Perelman School of Medicine
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Social and Behavioral Sciences Human Research Protocol Template *V4: 8 Jul 2022*

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PROTOCOL TITLE:

1. **Full Title:** Acute effects of cigarette packaging and charcoal filtration on perceptions, use behaviors, and harm exposure (IRB# 849152)
2. **Brief Title:** SKY Pilot

INTRODUCTION AND PURPOSE:

The US Food and Drug Administration (FDA) has the authority to regulate tobacco products, including their marketing and design.[1] There is modest empirical support that using cigarettes with charcoal filters may reduce exposure to some toxic constituents,[2–4] which could improve health outcomes for users of these products. However, studies have produced mixed conclusions about reduced harm resulting from use of charcoal filters, and it is further unclear if such effects occur with real world use of charcoal-filtered cigarettes, especially if marketed in misleading ways. The tobacco manufacturer Natural American Spirit (NAS) is using charcoal filters, combined with other misleading pack attributes (e.g., light colored packaging, brand name conveying 'lightness'), to promote a new cigarette product called 'Sky.' Although the Sky product marketing makes no explicit references to reduced harm, its marketing materials contain prominent implicit references to charcoal's purification properties. Although Sky is just one product, if this brand is commercially successful, other manufacturers may mimic NAS's marketing tactics to promote similar charcoal filtered cigarette products and implicitly mislead smokers about health risks.

This single laboratory session pilot study will examine the acute effects of cigarette filter type and packaging on initial product perceptions, use, and exposure. Forty adult daily smokers will be randomized to smoke two study-supplied commercially-available cigarettes interspersed by 45 minutes, completing pre- and post-cigarette carbon monoxide and questionnaire measures. We will use a 2 x 2 mixed factorial design to manipulate cigarette filter type (within-subject: charcoal vs. non-charcoal) and packaging (between-subject: light vs. dark).

OBJECTIVES:

This project will address the following specific aims:

Aim 1: Examine the acute effects of filter type on product perceptions, use behaviors, and exposure.
Hypothesis 1: Smokers will endorse more favorable product perceptions (i.e., greater subjective ratings and lower perceptions of harm), engage in greater smoking behaviors, and have higher tobacco exposure after smoking the cigarette with the charcoal (vs. non-charcoal) filter.

Aim 2: Assess the acute effects of packaging on product perceptions, use behaviors, and exposure.
Hypothesis 2: Light-colored (vs. black) packaging will be associated with lower perceptions of harm, subjective ratings consistent with lower harm products (e.g., milder taste, weaker strength), greater use behaviors, and greater tobacco exposure.

Aim 3: Examine the interaction of filter type and packaging on product perceptions, use, and exposure.
Hypothesis 3: The combination of light-colored packaging with the charcoal filter (actual product) will have the lowest perceptions of harm relative to other conditions, greatest use behaviors, and greatest tobacco exposure.

BACKGROUND:

The FDA can regulate tobacco products to reduce their negative health impact. Cigarette smoking remains the leading cause of preventable death.[5] In 2009, the Family Smoking Prevention and Tobacco Control Act (FSPTCA) granted the U.S. Food and Drug Administration (FDA) the authority to regulate the tobacco industry with the intent of protecting the public from tobacco-caused morbidity and mortality.[1] The FSPTCA allows the FDA to regulate the distribution, marketing, and manufacture of tobacco products, provided that rigorous empirical data supports that any regulatory actions taken ultimately benefit public health.[1]

The potential and pitfalls of charcoal filters on cigarettes. Within the FDA's regulatory authority is the ability to regulate cigarette design features,[1] such as filter composition and design. There is modest empirical support that using cigarettes with charcoal filters may reduce exposure to some toxic constituents, which could improve health outcomes for users of these products.[2–4] However, there are mixed conclusions about reduced harm resulting from use of charcoal filters in these and other studies, prompting a need for further research on how charcoal filters impact cigarette use and toxicant exposure.

The tobacco industry relies on marketing/packaging to stay relevant. The tobacco industry has a long history of exploiting product marketing to alter consumer perceptions and maintain sales.[6–8] "Light" cigarettes were promoted implicitly as reduced harm products to health-concerned smokers[9] through their labeling and light colored packaging,[10] yet contained as much nicotine as traditional cigarettes, and increased smokers' puffing behavior and consequent harm exposure.[11] Because the industry has previously used marketing to fuel false perceptions of tobacco product harms, as other regulations appear imminent, such as banning menthol or reducing nicotine levels in cigarettes,[12] the tobacco industry will likely search for innovative ways to promote its products. Packaging is and likely will remain the "final communication vehicle" between the industry and consumers.[13] Despite being required to remove misleading descriptors (i.e., "light") from cigarette packaging, the industry has used color to implicitly retain this information (e.g., gold = light; red = full-flavor).[14] The effects of misleading packaging may be further exacerbated by other design features that reduce perceptions of harm.

NAS promoting a product with implicit health claims; others may follow. The tobacco manufacturer Natural American Spirit (NAS) is using charcoal filters, combined with other misleading marketing attributes (e.g., light colored packaging, brand name conveying 'lightness', website claim that the charcoal for the filters 'is derived from coconut'), to promote a new cigarette product called 'Sky.' Although the Sky product marketing makes no explicit references to reduced harm, its marketing materials contain prominent implicit references to charcoal's purification properties. Although Sky is just one product, if this brand is commercially successful, other manufacturers may mimic NAS's marketing tactics to promote similar charcoal filtered cigarette products and implicitly mislead smokers about health risks.

Tobacco regulatory relevance. By examining the effects of cigarette filter type and pack color on product perceptions, use behaviors, and exposure, this work directly addresses multiple research priorities of the FDA Center for Tobacco Products (CTP), including behavior (how changes in design and packaging affect tobacco use behaviors and perceptions), marketing influences (how marketing impacts abuse liability and product initiation), and toxicity (how product design characteristics impact constituent exposure).

INNOVATION.

This project is innovative for several reasons. To our knowledge, this is the first formal study to address the effect of placing charcoal cigarettes in different packaging contexts, providing the FDA with evidence informing regulatory decisions regarding both cigarette design and marketing. We will study two industry-created packages, primarily defined by their color (black vs. white) and representing extreme ends along a continuum of implicit harm, thus expanding upon previous work using traditional colors (e.g., blue, red) to assess the impact of novel packaging on consumer reactions. By using identical cigarette rods that have different filter compositions, we will also be able to disentangle effects of cigarette design from packaging/other marketing. Finally, smokers will sample the product, simulating actual initial novel product use, rather than respond to product marketing only, building upon previous work on pack color effects using survey methods.[15]

CHARACTERISTICS OF THE STUDY POPULATION:

1. Target Population and Accrual:

We aim to enroll, defined as completing the informed consent process, 60 adult smokers from the greater Philadelphia region to obtain 40 eligible study completers (approximately 20 male and 20 female). Recruitment is anticipated to begin in August 2021 and will continue for 2 years. This accrual projection is based on our experience running similar studies with non-treatment seeking smokers requiring multiple visits. As this study consists of a single visit, we do not anticipate significant retention issues, though we do expect some individuals who enroll could be later be deemed ineligible or withdraw their participation.

2. Key Inclusion Criteria:

Eligible subjects will be:

1. Male and female smokers who are between 21 and 60 years of age and self-report smoking at least 5 cigarettes per day for at least the past 12 months.
2. Smokers of primarily non-menthol cigarettes of brands other than Natural American Spirit.
3. Not currently undergoing smoking cessation treatment or trying to quit.
4. Able to communicate fluently in English (speaking, writing, and reading).
5. Capable of giving written informed consent, which includes compliance with the requirements and restrictions listed in the combined consent and HIPAA form.

3. Key Exclusion Criteria:

Subjects who self-report and/or present with the following criteria will not be eligible to participate in the study:

<u>Smoking Behavior</u>

1. Use of menthol or Natural American Spirit cigarettes as preferred/regular brand (defined as using >20% of the time).
2. Use of research cigarettes in the past 6 months (i.e., past 6-month participation in applicable previous CIRNA studies).
3. Enrollment or plans to enroll in a smoking cessation program in the next month.
4. Provide an initial Carbon Monoxide (CO) reading < 5 parts per million (ppm).

<u>Alcohol/Drugs</u>

1. History of substance abuse (other than nicotine) in the past 12 months and/or currently receiving medical treatment for substance abuse.
2. Current alcohol consumption that exceeds 25 standard drinks/week.

<u>Medical</u>

1. Women who are pregnant, planning a pregnancy, and/or lactating.
2. Any impairment including, but not limited to, visual, physical, and/or neurological impairments preventing the completion of procedures included within this protocol. Notable impairments will be evaluated by the PI and eligibility will be determined on a case-by-case basis.
3. Color blindness.
4. Serious or unstable disease within the past 12 months (e.g. heart disease, cancer). Applicable conditions will be evaluated by the Principal Investigator and eligibility will be determined on a case-by-case basis.

<u>Psychiatric</u>

As determined by self-report:

1. Lifetime history or current diagnosis of psychosis, bipolar disorder, and/or schizophrenia.
2. Current diagnosis of major depression. Subjects with a history of major depression, in remission for 6 months or longer, are considered eligible.

Other
Additionally, participants may be deemed ineligible for any of the following general reasons at any point throughout the study, as well as during the initial telephone screen, at the discretion of the PI:

- Significant non-compliance with protocol and/or study design.
- Past, current, anticipated, or pending enrollment in another research program over the study period that could potentially impact study data.
- Any medical condition, illness, disorder, adverse event (AE), or concomitant medication that could compromise participant safety or significantly impact study performance.

4. Subject Recruitment and Screening:

We will recruit participants from the greater Philadelphia region primarily through digital media (e.g., internet postings, television ads), and secondarily through print ads and contacting former study participants. Those interested in participating will either directly contact study personnel via e-mail, telephone, or via completing a short REDCap eligibility survey. Prospective participants will ultimately complete a short telephone eligibility screen survey with staff; those eligible will be scheduled for the single laboratory session.

5. Early Withdrawal of Subjects:

Subjects may withdraw from the study at any time. They may also be discontinued from the study at the discretion of the PI for lack of adherence to the study procedures, or to protect the subject for reasons of safety or for administrative reasons. It will be documented whether or not each subject completes the study. Participants who withdraw or leave the study early will not be contacted following their withdrawal.

5. Vulnerable Populations

No children, pregnant women, fetuses, neonates, or prisoners are included within this research study.

6. Populations Vulnerable to Undue Influence or Coercion

Educationally or economically disadvantaged persons or cognitively impaired persons will not be targeted for recruitment; however, they may be included in the current study. Because recruitment efforts for this study will be targeted to the greater Philadelphia area, University of Pennsylvania employees and students may be exposed to these advertisements and choose to respond. Status of participation in the current study will be independent of the participant's work or school activities.

STUDY DESIGN:

We will recruit 40 adult daily, non-menthol smokers to a single 2-hr laboratory study where they will smoke two study-provided [commercially available] cigarettes, each for a 10-min *ad lib* period, and then complete product perception and use measures. Smoking sessions will be video recorded and scored to capture puffing behavior, and carbon monoxide (CO) assessments will be collected before and after smoking to assess changes in acute smoke exposure. We will use a 2 x 2 mixed factorial design to manipulate the study-provided cigarette's packaging (between subject factor: light colored 'Sky' package vs. black NAS package; both industry-made) and filter type (within-subject factor: charcoal filter vs. non-charcoal filter; cigarettes will appear identical despite differences in filter composition). Primary outcomes will be product perceptions (risk perceptions, subjective ratings), use behaviors (puffing behavior and purchase task), and acute toxicant exposure (changes in CO). Our laboratory has extensive experience with administering cigarette products within similar study designs.

METHODS:

1. Study Instruments:

Independent variables:

Cigarette pack type (between-subject condition): We will purchase and repurpose industry-created cigarette packages to randomly assign participants to smoke a study supplied-cigarette in either light colored (i.e., NAS 'Sky') or black (i.e., NAS 'Black') packs.

Cigarette filter type (within-subject condition): We will manipulate cigarette filter type by providing smokers with two cigarettes, one with a charcoal filter and one without a charcoal filter, in counterbalanced order. We will use the NAS 'Orange' and 'Sky' varieties as the non-charcoal and charcoal cigarettes, respectively, as these cigarettes are identical in appearance despite differences in filter composition.

Screening/Descriptive Measures:

Height/weight: Research staff will measure and document participant height and weight utilizing a standard physician's scale.

Medical history: A Medical History Form (led by the research staff) will be completed to review for applicable contraindications previously listed under Key Inclusion/Exclusion Criteria.

Demographics, Smoking history, Cigarette characteristics, and Nicotine Dependence (FTND): Standard questionnaires will be administered to assess participants': demographics, age at smoking initiation, current smoking rate, previous quit attempts, and own cigarette brand characteristic information (Cigarette Brand Form). Cigarette characteristics will include: length (king/regular, 100, 120, other), filter status (filtered vs. nonfiltered), pack type (soft vs. hard), tar and nicotine yield, and brand name/variety. We will also administer the Fagerstrom Test for Cigarette Dependence (FTCD),[16] a 6-item, self-report measure of nicotine dependence. The FTCD scale has satisfactory internal consistency (Cronbach's alpha = .64) and high test-retest reliability (r =.88).

Alcohol use: We will administer an alcohol use questionnaire to assess alcohol consumption over the past 7 days.

Primary Outcome Measures:

Product perceptions will be assessed using multiple questionnaires:

a. Risk beliefs: A previously validated 8-item scale[17–19] will be administered at the beginning of the study session (regarding their own brand) and after each cigarette smoked in the laboratory (regarding these cigarettes), while physically viewing the pack, to assess participant's perceptions of harms from using the product. We will examine both a summed composite score and individual items rated on a 5-point Likert scale (1 = "definitely untrue", 5 = "definitely true") that evaluate participants' preferred brand and the cigarettes they smoked on the following beliefs: a) "lower in nicotine", b) "lower in tar", c) "less addictive", d) "less likely to cause cancer", e) "has fewer chemicals", f) "is healthier", g) "makes smoking safer", h) "helps people quit smoking."

b. Perceived health risks: At the beginning of the study session and after using each laboratory cigarette, participants will complete a 13-item measure[20] asking them to indicate on a 7-point Likert scale (1 = "very low risk", 7 = "very high risk") their risk of developing 11 health conditions (i.e., lung cancer, heart disease, stroke, high blood pressure, diabetes, asthma, liver disease, emphysema, respiratory infections, other cancers, and addiction) based on regular use of their preferred brand and each cigarette they sampled. Two additional items will ask about overall risks of using the cigarettes for themselves and for others.

c. Subjective ratings: Subjective ratings will be measured after each cigarette smoked during in-person visits using 14 individual items assessing various cigarette characteristics (e.g., strength) used by the tobacco industry and our laboratory.[17,21–23] Items are rated on a 100 mm visual analog scale with item-specific anchors (e.g., strength: 0 = "very weak," 100 = "very strong"); lower scores indicate less favorable ratings.

Product use

a. Video-scored smoking behavior: Participants' puffing behavior will be collected using a validated procedure to score video recorded smoking sessions.[24] We previously demonstrated that video-observed puffing behavior measures are interchangeable with those collected by electronic topography devices. We

will quantify puffing behavior for this study using the same procedures to obtain estimated number of puffs taken, the duration of each puff, and interpuff interval (time between puffs).

b. Cigarette purchase task: Behavioral economic indices of demand will be measured using a hypothetical purchase task. Participants will be asked how many cigarettes (preferred brand and study-supplied) they would purchase and consume in the next 30 days across a range of prices, from free up to high amounts at which purchase/consumption is expected to drop off.

Exposure:

a. Carbon monoxide (CO): CO will be measured in parts per million (ppm) using the Vitalograph BreathCO carbon monoxide monitor (Lenexa, KS) at the onset of the laboratory visit, as well as before and after each cigarette smoked. CO at the onset of each visit represents daily exposure, while CO boost – the change in CO values resulting from smoking a cigarette – crudely estimates smoke exposure due to smoking an individual cigarette.

Secondary Outcome Measures and Covariates:

Craving: Craving will be assessed using at the beginning of the session using the Questionnaire on Smoking Urges (QSU). A "Right Now" frame of reference to determine factor subscales and a summary score from a 32-item Likert-format self-report instrument will be used to assess smoking urges and cravings over the course of the study. Questionnaire items are separated into four areas: 1) desire to smoke, 2) anticipation of immediate positive outcome from smoking, 3) anticipation of immediate relief from nicotine withdrawal or relief from negative affect, and 4) intentions to smoke.

Withdrawal: A Withdrawal Symptom Checklist (WSC), using a "Right Now" frame of reference, will be used to measure withdrawal symptoms at the beginning of the session. The checklist consists of 21 items such as cravings, irritability, difficulty concentrating, restlessness, impatience, anxious/tense, insomnia, drowsiness, nausea, tremors, increased heart rate, general physical complaints (e.g., sweating, dizziness), increased hunger, increased eating, headache, gastrointestinal disturbance, depression, fatigue, urges to smoke, and decreased heart rate. Participants will rate the intensity of their symptoms on the following scale: 0 = not present, 1 = mild, 2 = moderate, 3 = severe.

Attitudes and intentions (to use product): Attitudes toward using both participants preferred brand and the study-supplied cigarette be assessed using the mean of an eight-item, seven-point semantic differential scale[25,26] that asks, "Which of the words below would best describe your continued use of this product?" Items were a) bad/good, b) unenjoyable/enjoyable, c) unpleasant/pleasant, d) foolish/wise, e) difficult/easy, f) more/less harmful, g) not under/under my control, and h) less/more healthy. Higher and lower scores respectively indicate more and less favorable attitudes. Two Likert-type items will assess participants' intentions to purchase and use the study-supplied cigarettes regularly.

Quitting motivation (contemplation ladder): The contemplation ladder will be used to assess readiness to consider smoking cessation. Based on the stages of change model, the contemplation ladder is designed to measure a smokers' position on an 11-point (0-10) range, from having no thought of quitting to taking action to quit, and has been successfully employed in several diverse smoking populations. We will assess quitting motivation using the contemplation ladder as a potential covariate that could make participants more or less susceptible to effects of the study manipulates.

Final cigarette rating scale: At the end of the study, participants will be asked to recall how much they like their preferred brand and each cigarette they smoked (i.e. study-supplied) on a 10-point Likert-format scale (1= very little; 10= very much).

Brand appeal: Participants will be asked to complete a 6-item measure of brand appeal regarding their preferred brand and the two study-supplied cigarettes they smoked during their in-person session. They will be asked to rate the design of the brand of cigarette they currently smoke (or just tried) on the following 6 items: 1) stylish, 2) fashionable, 3) cool, 4) high quality, 5) attractive, and 6) appealing. Responses will be scored using a 7-point likert scale with anchors of "Strongly Agree" and "Strongly Disagree."

Mouth-level nicotine exposure and compensatory smoking: We will collect and store the filters of the two cigarettes smoked during laboratory sessions for potential future analysis regarding mouth-level nicotine exposure (approximated using the biomarker, solanesol) and compensatory smoking (estimated via digital image analysis).

2. Group Modifications:

There will be no differences in study procedures or questionnaire administration; all participants will complete the same procedures and questionnaires following randomization to filter type and packaging conditions.

3. Method for Assigning Subjects to Groups:

Participants will be randomly assigned to smoke two study-supplied cigarettes from 4 possible combinations of filter type and packaging conditions:

1. Charcoal filter cigarette in light-colored pack (NAS Sky cigarette in NAS Sky pack [i.e., actual product])
2. Charcoal filter cigarette in black-colored pack (NAS Sky cigarette in NAS Black pack)
3. Non-charcoal filter cigarette in light-colored pack (NAS Orange cigarette in NAS Sky pack)
4. Non-charcoal filter cigarette in black-colored pack (NAS Orange cigarette in NAS Black pack)

Each participant will smoke one charcoal filtered and one non-charcoal filtered cigarette, in counterbalanced order (i.e., the within-subject condition), but the participant will be assigned the same package color for both cigarettes (i.e., the between subject condition). Randomization group (filter order and package color) will be determined via internal database and assigned prior to participants' arrival for the session.

4. Administration of Surveys and/or Process:

The following measures will be assessed by staff at the start of the laboratory session:

1. Session onset CO
2. Medical history
3. Height and weight
4. Cigarette brand characteristics

The following measures will be completed by participants prior to trying to smoking any laboratory cigarettes:

1. Demographics
2. EtOH
3. Tobacco use history
4. FTCD
5. Contemplation ladder
6. Craving (QSU)
7. Withdrawal (WSCW)
8. Risk beliefs (own brand)
9. Perceived health risks (own brand)
10. Purchase task (own brand)
11. Brand appeal (own brand)
12. Pre-cigarette CO reading(s)

The following measures will be completed by participants after each cigarette smoked during the session:

1. Post-cigarette CO reading(s)
2. Subjective ratings
3. Risk perceptions
4. Perceived health risks
5. Attitudes and intentions
6. Purchase task
7. Brand appeal

The following measures will be completed by participants at the conclusion of the session:

1. Final cigarette rating scale
2. NAS & charcoal knowledge

5. Data Management:

A data management system (DMS) developed by the CIRNA Data Management Team will facilitate the operational facets of this study, including determining initial eligibility and producing lists of subjects for telephone contacts for scheduling, and data entry. The DMS uses the relational database product Microsoft Access as the primary software platform for data entry and validation, storage, retrieval, modification, and security. The DMS ensures data integrity through range and validity checks during the data entry process. Daily backups are performed to protect data from accidental destruction or corruption.

The CIRNA Data Manager will work closely with the PI, Dr. Mercincavage, to develop an understanding of the data collection, storage, and quality assessment needs for the study (e.g., design and development of data collection forms and any additional administrative CRFs) to ensure that standardized, uniform data collection and management procedures throughout the duration of study enrollment. The Data Manager will work closely with the PI and senior personnel to design, develop, and test an appropriate database structure to support the requirements of the DMS and to promote data security and integrity. Electronic audit trails of changes to database contents are incorporated into the design and will capture and record those changes automatically. In addition to the study database where actual results will be maintained, a development database will be created. The development database is a working environment that facilitates the development, testing, troubleshooting, enhancement, and training for the DMS without adversely affecting the integrity of the collected project data.

Prior to deployment for use by study staff, the database and DMS will be subjected to extensive functional testing according to a written test plan intended to verify the proper functioning of all DMS components. Any components that do not function as intended will be identified and evaluated by the development team to determine appropriate corrective action. Testing will also include an evaluation by user representatives for adherence to the requirements established by the intended users for the DMS. Successful completion of user acceptance tests will mark the end of development and predicate the deployment of the DMS for use in storing and managing active trial data. Any modifications made to the DMS will be conducted in accordance with change control procedures.

Data Storage: All data will be stored in an electronic Access database or in REDCap, and will be managed by the Data Manger. The database will be hosted on a secure computing server and will be restricted to individuals authorized to work on the trial via individual user accounts with passwords. Specific privilege assignments within the database will also be employed to limit the types of functions that authorized users can perform to those that are appropriate for their role in the trial. Additional measures to prevent unauthorized external access to the database will be employed using network firewall technologies. The Data Manager will maintain the database in an appropriate manner for the retention period required by regulation. Database administration includes user account maintenance, database security, performance monitoring, and database change management.

Data Processing: The data entry screens will resemble the data collection forms as closely as possible to allow visual referencing during data entry. This data entry module will be configured for single data entry. Participant data will either be entered into REDCap using smart phones, computers, or tablets or be collected by research staff, recorded on study-specific CRFs, and scanned in or entered directly into the appropriate DMS module. Data entry checks will be included in the entry screen designs where appropriate to limit the opportunity for erroneous entries due to mistyping. Such data entry checks would include value range comparisons, valid data type checks, required value checks, and/or skip pattern enforcement. Following telephone eligibility screening, staff will perform subject registration. A randomization module will allow staff to randomize eligible subjects into one of the four randomization groups. At the randomization attempt, the DMS will check the eligibility data to confirm validity. A randomization assignment will then be provided.

Data Quality Assurance: The Data Manager will work closely with the PI to develop a data quality module that will identify data items that may have been collected or entered into the database incorrectly. The module will run automatically to inspect all newly entered or modified data. Staff will review data validation results and take any required corrective action for invalid data. Queries will be recorded and tracked in the data quality module.

Corrections identified for individual data items will be managed by the research staff. All changes made will be recorded in an electronic audit trail and documented using change control procedures.

Monitoring of study progress will be accomplished, in part, through reviewing a set of standard enrollment, tracking, and quality review monitoring reports created by the Data Manager. Data audits will occur after the first participants are enrolled, as well as periodically throughout the recruitment period, to detect data entry errors. Eligible participants will have their source document information compared with the data entered in the database. Any errors will be investigated, resolved, and a plan will be implemented to prevent further errors should concerning patterns emerge.

The Data Manager will develop a module to assist study staff in participant recruitment and retention tracking. This module will accept and store contact information for potential subjects and will include data items to indicate the completion status of significant events. The tracking module will include information about contact and visit schedules to assist in preparing communications to potential and active participants concerning scheduled events. The module will also allow for incentive-related inventory management.

6. Subject Follow-up:

Not applicable. We will not follow up with participants after they complete the single study visit.

STUDY PROCEDURES:

1. Detailed Description:

Telephone eligibility interview (duration: ~0.5 hours): Trained personnel will determine participants' initial eligibility during a structured telephone interview. Those who meet eligibility criteria will be scheduled for the in-person visit.

Laboratory visit (duration: ~2.5 hours): The single study visit will occur at the Center for Interdisciplinary Research on Nicotine Addiction (CIRNA). Upon entering the CIRNA for this session, participants will complete the following:

1. Confirm the accuracy of information (i.e. name, address, phone number, email [if applicable], date of birth, age, ethnicity, race, and cigarette brand type) provided during the initial Telephone Eligibility Screening.
    a. Participants must bring in a pack of their own preferred brand of cigarettes to verify their cigarette brand type.
        i. If a participant forgets to bring a pack of their preferred brand of cigarettes, their session may be rescheduled to a later date or the participant may be deemed ineligible at the discretion of the PI.

2. Hear a study description where all study procedures will be reviewed.
    a. The combined informed consent and HIPAA will be read verbatim. All questions will be answered as appropriate after which the combined informed consent and HIPAA form will be completed (signed and dated) by the participant and a member of the research staff.

3. Perform a CO breath assessment and self-report smoking behavior over the past 24 hours to control for prior tobacco exposure.
    a. Participants with a CO reading < 5 ppm will be ineligible.

4. Height and weight measurements.

5. Complete a Medical History Form with a member of the research staff to review for applicable contraindications previously listed under Key Inclusion/Exclusion Criteria.

6. Complete questionnaires on cigarette characteristics (Cigarette Brand Form_*Staff should physically view preferred brand of cigarette pack), demographics, ETOH history, smoking history, nicotine dependence (FTND), craving (QSU), withdrawal (WSC), quitting motivation (contemplation ladder), risk perceptions (Risk Beliefs & Perceived Health Risks), Purchase Task, and Brand Appeal.

7. Smoke two study provided cigarettes interspersed by 45 minutes in the smoking lab while video-recorded.
    a. Participants will complete a harm perceptions questionnaire before smoking each cigarette.
    b. CO will be assessed before and after each cigarette smoked in the lab.
    c. Subjective Cigarette Ratings (VAS), Risk Beliefs, Perceived Health Risks, Purchase Task, Attitudes/Intentions, and Brand Appeal will be assessed after each cigarette smoked in the lab.
    d. Used cigarette filters will be collected and stored for potential future analysis.

8. Complete the Final Cigarette Rating Scale and NAS & Charcoal Knowledge questionnaires.

9. Receive Debrief Script and study payment
    a. Participants will be debriefed as to the full purpose of the study and compensated for their time.

2. Data Collection:

As detailed in the Data Management section, we will use both paper and electronic forms (via REDCap) surveys to collect participant data.

3. Genetic Testing:

Not applicable.

4. Use of Deception:

To avoid biasing participants' perceptions and use of the study cigarettes, we will not explicitly state in any materials (e.g., flyers, consent form) that the study's purpose is to evaluate the effects of cigarette packaging and filter composition. Instead, individuals will be told that we are recruiting volunteers to "evaluate different commercially available cigarettes."

Deception is acceptable in the present study because the study is minimal risk, and participants will be debriefed within the same session that the deception occurs.

Deception is necessary and scientifically valid in this instance because we are interested in how certain design and marketing features used to promote cigarettes implicitly affect smokers' perceptions and use of those products; if we were to inform participants that we were specifically interested in their reactions to the filter and packaging, they may respond in ways that they otherwise would not.

To inform subjects prospectively of the use of deception/incomplete disclosure, we have included the following suggested consent language on our consent document (see Informed Consent document): "In some research studies, the investigators cannot tell you exactly what the study is about before you participate in the study. We will describe the tasks in the study in a general way, but we can't explain the real purpose of the study until after you complete these tasks. When you are done, we will explain why we are doing this study, what we are looking at, and any other information you should know about this study. You will also be able to ask any questions you might have about the study's purpose and the tasks you did. Though we may not be able to explain the real purposes of the study until after you complete the tasks, there are no additional risks to those that have been described in this consent form."

Upon completing the full survey, participants will be debriefed of the true study purpose. They will be told that we were specifically interested in understanding the effects of cigarette packaging and filter type on their perceptions and use of the product, and that we were initially vague about our procedures to avoiding biasing their responses toward the study manipulations.

5. Statistical Analysis:

Analytic plan. Main and interaction effects of filter and pack type will be analyzed using univariate analysis of variance (ANOVA) models in SPSS IBM Statistics v26. Primary outcomes are continuous, and based on previous work[17,21,22] are expected to meet normality assumptions. Analyses will first include only main and interaction effects, then will include as covariates any baseline variables demonstrating a bivariate association of $p < 0.25$ with a given outcome measure.

Power analysis and sample size. A priori power analyses were conducted for primary aims using G*Power v3.1.9.2. These analyses determined that a target sample size of 40 will be adequate to detect a significant small-to-medium effect (partial $\eta^2 = .05$, $\alpha = 0.05$, within-subject correlation = 0.5) of the 2 x 2 between-within subject interaction on a univariate outcome with 80% power.

RISK/BENEFIT ASSESSMENT:

1. Risks:

The potential risks to participants, and their likelihood and seriousness, are minimal and described below. Participants can choose, as an alternative, to not enroll in this study.

Emotional distress: Some subjects may experience some emotional distress during the study due to learning their CO levels or completing questionnaires. These events happen very rarely and in almost all cases are short-lived and of low intensity. If upon assessment in the study the participant exhibits severe high levels of emotional distress, the participant will be offered a referral for mental health services in the area.

Cigarette smoking: Although smoking is associated with many diseases, we do not believe the risk is beyond everyday risk as all participants must report smoking at least 5 cigarettes per day to be eligible for this study, which exceeds the number of cigarettes that they would smoke during the single study session. We will inform participants that continued smoking has been shown to cause diseases such as emphysema and cancer.

Confidentiality and loss of privacy: Communications made among study staff regarding participants will use study identification number only and not include names or any other personal identification numbers. Participant data will be kept in locked files which are only accessible to staff. In all data sets we will only include identification numbers to label each participant. No names or other unique identifiers will appear in data sets. Only study-specific staff, identified in institutional review board-approved materials, will have access to the list of names matched to identification numbers.

COVID-19: By attending the laboratory visit, participants may place themselves at increased risk for exposure to the COVID-19 virus. Additionally, if participants choose to use public transportation to get to their appointments, they may place themselves at increased risk for exposure to the COVID-19 virus. We advise participants to wear a mask and practice social distancing while using public transportation. All participants will be provided the IRB recommended COVID-19 Informational Sheet before agreeing to take part in this research study. The CIRNA will follow guidelines to ensure minimal contact between participants and staff to mitigate exposure to the COVID-19 virus. Details can be found within the Spring Semester Research Resumption Phase Plan for the 4th Floor.

Other risks: This research may involve risks that are currently unforeseeable.

2. Benefits:

Individuals will not benefit directly from their participation in this study. The anticipated benefit of this research to society (i.e., indirect benefit) is to provide data regarding the effects of cigarette filter composition and packaging on product perception, use, and exposure outcomes, which may be used to guide decisions related to regulating cigarette design and marketing.

Although this study is not a cessation trial, participants may be motivated to seek cessation. Information about ongoing cessation trials in our Center and in the City of Philadelphia is available for participants interested in cessation.

3. Subject Privacy:

Only individuals who have responded to recruitment efforts or who have agreed to be contacted about studies at our Center will be contacted over the phone. If an individual cannot be reached immediately, staff will identify themselves only as calling from the University of Pennsylvania; no mention will be made of the inquiry regarding study participation. Participants will undergo an initial telephone screening where preliminary eligibility for the study will be determined. Only if a participant is initially eligible will they be asked to attend an in-person visit to confirm eligibility. All data will be collected by staff who have completed the CITI-Protection of Human Subjects Research Training and HIPAA Compliance Training. Once enrolled, information will never be recorded with identifiers other than study ID. A separate list of names with ID numbers will be accessible only by authorized personnel. All records will be kept in locked filing cabinets to maintain confidentiality. All analyses will be conducted on de-identified data.

Data will be accessible only to the Study Investigators, study staff, applicable Center staff, UPenn IRB, Office of Clinical Research, authorized UPENN staff (e.g. accounting and billing matters), National Cancer Institute, and the FDA. Communications made among study staff regarding participants will use identification number only and not include names or any other personal identification numbers. Participant data will be kept in locked files which are only accessible to staff. In all data sets we will only include identification numbers to label each participant. No names or other unique identifiers will appear in data sets. Only study-specific staff, identified in institutional review board-approved materials, will have access to the list of names matched to identification numbers. Electronic data will be password protected and will be stored on an institutionally secured and managed server. Per language in our informed consent form and standard procedures across the CIRNA, we retain participant PHI indefinitely unless participants request in writing that they wish to revoke access to this information.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify a subject directly. At most, the website will include a summary of the results. Subjects may search this website at any time.

4. Subject Confidentiality:

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization.

How will confidentiality of data be maintained? Check all that apply.

☒ Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

☒ Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.

☒ Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

☒ Whenever feasible, identifiers will be removed from study-related information.

☐ A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

☐ A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

☒ Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

☐ Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

☐ Other (specify):

Additionally, per NIH policy, sensitive information obtained during the course of the study is protected by under a Certificate of Confidentiality. All recipients of a Certificate shall not:

- Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

Disclosure is permitted only when:

- Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding;
- Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
- Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

Since self-report data will be collected and stored as part of this study, it is possible that subject privacy or confidentiality can be threatened. To address this concern, the data management system has set up several safeguards to prevent unauthorized access to participant data. In the subject map table, an automatically generated index number is assigned to a subject's study identification number. A linked subject identification table is created to store subject name, address, and telephone contact information. This table uses the automatically generated index number rather than the study identification number. The master subject map and subject identification information are maintained in separate locations. Using this method, no identifying subject information is directly linked to bio-samples or results. Any publication of data will not identify participants by name or with an identifier that could be used to reveal identity.

Video recordings of participants' smoking sessions will not include other identifying information (e.g., name) other than their face. Video recordings will be kept on password-protected computers accessible to study staff only. Recordings will be maintained for a period of at least four years after the study is terminated, completed, or the date that the records are no longer considered necessary.

5. Protected Health Information

The following protected health information (PHI) may be collected as part of this study:
• Name
• Street address, city, county, zip code
• All elements of dates (except year) for dates directly related to an individual and all ages over 89
• Date of birth

• Social Security Number (compensation purposes)
• Telephone number(s) and e-mail addresses
• Results from all questionnaires, tests, and procedures
• Any other unique identifying number, characteristic, or code
• Full face photographic images and any comparable images

Data listed above will be accessible to:
• Investigators and the study team
• Authorized members of UPENN Staff (e.g. accounting and billing matters, provide treatment, etc.)
• UPENN IRB
• Greenphire
• Office of Clinical Research
• The Office of Human Research Protections
• The Food and Drug Administration (FDA)
• The National Institutes of Health

6. Compensation:

Participants will be compensated up to $100 via ClinCard for successfully completing all study requirements at the end of the single laboratory session ($90 visit compensation, $10 travel reimbursement). Those determined to be ineligible during the study session will receive travel compensation only ($10).

Participants will be asked to complete a W-9 tax form at the conclusion of the study because the University of Pennsylvania is required to report to the Internal Revenue Service (IRS) any cumulative payments for participation in research studies at the University of Pennsylvania that exceed a total of $600 in a calendar year. A W-9 will aid the Center in tracking and reporting those who participate in multiple projects at the Center and accrue over $600 in a calendar year.

7. Data and Safety Monitoring:

The PI will be responsible for the overall monitoring of the data and safety of participants, assisted by other study personnel. Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the PI or designated member of the research team to the IRB.

8. Investigator's Risk/Benefit Assessment:

The PI feels the benefits of study participation outweigh the risks, given that the risks of participating in this study are minimal and largely relate to confidentiality/privacy concerns, and that the anticipated benefits to society include increased knowledge of how cigarette packaging and filtration influence product perceptions, use, and exposure, which by extension, may be used to inform regulation of both cigarette marketing and design to subsequently reduce tobacco-caused disease.

INFORMED CONSENT:

1. Consent Process:

A fully trained study staff member will obtain informed consent using the combined consent and HIPAA authorization form approved by the University of Pennsylvania IRB. The consenting process will occur in-person at the CIRNA prior to the initiation of any study procedures and will involve a discussion of the study requirements and procedures. Participants will have an opportunity to ask any questions and/or express concerns, which will be documented on a "Questions Form." Participants can elect not to participate and may withdraw at any time without penalty. Participants will receive a copy of the combined consent and HIPAA authorization form for their records. In addition, participants will be given the Principal Investigator's contact information (located on the consent) should they wish to speak to the Investigator during the course of the study regarding their consent or the study procedures. The consent process will take place in English. There will be no waiting period, no coercion

to participate, and all participants will be considered competent to provide informed consent (i.e., they will be asked if they understand what they are consenting for). If the participant has difficulty or is unable to understand the consent form or other procedures, they will be excluded from the study. The original signed combined consent/HIPAA authorization and Questions forms will be centrally stored in Regulatory Consent Binders.

2. Waiver of Informed Consent:

Not applicable.

RESOURCES NECESSARY FOR HUMAN RESEARCH PROTECTION:

1. Qualifications of Investigators

Brief highlights are presented below for key investigators.

Melissa Mercincavage, Ph.D., Principal Investigator: Dr. Mercincavage is an Assistant Professor in the Center for Interdisciplinary Research on Nicotine Addiction (CIRNA) in the Department of Psychiatry and the Tobacco Center of Regulatory Science at the University of Pennsylvania (UPENN). She will oversee operations for the study and will have responsibility for the design, implementation, and evaluation of the proposed research. Dr. Mercincavage has previously conducted laboratory-based smoking studies of similar design and duration related to informing the tobacco regulatory science field. She will be responsible for overseeing the study materials for institutional review board approval, programming study equipment, overseeing training, conducting analyses and manuscript preparation.

Andrew A. Strasser, Ph.D., Co-Investigator: Dr. Strasser is Professor of Psychiatry at UPENN, Director of the Biobehavioral Laboratory in the CIRNA, and Co-Principal Investigator of the UPenn-Rutgers Tobacco Center of Regulatory Science (TCORS). Dr. Strasser has been conducting smoking research for over 20 years, with expertise in assessing smoking behavior and biomarker data, and has several ongoing NIH-funded projects involving health communication and smoking, including clinical trials assessing effects of tobacco product marketing on smoking behaviors and exposure. Dr. Strasser will serve as a Co-Investigator on this project and will provide guidance on study design and execution, data analyses, and manuscript and grant preparation.

Andrea C. Johnson, Ph.D., Co-Investigator: Dr. Johnson is a Postdoctoral Researcher at the UPenn-Rutgers TCORS and the Center for Interdisciplinary Research on Nicotine Addiction at the University of Pennsylvania. Dr. Johnson will serve as a Co-Investigator on this project. She will assist Dr. Mercincavage in overseeing the proposed research, executing protocols, conducting analyses, and preparing manuscript submissions.

2. Research Staff and Assurances about Training

The following research staff will be directly involved with the implementation and execution of the current study:

- Melissa Mercincavage, Ph.D., Principal Investigator
- Andrew A. Strasser, Ph.D., Co-Investigator
- Andrea Johnson, Ph.D., Co-Investigator
- Teresa DeAtley, Ph.D., Postdoctoral Researcher
- Matthew Stone, Ph.D., Postdoctoral Researcher
- Victoria McLaughlin, Project Manager
- Valentina Souprountchouk, Project Manager
- Catherine Kreider, Project Manager
- Susan Ware, Database Developer/Manager
- Linda Mangino, Fiscal Coordinator
- Kendra House, Research Staff
- Amanda Lopez, Research Staff
- Emma Pitcher, Research Staff
- Lizza Waugh, Research Staff

- Julia Villasenior, Research Staff
- Brianna Lenza, Research Staff

Staff training will be overseen by the PI and consist of an initial explanation and review of the protocol, informed consent form, CRFs and laboratory tasks, data management system, and all study-specific SOPs. In addition, during a standardized training period, the duties of each staff member will be clearly outlined, and all applicable regulations will be reviewed. Training interactions will be documented in a training log, which will be maintained within the regulatory binder. Senior personnel will supervise junior staff and provide re-training as needed. All personnel working on this project will complete required training in the protection of human subjects and the protection of personal identifiable information (i.e. HIPAA) before interacting with study data or research participants. All human subject and privacy protections certifications will be maintained in the regulatory binder.

Until COVID-19 research operation restrictions at UPenn are removed, training will be conducted primarily via BlueJeans, a HIPAA-compliant platform used by Penn Medicine for video conferencing purposes. Conducting training via BlueJeans will ensure all training procedures are completed appropriately while meeting COVID-19 social distancing guidelines.

3. Access to Target Population / Recruitment

Using proven strategies from prior studies conducted at the CIRNA (previous Mercincavage and Strasser protocols) we will recruit participants from the greater Philadelphia region primarily through digital media (e.g., internet postings, television ads), and secondarily through print ads and contacting former study participants. Our team has been highly successful using these methods to recruit adult, non-menthol smokers.

4. Research Facilities

This single-session study will take place in the CIRNA at the University of Pennsylvania. The facilities available for this project include physio rooms, ventilated smoking laboratories, storage rooms, office space for study personnel, and data management facilities. The lab has 5 Carbon Monoxide devices (Vitalograph) and several laboratory-housed computers are available to conduct data processing. Data are maintained on a firewall protected, secure server with continual backup. Paper data and participant charts are stored in locked cabinets in a secured storage room.

5. Timeline and Feasibility

The study will take place over a period of 2 years or until 40 participants complete the study. However, each individual's participation will take no more than 3 hours total. Ensuring enough time to properly sanitize experiment rooms and study equipment between participant visits, we have the capacity to recruit 2 subjects per day. Because this study consists of a single visit, we do not anticipate retention issues.

REFERENCES

1. U.S. Congress. *Family Smoking Prevention and Tobacco Control Federal Reform Act.*; 2009.
2. Goel R, Bitzer ZT, Reilly SM, et al. Effect of Charcoal in Cigarette Filters on Free Radicals in Mainstream Smoke. *Chem Res Toxicol*. 2018;31(8):745-751.
3. Reilly SM, Goel R, Trushin N, et al. Effects of Charcoal on Carbonyl Delivery from Commercial, Research, and Make-Your-Own Cigarettes. *Chem Res Toxicol*. 2018;31(12):1339-1347.
4. Muscat JE, Takezaki T, Tajima K, Stellman SD. Charcoal cigarette filters and lung cancer risk in Aichi Prefecture, Japan. *Cancer Sci*. 2005;96(5):283-287.
5. U.S. Department of Health and Human Services. *The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General*. Government Printing Office; 2014.
6. Moodie C, MacKintosh AM, Brown A, Hastings GB. Tobacco marketing awareness on youth smoking susceptibility and perceived prevalence before and after an advertising ban. *Eur J Public Health*. 2008;18(5):484-490.
7. Pederson LL, Nelson DE. Literature review and summary of perceptions, attitudes, beliefs, and marketing of potentially reduced exposure products: Communication implications. *Nicotine Tob Res*. 2007;9(5):525-534.
8. Apollonio DE. Marketing to the marginalised: tobacco industry targeting of the homeless and mentally ill. *Tob Control*. 2005;14(6):409-415.
9. Pollay RW, Dewhirst T. The dark side of marketing seemingly “Light” cigarettes: successful images and failed fact. *Tob Control*. 2002;11(Supplement 1):i18-i31.
10. Hammond D, Dockrell M, Arnott D, Lee A, McNeill A. Cigarette pack design and perceptions of risk among UK adults and youth. *Eur J Public Health*. 2009;19(6):631-637.
11. National Cancer Institute. *Risks Associated with Smoking Cigarettes with Low Machine-Measured Yields of Tar and Nicotine*. National Institutes of Health; 2001.
12. Maloney J. Biden Administration Considering Rule to Cut Nicotine in Cigarettes. *Wall Street Journal*. https://www.wsj.com/articles/biden-administration-considering-rule-to-cut-nicotine-in-cigarettes-11618859564. Published April 19, 2021. Accessed April 19, 2021.
13. Hulit M. In: *Marketing Issues Corporate Affairs Conference*. ; 1994.
14. Falcone M, Bansal-Travers M, Sanborn PM, Tang KZ, Strasser AA. Awareness of FDA-mandated cigarette packaging changes among smokers of “light” cigarettes. *Health Educ Res*. 2015;30(1):81-86.
15. Delnevo CD, Jeong M, Ganz O, Giovenco DP, Miller Lo E. The Effect of Cigarillo Packaging Characteristics on Young Adult Perceptions and Intentions: An Experimental Study. *Int J Environ Res Public Health*. 2021;18(8):4330.
16. Fagerstrom K. Determinants of tobacco use and renaming the FTND to the Fagerstrom Test for Cigarette Dependence. *Nicotine Tob Res*. 2012;14(1):75-78.
17. Mercincavage M, Saddleson ML, Gup E, Halstead A, Mays D, Strasser AA. Reduced nicotine content cigarette advertising: How false beliefs and subjective ratings affect smoking behavior. *Drug Alcohol Depend*. 2017;173:99-106.
18. Strasser AA, Tang KZ, Tuller MD, Cappella JN. PREP advertisement features affect smokers’ beliefs regarding potential harm. *Tob Control*. 2008;17(Supplement 1):i32-i38.
19. Lochbuehler K, Tang KZ, Souprountchouk V, et al. Using eye-tracking to examine how embedding risk corrective statements improves cigarette risk beliefs: Implications for tobacco regulatory policy. *Drug Alcohol Depend*. 2016;164:97-105.
20. Pacek LR, McClernon FJ, Denlinger-Apte RL, et al. Perceived nicotine content of reduced nicotine content cigarettes is a correlate of perceived health risks. *Tob Control*. Published online In press.
21. Mercincavage M, Souprountchouk, V, Tang KZ, et al. A randomized controlled trial of progressively reduced nicotine content cigarettes on smoking behaviors, biomarkers of exposure, and subjective ratings. *Cancer Epidemiol Biomarkers Prev*. 2016;25:1125-1133.
22. Mercincavage M, Albelda B, Mays D, et al. Shedding ‘light’ on cigarette pack design: Color differences in product perceptions, use, and exposure following the U.S. descriptor ban. *Tob Control*. Published online in press.
23. Strasser AA, Ashare RL, Kaufman M, Tang KZ, Mesaros AC, Blair IA. The effect of menthol on cigarette smoking behaviors, biomarkers and subjective responses. *Cancer Epidemiol Biomarkers Prev*. 2013;22(3):382-389.
24. Mercincavage M, Karelitz JL, Kreider C, Souprountchouk V, Albelda B, Strasser AA. Comparing video observation to electronic topography device as a method for measuring cigarette puffing behavior. *Drug Alcohol Depend*. 2021;221:108623.
25. Strasser AA, Cappella JN, Jepson C, et al. Experimental evaluation of antitobacco PSAs: Effects of message content and format on physiological and behavioral outcomes. *Nicotine Tob Res*. 2009;11(3):293-302.
26. Yzer MC, Cappella JN, Fishbein M, Hornik R, Ahern RK. The effectiveness of gateway communications in anti-marijuana campaigns. *J Health Commun*. 2003;8(2):129-143.