-cigarettes would be available to smokers were menthol cigarettes to be banned, to most closely mimic naturalistic conditions we will not ask subjects to abstain from e-cigarettes. However, since the risks of e-cigarette use are unclear as are their impact on cigarette cessation, we will also not encourage their use. In order to approximate what would likely occur were a menthol ban to be enacted, no specific instructions will be given to subjects about how to effectively quit but subjects will be encouraged to call the Smoking Quitline to obtain support for their cessation attempt. At each visit, exhaled carbon monoxide concentrations will be measured and subjects will complete questionnaires assessing craving and withdrawal symptoms, smoking urges, perceived health risk, and motivation to quit smoking. Subjects will also complete a food diary to assess menthol intake from sources other than cigarettes. A questionnaire assessing level of support for a menthol ban will be assessed at baseline, the week 0 (i.e. their quit day) visit and post-quit visits. At the baseline visit subjects will set a quit date which will be the day of their week 0 visit (i.e. they are not to smoke after the visit). If subjects wish to quit smoking the next day, that will also be allowed. At each visit, subjects will return all unused study product. In order to encourage smokers to bring back all unused product, subject payment will increase by the market value of the brand of cigarettes that they received (i.e. currently about $8 per pack for most brands) based on how much they return. Since subjects will be provided cigarettes during the first month, they will not receive additional compensation (although parking will be provided). Returned cigarettes may be provided to the same subject as part of their subsequent supply but will not be used for any other subjects.

At all visits, subjects will be asked to provide a urine sample. The urine will be used to measure cotinine concentrations and may in the future also be used to measure other markers related to smoking menthol cigarettes (such as other nicotine metabolites, menthol concentrations, tobacco toxicants, etc.). Subjects will also be asked to bring in their smoking diary in which they are to record cigarettes smoked as well as any other tobacco or nicotine products used (including e-cigarettes).

Follow up visits: Starting at Week 0 (quit date); subjects will attend follow up visits at weeks 1, 2, 4, 6, 8, 12 and 26. At each of these visits subjects will be asked if they have smoked at all since their previous visit. Exhaled carbon monoxide (CO) will be measured with an exhaled CO less than 8 ppm and a urine cotinine concentration of less than 50 ng/ml confirming abstinence (16). Smoking diaries will be used to determine time to lapse (time from their quit attempt until any smoking occurs) and time to relapse (time from their quit attempt until the first day of seven consecutive days that a cigarette is smoked).

Subjects will be paid $20 for the screening visit, $30 for each of the 7 visits between week 0 and week 12 with a $100 bonus if they complete all visits up to week 12 and have complied with study related procedures. We anticipate that it will be more difficult to retain subjects through the 6 month visit; therefore subjects will receive $60 for that visit. Since it is imperative that subjects honestly report any smoking during the study (in order to calculate time to lapse), payment during the cessation phase will not be contingent on successful abstinence. Subjects that relapse and resume smoking during the study will still be eligible to continue in the study. However, subjects that fail to follow study procedures (e.g. provide urine samples, fill out questionnaires, etc.) will be removed from the study.

Data and Safety Monitoring Plan:

Risks that subjects are exposed to as a result of enrolling in the study are minimal. Subjects will be asked to quit smoking after a 4 week period during which they either switch to smoking a non-menthol brand of cigarette or continue to smoke their current brand of menthol cigarettes. Since we will be enrolling smokers, asking them to continue to smoke for a four week period would not be expected to increase risk of tobacco related illness beyond that which would have otherwise occurred. Smoking cessation would lead to health benefits for subjects. The study procedures will consist of filling out questionnaires and providing breath and urine samples. It is not anticipated that these activities would pose any risk to subjects.

This study will be submitted for approval by the University of Minnesota Institutional Review Board. The study will be explained to all subjects who will have an opportunity to ask any questions prior to signing an informed consent form. Informed consent will be obtained by one of the investigators or a study coordinator trained in the protection of human subjects, per university guidelines. No study related procedures will take place until an informed consent form has been signed. Subjects with serious or unstable medical conditions (based on self-report) will be excluded from the study since their pattern of smoking may be influenced by their concurrent disease states.

To ensure confidentiality, all subjects will be assigned a study identification code to be used on all data collection forms except those for which use of personal identifiers is mandatory (e.g., informed consent form). Forms that link the name of the participant and the subject identification code will be kept in a locked cabinet or office or in an electronic file stored on password protected secure computer servers that meet university guidelines for ensuring confidentiality. Access to subject identifiable information will be limited to those that require this information such as study investigators or others who have direct contact with study subjects (e.g., study coordinator).

At each visit, subjects will be asked if they are experiencing any adverse effects or difficulties with the study. The Principal Investigator will review all reports to determine if changes are needed to any of the study related procedures or if the subject has symptoms / difficulties that would warrant discontinuation from the study.

Data Analysis

Time to lapse: The primary outcome, time to lapse following the week 0 visit, will be evaluated using a two-sided log-rank test. Since drop-outs could be more likely to lapse, we will perform two tests: one censoring drop-outs at the time of their last visit, and one considering drop-outs as lapsed at the time of their last visit. Randomization of 140 subjects should balance the groups with respect to potential confounding factors, and therefore no adjustment for other factors is planned. The same procedure will be used for the secondary outcome of time to relapse.

Other outcomes: Several continuous outcomes will be measured at baseline and subsequent time points, such as motivation and self-efficacy to quit, support for a menthol ban, severity of craving, perceived health risk, urinary cotinine concentrations, and exhaled CO. We will first calculate the change in each subject's outcome from baseline to the week 26 visit, and compare the study groups using two-sided, two sample t-tests. This will provide a straightforward comparison of whether cessation of menthol use affects long-term nicotine use and perceptions. Second, we will use analysis of variance (ANOVA) with repeated measurements to further analyze trends over all visits in the study period, with group, time, and interaction effects. This would identify more precisely when particular changes took place, or if any group differences emerged around the quit attempt but diminished by the end of the study. Changes in tobacco product use within groups will be summarized qualitatively and by descriptive statistics such as proportions.

Power and Sample Size: Our primary outcome is time to lapse. Previous studies have found that during a cessation attempt most participants lapse within one week, at a median of 2-3 days after their quit attempt (35, 36). We plan on enrolling 140 subjects randomized 1:1 with an approximately 15% post-randomization visit dropout rate, leaving 120 subjects with data on time to lapse. This gives us over 80% power to detect a 1.7-fold difference using a significance cutoff of 0.05. We believe that such a difference would be a meaningful indicator of smoking success. The 1.7 fold difference in time to lapse is substantially smaller than is typically seen with medication studies. For example, an analysis by Shiffman et al (J Consult Clin Psychol 2006;74:276-85) found that the median duration of abstinence (i.e. time to lapse) was 6 days for active nicotine patch and 2 days for placebo. That would correspond to a 3 fold difference. Directly comparable data for other interventions is not available, however in a study comparing placebo to five different pharmacotherapy options (i.e. bupropion, nicotine lozenge, patch, bupropion + lozenge, patch + lozenge), the time until 50% of participants in the placebo group lapsed was approximately 6 days whereas the time for all other groups (except for nicotine lozenge) the time until 50% of participants lapsed was over 20 days (Japuntich et al. J Consult Clin Psychol 2011;79:34-42), an over 3-fold difference. Likewise, we

would have 80% power to detect an effect size of 0.6 in continuous secondary outcomes (i.e. a difference in group means of 0.6 times the outcome's standard deviation). Since it is not clear what the smallest difference is that would be important to detect, we believe that this samples size will be able to detect a meaningful difference.

Data and Record Keeping:

Data will be managed by the study coordinator(s). To ensure confidentiality, all subjects will be assigned a study identification code to be used on all data collection forms except those for which use of personal identifiers is mandatory (e.g., informed consent form). Forms that link the name of the participant and the subject identification code will be kept in a locked cabinet or office or in an electronic file stored on password protected secure computer servers that meet university gguidelines for ensuring patient confidentiality. Access to subject identifiable information will be limited to those that require this information such as study investigators or others who have direct contact with study subjects (e.g., study coordinator).

Data for this study will be entered into a REDCap database. This database is housed on secure servers which are operated by the University of Minnesota Academic Health Center's Information Systems group (AHC-IS). Access to the database will be restricted to members of the study team by username and password. Specific information regarding the database design and features can be found on the Clinical and Translational Science Institutes website, http://www.ctsi.umn.edu/research/tools-software/REDCap/ .

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