DOCUMENT: Study Protocol

PROTOCOL TITLE: Complimentary Electronic Cigarettes for Harm Reduction among Adult Smokers with Asthma

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Brown University
Application for Full Board / Expedited IRB Review

Protocol Title: Complimentary Electronic Cigarettes for Harm Reduction among Adult Smokers with Asthma

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Is this a graduate student project?* ☐ Yes ☒ No

If student PI, please provide the following:

Advisor: **Phone number:**

Department: **Email address:**

Is this an undergraduate student project?* ☐ Yes ☒ No

If yes, name of undergraduate student:

Human Subjects CITI training is complete (PI, advisor (if student PI)): ☒ Yes ☐ No

Good Clinical Practice (GCP) training is complete (clinical trials only): ☒ Yes ☐ No ☐ N/A

**HIPAA training is complete (if using PHI): ☒ Yes ☐ No ☐ N/A **

Are there multiple sites involved with this study? ☐ Yes ☒ No

a) If "yes," review the Application for IRB Authorization Agreement

Funding Source(s):

- If externally funded, provide the following:

  Project title: Center for Addiction and Disease Risk Exacerbation (PI: Monti)

  Grant/Contract #: 1P20GM130414

- If there is no external funding for the project, write "University;" if funded by a specific internal funding mechanism (e.g., Mellon Mays Fellowship, Royce Fellowship, UTRA, OVPR Seed funds, etc.) please specify**:**

PART I. HUMAN SUBJECTS RESEARCH SCREENING

Full Board/Expedited studies must meet the federal definition of "Human Subjects Research." Answer the following questions to determine if your proposed study meets the federal definitions of both "Research" and "Human subjects."	
☒ Yes ☐ No	Is this study a systematic investigation?
☒ Yes ☐ No	Is the *primary design intent* of this study to contribute to generalizable knowledge?
☒ Yes ☐ No	Is the information being obtained *about* living individuals?
☒ Yes ☐ No	Will you collect information through some type of intervention or interaction? **OR** Will you have access to individually identifiable information? **OR** Will you have access to private information?
STOP	If you answered "no" to any of the above questions, your study does not meet the definition of "Human Subjects Research." You are not required to submit an Application for IRB review to the Brown HRPP.
Before proceeding, be sure to review the revised Common Rule categories for Exemption to determine if your study meets criteria for Exempt review and the Application for Exemption.	

PART II. RISK ASSESSMENT & EXPEDITED ELIGIBILITY SCREENER

1. Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

Using this definition, do you believe this research presents:

☒ No greater than minimal risk (**Expedited**)	Briefly justify this selection (and proceed to Question 2): Expedited review is suggested for the study because procedures are not expected to nor are likely to result in harm greater than encountered during daily life or during the performance of routine physical or psychological examinations. The complimentary electronic cigarettes provided to participants (JUUL) are a popular, commercially available nicotine The commercial availability of this product results in a lack of requirement for FDA Investigational Tobacco Product approval for its use in research. The use of electronic cigarettes broadly and JUUL specifically is consistent with the nicotine use patterns of proposed participants (i.e., regular smokers who are unwilling to quit), and the use of these products is expected to be associated with reduced harm versus their typical use. Procedures for blood collection are consistent with minimal risk, as defined by category 2. Collection of spirometry lung function is consistent with minimal risk routine clinical practice, as defined by category 4. Other physical and psychological tests are non-invasive and do not present risk beyond what is encountered in typical clinical or academic settings.
☐ Greater than minimal risk (**Full Board**)	Briefly justify this selection (and proceed to Part III):

2. Below are Research Categories *eligible* for Expedited Review. Select one or more of the categories that are applicable to your proposed research, if any.	
☐ Category 1	Clinical studies of drugs and medical devices only when condition (a) or (b) is met (please select one):

	☐ (a) research on drugs for which an IND application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review); OR ☐ (b) research on medical devices for which (i) an IDE exemption application is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
☒ Category 2	Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: ☒ (a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these participants, the amounts drawn must not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; OR ☐ (b) from other adults and children, considering the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these participants, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.
☐ Category 3	Prospective collection of biological specimens for research purposes by noninvasive means. Examples may include: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicated a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removal at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routing prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
☒ Category 4	Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples may include: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
☐ Category 5	Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). NOTE: Some research in this category may be Exempt. Review the categories for Exemption before selecting this option.
☐ Category 6	Collection of data from voice, video, digital, or image recordings made for research purposes.

☒ Category 7	Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. NOTE: Some research in this category may be Exempt. Review the categories for Exemption before selecting this option.

PART III. RESEARCH DESIGN & METHODS

1. **Introduction and Background.** *In reviewing the protocol, the IRB must consider the rationale for the study and the importance of the knowledge that may reasonably be expected to result.*

- **Briefly** summarize the nature, scientific or scholarly rationale and significance of the proposed study and any relevant background information on the topic in lay language. Explain the relevance of the study to previous and/or continuing work in the field. Discuss why novel inquiry is necessary. If there is a gap in knowledge, explain how it is anticipated that this research will address the gap. If this research is intended to replicate previous research, provide rationale.

Structure of overall study: This study is part of a larger Center for Biomedical Research Excellence (COBRE) grant which will enhance the research infrastructure of Brown University's School of Public Health. The grant will establish a new Center for Addiction and Disease Risk Exacerbation (CADRE) investigating the interrelationship between substance use and chronic diseases. This study described in this protocol will investigate whether providing complimentary electronic nicotine delivery systems (ENDS) to adults with asthma who smoke regularly and are unwilling to quit will increase substitution of smoking for ENDS and improve lung function. This project, and all projects at CADRE, are supported by the Clinical Laboratory Core (CLC) which will oversee the collection and storage of data and biological samples.

Background in lay language: Smoking is the leading cause of preventable disease and death in the US. One central smoking-related disease and the primary driver of smoking-related death is chronic obstructive pulmonary disorder (COPD). Smokers with COPD experience 85 times the rate of death than non-smokers with COPD between ages 55-64 and 20-30 times the rates of death after age 65. Asthma, a condition characterized by variable, recurring, and treatable airway obstruction, significantly increases the risk for developing COPD. Given the health burden of tobacco-use related respiratory disease, identifying ways of improving pulmonary function and preventing the development or progression of COPD among smokers – particularly those with extant respiratory conditions such as asthma – is a key public health goal.

Critically, smoking rates remain staggeringly high with 16.7% of US adults (41.1 million) smoking combustible tobacco. In light of the high rates of continued use and considerable disease burden of smoking, identifying novel harm reduction strategies is a significant public health target. One possible harm-reduction strategy for combustible tobacco is substitution with electronic nicotine delivery systems (ENDS). Reduced exposure to tobacco constituents has contributed to the public health view that while ENDS are not without harm these harms are reduced relative to combustible tobacco. Importantly, in smokers unwilling to quit, providing ENDS and encouraging switching from combustible cigarettes could reduce smoking-related harms and provide opportunities for cessation without typical rates of relapse. Studies of "healthy" smokers have also shown improved pulmonary function associated with substituting combustible tobacco for ENDS.

The current study aims to evaluate the effect of a randomized controlled clinical trial of complimentary ENDS provision to adults with asthma on tobacco use behaviors (including substitution of smoking for ENDS use), pulmonary function, asthma control and symptomatology, and related inflammatory and disease outcomes over 16 weeks. This study is significant because smoking is strongly linked to respiratory diseases such as COPD and asthma and targeting adults with asthma for harm reduction could reduce the public health burden of these diseases. Furthermore, given the limited research on this target population and the difficulty of promoting smoking cessation in people

who are unwilling to quit, using ENDS to facilitate substitution of smoking for ENDS represents a novel direction for harm reduction research.

2. **Specific Aims and Study Objectives.** *The IRB must evaluate the objectives of the research in order to determine whether the risks to participants are reasonable in relation to the importance of the knowledge that may be gained.*

Primary Aims and Hypotheses

Aim 1a. Assess the effects of 8 weeks of complimentary ENDS provision on cigarette use, ENDS use, and nicotine dependence, among adults with asthma over a 16 week period.

> **Hypothesis 1.** ENDS participants will smoke fewer cigarettes/day and demonstrate reduced cigarette dependence than control participants.

Aim 1b. Examine the effect of ENDS provision on respiratory function in adults with asthma.

> **Hypothesis 2.** ENDS participants will exhibit better asthma control and improved pulmonary function on measures of spirometry (i.e., PEF, FEV1, FVC, FEV1/FVC ratio, FEF25-75) and self-reported respiratory symptoms (wheezing, bronchitis, shortness of breath, mucus production, and other symptoms).

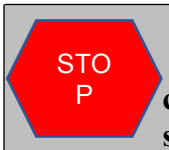
Secondary Aims

Aim 2a. Examine the effects of ENDS provision on inflammatory and disease biomarkers, including (IL-6, TNF-α, CXCL9, MMP9, FENO) and tobacco toxicant exposure (cotinine, CO, NNAL) at weeks baseline and week 8.

> **Hypothesis 4.** Levels of both inflammatory biomarkers and tobacco toxicant exposure will be improved among participants randomized to ENDS relative to assessment-only control.

Aim 2b. Examine the effect of ENDS provision on intention to quit smoking and smoking cessation self-efficacy.

> **Hypothesis 5.** ENDS participants will have higher quit intentions, and smoking cessation self-efficacy than controls.



If your study ONLY involves the use of identifiable secondary data / biospecimens, including coded data from which you may be able to ascertain identity, skip to PART VI. Otherwise, please continue.

3. Materials, Methods and Analysis. *The study design, methods and procedures must be adequately described in order for the IRB to understand all activities in which human subjects will participate. The IRB must also be able to differentiate those procedures that are performed for research purposes from those that are performed for routine care or evaluation.*

Design Overview: This study will use a between-subjects (N=30) randomized (unequally allocated 2:1), controlled design to investigating the influence of complimentary ENDS provision on combustible cigarette and ENDS use (including substitution of smoking for ENDS use), cigarette dependence, pulmonary function, and clinical indicators and biomarkers over 16 weeks. Eligible participants will be randomized to one of two conditions: 1) receive ENDS and e-liquid for 8 weeks, including encouragement to fully switch from cigarettes to ENDS; or, 2) an assessment-only control condition wherein participants may continue their usual cigarette smoking behaviors. The study involves initial and in-person screening, a baseline session and 8 weekly visits, and a 16-week follow-up visit (i.e., 8 weeks after discontinuation of complimentary ENDS provision to the experimental group).

ENDS selection: We intended to use JUUL for the ENDS condition due to its market share and nicotine delivery comparable to combustible cigarettes. However, due to shifting perceptions of JUUL related to EVALI and because the products have similar nicotine delivery profiles, we chose the VUSE Alto.

Initial Screening: Potential participants will be recruited from the community, through referral from established community partnerships with immunology clinics facilitated by co-investigator and project mentor Elizabeth McQuaid, and through recruitment and advertising partner BuildClinical (see section 5 for complete recruitment information). Computer-assisted screening will determine initial eligibility. Initial screening will query age, self-reported asthma history and symptoms, current smoking and ENDS use pattern, and intentions to quit smoking or engagement in behavioral or pharmacological smoking cessation. For adults meeting initial eligibility criteria, a research assistant (RA) will explain the purpose and procedures, provide information on confidentiality, answer questions, and schedule in-person screening, baseline assessment and randomization at Brown University's School of Public Health. All initial screening data will be destroyed once initial eligibility is determined.

Baseline Visit (In-person Screening, Consent, and Randomization): Informed consent for in-person screening will be obtained. During the in-person screening, the CADRE CLC nurse practitioner will evaluate medical history to determine eligibility. In-person screening will include psychiatric screening, urine pregnancy test (for women), urine drug screen, breath alcohol via breathalyzer, and exhaled carbon monoxide via Bedfont Micro Smokerlyzer. Participants who arrive at the study intoxicated will be asked to stay at the study location until their Breath Alcohol (BrAC) reaches 0.04%, at which point they will be provided with transportation home by the study team. Participants will complete a medical screening questionnaire assessing their asthma and other medical history; the CLC nurse practitioner (NP) will evaluate medical eligibility and contraindications to nicotine use. Participants meeting all study criteria will complete informed consent (see section 5) and be enrolled in the study. Any participant reporting a course of oral steroids over the prior month will be rescheduled to a later date. Participants may also choose to be scheduled at a later date. Participants will be asked to withhold any short-acting β2-agonists (SABA) for 8 hours prior to testing; if significant symptoms requiring SABA use occur, the assessment will be rescheduled. Measures will be completed per the schedule of measures below (see Table 1), including: demographic measures; measures of tobacco use, use history, and dependence; pulmonary function and asthma quality of life, symptomatology, and control; measures of mood; measures of cannabis use; and clinical biomarkers. Additionally, shared CLC measures will be administrated as described below. Following completion of baseline measures, participants will be randomized to complimentary ENDS condition or assessment-only control. Following completion of all scheduled measures and randomization, participants in the experimental condition will meet with aCAAS research staff unaffiliated with the project and will be allowed to experiment with available VUSE flavors. Participants will then be

provided with a complimentary VUSE device and VUSE pods consistent with their preferred flavor. Participants will be provided with a number of VUSE pods comparable to 150% of their weekly consumption of nicotine based on their responses to the baseline timeline follow-back (TLFB). This quantity will ensure that participants have adequate VUSE pods to fully substitute combustible cigarettes within a reasonable margin of error (e.g., timing/ scheduling of the next session), should they choose to do so. As each standard VUSE pod provides an amount of nicotine comparable to one pack of cigarettes (i.e., 20 cigarettes), we will compute participants' average weekly cigarette consumption in packs and provide 1.5x that number of VUSE pods rounded up to the nearest two pods (VUSE Alto pods are packaged in sets of 2 pods). VUSE recipients will either return to lab each week with all used and unused VUSE pods or CAAS research staff will meet participants at their home to collect unused pods as a secondary verification of self-reported ENDS use behavior.

- **CLC Measures**: Aim 3 of CADRE's CLC is to create a database of factors (biological, environmental, social, and behavioral) associated with the development and progression of substance use disorders (SUDs) and chronic disease. Measures to be included in all projects in service of this aim include: the MINI 7.0.2. (brief patient-completed structured clinical interview for DSM-5 disorders), measures of stigma, trauma, family history of alcohol/substance use, affective dysregulation (anhedonia), behavioral dysregulation (impulsivity), sleep, physical activity, health-related quality of life, saliva samples for cortisol analysis, and blood samples from which DNA will be extracted and biobanked for future analysis. We will ask all participants for permission to keep and use their biological samples for future research for as long as needed, including permission to share their de-identified information and biospecimens with other academic and medical institutions consistent with the data sharing plan of the CADRE. Permission will be requested using a separate checkbox on the consent form so that participants may consent for study participation but opt out of genetic testing and biobanking. Samples will be biobanked in the CLC Laboratory for future analysis by CADRE-affiliated investigators studying chronic diseases. Biomarkers collected in all projects include: enzymes aminotransferase and alanine aminotransferase (AST, ALT), markers of liver damage; creatinine and blood urea nitrogen, markers of kidney function; salivary cortisol, a marker of stress response; soluble CD14 (sCD14), a marker of monocyte activation; tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), pro-inflammatory cytokines; kynurenine/tryptophan ratio (Kyn/Tryp), implicated in neuropsychiatric symptoms associated with immune activation; and monocyte chemoattractant protein 1 (MCP-1), a chemokine that regulates migration and infiltration of monocytes/macrophages and is involved in various neuroinflammatory disorders. All measures are described in the CLC Research Plan. The CLC measures will be included in each project's baseline assessment battery, along with project-specific measures, by the CLC's data management team to ensure uniformity in item wording and response format across projects.

Table 1. Schedule of Measures				
Measures	**Baseline**	**Weeks 1-7**	**Week 8**	**Week 16**
Primary purpose of visit	*- Screening, randomization, and baseline*	*- Weekly assessments*	*- Weekly assessments - Clinical inidicators and biomarkers*	*- Follow-up*
Shared and Demographic Measures				
CLC Measures (see above)	X			
Screening (Eligibility) and Participant Safety Specific Measures				
Mini International Neuropsychiatric Interview (MINI 7.0.2)	X			
Breath alcohol (screening and participant safety)	X	X	X	X
Health Changes Questionnaire (participant safety ONLY)		X	X	X
Smoking Stages of Change Questionnaire	X			
Tobacco Use/Dependence Measures				
Combustible and ENDS Timeline Follow-Back (TLFB)	X	X	X	X
Minnesota Nicotine Withdrawal Scale (MNWS)	X	X	X	X
Brief Questionnaire on Smoking Urges (B-QSU)	X	X	X	X
Cigarette Use History (PATH Adapted)	X			
Fagerström Test for Cigarette Dependence (FTCD)	X		X	X
Penn State Dependence Index (PS)	X		X	X
Wisc. Inventory for Smoking Dep. Motives-Brief (WISDM)	X		X	X
Smoking Cessation Self-Efficacy Scale	X		X	X
Perceived Health Risk Scale	X		X	X
Respiratory Function Measures				
Pulmonary Function Test (PFT) via Spirometry	X		X	X
- Forced Expiratory Volume (FEV_1)				
- Forced Vital Capacity (FVC)				
- Forced Expiratory Flow 25%-75% (FEF_{25-75})				
- Peak Expiratory Flow (PEF)				
Mini-Asthma Quality of Life Questionnaire	X	X	X	X
Asthma Symptoms Utility Index (ASUI)	X		X	X
Asthma Control Test (ACT)	X		X	X
Biomarkers (blood and breath)				
Carbon monoxide (CO)	X		X	X
Exhaled Nitric Oxide (FENO)	X		X	X
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	X		X	
Cotinine	X		X	
Interleukin-6 (IL-6)	X		X	
Tumor necrosis factor α (TNF- α)	X		X	
Matrix Metallopeptidase 9 (MMP-9)	X		X	
Chemokine ligand 9 (CXCL-9)	X		X	
Mood Measures				
Patient Health Questionnaire 9 (PHQ-9)	X		X	X
Generalized Anxiety Disorder 7 (GAD-7)	X		X	X
Cannabis Use/Dependence Measures				
Cannabis Use Disorders Identification Test-Revised (CUDIT-R)	X			

Weeks 1-8, 16: Participants who choose transportation to CAAS but arrive at the study intoxicated will be asked to stay at the study location until their Breath Alcohol (BrAC) reaches 0.04%, at which point they will be provided with transportation home by the study team. Participants will

complete scheduled measures per Table 1, including: measures of health changes, tobacco use; and asthma quality of life. These measures can either be completed at CAAS or remotely over the phone. **On Weeks 8 and 16,** participants will also complete measures related to tobacco dependence, smoking cessation self-efficacy, asthma symptomatology and control, and mood. **On week 8,** pulmonary function tests (i.e., spirometry) and breath CO will be collection, as will blood for clinical laboratory tests. During baseline and Weeks 1-7, following completion of the schedule of measures, participants in the experimental condition will meet with CAAS research staff and will be provided with VUSE pods consistent with their preferred flavor and in an amount equal to that of the baseline week. Participants will be able to select any preferred flavor each week. Participants can choose whether the Weeks 1-7 visits to collect used and used pods and receive new pods occurs at CAAS or outside the home of the participants. **On Week 16**, following completion of the measures schedule, the study will end.

NOTE: The focus of this section is on methods and procedures. Risks will be described later.

THE BLUE TEXT IN THE FOLLOWING SECTIONS IS A GUIDE TO ENSURE ALL RELEVANT INFORMATION IS INCLUDED IN YOUR APPLICATION. YOU MAY DELETE THE BLUE TEXT BEFORE SUBMISSION

4. **Participant Population.** *In order to approve research, the IRB must determine that the selection of participants is equitable and reasonably related to the purpose and aims of the research. The IRB must also consider whether adequate safeguards are in place to minimize any risks that are unique to vulnerable populations. To make this determination, the IRB must review all methods and materials used to contact and recruit potential participants, including letters, flyers, emails, etc.*

Thirty individuals age 21-65 with asthma and without other causes of airway obstruction such as COPD who are current combustible tobacco smokers and are not intending or planning to quit smoking will be screened and randomized. The rationale for including individuals with asthma who are not intending or planning to quit is that the risk for worsening respiratory symptoms is high with continued smoking, individuals are not otherwise engaged in behaviors such as smoking cessation which could reduce harm, and age 21-65 is a unique risk period for asthma exacerbation. By providing some eligible individuals in the experiment with ENDS and measuring pulmonary function, symptomatology, and biomarkers, we will expose these individuals to a level of risk that is either comparable or less (i.e., harm reduction associated with reduced smoking following complimentary ENDS provision) than that encountered in their day-to-day lives.

Inclusion Criteria

a) Male or female (50%), 21 to 65 (inclusive) years of age;
b) Persistent or intermittent asthma symptoms (i.e., episodic symptoms of airflow obstruction / airway hyperresponsiveness (AHR) as documented in CLC review of medical history);
c) Currently prescribed SABA medication;
d) Past-year smoking of ≥5 cigarettes/day;
e) Exhaled CO ≥ 6 ppm at baseline;
f) Zero breath alcohol during informed consent for participation;
g) English-speaking at an 8th grade level.

Exclusion Criteria

a) Intention to quit smoking during the next 30 days;
b) Current engagement in any smoking cessation treatment;
c) Current self-identification as regular ENDS user or using ENDS > 2 days / week;

d) Medical contraindication to nicotine;
e) Pregnancy (due to toxicity of nicotine and tobacco products);
f) Urine-screened or past-month self-reported use of illicit substances (amphetamine, cocaine, methamphetamine, opioids, benzodiazepines);
g) Current psychosis, mania, or suicidal ideation;

Note: Cannabis use will be assessed but not excluded.

Participants will need to speak English and be able to understand informed consent and questionnaires in English, which will be written at an 8th grade level.

Potential participants will be recruited from the community and through referral from established community partnerships with immunology clinics facilitated by co-investigator and project mentor Elizabeth McQuaid. Potentially eligible participants will be invited for an in-person screening, where they will provide written informed consent and undergo a physical examination in the CLC.

Sample Size Considerations

Tobacco use outcomes: Power and sample size calculations were conducted in GPower 3.1 based on between- and within-subjects analyses. Dr. Tidey's pilot trial examining 6 weeks of complimentary ENDS provision on tobacco use behaviors and nicotine dependence at weeks 6 and 10 (i.e., 4 weeks after final ENDS provision) found significant reductions between baseline and both time points in average cigarettes per day (baseline=19.6(8.2); week 6=6.7(7.9), d=1.64; week 10=8.8(8.3), d=1.12) and cigarette dependence (baseline=5.94(1.96); week 6=3.89(2.78), d=.88; week 10=3.50(3.08), d=1.03); all with large effects. However, given the unknown effect of providing free ENDS to adult smokers with asthma and the limited interpretability of effect sizes from pilot trials we chose to use a more conservative medium-large (d=0.65) effect size. With our planned enrollment (N=30), anticipated 10% dropout, and target power (1-β=.8), sample size was adequate to detect within-subject repeated measures (Aim 1) differences in the intervention (ENDS) group but was inadequate to detect between-subjects effects (i.e., group differences). Although power is below .80 to detect group differences, this pilot proposal will help determine the magnitude of these effects and inform the design of future research.

Respiratory outcomes: Investigations of respiratory symptoms and lung function change in 'healthy' smokers switching to ENDS have found very large (h=1.94) within-subjects effects for cough, very large (h=1.50) within-subjects effects for shortness of breath, and large (d=.998) within-subjects effects for FEF25-75; also found were large (d=.921) between-subjects effects comparing successful to failed switchers. As these improvements may be even more pronounced for adults with asthma, the current planned enrollment achieves adequate power to examine these within-subjects (but not between-subjects) outcomes within the ENDS condition per the power and sample size analyses outlined above (Aim 3). However, analysis of spirometry are limited by the short follow-up period for the proposed pilot within-which changes in these metrics are not anticipated. As with the tobacco use outcomes, although power is below .80 to detect group differences, this pilot proposal will help determine the magnitude of these effects and inform the design of future research.

Biomarker: The effect of complimentary ENDS provision on biomarkers of exposure, toxicity, and inflammation in adults with asthma in real-world use conditions should be considered exploratory and preparatory for future intervention design.

5. Recruitment Methods

- Describe the process and/or method by which participants will be identified, approached, and recruited for the research, including the following:

Recruitment procedures will be modeled after previous successful strategies utilized by mentors Tidey and McQuaid. Adults with asthma will be recruited from the community and through referral from established community partnerships with immunology clinics facilitated by mentor McQuaid's ongoing asthma research program.

Community Recruitment: Recruitment from the community will involve: (a) posting flyers or paid advertisements with QR codes, hyperlinks, and telephone numbers; (b) paid advertisements on social media sites (e.g., Instagram, Snapchat, Facebook); and, (c) distributing information through the Center for Alcohol and Addiction Studies (CAAS) website.

BuildClinical Recruitment: BuildClinical recruitment involved targeted web advertising on search and social media platforms delivered via BuildClinical's patient advertising network. BuildClinical will use approved study advertisements through their advertising network to direct individuals to a landing page consisting of the questions from our online screener but hosted at BuildClinical. Potentially eligible participants then provide contact information and are taken through the rest of our "General Recruitment" procedures below.

Clinic Recruitment: Recruitment from community partnerships will build off the Dr. McQuaid's successful Childhood Asthma Research Program (CARP) and the Community Asthma Programs (CAP) at Rhode Island Hospital/Hasbro Children's Hospital. Dr. McQuaid and her colleague, Dr. Daphne Koinis-Mitchell, have a well-established infrastructure for recruiting research participants with asthma. This has served as the basis for recruitment of approximately twenty funded projects since 2010. Currently, CARP research staff are screening for four active studies and enrolling approximately 600 participants/year. Our primary recruitment avenue is the clinics at Rhode Island Hospital/Hasbro Children's Hospital (RIH). We will recruit participants from 1) the Community Asthma Programs, 2) the RIH Ambulatory Clinics, and 3) the RIH Asthma and Allergy Center. Although the focus of Dr. McQuaid's research team is children with asthma, CARP has successfully recruited parents of children with asthma and adult smokers into numerous protocols (e.g. 1R01 HL062165 & 2R01 HL062165). The RIH/Hasbro Ambulatory Clinics has over 126,000 routine visits each year; we also maintain a database of research participants that currently contains over 3000 families; given the heritability of asthma, our experience is that 20-25% of these families will have adults with asthma in the household. Across settings, adults complete a "consent-to-contact" form that indicates consent to be called and screened for research participation.

General Recruitment: The PI or a designated RA will call or speak with any adults who indicate interest through independently contacting CAAS (i.e., community recruitment) or indicate interest through a consent-to-contact form (community partnerships). Computer-assisted pre-screening will determine potential eligibility. Alternatively, participants may complete an online pre-screening survey. Participants who are potentially eligible will be able to provide their contact information. For potentially eligible individuals identified either through telephone computer-assisted pre-screening or who are found to be potentially eligible in the online pre-screening survey, the PI or RA will explain the purpose and procedures, provide information on confidentiality, answer questions, and schedule in-person screening. Potentially eligible individuals will also provide consent for screening and a HIPAA authorization, after which the PI will submit a Physical Query Form on behalf of the individual to obtain their asthma-specific medical background (see eligibility criteria). At the in-person screening, research staff will review the signed consent for screening form with individuals to ensure continued knowledge of consent procedures. Potentially eligible individuals will then undergo a chart review of medical history (from the returned Physician Query Form) completed by the CLC NP and complete all screening measures. Those meeting all criteria will be enrolled into the study by the PI (Dr. Alexander Sokolovsky) with the support of the RA.

Biomedical assessments involving urine will be performed by the RA while those involving blood will be collected by a phlebotomist or NP.

- For research involving an intervention (e.g. behavioral intervention, drug/device studies, etc.):

Standard of care treatment for adults with asthma involves behavioral smoking cessation with or without the support of nicotine replacement therapy (NRT; e.g., nicotine patch) or pharmacotherapy (e.g., varenicline). However, the current study targets adults who explicitly deny any quit intentions for the next 30 days and excludes those who are engaged in smoking cessation treatment (i.e., those adults who do not wish to engage in standard of care treatment at this time; see exclusion criteria). For those participants in the study who are randomized to the assessment only control, there are no expected changes in care or behavior.

Intervention involves complimentary provision of ENDS (VUSE), VUSE cartridges, and brief encouragement to switch to ENDS for 8 weeks. For those participants in the study who are randomized to the complimentary ENDS condition, intervention represents an escalated level of care.

Treatment providers have no role in the current research project.

6. **Compensation / Reimbursement**

- If participants are to receive compensation for their time, please describe the following or simply state "no compensation will be offered":

Compensation schedule and amount is described below:

Screening will take between 1 – 2 hours and participants will receive $25 ($25 total)
Baseline (Visit 1) assessment will take ~2 - 3 hours and participants will receive $50 per visit ($50 total)

Week 1-7; 16 (Visits 2-8; 10) will take ~20 min and participants will receive $25 per visit ($200 total)
Weeks 8 (Visit 9) will take ~1 hour and participants will receive $50 per visit ($50 total)

Participants will be compensated in cash for the sessions that they complete. Those completing all study visits will receive $300 total. Those completing all study visits will be eligible to win an additional $100 Amazon gift card. The amount of compensation is based on the time spend in each session and based on other similar studies at Brown University. Participants will receive parking validation (for Brown School of Public Health), RIPTA tickets (both ways), or compensation for taxi or ride-share services (e.g., Uber) as reimbursement for travel costs.

- If there is the possibility that there will be costs to the participant or to a third party (e.g., an insurer), identify the specific expenses (e.g., drug tests, procedures, hospitalization, travel, etc.) and provide a justification for those costs.

There are no third party costs associated with this project.

7. **Potential Research Risks / Discomforts to Participants.** *In order to approve the research, the IRB must consider the risks posed to participants by the research and any efforts to mitigate those risks. The IRB needs to determine that the risks have been both minimized and are reasonable in relation to the anticipated benefits to participants, as well as to the importance of the knowledge that may be gained. The IRB will also consider whether the informed consent process provides potential participants with an accurate and fair description of the risks or discomforts.*

Potential risks: Potential risks are minimal. They include subjective discomfort, questions of coercion, breach of confidentiality, risk of increased smoking, and risk of irritation from ENDS vapor.

None of these risks are considered serious using criteria of the Food and Drug Administration (FDA). Risks are described below:

(a) Subjective discomfort: Participants may feel uncomfortable answering questions about their substance use, including the use of multiple tobacco products. We will remind participants that they can stop their participation at any time without penalty or loss of benefits. However, the likelihood of experiencing subjective discomfort is low based on our experience with comparable methods in research studies at CAAS. Additionally, discomfort from providing biological samples is also low based on past experiences with these methods. Participants who are unwilling to provide biological samples will be reminded that they can choose not to participate.

(b) Coercion: Coercion due to the monetary compensation provided in this study is also a risk. However, the risk of coercion is low. The maximum total amount of compensation provided during the study is $300 over 16 weeks and eligibility to win a $100 Amazon gift card.

(c) Breach of confidentiality: It is as possibility that data collection could result in breach of confidentiality. A breach in confidentiality in self-report data could reveal that participants are engaging in illegal behavior (e.g., illicit drug use in Rhode Island). However, the risk of breach of confidentiality is also low given adequacy of the data safety and monitoring plan.

(d) Risk of increased smoking: It is possible that participation in the study could result in increased smoking; however, this risk is low given the significant body of prior research findings.

(e) Irritation from ENDS vapor: It is possible that participants who use ENDS could experience irritation from their use of these products; however, this risk is low given evidence regarding the sensory profile of using ENDS and the selection of the VUSE device which is a commercially available and popular ENDS product with high quality design and manufacturing.

(f) Risks associated with blood draw: It is possible that participants will experience physical risks associated with blood draw, including: exposure to blood-borne viruses, infection at the sampling site, pain or discomfort, hematoma, excessive bleeding, nerve damage, and vasovagal reaction or fainting.

Protection Against Risks: The risks of this study include (a) subjective discomfort, (b) coercion, (c) breach of confidentiality, (d) risk of increased smoking, (e) irritation from ENDS vapor, and (f) risks associated with blood draw. There risks are protected against in the following ways:

(a) Subjective discomfort: Participants who feel uncomfortable at any time will have the opportunity to refuse to answer questions that make them uncomfortable. Participants will also be able to withdraw from the study without penalty. If participants feel uncomfortable at any time, they can choose not to answer a question. Discomfort related to providing biological samples will be minimized by employing CADRE CLC whose staff will operate with a high level of medical training and professionalism when conducting procedures, with considerable emphasis placed on communicating to the study participant that participation is voluntary. Participants will be debriefed following each assessment to evaluate their level of discomfort and provided with the opportunity to discuss discomfort with project staff.

(b) Coercion: Concerns regarding coercion may arise from the compensation offered for study completion. Participants will be able to receive up to $300 for completing all study visits. Those completing the full study will also be eligible to win a $100 Amazon gift card. Considering that weekly assessments require considerable effort, as well as,

potentially, transportation to and from CAAS, or meeting with study staff at home, compensation is commensurate with the time and effort involved. We include the final full-study bonus payment and eligibility into a raffle drawing because high attrition may reduce statistical power in this study. Participants will be free to discontinue at any time without penalty and will receive compensation proportional to the portion of the assessments completed.

(c) Breach of confidentiality: Participant responses to the baseline questionnaire will be collected using Brown University's Qualtrics service. This secure system and our data collection practices will ensure the secure transmission and storage of survey responses. All biological, behavioral, and questionnaire data obtained from participants will be assigned unique IDs generated for the study, with separate IDs generated for biological and self-report data. Data will be stored without identifiers in either a double locked cabinet or password-protected and network secured computers at CAAS. Study consent forms and tables linking participants identifying information to their unique ID codes will be stored separately in a locked file cabinet within the office of the Principal Investigator, located on a separate floor of the building. All information collected as part of this study will only be accessible to research staff. All interactions with participants will be conducted in private rooms. Biological samples will be obtained in a private bathroom or clinical assessment room, per the procedures of the CADRE CLC.

(d) Risk of increased smoking: As this study is a trial of complimentary ENDS to adult smokers with asthma who are unwilling to quit, the risk of increased smoking will primarily be reduced by providing ENDS and encouraging substitution in that condition - an intervention with growing empirical support. At the conclusion of the study risk will be further reduced by providing brief advice to quit and referral to a quitline.

(e) Irritation from ENDS vapor: The most frequently reported side effects of vaping are mild (e.g., throat or mouth irritation) and will be comparable to what participants experience outside of the laboratory given current exposure. Should participants experience irritation from ENDS vapor, they will be able to choose a different vapor at the subsequent assessment (i.e., weekly).

(f) Risks associated with blood draw: During the informed consent process, participants will be advised of the necessity of obtaining repeated blood samples during the study. Screening will exclude individuals who report psychological discomfort caused by blood draw or the sight of blood, or who report history of adverse reaction to standard blood draw procedures. The total volume of blood to be collected is modest. Blood draw procedures will follow World Health Organization guidelines for safe and well-tolerated procedures to minimize risk of infection or other complications. The CLC NP will collect the blood samples. Risk reduction strategies are to use sterile, single-use implements; surface disinfectant; proper hand hygiene; application of 70% isopropyl alcohol to the blood draw site; minimal vein probing; application of pressure after drawing blood; and non-latex vinyl gloves. Blood draw by a licensed professional using these risk reduction methods makes the occurrence of negative outcomes very unlikely.

8. **Potential Benefits of the Research. NOTE: Compensation for participation is not a benefit and should not be included in this section.** *In order to approve this research, the IRB must determine that the potential benefits to research participants are reasonable in relation to the potential risks. Very often, research at Brown does not include potential direct benefits to participants, but may only benefit society as a whole by helping researchers.*

It is not likely that participants in this study will benefit directly from participation. However, some participants may benefit from receiving complimentary ENDS that may facilitate substation of smoking for ENDS use. It is also possible that participation in this clinical trial will increase awareness of one's own patterns of smoking, which may potentially lead to changes in tobacco use behaviors.

Furthermore, participants may benefit from receiving results of clinical tests when such results indicated that medical attention is warranted (e.g., high blood pressure).

The risk/benefit ratio is seen as favorable for participants as risks are minimal and outweighed by the potential benefits detailed here, and benefits of the knowledge gained: Given the considerable public health burden of smoking-related respiratory diseases and the growing popularity of ENDS, knowledge about the potential health benefits of switching from smoking to ENDS for asthma control and pulmonary outcomes is important to guide clinical practice and public policy. If ENDS use leads to reduced smoking or increased substitution, and improved asthma control and pulmonary function among adults with asthma, this study could have significant implications for public health and result in reduced morbidity and mortality from smoking-related respiratory disease. Knowledge gained from this study will thus benefit both the target population (adult smokers with asthma) and health policy makers, particularly those interested in function-impairing chronic disease. The importance of the knowledge to be gained relative to the minimal risks outlined above is considerable.

PART IV. APPENDICES SCREENER

Please complete & attach the following Appendices to this Application, as applicable.

Incl.	N/A	
☐	☒	Appendix A. Children as Subjects *To be attached when minors are included as participants [please be aware of the age of majority for your specific research site(s)]*
☐	☒	Appendix B. Prisoners as Subjects *To be attached when prisoners are included as participants.*
☐	☒	Appendix C. Use of Drugs *To be attached when the research includes the use of FDA-regulated or unregulated drugs.*
☐	☒	Appendix D. Use of Devices *To be attached when the research includes the use of FDA-regulated or unregulated devices.*
☐	☒	Appendix E. Prescription Drug / Medication Management *To be attached when study procedures include administering prescription medications to study participants.*
☒	☐	Appendix F. Mental Health Safety Plan *To be attached when participants may experience significant emotional distress, or be at risk of themselves or others.*

PART V. INFORMED CONSENT

Informed consent is a *process*, not just a form. The IRB must ensure the informed consent process clearly discloses and facilitates the understanding of all information needed to make an informed decision to participate while promoting the voluntariness of participation.

Please review the Consent/assent templates and related guidance on the HRPP Forms & Templates page before developing your consent forms.

1. **Describe the informed consent process, including:**

There are 2 key elements of informed consent for this project:

1) Informed Consent for release of medical record information (Physician Query Form) and in-person screening will be obtained at the conclusion of the initial screening through a verbal script (phone) with a paired signature on an online consent form. As consent for screening will be obtained prior to the in-person screening, research staff will review this signed consent form with the potentially eligible individual at the in-person screening visit to ensure ongoing awareness of study procedures.
2) Informed consent for study participation following in-person screening will be obtained in a private room in the laboratory suite of the Center for Alcohol and Addiction studies. Breath alcohol concentration of 0.00% will be confirmed when obtaining consent for participation. The nature of the study will be described in written format in the informed consent documents.

Written informed consent will be obtained by the PI or RA, who will have completed all applicable CITI and HIPAA training and will be trained by the PI in informed consent procedures.

2. **Facilitate Understanding**

Participants will be encouraged to ask questions about the study during the entirety of the consent process and throughout their participation in the study. Participants must be able to read and speak English in order to participate. Participants who express hesitation to proceed wit the experimental session will be reminded that they have the right to withdraw from the study at any time. Participants who decide to withdraw from the study prior to completion will be paid for their participation up to that point. The names and office phone number of the PI (Dr. Sokolovsky) and study staff will be provided on the consent document in case questions arise.

3. **Documentation**

Informed consent for the release of medical record information will be documented by having participants sign a release of medical information form as noted above.

Informed consent for the release of medical information and for in-person screening will be documented by having participants sign an online form (Qualtrics) as noted above. Informed consent for project participation will be documented by having the participant sign informed consent forms. The original signed consent forms will be kept in a locked filing cabined in the PI's office and participants will be offered a copy of the signed forms.

4. **Additional Considerations**

Protected Health Information (PHI): The researchers request a HIPAA waiver of authorization for the purpose of 1) screening potential participants from community partnerships through the Childhood Asthma Research Program and Rhode Island Hospital (RIH); and 2) sharing limited personal identifying information from RIH to Brown University. Under the waiver of authorization, CARP research staff who are already screening for four active asthma-related projects at RIH will additionally use patient medical records to assess eligibility criteria such as age, current smoking, and asthma status for this proposal. All patients screened by CARP research staff will have already signed "consent-to-contact" forms for research study recruitment. Demographic PHI (contact information) of potentially eligible participants listed on their signed consent-to-contact forms will be shared with the Brown University RA for recruitment. No medical information will be shared at this point between RIH and Brown University.

Necessity of PHI to conduct the study: Use of PHI is necessary to assess basic eligibility criteria using information that exists only in the individual's medical record, including diagnosis.

Protection of identifiers: No medical information will be shared between RIH and Brown University and *only* demographic PHI listed on consent-to-contact forms (e.g., telephone numbers) will be used to contact potential participants. All recruitment-related PHI will be destroyed once recruitment is completed.

Destruction of identifiers: Only demographic PHI (e.g., telephone numbers) listed on consent-to-contact forms will be shared between RIH and Brown University. This information will not be linked to a participant's study record, and will only be used to establish initial contact. All recruitment-related PHI will be destroyed by CARP and Brown University staff once recruitment is completed.

Reuse of identifiers: The PI will attest in writing prior to the commencement of research activities that no PHI shared from RIH to Brown University will be reused for any purpose outside the scope of the original study.

Risk assessment: Review of medical records at RIH by CARP staff will be conducted by trained research staff who are currently recruitming for multiple other studies for project mentor Dr. Elizabeth McQuaid and her colleague Dr. Daphne Koinis-Mitchell. Staff at CARP have expertise in the clinical setting, including best practices for records review and protection of privacy. The minimum amount of information needed to establish eligibility will be collected from medical information. Furthermore, only contact information listed on a signed "consent-to-contact" form will be shared to facilitate recruitment. This personal information will not be associated with any possible subsequent records of study participation. Lastly, the use of PHI for recruitment is independent of the previously noted release of medical record information for which a signed release will be obtained and no waiver of authorization is required.

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Proceed to PART VII. DATA SECURITY ASSESSMENT

PART VI. USE OF SECONDARY DATA / BIOSPECIMENS

1. From what source(s) will you acquire or access the data / biospecimens?

2. Do any of the source(s) require a Data Use Agreement (DUA) or other Agreement that requires institutional signature to obtain, access or use the data / biospecimens? ☐ Yes ☐ No

If "yes," please include a copy of the Agreement(s) with this submission and also follow the Data Use Agreement review and signature processes.

3. Describe the type(s) of data and date range(s) of the data you will use and the characteristics of the study research population (e.g., age range, sex, and any other pertinent demographic information.)

Proceed to PART VII. DATA SECURITY ASSESSMENT

PART VII. DATA SECURITY ASSESSMENT

1. Do the study data / biospecimens include identifiers? Video and audio recordings are considered identifiable.

☒ Yes ☐ No*

If "no," I affirm that I have read and will abide by the Level 1 Risk Minimum Security Standards: ☐ Yes ☐ No
Proceed to Part VIII.

If "yes," answer the following questions.

A. Describe the identifiers associated with the data / biospecimens.

Data and biospecimens collected for the study will be deidentified (identifiers will be stored separately from study data and biospecimens). Research staff will maintain a file that contains links of personal identifiers with unique study IDs. This file will be kept for the duration of the study and will be destroyed at the conclusion of the study by the PI.

B. Justify why identifiers are required to conduct the research.

Identifiers are needed because the study involves multiple sessions and the collection of clinical data. The study must be able to contact participants for follow-up appointments and to relay select clinical information as detailed in the consent form.

C. Described the proposed research use of the identifiable data / biospecimens.

Data and biospecimens will be deidentified for research use.

D. Self-classify the Risk Level of these data / biospecimens (select the *highest level of risk* for all data / biospecimens being collected).

☒ Level 2 Risk
☐ Level 3 Risk

2. How will study data / biospecimens be collected?

☒ Brown desktop
☐ Laptop
☐ Departmental server
☐ CIS managed server
☒ Brown Qualtrics
☐ REDCap; Please describe what instance of REDCap is being used (Brown does not have an instance of REDCap):
☐ MTurk (AMT)
☐ Text messaging à You must complete the Text messaging section after completing Qs 3 – 5.
☐ Mobile App (on tablet, iPad, Phone) à You must complete the Mobile App section after completing Qs 3-5.
☐ Zoom
☐ Other audio / videoconferencing tool; please describe the tool:
☒ Paper records, including photographs. Please describe, including how you will securely store the paper records: Participants will provide contact information on paper forms so that they can be contacted by study staff. Participants will complete paper research questionnaires that will be identified by the participant's study ID but will not contain other personal identifiers. Paper records with

participants' study IDs will be stored in a locked filing cabinet in the office of the PI separate from any other research records.

☒ Web-based site / survey / other tool not listed above à You must complete the Web-based Other section after completing Qs 3 – 5.

☐ Other; please describe:

3. Who will have access to the study data / biospecimens?

☐ A. Brown PI only. How will unauthorized access by others be prevented?

☒ B. Brown PI and other Brown research team members. How will unauthorized access by others be prevented?

All biological, behavioral, or questionnaire data obtained from participants will be assigned a unique ID generated only for this study. These unique IDs will be used to identify study participants on all research materials, digitally stored data, tracking forms, and data management databases. Research staff who correspond with participants throughout the study will have access to individual contact information but not to participant responses. Participant identifying information will never be stored with study data and will not appear on any report generated as a result of this study. For biological samples processed externally, a separate identification number will be generated that will allow research staff to link metadata about a given participant with laboratory responses while also providing a second firewall of confidentiality between study data (i.e., biological and self-response data will not be able to be linked based on the IDs on these samples). Linked tables will not have any participant-provided study data. All data information sources will be double locked in a locked cabined or password protected secured computer in a locked room. External unauthorized access will be prevented by keeping data on the secure fileserver at the Center for Alcohol and Addiction Studies with firewall protections and all Brown University security procedures in place. Only the PI and research assistants trained in research with human subjects will have access to any project data.

☐ C. Data will be shared with research collaborators external to Brown. This data sharing intent **must** be described as part of your consent process / form. Please describe how you will securely share / transfer the data outside of Brown:

*Note that an Outgoing Data Use Agreement **is required when sharing identifiable data external to Brown**. Please follow the procedures outlined here. You do not need to submit a copy of a DUA to the HRPP. This will be linked by the ORI administratively.*

4. Where will the study data / biospecimens be stored?

☒ Departmental server
☐ CIS managed server
☐ Stronghold
☐ Campus file storage
☐ REDCap
☐ Other. Please describe:

5. If traveling with your data, describe how your data will be secured.

N/A

6. For how long will you retain identifiable data / biospecimens? How will you destroy identifiers when no longer required?

Personally identifying information used for recruitment will be destroyed at the end of recruitment. Personal identifying information from project participation will be retained until the completion of data collection. At the end of the study, the password-protected file linking study data and biospecimens to personal identifying information will be deleted by the study PI.

Text Messaging (only complete if instructed above.)

1. Are you using the current text messaging service available on the device?

☐ Yes ☐ No	If "no," you must also complete the Mobile App section.

2. Whose device will be used? ☐ Participant's personal phone ☐ Brown-issued phone

3. Content of messaging: (If brief, insert here; otherwise, please provide as an attachment)

4. Is the communication one-way or two-way? ☐ One-way ☐ Two-way

Mobile App (only complete if instructed above.)

1. Name of the mobile app:

2. Has this site / tool been reviewed by CIS IT Security?

☐ Yes ☐ No	If "no," answer the following: a. Who created the site / tool (vendor name or off the-shelf app creator name)? b. Where is it hosted? c. Is the site / tool scanned for security vulnerabilities? ☐ Yes ☐ No d. What version of software is being used, if applicable: ☐ N/A or e. How are the data encrypted?

3. Whose device will be used? ☐ Participant's personal phone ☐ Brown-issued phone
If Participant's person phone:
a. How is the app downloaded to the device?
b. Is a password or PIN required for the app? ☐ Yes ☐ No

4. Will data be stored on the device for any period of time?

☐ Yes ☐ No	a. If "yes," please describe (i.e., queue on phone and then transmitted to server): b. Is the app data encrypted on the device? ☐ Yes ☐ No

5. Device features mobile app can access ☐ N/A
☐ Device ID and call information
☐ Identity
☐ Contacts
☐ Camera
☐ SMS or chat
☐ Storage
☐ Device and application history
☐ Phone
☐ Photo / media / files
☐ Microphone

☐ Location ☐ Other; please describe:	
6. Will a third-party have access to research data through this app? ☐ Yes ☐ No	
7. Is data transmitted by the device?	
☐ Yes ☐ No	If "yes," how is it encrypted in transit?
8. Are phone numbers or mobile identification numbers stored with the data? ☐ Yes ☐ No	
Web-based Other (only complete if instructed above.)	
1. Name of the site / tool: BuildClinical – BuildClinical is a patient recruitment and advertising tool. Individuals who respond to BuildClinical's advertisements (approved study advertisements) are taken to a landing page hosted at BuildClinical which comprises the Online Screener items. Potentially eligible individuals who pass prescreening will provide contact information and be funneled into our General Recruitment procedures. No data about individuals other than contact information is stored by BuildClinical. This tool has been approved by CIS IT and is in use by other projects at Brown University.	
2. Has this site / tool been reviewed by CIS IT Security?	
☒ Yes ☐ No	If "no," answer the following: a. Who created the site / tool (vendor name or off the-shelf app creator name)? b. Where is it hosted? c. Is the site / tool scanned for security vulnerabilities? ☐ Yes ☐ No d. What version of software is being used, if applicable: ☐ N/A or e. How are the data encrypted?
☐ Yes ☐ No	If "no," answer the following: a. Who created the site / tool (vendor name)? b. Where is it hosted? c. Is the site / tool scanned for security vulnerabilities? ☐ Yes ☐ No d. What version of software is being used, if applicable: ☐ N/A or e. How are the data encrypted?
3. Is informed consent being obtained via this site / tool?	
☐ Yes ☒ No	If "yes," how is re-identification prevented?
4. Does the technology allow for the explicit exclusion of the collection of IP address of the participant's connection?	
☐ Yes ☒ No	If "yes," will you use this option to exclude the collection of IP address? ☐ Yes ☐ No

Brown Qualtrics: CIS has pre-vetted Brown Qualtrics for collection/storage of up to Risk Level III data. Qualtrics is the preferred survey tool for all Brown research data collection.

REDCap: Brown does not currently have its own instance of REDCap. Access to REDCap through a Lifespan collaborator must be explicitly identified.

Data collection: The expectation is that data collection *devices* will only store data during active data collection. Data must then be transitioned to more secure long-term storage solutions.

Departmental/CIS managed servers: If data are collected/entered directly onto a Departmental or CIS managed server, **you must ensure** that the server meets the security standards described in the Minimum Security Standards for Servers based on the Risk Level of the data identified in 1D.

Proceed to PART VIII. INTERNATIONAL RESEARCH

PART VIII. INTERNATIONAL RESEARCH

1. Does the research involve human subjects activities outside of the United States?

☐ Yes ☒ No

If "yes," please list the countries:

If "no," you are not required to complete this Part of the application. Proceed to PART IX. ATTACHMENTS.

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b. What is the status of permissions / approvals from local ethics boards or committees?
☐ Received; please append to this Application.
☐ Pending
☐ N/A. Please explain:

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c. Will this research take place in a non-public setting (including a school, hospital or clinic) for which local permission is required? ☐ Yes ☐ No
If "yes," please append a letter(s) of support or permission(s) to this Application.

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d. Describe how you have taken into account any social, political, or cultural issues that may impact participants.

☐ I have reviewed the current version of the *International Compilation of Human Research Standards* and agree to abide by relevant local laws, regulations and guidelines.

☐ I have reviewed the *General Data Protection Regulations guidance* and will abide by any requirements.

☐ I have reviewed ORI's export control guidance on international travel, international collaborations, and international shipping (*if applicable*)

Proceed to PART IX. ATTACHMENTS

PART IX. ATTACHMENTS

Please attach the following materials to this Application for Full Board / Expedited IRB Review, as applicable.

Incl.	N/A	
☒	☐	Informed consent documents / scripts: 1) Consent for Screening; 2) Consent for Research Participation
☒	☐	Data collection materials (questionnaires, surveys, interview scripts, etc.)
☐	☒	Permissions, approval documents, and/or support letters identified in PART VII.
☒	☐	Recruitment materials (emails, flyers, letters, scripts, posters, brochures, etc.)
☐	☒	Application for IRB Authorization Agreement
☐	☒	Data Use Agreement from data provider(s)
☒	☐	Data Safety Monitoring Plan
☒	☐	Other: Physician Query Form

PART X. CONFLICT OF INTEREST

The *Brown University Conflict of Interest Policy for Officers of Instruction and Research* *("COI Policy")* defines the term "Investigator" as "the project director or principal investigator and any other person, regardless of title or position (e.g., full or part-time faculty member, staff member, student, trainee, collaborator, or consultant), who is **responsible** for the **design, conduct, or reporting** of sponsored research."

Using this definition of "Investigator," please ensure that all Investigators on this protocol answer questions (1) and (2) below. Attach additional sheets for any Investigators who are not the PI; additional sheets are available on the HRPP website.

1. Have you completed a conflict of interest disclosure (i.e. *COI Reporting Form*) within the past 12 months and is it accurate and up-to-date as of the time of this submission, as required by Brown's COI Policy? (You may access the InfoEd system here to confirm.)

☒ Yes ☐ No	If "no," please do so before submitting this Application

2. Do you have a significant financial interest (SFI) that is related to this research protocol?
"Related" could mean the research involves products, technology, intellectual property, or services made, owned, or provided by the entity/ies in which you have an SFI. It could also mean that the SFI could be affected by the proposed research or its results.

☐ Yes ☒ No	If "yes," please identify the SFI and explain the relatedness:
☒	Additional COI sheets for Investigators are attached to this Application. ***(Required for Advisors)***

PART XI. INVESTIGATOR & FACULTY ADVISOR AGREEMENTS / PRINCIPAL INVESTIGATOR RESPONSIBILITIES

A. Conduct of the Research

1. I accept responsibility for the ethical conduct of this research and protection of participants as set forth in the Belmont Report, Common Rule, and Brown University policies.
2. I accept responsibility for ensuring this research is conducted in accordance with:
   a) Sound research design and methods;
   b) The parameters of the research plan and activities described in this Application;
   c) The applicable terms of the grant, contract, or other signed funding agreements;
   d) Applicable laws and regulations, including those protecting the rights, safety and welfare of human subjects.
3. I certify that I am, or my faculty advisor is, sufficiently qualified by education, training and experience to assume responsibility for the proper conduct of this research. I accept responsibility for ensuring that all member of the research team have or will complete human subjects CITI training before any work with participants or identifiable data / biospecimens begins.
4. I accept responsibility to personally conduct and/or directly supervise this research. I certify that I have sufficient time and resources to properly conduct and/or supervise this research.

B. Ensuring and Maintaining Compliance

1. I will comply with relevant regulatory and institutional reporting requirements, including Brown University's *Reportable Events Policy*.
2. I understand that it is my responsibility to ensure that any research personnel, including myself, responsible for the design, conduct or reporting of the research declares any conflicts of interest related to this research. I will ensure that any changes that impact my or other research personnel's answers to the questions in PART IX. Conflict of Interest, are reported promptly to Brown's HRPP.
3. I will ensure that prospective agreement and/or informed consent is obtained and a copy is provided to participants, when appropriate.
4. If there are changes to the research described in this Application for Full Board / Expedited IRB Review that may impact the study's classification as Full Board or Exepdited research, I will promptly notify the Brown HRPP of such changes.
5. I will notify the Brown HRPP when I have completed all activities involving human subjects or identifiable participant data or identifiable biospecimens.
6. I will maintain approval, as applicable, with collaborative parties, including approvals from other countries or jurisdictions.
7. I will cooperate with any post-approval monitoring or auditing of study activities and/or study records as requested and/or required by the Brown ORI, the Brown IRB, funding entities, sponsors, and/or any federal or state regulatory agencies.

C. Study records, Reports and Documentation

1. I will maintain all research protocol materials and consent materials for the duration of this study.
2. I will maintain research records for at least three years following the end of this research, or for a longer length of time if specified in applicable regulations or sponsor requirements. I will take measures to prevent accidental or premature destruction of these records.
3. I will abide by all terms of any Data Use Agreement (or equivalent agreement) related to this study, including those agreed to electronically (through an online attestation).
4. I will ensure that the data security measures for acquisition, collection, transfer and use of study data described in PART VI. of this Application are adhered to by all members of the research team.

By my signature below, I certify that I have read and agree to uphold all of you and/or Advisor Responsibilities in PART XI.

Principal Investigator signature: **Date:** 2/28/2023

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An Advisor's signature is required for all graduate/medical student projects

Advisor certifies the following: Advisor has read the complete protocol, approves this project, and will remain available to advise the student throughout the course of the proposed human subjects research, or will transfer responsibilities to another Advisor if unable to advise for the entirety of the project.

Advisor's name (please print):

Advisor's signature: **Date:** Click here to enter a date.

For IRB Use Only

Signature of the IRB:

Date of IRB approval: Click here to enter a date.