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Isradipine enhancement of virtual reality cue exposure for smoking cessation

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Study Protocol

Eligibility Screening

Internet Prescreen. Individuals interested in participating in the study will be directed via various recruitment strategies to an Internet prescreen using REDCap. This prescreen is a joint prescreen used by several other IRB-approved smoking studies[1]. The prescreen procedure is the first point of contact for participants, and it will allow us to ask critical information about the potential participant's willingness and ability to commit to the frequency of clinic visits as well as the assessment of inclusion criteria. If a participant passes the Internet Prescreen, they will be directed to a scheduling platform called You Can Book Me. Participants will sign up for a time slot for the phone screen.

Phone Screening. The phone screen is an opportunity for research assistants to give potential participants more information about the study and to further assess inclusion/exclusion criteria. Research assistants will follow a phone screen script (see attachment) which includes the Columbia-Suicide Severity Rating Scale (C-SSRS; see Measures). If there is evidence of a suicidal risk, the trained research assistants will follow the Suicidality Standard Operating Procedures (see attachments). Participant responses will be stored on REDCap. Participants who are interested and eligible will schedule an additional phone screen with the study nurse, Dr. Cara Young, to discuss their medical history. Participants who are not interested, or ineligible will be provided with smoking treatment referrals (see phone screening script).

Baseline Survey. The Baseline survey will be administered during CET 1 during the waiting period for the study drug. This will include further demographic measures, medical questions, and baseline smoking measures such as the Smoking Cue Appeal Survey (SCAS) and Overall Anxiety Scale (OASIS). Previously, all of these questions were included in the Internet Prescreen survey. The Internet Prescreen has been shortened to more effectively recruit participants.

In-Person Physical Exam. The ICD will be sent to participants via REDCap before the appointment so that they have time to read through the form and give their informed consent by signing the form digitally with a mouse or mouse pad. Upon arrival, if the participant has not signed the ICD, they will first read the ICD on a computer or iPad and provide their signature if they choose to participate. A study coordinator will be available to answer any questions the participant may have about the study and participation. If the individual chooses to sign the informed consent, he or she will proceed with the physical exam. Study personnel trained in advanced health assessment (PI, Cara C. Young, PhD, RN, FNP-C or other qualified study personnel under the supervision of Dr. Young) will conduct a cardiac and respiratory exam to determine if it is safe for them to take the study medication. In addition to a cardiac and respiratory focused history and physical exam, vital signs to include temperature (Temp), pulse (P), respiratory rate (RR), and blood pressure (BP) will be obtained. Participants will be immediately excluded from the study if any abnormal findings are identified within the cardiac or respiratory physical exam. Vital signs outside normal limits will be handled thusly, (a) BP < 90/60 or >140/90, BP will be reassessed in 5 minutes. If BP is still outside limits participants will reschedule their physical exam within 1 week. If upon return BP is < 90/60 or >140/90 participants will be excluded from the study; (b) P < 60 or >100, recheck in 5 minutes. If P is still outside limits, participant will reschedule their research session within 1 week. If upon return P is < 60 or >100 participant will be excluded from the study; (c) RR >20, RR will be reassessed in 5 minutes, if RR is still outside limits, participants will reschedule their physical exam within 1 week. If upon return RR is >20 participant will be excluded from the study; (d) Temp > 100.4, participants will reschedule their research session within 1 week. If upon return Temp is >100.4 participants will be excluded from the study. If the advanced practice nurse deems it is unsafe for the participant to take the study medication, they will be notified, thanked for their time, and dropped from the study. All eligible participants will continue with the rest of the visit which includes introduction to the goals of research study, and an explanation of data collection documents. Research personnel will also discuss the potential side effects of isradipine with potential participants.

Randomization

Santiago Papini or Alex Perrone will oversee the randomization to either CE+ISR or CE+PBO conditions. Both participants and study personnel will be blind to study condition, and study medication will be labeled by either "A" or "B" by the pharmacy in order to blind the medication administration. A random number generator will be used to assign individuals to either condition. Only Mr. Papini or Mr. Perrone will have the information necessary to break the blind. Prior to data analyses, Mr. Perrone will check the balance of randomization and control for any factors that are imbalanced.

Intervention Modules

Abstinence Challenge. Eligible participants will be required to abstain from smoking beginning 24 hours prior to the physical exam that occurs on the day of the first CE session and up until the time of the second session. Abstinence status will be verified by a Vitalograph Breathco Carbon Monoxide monitor (≤4 ppm). If a participant is not abstinent at the time of the physical exam and CE session 1, the participant will be asked to re-schedule within 1 week. In order to ensure compliance with alcohol abstinence 24 hours prior to CE session 1 and 24 hours after CE session 1, abstinence status will be verified by an AlcoBreath measurement at the beginning of CE session 1 and the beginning of CE session 2. If a participant is not abstinent at the time of CE session 1, the participant will be asked to re-schedule within 1 week.

Ecological Momentary Assessment (EMA). Eligible participants will be asked to respond to surveys delivered via text message or email up to 15 times per day 24-hours prior to the physical exam and up until the time of Cue Exposure Session 2 (48 hours total). Participants will be asked various questions related to smoking craving, behavior, and cues (see attached Short Smoking Log).

Cue Exposure (CE). The two 60-minute CE sessions will be conducted to expose participants to interoceptive and situational cues for tobacco use and craving (see Cue Exposure Therapy Protocol attachment). In the first session, participants will receive a dose of ISR or PBO and begin the CE session after waiting 75 minutes. The overarching goal of CE is to expose participants to triggers that will produce high cravings, and to repeat exposure to those triggers in a controlled setting in order to allow the craving to come down on its own. Because not all smokers respond equally to the same triggers, clinicians are trained to apply a variety of approaches. These can include exposure to slides, videos (on a traditional flat screen as well as in 360 video headsets) depicting smoking cues (visual exposure), exposure to emotions and imagined situations that most reliably triggered an urge to smoke (emotional/imaginal), and exposure to a participant's own cigarettes (in vivo). The second session will be conducted 24 h after the first in a medication-free state. Clinicians will record craving throughout the CE sessions (see Reported Craving During CE attachment).

Isradipine or Placebo. All capsules will be identical in appearance to maintain the blind design of the study. Study capsules will be prepared containing: (a) 15 mg immediate release isradipine or (b) pill placebo. Individual doses of study medications, prescribed by Dr. Young, will to be dispensed to patients by study personnel 75 minutes prior to CE 1 and patients will be asked to remain in the clinic until session time. Because all pill taking is observed, no pill counts are necessary to help ensure adherence to the randomized drug condition. The drug will be prepared at Abrams Royal (8220 Abrams Road, Dallas, TX 75231). All medications will be stored in a locked refrigerator. Upon completion of recruitment, unused medication will be returned to the pharmacy for proper disposal.

SUMMARY OF VISITS

	Physical Exam	**Cue Exposure Day 1**	**Cue Exposure Day 2**
Length:	30 minutes	2.5 hours	1 hour

Purpose:	- Ecological Momentary Assessment 24-hours prior to Day 1 visit (text) -Determine your eligibility by ensuring that it is safe for you to take isradipine. - Receive $10 cash payment.	-Take isradipine or placebo, wait 75 min, do 60 min of cue exposure. - Receive $30 for Day 1 and $2 per EMA response (up to $30), for a total of up to $60 for Day 1.	- Ecological Momentary Assessment 24-hours prior to Day 2 visit (text) - Do 60 min of cue exposure without taking isradipine or placebo (no medication). - Receive $50 for Day 2 and $2 per EMA response (up to $30), for a total of up to $80 for Day 2.

Measures
Assessment Instruments

Screening Measures
Initial Eligibility Screen. This questionnaire will assess some of the basic inclusion and exclusion criteria. This will be collected in the online prescreen.

Demographics. Participants will be asked to provide standard demographic information (i.e. age, gender, race/ethnicity, level of education, etc.) as well as history of medical problems. This will be collected in the online prescreen.

Suicide. The Columbia Suicide Severity Rating Scale (C-SSRS; Posner, Oquendo, Gould, et al. 2007) is a standardized measure of current and past self-injurious behavior, suicidal intent, and suicidal behaviors. The C-SSRS has demonstrated good reliability and validity (Hammad et al., 2006; Posner et al., 2007). The C-SSRS will be administered as part of the diagnostic interview in order to assess for a history of suicide attempts or current suicidal thoughts or plans. This will be collected during the screening visit. The IRB-approved standard operating procedures for individuals who pose a suicide risk will be followed (see attached Suicidality SOP).

Vital Signs. Temperature (Temp), pulse (P), respiratory rate (RR), and blood pressure (BP) will be obtained. This will be collected during the screening visit, CE visit 1 and 2.

Medical evaluation. A study advanced practice nurse will review the patient's medical history and conduct a complete physical examination if deemed necessary. This will be collected during the screening visit.

Overall Anxiety Scale (OASIS): The OASIS is a 5 question self-report instrument that measures transdiagnostic anxiety symptoms (Norman et al., 2006).

Measures of smoking behavior, nicotine dependence, withdrawal symptoms, and sleep measures

Fagerström Test for Nicotine Dependence (FTND). The FTND is a 6-item scale designed to assess gradations in tobacco dependence (Heatherton et al., 1991). This measure will serve to quantify nicotine dependence, which will be used as a covariate in the primary analyses. This will be collected during the screening visit.

Minnesota Withdrawal Scale (MWS). Given its potential relation to outcome, we will monitor withdrawal severity using the Minnesota Withdrawal Scale, a reliable and sensitive 10-item scale (Hughes & Hatsukami, 1986). This will be collected at CE visit 1 and 2.

Smoking Cue Appeal Survey (SCAS). The Smoking Cue Appeal Survey (Murray, McHugh, Rowley, Sirota, & Otto, 2010) measures cue appeal to sensory smoking cues. An initial study demonstrated good psychometric properties associated with smoking status and craving (Murray et al., 2010). This will be collected during the screening visit, CE visit 1 and 2.

Pittsburgh Sleep Quality Index (PSQI) and Sleep Diary. The Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a self-reported questionnaire which assesses sleep quality and disturbances. The question items group into seven component scores: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. In addition, a short self-report sleep diary will be administered in order to record the previous night's sleep. The sleep measures will be used to examine the impact of sleep on the efficacy of exposure therapy and may also be used as a covariate in primary analyses. The PSQI will be collected at CE visit 1 and the Sleep Diary will be collected at CE visits 1 and 2.

Perceived Treatment. A single self-reported item will be asked to examine whether the participant believes they received the active treatment study drug or a placebo.

Measures of research integrity, safety, and acceptance

Vital Signs. Participants' blood pressure and heart rate will be assessed. This will be collected during the screening visit, CET visit 1 and 2.

Patient Adherence. Patient adherence will be assessed by taking attendance at each session.

Researcher Adherence. Each session (for those participants who give consent to be videotaped) will be videotaped and 10% will be rated shortly thereafter by independent raters to assess therapist adherence to, and competence with, the experimental protocol. Participants are not required to be videotaped and will indicate on their ICD whether or not they are willing to participate in the recording of sessions. Sessions from CE visit 1 and 2 will be reviewed.

Concurrent Treatment. Use of medications other than nicotine patch or other aids to smoking cessation and participation in any concurrent psychotherapeutic treatment will be assessed. This will be collected during the screening visit, CE visit 1 and 2.

Safety Monitoring and Concerns**.** At each visit, participants will be asked about side effects of the study medication and procedures. Adverse Events forms will be utilized to track any symptoms expressed during study visits. Forms will be reviewed each visit by the study PI, and participants who report significant symptoms or adverse reactions will be interviewed separately. This will be collected during the screening visit, CE visit 1 and 2.

AlcoBreath Screening. Participants will be asked to breathe into an AlcoBreath tube in order to assess for the presence of alcohol. Although there are no absolute contraindications to co-administration of isradipine with alcohol, both substances are metabolized through the liver. Participants are advised to refrain from alcohol for at least 24 hours prior to administration of isradipine and 24 hours after administration of isradipine. This will be collected during the screening visit, CE visit 1 and 2.

Assessment Schedule

Participants will receive thorough assessments prior to and over the course of this study, summarized in the table below.

Measure (number of items)	Online/phone Screen	Daily monitoring until quit attempt	Physical Exam	CE visit 1	CE visit 2
Initial eligibility screen	X				
Demographics	X				
Columbia Suicide Severity Rating Scale - CSSRS	X				
Overall Anxiety Scale OASIS (5)	X				
Fagerström Test for Nicotine Dependence - FTND (6)	X				
Medical history	X				
Carbon Monoxide (2)			X	X	X
Minnesota Withdrawal Scale - MWS (15)				X	X
Smoking Cue Appeal Survey -SCAS (8)	X			X	X
Pittsburgh Sleep Quality Index - PSQI				X	
Sleep Diary				X	X
Therapist Adherence				X	X
Patient Adherence		X		X	X
Adverse Events			X	X	X
Vital Signs			X	X	X
AlcoBreath			X	X	X
Perceived Treatment					X
Smoking log surveys		X			

Data Analyses

<u>Specific Aim 1: Effect on Long Term Craving</u>

To examine effects on the target of engagement, we will test the hypothesis that CE+ISR, compared to CE+PBO, will have a greater reduction in reduce subjective craving to smoking cues in a subsequent medication-free cue exposure conducted 24-hours later (CE 2).

<u>Analytic approach:</u> A mixed factorial ANOVA will be used to test whether reduction in craving over the course of CE session 2 significantly differ across groups (CE+ISR vs. CE+PBO). More specifically, a 2X2 mixed (within-between) factorial ANOVA will be conducted with Group (2 levels: CE+ISR vs. CE+PBO) as the between-subject variable and Trials (2 levels: the first and last trials during the CE session 2) as the within-subject variable to examine the Group X Trial interaction effects on craving. A separate analysis (ANCOVA) for the same model will be conducted, controlling for sex and baseline nicotine dependence. In addition, potential moderating roles of sex and baseline smoking severity on the effect of CE+ISR (vs. CE+PBO) on craving at the first trial during the CE session 2 will be explored by using two-way ANOVA to test the Group X Moderator interactions or linear regression models with Group X Moderator interaction terms.

Specific Aim 2: Feasibility and Acceptability of Implementation: Descriptive statistics will be calculated for the questionnaire to assess overall clinic staff views of feasibility, acceptability, and ease of implementation. A qualitative descriptive approach[81] will be used to analyze semi-structured interview transcripts using content analysis to systematically code and categorize for trends and patterns in the textual data to remain as close to the staff's experiences as possible[82]. We have successfully used similar approaches in prior studies.[83–85]

C3g. Sample size and power considerations

Based on the sample size calculation using G*Power, a total sample size of 102 (n=51 for each group) will be sufficient to detect a small effect size (f=0.1) in Group (between-subject) by Trial (within-subject: craving ratings for the first and last trials during CE session 2) interaction on craving using mixed (within-between) factorial ANOVA/ANCOVA, with 80% power, an alpha of 0.05, and a correlation coefficient between repeated measures (the first and last trial) of 0.75.

D. Limitations and alternative considerations

While a variety of indirect measures of craving have been proposed for humans, including behavioral indicators (e.g., rate and latency of consumption, inter-puff-interval), psychophysiological measures (e.g., startle eye-blink, skin conductance response, and heart rate) and cognitive measures (e.g., attentional and cognitive biases to drug cues), the advantages of these over subjective report is not clear.[86] Meta-analysis of cue reactivity research show robust increases in subjective craving compared to physiologic indices.[7] Although functional MRI is a powerful tool for understanding the neural mechanisms of human addiction[34,35,87], it is not feasible for this project. Importantly, treatment research employing prospective analyses[10] and ecological momentary assessment[88] have demonstrated that subjective craving post-cessation and through the abstinence phase is a robust predictor of relapse, indicating the value of a simple, direct, measure of craving and as a potential mechanistic target

The University of Texas at Austin

Consent to Participate in Research

Basic Study Information

Title of the Project: Isradipine and Virtual Reality Cue Exposure for Smoking Cessation
Principal Investigator: Cara Young, PhD, The University of Texas at Austin
Co-Principal Investigator: Jasper Smits, PhD, The University of Texas at Austin
Study Sponsor: National Institute on Drug Abuse (NIDA)

Invitation to be Part of a Research Study

You are invited to be part of a research study. This consent form will help you choose whether or not to participate in the study. Feel free to ask if anything is not clear in this consent form.

Important Information about this Research Study

Things you should know:

• The purpose of this study is to examine the efficacy of 15 mg of isradipine compared to placebo for tobacco craving reduction.
• In order to participate, you must be deemed eligible based on a brief phone screen with the study advance practice nurse, Dr. Cara Young, to discuss your medical history.

• If you choose to participate, you will be asked to choose a quit day to quit smoking for 48 hours and attend a thirty-minute physical exam in-person. If you are deemed physically healthy, you will engage in the first in-person Cue Exposure Therapy (CET) session immediately after the physical exam. The second session will occur in-person the following day. The first in-person session is 2.5 hours, the second in-person session is 1 hour.

• Risks or discomforts include withdrawal due to smoking abstinence, possible side effects of isradipine (described in detail below), possible discomfort due to exposure to smoking cues in a 360 degree

• Taking part in this research is voluntary. You do not have to participate, and you can stop at any time.

More detailed information may be described later in this form.

Please take time to read this entire form and ask questions before deciding whether to take part in this research study.

What is the study about and why are we doing it?

The purpose of this study is to examine the efficacy of 15 mg of isradipine in comparison to placebo (a pill containing no medication) for tobacco craving reduction.

What will happen if you take part in this study?

The objective of the medical phone screen is to review your medical history to determine your eligibility for participation in this research study. If you agree to participate, the first part of your

in-person visit is a 30-minute physical exam. During the physical exam, your heart rate, blood pressure, and CO will be measured. You will be asked about any cardiovascular or respiratory conditions you may be experiencing.The results will be stored on a confidential, secure, HIPAA compliant server without identifying information. Our study advance practice nurse, Dr. Cara Young, will review the report to ensure that there is no risk for isradipine administration. Together, these procedures provide the information required for the study advance practice nurse to determine whether you can safely participate in this research study.

If you qualify for the study based on the outcome of the screening assessment, you will be enrolled in the study. Inclusion in the study will involve:

• Choosing a quit day. Because we want to measure craving during nicotine withdrawal, you will select a day in which you will have the physical exam. You will be required to stop smoking 24 hours before the exam, until the end of the study. If deemed eligible, the first Cue Exposure Therapy Session (CET) will take place immediately after the physical exam. The second session will occur 24 hours later (two consecutive days). Together, you will have to remain quit for 48 hours. We will verify abstinence on both days with a carbon monoxide (CO) monitor.

• Complete short smoking logs 24-hours prior to each visit. You will receive up to 15 notifications per day to complete the short smoking log prior to the two visits. You will be asked to complete the logs as soon as you receive them. Each log should take less than 30 seconds to complete.

• Attend two consecutive visits. The purpose of the Cue Exposure Therapy (CET) is to measure your craving levels while we show you smoking related cues. In the first visit only, after the physical exam, you will be randomly assigned (like the flip of a coin) to receive either isradipine or a placebo pill 75 minutes before the first session of CET. You have a 1 in 2 chance of receiving the study drug. Please note: A placebo is an inactive substance given in the same form as the active drug (like a sugar pill). The second session will take place 24 hours after the first and will not include medication. During these visits you will also complete questionnaires related to smoking, your mood, and sleeping patterns. You will also breathe into devices that measure alcohol, and carbon monoxide. You have the option to consent to allow these sessions to be videotaped so that supervisors can monitor staff and procedures. The first visit will take approximately 2.5 hours (due to 75-minute medication wait period) and the second visit will take approximately 1 hour.

Neither you nor the study personnel will be able to choose your group. The study will be "double-blinded," meaning that neither participants nor study personnel will know which kind of tablets the participants are taking. However, in case of an emergency, study personnel can find out which dose you are taking.

It is unlikely that you will experience any symptoms from taking this pill. In case you do experience any side effects, a clinician, Cara Young, PH.D., will be available to answer any questions or concerns you may have (cell phone number: 816-596-6056).

	Physical Exam	Cue Exposure Day 1	Cue Exposure Day 2
Length:	30 minutes	2.5 hours	1 hour
Purpose:	- Ecological Momentary Assessment 24-hours prior to Day 1 visit (text) -Determine your eligibility by ensuring that it is safe for you to take isradipine. - Receive $10 cash payment.	-Take isradipine or placebo, wait 75 min, do 60 min of cue exposure. - Receive $30 for Day 1 and $2 per EMA response (up to $30), for a total of up to $60 for Day 1.	- Ecological Momentary Assessment 24-hours prior to Day 2 visit (text) - Do 60 min of cue exposure without taking isradipine or placebo (no medication). - Receive $50 for Day 2 and $2 per EMA response (up to $30), for a total of up to $80 for Day 2.

This is a research study and, therefore, not intended to provide a medical or therapeutic diagnosis or treatment. The intervention provided during this study is not necessarily equivalent to the standard method of prevention, diagnosis, or treatment of a health condition.

How long will you be in this study and how many people will be in the study?

Participation in this study will last approximately four and a half hours and 102 subjects will be enrolled in the study.

What risks and discomforts might you experience from being in this study?

There are some risks you might experience from being in this study. The physical exam is designed to evaluate the safety of the procedures, your medication use, and drug allergies. There are minimal risks associated with the screening procedures or devices. If you have any discomfort you should notify the investigators as soon as possible. If the discomfort cannot be relieved, the session may be stopped. We will provide referrals to psychological services in the area.

There are minimal risks associated with the questionnaires such as possible discomfort involved in answering some of the questions. You will not be forced to do anything you do not want to do, and you can terminate any of these procedures at any time.

The possible side effects for isradipine include: edema, tingling of hands or feet, unusual weight gain or loss, chest pain, difficult or labored breathing, wheezing, shortness of breath,

dizziness/faintness/lightheadedness, fast/irregular/pounding/racing pulse, feeling of warmth, full or bloated feeling, nausea/vomiting/diarrhea/constipation, pressure/soreness in the stomach, swelling of abdominal or stomach area, tightness in chest, unusual tiredness or weakness, blurred vision, confusion, flushing, sweating, headache. However, most of these side effects occurred as commonly as with placebo in placebo-controlled trials. Edema, palpitations, fatigue, and flushing appear to be dose related, particularly at doses >15-20 mg per day. Although there are no absolute contraindications to co-administration of isradipine with alcohol, both substances are metabolized through the liver. Participants are advised to refrain from alcohol for at least 24 hours prior to administration of isradipine and 24 hours after administration of isradipine. You will be asked to breathe into a tube so that members of the study team can perform an alcohol screen. It is unlikely that you will experience any symptoms from taking this pill. In case you do experience any side effects, our study advance practice nurse, Cara Young, PH.D., will be available to answer any questions or concerns you may have. Isradipine has been used in previous studies with individuals with substance use. Isradipine is approved for the treatment of high blood pressure in the United States by the Food and Drug Administration, but it is not approved for the treatment of tobacco craving and use.

The exposure to smoking cues may make some individuals anxious but these procedures are very well accepted. There may be some risks associated with the use of 360 video for the cue exposure. However, new systems such as the one we are using have made the likelihood that this will occur extremely small. Mild to moderate physical discomfort as a result of cyber sickness, a form of motion sickness may occur. Symptoms can include blurred vision, sweating, eyestrain, salivation, headaches, vertigo, dizziness, nausea, and vomiting. Symptoms are temporary and resolve within a few minutes to a few hours. Each exposure to the 360 video is for a short duration (maximum of 5 minutes) making cyber sickness significantly less likely than if the exposure were for a longer period of time to occur. Researchers will be trained in the case of a participant experiencing cyber sickness, and participants will be free to terminate the experiment at any time should they experience any discomfort. Cue exposure therapy and/or isradipine may involve risks, which are currently unforeseeable. The researchers will let you know about any significant new findings (such as additional risks or discomforts) that might make you change your mind about participating in this study.

How could you benefit from this study?

There are no direct benefits to participants for participating in this study. All participants will receive brief treatment with CET, a type of psychotherapy that has previously been shown to reduce cigarette cravings in some individuals.

What will happen to the samples and/or data we collect from you?

The electronic and self-report data obtained will also be assigned an ID number and will be stored on the lab's hard drive, which will be password protected.

If you choose to participate in this study and grant the staff permission, your sessions will be audio recorded. The recordings will be heard or viewed only for research purposes by the investigator and his or her associates. Any audio recordings will be stored securely and only the research team will have access to the recordings. Recordings will be kept for three years and then erased.

How will we protect your information?

The study is confidential. In order to protect your confidentiality, any information about you obtained as a result of participation in this research will be kept as confidential as legally possible. However, your research records, just like hospital records, may be subpoenaed by court order or may be inspected by federal regulatory authorities. A record of your participation will be kept in a confidential form, such that your name will be assigned an ID number. By doing this, information you provide cannot be directly linked to your name. Furthermore, information with identifying information, such as the consent form, will be kept separately from data that has been assigned an ID number. All of the information you provide will be double-locked (in a locked cabinet, within a locked lab) at all times.

We may share your data with other researchers. Your data may be used for future research very different than this research study. If we share your data we will remove any information that would let others know that these data came from you. However, we will not come back to you to ask for your consent if we share your data. We plan to publish the results of this study. To protect your privacy, will not include any information that could directly identify you.

The principal investigator for this study (Cara Young, Ph.D.), other designees of the research team, and representatives from the Institutional Review Board and regulatory authorities, will be granted direct access to your research records for verification of research procedures and use of data. If it becomes necessary for the Institutional Review Board to review the study records, information that can be linked to you will be protected to the extent permitted by law. Your research records will not be released without your consent unless required by law or a court order.

Information about you may be given to the following organizations:

- The study sponsor and/or representative of the sponsor
- Representatives of UT Austin and the UT Austin Institutional Review Board

A description of this study will be available on http://www.ClinicalTrials.gov as required by U.S. law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

What will happen to the information we collect about you after the study is over?

We will keep your research data to use for future research purposes not detailed within this consent form. Your name and other information that can directly identify you will be kept secure and stored separately from the research data collected as part of the project.

What if we learn something about your health that you did not know?

As part of this study, we may learn medically relevant information about you. If we learn something that you and your doctor did not know, we refer you to the relevant healthcare services and/or communicate relevant health information to your doctor, under the guidance of the study advance practice nurse, Dr. Cara Young.

How will we compensate you for being part of the study?

After completing the physical exam, you will receive $10. You will receive up to $30 each for completing the smoking logs for Day 1 and $30 Day 2 ($60 total, $2 per response). For completing Cue Exposure Day 1, you will receive $30. For completing Cue Exposure Day 2, you will receive $50. The total compensation is $150.

Who will pay if you are hurt during the study?

In the event of a research-related injury, it is important that you notify the Principal Investigator of the research-related injury immediately. You and/or your insurance company or health care plan may be responsible for any charges related to research-related injuries. Compensation for an injury resulting from your participation in this research is not available from The University of Texas at Austin.

You are not waiving any of your legal rights by participating in this study.

What if you become pregnant during the course of the study?

Pregnancy will be a reason to stop study treatment. If you become pregnant during the study, you may be discontinued from study participation for safety reasons.

What other choices do you have if you do not take part in this study?

An alternative is to choose not to participate in this research study. You may elect to consult with a primary care advance practice nurse if you are interested in treatments for tobacco use.

Your Participation in this Study is Voluntary

It is totally up to you to decide to be in this research study. Participating in this study is voluntary. Your decision to participate will not affect your relationship with The University of Texas at Austin. You will not lose any benefits or rights you already had if you decide not to participate. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to answer any questions you do not want to answer.

If you decide to withdraw before this study is completed, your de-identified data will be retained and analyzed unless we receive a written request to destroy or exclude the data from any analysis.

Contact Information for the Study Team

If you have any questions about this research, you may contact:

Dr. Cara Young
Phone: 816-596-6056
Email: cyoung@mail.nur.utexas.edu

Or

Alejandra Gonzalez-Badia
Phone: 915-777-0823
Email: alejandra.gonzalez@austin.utexas.edu

Contact Information for Questions about Your Rights as a Research Participant

If you have questions about your rights as a research participant, or wish to obtain information, ask questions, or discuss any concerns about this study with someone other than the researcher(s), please contact the following:

The University of Texas at Austin Institutional Review Board
Phone: 512-232-1543
Email: irb@austin.utexas.edu

Please reference the protocol number found at the top of this document.

Your Consent

By signing this document, you are agreeing to be in this study. We will give you a copy of this document for your records. We will keep a copy with the study records. If you have any questions about the study after you sign this document, you can contact the study team using the information provided above.

I understand what the study is about and my questions so far have been answered. I agree to take part in this study.

_____

Printed Subject Name

_____

Signature Date