IRB # 00002116

PROTOCOL TITLE:

Development and Implementation of a Tobacco and ENDS Use Intervention for Adolescents and Young Adults in the Pediatric Hospital

PRINCIPAL INVESTIGATOR:

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REVISION HISTORY

This Revision History table is provided for the benefit of study team version control. If this table will not be useful please delete it.

Revision #	Version Date	Summary of Changes	Consent Change?
1	4.24.23	Addition of Twilio to send secure text messages through REDCap	yes
2	6.9.23	Addition of exploratory aim of genetic variation and collection of voluntary salivary samples from all participants	yes
3	6.21.23	Clarification of reconsenting process for participants who turn 18 years old during study	
4	7.12.23	Clarification of eligibility criteria, must be an ENDS user (cannot be solely a traditional cigarette user, can be co-user)	
5	7.28.23	Addition of hospital staff as participants and information about the interviews for them	
6	7.28.23	Inclusion of vulnerable population, wards of the state	
7	2.21.24	Addition of another salivary testing option for participants.	yes
8	5.24.24	Addition of option for blood salvage samples for genomic sequencing.	yes
9	8.30.24	Adding additional study site, Children's Hospital of Los Angeles (CHLA). The current	Yes

		study PI (Masonbrink) will be starting a position there on November 1, 2024. At the time of her departure we will change the CMH study PI to Dr. Melissa Miller (currently a Co-Investigator). CHLA will be added as a study site but will complete external reliance on the CMH IRB and no data collection will occur at CHLA.	

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DATA MANAGEMENT

STUDY INFORMATION

1.0 Study Summary*

1.1 Synopsis

Study Title	Development and Implementation of a Tobacco and ENDS Use Intervention for Adolescents and Young Adults in the Pediatric Hospital
Study Design	Randomized controlled pilot study with 3-month follow up to evaluate preliminary efficacy as well as implementation outcomes (i.e., acceptability, feasibility, fidelity) of a tobacco use and vaping cessation program. All data collection will occur at Children's Mercy Hospital (CMH) but we will have a second study stie (CHLA; added due to change in position of PI Masonbrink) where no data collection will occur, but data containing PHI may be shared.
Primary Objective	We will evaluate preliminary efficacy (i.e., 30-day self-reported abstinence with biochemical verification) as the primary outcome.
Secondary Objective(s)	We will assess self-reported motivation and confidence to quit and implementation outcomes (i.e. acceptability, feasibility, and fidelity) immediately post-intervention and at 3-month follow up.
Study Population	Adolescents and young adults (AYAs; 14-21 years old) admitted to the hospital
Sample Size	144 AYA, up to 144 parents, up to 10 hospital staff
Study Duration for Individual Participants	3 months
Study Specific Abbreviations/ Definitions	Adolescents and young adults (AYAs) electronic nicotine delivery system (ENDS) American Academy of Pediatrics (AAP) United States (US) United States Preventive Service Task Force (USPSTF) Motivational interviewing (MI) SBIRT (Screening, Brief Intervention, Referral to Treatment) clinical decision support (CDS) Emergency department (ED) Nicotine replacement therapy (NRT) Electronic health record (EHR) Consolidated Framework for Implementation Research (CFIR) Randomized controlled trial (RCT)

2.0 Objectives*

2.1 Purpose, specific aims or objectives:

Design and iteratively refine a tobacco and ENDS use intervention for AYAs. We will draw on promising primary care and hospital-based approaches to develop and iteratively refine, based on survey and interviews of key stakeholders, a novel intervention to screen for and treat current tobacco and ENDS use in hospitalized AYAs.

Evaluate preliminary efficacy and implementation outcomes of the tobacco and ENDS use intervention. We will conduct a randomized pilot trial with 3-month follow up to assess preliminary efficacy and implementation of the intervention in hospitalized AYAs with current tobacco and ENDS use. Self-reported 30-day abstinence with biochemical verification at 3 months will be the primary outcome and secondary outcomes will include implementation measures (e.g., acceptability, feasibility, fidelity).

Exploratory secondary aim: We will explore the impact of individual-level factors (e.g., CYP2A6 genotype, nicotine metabolite ratio, sex) at baseline with our primary outcome (past 30 day ENDS use abstinence).

2.2 Hypothesis to be tested/Exploratory study design:

We hypothesize the intervention arm will have higher rates of biochemically confirmed self-reported tobacco use abstinence (preliminary efficacy; primary outcome) compared to the control arm at 3 month follow up.

3.0 Background*

Tobacco use is the single leading cause of preventable death, disability and disease in the United States (US). Adolescence is a critical developmental period for intervention because 90% of adult tobacco users initiate during this period.[1] Although tobacco control efforts have led to declining rates of combustible cigarette use, electronic nicotine delivery system (ENDS) use among youth has risen dramatically in the past decade. ENDS, which include electronic or "e"-cigarettes, pod-based or disposable vaping devices, and vape pens, are now the most common tobacco product used by adolescents and young adults (AYAs).[2,3] Between 2011-20, current (past 30-day) ENDS use increased from 1.5% to 20% among high school students and from 0.6% to 5% among middle school students.[2–4] ENDS use is linked with increased use of cigarettes, alcohol and other illicit substances, as well as adverse health outcomes among AYAs.[5–9] Recently there was an outbreak of hospitalizations for e-cigarette and vaping-associated lung injury including among youth (≤ 18 years).[10,11]

The American Academy of Pediatrics (AAP) and the US Preventive Service Task Force (USPSTF) recommend counseling using the 5 A's Framework (Ask, Advise, Assess, Assist, Arrange) and motivational interviewing (MI) techniques to address tobacco use at every adolescent clinical visit.[12–14] This recommendation is based largely on research from the primary care setting, although many adolescents do not routinely attend primary care visits. With more than 1.5 million AYA hospitalizations annually, the hospital setting offers an untapped venue for identifying and treating AYA cigarette and ENDs use.[15–18] Many hospitalized AYAs are at increased risk for tobacco use as well as tobacco-related poor health outcomes due to underlying comorbidities (e.g., mental health disorders, diabetes, asthma).[5,6,16] In addition, the rising prevalence of ENDS use may be linked with increased risk for hospitalizations for respiratory illnesses as well as an increased risk for unrecognized and untreated nicotine withdrawal among hospitalized AYAs.[1,17–19] Although research on tobacco and ENDS use among hospitalized AYAs is sparse, our preliminary data indicate that 28% report any tobacco use, and 15% report current ENDS use.[20]

While there is strong evidence supporting the feasibility and effectiveness of treating tobacco use during adult hospitalizations and promising evidence for substance use treatment (e.g., alcohol) during

hospitalization among AYAs,[21–26] no interventions for tobacco and ENDS use have been developed or tested in the pediatric hospital setting. In primary care-based tobacco treatment for AYAs there are limited ENDs use treatment interventions.[27] In this proposal, we aim to address these limitations by initiating a line of research focused on treating tobacco and ENDS use among AYAs in the hospital.

Drawing on related work in the hospital and primary care settings, we will adapt components of the most efficacious tobacco and ENDS use interventions (e.g., 5 A's Framework, MI) to design an intervention that accounts for important hospital-specific contextual factors. We will use the Proctor and CFIR (Consolidated Framework for Implementation Research) frameworks to evaluate implementation such as determining the optimal process for tobacco and ENDS use screening and treatment while managing acute illness; coordinating care with the medical team; and using confidential computerized decision support (CDS) systems to achieve systematic and high-quality implementation.[28,29] We will also identify and utilize feasible post-discharge follow-up strategies.

4.0 Study Design*

Health Services/Programmatic Activities

Design and iteratively refine a tobacco and ENDS use intervention based in clinical practice guidelines for AYAs

Research Activities

- Conduct a pilot RCT to assess implementation of the evidence-based intervention in the pediatric hospital setting with 3-month follow up to assess preliminary efficacy and implementation outcomes. We will evaluate preliminary efficacy (i.e., 30-day self-reported abstinence with biochemical verification) as the primary outcome. We will also assess self-reported motivation and confidence to quit and implementation outcomes (i.e. acceptability, feasibility, and fidelity) immediately post-intervention and at 3-month follow up. We will conduct 4 follow up phone sessions with AYA post hospitalization. These phone calls will consist of counseling provided by the health educator and will last approximately 30 minutes. Parents of AYA will complete a post intervention survey. Hospital staff will be asked to complete a post intervention survey and interview.

All data collection will occur at Children's Mercy Hospital (CMH) however we will have a second study stie (CHLA; added due to change in position of PI Masonbrink November 1, 2024) where no data collection will occur, but data containing PHI may be shared for analysis.

5.0 Research Interventions*

5.1 Description: We will conduct a prospective, pilot trial with 3-month follow up to assess preliminary efficacy and implementation outcomes. Hospitalized AYAs with current (past 30-day) ENDS use (including those with co-use of cigarettes) will be randomized 2:1 to receive either novel intervention or control intervention that will consist of brief advice and printed quit line referral as part of their clinical care. We will evaluate preliminary efficacy (i.e., 30-day

self-reported abstinence with biochemical verification) as the primary outcome. We will also assess self-reported motivation and confidence to quit and implementation outcomes (i.e. acceptability, feasibility, and fidelity) immediately post-intervention and at 3-month follow up.

We will screen the EMR to identify potential eligible participants and send a text page to the medical team to notify them that we will approach the potential participant. The text page will state "Your patient is potentially eligible to participate in Dr. Masonbrink's research study about vaping and tobacco use. Please call us if you have concerns about our team approaching the patient." The study team will then approach the eligible participant and give brief information about the study (e.g., "We are doing a research project to learn how we can help adolescents and young adults stop vaping and using tobacco products. Are you interested in hearing more about this?"). The study team will then review and consent the eligible participants. Randomization of consented participants will be stratified on sex and age using a 2:1 ratio within strata via computer generated assignment sequence placed in sequentially numbered sealed envelopes. Control participants will receive brief advice from the health educator regarding tobacco and ENDS use cessation and printed referral to a quit line. Intervention participants will receive our vaping and tobacco use cessation intervention based in clinical practice guidelines and administered by a health educator. Intervention participants will be eligible to receive a prescription for nicotine replacement therapy based on current clinical practice guidelines if they demonstrate risk for nicotine withdrawal. All participants will complete a post-intervention survey and a 3-month survey sent via email, text message via Twilio, and/or mailed paper survey so the research team is not directly involved in outcome data collection. Four phone calls will be conducted on the intervention group post hospitalization to provide smoking cessation counseling. These calls will take approximately 30 minutes. Parents/guardians of AYAs will be asked to complete a post-intervention survey which will be administered by the health educator and will take approximately 15 minutes.

Hospital Staff will be asked to complete a post-intervention survey and interview conducted by the health educator to assess acceptability and disruption of the intervention, it will take approximately 10 minutes, the only PHI that will be collected is to compensate them and will include no sensitive data.

Participant demographics and clinical characteristics (e.g., age of initiation, nicotine dependence) will be assessed at baseline. Preliminary efficacy will be assessed via self-reported 30-day point prevalence tobacco/ENDS abstinence using the timeline follow-back method at 3-month follow-up. To obtain a biochemically verified outcome and to encourage accurate self-reporting we will assess salivary cotinine via mailed samples from all participants (not currently on NRT) who report abstinence. We will assess this by either mailing a saliva specimen home collection kit to then be return mailed (pre

addressed and paid) to our study team or we will also offer the option of completing a home saliva cotinine test which do not require return mailing. For this option home saliva cotinine tests will be mailed to the participant. The study team will then schedule a secure Microsoft Teams video call to witness saliva test completion and results or photos of the test results can be emailed at a convenient time to phmteenresearch@cmh.edu . Although accurate verification will not be possible with participants who are occasional users or those on NRT, this will also allow us to evaluate the feasibility of confirming abstinence by collecting saliva specimens by mail or completing witnessed (via Microsoft Teams secure video or securely emailed photos) home saliva cotinine tests in this population which will be informative for future studies with daily ENDS users. Secondary efficacy outcomes will include self-reported motivation and confidence to quit immediately post-intervention and at 3-month follow up. We will assess acceptability with the overall intervention and intervention components via survey immediately post intervention (AYAs and parents) and at 3 month follow-up (AYAs). We will also explore our secondary objective by obtaining a voluntary saliva or salvage leftover blood samples at baseline from all participants to assess genotyping the impact of individual-level factors (e.g., CYP2A6 genotype, nicotine metabolite ratio, sex) at baseline with our primary outcome (past 30 day ENDS use abstinence).

Acceptability will also be evaluated via participant enrollment and session completion rates. Study Procedures: Data from AYAs and parents/guardians will be collected using confidential electronic survey collection via REDCap.. AYAs who decline to participate will be asked to provide age, sex, race and ethnicity to facilitate identification of participation bias.

SUBJECT MANAGEMENT

6.0 Inclusion and Exclusion Criteria*

6.1 Eligibility Criteria:

AYA patients	Inclusion: 14-21 years, current or past 30-day ENDS use, hospitalized, English speaking Exclusion: severe illness, severe psychiatric illness or cognitive impairment
Parents/Guardians	Inclusion: AYA agrees to parent/guardian surveys

Hospital Staff	Inclusion: Staff of enrolled AYA agrees to participate

6.2 Equitable Selection*:* There are no exclusions based on sex or race/ethnicity. We will plan to enroll a balanced study sample by reviewing the EHR and approaching a study population that is representative of the hospitalized AYAs at our hospital. As a majority of patients are English speaking we will plan to enroll English speaking participants, we will provide a parent information sheet in Spanish for participants whose parents speak Spanish but the enrolled participant must be English speaking.

6.3 Vulnerable Populations: *Check any vulnerable populations <u>that are being targeted</u> for enrollment into the study: (Members of the following populations may not be included as participants in the research unless selected here.)*

☐ Children/Minors (under 7 years of age)
☒ Children/Minors (7-17 years of age)
☐ Neonates (infants less than 30 days old)
☐ Neonates of Uncertain Viability (infants less than 30 days old)
☐ Non-Viable Neonates (infants less than 30 days old)
☒ Wards of the State
☐ Fetuses
☐ Pregnant Women
☐ Adults with impaired decision-making capacity
☒ CM Employees
☐ CM Students/Residents/ Fellows
☐ Economically or Educationally Disadvantaged Persons
☐ Prisoners

<u>Adolescents aged 14-17 years:</u>
Adolescent assent procedures will follow practices accepted by the Society for Adolescent Health and Medicine and current regulatory guidelines and align with those previously used for CM studies involving adolescents
All adolescents will be encouraged to ask questions, provided necessary time to consider participation, and able to stop participation at any time, should they choose to do so.
All adolescents will be assured that their decision to participate or not will have no impact on their relationship with and care received at CM.

<u>Wards of the State:</u>
Another population that requires close attention are those who are wards of the state. This population is extremely important to capture, as they are known to have higher risk

for all of the factors being studied here and likely benefit from prevention at every medical encounter.

Hospital staff as participants: We will enroll CMH employees (hospital staff) in the study. We will minimize the potential for employees to feel coerced or unduly influenced to participate in the study by ensuring that employee will not be recruited or enrolled by their direct supervisor. Participation in the study is completely voluntary and does not impact the AYA patient's participation.

7.0 Local Number of Subjects

144 AYA and up to 144 parents of AYA, up to 10 hospital staff members will be recruited at CMH (the lead study site).

8.0 Identification and Recruitment of Potential Participants*

8.1 Identification of Potential Participants:

How will participants be identified? (Check all that apply)

☐ Chart reviews

☐ By their treating physician who will then provide the study team's contact information to the potential subject/family

☐ By their treating physician who will obtain patient/family permission to share contact information with the study team

☐ By a partnering community-based organization who will then provide the study team's contact information to the potential subject/family

☐ By a partnering community-based organization who will obtain patient/family permission to share contact information with the study team

☐ Self-refer in response to IRB approved advertisements or websites

☒ Through Cerner or other CM sources (e.g. databases, billing records, pathology reports, admission logs, etc.) May involve access of records by individuals not involved in the patient's care.

☐ List of candidates provided through the Data Report Request Form

☐ Registry of individuals interested in research opportunities

☐ Past subject list

☐ Participants will roll-over from another research study: Study #_____

☒ Other: Hospital staff of enrolled AYA will be identified at bedside.

8.2 Pre-Screening prior to HIPAA Authorization

Will any of the identification methods checked above involve access to Protected Health Information (PHI) prior to obtaining HIPAA Authorization?

☒ Yes

☐ No

- *If yes, a "Partial Waiver of HIPAA Authorization" is required. Be sure to make this selection in the "HIPAA & Confidentiality" section below and complete* ***Addendum E: Waiver/Alteration of HIPAA Authorization***

8.3 Recruitment of Potential Subjects:

All data collection will occur at CMH, the lead study site. The research team will use the EHR to identify and recruit a heterogeneous sample of eligible AYAs for the pilot RCT. The health educator will monitor the EHR to identify, notify the medical team and then enroll and consent eligible AYA participants. Recruitment will occur at flexible times to minimize hospital care disruptions. Hospitalized AYAs with current (past 30-day) ENDS use (including those with co-use of cigarettes) will be randomized 2:1 to receive our novel intervention or control intervention that will consist of brief advice and printed quit line referral. Data from AYAs and parents/guardians will be collected using confidential electronic survey collection via REDCap. The health educator will recruit, screen, consent, and randomize eligible participants. AYAs who decline to participate will be asked to provide age, sex, race and ethnicity to facilitate identification of participation bias.

Randomization of consented participants will be stratified on sex and age using a 2:1 ratio within strata via computer generated assignment sequence placed in sequentially numbered sealed envelopes.

Parents of enrolled AYA will be identified at the bedside or given a phone call to ask about interest in the study. The health educator obtain verbal consent from parents in person or by phone.

Hospital staff of enrolled AYA will be identified at bedside. The health educator will obtain verbal consent from hospital staff in person.

9.0 Surveys and Psychometric Testing:

- Data Collection:

  All participants will complete a post-intervention survey and a 3-month survey sent via email, text message via Twilio, and/or mailed paper survey so the research team is not directly involved in outcome data collection. Parents/guardians of AYAs will be asked to complete a post-intervention survey. Hospital staff of AYAs will be asked to complete a post-intervention survey and interview (n=up to 10). A member of the study team, the health educator will complete brief survey items and field notes after each session.

  Measures: *Participant demographics and clinical characteristics* (e.g., age of initiation, nicotine dependence) will be assessed at baseline. The outcome measures, method of assessment, relevant stakeholders and detailed description are depicted in Table 3 and sample survey items in Table 4. *Preliminary efficacy* will be assessed via self-reported 30-day point prevalence tobacco/ENDS abstinence using the timeline follow-back method at 3-month follow-up.[73] To obtain a biochemically verified outcome and to encourage accurate self-reporting we will assess salivary cotinine from all participants (not currently on NRT) who report abstinence. We will assess this by either mailing a saliva specimen home collection kit to then be return mailed (pre addressed and paid) to our study team or we will also offer the option of completing a home saliva cotinine test which do not require return mailing. For this option home saliva cotinine tests will be mailed to the participant. The study team will then schedule a secure Microsoft Teams video call to witness saliva test completion and results or photos of the test results can be emailed at a convenient time to phmteenresearch@cmh.edu. If video call is performed the Microsoft Teams video call will not be recorded. If photos are emailed, the photos will be uploaded to REDCap and then deleted from the email. Secondary efficacy outcomes will include self-reported motivation and confidence to quit immediately post-intervention and at 3-month follow up.[65, 74,75] We will assess *acceptability* with the overall intervention and intervention components via survey immediately post intervention (AYAs and parents) and at 3 month follow-up (AYAs). Acceptability will also be evaluated via participant enrollment and session completion rates. *Feasibility* will be assessed via intervention duration in minutes from audio recordings and Dr. Masonbrink and the health educator will complete a brief survey and record field notes to assess feasibility (e.g., impact on workflow, disruption, suitability). To assess *fidelity* we will review audio recordings and rate health educator intervention and control sessions based on a previously developed fidelity rating scales.[76]

10.0 Additional Research Activities

10.1 Data collection from the medical record: The research team will use a REDCap instrument to collect some demographic information (eg, age, insurance type) from the medical record for each participant. Additionally, upon completion of enrollment, we will collect additional medical record data based on Cerner orders and/or prescription information (to assess for prescription of NRT).

10.2 Refusal Log: The study team will maintain a refusal log to assess potential differences between AYAs that participate and those that do not. AYAs who decline to participate will be asked if they will provide information anonymously. If they agree to do this, they will complete an anonymous survey to assess age, sex, gender, race/ethnicity, primary language, and reason for not participating. This survey will be administered via REDCap/tablet computer. If the adolescent declines to complete the refusal survey, the study team member will complete survey items on age and sex (available via EHR) and reason for study declination, if provided.

10.3 Blood and Other Specimen Collection:

- To explore the impact of genetic variation on electronic cigarette use, nicotine dependence and cessation outcomes, DNA will be isolated from each participant and genotyping/sequencing will be completed by CMRI Genomics core or a similar service. This will allow for detection of known SNPs of interest and creation of an exploratory dataset for future inquiry as new questions arise. To evaluate this exploratory outcome we will collect a salivary or salvage leftover blood (collected during hospital stay) samples from all participants at baseline.
- A saliva sample kit will be mailed to the participant's home with a pre-paid label for their return of the sample or participants will have the option of completing a salivary cotinine test at home that will be witnessed by a study team member through secured Microsoft Teams video calling or photos will be securely emailed to a research specific email address. If using the return mailing option participants will collect saliva according to included instructions and send the sample back in the package we provide them.
- No extra samples will be collected during this time.

11.0 Follow-up

- All AYA participants (both control and intervention arms) will be asked to complete a follow-up Survey at 12 weeks (completion window 10-14 weeks).
- AYA participants will receive an email and/or text via Twilio inviting them to complete the follow-up survey using a weblink provided. We will send up to 2 emails and/or 2 text reminders, as needed. If by

week 13 the participant has not completed the follow-up survey, a study team member will call them using the phone number(s) provided to remind them about the survey (maximum number of phone calls = 3). If needed at the time of the call, the follow-up survey weblink will be sent via email and/or text via Twilio.

12.0 Genetic Analysis Information

Single nucleotide polymorphism (SNPs) analysis and genomic sequencing may occur as part of this study for research purposes only to explore the impact of genetic variation on pharmacokinetics, pharmacodynamics and/or disease.

13.0 Sharing of Results with Subjects

13.1 Results from genetic analysis will not be shared individually with participants. We will not share results of research procedures with participants.

14.0 Risks to Subjects*

14.1 Breach of confidentiality: As with any study, there is potential for breach of confidentiality. Strict measures will be taken to ensure participant privacy and confidentiality. All data will be managed in accordance with hospital institutional review board and HIPPA requirements to ensure confidentiality and protection of research participants. Participants will provide assent/consent and complete data collection privately to maintain confidentiality. Study personnel will not use study data and records for any purpose other than conducting the study. Only researchers involved in this study will have access to the collected data. All data will be de-identified then stored in the secure REDCap database, and all participants will be assigned a unique identification number. The contact information needed to facilitate the 3-month Follow-up will not be linked to survey data. All personally identifiable information will be kept strictly confidential and stored in REDCap and only accessible by Dr. Masonbrink and the necessary, designated study staff at both study sites, including CMH and CHLA. At the completion of data collection and gift card provision, personally identifiable information will be destroyed.

14.2 Mandatory reporting: During the consent process, we will inform participants that we are unable to maintain confidentiality if they verbally disclose abuse that requires a mandated report by state law or

relationship behaviors that raise significant concern for safety of a minor (i.e., < 18 years of age) adolescent participant.

14.3 Emotional distress: Participants may experience distress triggered by the study topic. However, our prior experience with similar studies and available published evidence suggests this risk is minimal. We include information in the assent/consent process that reminds participants that they are not required to answer questions that make them feel uncomfortable and may choose to terminate study participation at any time. CMH social workers are available 24 hours daily for patients and families; participants will be informed of this availability during the informed consent process, as well as upon interview completion. Additionally, each participant will receive a list of teen community resources (e.g., teen resource center, mental health resources, substance use disorder treatment resources, national suicide hotline), such that they may contact needed resources at any time without disclosure of need to the study team.

14.4 Study risks are not greater than minimal for all participants.

15.0 Potential Benefits*

15.1 Participants may benefit directly from the teen resource list that will be provided to each participant. Information provided in the teen resource list and the intervention may enable participants to reduce or quit smoking and/or vaping, to provide support for peers who use tobacco and/or ENDS use, and to access CM and community resources for common issues, including substance use disorders. Intervention participants may benefit directly from the knowledge and resources gained through the intervention itself by receipt of MI-based counseling with the health educator and Dr. Masonbrink, possible prescription of nicotine replacement therapy if indicated and follow up through booster sessions and/or text messaging program. Control participants may benefit from receipt of brief advice to quit tobacco use by a health professional and referral to a quit line. Indirect benefit from this study may include potentially decreasing prevalence of AYA tobacco and/or ENDS use and adverse health outcomes.

15.2 Benefits to society/science may include 1) improved care of AYAs treated receiving care in the pediatric hospital in the future, and 2) better understanding of effective interventions to promote tobacco and ENDS use cessation among youth. In the long term, the findings of this study could contribute to a reduction in tobacco and ENDS use among AYAs and associated negative outcomes, which include cancer, cardiorespiratory illnesses and death. The minimal risks of participation are reasonable in relation to these generalizable benefits.

16.0 Investigator Assessment of Risk/Benefits Ratio*

16.1

Select as applicable:	**Pediatric Risk Category:**	
☒	Category 1	Research not involving greater than minimal risk (45 CFR §46.404 and 21 CFR §50.51)
☐	Category 2	Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. (45 CFR §46.405 and 21 CFR §50.52)
☐	Category 3	Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. (45 CFR §46.406 and 21 CFR §50.53)
☐	Category 4	Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (45 CFR §46.407 and 21 CFR §50.54)
Select if applicable:	**Adult Risk Category:**	
☒	Not Greater than Minimal Risk	
☐	Greater than Minimal Risk	

17.0 Payment, Reimbursement and Tangible Property provided to subjects*

Is payment, reimbursement, or tangible property part of the study?

☒ Yes ☐ No *(If No, delete the following subsections)*

17.1 ***Payment to Subjects:*** *If providing payment for participation (e.g. cash equivalent for participation, payment for time off work), select the form of payment:*

☐ Greenphire/ClinCard
☐ Gift Card: (Merchant:_____)
☒ Other: ___Clinical Conductor (CCpay)_____

Note: "Gift Card" and "Other" options require approval by Research Administration. Upon submission in myIRB, ORI staff will initiate the Research Administration approval process.

Payment Schedule:
Formative stage: Parents of AYA will receive $20 for participation. Hospital staff of AYAs will receive $10 for participation.

Research stage: Pilot RCT: AYAs will receive $15 for study enrollment and $20 for 3-month follow up survey completion. For eligible participants who agree to complete a saliva sample at the 3 month follow up they will receive $25 once the sample is completed/received. Total potential payment for one AYA participant is $60. We will also provide NRT prescription free of charge for AYA participants assigned to the intervention group and for which this is clinically indicated.

17.2 Reimbursement: *N/A*

17.3 Tangible Property: *N/A*

18.0 Compensation for Research-Related Injury

18.1 Being in this study involves no more than minimal risk, therefore we do not require compensation for research-related injury.

19.0 Economic Burden to Subjects

Participants may incur costs related to text messaging and data charges for surveys completed on their cellular phone. Participants may incur costs related to follow up after the hospital visit during which they enrolled in the study (e.g., if they follow up in the CM adolescent clinic).

20.0 Parental Permission and Adult Consent Process*

Waiver of Documentation of Permission/Consent

Permission/Consent form provided but signature will **NOT** be obtained (e.g. verbal consent)
Must complete *Addendum A: Waiver of Documentation of Permission/Consent*

☒ **Waiver of written documentation of permission of parent/LAR for pediatric participants**

Study group(s) to which this method applies: Parents of Adolescent participants (14-17 years old). An information sheet will be left in the room/given to parents of adolescents who decide to participate in the study.

☒ **Waiver of written documentation of consent of adult participants**

Study group(s) to which this method applies: Parents as Participants; Parents will give verbal consent to participate in the study and complete a survey.

☐ **Waiver of written documentation of consent of participants turning 18**

Study group(s) to which this method applies:

Waiver or Alteration of Permission/Consent

Adult consent will **NOT** be obtained, or you propose to alter a required element of consent.
Must complete *Addendum B: Waiver of Permission/Assent/Consent*

☒ **Waiver/Alteration of permission of parent/LAR for pediatric participants** We request a waiver of parent/LAR permission for adolescent participants 14-17 years of age admitted to the hospital without a parent/LAR present.

We will enroll wards of the state and children in foster care, consistent with the above process legal guardians will be given brief information about the study but we will waive consent from a legal guardian. We feel this is appropriate, as there is very low risk for harm to the participants.

☐ **Waiver/Alteration of consent of adult participants**

Study group(s) to which this method applies:

☐ **Waiver of consent of participants turning 18**

Study group(s) to which this method applies:

Written Informed Permission/Consent

☐ **Written informed permission of parent/LAR for pediatric participants**

Study group(s) to which this method applies:

☒ **Written informed consent of adult participants**

Study group(s) to which this method applies: AYA participants age 18-21 years of age will provide written consent using eConsent.

☒ **Written informed consent of participants turning 18**

This includes the continued access to and use of their PHI by the study team.

Study group(s) to which this method applies: If a participant turns 18 during the course of the study they will be asked to reconsent at a subsequent study interaction which will provide written consent using eConsent.

Additional Methods

☒ **Obtaining permission/assent/consent of non-English speaking parents or participants**

Must compete *Addendum C: Non-English Speaking Subjects*

☐ **Surrogate decision maker consent form adults not capable of consenting for themselves**

Must complete *Addendum D: Surrogate Decision Maker Consent*

Study group(s) to which this method applies: N/A

20.2 Permission/Consent/Consent at 18 Discussion: The 3-month follow-up survey will include a question asking the patient if they have turned 18 since they enrolled in the study. For those that answer "yes," we will use branching logic to ensure that they consent to participate at this point.

20.3 Documentation of Permission/Consent/Consent at 18: For those who turn 18 while enrolled in the study we will review the consent form with the adult participant and obtain eConsent for continued study participation.

21.0 Assent of Pediatric Subjects

21.1 Select the option(s) that apply to the study:

☐ **Obtaining assent of pediatric participants is NOT POSSIBLE due to:**

- ☐ *The capability of the participants (considering the ages, maturity, physical and/or psychological state) is so limited that they cannot reasonably be consulted.*
- ☐ *The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the participants and is available only in the context of the research.*

☐ **Obtaining assent of pediatric participants is NOT PRACTICLE given the context of this study** (e.g., minimal risk, no direct contact with subjects). **Must complete *Addendum B: Waiver/Alteration of Permission/Assent/Consent***

☒ **Assent of pediatric participants WILL BE SOUGHT following assessment of ability to assent.**

21.2 Assessment of Ability to Assent: Research team members will verify with the clinical care team that the patient has the capacity to assent.

21.3 Assent Discussion: Informed assent will occur during the hospital visit in a private setting (i.e., parent/LAR will not be present during the assent process). The study team will:
1) Provide ample opportunity for potential participants to ask questions and to consider participation, including coming back later during the visit to allow the participant time for consideration.
2) Use teach-back to confirm comprehension of study procedures.
3) Communicate that current and future care at CM will not be impacted by the decision to participate in the study or not.

21.4 Documentation of Assent or Inability to Assent: We will use eConsent to document participant assent

22.0 HIPAA and Confidentiality

HIPAA regulations apply to this study if the data used or accessed relates to:

- The past, present or future physical or mental health or condition of an individual;
- The provision of health care to an individual; OR
- The payment for the provision of health care.

22.1 HIPAA Authorization

☒ Full Written HIPAA Authorization will be obtained (within the p/a/c form or standalone form)

☒ *Partial Waiver of HIPAA Authorization (e.g. waiver for recruitment and pre-screening purposes only)* We request a partial waiver of HIPAA Authorization for:

- Use of Cerner to facilitate recruitment and pre-screening.

☒ Alteration of HIPAA Authorization (some but not all required elements of an Authorization are present, e.g. signature will not be obtained)

Adolescent participants (14-17 years old): An information sheet will be provided to parents, parent signature will not be obtained

Parent as Participant (survey): A brief verbal consent will be obtained, participant signature will not be obtained

Hospital staff as participants: A brief verbal consent will be obtained, participant signature will not be obtained.

☒ Waiver of HIPAA Authorization (authorization will NOT be obtained)
For participants under 18 years old without a parent or guardian present we request a waiver of HIPAA authorization to enroll without parental/guardian permission or consent

☐ If Other, explain:

22.2 Data confidentiality:

- PHI will be stored in a secure CM REDCap file, accessible only to members of the study team members at both study sites, including CMH and CHLA.
- We will destroy PHI at the earliest opportunity. We will maintain PHI through completion of enrollment and data analysis. PHI will then be deleted.
- PHI will only be accessed by members of the study team as necessary for study procedures. Good Clinical Practice guidelines will be followed in order to ensure that study data is not disclosed to unauthorized persons.
- Study team training will include the importance of data confidentiality and mechanisms to protect confidentiality.

22.3 As this is an NIH-funded study, a Certificate of Confidentiality will be issued for this study.

23.0 Provisions to Protect the Privacy Interests of Subjects*

23.1 The study team will take great care to protect participant privacy.

Recruitment and enrollment will occur privately.

Participants will be assigned a study number. Surveys will be completed confidentially and will not contain identifying information. We will use a unique, participant-created code to link study surveys over time, such that participant identity is not linked to the study survey data. Contact information used to facilitate follow-up survey completion will be stored in a separate REDCap tool and thus not linked to study data. Identifying information necessary for gift card provision will be obtained upon survey completion via a separate REDCap tool and thus this information will not be linked to an individual participant's survey data.

All data will be managed in accordance with the CM Institutional Review Board and HIPAA requirements to ensure confidentiality and protection of research participants. Study team members will not use study data and records for any purpose other than for conducting the study. PHI will be kept in a password protected database that is separate from the study survey database. PHI will be deleted at the earliest opportunity. There are no patient identifiers recorded in the permanent research record. Clinical information will not be released without written permission of the participant, except as necessary for monitoring by IRB, the FDA, the OHRP, the Sponsor, or the Sponsor's designee.

23.2 To ensure participants feel at ease with study procedures, we will thoroughly explain study procedures, ensure ample opportunity for questions at any point during the study, provide assurance that participation is voluntary and can be terminated at any point, and provide assurance that the decision to participate or not will not impact the participant's relationship with CMH. If eligible participants do not want to participate in the research but are interested in learning more about how to quit smoking or vaping we will inform them that they can ask their medical team for more information.

23.3 Study team members will only have access to data required to complete their designated study duties. Study team member training will include necessity of and mechanisms to protect privacy and confidentiality.

24.0 Withdrawal of Subjects*

24.1 All participants may withdraw from the study at any time by notifying the research team. If a participant withdraws from the study, any data collected up to that point will be kept and deidentified for analysis purposes.

DATA MANAGEMENT

25.0 Data Collection*

25.1 Sources of data include surveys and medical records of AYA participants, parent surveys and Health Educator field notes.

25.2 Sensitive Data: Study data includes report of substance use and receipt of NRT prescription during hospital visit.

25.3 Identifiable Data: PHI sufficient to enable delivery of the study follow-up survey will be recorded.

25.4 .

1. Name/Initials	☐ Accessed only	☒ Recorded
2. All elements of date (except year) directly related to an individual (e.g. date of birth, admission date, discharge date, date of death)	☐ Accessed only	☒ Recorded
3. Medical record number	☐ Accessed only	☒ Recorded
4. Account number	☐ Accessed only	☒ Recorded
5. Health plan identification number	☐ Accessed only	☐ Recorded
6. Social Security Number	☐ Accessed only	☐ Recorded
7. Device identifiers and serial number	☐ Accessed only	☐ Recorded
8. Certificate/License number	☐ Accessed only	☐ Recorded
9. Telephone number	☐ Accessed only	☒ Recorded
10. Fax number	☐ Accessed only	☐ Recorded
11. Email addresses	☐ Accessed only	☒ Recorded
12. Web addresses (URLs); Internet IP addresses	☐ Accessed only	☐ Recorded
13. Street address, city, county, precinct, zip code or equivalent geographical codes	☐ Accessed only	☒ Recorded
14. Full face photographic images and any comparable images	☐ Accessed only	☐ Recorded
15. Biometric identifiers, including finger and voice print	☐ Accessed only	☒ Recorded
16. Vehicle identifiers and serial numbers, including license plate number	☐ Accessed only	☐ Recorded
17. Any other unique identifying number, characteristic or code that may help identify individual participants including their initials (e.g. student or employee ID number)	☐ Accessed only	☒ Recorded
18. Elements of date, including year, for persons 90 years or older	☐ Accessed only	☐ Recorded
19. Other:	☐ Accessed only	☐ Recorded

26.0 Adverse Events and Unanticipated Problems*

26.1 Monitoring: The PI and study team will meet weekly during enrollment and the 3-month follow-up period to identify and discuss adverse events and unanticipated problems. Study team members will promptly notify the PI if an adverse event or unanticipated problem is identified.

26.2 Reporting: We will follow Policy 5.11 Reportable Events of the CM Research Program Policies and Procedures in regards to reporting adverse events and other unanticipated problems to the CM IRB.

26.3 Plans for Assuring Compliance with Requirements Regarding Reporting of Adverse Events

Serious adverse events will be monitored and handled as described below:
Definition: Consistent with the definition by the US Food and Drug Administration (FDA), a serious adverse event includes any event experienced by a participant while in the study that:

- Is fatal
- Is life-threatening (participant was at risk of death from the event as it occurred)
- Is disabling or incapacitating
- Requires inpatient hospitalization or prolongs a current hospitalization
- Is a congenital anomaly in the offspring of a subject who received the study medication
- Requires intervention to prevent permanent impairment or damage

Monitoring: Information about serious adverse events experienced by study participants will be monitored by the following means:

- Report given by study participant to study staff either in person or by telephone
- Report given to study staff by study participant's family or friends either in person or by telephone
- Report by the participant's physician or other health care provider involved in their care
- Report from a hospital or other facility where the study participant(s) is being treated for the serious adverse event
- Other persons who may have knowledge of the serious adverse event

Procedure: Upon receiving report of a serious adverse event:

- The study staff will page Dr. Masonbrink as soon as possible
- The study staff will give the necessary information to Dr. Masonbrink
- Dr. Masonbrink will obtain other necessary information and complete the FDA "MED WATCH" form for each serious adverse event
- Dr. Masonbrink will make a decision whether to stop the study temporarily or

permanently and inform study staff of this decision
• Dr. Masonbrink will submit the serious adverse event to the Institutional Review Board at the Children's Mercy Hospital within 7 days of learning of the event and will work with the IRB to determine the need for changes to study procedures and the study protocol
• Dr. Masonbrink will provide a completed copy of the FDA "MED WATCH" form to the Data Safety and Monitoring Board within 7 days of learning of the event
• Dr. Masonbrink will submit the serious adverse event to the NIDA program officer within 7 days of learning of the event
• A copy of the completed "MED WATCH" form will be kept in the study file

27.0 Data Analysis*

27.1

Measures: *Participant demographics and clinical characteristics* (e.g., age of initiation, nicotine dependence) will be assessed at baseline. The outcome measures, method of assessment, relevant stakeholders and detailed description are depicted in Table 3 and sample survey items in Table 4. *Preliminary efficacy* will be assessed via self-reported

Table 3: Assessment of Proctor Outcome Measures

Outcome Measure	Definition	How/What Assessed	Team member/ Stakeholder(s)	Description
Preliminary Efficacy	Impact on treatment outcomes of the intervention vs. control	Survey	AYA participant	Self-reported and biochemically verified (salivary cotinine) 30-day tobacco/ENDS use abstinence at 3-mo follow up survey (primary outcome) Self-reported motivation & confidence immediately after intervention and at 3-mo follow up survey
Acceptability	Participant satisfaction with the intervention components	Survey Study process data	AYA participant, Parent/Guardian AYA participant	Likert-scale AYA and parent/guardian survey items on intervention satisfaction after the session (AYAs and parent/guardians) and at 3-mo survey (AYAs only)* Proportion of eligible patients who enroll, complete the intervention & booster sessions
Feasibility	Intervention fit within the context; suitability for everyday use; practicality	Field notes, session length, & survey items	Health Educator, Dr. Masonbrink	Mean score of Likert-scale items on intervention feasibility (immediately post intervention*; Session duration (minutes) from audio-recordings; Health educator field notes of interruptions to workflow and modifications to care
Fidelity	Extent to which the intervention is delivered as intended?	Audio-recordings of Health Educator and Dr. Masonbrink's sessions	Health Educator, Dr. Masonbrink	Drs. Masonbrink and Catley will review audio-recordings and perform fidelity scoring of intervention sessions utilizing adapted fidelity rating scales

*For outcomes assessed by 5-point Likert-scale survey items, we will calculate mean scores of survey items by categories (e.g., mean AYA satisfaction/acceptability for each intervention component and for the overall intervention). Mean scores ≥ 4 will be considered satisfactory.

30-day point prevalence tobacco/ENDS abstinence using the timeline follow-back method at 3-month follow-up.[73] To obtain a biochemically verified outcome and to encourage accurate self-reporting we will assess salivary cotinine from all participants (not currently on NRT) who report abstinence. We will assess this by either mailing a saliva specimen home collection kit to then be return mailed (pre addressed and paid)

to our study team or we will also offer the option of completing a home saliva cotinine test which do not require return mailing. For this option home saliva cotinine tests will be mailed to the participant. The study team will then schedule a secure Microsoft Teams video call to witness saliva test completion and results or photos of the test results can be emailed at a convenient time to phmteenresearch@cmh.edu, a secure email address created specifically for this research study. Although accurate verification will not be possible with participants who are occasional users or those on NRT, this will also allow us to evaluate the feasibility of collecting saliva by mail or completing secure video or photos witnessed home saliva cotinine tests in this population which will be informative for future studies with daily ENDS users. Secondary efficacy outcomes will include self-reported motivation and confidence to quit immediately post-intervention and at 3-month follow up.[65, 74,75] We will assess *acceptability* with the overall intervention and intervention components via survey immediately post intervention (AYAs and parents) and at 3 month follow-up (AYAs). Acceptability will also be evaluated via participant enrollment and session completion rates. *Feasibility* will be assessed via intervention duration in minutes from audio recordings and Dr. Masonbrink and the health educator will complete a brief survey and record field notes to assess feasibility (e.g., impact on workflow, disruption, suitability). To assess *fidelity* we will review audio recordings and rate health educator intervention and control sessions based on a previously developed fidelity rating scales To assess *preliminary efficacy*, differences in self-reported and biochemically verified 30-day tobacco/ENDS use abstinence at 3-month follow up (primary outcome) will be analyzed using a generalized linear model assuming an underlying binomial distribution and logit link function to compare between study arms. Motivation and Confidence to quit will be analyzed using a repeated measures analysis of variance. Potential differential outcomes based on sex and demographic factors will be explored. Chi-square (categorical variables) and Wilcoxon Rank Sum (continuous variables) tests will be used to assess participation bias. For *acceptability*, we will calculate the proportion of AYA participants and parents/guardians in the intervention arm with mean ratings of satisfaction and acceptability of ³ 4 on the 5-point Likert scale. In addition, frequencies and percentages will be used to describe the enrollment and session completion rate. For *feasibility* we will conduct thematic analysis of field notes and conduct simple descriptive analyses (means, frequencies, percentages) of the brief survey items completed by Dr. Masonbrink and the health educator and session length data. *Fidelity* will be summarized utilizing similar descriptive analyses of the fidelity ratings (e.g., percentage of intervention steps completed; mean rating of key MI skill adherence).

CYP2A6 genotype-predicted phenotype (slow, intermediate, extensive) and other genetic variants of interest may be explored as co-variants in the analysis. Given the exploratory nature of the genetic analysis, we are likely underpowered to find significant association across numerous genetic co-variants, but these data may inform future studies designed to evaluate the relationship.

27.2 Our proposed sample size [n=144 (96 treatment, 48 control)] is well within the recommendations for behavioral intervention development pilot trials based on what is feasible to recruit in our hospital and judged to be sufficient to evaluate efficacy (i.e., self-reported/biochemically verified abstinence) in a preliminary behavioral design trial.[63,64] With respect to percentage reporting self-reported and/or biochemically confirmed abstinence at 3-mo follow up the margin of error (ME) around our observed outcomes depends on the observed proportion with the largest ME occurring when the proportion is 50%. Our sample size is sufficient to provide a ME of 10% (if the proportion is 50%) or less.

28.0 Data and Specimen Management*

Data Management: Data will include that obtained from the study surveys and medical record, as described above.

Data will be collected via REDCap or paper survey or EHR review. Data from the surveys and EHR will be stored in REDCap. Paper surveys, if used in the event of a REDCap or other IT issue, will be stored in a locked office of the investigators.

Deidentified data will be exported from REDCap to statistical programs for analysis (e.g., SAS, SPSS, Excel). All data will be securely stored on password-protected CM servers.

Strict measures will be taken to ensure participant privacy and confidentiality. Participants will be assigned a unique study identification number. Additionally, survey data will be collected using a unique, participant-created code such that a link between participant survey number and participant identity do not need to be linked.[39] The study REDCap project will be set up such that the study team will not be able to link survey data to individual participant identity. All personally identifiable information needed to facilitate data collection and intervention fidelity review will be kept strictly confidential, stored on REDCap, and accessible only to designated study team members. Only study team members needing access to data to fulfill their study responsibilities will have access to the data. Non-study team members will not have access to the data.

Data will be stored per CM records retention policy.

28.1 Specimen Management: *Describe how specimens will be handled, including:*

Genetic data and biospecimens will be stored up to 5 years for this study (IRB STUDY00002116); biospecimen storage will occur in the existing Adolescent Medicine Pharmacogenetic Repository.

If this study involves storing of data or banking of leftover specimens for future research, indicate how the use will be managed:

☐ Contributing data and/or leftover specimens to an existing CM repository protocol (myIRB#_____)

☐ Contributing data and/or leftover specimens to an existing non-CM repository (Institution/Repository Name: _____)

☒ Not contributing to an existing repository for the management of data/specimens for future research use.

☒ Other: Samples will be stored in the Adolescent Medicine Pharmacogenomic Repository (AMP) (IRB#13020033).

Saliva or salvaged blood samples will be stored in the AMP freezer space until time of analysis. The samples will be accessed by study team members and lab members needed to analyze the samples. All personnel are CM researchers. All samples will be deidentified and marked in with a systematic record number including no individual identifying information.

For participants who begin the study as a minor and turn 18 they will be asked to reconsent at a subsequent study interaction which will provide written consent using eConsent.

30.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Although this study represents no more than minimal risk to participants, we will exercise the following provisions to ensure participant safety. *Dr. Masonbrink will have overall responsibility for monitoring the safety of participants and data. The data and safety monitoring plan will be developed in accordance with NIH guidelines and code of federal regulations established by the Department of Health and Human Services (45 CFR 46; the Common Rule). Dr. Masonbrink will share reports of preliminary data with Dr. Catley (primary mentor) monthly through the duration of participant enrollment and data collection. In the unlikely event of an adverse outcome associated with the study protocol, the outcome will be documented and, as appropriate, reported to the Institutional Review Board, FDA and NIH.*

Regulatory Requirements & Site Performance

This multi-site collaborative research study (see below under Multi-Site Research) is approved by the CMKC Institutional Review Board (IRB) and will comply with all applicable regulatory requirements. The committee will monitor subject accrual and retention and ensure that the study cohort is balanced for age, gender, race/ethnicity.

Monitoring Committee A Data Safety Monitoring Board (DSMB) will be established, to periodically review and evaluate accumulated study data for participant safety, study conduct and progress, and efficacy. Based on these assessments, the DMSB will make recommendations regarding the continuation, modification, or early termination of the study. The committee will meet twice yearly (via teleconference) to review the studies associated with this application and to monitor any adverse events. Documentation of the meetings will be recorded and stored in the Division of Pediatric Hospital Medicine at CMKC. The DMSB membership will include experts in adolescent health and tobacco use and investigators with expertise in the conduct and methodology of trials for behavioral interventions. Members of the DSMB will review the written protocols, informed consent procedures, and plans for data and safety monitoring. The DSMB reporting guidelines will then be individualized for the study, taking into consideration the population under study, the known or anticipated adverse outcomes or risks of the study procedures, and any other data monitoring or oversight required. The DSMB will review data quality and timeliness, adherence to the study protocol, participant recruitment and consenting procedures, accrual and retention figures, and all adverse and other events and outcomes. For the purposes of DSMB review, adverse and other events will be defined broadly to include any negative occurrence experienced by a participant during the course of their participation in the study regardless of any investigator-determined attribution to the study protocol or procedure. This allows the DSMB to independently evaluate attribution for the event. Through these reviews the DSMB determines whether cumulative data indicate the need to change the research design, to modify information presented to participants, or to terminate the project. New scientific developments outside the study that may impact participant safety or the ethics of the study are considered in making these determinations. Pre-specified stopping rules are established in consultation with the investigator and are employed if significant benefits or risks have developed, if trial management issues prevent successful completion, or if compelling ethical concerns arise. Again, should it be deemed necessary to have a DSMB, we will elucidate the plan in greater detail in accordance with institutional guidelines.

30.1 *In addition to the Principal Investigator, which individual or group will be responsible for monitoring the data and safety for this study?*

☐ Sponsor or Sponsor Designee (including the Sponsor CRO)

☒ Data and Safety Monitoring Board (DSMB) or Data Safety Monitoring Committee (DSMC)
☐ Independent Monitor (s)
☐ Internal Committee at CM
☐ Other: _____

30.2 Data Safety Monitoring Plan: Please see Data Safety and Monitoring plan in IRB documents for details.

STUDY MANAGEMENT

31.0 Setting & Locations*

31.1 *Describe the sites or locations where the research will be conducted.*

- *Identify where research procedures will be performed including any non-CM affiliated locations. For any non-CM affiliated locations, upload a letter of support in myIRB which states that the site is aware that research will be conducted on their premises.*
- *Describe the composition and involvement of any community advisory board.*
- *For research conducted outside of CM and its affiliates describe:*
  - *Regulations or customs affecting the research*
  - *The local scientific and ethical review structure*
- *Describe the availability of medical or psychological resources that subjects might need as a result of taking part in the study.*

32.0 Multi-Site Research

Is this a multi-site or collaborative research study?

☐ No If no, you do not need to complete this section.

☒ Yes If yes, continue below:

☐ ***Multi-Site Research:*** *Multiple sites will be engaged in this human research project. Sites will use the* ***same*** *protocol to conduct the* ***same*** *human research activities (except for minor variations due to local context considerations).*

☒ ***Collaborative Research:*** *Multiple sites will be engaged in this human research project. Sites will* ***not*** *be performing the* ***same*** *research activities. The Site submission will specify the specific research activities each site will perform.*

REQUIRED*: Enter summary of site-specific activities that differ from the overall protocol:* The study P.I. Abbey Masonbrink, MD MPH, will start a

new position at Children's Hospital of Los Angeles (CHLA) on November 1, 2024. At that time we will assign a new CMH site PI (Dr. Miller, currently co-Investigator) and Dr. Masonbrink will be added as an external collaborator at CHLA with a external reliance on CMH IRB. No study participants will be enrolled at CHLA but data containing PHI will be shared with Dr. Masonbrink and necessary study team members at CHLA for data analysis and dissemination (manuscript and future grant preparation.

☐ ***Student(s)*:** Student(s) will help with this project and will be engaging their home institution.

☐ **Visiting *Resident(s) /* Visiting *Fellow(s)*:** Visiting Resident(s) / Visiting Fellow(s) will help with this project and will be engaging their home institution.

Is Children's Mercy (CM) acting as the single IRB of Record (sIRB)?

☐ ***No, each site is getting their own IRB approval.***

☒ **Yes, some or all sites will rely on the CM as the sIRB**.

- ***Reliance is required*** *for non-Exempt* ***NIH*** *or other* ***Federally Funded*** *research where:*
  - *The institution's employees or agents intervene or interact with human subjects for research purposes;*
  - *The institution's employees or agents obtain individually identifiable private information or identifiable biospecimens about human subjects for research purposes; or*
  - *The institution receives a direct HHS award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.*

If CM is sIRB for another site, complete the chart for that site(s) (*Add a new row for each site relying on the CM IRB, delete chart if not acting as sIRB):*

Site Name	Enrollment Goal for Site(s) *Choose One*	Relying on CM IRB?
CHLA	☐ **Site Enrollment Goal:** N/A ☒ **Site will not enroll:** No study subjects will be	☒ External Site will rely on the CM IRB as the IRB of Record using a reliance agreement. ☐ **Not Applicable**. Site will **not** interact or intervene with human participants or their identifiable data / identifiable biospecimens.

	enrolled, however data containing PHI will be shared with this study site for analysis.	Site is also not a primary NIH or federal grant recipient.

32.1 ***Multi-Site Research:***

All study procedures will occur at CMH. However, some co-investigators are from non-CM institutions: Karen Wilson MD MPH (University of Rochester Medical Center, Rochester NY), Kimber Richter, PhD (University of Kansas Medical Center). These study members are categorized as not participating in human participants research as they will at no time interact with study participants or have access to identifiable data. The study P.I. Abbey Masonbrink, MD MPH, will start a new position at Children's Hospital of Los Angeles (CHLA) on November 1, 2024. At that time we will assign a new CMH site PI (Dr. Miller, currently co-Investigator) and Dr. Masonbrink will be added as an external collaborator at CHLA with a external reliance on CMH IRB. No study participants will be enrolled at CHLA but data containing PHI will be shared with Dr. Masonbrink and necessary study team members at CHLA for data analysis and dissemination (manuscript and future grant preparation.