



BMJ Open Measuring young adult appeal for menthol and non-menthol cigarettes: protocol of a clinical trial using both laboratory and intensive longitudinal methods (PRISM)

Amy M Cohn ¹, Wallace Pickworth,² Janet Audrain-McGovern,³ James Murphy,⁴ Andrea C Villanti ⁵, Donald Hedeker,⁶ Delaney Dunn,⁷ Riley Wyatt,⁷ Taylor Niznik,⁷ Whitney Cotten,⁷ Michael Smith,⁷ Sarah J Ehlike⁷

To cite: Cohn AM, Pickworth W, Audrain-McGovern J, *et al.* Measuring young adult appeal for menthol and non-menthol cigarettes: protocol of a clinical trial using both laboratory and intensive longitudinal methods (PRISM). *BMJ Open* 2022;**12**:e058823. doi:10.1136/bmjopen-2021-058823

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-058823>).

Received 09 November 2021
Accepted 03 March 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Amy M Cohn;
amy-cohn@ouhsc.edu

ABSTRACT

Introduction Although the Food and Drug Administration banned other characterising flavours in cigarettes, menthol cigarettes are still available to consumers. Young adult new smokers are initiating with menthol cigarettes, such that the prevalence of young adults menthol versus non-menthol smokers is increasing. Experimentation with menthol cigarettes is associated with progression to regular smoking and nicotine dependence. This ongoing clinical trial in young adult smokers measures appeal and the reinforcing value of smoking menthol versus non-menthol cigarettes and the impact of these variables on changes in smoking behaviour at a 6-month follow-up.

Methods and analysis Reinforcement for menthol smoking is assessed in the laboratory using a validated behavioural economic choice task, and appeal is measured in the natural environment using ecological momentary assessment (EMA). Analyses will examine differences between menthol and non-menthol cigarette smoking on measures of subjective response in the laboratory and via EMA, and how subjective response mediates the association between menthol preference at baseline and smoking outcomes at follow-up.

Ethics and dissemination This protocol was approved by the University of Oklahoma Health Sciences Center Institutional Review Board (#10581). The findings will isolate the unique effects of menthol in smoking and will help inform regulatory decisions about the abuse liability of menthol cigarettes. Findings will be disseminated through peer-reviewed journal articles and presentations at national and international conferences.

Trial registration number NCT03953508.

INTRODUCTION

Background

Although the Food and Drug Administration (FDA) banned other characterising flavours in cigarettes, menthol cigarettes are still available to consumers. Menthol cigarette smoking has increased in young adults. Experimentation with menthol cigarettes,

Strengths and limitations of this study

- This is the first study to examine differences in subjective response to menthol and non-menthol cigarette smoking in young adults, using both laboratory assessments, behavioural economic paradigms and daily diary surveys.
- Laboratory studies have high internal control, allowing for causal inference of acute subjective response to menthol smoking, and daily diary surveys allow for measurement of context-dependent fluctuations in cigarette smoking appeal in the natural environment.
- Examining the predictive value of menthol's appeal on future smoking behaviour at a 6-month follow-up through the combination of both laboratory and real-world daily diary assessments will demonstrate important causal links between cigarette characteristics and smoking behaviour that are necessary to inform Food and Drug Administration policies towards menthol. Participants are not asked to switching their usual brand flavour (menthol or non-menthol) during daily diary assessments, as this may impact compliance with daily reporting and result in study attrition.
- Processes related to quitting smoking are not assessed.

versus non-menthol cigarettes, is linked to a greater likelihood of progressing to regular smoking and nicotine dependence.^{1–3}

Menthol adds a pleasant minty flavour to tobacco and imparts cooling sensations in the mouth and throat.^{4–9} Menthol's pleasurable taste and other sensory effects (eg, throat grab) may encourage the perception that menthol is 'easier' to smoke and thus enhance greater exposure to nicotine.^{10 11} Over time, the conditioned reinforcing aspects of menthol flavouring in cigarette smoking

enhances the rewarding effects of inhaled nicotine and strengthens the learnt association between smoking and reward, beyond nicotine alone.^{12 13} A key unanswered question is whether in newer and younger users menthol increases the appealing and reinforcing properties of cigarette smoking beyond non-menthol smoking.

Objectives

This ongoing clinical trial in young adult smokers measures appeal and the reinforcing value of smoking menthol versus non-menthol cigarettes and the impact of these variables on changes in smoking behaviour at a 6-month follow-up. Reinforcement for menthol smoking is assessed in the laboratory using a validated behavioural economic choice task, and appeal is measured in the natural environment using ecological momentary assessment (EMA). Analyses will examine differences between menthol and non-menthol cigarette smoking on measures of subjective response in the laboratory and via EMA, and how subjective response mediates the association between menthol preference at baseline and smoking outcomes at follow-up.

This study anticipates enrolling 125 menthol and 125 non-menthol young adult smokers into three separate study phases. Aim 1 (phase 1) examines the absolute and relative reinforcing value (RRV) of menthol versus non-menthol cigarette smoking using a validated behavioural economic choice task. Aim 2 (phase 2) examines the subjective effects (appeal) of menthol versus non-menthol

cigarette smoking (own brand) during 14 days of EMA in the natural environment. Aim 3 (phase 3) examines the association of laboratory and EMA measurements of menthol reinforcement on 6-month smoking outcomes (progression, increased nicotine dependence and lower cigarette harm perceptions).

Design

This study consists of three phases in a mixed between-within subjects crossover design, where participants complete all phases of the study. Phase 1 uses smoking topography and a behavioural economic choice task paradigm to assess absolute and RRV of menthol and non-menthol cigarette smoking.¹⁴ In phase 1, participants will abstain from smoking (≥ 12 hours) prior to each of three laboratory sessions: ad libitum smoking of one's preferred/usual brand cigarette (session 1), smoking 3–5 puffs of a commercially available experimental cigarette (session 2) and completing a behavioural economic choice task to earn puffs of a menthol and/or non-menthol cigarette (session 3). In phase 2, participants will complete a 14-day daily monitoring regimen using a smartphone-based app to assess subjective appeal from smoking their preferred cigarette brand. In phase 3, changes in smoking behaviour and attitudes will be examined at a 6-month follow-up (see [table 1](#)).

Table 1 Schedule of enrolment, study visits and assessments

	Study period							
	Screening	Phase 1 Laboratory visits			Phase 2 Daily monitoring	Phase 3 Follow-up (postbaseline)		
Timepoint**	0	t ₁	t ₂	t ₃	1–14 days	2 months	4 months	6 months
Enrolment:		x						
Eligibility screen	x							
Informed consent		x						
Pregnancy urine test		x	x	x				
Interventions:								
Random number generation			x	x				
Smoke Camel Crush menthol cigarette			x	x				
Smoke Camel Crush non-menthol cigarette			x	x				
Smoke usual brand cigarette		x			x			
Assessments:								
Tobacco use behaviour	x	x			x	x	x	x
Subjective response to smoking		x	x	x	x			
Cigarette smoking frequency		x			x	x	x	x
Smoking topography (eg, puffing behaviour)		x	x	x				
Choice task				x				

METHODS: PARTICIPANTS, INTERVENTIONS AND OUTCOMES

Study setting

Participants will be recruited from TSET Health Promotion Research Center, located in Oklahoma City, using methods that have been used in previous studies by the principal investigator: local newspapers (including at local colleges/universities), online (eg, Facebook and Instagram), community flyers, snowball techniques and a database of interested callers from past smoking studies. Men and women of any ethnic or racial group are eligible if they meet inclusion/exclusion criteria. All recruitment materials direct participants to complete an online screening or call the study number to determine eligibility. For print ads, a QR code is included. Recruitment began in August 2020 but was interrupted because of COVID-19 in February 2020. Recruitment was paused in March 2020 and began again August 2020, after the protocol was redesigned for remote and socially distanced administration.

Eligibility criteria

Inclusion criteria: (1) ages 18–26 years; (2) currently smoke cigarettes 'somedays' or 'everyday'; (3) report a strong preference for menthol or non-menthol cigarettes (ie, smoke one type $\geq 80\%$ of the time); (4) able to read and understand the informed consent; and (5) willing to abstain from nicotine-containing products or other combustible products (eg, smoked cannabis) for ≥ 12 hours prior to each smoking session (confirmed by carbon monoxide (CO) ≤ 8 ppm). Exclusion criteria: (1) current use of nicotine replacement therapy; (2) currently pregnant, planning to become pregnant (verified by pregnancy test at each study visit/session) or breast feeding; (3) self-reported diagnosis of lung disease, including asthma, cystic fibrosis or chronic obstructive pulmonary disease; or (4) self-reported history of cardiac event or distress within the past 3 months.

Interventions

Eligible participants will smoke both menthol and non-menthol versions of a commercially available Camel Crush cigarette (R.J. Reynolds, Winston-Salem) in visit 2, phase 1.¹⁵ The order of administration for smoking the menthol and non-menthol version of the Camel Crush cigarette will be via REDCap procedure in which assignment to smoke menthol or non-menthol first is randomly generated. These cigarettes were chosen because they contain a small, menthol-filled capsule that breaks open when squeezed and releases menthol into the cigarette. They are well suited to isolate menthol's effects because there is no menthol flavour prior to squeezing and minimal menthol variation after crushing. They also have similar levels of nicotine, cotinine and NNK, before and after crushing.¹⁶

Outcomes

Aim 1/phase 1 primary outcomes

Primary outcomes for aim 1/phase 1 are: (A) the absolute reinforcing value (ARV) of menthol cigarettes from session 1 and (B) the RRV of menthol cigarettes from session 3 based on choice task responding. ARV of

menthol cigarettes will be operationalised as between-subject differences in subjective ratings of menthol versus non-menthol cigarettes (satisfaction, reward, craving reduction and physical sensations) during the ad libitum smoking session. RRV will be measured by evaluating motivation to 'work harder' for menthol versus non-menthol cigarette puffs or for one's own brand from visit 3 (eg, breakpoint). This is operationalised by the highest trial (breakpoint) that a participant successfully works for a menthol versus non-menthol cigarette puff. Higher values reflect greater RRV of menthol cigarettes relative to non-menthol cigarettes. Secondary outcomes: (A) total number of responses for the menthol versus the non-menthol-cigarette on the choice task; (B) CO boost; and (C) puff topography (number of menthol vs menthol cigarette puffs consumed, number of minutes smoked and interval between puffs). Exploratory analyses will compare ARV and RRV.

Aim 2/phase 2 primary outcomes

Primary outcomes for Aim 2/phase 2 are: (A) within-day subjective response (craving reduction, satisfaction, psychological reward and physical sensations like throat grab) to the most recent cigarette smoked (menthol vs non-menthol) and (B) between-day subjective response. Secondary outcomes: (A) aggregate ratings of subjective response (over the course of 14 days) by baseline menthol brand preference (at the person-level, rather than by day); (B) changes over the course of days (creating an average change score for each person) in subjective response ratings; (C) within-person variability in subjective response to smoking by calculating the SD for each person; (D) cigarettes per day (CPD) (within-day, over days); and (E) craving intensity (within-day, over days).

Aim 3/phase 3 primary outcomes

Primary outcomes for aim 3/phase 3 three are: (A) number of days smoked cigarettes in the past 30 days, (B) number of cigarettes smoked per day in the past 30 days, (C) nicotine dependence severity; and (D) continuous ratings of harm perceptions (relative and absolute). Secondary outcomes: (A) number and frequency of use of non-cigarette tobacco products in the past 30 days (or onset of using a new tobacco product, if no use reported at baseline), (B) number and use of non-cigarette flavoured tobacco products in the past 30 days (including assessment of the type of flavour used, like candy, fruit, alcohol, etc) and (C) intentions to use menthol cigarettes (among non-menthol smokers at baseline). Intentions to use menthol cigarettes will also be assessed at follow-up among those reporting non-menthol as their preferred brand at baseline, using a modified three-item algorithm: (1) 'Do you think that you will try a menthol cigarette in the next 6 months?', (2) 'Do you think you will use a menthol cigarette anytime during the next month?' (we will assess next month and 6 months to increase variability); and (3) 'If one of your best friends offered you a menthol cigarette, would you use it?' ('definitely yes,' to

'definitely not'). Because of a range of possible responses, intentions may change among some participants, making it a reasonable outcome measure.

Participant timeline

The main outcomes of interest are RRV of menthol versus non-menthol smoking assessed in the laboratory and subjective response to smoking menthol versus non-menthol cigarettes assessed via a 14-day daily monitoring regimen. Study eligibility will be confirmed via telephone by a trained research technician. Individuals are eligible will be invited to their first visit (session 1) to complete informed consent and a baseline questionnaire of tobacco use behaviour, tobacco use history, perceptions of tobacco use and other health behaviours related to tobacco use (eg, alcohol use and cannabis use), and then smoke their usual brand cigarette. Participants will be instructed to be abstinent from nicotine at this first session. Participants will then complete two other laboratory smoking sessions, scheduled a minimum of 48 hours apart. After completing the phase 1 laboratory smoking sessions, participants will then begin a regimen of 14 days of daily monitoring, where they will answer questions about their cigarette smoking and other tobacco use, twice a day, using smartphone-based app. At the completion of the 14 days of daily monitoring, participants will take a brief survey to assess satisfaction with and reactivity to the daily surveys. Follow-up surveys will occur again at 2, 4 and 6 months postbaseline to assess tobacco use behaviours (see [table 1](#) for schedule of events).

New methods addressing COVID-19 restrictions

The order in which study phases can occur may differ in response to the COVID-19 virus. Participants will be offered socially distanced in-person visits or remote study sessions, at their choice. Online informed consent and baseline survey will be offered. Once consent is obtained and the baseline survey is complete, a participant will have the option to begin phase 2 EMA, as this can be done remotely. Remote smoking sessions will be offered after EMA for those who do not wish to attend in person. Participants who complete the entire study remotely will also be given a smartphone compatible portable CO monitor (Bedfont iCO Smokerlyzer) and asked to use the iCO reading to verify smoking status at the beginning of each remote smoking session (≤ 8 parts per million/ppm) and exhaled CO (exposure) following smoking. Each participant will be provided their own iCO Smokerlyzer free of charge. Remote smoking sessions will occur via Zoom video. The order of administration of study phases is coded and will be examined as a potential covariate in final analytic models.

Sample size

For aim 1/phase 1, we expect a 15% attrition rate over the course of the three laboratory sessions, leaving a total of 213 participants. In the mixed 2×2 analysis of variance (ANOVA) models, for two-tailed tests, with $\alpha=0.05$,

a null hypothesis of no effect, an alternative hypothesis with 'medium' effect (partial $\eta^2=0.06$), the observed power for a sample size of $n=213$ is adequate. For aim 2/phase 2, we will obtain 5600–5950 (out of 7000) random person-reports for 14 days (nested within ~250 subjects), assuming an 80%–85% compliance rate.

For aim 3, we assumed a conservative 20% attrition rate for the 6-month follow-up. Our projected sample size would provide 0.80 power ($\alpha=0.05$) to detect small to medium effect sizes¹⁷ for laboratory and EMA-derived slopes on the outcomes of interest.

Recruitment

Recruitment and enrolment will occur at the laboratory of the TSET Health Promotion Research Center, in Oklahoma City, Oklahoma, which is specifically designed for the observation and measurement of cigarette smoking and tobacco use behaviour. The team will use methods that have been successful in previous studies: local newspapers (including at local colleges/universities), radio, online (eg, Craigslist; Facebook; Instagram; Snapchat), community flyers, snowball techniques and our database of interested callers from past smoking studies. The laboratory's close proximity (<10–20 miles) to several colleges and universities will further aid in our ability to recruit the sample of young adults.

Planned start date: August 2020.

Planned end date: October 2022.

METHODS: ASSIGNMENT OF INTERVENTIONS (FOR CONTROLLED TRIALS)

Not applicable; this is not a controlled trial.

METHODS: DATA COLLECTION, MANAGEMENT AND ANALYSIS

Data collection methods

Phase 1: laboratory smoking topography and subjective response to smoking

Phase 1 (aim 1) will be a 2 (menthol preference: yes/no) × 2 (cigarette type: usual brand vs experimental cigarette) factorial design, with cigarette type as a within-subjects factor. After determining initial eligibility via telephone, >12-hour abstinent smokers (CO-verified ≤ 8 ppm) complete each of three lab sessions.

Session 1: baseline assessment and ad libitum smoking

Session 1 measures ARV of menthol versus non-menthol cigarette smoking via a 60 min ad libitum smoking session of one's usual cigarette type (menthol or non-menthol). During scheduling for session 1, participants will be reminded to bring their own cigarettes to the and are asked to abstain from nicotine and tobacco products for at least 12 hours prior to each study visit. Participants who attend an in-person session are reminded to wear a mask and that they will be asked about any changes in COVID-19 symptoms since they completed the telephone screener. If an individual selects virtual study sessions,

they are asked to complete the visit 1 procedures remotely using a remote topography device and iCO CO reader to confirm smoking recency.

For remote or in-person sessions, participants smoke through a mouthpiece of the CRESS Smoking Topography Device, which records puff volume, duration and velocity, and interpuff interval for each puff and their aggregate averages.^{18–21} Before and after smoking, heart rate, blood pressure (if session is in person), nicotine withdrawal and exhaled CO (eg, CO boost, measured in parts per million) are collected. After smoking, subjective response to smoking (eg, smoking satisfaction, craving reduction, psychological reward, sensory effects, for example, throat hit) is measured. Note: blood pressure and heart rate are not collected if sessions are completed remotely.

Session 2: sampling experimental cigarettes

Session 2 familiarises participants with the experimental cigarette (Camel Crush) by having them take a minimum of three and up to 5 puffs each of a menthol (ie, 'crushed' filter and non-menthol version (counterbalanced) and complete subjective ratings, smoking exposure (CO boost), and smoking behaviour (topography). All participants are abstinent for this session (verified CO ≤ 8 ppm). There is a 20min washout period between each cigarette smoked (eg, menthol and non-menthol version of the Camel Crush). Before and after smoking, heart rate, blood pressure (if the session is in person), withdrawal symptoms and exhaled CO (eg, CO boost, measured in parts per million/ppm) are collected. After smoking, subjective response to smoking (eg, smoking satisfaction, craving reduction, psychological reward and sensory effects like throat hit) is measured. If an individual is unable to come to the lab due to COVID-19, they are asked to complete the visit 2 procedures remotely using a remote topography device and portable CO reader, via password protected video conferencing.

Session 3: behavioural economic choice task

Session 3 assesses the RRV of menthol versus non-menthol usual brand cigarettes via a computerised behavioural economic choice task that has been used and validated by Audrain-McGovern.^{14 22 23} Following confirmation of abstinence (expired CO ≤ 8 ppm). Participants complete a behavioural economic choice task whereby they can earn points for puffs of a menthol versus non-menthol cigarette by clicking targets or images on the computer screen. Images on the choice task will be brand neutral and include an image of a cigarette with a mint/menthol leaf and an image cigarette with a brown tobacco leaf to indicate menthol and non-menthol flavouring. With this choice task, we are able to isolate the unique effects of menthol on smoking by controlling for the potential impact of cigarette brand familiarity on ratings of RRV.

Using a concurrent schedule, participants are able to switch from working on one computer screen to the other as often as they desire. The reinforcement schedule in the non-menthol earning screen remains constant at

a fixed ratio FR-25 (25 targets achieved to earn a puff) while the reinforcement schedule for the menthol cigarette increases (require more effort) with a progressive ratio schedule of PR-25 \times over 10 trials, such that 25, 50, 75, 100, 125, 150, 175, 200, 225 and 250 targets have to be 'hit' to earn a puff. Reinforcement is defined by the breakpoint, or the highest trial (out of 10 trials) that is completed for menthol cigarette puffs.

The computer task is performed until 10 trials are completed, and a total of 10 points (or puffs) are accumulated. Per paradigm protocol, cigarette puffs earned are taken at the end of the procedure.¹⁴ As in visits 1 and 2, subjective response (eg, smoking satisfaction, craving reduction, psychological reward and sensory effects like throat hit), smoking exposure (CO boost) and behaviour (topography) are measured. To ensure that choice task responses are based on reinforcer preference rather than departure from the laboratory, the choice task is followed by a 30 min wait in the laboratory (if the session is taken in person). If the session is taken remotely, there may not be a 30 min wait period. During this 30 min wait period, participants are queried about potential reactivity (ie, behaviour change or increased awareness of behaviour and attitudes) to the laboratory visits with a brief survey. They are then given instructions for the EMA phase of the study if they have not already completed phase 2.

Phase 2: EMA

Phase 2 examines the subjective effects (appeal) of smoking menthol versus non-menthol cigarettes (own brand) in the participant's natural environment using EMA. Participants complete 14 days of EMA of smoking behaviour and subjective response (satisfaction, craving reduction, psychological reward and sensory effects like throat hit) twice a day, smoking as usual. (Note: if participants are enrolled when there are COVID-19 restrictions on in-person data collection, they begin the daily EMA after they complete the baseline survey and before they attend the 3-person lab visits). Participants answer a set of questions about their smoking behaviour via a smartphone-enabled app installed on their phone (or a study provided phone, at their choosing). Phones are mailed back using a preaddressed stamped envelope provided by the study team, or returned in person to the study lab at the end of the 14-day monitoring period. Prompts (eg, notifications to the telephone) are programmed to occur at random times within each block, one corresponding to the morning and one the evening. Prompts are programmed to coincide with respondents' sleep-wake cycle (ie, the usual time they wake up and go to bed). At the completion of EMA, participants complete a brief assessment to query about satisfaction with and reactivity to the EMA assessments. EMA entries are expected to last ~5min. Participants who miss EMA surveys or the EMA reactivity survey are given the opportunity to complete the surveys by invitation via REDCap.

Phase 3: follow-up assessment of tobacco use behaviour and attitudes

Participants complete a follow-up survey that is scheduled to occur 6 months after they are enrolled in the study to assess cigarette smoking (frequency and intensity in the past 30 days), nicotine dependence, absolute smoking harm perceptions ('How harmful are cigarettes to your health?') and relative smoking harm perceptions ('Compared with non-menthol cigarettes, how harmful to your health are menthol cigarettes?'). Follow-up assessments can be completed either in-person, online or via telephone. Participants are asked to complete two interim assessments (2 months and 4 months postenrolment) to enhance retention rates through the 6-month follow-up. These surveys are brief and query about tobacco use behaviour in the past 30 days. Participants are given a reminder notification approximately 2 weeks before their scheduled follow-up assessment.

Measures

Measures with known psychometric properties from the PhenX Toolkit and published studies were selected when possible. Most measures listed further are standard instruments commonly used in tobacco studies (see [table 1](#)).

Demographics

At the baseline, we collect information about age, race, ethnicity, income, employment status, relationship status, sexual orientation, educational attainment and tobacco expenditure habits.

Tobacco use history and patterns

At baseline, participants are asked about lifetime, past year and past 30-day use of cigarettes, e-cigarettes, large cigars, little cigars/cigarillos, hookah and other tobacco products (chew, dip, snuff, snus and pipe). Participants are also asked about age at first tobacco use, the tobacco product used at initiation, motivation to quit smoking, peer tobacco use and tobacco marketing exposure. To measure nicotine dependence, participants are asked how soon after waking they smoke their first cigarette (within 5 min, 6–30 min, 31–60 min and after 60 min), a validated item from the Fagerström Test of Nicotine Dependence.^{24 25}

Menthol cigarette use, attitudes and perceptions of menthol cigarettes

At screening, participants are asked whether the cigarettes they typically smoke are flavoured to taste like menthol or non-menthol, and at baseline, participants are asked whether their first cigarette smoked was a menthol or non-menthol cigarette. Attitudes and perceptions about menthol cigarettes are assessed using a 59-item questionnaire with five subscales (medicinal effects, image, less harmful, tradition and taste/sensation) developed by Allen *et al.*²⁶ Three subscales (medicinal effects, less harmful and taste/sensation) are used in the current study.

Absolute and relative cigarette harm perceptions

Absolute harm perceptions of menthol and non-menthol cigarettes are assessed at baseline using a single question stem: 'How harmful do you think the following products are to health?', with separate queries for 'menthol cigarettes' and 'non-menthol cigarettes'. Response options for each item are 1='not at all harmful' to 5='extremely harmful'. To measure relative harm of menthol versus non-menthol cigarettes, participants are asked 'Compared to non-menthol cigarettes, do you think that menthol cigarettes are much less harmful to a person's health, a little less harmful, about the same, a little more harmful, much more harmful to health?'.

Safety measures

Pregnancy tests are performed for all female participants at baseline and prior to engaging in a smoking session. The Adverse Events Questionnaire, designed specifically for this study, asks about adverse events experienced at baseline and then since the last visit.

Smoking topography

Data on cigarette smoking behaviour is collected as inter puff interval, total time smoking, inhalation volume and number of puffs, in real-time during smoking through a mouthpiece of the Clinical Research Support System (CRESS; Borgwaldt KC, Richmond, Virginia, USA), a transducer-based smoking topography data collection device. These data will be collected in electronic files coded with participant identification number.

Presmoking and Postsmoking measures

Participants complete assessments of nicotine withdrawal and craving prior to smoking using the Minnesota Nicotine Withdrawal Scale (MNWS)²⁷ and the Questionnaire on Smoking Urges.²⁸ Heart rate and blood pressure are taken before smoking, as well as expired CO. We note that some vitals sign measurements may not be taken if sessions are completed remotely. After smoking, participants complete assessments of expired CO, subjective response to smoking with the Cigarette Evaluation Questionnaire (CEQ),²⁹ the Duke Sensory Questionnaire,³⁰ the Nicotine Drug Effects Questionnaire,³¹ as well as the MNWS. Exhaled CO (parts per million, ppm) will be collected via a Bedfont Micro+Smokerlyzer Monitor if the session is completed in-person or a via a portable iCO Smokerlyzer (Covita) if the session is completed remotely.

EMA measures

EMA measurements parallel the constructs used in the laboratory assessments (eg, craving, subjective response). Subjective ratings are queried using items from the modified Cigarette Evaluation Questionnaire, which adds an additional item from the CEQ to assess enjoyment from smoking.³² Questions also assess the use of alternative tobacco products (e-cigarettes, large cigars, little cigars/cigarillos) since the previous assessment, characterising flavours (eg, fruit, chocolate) of each product used, cigarette craving, positive and negative mood and other

factors associated with smoking (alcohol and cannabis use). To minimise the response burden, EMA will prompt use-relevant probes via skip patterns. Missed EMA assessments are retrospectively assessed via a REDCap survey.

EMA application

This study uses a mobile phone application provided by the NCI Designated Stephenson Cancer Center mHealth Shared Resource called the Insight mHealth Platform <https://healthpromotionresearch.org/Mobile-Health-Technology>. Insight software is customisable for each research project, uses a web-based content management system (CMS) for easy access across multiple browsers and uses an architecture that enables the incorporation of new features. Users of this service log into the web-based CMS and follow step-by-step guide to create and manage research studies, enrol and monitor study participants, create questionnaire items, create different types of surveys (eg, baseline, follow-up, random, daily, participant initiated and sensor initiated) and create specific assessment rules (eg, two versus four random assessments per day). Once study parameters and content are created in the CMS, researchers transfer their study materials into the Insight smartphone application shell. Data are encrypted within the smartphone application and automatically and securely uploaded into the mHealth server database. Encrypted data can be downloaded from the mHealth servers by approved users at any time. Insight works offline (eg, in aeroplane mode) after the initial application download. Study team members have access to participant data through specified roles with secure logins and can only access data for their projects. All study-provided phones will be 'wiped' and 'sanitised' once the monitoring period is complete. The app can be disabled remotely.

Follow-up assessments

Participants complete a follow-up 6 months after enrolment to assess past 30-day use of all baseline tobacco products (cigarettes, e-cigarettes, large cigars, little cigars/cigarillos, hookah and other tobacco), nicotine dependence severity, absolute smoking harm perceptions ('how harmful are cigarettes to your health?') and relative smoking harm perceptions (compared to non-menthol cigarettes, how harmful to your health are menthol cigarettes?). Questions about cessation attempts and new tobacco product initiation, and curiosity to use (where applicable) are assessed. To reduce the potential for attrition, we ensure confidentiality, provide incentives, include brief interim surveys at 2 and 4 months post-enrollment and provide phone, email and/or text message reminders.

Retention

Participants are compensated using an incentive paradigm to ensure participant retention in all three laboratory visits and completion of all daily EMA surveys. Participants receive \$35 for completing the baseline

survey, \$45 for completing the session 1 smoking session, \$45 for completing session 2 and \$45 for completing Session 3. Participants are compensated for EMA based on the following compensation schedule: they receive \$1 for each completed EMA survey (totaling \$28), a \$10 bonus each week for completing all EMA surveys in a week (totaling \$20) and a \$50 bonus if they complete 85% of the EMA surveys over the courses of 2 weeks (23/28 surveys). Participants can therefore be eligible to receive a total of \$98 if they complete all EMA surveys. Participants are fully compensated for their final week of EMA and the EMA bonus on return of the smartphone after the 2 weeks of EMA monitoring.

There is a brief post-EMA survey to assess reactivity, for which they are paid \$15, and then a 6-month follow-up for which they are paid \$55. Participants are compensated \$15 each for completing brief interim surveys at 2 and 4 months post-enrollment. Participants who refer an individual who is eligible and signs informed consent to participate receive a \$25 referral bonus (limited to one person), and those who complete all phases of the study are eligible for a \$100 bonus. Participants are also compensated \$10 for each in-person visit if they do in-person sessions (up to \$30). If a participant chooses to complete the study remotely, they are compensated \$10 for coming to the research site to pick-up/drop-off study materials (eg, study phone, remote topography machine, Camel Crush cigarettes), also up to three times (total of \$30 for travel). Total possible compensation is \$523, including the referral bonus.

Providing bonus payments, escalating incentives and immediate incentive payments (reloadable gift card) are three methods used by the principal investigator and team members in previous studies to enhance study retention and research cigarette and EMA compliance. We will ensure confidentiality, provide monetary incentives and provide mail, telephone and/or text message reminders for study visits and the follow-up assessments. Participants will be offered web assessments for the 30-day follow-up to boost retention. If attrition rates are >20%, we will intensify telephone reminders and increase incentives as budget allows.

Data management

Data will be acquired through self-report questionnaires, biochemical measures and laboratory choice procedures. Smoking topography data will be collected in real time during smoking through a mouthpiece of the Clinical Research Support System (CRSS; Borgwaldt KC), a transducer-based smoking topography data collection device. These data will be collected in electronic files coded with participant identification number. Exhaled CO will be collected via Bedfont Micro+ Smokerlyzer CO Monitor and measured in parts per million (ppm) immediately before and up to 10 min after laboratory smoking.

For clinical trial data collection, the research facility uses an electronic data capture system to maintain 21 CFR Part 11 compliance and Good Clinical Practice (GCP)

standards. The research staff members are responsible for collecting and recording all data. This task includes ensuring that all source documents exist for the data in the permanent hard copy participant record folder (case report form), ensuring all fields are completed appropriately, and all corrections are done according to GCP.

The principal investigator will be responsible for overseeing and completing the monitoring process for the research. The research staff members are responsible for collecting and recording all data. This task includes ensuring that all source documents exist and ensuring all fields are completed appropriately. Any inconsistencies/deviations from the study protocol will be documented. Staff training will consist of an explanation of the protocol and review of the study surveys and participant record forms. In addition, the duties of each staff person will be outlined, and all applicable regulations will be reviewed and questions will be answered. Senior personnel will supervise junior staff and provide retraining in the study protocol as needed.

Statistical methods

For aim 1/phase 1 analyses, a 2 (menthol preference) \times 2 cigarette type (usual brand vs experimental brand) mixed ANOVA will be conducted to examine main effects and interactions on the outcomes of interest. Models will examine CPD, nicotine dependence, race/ethnicity, gender and age of smoking onset as potential covariates. If nicotine dependence and CPD are collinear, the most significant predictor of the outcome will be retained in the model. Significant interactions will be followed up with individual contrasts of cell means using Fisher's least significant difference tests. In exploratory analyses, a 2 (menthol preference) \times 4 (race/ethnicity: white, black, other and Hispanic) between-subjects ANOVA and a 2 (menthol preference) \times 2 (gender) between-subject ANOVA will be conducted separately for the baseline visit (session 1) to evaluate differential reactions to own brand cigarette smoking by race/ethnicity and by gender. Comparison of usual brand and experimental cigarette ratings will also be made to determine the perceived similarity of the experimental cigarette to one's brand and as a function of gender and race/ethnicity. Covariates with $p < 0.05$ will be retained in the final models.

For aim 2/phase 2 analyses, patterns of missing data, attrition rates, distributional properties of dependent and other measures, and correlations among all measures will be assessed. We will control for potential variables related to missing data and use multiple imputation methods (expectation maximisation algorithm). Analysis of EMA data will use hierarchical linear modelling (which provides flexibility in handling missing data such that robust estimates can be obtained even when data are missing at random). Models for aim 2 will examine effects of cigarette type (menthol vs non-menthol) at the day-level and episode-level on predictions of subjective response (satisfaction, reward, craving reduction, physical sensations like throat grab), and subjective response

at time t (eg, morning) predicting smoking behaviour (number of cigarettes, any smoking, craving) occurring at subsequent points in time to determine the impact of subjective response on continued use by menthol status (controlling for cigarette consumption and subjective response from the previous report). Within-person slopes capturing associations between cigarette type (menthol vs non-menthol) and subjective response will be saved and used in aim 3 regression models to predict 6-month smoking outcomes. Covariates with $p < 0.05$ will be retained in final models. Analyses will control for the order in which study phases were completed (eg, phase 1 vs phase 2 first). It is possible that some participants may stop smoking over the course of the 6 months. We will examine baseline, laboratory and EMA findings that set these individuals apart from those who continue to smoke.

The main outcome analyses for aim 3 will examine the predictive validity of laboratory (phase 1) and EMA (phase 2) outcomes on changes in the 6-month outcomes of interest and the degree to which laboratory and EMA ratings of appeal/reinforcement account for (ie, mediate) the association between menthol brand preference at baseline and smoking behaviour change at 6 months. Hierarchical regression models (continuous or binary logistic) will predict the 6-month outcome of interest, controlling for baseline levels of the outcome in interest and relevant demographics (gender, race/ethnicity and age of smoking onset) in step 1, baseline menthol status in step 2, and then laboratory or EMA-derived slopes step 3. Models will be conducted separately using phase 1 and phase 2 measurements of appeal/reinforcement. Mediation will be reflected by a reduction in the association between baseline menthol preference and smoking outcomes after including the requisite measure of appeal/reinforcement in the model. Covariates with $p < 0.05$ will be retained in the final models.

Exploratory analyses will examine changes over time in tobacco use behaviour from baseline, 2, 4 and 6 months postbaseline. All data collected during the course of the study, survey and biospecimen results will be maintained for future use in cross-reference against new and continued data collection.

METHODS: MONITORING

Data monitoring

During the course of the study, safety and data quality monitoring will be performed on an ongoing basis by the principal investigator and study personnel, who will also review potential adverse events. Team members meet weekly with the principal investigator and discuss enrolment, consent, eligibility, adherence to/compliance with EMA and data collection. If a female participant becomes pregnant during the laboratory smoking phases of the study, she will be immediately withdrawn from the study. All adverse events and serious adverse events will be documented and recorded in accordance with the University

of Oklahoma Health Sciences Center (OUHSC) and National Institutes of Health (NIH) policies. This information will, in turn, be reported immediately to all necessary regulatory committees. Any serious adverse event will be reported to the Institutional Review Board and the NIH project officer within 48 hours of occurrence. At each study visit, the participant will be directly asked about adverse events that may have occurred, and during the visit participants will be monitored for any adverse effects associated with their cigarette smoking. An annual report summarising all adverse events will also be submitted. Drop-out rates and reasons for dropout will also be monitored to ensure the integrity of the study protocol.

Harms

Participants will not be exposed to any more risk than the usual risk they expose themselves to by choosing to smoke. Questionnaires, smoking topography and CO measurement are all non-invasive and involve minimal risk to study participants. According to new statute passed in early 2020, tobacco products, including Camel Crush cigarettes, are available in convenience stores to persons 21 years of age and older. Potential risks to participants include: (1) risk of using cigarettes, (2) loss of confidentiality or privacy and (3) potential discomfort from being asked to abstain from nicotine. The laboratory where visits will be completed was constructed with a special ventilation system for quickly removing smoke from the experimental rooms to reduce excess smoke exposure to participants and researchers. Smoking cessation resources will be available to all participants at completion of the study, or earlier if requested, and participants will be provided with a list of cessation resources including the Oklahoma Helpline, a free, 24/7, telephone-based resource to provide tobacco cessation counselling. A Federal Certificate of Confidentiality is automatically provided by the NIH to protect against disclosures or release of data.

Auditing

N/A.

ETHICS AND DISSEMINATION

Research ethics approval

This protocol and the informed consent have been reviewed and approved by the University of Oklahoma Health Sciences Center (OUHSC) IRB (IRB #10581) with respect to compliance with applicable research and human subjects regulations (see online supplemental appendix 1 for IRB-approved consent). An annual continuing review is required, which includes the total number of participants enrolled and any reports of adverse and/or serious adverse events, as well protocol deviations.

Protocol modifications

Any modifications to the protocol that may impact the conduct of the study, potential benefit of the participant or safety of the participant, including changes in the study objectives, study design, participant population, sample size, study procedures or significant administrative

aspects will require a protocol modification to the IRB. Such modification will be approved by the OUHSC IRB prior to implementation. Administrative changes to the protocol that may have no effect on the way the study is conducted or on participant safety or benefit may be approved administratively.

Consent or assent

Informed consent is obtained from each individual prior to participation in the study. All participants are informed that they may withdraw from the study at any time without penalty and will be paid for what they have completed up to that point.

If recruited during university normal operating procedures (when in-person data collection is allowed), eligible participants will provide written consent in person immediately before their first laboratory visit begins. This will take place in the lab. Trained staff will go over the consent document with the participant, then ask if he or she has any other questions before signing. Each participant will be allowed time to read the consent document and ask questions before any data are collected. A copy of the consent form will be given to the participant.

To provide consent electronically, participants will be sent a link to the eIC via REDCap. REDCap has a feature that allows for version control, automatic time and date stamp and electronic signature (using a fingertip, computer mouse, or stylus on a tablet screen). To ensure that the eIC is presented appropriately and that subjects will have enough time to dedicate to the eIC process, an eligible and interested participant will be told by a study personnel, at the end of the phone screening session, approximately how long the consent review process will take and will review with them the information that will be in the eIC. The eIC will record the timestamp of participant's acceptance or declination and a copy of the signed eIC will be sent to the participant via email. No personal information, other than the participant's name, will be collected in the eIC. Participants will be reminded that their participation is voluntary. Additionally, they will be reminded that they are allowed to discontinue participation in the study at any time, without any loss of benefits or other negative consequences. Participants will be given ample opportunity to read the consent and have any questions related to the consent, the study or participation answered by the research team member. The participant will have the option to decline participation or withdraw from the study at any time. Individuals will be given as much time as they need to make a decision about participation. If the individual decides to participate, he or she will be given the opportunity to sign the consent and the research team member will sign as a witness (if the consent is completed in-person). The participant will be given a copy of the consent form to keep for his or her records. All research team members will complete an approved course on the protection of human subjects and be trained on how to clearly describe study procedures and the obtain informed consent process.

Confidentiality

All research data will be labelled using numerical codes. All data are managed and analysed on-site by project staff; no transmission of identifiable data outside of research centre will occur. Research data without identifiers will be maintained in a locked file cabinet or on a password-protected server, which can only be accessed by approved study personnel. Paper-pencil versions of study consent forms will be stored in a locked filing cabinet; electronic versions of consent forms will be stored on a secure server that can only be accessed by approved personnel. Consent forms with participant name do not contain any research data or study ID and cannot be linked to participant's research data. Controlled user access to database systems will ensure that only appropriate and authorised personnel are able to view, access and modify study data. All records that contain names or other personal identifiers that link participant ID numbers will be kept on a password-protected server that can only be accessed by approved study personnel. This information will be used for payment and contact purposes only. Participants' study information will not be released outside of the study without the written permission of the participant, except as is necessary by any relevant monitoring or regulatory authorities.

Declaration of interests

There are no conflicts of interest to report.

Access to data

The principal investigator and approved team members will be given access to the cleaned data sets. To ensure confidentiality, data dispersed to project team members who are not employed at the University of Oklahoma Health Sciences Center (OUHSC) will be deidentified and not contain any identifying participant information.

Ancillary and post-trial care

Smoking cessation resources will be available to all participants at completion of the study, or earlier if requested, and participants will be provided with a list of cessation resources including the Oklahoma Helpline, a free, 24/7, telephone-based resource to provide tobacco cessation counselling.

Dissemination policy

Trial results

The sponsor and PI are committed to the open and timely dissemination of research outcomes. Manuscript and conference submissions to peer-reviewed outlets, focused on the primary and secondary outcomes, will assist with the dissemination of results from this study and will provide a critical empirical foundation to support FDA's proposed regulatory actions to ban or restrict menthol in cigarettes. Results of the study will be reported in ClinicalTrials.gov to increase availability of information to the public and ensure that study results occur in a timely manner.

Authorship

Topics suggested for presentation or publication will be circulated to the PI and team members. We will follow the recommendations set forth by the International Committee of Medical Journal Editors for defining the roles of authors and contributors in publications or presentations that arise from the data.

Reproducible research

Investigators in the proposed activity recognise that promising new methods, technologies, strategies or computer software may arise during the course of the research. The study team is aware of and agrees to abide by the principles for sharing research resources as described by NIH in 'Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources'. While the investigators expect that research tools will be freely shared with the research community, opportunities for technology transfer and translational research will be explored as appropriate. Any data shared will be deidentified and follow the regulations set forth in the university's applicable human subjects protection guidelines. NIH policy expects that grant recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication. The investigators on this grant are committed fully to the principles of research resource sharing through publications, presentations, web sites, direct principal investigator contact and other means as possible.

Data availability

Data are sensitive, and the priority in sharing data will be protecting study participants' privacy. This will not be a public use dataset. Data will be available for certain types of sharing in accordance with the terms of a data-sharing agreement and only after the publication of major findings of the study. Only researchers certified in the protection of human subjects will be considered for access to the data.

Patient and public involvement statement

There was no active involvement of patients or the public in the development of this research. Patient and public involvement in this grant funded was not feasible, given the timeline for project submission and the timeline and budget constraints of the funding mechanism.

Biological specimens

N/A.

STUDY STATUS

Study recruitment began in August 2020 and is ongoing. The target sample size is 250. At the time of this submission, October 2021, 336 individuals had been screened for the study; 65 had consented, completed the baseline survey and started EMA; and 35 had completed all three laboratory sessions (either remotely or in-person).

Author affiliations

¹Department of Pediatrics, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

²Battelle Memorial Institute Baltimore, Baltimore, Maryland, USA

³University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

⁴Department of Psychology, The University of Memphis, Memphis, Tennessee, USA

⁵Department of Psychiatry, University of Vermont, Burlington, Vermont, USA

⁶University of Illinois at Chicago, Chicago, Illinois, USA

⁷The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

Contributors AMC conceived of the study. AMC, WP, JA-M, JM and ACV initiated the study design, and DD, RW, TN, WC, MS and SJE helped with implementation. AMC and DH will contribute to statistical analyses. MS, TN, RW and SJE contributed to data acquisition and protocol development; all authors contributed to the review of this manuscript and provided comments. All authors read and approved the final manuscript. AMC is the primary grant holder.

Funding This study is funded by a grant from the National Institute on Drug Abuse and the Food and Drug Administration Center for Tobacco Products, R01DA046359, awarded to AMC.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

Author note Committees: principal investigator: design and conduct of the study, preparation of protocol and revisions, managing data collection and research personnel team, budget administration and publication of study results. Research technicians and sponsored programme coordinator: maintenance of trial IT system and data entry, data verification, assisting with protocol revisions, recruitment, screening, data collection and participant tracking. Coinvestigator and consultants: publication of study results and advice for principal investigator.

ORCID iDs

Amy M Cohn <http://orcid.org/0000-0001-9034-4293>

Andrea C Villanti <http://orcid.org/0000-0003-3104-966X>

REFERENCES

- Nonnemaker J, Hersey J, Homs G, *et al*. Initiation with menthol cigarettes and youth smoking uptake. *Addiction* 2013;108:171–8.
- Hersey JC, Ng SW, Nonnemaker JM, *et al*. Are menthol cigarettes a starter product for youth? *Nicotine Tob Res* 2006;8:403–13.
- Wackowski O, Delnevo CD. Menthol cigarettes and indicators of tobacco dependence among adolescents. *Addict Behav* 2007;32:1964–9.
- Carpenter CL, Jarvik ME, Morgenstern H, *et al*. Mentholated cigarette smoking and lung-cancer risk. *Ann Epidemiol* 1999;9:114–20.
- Kreslake JM, Wayne GF, Alpert HR, *et al*. Tobacco industry control of menthol in cigarettes and targeting of adolescents and young adults. *Am J Public Health* 2008;98:1685–92.
- Kreslake JM, Wayne GF, Connolly GN. The menthol smoker: tobacco industry research on consumer sensory perception of menthol cigarettes and its role in smoking behavior. *Nicotine Tob Res* 2008;10:705–15.
- Lee YO, Glantz SA. Menthol: putting the pieces together. *Tob Control* 2011;20 Suppl 2:ii1–7.
- Ferris Wayne G, Connolly GN, Wayne GF, Application CGN. Application, function, and effects of menthol in cigarettes: a survey of tobacco industry documents. *Nicotine Tob Res* 2004;6 Suppl 1:43–54.
- Carpenter CM, Wayne GF, Connolly GN. The role of sensory perception in the development and targeting of tobacco products. *Addiction* 2007;102:136–47.
- US Food Drug Administration. *Tobacco products scientific Advisory Committee (TPSAC). menthol cigarettes and public health: review of the scientific evidence and recommendations*. Rockville, MD: US food and drug administration. center for tobacco products, 2011.
- US Food Drug Administration. *Preliminary scientific evaluation of the possible public health effects of menthol versus nonmenthol cigarettes*, 2013.
- Hymowitz N, Mouton C, Edkholdt H. Menthol cigarette smoking in African Americans and whites. *Tob Control* 1995;4:194–5.
- Finkenauer R. *Emotion, motivation, and executive functioning as predictors of smoking status*. Wayne State University, 2009.
- Audrain-McGovern J, Strasser AA, Wileyto EP. The impact of flavoring on the rewarding and reinforcing value of e-cigarettes with nicotine among young adult smokers. *Drug Alcohol Depend* 2016;166:263–7.
- Strasser AA, Ashare RL, Kaufman M, *et al*. The effect of menthol on cigarette smoking behaviors, biomarkers and subjective responses. *Cancer Epidemiol Biomarkers Prev* 2013;22:382–9.
- Gordon SM, Brinkman MC, Meng RQ, *et al*. Effect of cigarette menthol content on mainstream smoke emissions. *Chem Res Toxicol* 2011;24:1744–53.
- Cohen J. *Statistical power analysis for the behavioral sciences*. 2nd ed. Lawrence Erlbaum, 1988.
- Pickworth WB, Moolchan ET, Berlin I, *et al*. Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery. *Pharmacol Biochem Behav* 2002;71:55–61.
- Pickworth W, Canlas L, Rosenberry Z, *et al*. Make your own cigarette smoking: toxicant exposure and behavioral changes. *Drug Alcohol Depend* 2014;140:e177.
- Rosenberry ZR, Pickworth WB, Koszowski B. Large Cigars: smoking topography and toxicant exposure. *NICTOB* 2016;63(30):ntw289.
- Pickworth WB, Rosenberry ZR, O'Grady KE, *et al*. Dual use of cigarettes, little Cigars, Cigarillos, and large Cigars: smoking topography and toxicant exposure. *Tob Regul Sci* 2017;3:72–83.
- Audrain-McGovern J, Strasser AA, Ashare R, *et al*. Reinforcing value of smoking relative to physical activity and the effects of physical activity on smoking abstinence symptoms among young adults. *Exp Clin Psychopharmacol* 2015;23:477–85.
- Audrain-McGovern J, Wileyto EP, Ashare R, *et al*. Reward and affective regulation in depression-prone smokers. *Biol Psychiatry* 2014;76:689–97.
- Fagerstrom KO, Heatherton TF, Kozlowski LT. Nicotine addiction and its assessment. *Ear Nose Throat J* 1990;69:763–5.
- Heatherton TF, Kozlowski LT, Frecker RC, *et al*. The Fagerström test for nicotine dependence: a revision of the Fagerström tolerance questionnaire. *Br J Addict* 1991;86:1119–27.
- Allen B, Cruz TB, Leonard E, *et al*. Development and validation of a scale to assess attitudes and beliefs about menthol cigarettes among African American smokers. *Eval Health Prof* 2010;33:414–36.
- Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry* 1986;43:289.
- Cox LS, Tiffany ST, Christen AG. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. *Nicotine Tob Res* 2001;3:7–16.
- Westman E, Levin E, Rose J. *Smoking while wearing the nicotine patch. is smoking satisfying or harmful*. Slack Inc 6900 grove RD, THOROFARE, NJ 08086, 1992: A871.
- Behm FM, Rose JE. Reducing craving for cigarettes while decreasing smoke intake using capsaicin-enhanced low TAR cigarettes. *Exp Clin Psychopharmacol* 1994;2:143–53.
- Morean ME, de Wit H, King AC, *et al*. The drug effects questionnaire: psychometric support across three drug types. *Psychopharmacology* 2013;227:177–92.
- Cappelleri JC, Bushmakini AG, Baker CL, *et al*. Confirmatory factor analyses and reliability of the modified cigarette evaluation questionnaire. *Addict Behav* 2007;32:912–23.

701G Consent | OUHSC IRB Version Date: 03/12/2019
IRB Number: 10581

Consent Form to Participate in a Research Study

University of Oklahoma Health Sciences Center (OUHSC)

Study Title: Menthol and non-menthol cigarette smoking in young adults

Sponsor: National Institute on Drug Abuse/Food and Drug Administration Center for Tobacco Products (CTP)

Principal Investigator: Amy M. Cohn, PhD

Phone Number: 405-271-1903

KEY INFORMATION ABOUT THE RESEARCH STUDY

You are being asked to participate in a research study. Research studies are voluntary and include only people who choose to take part. This consent form begins with a 'Key Information' section to provide important information to help you decide whether or not to participate in this study. More detailed information is provided after the key information. Please take your time, discuss this with family and friends, and ask the investigator and study team any questions you may have.

WHY HAVE I BEEN ASKED TO PARTICIPATE IN THIS STUDY?

You are being asked to participate in this research study because you are a current smoker and meet study eligibility criteria. This study is being conducted by the University of Oklahoma Health Sciences Center and is funded by the National Institutes of Health (NIH). Joining the study is voluntary. You do not have to answer any questions that make you feel uncomfortable. You can stop participating or answering questions at any time.

WHY IS THIS STUDY BEING DONE AND HOW LONG WILL IT LAST?

The purpose of this study is to understand why people smoke menthol and non-menthol cigarettes. We are interested in how smoking these cigarettes affects your smoking, how you feel, and attitudes about different types or brands of cigarettes. We think that you will be in the study for 6 months.

WHAT WILL I BE ASKED TO DO IN THIS STUDY?

Before any study-related tests and procedures are performed, we will ask you to read and sign this consent document. Then, we will ask you to take part in the following study activities:

- Complete a baseline survey where you will answer questions about your personal history, tobacco use behavior, attitudes, and tobacco-related behaviors
- Take part in three in-person laboratory visits which may last up to 2 hours each. You will be asked to refrain from cigarette smoking or using other nicotine products for at least 12 hours before each visit. At each lab visit, we will ask you to have a smoking session. You will provide breath samples to measure when you last smoked. You will also complete questionnaires about your behavior and mood, both before and after smoking. We will also measure your heart rate and blood pressure before and after smoking. Note: You may complete these visits remotely, via password protected video in the event social isolation is necessary, or at your choosing.
- You will complete daily surveys about your mood and behavior through a phone application for 14 days. At the end of the 14 days (2-weeks) you will complete a survey asking about your experience with the phone surveys.
- Finally, at 2, 4, and 6 months after your initial enrollment, we will do a short survey in-person, online, or via the phone (your preference) about your tobacco use and behavior.



701G Consent | OUHSC IRB Version Date: 03/12/2019
IRB Number: 10581

For a complete description of the study procedures, refer to the Detailed Information section of the consent form.

WHY MIGHT I WANT TO PARTICIPATE IN THIS STUDY?

If you agree to take part in this study, you may benefit directly through increased understanding of factors underlying your use of cigarettes. We also hope that the information learned from this study will benefit other people in the future.

WHY MIGHT I NOT WANT TO PARTICIPATE IN THIS STUDY?

This study has minimal risk however there are known complications that arise from smoking cigarettes that may affect the individual or an embryo, fetus, or infant. The researchers do not know all of the side effects that could happen. For a complete description of known risks, refer to the Detailed Information section of the consent form.

WHAT OTHER OPTIONS ARE THERE?

You may choose not to participate in this study. If at any point during the three in-person study visits you decide to stop smoking, you will be reimbursed for your time up to that point and be released from the study. We will not ask you to smoke cigarettes if you decide you want to stop smoking. We will also provide you with a list of places where you may choose to seek treatment. If you decide to stop smoking after the in-person study visits, you will still be able to continue in the study and unless you tell us you want to drop-out of the study.

HOW WILL PARTICIPATING IN THE STUDY AFFECT ME FINANCIALLY?

You will be paid for your time and effort. Below describes the compensation for completing each phase of the study:

- Completing the baseline survey: \$35
- Completing the daily surveys: up to \$98 (if you complete all surveys)
- Visit/Session 1 \$45 (if eligible and decide to participate); \$25 if you are not eligible at this first visit.
- Visit/Session 2 - \$45
- Visit/Session 3 - \$45

Below describes the compensation for completing the daily telephone surveys for 14 days:

- \$1 for each completed telephone survey x 28 (14 days x twice a day) surveys = \$28
- \$10 bonus for each week if you complete all surveys for that week x 2 weeks = \$20
- \$50 bonus if you complete 85% of the telephone surveys (23 of 28) during the 2 weeks

Follow-up Surveys

- \$15 for completing the 2-week follow-up survey (at the end of the daily surveys), the 2-month follow-up survey, and the 4-month follow-up survey (total of \$45)
- \$55 for completing the final follow-up survey (at 6-months)
- \$100 bonus for completing all phases of the study

Travel

- \$10 for each of three in-person lab visits or \$10 for curbside pickup/delivery of study materials if you take the study remotely (up to \$30 total)



701G Consent | OUHSC IRB Version Date: 03/12/2019

IRB Number: 10581

If you refer someone who is eligible and agrees to participate, you will receive a \$25 referral bonus. You will receive a maximum of one referral bonus.

The total possible compensation (including referral) is \$523.

You will be asked to provide your social security number, your residency status (a copy of your green card must be provided if applicable), and whether you are a University of Oklahoma employee for tax reporting purposes. If you are unwilling or unable to provide your social security number, residency status (and green card if applicable), or University of Oklahoma employment status you will not be eligible to participate in the research study.

For additional information about possible costs, please refer to the Detailed Information section of the consent form and ask the study team about any expected additional costs or insurance problems.

DETAILED INFORMATION ABOUT THE RESEARCH STUDY

The following pages of the consent form will provide you with more information about this study. Please take your time in reviewing this information and ask the investigator and study team any questions you may have.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 250 people will take part in this study in Oklahoma. All of these individuals will participate at this location.

WHAT IS THE STATUS OF THE DRUGS/DEVICES/PROCEDURES USED IN THIS STUDY?

At the in-person laboratory visits, you will smoke your own or usual cigarette brand and commercially available Camel Crush cigarettes in this study. The Food and Drug Administration Center for Tobacco Products regulates cigarettes.

WHAT IS INVOLVED IN THE STUDY?

If you are eligible and agree to participate, this study will require you to complete

- 3 in-person visits to our laboratory or 3 virtual study sessions,
- Daily cell phone surveys for 14 days (on your phone or a study provided phone),
- Interim surveys at 2-weeks, 2 months, and 4 months after you are enrolled, and
- A final follow-up survey 6 months after you are enrolled.

The first visit /session will last about 2.5 hours.

The three in-person visits or virtual sessions will be scheduled at least 2 days apart and will last between 1 and 2 hours, depending on the session. We will ask that you refrain from cigarette smoking and using other nicotine products for at least 12 hours before each in-person visit.

If you are female, to be eligible you cannot be pregnant, breastfeeding, or plan to become pregnant. If you do become pregnant, please notify the study staff as soon as possible. We will ask you to take a pregnancy test at every in-person study visit or virtual session. We expect that if you are a female of child bearing age who is able to conceive, you will use reliable contraception and not be planning pregnancy or breastfeeding during the study. Participants with a positive pregnancy test at any in-person visit will be notified and will

701G Consent | OUHSC IRB Version Date: 03/12/2019

IRB Number: 10581

not be able to continue participation in the laboratory portion of the study. If you become pregnant, please let staff know as soon as possible.

Special Note about Response to the Coronavirus Outbreak (COVID-19)

In order to protect your health and the health of the staff members, the order in which you complete the activities of this study (daily phone surveys and in-person laboratory sessions) may vary due to COVID-19 restrictions that could be imposed at the national, local, or university-level. When the university is operating “as normal”, you will complete the 3 in-person laboratory sessions first, and then begin the daily phone assessments after the final in-person session. You will complete the baseline survey during the first in-person visit.

If you are being recruited when in-person data collection activities are limited or restricted due to COVID-19, you will be asked to provide consent online (by electronically signing this document), complete the baseline survey online, and then begin the daily phone surveys after that, before the lab visits. One of our research staff will schedule a brief phone call with you to explain how to complete the daily surveys, before you start them. Once we are able to begin in-person data collection in the laboratory, you will be contacted by a member of our team to determine if you are still interested in attending in-person visits and eligible to participate. If you are interested and meet eligibility criteria, we will schedule the 3 in-person laboratory sessions. We will make every effort to contact you and schedule those sessions as soon as we can after you are enrolled. Given the uncertainty of the COVID-19 outbreak, we are unable to say how long you may need to wait. In both instances, you will be compensated for the portion of the study you have completed up to that point. If in-person visits are deemed unsafe and social isolation persists, remote/virtual smoking sessions may also be provided as an option in place of in-person laboratory visits. If you select remote/virtual visits, you will be provided a smartphone compatible portable carbon monoxide (iCO) monitor and so that we can test your breath for carbon monoxide at the beginning of each remote (video) smoking session and after you smoke each cigarette.

Study Procedures

In-Person Laboratory Visits. At each in-person visit, you will participate in a smoking session. During the first visit, you will smoke your own cigarettes as you wish, during a 60-minute smoking session. At all lab visits, we will ask you to have a smoking session similar to the first in-person visit. You will provide breath samples to quantify when you last smoked. You will also complete questionnaires about your behavior and mood, both before and after smoking. We will also measure your heart rate and blood pressure before and after smoking.

Visit 1: We will review eligibility criteria similar to what you answered over the phone. We will also take your heart rate and blood pressure. If you are still eligible at this point and you agree to participate, we will ask you to provide some additional information about yourself and your use of cigarettes, other tobacco products, and behaviors related to tobacco use. We will then ask you to participate in your first smoking session. During this session, you will smoke your own cigarette that you brought with you today. Before you smoke, we will test your breath for carbon monoxide, and check your heart rate and blood pressure. You will smoke your cigarette through a mouthpiece that allows us to measure the puffs you take. After you finish smoking, we will conduct another breath test, and check your heart rate and blood pressure. Both before and after smoking we will have you answer some questionnaires about how you are feeling.

Visit 2: For your following visits, you will be asked to smoke a few puffs of two different types of study cigarettes. One will be flavored to taste like mint/menthol and the other will be flavored to taste like traditional tobacco flavoring. These are commercially available cigarettes. The order in which you smoke

701G Consent | OUHSC IRB Version Date: 03/12/2019
IRB Number: 10581

the two types of study cigarettes will be randomly chosen. Before you smoke, we will test your breath for carbon monoxide, and check your heart rate and blood pressure. You will smoke the cigarette through a mouthpiece that allows us to measure the puffs you take. After you finish smoking, we will conduct another breath test, and check your heart rate and blood pressure. Both before and after smoking we will have you answer some questionnaires about how you are feeling.

Visit 3: For your final visit, you will be asked to complete a computer task in which you hit targets on a computer screen of cigarettes. You can “earn” cigarette puffs for each target you correctly hit on the computer screen, for up to 10 puffs after completing the computer task. After the task is complete, you can smoke the puffs that you earned. You will wait in the laboratory to fill out some survey questions about how you are feeling and we will talk to you about how to complete the daily surveys for the next phase of the study (if you have not already completed them). As with the previous visit, we will test your breath for carbon monoxide when you first arrive. We will check your heart rate and blood pressure immediately before and after you smoke. You will smoke the cigarette through a mouthpiece again. Both before and after smoking we will have you answer some questionnaires about how you are feeling.

At all lab visits, we will ask you to have a smoking session similar to the first study session. You will provide breath samples to quantify when you last smoked. You will also complete questionnaires about your behavior and mood, both before and after smoking. We will also measure your heart rate and blood pressure before and after smoking.

Daily Surveys. For every morning and evening, you will receive an automated notification on a cell phone to answer some questions about how you feel, your smoking behavior, and other behaviors through an app that we will install on your phone or a study-provided phone (if your phone does not have the Android operating system). The notifications will be scheduled to happen during times of the day or evening when you are typically awake. During this phase, which will last for 14 days, you should engage in your normal life routines and smoke as you normally would. At the end of the 14 days, we will ask you to take a brief survey (either online or via the telephone) to ask how you are doing and find out your experience with the daily surveys. If you are enrolled in the study under normal operating conditions, you will begin the daily surveys after your third lab visit. If you are enrolled during a time of COVID-19 restrictions, you will begin the daily surveys after you complete the baseline survey online and have a brief training with one of our program staff about how to do them.

Finally, 2, 4, and 6 months after you enroll in the study, we will do a short survey with you, preferably in our lab, but if you cannot make it, we can do it over the phone or online. This survey will ask about your smoking and tobacco use and tobacco-related behaviors. We will contact you about once per month to keep in contact so we may schedule these follow-up surveys.

Update about the impact of Tobacco 21 regulation on study recruitment

Because of the new Tobacco 21 regulations at the state and federal level, individuals under the age of 21 are not allowed to purchase tobacco products, and the research team is no longer allowed to “furnish” tobacco products to individuals under the age of 21. As a result, individuals ages 18 to 20 enrolled in the study will complete a modified study protocol, where they will smoke their usual brand cigarette (e.g., as outlined in Lab Visit 1), they will complete the daily diary assessments, and they will complete all follow-up assessments. These individuals will not smoke the experimental cigarettes (lab Visits 2 and 3), until or unless a waiver of approval to provide these experimental cigarettes has been given by the state.

CAN I WITHDRAW FROM THE STUDY?

701G Consent | OUHSC IRB Version Date: 03/12/2019

IRB Number: 10581

You can stop participating in this study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher. Refusal to participate or withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you withdraw, you will be compensated for your time up to that point. Your data up to that point may be used for study purposes unless you request otherwise

There may be circumstances under which your participation may be terminated by the investigator without your consent. We may discontinue you from the study if we believe being in the study may put you at significant risk; if you are unable or unwilling to follow study procedures, such as keeping your visit appointments, or unwilling or unable to abstain from nicotine or tobacco products; or if you are female and are pregnant or breastfeeding, or become pregnant.

WHAT ARE THE RISKS OF THE STUDY?

The cigarettes you smoke during this study will be your own brand and the study cigarettes that we provide to you will be commercially available.

The study cigarettes contain tobacco and nicotine. Although smoking is associated with disease, we do not expect the disease risk to be significantly greater when smoking the study cigarettes versus the cigarettes you typically smoke. At the end of the study, you will be offered resources to help you stop smoking. Quitting smoking can greatly reduce risks to your health.

Some questions may make you feel uncomfortable. You may refuse to answer any questions. However, if you refuse to answer questions that are required to determine your eligibility for the study, you will not be able to continue in the study. There is a potential risk for an unanticipated breach of confidentiality. Below we describe the methods we will follow to ensure your confidentiality is maintained.

In addition to the risks described in the Key Information section, you may also be at risk for acute side effects of nicotine including headache, nausea/vomiting, increased heart rate, increased blood pressure, runny/stuffy nose, change in taste, heartburn, hiccups, sweating, or diarrhea. You should discuss these with the researcher and/or your regular doctor. Other drugs may be given to make side effects less serious and uncomfortable. Many side effects go away shortly after the cigarettes are stopped, but in some cases side effects can be serious or long lasting and permanent.

For more information about risks and side effects, contact Amy Cohn, PhD or the study coordinator at 405-271-7759 24 hours a day. We are available Monday through Friday during regular business hours (9am-5pm) to return phone calls.

REPRODUCTIVE RISKS FOR WOMEN:

If you are a female, you must not be and should not become pregnant nor breast-feed an infant while participating in this study. Smoking cigarettes while you are pregnant or breastfeeding may involve risks to an embryo, fetus, or infant, including birth defects which are currently unforeseeable. In order to reduce your risk of pregnancy, you or your partner should use one or more of the acceptable methods of birth control listed below, regularly and consistently, while you are in this study.

Acceptable methods of birth control (continuing throughout the study) include:

- An approved oral contraceptive (birth control pill)
- Intra-uterine device (IUD)



701G Consent | OUHSC IRB Version Date: 03/12/2019

IRB Number: 10581

- Hormone implants
- Contraceptive injection (Depo-Provera)
- Barrier methods (diaphragm with spermicidal gel or condoms)
- Transdermal contraceptives (birth control patch)
- Vaginal contraception ring (birth control ring)
- Sterilization (tubal ligation, hysterectomy or vasectomy)

Certain drugs may interact with contraceptive agents and reduce their effectiveness; therefore, you should inform the study staff of all medications (prescription and over-the-counter) that you are currently taking or begin taking during the study.

IN CASE OF PREGNANCY:

If you become pregnant or suspect that you are pregnant, you should immediately inform the study personnel. We will perform a pregnancy test at each in-person visit. If pregnancy is confirmed, you will be withdrawn from the study. Payment for all aspects of obstetrical, child, or related care will be your responsibility.

TO WHAT EXTENT WILL MY INFORMATION BE KEPT CONFIDENTIAL?

Efforts will be made to keep your personal information confidential. You will not be identifiable by name or description in any reports or publications about this study. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. You will be asked to sign a separate authorization form for use or sharing of your protected health information.

There are organizations outside the OUHSC that may inspect and/or copy your research records for quality assurance and data analysis. These organizations may include the US Food & Drug Administration and other regulatory agencies, and the National Institutes of Health. The OUHSC Human Research Participant Program office, the OUHSC Institutional Review Board, OUHSC Office of Compliance, and other University administrative offices may also inspect and/or copy your research records for these purposes.

We work with a university vendor who supplied the mobile application for the automated daily phone surveys. The company will take appropriate steps to protect your privacy. Your information is stored securely and separately from your survey responses. Your personal information will not be sold or given to any other people or companies for any purpose.

Posting Study on ClinicalTrials.gov:

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. However, this website will not include information that can identify you. At most, the website will include a summary of the study and results. You can search this website at any time.

Certificate of Confidentiality:

To help protect your privacy, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. This Certificate means that the researchers cannot be forced (for example by court subpoena) to share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

701G Consent | OUHSC IRB Version Date: 03/12/2019
IRB Number: 10581

The Certificate cannot be used to resist a demand for information from personnel of the U.S. government that is used for checking or evaluating federally-funded projects or for information that must be disclosed in order to meet the requirements of the US Food and Drug Administration.

The protection offered by the Certificate of Confidentiality does not prevent us from being required by applicable state law to report information about suspected or known sexual, physical, or other abuse of a child or older person, or a subject's threats of violence to self or others. If any member of the research team is given such information, he or she will be required to make a report to the appropriate authorities.

The Certificate, however, does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. This means that you and your family should actively protect your own privacy.

Identifiable Private Information:

- Your information may be used for future studies without your additional consent. We will remove direct identifiers from your information/specimen and assign a code. The key to this code will be kept separately and only the researcher and approved study personnel for this study will have access to the code. If your information is shared with another investigator for research purposes, they will not be able to re-identify you.

WHAT ARE THE COSTS?

You may have some travel costs for your study visits and you will be using your own cigarettes for part of the study. You will be reimbursed \$10 for each in-person visit, or \$10 for three curbside pick-up/drop-offs of study materials if you take the study remotely. You can earn up to \$30 total for travel. If you use your personal phone to complete the daily automated phone calls, we will reimburse you \$40 for the 2 weeks that you have it, or you may have a study phone provided to you if your phone does not have the Android operating system. There are no other costs to you.

WHAT IF I AM INJURED OR BECOME ILL WHILE PARTICIPATING IN THIS STUDY?

You will be watched throughout the study for Adverse Events. All Adverse Events will be recorded and will be followed until they are resolved or stabilized. Formal policies are in place for emergency procedures. If you are injured as a direct result of taking part in this study an Emergency Medical Service will take you to a medical center.

Complications arising as a result of the natural progression of an underlying or pre-existing condition may be billed to you or your insurance. Please check with the investigator or with your insurance company if you have questions.

No other funds have been set aside by the University of Oklahoma Health Sciences Center or the National Institutes of Health to compensate you in the event of injury, illness, or for other damages related to your event of injury or illness.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.



701G Consent | OUHSC IRB Version Date: 03/12/2019

IRB Number: 10581

If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time. Please be sure to discuss leaving the study with the principal investigator or a staff member. You may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled.

We will provide you with any significant new findings developed during the course of the research that may affect your health, welfare, or willingness to continue your participation in this study.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished. You consent to this temporary restriction.

WHOM DO I CALL IF I HAVE QUESTIONS, SUGGESTIONS, OR CONCERNS?

If you have questions, concerns, or complaints about the study or have a research-related injury, contact Amy M. Cohn, PhD at 405-271-1903 or the study coordinator at 405-271-7759 or at PrismStudy@ouhsc.edu.

If you cannot reach the Investigator or wish to speak to someone other than the investigator and for questions about your rights as a research participant, contact the OUHSC Director, Office of Human Research Participant Protection, at 405-271-2045.

SIGNATURE:

By signing this form, you are agreeing to participate in this research study under the conditions described. You have not given up any of your legal rights or released any individual or entity from liability for negligence. You have been given an opportunity to ask questions. You will be given a copy of this consent document.

I agree to participate in this study:

PARTICIPANT SIGNATURE (age ≥18)

Printed Name

Date

**SIGNATURE OF PERSON
OBTAINING CONSENT**

Printed Name

Date