VCU IRB #: HM20018382 / Clinicaltrials.gov #: NCT04219189

Study Title: Evaluating the acute effect of vaping on food intake/The Acute Effect of Vaping on Food Intake

Study Protocol with Statistical Analysis Plan*

*please note this document was abstracted from the approved IRB smartforms/documentation as there is not a separate protocol document

Protocol Approval Date: 8/4/2023

Major Changes to Protocol Approved by Human Subjects Protection Review Board:

Amendment approved 8/17/2021 - Regarding exclusion criteria, we added the following: women using progestin IUDs, women using injections such as Depo-Provera, and women who received a hysterectomy and still have ovaries present. The additional exclusion criteria was added because women who are currently under these conditions will have differing hormone levels from those recommended to perform this study.

Amendment approved 4/5/2022 – Regarding inclusion criteria we amended e-cigarette frequency: reports either every day e-cigarette use with liquid containing at least 0.3% (~3 mg/ml) nicotine or some day e-cigarette use (at least 3 days a week) with liquid containing at least 3% (~30 mg/ml) nicotine for the past 30 days. Our amended criteria allows for individuals who use lower nicotine concentration e-cigarette liquids at higher frequencies as well as those who meet our original criteria which focused on users of higher nicotine concentration liquids.

Amendment approved 7/21/2022 - We met with IRB staff/faculty about the FDA's recent marketing denial order for JUUL e-cigarettes, the study product we use in this study. They recommended we submit an amendment with some additional language to our informed consent form (ICF). These updates are included in the ICF and ICF video.

Amendment approved 8/31/2022 - We submit changes that were requested by the IRB regarding the ITP application submitted to the FDA for review including: 1) text has been added under study procedures in the smartform, 2) Revisions to the informed consent form that address the recent development from the FDA, and 3) uploading a copy of the protocol that was submitted to the FDA in the ITP application.

Amendment approved 8/4/2023 – VCU’s FDA Program Manager, has recommended that all studies should be designated as FDA-regulated if the study involves protocol-directed nicotine use. This study involved JUUL electronic nicotine delivery system use which has not been authorized or denied by the FDA.

Background, Rationale and Goals

* **Describe the study's background and what is currently known from the scientific literature, including citations, or upload a citation list in document upload. Use lay language whenever possible.**

Weight control is a common motive for cigarette smoking (1,2) and concerns about gaining weight are a significant barrier to quitting smoking (3,4). Nicotine suppresses appetite and increases resting metabolic, and also serves as a behavioral alternative to eating or a distraction from hunger or food craving (5,6). In rodents, systemic nicotine infusion has been shown to suppress ad libitum food intake due to significantly reduced meal sizes while meal numbers were not altered (7). In humans, data on the acute effects of nicotine, or cigarette smoking, respectively, on energy intake are scarce and contradictory. A small study (N=14) showed that acutely, smoking two cigarettes within a 15-minute period elicited a significantly lower energy intake (673 ± 245 kcal) during an ad libitum meal (45 min after the last cigarette) compared to the control condition of holding the cigarette without lighting it (825 ± 310 kcal) (8). In contrast, another study did not find any significant effect of a sham cigarette on hunger ratings or caloric intake of ten male and ten female smokers (9).

To our knowledge, data on the acute effect of e-cigarette use ('vaping') on ad libitum food intake are non-existent. Given that many e-cigarette users report vaping for weight control and that certain e-cigarettes are being actively marketed for weight management and/or suppression of food cravings (10), addressing this research gap is of the utmost importance.

Therefore, the aim of this study is to examine the acute effect of vaping on food intake during an ad libitum meal.

1. Pinto BM, Borrelli B, King TK, Bock BC, Clark MM, Roberts M, et al. Weight control smoking among sedentary women. Addict Behav. 1999 Feb;24(1):75–86.
2. White MA. Smoking for weight control and its associations with eating disorder symptomatology. Compr Psychiatry. 2012 May;53(4):403–7.
3. Beebe LA, Bush T. Post-cessation weight concerns among women calling a state tobacco quitline. Am J Prev Med. 2015 Jan;48(1 Suppl 1):S61-64.
4. Clark MM, Hurt RD, Croghan IT, Patten CA, Novotny P, Sloan JA, et al. The prevalence of weight concerns in a smoking abstinence clinical trial. Addict Behav. 2006 Jul;31(7):1144– 52.
5. Audrain-McGovern J, Benowitz N. Cigarette Smoking, Nicotine, and Body Weight. Clin Pharmacol Ther. 2011 Jul;90(1):164–8.
6. Metsios GS, Stavropoulos-Kalinoglou A, Nevill AM, Douglas KMJ, Koutedakis Y, Kitas GD. Cigarette smoking significantly increases basal metabolic rate in patients with rheumatoid arthritis. Ann Rheum Dis. 2008 Jan;67(1):70–3.
7. Bláha V, Yang ZJ, Meguid M, Chai JK, Zadák Z. Systemic nicotine administration suppresses food intake via reduced meal sizes in both male and female rats. Acta Medica (Hradec Kralove). 1998;41(4):167–73.
8. Yannakoulia M, Anastasiou CA, Zachari K, Sidiropoulou M, Katsaounou P, Tenta R. Acute effect of smoking and smoking abstinence on energy intake and appetite-related hormones blood concentrations. Physiol Behav. 2018 01;184:78–82.
9. Perkins KA, Sexton JE, DiMarco A, Fonte C. Acute effects of tobacco smoking on hunger and eating in male and female smokers. Appetite. 1994 Apr;22(2):149–58.
10. Morean ME, Wedel AV. Vaping to lose weight: Predictors of adult e-cigarette use for weight loss or control. Addict Behav. 2017;66:55–9.
11. Goniewicz ML, Boykan R, Messina CR, Eliscu A, Tolentino J. High exposure to nicotine among adolescents who use Juul and other vape pod systems ('pods'). Tobacco Control. 2018 Aug 30;tobaccocontrol-2018-054565.
12. Digard H, Proctor C, Kulasekaran A, Malmqvist U, Richter A. Determination of Nicotine Absorption from Multiple Tobacco Products and Nicotine Gum. Nicotine Tob Res. 2013 Jan 1;15(1):255–61.

* **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
Given that many e-cigarette users report vaping for weight control and that certain e-cigarettes are being actively marketed for weight management and/or suppression of food cravings (10), addressing this research gap is of the utmost importance.

The aim of this study is to examine the acute effect of vaping on food intake during an ad libitum meal.

We expect that the vaping condition will result in significantly less food intake compared to the no-vaping control condition.

* **Describe the study's specific aims or goals. Use lay language whenever possible.**
The goal of this study is to test whether vaping a nicotine-containing e-cigarette prior to eating a meal changes eating behavior (as measured by calories ingested) and associated subjective effects.

* **Describe the scientific benefit or importance of the knowledge to be gained:**

The benefits of this research are of a scientific nature. Specifically, we aim to use study results to inform our understanding of the influence of e-cigarettes on eating behavior as well as their use as weight control strategy by users.

In particular, the use of ECIGs has become increasingly popular, especially among individuals aged 18-24. New public health recommendations and policy are being targeted at this age group (and other age groups) and effects need to be studied/tested in this age group to inform their implementation. If we cannot study the age group that public health recommendations and policy are targeting, we cannot inform them effectively.

* **Describe any potential for direct benefits to participants in this study:**
None.

* **Describe any potential for direct social impact in this study . For example, any engagement with specific communities to respond to community-identified needs, or ways the study will strengthen the well-being of the specific communities if applicable:**
No direct social impact is expected from this study.

Study Population

* **Provide the maximum number of individuals that**

1. **May participate in any study interaction or intervention (Including screening, consenting, and study activities) AND/OR**
2. **You obtain any data/specimens about (regardless of identifiability)**

at VCU and at other sites under the VCU IRB's oversight. See the help text for additional guidance.
100

If this is a multi-Center Project, what is the maximum anticipated number of subjects across all sites?

* **Provide justification for the sample size by explaining how you arrived at the expected number of participants and why this number is adequate for answering the research questions:**
The study by Yannakoulia et al. (8) showed a 152 ± 190 (mean +SD) kcal lower food intake during the ad libitum meal for the smoking group compared to the sham group, 45 minutes after the 15-minute smoking/sham condition. Assuming a more conservative mean difference in food intake between the vaping and control condition in our study of 100 ± 200 (mean +SD) kcal (effect size of 0.50) following similar procedures (20 min vaping condition followed by a 45 min break before the food intake test), the sample size needed to detect a significant difference between the two conditions with a power of 80% and an α-level of 0.05 (two-sided) is 34.

Including ineligible individuals and expected dropout, we estimate up to 100 individuals may be consented over the course of the study. Please note that initial telephone/web screening is performed under separate protocols - HM20007677 and HM20002567.

* **List the study inclusion criteria:**
o 18 – 65 years of age (ID card verified) - please note ages 18-20 will only be enrolled following July 1, 2020 per new Virginia law (see below).

o Reports either every day e-cigarette use with liquid containing at least 0.3% (~3 mg/ml) nicotine or some day e-cigarette use (at least 3 days a week) with liquid containing at least 3% (~30 mg/ml) nicotine for the past 30 days.

Please note that beginning July 1, 2020, per Chapter 524 of the 2020 Acts of Assembly, which the Governor signed on March 31, 2020, Virginia law now permits us to recruit individuals aged 18-55. This law "Provides an exception to the law prohibiting possession of tobacco products, nicotine vapor products, or alternative nicotine products by a person less than 21 years of age when such possession is part of a scientific study being conducted by an organization for the purpose of medical research to further efforts in cigarette and tobacco use prevention and cessation and tobacco product regulation, provided that such medical research has been approved by an institutional review board pursuant to applicable federal regulations or by a research review committee."

* **List the study exclusion criteria:**
o being unwilling to consume the foods provided due to: a) dietary limitations or preferences or b) allergies to the foods provided.

o being unwilling to take 20 puffs from a JUUL device containing a 5% nicotine pod

o self-reported current, diagnosed medical condition(s) will be excluded automatically: heart-related conditions (e.g., recent heart attack/stroke, coronary heart disease), severe immune system disorders (e.g., HIV/AIDS, multiple sclerosis), respiratory disorders (e.g., COPD, asthma), kidney diseases, liver diseases (e.g., cirrhosis), or seizures

o observed high blood pressure at screening (systolic >140; diastolic >90)

o other self-reported current, diagnosed medical conditions (e.g., specific food allergies, diabetes, thyroid disease, lyme disease) will be considered for exclusion after consultation with the PI and medical monitor

o self-reported current, diagnosed psychiatric conditions or who report current psychiatric treatment or psychotropic medication use

o past month use of cocaine, opioids, benzodiazepines, methamphetamine, or other (non-cannabis) illicit drugs

o self-report of >25 days out of the past 30 for alcohol use or >20 days out of the past 30 for cannabis use.

o women who are breast-feeding or test positive for pregnancy (by urinalysis at screening)

o women using progestin-IUDs for birth control

o women using birth control injections (e.g., Depo-Provera)

o women who received a hysterectomy and still have ovaries present

o self-report intending to quit tobacco/nicotine products in the next 30 days

Study Procedures

* **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
Given that many e-cigarette users report vaping for weight control and that certain e-cigarettes are being actively marketed for weight management and/or suppression of food cravings (10), addressing this research gap is of the utmost importance.

The aim of this study is to examine the acute effect of vaping on food intake during an ad libitum meal.

We expect that the vaping condition will result in significantly less food intake compared to the no-vaping control condition.

* **Describe the study's specific aims or goals. Use lay language whenever possible.**
The goal of this study is to test whether vaping a nicotine-containing e-cigarette prior to eating a meal changes eating behavior (as measured by calories ingested) and associated subjective effects.

* **Choose all types of recruitment materials that may be used and upload them below:**

- [x] **E-mail invitations**
- [x] **Phone Solicitation scripts (i.e. cold calls or random-digit-dialing)**
- [x] **Flyers, Mailed Letters or Newspaper/TV/Radio Ads**
- [ ] TelegRAM announcements
- [x] **Website text**
- [ ] Study-specific web sites (provide the design and text)
- [ ] Social Media
- [ ] EPIC MyChart Patient Portal research study descriptions
- [x] **VCU TelegRAM announcement**
- [ ] Psychology Research Participant Pool (SONA) study descriptions
- [ ] Scripts for announcements made to groups
- [x] **Other recruitment document**
- [ ] No recruitment materials

* **If Other was selected above, describe the recruitment document that will be used:**
Craigslist.org advertisements

* **Describe the study procedures/methods for identifying and recruiting participants. Address all of the following three aspects of recruitment in your response.**

1. Identification of potentially eligible participants or secondary data/specimens of interest.
- What database(s) will be queried to identify secondary data/specimens
- How VCU Informatics or VCU IRDS will be used for cohort identification (when applicable, see help text)
- How potential participants' contact information will be obtained

2. Recruitment procedures to invite participation in the study (when applicable):
- How each of the written or verbal recruitment materials and reminders (selected above) will be used
- Who will contact, approach, or respond to potential participants
- Locations where recruitment procedures will take place
- The timing and frequency of recruitment attempts

3. Eligibility screening prior to consent and how those activities will be carried out (when applicable)

See the help text for additional guidance.

Flyers will be posted around VCU (e.g., public poster boards in classroom buildings, dorms), on community message boards, laundromats, convenience stores, libraries. Websites used for recruitment will include the VCU Telegram and craigslist. All of these advertisements direct participants to the phone number or websites used for our registries (HM20002567/HM20007677) but the advertisements themselves are specific to this study (HM20018382). Advertisements may also be placed on the laboratory websites associated with each registry (https://cstp.vcu.edu/ or https://blogs.vcu.edu/cobbco/). Advertisements posted on laboratory websites may use Telegram or Craigslist format or the non-tear-off image format.

Interested individuals will respond to recruitment materials by visiting the screener survey/registry webpage (HM20002567/HM20007677) or calling a dedicated study line answered by HM20002567/HM20007677 staff for screening. The informed consent document posted on the webpage is either read by the participant directly (online) or read verbally by HM20002567/HM20007677 staff. After participants agree to either an eligibility screening online or over the telephone (using the identical survey), the screening questions will be completed/asked. Individuals may also consent to join the research registry as part of HM20002567/HM20007677. Individuals who consent to the registry and complete screening questions will be evaluated for eligibility by HM20002567/HM20007677 staff, these individuals will always be concurrent staff on the current protocol (HM20018382).

If potentially eligible, HM20002567/HM20007677/HM20018382 staff will use administrative features (i.e., administrative fields/forms) in REDCap to create an internal report that is used to contact/follow-up potentially eligible and enrolled participants for the current protocol using their registry ID. No data will be directly transferred to the current protocol to or from either registry. Use of administrative fields and study staff that are aware of their responsibilities on related protocols eliminates the need for this additional activity.

The previously mentioned study ID is used to identify all subsequent study-related information/data. Following enrollment, the study ID is added to the participant's registry record/ID (HM20002567/HM20007677) in an administrative form thus electronically linking the registry ID (where contact information is housed) to their study ID (HM20018382). This technique is used so we can communicate effectively with participants as well as reduce the number of places/REDCap projects where participant contact information is stored. The study ID field (HM20018382) is deleted from the registry project (HM20002567/HM20007677) when recruitment for the study has been completed.

* **Does this study have a separate protocol document (i.e. a multisite or sponsor's protocol) that contains a detailed description of the study's methodology?**

- ○ Yes
- ◉ **No**

* **Since a separate protocol document is not uploaded, describe the proposed research using language understandable to those IRB committee members whose expertise is not scientific. The description must include:**

1. A statement explaining the study design
2. A detailed description of all the procedures that will be followed to carry out the study, preferably in sequential order, and in sufficient detail that the study's methods could be replicated
3. The schedule and frequency of when and how procedures will be conducted (e.g. in person, online, phone, paper, etc.)
4. A description of all research measures/tests/interventions that will be used, including analyses/tests conducted on specimens/biological samples (if applicable)

See the help text for additional guidance
Overview. This study involves 34 ECIG users who will complete 2, within-subject, laboratory conditions that differ by the product used: 1) JUUL e-cigarette with a 5% nicotine pod (tobacco flavor), 2) no ECIG use / participants sit in an empty room with an uncharged JUUL loaded with an empty pod for 20 minutes. The condition orders (i.e., 1 then 2, or 2 then 1) will be randomly ordered and assigned following enrollment. New recruits will replace participants who do not complete the study. Accrual ends when the required number of completers (N=34) is reached.

Products. For the session involving e-cigarette use, we will provide a pre-charged JUUL e-cigarette device and a new nicotine-containing pod containing (labeled as 5% nicotine; nicotine content will be verified independently for a random selection of products). The e-cigarette products will be sourced commercially (e.g., https://www.juul.com/). Please note we are unable to test each pod used during the study as accessing the liquid for testing requires tampering with the pod seal.

The anticipated amount of nicotine that will be absorbed with 20 puffs of this e-cigarette product is approximately 1.6 mg (Goniewicz et al., 2018, High exposure to nicotine among adolescents who use Juul and other vape pod systems (‘pods’).Tobacco Control), which is equal to approximately 1.5 cigarettes (Digard et al. 2013. Determination of Nicotine Absorption from Multiple Tobacco Products and Nicotine Gum. Nicotine Tob Res).

Test Meal. The test meal will be a buffet, consisting of several commercially available, sweet and salty snacks, such as crackers, cookies, cheese, chicken, carrots, chips, etc. This makes the amount of food consumed easily quantifiable and the small size of the snacks allows repeated serving at the second study visit without participants remembering the precise consumption at the first visit. Specifically, each food will be weighed before the participant eats. The amount of each food remaining after the participant eats will also be weighed. Food intake is calculated by difference; i.e., food selection minus plate waste. The energy and nutrient content of food intake is determined by matching each food the same or similar items in a nutrient database.

Recruitment and Enrollment.

At the in-person informed consent/screening appointment, participants will first complete informed consent procedures, consent may include the use of a recorded tool/presentation. After agreeing to be in the study, participants are assigned a unique numeric code (study ID) specific to this protocol. Then they will be asked to complete self-report baseline questionnaires, expired air CO/blood

pressure/heart rate/height/weight measurement, and provide a urine sample to assess pregnancy status if female. Age will be verified using a participant-provided identification card (any valid card with birth date is acceptable). Participants will be then familiarized with study measures and procedures used during sessions prior to scheduling their first session.

Potential participants will be recruited by IRB-approved advertisements, as well as referral from current participants. Once initial screening is completed (either over the phone or via the internet), participants will be invited to the lab to complete in-person informed consent, additional screening, and familiarization with study procedures (approximately 1.5 hrs, $15/hour compensation).

Upon arrival for an in-person screening visit, participants will be asked questions about possible COVID-19 symptoms/exposures and have their temperature taken. If their answers to the questions are all “no” and their temperature is below 100.4 degrees, participants will be escorted to a session room. Once participants have been seated in a private study room, research staff will communicate with the participants primarily using Zoom as an intercom, to speak/interact with participants.

Prior to in-person data collection, staff will review the informed consent in person and ensure they understand the study, its risks and benefits, and their rights as research participants. Participants will have the opportunity to ask questions to the research staff, prior to signing the consent document. Following documentation of informed consent, participants will complete baseline measures to confirm eligibility, have their blood pressure and heart rate checked, provide a urine for pregnancy status assessment (women only), and provide an expired air carbon monoxide sample. Age will be verified by asking participants to provide some form of identification that includes a date of birth.

Procedure Overview. Following successful completion of an in-person baseline screening session where informed consent is provided and eligibility is confirmed, eligible participants will be asked to schedule the first of two study sessions. During each session, participants will complete compliance/safety procedures, complete a vaping or a control condition, answer study measures, and have an ad libitum buffet meal.

Detailed Procedure. Each study session will be separated by about 1 week. For premenopausal women only, we will attempt to schedule sessions during their luteal phase based upon the baseline Menstrual Questionnaire responses (to help control for hormone levels).

Prior to starting any session, participants will complete COVID-19 measures upon arrival to the lab (See: COVID-19 Measures) including having their temperature checked. Once participants have been seated in a private study room, research staff will communicate with the participants primarily using Zoom as an intercom, to speak/interact with participants.

For each session, participants will be asked to refrain from beverages (other than water), food, and tobacco/nicotine for ≥12 hours with verification of tobacco/nicotine use status upon arrival at the lab (must arrive before 11am). More specifically, upon arrival at the laboratory for each session, participants’ breath CO will be measured to ensure compliance with the overnight abstinence criteria (CO must be either < or equal to half of the CO [ppm] that the participant had at the in-person screening visit, or, if 10 ppm or less at screening, it must be equal to or less than 5 ppm before a session can begin).

The session times were chosen to minimize the discomfort participants may experience due to extended abstinence from food/tobacco. Participants will also be asked to sign a form stating whether or not they have been abstinent from beverages (other than water), food, and tobacco/nicotine for ≥12 hours. In addition, participants will have their blood pressure checked and be asked about any side effects/adverse events experienced since the last visit. Responses to these items will determine whether participants can continue with the session/study.

Once deemed abstinent and safe to participate, participants will begin a 1-hour waiting period. During this time, participants cannot eat or use their cell phones, although water and/or books/magazines will be provided. We have recently instituted this 1-hour waiting period in other studies, because we find, after looking at plasma nicotine levels which are analyzed months after participants complete studies, that some participants do not comply with the 12-hour nicotine/tobacco abstinence requirement. Adding this 1-hour waiting period ensures that all participants are abstinent for at least one hour before the session begins.

After the one-hour waiting period, participants are asked to either vape (20 puffs) or will complete the control condition, which involves the participant sitting with an uncharged JUUL loaded with an empty pod for 20 minutes. The anticipated amount of nicotine that will be absorbed with 20 puffs of a 5% nicotine JUUL pod is approximately 1.6 mg, which is equal to approximately 1.5 cigarettes. They then have an additional rest period which is followed by an ad libitum buffet meal (that is administered in a different laboratory room). This rest period is to allow for feelings of satiety to occur prior to completion of the Food Craving Questionnaire, which measures appetitive drive to eat. We will use unobtrusive video surveillance of the participants during the buffet meal (Zoom) that will be monitored by research staff via their VCU computers (video data is transmitted via internet) during the ad libitum buffet meal. Live video will be monitored using privacy screens to ensure confidentiality during sessions and data will not be stored or linked to participant IDs or used for any analysis purpose other than determining if an individual takes food (other than eating it) from the laboratory room during the session. Immediately before and after the vaping/control condition, as well as immediately before and after the ad libitum meal, participants fill out subjective questionnaires. At the end of the session, participants will have their blood pressure checked again.

A detailed timeline of each session is described below.

Experimental session timeline (times approximate):

0 Hr 00 Participant arrives, Sign document/CO test/BP check/side effects-adverse events questionnaires followed by 1-hour waiting

period
0 Hr 05 Rest Period #1 begins
1 Hr 05 Subjective questionnaires
1 Hr 10 Vaping or control condition (uncharged JUUL w/ empty pod))
1 Hr 30 Subjective questionnaires
1 Hr 35 Rest Period #2 begins (additional questionnaires/behavioral tasks)
2 Hr 10 Subjective questionnaires
2 Hr 15 Ad libitum buffet meal
2 Hr 45 Subjective questionnaires
2 Hr 50 BP check, Pay participant and schedule next session if needed

Measures.

Baseline measures. During the in-person baseline screening session, we will assess sociodemographic information, health and psychiatric conditions (including specific respiratory/gastrointestinal/other health symptoms associated with e-cigarette use), drug and alcohol use, history and patterns of tobacco, nicotine dependence, discounting behavior, and perceived harm and risk of tobacco products using standardized items from national surveys (e.g., PATH and/or the PhenX Toolkit). We will also assess eating behavior with the Eating Inventory Measure (administered on paper) and the Power of Food Scale. Demand for own brand e-cigarettes will be assessed using a hypothetical purchase task at varying amounts of money ($0-$20.48). We will also inquire about participant's Physical Activity at Baseline utilizing the International Physical Activity Questionnaire. Urine samples will be collected and tested immediately for pregnancy; a menstrual cycle questionnaire also will be assessed in order to better determine cycle phase. We will also be obtaining baseline physiological measures including: expired air CO, HR/BP, and height/weight. CO will be assessed via a BreathCO monitor (Vitalograph, Lenaxa, KS). HR/BP will be measured using equipment that sounds an alarm if safety parameters are exceeded (Model 506, Criticare Systems).

Please note, the Minute Discounting Task is a series of hypothetical decision scenarios. Each scenario presents a choice between receiving an amount of money now or an amount of money later. These choices are differentiated by the amount of money at each time point and the length of time between the time points. Participants make a choice for five decision scenarios which are automatically adjusted based upon individual responses; while there are approximately 30 potential scenarios, only five are presented to the participant. The task takes less than one minute to complete. Data is collected via Qualtrics survey. Data is stored within Qualtrics under usernames and passwords assigned to some lab staff.

Pre-session side effects/adverse events. Before each session begins we ask participants whether they have experienced specific respiratory/gastrointestinal/other symptoms (identical to measures collected at baseline) as well as any other changes in their health since their last visit. Answers given at the beginning of each session will be compared to the participants' previous answers, and if any symptoms have increased or new information is provided that may raise participant risk/influence study data collection, Dr. Lipato will be asked to review participant responses. In some cases, we may contact Dr. Lipato to determine if a session can proceed. Premenopausal women also will be asked about their menstrual cycle.

Session physiological measures. To measure compliance with tobacco/nicotine abstinence at the beginning of sessions, a BreathCO monitor will be used (Vitalograph, Lenaxa, KS). For safety purposes, blood pressure will be checked at the beginning and end of each session. Energy (kcal) and macronutrient intake via will be measured via directly weighed food provision and waste (food intake is calculated by difference).

Session subjective measures. Repeatedly within each condition, we will ask participants to complete items that originate from the following questionnaires: Food Craving Questionnaire-State, Visual Analog Scales. See measures document for more detail.

Data analysis (**Statistical Analysis Plan**). Subjective and physiological data will be prepared as reported elsewhere (Barnes et al., 2017; Rusted et al., 1998; Cobb et al., 2010). In general, analysis will involve a within-subject ANOVA or mixed linear models approach. For all ANOVAs, adjustments for sphericity violations and post-hoc testing using Tukey's HSD or planned contrasts with Bonferroni corrections will be used (Keppel, 1991). Depending on the amount of missing data, multiple imputation techniques may be used (Allison, 2001).

Other Product Information: E-cigarette companies have to apply to the Food and Drug Administration (FDA) and be approved for sale in U.S. markets. In June 2022, the FDA denied the marketing application from JUUL, the manufacturer of the e-cigarettes used in this study. The FDA determined that JUUL did not provide enough evidence about the toxicity of its e-cigarette device and pods in its application. However, the FDA has not received clinical information to suggest an immediate hazard associated with the use of JUUL devices or JUUL pods. The FDA decision to ban the sale of JUUL is not final yet due to ongoing legal disputes. When and if the FDA's decision to ban JUUL is final, it will be illegal to sell JUUL products. However, it will still be legal for researchers to study these products and for participants to use them.

-The above text has been added to the informed consent form for this study under Physical Risks to address recent developments regarding JUUL products from the FDA.

-An investigational tobacco product application describing the products provided and procedures used in this study was submitted for review to the FDA Center for Tobacco Products on 7/22/2022.