Document Cover Page

Official Title of the Study: Project Q Pilot: Smoking Cessation for Light Smokers

NCT Number: NCT03416621

Date IRB Approved: 1/17/2020

Project Q Pilot

PURPOSE OF THE STUDY

The purpose of this pilot study is to evaluate the feasibility, acceptability, and preliminary efficacy of an intervention to promote smoking cessation among light daily and intermittent smokers. The intervention will include a combination of cognitive-behavioral cessation counseling and cue exposure treatment. This pilot study aims to test tailored intervention strategies for light smokers. We will use data from this pilot as preliminary data for a P01 grant application we will resubmit to the National Cancer Institute in January 2020.

BACKGROUND & SIGNIFICANCE

Light daily and intermittent smokers (smoking ≤10 cigarettes per day or on some days) now represent almost half of all people who smoke; yet, smoking even a few cigarettes a day or even on some days increases morbidity and mortality[1]. Despite this, light smokers continue to be excluded from most cessation trials. Further, exclusion of light smokers from cessation trials contributes to health disparities as many light smokers are African American or Latinx, who suffer more from smoking-related diseases than Whites. Thus, researchers have been attempting to design interventions to help light smokers quit with some but limited success[2-6]. We argue that we do not understand enough about why light smokers have a different pattern, and therefore, cannot find effective ways to help them quit. Also, there are subgroups of light smokers. Some light smokers have always smoked 10 or fewer cigarettes a day (i.e., native light smokers) whereas others were formerly heavier smokers but now are light smokers (i.e., converted light smokers)[7]. To date, most researchers have designed interventions for light smokers that mimic those found effective for moderate to heavy smokers. These interventions have been based on the two-factor model for smoking behavior[8], addressing both nicotine dependence and situational and environmental responses to cues to smoke. Thus, the interventions included pharmacological agents that principally attenuate nicotine withdrawal effects or make nicotine less rewarding and behavioral and cognitive components that teach coping skills to overcoming urges in response to cues as well as increasing self-efficacy, outcome expectations, and problem-solving skills. However, these interventions have had limited success with light smokers. Different approaches might be necessary to help light smokers quit.

This pilot will build upon the hypothesis that while nicotine dependence may still play a role in light smoking, situational and environmental cues primarily drive light smoking. Thus, focusing on cue reactivity rather than just addressing nicotine dependence might be more effective at promoting cessation among light smokers. The behavioral aspect of cognitive-behavioral treatments might be more important for light smokers.

Thus, effective cessation programs for light smokers need to incorporate traditional cognitive strategies that promote self-regulation, behavioral learning strategies to optimize the ability to unlearn smoking cues, and elements to increase motivation, decrease barriers, increase self-efficacy and improve outcome expectations.

In this small, randomized controlled pilot trial, we will test the feasibility, acceptability, and preliminary efficacy of a combination of cognitive behavioral cessation counseling and cue exposure treatment, a cue driven treatment that has been found effective in the treatment of substance use. Further, we will extend cue exposure therapy beyond the clinic or laboratory by using interactive texting to help light smokers transfer their newly learned cue extinction skills into their natural environment. Interactive

texting will include both self-monitoring and extinction of cue extinction skills. Interactive texting for real-time data collection will include participants taking photographs of cues they identify as salient and triggering of their desire to smoke as well as texting when they smoke and their craving levels. We will incorporate the participants own photographs into their tailored cue exposure treatment conducted in the clinic

Specific Aims

Aim 1: To assess the feasibility of an enhanced cue exposure therapy intervention. This aim will specifically address the number of participants recruited and the number of participants who complete all study visits.

Aim 2: To evaluate and compare the acceptability of cue exposure therapy compared to standard smoking cessation counseling and support text messages as measured by participants' ratings of the usefulness of the intervention.

Aim 3: To compare the preliminary efficacy of an enhanced cue exposure therapy compared to standard smoking cessation and support messages in light smokers as measured by a) self-report 7-day point prevalence abstinence from smoking and b) biochemically validated smoking cessation.

DESIGN & PROCEDURES

Design

The two-arm trial compares Arm 1) standard smoking cessation counseling and 2) enhanced cue exposure treatment. For all arms, we will conduct a phone screening, provide smoking cessation counseling, and an in-person follow-up visit. The primary outcome will be feasibility and acceptability. The secondary outcome will be biochemically-validated cessation 1-week post-intervention.

Consent Process

Study staff will call people who express interest in the study and conduct a phone screening. Those eligible will be asked to come in-person to consent and complete the baseline visit. Study staff will meet potential participants to obtain informed consent.

Data Collection Methods

For all arms:

The baseline survey will include questions about demographics, smoking factors, and household information. The follow-up surveys will include some of the same questions as the baseline as well as process questions to assess helpfulness of the messages and participants' fidelity to the intervention protocol. The primary outcome will be assessed using seven-day point prevalence abstinence (e.g., Have you smoked any cigarettes in the past 7 days?) and biochemically validated through saliva analysis.

Saliva samples: Saliva samples from participants at baseline and follow-up will be used to biochemically validate the participant's smoking status. NicAlert strips will be used to measure the cotinine levels in the saliva at baseline and follow-up.

Text-message real-time data collection: We will ask participants in Arm 2 to text study staff every time they smoke and every time they have a strong urge to smoke for four consecutive days. The system will ask participants to rate their level of craving (1-10) and stress (1-10) via text. We will also ask participants in Arm 2 to take and text several photos of the situation in which they smoked/had the urge to smoke. Additionally, we will ask all participants to text the system every time they feel like smoking or

have an urge to smoke between Visits 2 and the follow-up visit. The system will ask the same questions about craving and stress but participants will not be asked to text a photo. For Arm 2 participants, the system will reply with a supportive message to encourage the participant not to smoke along with the questions. Participants will be instructed not to text while driving and only to text when it is safe to do so.

Cue exposure therapy measures: Participants will sit in front of a computer screen while the screen shows a PowerPoint presentation composed of a repeating set of images. Each set will include standardized smoking images and images that have been shown to make people who smoke want to smoke. These images will be from the International Affective Picture System (IAPS), a database of images designed to provide a standardized set of pictures for studying emotion and attention. Also, we plan to use 4-6 of the smoking images that participants have sent themselves. We will only show participants their images, not images taken by other participants. Additionally, participants will also be exposed to in vivo cues by following instructions to touch/hold/smell smoking paraphernalia, including cigarettes, ashtrays, and lighters.

A participant can miss completing any time point/study visit and it is not considered a protocol deviation.

STUDY INTERVENTIONS

Randomization

We will randomize participants into one of two arms: Arm 1) standard smoking cessation counseling and2) enhanced cue exposure treatment. The randomization will be automated and drawn from a random number generated list programmed onto the laptops. We will stratify randomization on the number of cigarettes per day and native /converted smoking status.

Intervention and Control Activities

Study staff will meet with all enrolled participants to conduct standard smoking cessation counseling (Visit 1: Baseline). At Visit 1, all participants will receive standard smoking cessation counseling, be asked to select a quit date. All participants will receive detailed instructions on how to collect real-time data on their smoking habits and craving levels. Arm 2 participants will be asked to identify smoking cues that they will photograph and also will receive detailed instructions on how to take and send pictures. Participants will select 4 consecutive days for collecting real-time data.

After Visit 1, participants in Arm 2 will text the study phone number every time they smoke for 4 consecutive days. The system will text questions related to the smoking encounter to the participant. Arm 2 participants will text a photo of the context in which they smoked. These photos will be used in in-person cue exposure therapy.

<u>Visit 2</u>

Arm 1 and 2 participants:

At Visit 2, all participants will meet in person with study staff to receive tobacco cessation counseling. All participants will complete a brief smoking assessment. Study staff will conduct smoking cessation counseling for both arms. The system will text the participant to collect data about the cue and the outcome. Questions include if the participant smoked or not, craving level, and stress level. Participants are instructed to continue to text the system up to the follow-up visit (approximately 4 weeks total).

Visit 2:
Arm 2 participants only:
Study staff will review a summary of their real-time smoking data and then explain the process for cue exposure therapy. Participants will first complete a brief assessment including a questionnaire of smoking urges (QSU) (10 items), Minnesota Nicotine Withdrawal Scale (MNWS) (10 items), and the Positive and Negative Affective Schedule (PANAS) (20 items). Study staff will then explain the process for cue exposure therapy.

Participants will sit in a room lit with a table lamp. They will sit in a comfortable chair in front of a computer screen to watch the presentation. The presentation will include repeating blocks of images. The image blocks include a mixture of standard photos and the individual's photos. After each block, the participants will see a slide instructing them to uncover a tray located in front of them that contains cigarettes, ashtray and lighter. They will be instructed to touch/hold/smell smoking paraphernalia on the tray. After approximately 2 minutes, they will be instructed to cover the tray.

After completing the cue exposure treatment (CET), the study staff will review how they can apply these processes outside the lab setting when the participant faces a cue to smoke over the next month. Each image viewed in the CET presentation will have a simple logo with words in the bottom right-hand corner. This image will be used as a retrieval cue to remind participants of the CET experience when in the real-world setting. Participants will be instructed to text the team anytime they feel an urge to smoke and need support to not smoke at that moment. The system will send the retrieval cue along with a supportive message.

Visit 3
Arm 1 and 2 participants:
After approximately one week, all participants will return for Visit 3. The procedures will be the same as Visit 2, completing the brief smoking assessment and standard smoking cessation counseling. Visit 3 is the last counseling session for Arm 1 participants.

Arm 2 participants:
Participants will also complete cue exposure therapy. This process repeats so participants will come in on a weekly basis for a total of 4 treatment visits (Visits 2, 3, 4, and 5) and will complete the same process as described for Visit 2.

Follow-up
For the final visit, participants from all arms will return to the Tobacco Cessation Lab to complete the follow-up assessment. This will occur one week after Visit 5 and one week after Visit 4, respectively. They will complete a questionnaire and we will assess abstinence via 7-day point prevalence. Participants will provide a saliva sample to biochemically validate their smoking status based on their cotinine levels. At the follow-up visits, we will ask participants if we can contact them after to ask for feedback on the pilot study. If they agree, we will call them or meet them in person to ask for their input.

Participants may also be asked at the time of visits to be audio-recorded for data or quality assurance purposes. They can refuse to be audio-recorded and can still participate in the study.

SELECTION OF SUBJECTS

Eligibility

For all arms:

Adults will be eligible to participate if they meet the following criteria:

- Age: ≥18
- Able to read and understand English
- Cognitively able to provide informed consent
- Daily smoker
- Smoke 1-10 cigs/day on average for the last year
- Express a desire to quit smoking in the next 30 days
- Access to a cell phone that can send and receive SMS text messages and take and send pictures

Exclusion criteria for all arms:

- Use (within the past 30 days) of:
    - Psychiatric medications including antidepressants (MAOIs, St. John's Wort), lithium, antipsychotics, or any other medications that are known to affect smoking cessation (e.g. clonidine);
- Current use of:
    - Wellbutrin, bupropion, Zyban, Chantix, varenicline, nicotine patch, nicotine replacement therapy or any other smoking cessation aid;
- Current participation in another smoking study at our Center or another research facility;
- Participated in Duke Smoking Cessation Program in the last year

SUBJECT RECRUITMENT & COMPENSATION

Screening and Recruitment

We will recruit participants into this low-risk study through Duke Center for Smoking Cessation, Facebook, flyers in public locations, DukeList, Duke Primary Care clinics through the Primary Care Research Consortium, and Durham Public Housing.

Staff will conduct the study in Hock Plaza. When participants call to express interest in a research study, staff will screen them for the study.

At participating clinics in Durham, Wake, Orange, and Chatham counties, with a HIPAA Waiver of Authorization, DHTS will conduct a DEDUCE query to identify potentially eligible patients. We will send patients who report tobacco use of "Light tobacco smoker" and/or "Current everyday smoker" "Smokes some days" a letter from their provider informing them of the study and asking them to call a study phone number if they prefer not to be contacted about study participation. If an email address is accessible for these patients, we may also attempt to email them these documents. We will call or text people who do not call to refuse to screen them for eligibility and set up a screening visit.

The Center for Smoking Cessation and the Nursing School will post Facebook ads through their Facebook accounts. The Facebook ad includes a link to a Qualtrics survey that asks the participant for their contact information. El Centro Hispano staff will refer light smokers to the Qualtrics link as well. Study staff will call those interested people who complete the Qualtrics survey to assess eligibility. The eligibility screening will: confirm a patient's age, smoking status, interest in quitting smoking, use of other tobacco products, pregnancy status, breastfeeding status, and history of serious adverse reaction to cycloserine in the past.

Participants can receive up to $150 to complete all aspects of the study. Participants will receive $50 for completion of surveys at Visit 1 and $100 at the follow-up visit. Participants will not receive

compensation for Visits 2, 3, 4 or 5 as these are intervention visits and we want the motivation to quit smoking to be intrinsic rather than extrinsic. Providing monetary compensation during these intervention sessions can interfere with this.

RISK/BENEFIT ASSESSMENT

Potential risks of study participation include breach of confidentiality with regard to identifiable personal information. Some of the questions participants will be asked might make them feel uncomfortable. All participants may refuse to answer any of the questions and may stop their participation in this study at any time. All of this is outlined in the written consent form the patient signs at the time of enrollment into the study.

Quitting smoking may cause nicotine withdrawal that may lead to headaches, irritability, weight gain, difficulty concentrating, poor sleep, increased appetite, anxious or depressed mood, and craving for cigarettes. Risks associated with drawing blood from the arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although very unlikely.

There may be a direct medical benefit to the participants as they might quit smoking. They also might find the intervention to be helpful. What we learn from the participants in the study will help us develop a P01 grant application being re-submitted to the National Cancer Institute in January 2020.

COSTS TO THE SUBJECT

There will be no additional costs to the participant as a result of being in this study.

DATA ANALYSIS & STATISTICAL CONSIDERATIONS

The purpose of this study is to evaluate the feasibility, acceptability, and preliminary efficacy of an intervention to promote smoking cessation among light smokers. The intervention arms will be compared using descriptive statistics. Results from these analyses will be used to prepare a P01 grant application.

Statistical Analysis of Feasibility Aim 1: For this feasibility aim, the two arms will be combined. We have two feasibility metrics. We will consider the intervention feasible if we enroll 6 light smokers per month and 75% complete at least 2 study visits.

Statistical Analysis of Aim 2: For this acceptability aim, we will ask participants in all arms how useful the intervention was (1="Not at all useful" to 5="Extremely useful"), whether the intervention will change their smoking (1="Will not change at all" to 5="Will change a lot"), and whether they would recommend the program to a friend (1="Definitely would not recommend" to 5="Definitely would recommend"). For the intervention to be deemed acceptable, 75% of participants in Arm 2 would have to rate each item a "4" or a "5." Note that this decision rule has nothing to do with the efficacy of the control arm. The percentage of participants endorsing "1", "2", "3", "4", and "5" on each of the three Likert-scaled items will be calculated and compared between arms. This comparison will be used to detect any unexpected, gross difference between arms. For example, if arm median on "how useful was the intervention?" were "2" and "5", this result would be considered both unexpected and noteworthy regardless of which arm did better.

Statistical Analysis of Aims 3 and 4: This aim will compare the arms on the efficacy of the intervention. We'll start by calculating an estimated prevalence (with 95% confidence interval) for the binary measure of point prevalence, with the confidence interval based on the standard formula for the standard error

or a binomial proportion. We're interested in all 3 pairwise comparisons between the groups, recognizing that only the comparison between groups 1 and 2 is randomized. Each of the comparisons would be based on a chi-square or Fisher's exact test as appropriate. Because this is a pilot study, which is not intended to be a definitive assessment of efficacy all 3 comparisons, we would use a cut-off value of p=0.05 for declaring statistical significance.

DATA & SAFETY MONITORING

The quality of data collection will be enhanced through extensive training of all personnel involved in data collection. Quality control checks will include feedback on protocol fidelity, interpersonal skills, and data entry and cleaning.

We will monitor participant safety by maintaining ongoing contact with staff and convening weekly meetings between the investigators and the project team. The study field staff will be trained and provided with a written protocol that instructs them to contact the Project Coordinator if any reportable AE occurs. The Project Coordinator will follow-up with participants within 48 hours to ensure that the event has been resolved and document actions. All non-reportable AEs will be reported to the Principal investigator at regular meetings and the IRB via annual reports.

PRIVACY, DATA STORAGE & CONFIDENTIALITY

Prior to any physical screening procedures, we will inform participants in their consent forms of the data storage and confidentiality safeguards, which are practiced according to current HIPAA regulations. Study records that identify participants will be kept confidential as required by law. Blood and urine specimens will be sent to LabCorp for processing. Name, date of birth, and gender will be included with each specimen. Except when required by law, participants will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS) (except to LabCorp). For records disclosed outside of DUHS, participants will be assigned a unique code number. The key to the code will be kept in a locked file in the PI's office separate from the locked file where the study records are stored.

People Designs, a Durham-based consulting and development firm, will manage the texting system. Texting data will be housed on a web-accessible interface behind the Duke firewall so that study staff can access the participant texts and data is stored securely. Only People Designs staff listed on the Outside Key Personnel list will have access to the system and text-based data.

Data will be collected by staff both in person and on the telephone. All participants will be assigned a code number that is the sole identifier on all study data forms. Survey data will be collected on paper-and-pencil surveys and entered into computers via a password protected REDCap form on a secure network server. Participants may also complete the surveys directly into REDCap. Study staff may enter data directly into REDCap during the interviewer-administered surveys. Access will only be granted to study staff who need to access the data. Staff will store active participant files in personal locking file cabinets. Access to this file will be limited to study personnel.

References

1. Jamal A, King BA, Neff LJ, Whitmill J, Babb SD, Graffunder CM. Current Cigarette Smoking Among Adults - United States, 2005-2015. *MMWR Morbidity and mortality weekly report.* 2016;65(44):1205-1211.
2. Ahluwalia JS, Okuyemi K, Nollen N, et al. The effects of nicotine gum and counseling among African American light smokers: a 2 x 2 factorial design. *Addiction (Abingdon, England).* 2006;101(6):883-891.
3. Cox LS, Nollen NL, Mayo MS, et al. Bupropion for smoking cessation in African American light smokers: a randomized controlled trial. *Journal of the National Cancer Institute.* 2012;104(4):290-298.
4. Cabriales JA, Cooper TV, Salgado-Garcia F, Naylor N, Gonzalez E. A randomized trial of a brief smoking cessation intervention in a light and intermittent Hispanic sample. *Experimental and clinical psychopharmacology.* 2012;20(5):410-419.
5. Gariti P, Lynch K, Alterman A, Kampman K, Xie H, Varillo K. Comparing smoking treatment programs for lighter smokers with and without a history of heavier smoking. *Journal of substance abuse treatment.* 2009;37(3):247-255.
6. de Dios MA, Anderson BJ, Stanton C, Audet DA, Stein M. Project Impact: a pharmacotherapy pilot trial investigating the abstinence and treatment adherence of Latino light smokers. *Journal of substance abuse treatment.* 2012;43(3):322-330.
7. Pollak KI, Fish LJ, Lyna P, Peterson BL, Swamy GK, Levine MD. Predictors of pregnant quitters' intention to return to smoking postpartum. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco.* 2015;17(6):742-745.
8. Shiffman S, Dunbar MS, Ferguson SG. Stimulus control in intermittent and daily smokers. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors.* 2015;29(4):847-855.
9. Rodrigues H, Figueira I, Lopes A, et al. Does D-cycloserine enhance exposure therapy for anxiety disorders in humans? A meta-analysis. *PLoS One.* 2014;9(7):e93519.
10. Ashare RL, Schmidt HD. Optimizing treatments for nicotine dependence by increasing cognitive performance during withdrawal. *Expert opinion on drug discovery.* 2014;9(6):579-594.
11. Santa Ana EJ, Rounsaville BJ, Frankforter TL, et al. D-Cycloserine attenuates reactivity to smoking cues in nicotine dependent smokers: a pilot investigation. *Drug and alcohol dependence.* 2009;104(3):220-227.
12. Nesic J, Duka T, Rusted JM, Jackson A. A role for glutamate in subjective response to smoking and its action on inhibitory control. *Psychopharmacology (Berl).* 2011;216(1):29-42.