Testing the Impact of Smartphone-based Messaging to Support Young Adult Smoking Cessation - Pilot

NCT05991934

3/19/25

JHSPH IRB Research Plan for New Data Collection

Use this template for new data collection and if you also will analyze secondary data. Answer the questions below and for numbered sections that do not pertain to your study, retain the section numbers and bolded questions, and write "N/A". Please start typing in the gray boxes provided.

PI Name: Johannes Thrul, PhD

Study Title: Testing the impact of smartphone-based messaging to support young adult smoking cessation

IRB No.: IRB00013413

PI Version No. / Date: V7, 03/19/2025

I. Aims of the Study: Describe the aims/objectives of the research and/or the project's research questions or hypotheses.

Clinical practice guidelines for smoking cessation emphasize cognitive behavioral therapy (CBT) to help patients develop coping strategies for urges. Mindfulness or Acceptance and Commitment Therapy (ACT) offer a different approach, which teaches smokers psychological flexibility through accepting negative experiences. While there is evidence for the efficacy of both CBT and Mindfulness/ACT smoking cessation interventions, it is unclear if these approaches are efficacious when implemented in real-time and with young adults. The overall goal of this proposal is to evaluate the efficacy of CBT and Mindfulness/ACT messages for young adults targeted at specific high-risk situations for smoking.

This research will address the following specific aims:

Aim 1: To test CBT and Mindfulness/ACT intervention message efficacy for reducing momentary smoking urges (N=80). To inform just-in-time interventions, it is crucial to test if CBT and Mindfulness/ACT based messages can reduce momentary smoking urges. We will conduct a micro-randomized trial (repeated within-subject randomizations of messages) to accomplish this. In line with our existing protocol, participants first collect EMA data for 14 days, allowing us to determine high-risk situations for smoking. In the following intervention phase, participants receive tailored messages triggered by geofencing of participants' high-risk locations for a total of 30 days. Tailoring is based on established predictors of smoking relapse (stress and presence of other smokers). The micro-randomized trial tests the efficacy of CBT versus Mindfulness/ACT versus control messages for reducing smoking urge 15 minutes post message delivery. Secondary outcomes include smoking or other tobacco use (including e-cigarettes), affect, and stress.

Aim 2: To test if exposure to urge reduction messages results in changes in smoking behavior over time compared to an EMA only control group (N=80). It is important to investigate if repeated messages in the micro-randomized trial impact smoking behavior over time, in contrast to just repeated assessment without messages. Thus, this study includes a conventionally randomized clinical-trial component. Parallel to the micro-randomized trial group, a control group completes EMA surveys only without intervention messages. This allows us to test if messages reduce smoking behavior. The primary outcome is number of cigarettes per day at end of treatment, 3-, and 6-months follow-up. Secondary analyses explore biochemically verified 7-day point prevalence abstinence, switching to e-cigarettes, and other tobacco outcomes. Post-hoc dose-response analyses investigate the long-term efficacy of CBT or Mindfulness/ACT messages on smoking behavior.

Aim 3: Explore moderation effects of substance co-use (cannabis, alcohol, other drugs) and exposure to specific location (home, work, bars) on urge reduction message efficacy. A crucial research question to inform future mobile interventions is how well intervention messages work in different situational contexts and when people are co-using other substances. Among intervention group participants, we will explore how urge reduction message efficacy may be moderated by substance co-use and exposure to specific settings.

II. Background and Rationale: Explain why this study is being done. Summarize briefly what is already known about the issue and reference previously published research, if relevant.

Tobacco smoking is the leading preventable cause of morbidity and mortality in the United States, and young adults have high smoking rates. Although most young adult smokers are interested in quitting, they underutilize professional cessation support. We need novel approaches to deliver evidence-based smoking cessation interventions to young adults. Smartphones have wide reach and integration into young adults' lives (96% own a smartphone). These devices offer great opportunities to deliver cessation interventions by delivering messages suggesting coping strategies "in the moment" when smokers need cessation support. However, few cessation apps deliver evidence-based intervention content with established acceptability and content tailored to individuals' needs. Moreover, mobile smoking cessation interventions have yet to account for the impact of substance co-use (e.g., alcohol, cannabis), frequent among young adults, on intervention effects.

One especially promising strategy for smartphone interventions is to target situations that elicit smoking urges. In our and others prior work, these urges emerged as the most important triggers of smoking. The probability of smoking greatly increases as urge levels rise, especially among light smokers, common among young adults. It is thus paramount for smartphone interventions to help young adults cope with these smoking urges.

III. Study Design:

A. Provide a BRIEF overview of your study design and methods. The study design must relate to your stated aims/objectives. DETAILS WILL BE REQUESTED LATER. *If your study also involves analysis of existing data, please complete Section XI, "Secondary Data Analysis of Existing Data" in the last part of this research plan. If your study ONLY involves analysis of existing data, please use the research plan template for secondary data analysis (JHSPH IRB Research Plan for Secondary Data Analysis of Existing Data/Specimens)*

Intervention message acceptability

To inform intervention development and efficacy, it is important to determine intervention message acceptability. Recruited from an online market research panel, each survey participant will complete a cross-sectional survey assessing acceptability of 10 randomly selected intervention messages. The primary outcome is the average Likert-scale response for four measures on acceptability of messages' (1) written content, (2) visual content, (3) helpfulness for coping with smoking urges and cravings, and (4) helpfulness for quitting smoking. Qualitative open-ended responses will help inform interpretation of quantitative findings. Analyses will be used to improve intervention messages and to examine message acceptability by age, gender, and race/ethnicity.

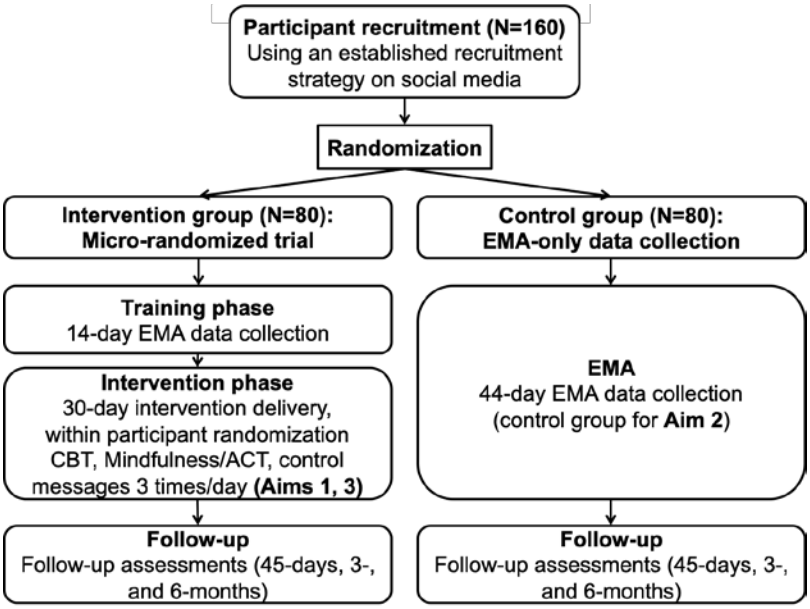
We will randomly select 10 messages for each of 300 young adult smokers, recruited from an online market research panel (Qualtrics), and assess message acceptability for content, graphic design, and helpfulness for a smoking cessation intervention by age, gender, and race/ethnicity.

We propose to test tailored smartphone-based messages to support young adults in quitting smoking (study overview in Figure). Our study addresses 3 specific aims.

For **Aim 1**, a micro-randomized trial (within-subject randomization) with 80 young adult smokers will investigate the efficacy of smoking cessation messages based on CBT and mindfulness/ACT for reducing smoking urge 15 minutes after message delivery.

In **Aim 2**, a built-in and conventionally randomized EMA-only control group will allow us to test if intervention messages result in changes in smoking behavior over time. The primary outcome will be self-reported number of cigarettes per day at end of treatment, as well as 3- and 6-month follow-up.

Aim 3 will explore moderation effects of substance co-use (cannabis, alcohol, other drugs) and exposure to specific locations (home, work, bars) on urge reduction message efficacy among intervention group participants.



Study overview

B. Provide a sample size and a justification as to how you arrived at that number. If you use screening procedures to arrive at a final sample a table may be helpful.

Message acceptability: A sample size of 300 participants receiving 10 randomized messages will yield 3,000 exposures. Given that we are testing 124 messages across 3,000 exposures, each message will have an average of 24.2 completed assessments. Kim et al. (2019) demonstrated that 25 evaluations per message is sufficient to estimate message acceptability by balancing accuracy and efficiency. Of the 10 randomly delivered messages, each participant will provide open-ended feedback on a random set of two of the messages. Thus, qualitative feedback will be given for 600 exposures or an average of 4.8 open-ended responses per message.

Aim 1: A sample size of 80 participants receiving 3 randomized messages per day for 30 days will provide 7,200 observations. Across person-days, there will be an average of one prompt per day for each of the 3 conditions CBT, Mindfulness/ACT, and control (balance across person-days). Power estimations were conducted using an online tool specifically developed for sample size calculations for micro-randomized trials by consultant Dr. Susan Murphy. Assuming a message randomization probability of 1/3 (33% CBT, 33% Mindfulness/ACT, 33% control), a quadratic effect over time (initially smaller as participants are getting used to the intervention, increasing over time to peak at day 20, and decreasing thereafter as participants may get desensitized), and an average compliance rate of 75%, linearly decreasing over time, a sample size of N=80 participants will allow for detecting a standardized mean difference between CBT, Mindfulness/ACT, and control conditions on the primary outcome self-reported smoking urge of d=0.1 with a power of 0.8 and an alpha level of 0.05. This measure of effect size is a generalization of Cohen's d (standardized mean difference), with the difference that the standardization is by the average standard error over the entire study, with multiple treatments for each person. A Cohen's d of 0.1 is considered a small effect. A previous EMA study found that playing Tetris (analogous to a CBT distraction technique) decreased substance use urges with a mean effect size of f^2=0.12 (medium sized effect). Given these effect sizes in the existing literature, we will be adequately powered to detect effects in Aim 1 analyses.

Aim 2: This aim will test between group differences in number of cigarettes smoked over time among micro-randomized trial (N=80) and EMA-only control group participants (N=80). Sample size calculations were based on findings from a recent app-based mindfulness meditation trial for smoking reduction. This trial only delivered intervention content for 14 days (as opposed to the 30 days proposed here) and found a significant reduction in 3.8 cigarettes/day in the intervention group compared to an increase in 0.8 cigarettes/day in the control group, which translates to an effect size of d=0.651 (f=0.326). Power estimation for between group repeated measures ANOVA and interactions were conducted with G-Power. Assuming an alpha level of 0.05, a sample size of N=160 will allow us to detect effects in reduction of cigarettes per day of f=0.326 and larger with a power of 0.80. Multiple imputation will be used for missing data and the full sample will be analyzed.

IV. Participants:

Describe the study participants and the population from which they will be drawn. Specify the inclusion and exclusion criteria. If you plan to include children, note their ages and whether you will include children in foster care. Note if the participants are particularly vulnerable in terms of cognitive limitations, education, legal migration status, incarceration, poverty, or some combination of factors.

A. Inclusion Criteria:

Participants will be young adult men and women who: 1) live in the U.S.; 2) read English; 3) are between 18 and 30 years of age; 4) own a smartphone with iOS and Android operating system and GPS capabilities; 5) are carrying their smartphone with them every day; 6) are willing to participate in the study for 44 days and give the research team access to the phone GPS data; 7) have smoked ≥100 cigarettes in their lives and currently smoke at least 1 cigarette per day on 3 or more days of the week (full trial: smoke at least 3 cigarettes per day on 5 or more days of the week); 8) are planning to quit smoking within the next 30 days.

B. Exclusion Criteria:

There are no additional exclusion criteria for participants that meet inclusion criteria.

***NOTE**: If you are recruiting participants or receiving, accessing, or using data from a U.S. health care provider, HIPAA review is likely to be required. If you plan to bring identifiable health information from a foreign country to a U.S. covered entity (e.g., lab at the Hopkins SOM), HIPAA may be triggered. Check "yes" to the HIPAA question in the PHIRST application.*

V. Study Procedures:

*In this section, provide details of your procedures, particularly as they relate to human subjects. If this is a multi-center study, make the role of JHSPH clear. If the JHSPH will serve as **data coordinating center**, indicate in the sections below which procedures JHSPH will not be performing. Additional information regarding data coordinating centers is requested in a later section. If your study will develop in phases, address each item below by phase.*

A. Recruitment Process:

1. Describe how you will identify, approach, and inform potential participants about your study. Include details about who will perform these activities and what their qualifications are.

Message acceptability testing

For the message acceptability testing, we will recruit a gender-balanced, nationally representative sample of participants via Qualtrics's online market research panel. A Qualtrics project manager will handle the recruitment process and work directly with our research team. Qualtrics partners with over 20 online sample providers and most samples come from traditional, actively managed, double-opt-in market research panels. The Qualtrics project manager recruits panel respondents by randomly selecting individuals from sites where

users are likely to qualify. Participants' names, addresses and dates of birth are third-party validated (*e.g.,* TrueSample, RelevantID, Verity, etc.). Invitations to participate in the survey are sent through email or on the survey platform with a generic message, a hyperlink to the survey, and the compensation offered. Some participants may also receive the invitation to participate via SMS or an in-app notification. Invitations do not include specific study details to avoid self-selection bias. Since participants are recruited from a variety of sources, incentives vary (*e.g.,* airline points, retail shopping points, cash, or gift cards), but is explicitly stated in the email before participants proceed to the survey link.

All other study phases and procedures

We will use multiple recruitment methods to achieve the target accrual. Participants will primarily be recruited through Facebook, Instagram, and Craigslist advertisements, a design and targeting strategy that we have previously used for recruiting young adult smokers for EMA studies and smoking cessation studies delivered through social media. Study ads will target all US states. Facebook is the social network with the highest number of users among adults and well-suited for recruiting study participants. Facebook ads can be targeted to different locations and key words, for example "smoking" and "tobacco" to target the population of interest. Moreover, Facebook advertisements will be displayed in the social medium Instagram as well. Recruitment of participants for medical research via Facebook has been shown to produce samples similar to traditional recruitment methods and is an efficient recruitment strategy for addiction research, reaching samples with high severity of substance use disorders. Additional study advertisements will be placed on social media platforms Reddit, Twitter, LinkedIn, and TikTok.

Additional social media campaign recruitment will be conducted by the company Patient Advertising Guru and their Research Study Rockstar social media campaign. This company will post and optimize social media advertisements. All advertisements will link to our Johns Hopkins Qualtrics screening survey, therefore not participant protected information will be collected by or shared with the company.

In addition to social media recruitment we will also advertise the study on ResearchMatch. ResearchMatch is a national online registry that connects researchers with people who are interested in participating in health-related research studies. Developed by major academic institutions and supported by the National Institutes of Health, ResearchMatch offers a secure, easy-to-use platform where potential participants can register and match with studies that align with their interests and eligibility. For this study, we will use ResearchMatch to advertise our project and connect with eligible participants. This approach allows us to efficiently recruit a diverse pool of participants who have expressed interest in being contacted about research opportunities. Recruitment through ResearchMatch will comply with all relevant privacy and ethical standards, and only those who meet the study's criteria will be invited to participate.

We will also use MyChart messaging at Johns Hopkins to recruit participants. Only individuals who meet the following criteria in their Electronic Medical Records will be sent these recruitment messages:

1. Age: 18–30, inclusive.
2. Location: all JH locations except ACH.
3. Patients were seen in the past year.
4. Has a U.S. address.
5. Active cigarette smoker (latest status within 1 year)
6. Have active MyChart proxy accounts.

These criteria were developed in collaboration with the MyChart recruitment committee at the ICTR and approved by them. The MyChart recruitment process follows their standard procedures. An approval letter from the MyChart recruitment committee and the MyChart message text to be sent to participants is provided with this submission. Like all other recruitment methods, the MyChart message will include a link to our Johns Hopkins Qualtrics screening survey.

2. Address any privacy issues associated with recruitment. If recruitment itself may put potential participants at risk (if study topic is sensitive, or study population may be stigmatized), explain how you will minimize these risks.

There are no physical or informational privacy issues associated with recruitment. Recruitment will be conducted remotely, without physical contact with potential participants. Potential participants will be able to access the ad-linked study information and eligibility questions according to their own freewill. Contact information from participants will only be collected after they have consented to participate in the study.

B. **Consent Process**:

1. Describe the following details about obtaining informed consent from study participants. If a screening process precedes study enrollment, also describe the consent for screening.

a. Who will obtain informed consent, and their qualifications:

Informed consent will be obtained online. Online consent will contain information and contact details of the study PI, Dr. Thrul. Dr. Thrul has completed training in responsible conduct of research and all CITI certificates are up to date.

b. How, where, and when the consent discussion(s) will occur:

Message acceptability testing
For the message acceptability testing, an electronic consent form will be presented to eligible participants at the beginning of the Qualtrics survey.

All other study phases and procedures
After clicking on the study ad link, potential participants will be presented with information on the research study's purpose and procedures, including contact information for Dr. Thrul for any questions. After viewing this information, interested potential participants can access the eligibility questions. After answering the eligibility questions, all eligible participants will then be presented with an electronic consent form. The form will provide the name of the PI (Dr. Thrul) and his email address and inform respondents that he, as the PI, has Johns Hopkins University Human Subjects approval to conduct the study. The consent form will contain a thorough description of the research project, including the procedures involved, the risks and benefits, compensation, and the right to non-participation.

c. The process you will use to determine whether a potential participant meets eligibility criteria:

All participants will be required to meet eligibility criteria and provide online consent prior to study involvement. Questions about inclusion and exclusion criteria will be provided to potential participants using a Qualtrics screening survey that will be accessed through a link in the study recruitment ads and for the message acceptability testing, via emails and notifications provided by Qualtrics. Participants will be eligible for the study if they endorse all inclusion criteria. For the message acceptability testing, endorsement of all inclusion criteria will sufficiently support study eligibility, since Qualtrics will have already verified participants' identities. For the intervention trial, after consenting to participate but before being enrolled into the study, participants will be required to send study staff a picture of a valid identification (e.g., driver's license) that has their name, picture, and birthdate to validate their age and the fact that they are a real person. Only the participant picture on the ID (headshot) will be retained for biochemical verification of smoking abstinence. The ID document will subsequently be deleted after validation of participant details. Pictures of participants on file will be deleted at the end of data collection.

d. Whether you will obtain a signature from the participant or will use an oral consent process:

To assess understanding of the information provided in the informed consent, eligible participants will be asked a series of three multiple-choice questions regarding the informed consent before being able to proceed with

the study. Answers will be collected and any wrong answer will result in the potential participant being prompted to review the full consent document before attempting the consent questions again. Potential participants will not be enrolled in the study if they answer the questions incorrectly four times.

e. Whether you will obtain a legally authorized representative's signature for adults lacking capacity:

N/A

f. If children are included in the study, if and how you will obtain assent from them:

N/A

g. If children are included in the study, how you will obtain permission for them to participate from their parent, legal guardian, or other legal authority (if child is in foster care or under government supervision):

N/A

h. If you are seeking a waiver of informed consent or assent, the justification for this request:

N/A

i. Whether you will include a witness to the consent process and why:

N/A

j. If the language is unwritten, explain how you will communicate accurate information to potential participants and whether you will use props or audio materials:

N/A

2. Identify the countries where the research will take place, and the languages that will be used for the consent process.

Country	**Consent Document(s) (Adult Consent, Parental Permission, Youth Assent, etc.)**	**Languages**
United States	Adult consent	English

C. **<u>Study Implementation</u>**:

1. Describe the procedures that participants will undergo. If complex, insert a table below to help the reviewer navigate.

Message acceptability testing

After informed consent, participants will be asked survey questions via Qualtrics on demographic information, smoking and tobacco use behaviors, and quit attempt history. The Avoidance and Inflexibility

Scale will measure the person's willingness to experience negative thoughts and affect. Message acceptability will be measured through four Likert-scale questions on message content, design, helpfulness for reducing smoking urges, and helpfulness for helping with quitting smoking. These will be asked for 10 randomly selected messages for each participant. Participants will complete open-ended feedback on two of the 10 randomly selected messages.

All other study phases and procedures

Training phase - EMA data collection

After informed consent has been obtained, participants will be asked for the contact information (email address and phone number) so that the study team can stay in contact. Final enrollment of a participant will depend on identity verification. Since data collection for this study will take place remotely, participants will be required to submit a picture of an official ID document for verification of their identity and age, a procedure that Dr. Thrul has found to be feasible in his previous studies. After verification of identity, participants will be enrolled into the study. Only the participant picture on the ID (headshot) will be retained for biochemical verification of smoking abstinence. The ID document will subsequently be deleted after validation of participant details for enrollment.

Baseline survey: Initially, all participants will complete a baseline survey on the online survey platform Qualtrics, to assess basic demographics, smoking and other tobacco use behavior, including e-cigarettes, nicotine dependence, quitting history and current quit motivation, frequency and intensity of smoking urges, and other substance use behavior including alcohol, cannabis, and other illicit drugs. Smoking-specific experiental avoidance, a measure to assess a person's willingness to experience negative mental states (e.g., urges, mood, thoughts), will be assessed with the Avoidance and Inflexibility Scale. Trait mindfulness will be assessed with the FIT-60 (Flexibility Index Test).[143] Baseline measures will also include trait negative affect and psychological distress.

EMA data collection: Before EMA data collections, participants will be contacted on the phone to received detailed instructions on how to use the EMA study app. Participants will use their own smartphones and the study app to collect data on smoking situations over the course of 14 days (EMAs of smoking situations and smartphone location sensor data). Participants will complete 3 randomly prompted EMA surveys per day and will report every time they smoke a cigarette. A random subset of these cigarette reports will trigger up to 3 EMA smoking survey prompts per day.

EMA momentary surveys: Smoking urges will be recorded with a single item in accordance with recommendations from the Society for Research on Nicotine and Tobacco. Additional questions will examine internal and external aspects of the situation. The number of questions asked will be limited to ensure they do not interfere with participants' daily activities. In addition, the EMA software will log participants geolocation based on GPS. All data will be time and date-stamped to allow time-specific analyses and determine high-risk periods for smoking.

EMA daily diaries: Thorough daily diaries will be collected to assess overall cigarettes, other tobacco product (including e-cigarettes), alcohol, cannabis, and other substance use (illegal drugs). Questions will also assess same occasion co-use of tobacco, alcohol, cannabis, and drugs (when participants were feeling under the influence of other substance).

Purpose of the EMA training phase: The EMA training phase serves multiple purposes: First, it allows participants to get used to the study app that will also deliver the intervention messages, and second, the collected data will allow us to generate an individual risk profile with regard to time of day and location (by combining timestamps, GPS data, and self-reported data) with the highest likelihood of smoking for each participant. We will use geofencing to generate geospatial buffers around these high-risk locations. In combination with time of day information to target high-risk time periods for smoking, these geofences will trigger delivery of intervention messages when a mobile device enters the area: A message can be triggered when a participant approaches a smoking location during one of the high-risk time windows. We will use our established protocol for triggering intervention messages that we have successfully used in a pilot trial.

Intervention phase - Micro-randomized trial with N=80 participants to determine message efficacy

The micro-randomized trial will determine if CBT and Mindfulness/ACT messages are superior to control messages in reducing the primary outcome momentary smoking urges. Based on participants' training

data collected in the initial 14 days of EMA monitoring, intervention messages will be delivered during time-periods and at high-risk locations for smoking. In the intervention phase, participants will be prompted to complete 3 geofence-triggered EMAs per day for a total of 30 days. Each EMA will be followed by an intervention message and the type of message (CBT, Mindfulness/ACT, control) will be randomly selected at each time point (within-subject randomization; see Figure). Each intervention message will also be tailored to situational factors from the EMA-pre data. Message tailoring will focus on two key situational triggers stemming from our conceptual framework: 1. Stress (high/low) and 2. Presence of other smokers (yes/no). For each situation, characterized by a combination of these 4 possible characteristics, several messages will be placed in separate message bins (4 bins for each CBT and Mindfulness/ACT messages, for a total of 8 bins). Control messages will thank participants for completing an assessment. Proximate outcomes will be assessed 15 minutes after message delivery and include urge levels, smoking or other tobacco product use since EMA-pre survey, affect, stress, and an evaluation of the last message (e.g., perceived usefulness of message, completion of suggested activity/intervention). In addition, participants will continue completing one brief retrospective EMA each morning. Just like the training phase, this retrospective EMA will assess cigarette and other tobacco product use, alcohol, cannabis, and drug use. Before we will embark on the full micro-randomized trial with N=80 participants, we will first conduct a brief pilot with N=10 participants to assess system functionality with current smartphones and operating systems.

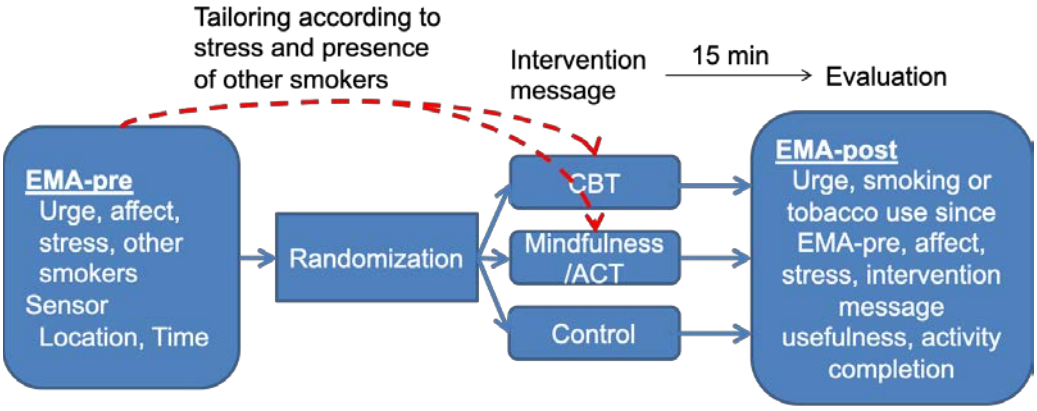


Figure: Flow-chart for delivery of each intervention message in the micro-randomized trial group

Built-in parallel-group RCT – EMA-only control group (N=80)

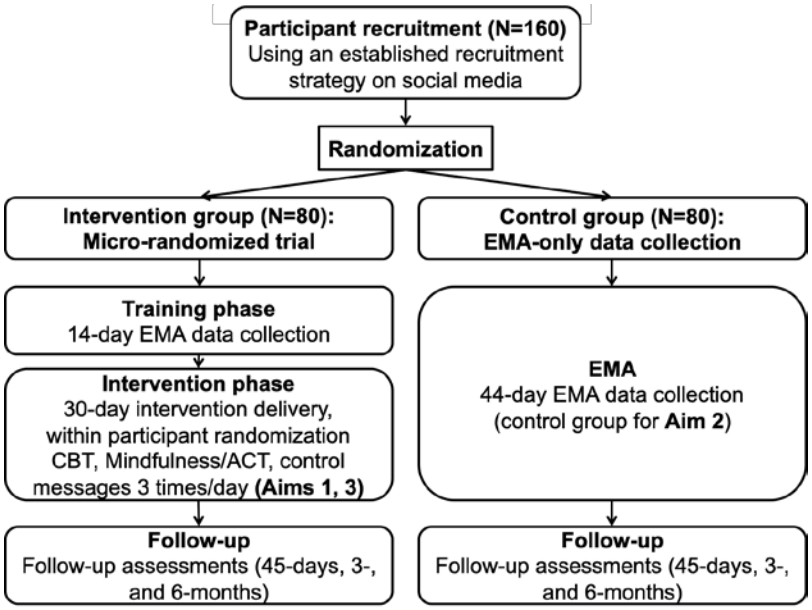
A total of N=80 participants will be randomized into an EMA-only control group, parallel to the micro-randomized trial intervention group (Figure: Study overview). This group will conduct 14-day EMA only training phase just like the micro-randomized trial group, but will not be switched over to the intervention phase after these initial 14 days. Instead, participants will continue the EMA-only data collection procedure for an additional 30-days (analogous to the 30-day intervention phase of the micro-randomized trial). During these 30 days, the EMA-only control group will continue to receive 3 randomly prompted EMA surveys per day and an additional 3 EMA surveys triggered by smoking reports. By comparing this control group to the micro-randomized trial intervention group, we will investigate if intervention message delivery results in changes in smoking behavior over time (see analytical strategy Aim 2).

Follow-up assessments

Follow-up assessment in both groups will be conducted at end of treatment (45 days), 3-months, and 6-months post-randomization. Surveys will be delivered online via Qualtrics and will assess current behavior (number of cigarettes/day, self-reported 7-day point prevalence abstinence), quit attempts, current quit motivation, frequency and intensity of smoking urges, and other substance use behavior including alcohol, cannabis, and other illicit drugs. Surveys will also assess baseline ACT measures: Avoidance and Inflexibility Scale and the FIT-60 (Flexibility Index Test).

Saliva cotinine will be used to **biochemically validate 7-day point prevalence abstinence** at each follow-up. Participants self-reporting smoking abstinence at any follow-up point will be mailed a saliva test-kit

(NicAlert test strip) and instructed to send one picture each of providing the saliva sample and the test kit result. We will only receive pictures of the test process and result and not receive an actual saliva sample. The picture of the test process (participant providing the saliva sample) will be used to confirm that the participant provided the sample him- or herself.



Study overview

2. Describe the number and type of study visits and/or contacts between the study team and the participant, how long they will last, and where/how they will take place.

There will be 4 main types of contacts between the study team and the participant. These contact types will be: 1) Baseline survey link email after consent; 2) An initial phone call to train participants on how to use the EMA study app; 3) EMA compliance check-ins during EMA data collection (email, text message, and phone calls if participants need help troubleshooting any procedures); 4) Follow-up survey link email and instructions for biochemical verification of smoking status. For the message acceptability testing, participants will come from Qualtrics market research panels and the study team will have no contact with participants.

3. Describe the expected duration of the study from the perspective of the individual participant and duration overall.

Message acceptability testing
Message acceptability testing will be conducted in one single survey using Qualtrics market research panels. The survey will take approximately 13 minutes to complete.

All other study phases and procedures

The phone call to train participants on use of the EMA study app will take approximately 15 minutes. The baseline survey will take approximately 30 minutes, the follow-up surveys at 45 days, 3 months, and 6 months will take approximately 15 minutes to complete each, and the momentary assessments will each take approximately 2 minutes to complete (2 minutes per assessment x 7 assessments per day x 44 days = 616 minutes total). The total time commitment will be 706 minutes, or approximately 12 hours. Pilot participants will not complete the 3 and 6 month follow up surveys, but will instead complete a brief 30 minute interview via phone or Zoom to describe their experience with study procedures. The overall time commitment will be the same for all participants.

Activity	**Time commitment – Pilot Participants**	**Time commitment – Trial Participants**
EMA study app training	15 mins	15 mins
Baseline survey	30 mins	30 mins
EMA smartphone data collection	44 days x 14 mins = 616 mins	44 days x 14 mins = 616 mins
45 day follow up survey	15 mins	15 mins
Follow-up interview	30 mins	-
3 months follow up survey	-	15 mins
6 months follow up survey	-	15 mins
Total	706 mins (approximately 12 hrs)	706 mins (approximately 12 hrs)

4. Provide a brief data analysis plan and a description of variables to be derived.

Analytical strategy Message Acceptability: To assess message acceptability across age, gender, and race/ethnicity.

Analyses for message acceptability testing will utilize a mixed methods approach. For the quantitiatve analyses, the **primary outcome** will be message acceptability expressed as the average score of Likert responses to helpfulness to cope with smoking urges or craving and to support quit attempts and acceptability of message content and design. Messages will be ranked by score and messages with low scores will be either modified in line with qualitative participant feedback or removed before moving to the next study phase. Analyses assessing message acceptability across age, gender, and race/ethnicity will include independent variables age, gender, race/ethnicity, educational attainment, psychological flexibility, smoking frequency, quit motivation, and past quitting attempts. These quantitative analyses on message acceptability will be supplemented with qualitative analyses involving inductive and deductive coding of participants' open-ended responses to inform how messages should be modified.

Analytical strategy Aim 1: To compare CBT and ACT intervention message efficacy.

Aim 1 analyses to test the hypothesis of a proximal benefit of urge reduction messages will be conducted using a centered and weighted least squares method, which estimates treatment effects and allows inclusion of covariates. The method is similar to GEE and multi-level models in that it accounts for dependence of responses within individuals due to repeated measures via the use of robust standard errors. Moreover, the method takes advantage of the sequential randomization to estimate causal treatment effects. The **primary outcome** will be participants' rating of **smoking urge** in EMA-post surveys, prompted 15 minutes after intervention message delivery, and controlling for the ratings in EMA-pre surveys. The main independent variable will be message type: **CBT versus Mindfulness/ACT versus a Control Message** ("Thank you for completing the survey"). We will also **test differences in efficacy between CBT versus Mindfulness/ACT**. We will use **multiple imputation** to impute missing data in EMA-post surveys.

Analytical strategy Aim 2: To test if urge reduction messages change smoking behavior over time.

Aim 2 analyses will use data from both the micro-randomized trial group (N=80) and the EMA control group (N=80). **Primary outcome:** The primary outcome will be self-reported number of cigarettes/day in the past week at 45-day, 3-, and 6-month follow-up. GEE will examine cigarettes/day at each follow up by group (micro-randomized trial vs. EMA-only control). Independent variables are group membership, variables that differ by group at baseline, gender, and nicotine dependence. Again, **multiple imputation procedures** will be used to impute missing data at follow-up.

Analytical strategy Aim 3: Explore moderation effects of substance co-use (cannabis, alcohol, other drugs) and exposure to specific location (home, work, bars) on urge reduction message efficacy.

Based on our data on high co-use of cigarettes with cannabis and alcohol, as well as changes in perceived reward of smoking cigarettes when under the influence of cannabis or alcohol, analyses in this aim will explore if message efficacy is moderated by substance co-use (whether a participant currently is under the influence of another substance, e.g., cannabis, alcohol, other drugs). Centered and weighted least squares

models[152] similar to those for Aim 1 will be estimated with predictors intervention message type (CBT, Mindfulness/ACT, control), substance use (cannabis, alcohol, other drugs, none), and their interaction. Based on existing evidence on alcohol and cannabis co-use as barrier to cigarette smoking cessation, we hypothesize that intervention message efficacy will be reduced when participants are under the influence of another substance. However, analyses for this aim will enable us to explore if specific types of messages (CBT, Mindfulness/ACT, and subconstructs) are more helpful in co-use situations.

Moreover, we will explore aspects of intervention message-situation fit. We will test if specific locations (e.g., home, work, bars) impact intervention message efficacy. Mixed models will be estimated containing the predictors intervention type (CBT, Mindfulness/ACT, control), location (home, work, bar, other locations), and their interaction. We will explore other situational characteristics and intervention message-situation fit based on affect, arousal, stress, and the presence of other smokers. We do not have specific hypotheses about moderation effects of location and other situational characteristics, but findings will inform future interventions using adaptive messages over time to improve intervention-message situation fit and intervention efficacy.

5. Answer the following **if they are relevant to your study design**:

A. If the study has different arms, explain the process for assigning participants (intervention/control, case/control), including the sequence and timing of the assignment.

We will use stratified block randomization to assign participants into the micro-randomized trial intervention group (N=80) and EMA-only control group (N=80). The stratification variable known to robustly impact smoking cessation success will be level of nicotine dependence (smoking within first 30 mins after waking, y/n).[131] Gender will be used as additional stratification variable. We will generate a randomization table and participants will be assigned after baseline completion.

B. If human biospecimens (blood, urine, saliva, etc.) will be collected, provide details about who will collect the specimen, the volume (ml) and frequency of collection, how the specimen will be used, stored, identified, and disposed of when the study is over. If specimens will be collected for use in future research (beyond this study), complete the "Biospecimen Repository" section below.

N/A

C. If genetic/genomic analyses are planned, address whether the data will be contributed to a GWAS or other large dataset. Address returning unanticipated incidental genetic findings to study participants.

N/A

D. If clinical or laboratory work will be performed at JHU/JHH, provide the JH Biosafety Registration Number.

N/A

E. If you will perform investigational or standard diagnostic laboratory tests using human samples or data, clarify whether the tests are validated and/or the lab is certified (for example is CLIA certified in the U.S.). Explain the failure rate and under what circumstances you will repeat a test. For all human testing (biomedical, psychological, educational, etc.), clarify your plans for reporting test results to participants and/or to their families or clinicians. Address returning unanticipated incidental findings to study participants.

N/A

F. If your study involves medical, pharmaceutical or other therapeutic intervention, provide the following information:

a. Will the study staff be blind to participant intervention status?

No

b. Will participants receive standard care or have current therapy stopped?

No

c. Will you use a placebo or non-treatment group, and is that justifiable?

Yes, control group will receive no intervention messages and only complete mobile surveys on their phones. This decision is defensible, since most smokers never receive evidence-based smoking cessation interventions and previous studies have demonstrated that if anything, repeated assessments of smoking on mobile devices result in lower cravings. Moreover, self-monitoring of smoking behavior is a standard component of evidence-based smoking cessation counseling. Therefore, the data collection acitivities the control group undertakes may result in reduced smoking urges and smoking behavior over time.
If requested, participants in both conditions request more intensive smoking cessation support outside of the study, they will be offered additional telephone counseling by the PI or referred to the Smokers Quitline (1-800-QUIT-NOW).

d. Explain when you may remove a participant from the study.

In the unlikely event that participants are significantly distressed by any aspect of their study participation, they will be offered the opportunity to discuss these issues with a PhD psychologist and smoking cessation counselor (Dr. Thrul, PI). If participants request more intensive smoking cessation support, they will be offered additional telephone counseling by the PI or referred to the Smokers Quitline (1-800-QUIT-NOW).

e. What happens to participants on study intervention when the study ends?

Participants will be referred to the Smokers Quitline (1-800-QUIT-NOW) if they desire additional smoking cessation support.

f. Describe the process for referring participants to care outside the study, if needed.

Participants will be referred to the Smokers Quitline (1-800-QUIT-NOW) if they desire additional smoking cessation support.

VI. Data Custody, Management, Security, and Confidentiality Protections:

Note: Principal Investigators are responsible for Data Protection and Use throughout the life of the study. You will need all of the following:

- *a data security plan that addresses each stage: data collection, transfer/analysis, storage, and sharing;*
- *a data management plan overseeing data access, storage, etc.;*
- *a data sharing plan that is consistent with obligations under the funding agreements associated with the study, and with the language in the consent documents.*

A. <u>Personally Identifiable Information (PII)</u>:

Please identify the Personally Identifiable Information (PII) that you may be collecting and using at any of the following stages of your study: ***Recruitment****, **Consent,*** *and* ***Study Implementation (Data Collection)***.

	Recruitment /Consent	**Data Collection**
Name, signature, initials, or other identifiable code	☒	☐
Geographic identifier: address, GPS location, etc.	☐	☒
Dates: birth, death, clinical service, discharge, etc.	☒	☐
Contact information: phone numbers, email address, etc.	☒	☐
ID: Social Security Number, driver's license number, etc.	☒	☐
Health record identifiers: medical record, insurance plan number, etc.	☐	☐
Account numbers	☐	☐
Device identifiers: e.g., implants	☐	☐
Internet identifiers: IP address, social media accounts	☐	☐
Biometric identifiers, including finger and voice prints	☐	☐
Audio recordings	☐	☐
Video or full face photographic images	☒	☒
Genomic/genetic data	☐	☐
Any other unique identifying number, characteristic, or code (note: this does not mean the unique code assigned by the investigator to code the data)	☐	☐
Other: Click here to enter text.	☐	☐

Recruitment:

Will you collect identifiers for the purpose of contacting potential participants? Yes ☒ No ☐

If **yes**, will you retain the identifiers after the recruitment contact has been made? Yes ☒ No ☐

B. Data Collection:

Collection of data for a research study can take on many forms. It can be as simple as gathering the data with pen and paper or developing an on-line adaptive survey that changes based on the participant's answers. Regardless of the method, PII collection for the purposes of identifying the participants will most likely be collected. Once collected, the raw data should go through a de-identification process to further protect PII.

In what form(s) will you collect and store PII? When you respond, refer back to the table above; think of PII collected during recruitment, consent, data collection, and other study purposes.

1. **Hard Copy/Paper:** Yes ☐ No ☒

   If yes, please answer the following:

   a. How will the data be kept secure during transfer from study collection site to storage site?

   b. Will the data be secured in a locked cabinet or room? Yes ☐ No ☐

   c. If study IDs/Codes are used, will they be stored separately from the study data? Yes ☐ No ☐

   d. Will the hard copy/paper be destroyed after data abstraction and cleaning are complete? Yes ☐ No ☐

      If No, when do you plan to destroy the hard copies?

2. **Electronic:** Yes ☒ No ☐

   If yes, please answer the following:

   a. Will the data be collected or stored on a portable device (laptop, mobile phone, tablet, PDA) Yes ☒ No ☐

      If Yes, will the device be protected by encryption? Yes ☒ No ☐

   b. Will the device(s) be study-owned or privately-owned (e.g., personally owned by data collectors or study participants?)
      Personally owned ☒ Study provided ☐
      Note: If personally owned, please address the privacy and data security risks under VII. Risks below.

c. Is the app (application)/website used for data collection being developed in-house (Hopkins) or by a 3rd party vendor? In-house ☐ 3rd party ☒

If 3rd party, provide the name of vendor and URL:

For the message acceptability testing, Qualtrics.

For the intervention, MetricWire Inc. – https://metricwire.com/

Identify Mobile Ecosystem (check all that apply): Apple ☒ Google ☒ Website ☐

d. Will the data be stored on a secure server (@JHSPH/on-site)? Yes ☒ No ☐

e. Will the data be stored in the Cloud/Web? Yes ☒ No ☐

f. Will it be encrypted? Yes ☒ No ☐

g. Will you be backing up your data? Yes ☒ No ☐

3. Mobile Apps Yes ☒ No ☐

FOR STUDIES USING MOBILE APPS: When the use of a mobile app is approved solely for a research use, the IRB either requires that it be restricted to people who consented to the research, or when a screen/script is used, for participants to understand that this is not a medical tool or a public app, but is for use only in a research study only. Please check the appropriate box(es) below that describe your study:

☒ Use of the app is restricted to people in the research, with access limited to those who have consented to the study.

☐ The consent information for participants clarifies that the app is not for clinical or public use but is restricted to this research study

4. **Audio Recording:** Yes ☐ No ☒

If yes, please answer the following:

a. Will you store the audio recording securely in a locked cabinet/room until transcription is complete? Yes ☐ No ☐

b. Will you use a transcription service? Yes ☐* No ☐

**If yes, if the PII comes from JHH/JHHS, you must use an approved vendor; otherwise, be aware of the data security protections that the transcription service provides.*

c. Will the audio recording be destroyed immediately after transcription? Yes ☐ No ☐

If no, why not? How long will it be retained?

4. **Photograph/Video:** Yes ☒ No ☐

   If yes, please answer the following:

   a. Will the photographs/videos be stored securely in a locked cabinet or room? Yes ☐ No ☒

   b. Will the photograph/video be destroyed? Yes ☒ No ☐

      If yes, when?

      The picture of the participant's ID will be destroyed at the end of the study when all study activities have been completed. The ID document will subsequently be deleted after validation of participant details. Only the participant picture (headshot) on the ID will be retained for biochemical verification of smoking abstinence. The participant picture needs to be retained until the end of the study to verify that the participant provided the saliva sample for biochemical verfication of smoking status. The picture of the participant providing a saliva sample will be destroyed as soon as we have confirmed the identity of the participant by comparing it to the ID picture of the participant on file. The participant picture on file will be deleted at the end of data collection.

C. PII De-Identification of Data Used for this Study:

1. When will you destroy the PII and/or the code linking the PII with the study ID?

   The PII (participants' names and contact information) and the code linking the PII with the study ID will both be destroyed after the final incentive is given to participants. GPS mobility data will be collected with the mobile app. These data will be stored separately from participant responses and can only be connected using the unique partipant study ID.

2. What is the method you will use to de-identify the data?

   All data will be identified only by arbitrary code numbers (study IDs). Participants' study IDs will be linked to participants' names and contact information in a password-protected file that is accessible only to the PI and study staff.

3. Is your research data governed by HIPAA (U.S. clinical data remaining within the covered entity)?

   a. Yes ☐ No ☒

   b. If yes, who is doing the de-identification?

   c. If yes, what level of de-identification will you achieve (Limited data set? De-identified?)

D. Data Storage and Analysis:

One of the keys to protecting PII is the proper use of tools to share and conduct your analysis. JH and JHSPH offers several options for you to consider. Please select the systems that you plan to use to protect your study data by clicking the box. Consult JHSPH IT for assistance if needed.
Check all systems used for data collection, storage and analysis.

☒ **JH Virtual Desktop**: The Hopkins Institute for Clinical and Translational Research (ICTR) provides a virtual Windows desktop (SAFE Desktop). It includes productivity software such as Microsoft Word and Excel, as well as statistical software, including SAS, Stata, R, R Studio, and Python. 100 GB of storage space is provided.

☒ **OneDrive-JHSPH**: Managed by JHSPH IT and available only to people with a JHSPH ID, a file storage and file sharing solution in the Microsoft cloud for faculty, staff, and students. With OneDrive, you can store files and access them anywhere with internet access. (https://my.jhsph.edu/Offices/InformationTechnology/ComputerSupport/SharedFolders/OneDrive-JHSPH/Pages/default.aspx)

☐ **JHU OneDrive**: Managed by IT@JH, personal cloud storage component of the Office 365 produce suite that allows users to store and share documents and files from any device with an internet connection. Share documents with colleagues, inside and outside of JHU (no JHED ID required). (https://it.johnshopkins.edu/services/collaboration_tools/OneDrive/)

☐ **JHSPH RedCAP**: These are departmentally managed applications. RedCAP is an application designed for collaborative research projects.

☐ **JHSPH HPCC:** High Performance Computing Cluster (HPCC: https://jhpce.jhu.edu/) can provide the high capacity computing required for very large data sets.

☐ **JHSPH Sharepoint:** For user-controlled private web sites, secure document storage, navigable directories, contacts and people searches, increased collaboration and sharing opportunities. (https://my.jhsph.edu/Offices/InformationTechnology/CommunicationServices/MyJHSPH/Pages/default.aspx)

☐ **Independent Departmental Servers and Systems**: These servers are typically managed by departmental or research team IT staff. Because these servers are not centrally managed by JHSPH IT, all documentation regarding data security protections will need to be provided by the owner/administrator of the server. This responsibility may fall to the data owners (PI).

☒ **Other**: Please provide details regarding any other systems being utilized, for example Qualtrics, ODK, etc. Examples may include servers and applications located at another university participating in your study or a 3rd party web-based application.

Screening, baseline, and follow up surveys will be collected using JHSPH Qualtrics.

Developed by MetricWire Inc., the MetricWire EMA system will collect the study's EMA survey data and GPS data through the MetricWire EMA study app. MetricWire is secure and HIPAA compliant and does not have any associated conflicts of interest.

Data on the participant's device are synced (encrypted in-transit) to the server and wiped from the mobile device when a connection is available. When the participant's device is not connected to the internet, data are stored (encrypted) on the device. When offline, the app/server periodically checks for a connection in the background and performs the sync/wipe of any response data. This allows triggers and data collection to occur offline while minimizing the amount of time data are stored on the device.

All participant generated data are stored in production information systems in hosted (cloud) environments and are not permitted to be stored on locally managed electronic devices such as MetricWire workstations.

User Identification
• All critical Information systems require a unique and valid User Login ID and password for each individual user
• Shared accounts for critical Information Systems are prohibited.
• All critical Information systems require Two-Factor Authentication (2FA) to prevent account Sharing

Encryption And Decryption
• MetricWire critical Information systems use symmetric AES-256-CBC for data encryption at the database level, with a random, unique initialization vector for each operation.
• Authentication is performed using HMAC-SHA-256 and HMAC-SHA-512.
• Encryption Keys are stored on a NIST FIPS 140-2 Certified Key Management Server
• All participant generated data are encrypted in transit using 4096-bit RSA keys

• Data are encrypted end to end through the entire application.
• Encryption keys and machines that generate keys are managed by MetricWire, protected from unauthorized access and encryption keys are regenerated after 365 days.
• MetricWire monitors the transmission activity of critical information systems automatically
• Information system owners review logs on a weekly basis and in accordance with quarterly risk assessments.

The MetricWire system will not store any PII. We will assign participant IDs as login information for your participants instead of their names, email addresses, or other contact information.

Once study data collection is completed, all data will be downloaded from the MetricWire backend server, stored on JHSPH OneDrive, and deleted from the MetricWire server. Data download from the MetricWire backend server will be done via an encrypted HTTPS protocol.

Only the research team at JHU will have access to the participant data.

E. <u>Other Data Security Measures:</u>

In addition to the details regarding data collection, please review the following questions. This additional information will be utilized to assist in the development of a comprehensive Data Security plan. This would include the systems used to analyze the data, data security contacts and additional requirements.

1. During the analysis phase, do you plan to use computer systems that are not managed by JHSPH or JH? Yes ☐ No ☒

If yes, please explain:

2. Do you have a designated person on your research team other than the PI who is the technical contact for a Data Security plan? Yes ☐ No ☒

   If yes, please provide a contact name:

3. Does your sponsor have other specific data security requirements for the study data? Yes ☐ No ☒

   If possible, please explain:

4. Please add any other information that you believe is relevant to data security.

   N/A

F. Certificate of Confidentiality:

All NIH studies include Certificate of Confidentiality protections with the grant; the consent form must include the C of C language provided in our template. Other funders may obtain C of C protections through NIH. (https://humansubjects.nih.gov/coc/index)

Does the study have Certificate of Confidentiality protections? Yes ☒ No ☐

G. Data Sharing and Disclosure:

a. Please describe your data sharing plan, including whether you plan to share your data with your sponsors or with other investigators. Explain whether the shared or disclosed data will be individually identifiable. **Your data sharing plan should be consistent with Sponsor requirements, and the consent document should include a description of your data sharing plan.**

In accordance with federal regulations, study data will be retained for at least 3 years after the study is complete. De-identified data may be shared with other investigators on a case-by-case basis.

b. Are there laws limiting data sharing in the country where the research site(s) is located? If yes, please address those limitations and how you will comply with them.

   N/A

c. Will you make your data publicly available? If yes, what is your plan for de-identification?

   N/A

d. Will you deposit it into a repository for broader use? If yes, identify the repository and provide information about the data protections.

N/A

H. JHM Clinical Records:

Will you use clinical data of 500 records or more from Johns Hopkins Hospital and its affiliates?
Yes ☐* No ☒

**If yes, please complete the JHM Data Security Checklist available on the JHSPH IRB website: www.jhsph.edu/irb and upload a copy of the checklist to the "Miscellaneous" section*.

VII. Risks of the Study:

A. Describe the risks, discomforts, and inconveniences associated with the study and its procedures, including physical, psychological, emotional, social, legal, or economic risks, and the risk of a breach of confidentiality. These risks should be described in the consent documents.

There are minimal risks associated with participation in this study. Participants will be encouraged to quit or reduce smoking, and smoking cessation/reduction can cause unpleasant physical and psychological states (urges to smoke, irritability). Other potential risks include boredom, discomfort, or annoyance with some of the questions or multiple EMA surveys over the course of the study period. We will make efforts to design the surveys in an appealing way and make them as short as possible so they will only minimally interfere with participants' daily activities. We will frame questions about smoking or tobacco use in non-judgmental language. An additional risk is a potential loss of confidentiality for the information that participants provide in the assessments, including their daily mobility patterns.

B. Describe steps you will take to mitigate or minimize each of the risks described above. Include a description of your efforts to arrange for care or referral for participants who may need it.

We have designed the surveys in an appealing way and made them as short as possible so they will only minimally interfere with participants' daily activities. We have framed questions about tobacco use in non-judgmental language.

All data are entered electronically and a database of survey responses is produced without names or contact information. Participants' contact information is gathered on a separate coded sheet and kept securely and separately from the individual's survey responses. The contact information will be kept in a password protected file and securely stored on JH Virtual Desktop, separately from any other participant data. Surveys and contact databases will be coded, and only study personnel actively involved in study recruitment will have access to these data. All quantitative data will be reported in aggregate and anonymously. All electronic data will be password protected and transferred between study personnel by secure websites.

Protecting participant data while using the smartphone app is critical because privacy concerns may inhibit use of the app. We will take precautions to ensure that participants are aware of steps they can take to protect their privacy and include a number of built-in features to protect privacy. Specifically, we will include the following features in the intervention to protect participant security and privacy when using the smartphone app:

a) Participants will be provided information about ways to protect their privacy when using their smartphone. We will send a message that contains a link to a webpage with information about security steps participants can take to protect their privacy (http://www.techlicious.com/tip/9-ways-to-secure-your-smartphone/). Steps may include setting a password to protect from others accessing their device and not using the app while connected to an unsecured wireless network. We will encourage participants to secure their entire smartphone

with the built-in “screen lock”. This can use a variety of identification mechanisms (password, face recognition, or fingerprint) that the participant determines is most convenient. Generally, we will encourage participants to use the lock/password features.
b) We will not retain data on participant’ smartphones. Rather, data will be stored on the MetricWire secure server, which is backed up on a continual basis. Data on participants’ smartphones will be deleted within several minutes after the information is captured to the server database.
c) All data will be transmitted directly between participant’s devices and the server. Transmissions will be encrypted.
d) At the beginning of the study, we will require all participants to “register” their phone (i.e., verify their credentials) to download the app and sync with the protected server. This will be a one-time event, but will ensure that only participants who pass the inclusion criteria and enroll in the study have access to the app.
e) Participants do not have the ability to see their data once it is submitted to the MetricWire secure server. For participant generated data, the EMA application interface functions in one direction only. This helps ensure that the participants submitted data remains secure even if the device is lost or stolen. In addition, MetricWire has the capability to prevent the participants’ version of the EMA application from connecting to the secure server in the event the phone is lost or stolen.

In the unlikely event that participants are significantly distressed by any aspect of their study participation, they will be offered the opportunity to discuss these issues with a PhD psychologist and smoking cessation counselor (Dr. Thrul, PI). If participants request more intensive smoking cessation support, they will be offered additional telephone counseling by the PI or referred to the Smokers Quitline (1-800-QUIT-NOW).

C. Describe the anticipated frequency and severity of the harms associated with the risks identified above; for example, if you are performing “x” test/assessment, or dispensing “y” drug, how often do you expect an “anticipated” adverse reaction to occur in a study participant, and how severe do you expect that reaction to be?

We don’t anticipate the reaction of boredom, discomfort, or annoyance with some of the questions to be very frequent or severe.

D. Describe the research burden for participants, including time, inconvenience, out of pocket costs, etc.

Participants will be responsible for the costs of their phone bill, including data usage, for completing the smartphone-based assessments. However, data usage of the app is very low, since only self-reported survey data and GPS datapoints will be transmitted. The overall data usage for EMA data over the 44-day study period will be less than 5 MB, or about the equivalent of streaming 3 minutes of music. GPS data will use more volume to transmit and can add up to 10 MB/day, for a total of 440 MB over the 44 day study period. If the participant's device restricts using mobile data roaming for upload, the app will store data (encrypted) until a wifi connection is available and automatically sync the data. If the participant allows mobile data roaming, the Metricwire app will hold the data back until wifi is available, if it is greater than a few MB (~5 MB) to avoid impacting the participant’s data plan.

E. Describe how participant privacy, and if relevant – family privacy - will be protected during data collection if sensitive questions are included in interviews, or if study visits occur in the home setting.

All information obtained from participants will be kept confidential. All data will be de-identified and coded. Participant contact information will be kept in a separate file secured on the JHSPH server (JH Virtual Desktop). The contact information will never be shared with anyone and will only be used by the study team to contact participants. All data will be stored on password-protected computers and databases, and securely transferred or transmitted (encrypted in transit).

VIII. <u>Direct Personal and Social Benefits</u>:

A. Describe any potential direct benefits the study offers to participants ("payment" for participation is not a direct personal benefit).

Benefits to participants include the possibility that they will reduce or quit their smoking as a result of the smartphone app-based self-monitoring of their smoking behavior and the smoking cessation messages the intervention will deliver.

B. Describe potential societal benefits likely to derive from the research, including value of knowledge learned.

Every year, more than 400,000 Americans die prematurely due to tobacco use. Smoking cessation at any age significantly reduces the risks of developing future health problems. Quitting smoking before age 30 is especially effective and reduces the disease risk to levels found among never smokers. Unfortunately, young adults have high smoking rates and few young adult smokers trying to quit utilize evidence-based cessation methods (e.g., pharmacotherapy or behavioral support) or succeed. Developing effective methods to help young adult smokers quit is among the most important challenges in tobacco research. This application will investigate a novel approach to smoking cessation that is empirically and theoretically supported, has good potential to be effective, and reach an underserved population of smokers.

Although there is some risk to participants, we estimate this risk to be small and outweighed by the knowledge that society will gain.

IX. Payment or Token of Appreciation:

A. Do you plan to provide a non-monetary token of appreciation (food, soap, tea, chlorine tablets, etc.) to study participants? If yes, please describe below.

N/A

B. If you plan to provide a monetary payment, describe the form, amount, and schedule of payment to participants. Reimbursement for travel or other expenses is not "payment," and if the study will reimburse, explain.

Message acceptability testing
For message acceptability testing, since participants are recruited from a variety of sources, incentives vary (e.g., airline points, retail shopping points, cash, or gift cards), but are explicitly stated in the email before participants proceed to the survey link. Incentives will be provided directly to participants from Qualtrics, without any involvement from our research team.

All other study phases and procedures
Participants will receive electronic gift cards (e.g., Amazon), with amounts tied to their level of participantion and compliance with study procedures.

Participants will receive $10 for completing the baseline survey and starting data collection using the smartphone app. Participants will receive $2 for each day of participation in the EMA surveys ($2 x 44 days = $88) plus an extra incentive of $90 if they complete at least 75% of the prompted assessments. Completion of 3- and 6-month follow-up surveys will be compensated with $20 gift cards each. All payments will come in the form electronic gift cards and will be emailed to participants intermittently during and after participation in the study (after baseline, EMA data collection at 45 days, 3 months follow-up, 6 months follow-up).

The N=10 participants in the initial pilot study will receive all of the same incentives and schedule with the exception that they will not complete the 3 and 6 month follow-up surveys, but will instead complete a brief 30 minute interview to talk about their study experience after 45 days. They will receive $40 for participating in the interview. The total incentive amount of $228 will be the same for pilot participants as well as for participants in the trial.

C. Include the possible total remuneration and any consequences for not completing all phases of the research.

The maximum total compensation is $228. Participants will be compensated according to how many surveys they complete and will be partially compensated if they drop out before completing all study activities.

X. Study Management:

A. Oversight Plan:

1. Describe how the study will be managed.

Study PI Dr. Thrul will oversee and manage all aspects of the study including programming of data collection instruments and procedures, participant recruitment and retention, data collection, management, analysis, and interpretation of results, as well as dissemination of study findings. Dr. Thrul will hold weekly meetings with study staff (TBN) and bi-weekly calls with study co-investigators (Drs. Mendelson, Latkin, Moran, Zipunnikov). TBN study staff will assist with participant recruitment, retention, data collection, processing, and dissemination of results. Study staff will be directly supervised by Dr. Thrul. Co-investigators have complementary expertise in adolescent health (Mendelson), clinical trials and substance use (Latkin), health communication (Moran), and biostatistics (Zipunnikov) and will consult on all aspects of the study.

2. What are the qualifications of study personnel managing the project?

As the PI, Dr. Thrul will provide primary oversight of the study. He has expertise in conducting EMA studies with young adult smokers and delivering technology-based smoking cessation interventions for this population. Dr. Thrul conducted one of the first studies using participants' own phones to collect EMA data on young adults' smoking. Moreover, Dr. Thrul has published on questions of tobacco and cannabis co-use and conducted a large EMA study with N=149 young adults in the San Francisco Bay Area on tobacco, alcohol, and cannabis co-use. Dr. Thrul is experienced in using online recruitment techniques, including Facebook and Craigslist, to recruit hundreds of participants for substance use studies. This experience naturally informs sample recruitment, survey design, and EMA data collection in the current study.

3. How will non-professional personnel (data collectors) involved with the data collection and analysis be trained in human subjects research protections? (Use the JHSPH Ethics Field Training Guide available on the JHSPH IRB website: www.jhsph.edu/irb)

All data will be collected digitally and remotely. All study investigators (Drs. Thrul, Mendelson, Latkin, Moran, Zipunnikov) have completed required Johns Hopkins University training and certification in the conduct of research with human subjects.

4. If the PI will not personally be on-site throughout the data collection process, provide details about PI site visits, the supervision over consent and data collection, and the communication plan between the PI and study team.

Data will be collected remotely (online), and the PI and study team will be present at Johns Hopkins and/or regularly communicate via email, phone, and video conferencing software.

B. Recordkeeping:

Describe how you plan to ensure that the study team follows the protocol and properly records and stores study data collection forms, IRB regulatory correspondence, and other study documentation. For assistance, contact: housecall@jhu.edu

Dr. Thrul will personally train the study team in the study protocol. Compliance with the study protocol will be reviewed in weekly team meetings.

C. **Safety Monitoring:**

1. Describe how participant safety will be monitored as the study progresses, by whom, and how often. Will there be a medical monitor on site? If yes, who will serve in that role?

Study data collection will be conducted remotely, and we will not have any in-person contact with study participants. In the event that a participant expresses serious distress during any of the EMA compliance contacts, the study team will provide information on medical emergency services (911) or the National Suicide Prevention Lifeline. Adverse events will be reported to the IRB by study PI Dr. Thrul.

The proposed study will utilize a Data and Safety Monitoring Plan (DSMP). A DSMP is appropriate for the trial proposed because: 1) This study does not involve a large number of subjects, 2) It does not involve a multi-site trial, and 3) It poses only minimal risks to participants. This plan will include safety monitoring when participants are contacted for study retention, as well as preparation of regular reports for the Johns Hopkins IRB and NIH, as appropriate, to update them on recruitment and any adverse events.

Who will be responsible for the monitoring?

Data and safety monitoring for the human subjects aspects of the research will be the responsibility of the PI, Dr. Thrul, with support from Co-Investigator Dr. Latkin, who has several decades of experience in running clinical trials for substance use treatment. Dr. Thrul will be responsible for reporting changes to the study protocol, any relevant adverse event or serious adverse event information, changes to the study's risk/benefit ratio, and/or acceptability of study continuation to the IRB as well as to NIH. The PI will also promptly report IRB actions (other than acceptance of reports) to NIH.

What will be monitored?

The DSMP will address the following areas: 1) The progress of the research study, including assessments of data quality and participant recruitment, accrual, and retention; 2) Review of outcome and adverse event data to determine whether there is any change to anticipated benefit-to-risk ratio of study participation, and whether the study should continue as originally designed, should be changed, or terminated; 3) The security for data transmitted wirelessly between the participants smartphones and secure servers; and 4) Review of study procedures designed to protect the privacy and confidentiality of participants' data.

What will be the frequency of monitoring?

Each of the above areas will be addressed in monthly meetings with the study team. All study data in these areas will be summarized on a yearly basis. After reviewing the data and protocol together with the study team, Drs. Thrul and Latkin will determine whether any changes need to be made to the protocol or consent forms.

How and when will reports be submitted to the IRB?

The yearly summary reports will be submitted with the annual IRB renewal. As described above, any adverse events will be promptly reported to the IRB and NIH, as appropriate, by Dr. Thrul.

2. If a Data Safety Monitoring Board (DSMB), or equivalent will be established, describe the following:

a. The DSMB membership, affiliation and expertise.

N/A

b. The charge or charter to the DSMB.

N/A

c. Plans for providing DSMB reports to the IRB.

N/A

3. Describe plans for interim analysis and stopping rules, if any.

Participants would be removed from the study only in the unlikely event that the study is cancelled. We do not foresee any other scenarios where a participant might be removed from the study beyond dropping out on his or her own.

D. **Reporting Unanticipated Problems/Adverse Events (AEs) to the IRB (*all studies must complete this section*)**:

Describe your plan for reporting to the IRB and (if applicable) to the sponsor. Include your plan for government-mandated reporting of abuse or illegal activity.

Unanticipated adverse events will be reported to the Johns Hopkins University IRB by PI Dr. Thrul, as appropriate, to ensure the safety of subjects.

NOTE: The IRB does not require PROMPT reporting of all AEs, only those that are **unanticipated, pose risk of harm to participants or others, and are related to the study**. Anticipated AEs may be reported with the Progress Report.

E. **Other IRBs/Ethics Review Boards:**

If other IRBs will review the research, provide the name and contact information for each IRB/ethics review board and its Federal Wide Assurance, if it has one (available on OHRP's website at http://www.hhs.gov/ohrp/assurances). **For federally funded studies, subrecipient AND subrecipient's IRB MUST have a Federal Wide Assurance (FWA) number.**

Non-JHSPH IRB/REC	FWA Number
N/A	

F. **"Engaged" in Human Subjects Research:**

For studies that involve collaboration with non-JHSPH institutions, complete the chart below by describing the collaboration and the roles and responsibilities of each partner, including the JHSPH investigator. This information helps us determine what IRB oversight is required for each party. Complete the chart for all multi-collaborator studies.

Insert collaborator names and FWA numbers, if available. Note who will be "engaged" in human subjects research by filling in the following table:

	JHSPH		
For federally funded studies, collaborators' FWA	00000287		
Primary Grant/Contract Recipient			
Grant/Contract Subrecipient			
Hiring Data Collectors			

Training Data Collectors			
Obtaining Informed Consent and/or Identifiable Data			
Accessing/Analyzing Identifiable Data			
Overseeing storage, access and use of biospecimens			

COMPLETE THE FOLLOWING SECTIONS WHEN RELEVANT TO YOUR STUDY:

XI. Secondary Data Analysis of Existing Data:

A. **Study Design:**

1. Describe your study design and methods. The study design must relate to your stated aims/objectives.

2. Provide an estimated sample size and an explanation for that number.

3. Provide a brief data analysis plan and a description of variables to be derived.

B. **Participants:**

1. Describe the subjects who provided the original data and the population from which they were drawn.

Note: If you are receiving, accessing, or using data from a U.S. health care provider, the need for HIPAA review is likely. If you plan to bring identifiable health information from a foreign country to a U.S. covered entity (e.g., lab at the Hopkins SOM), HIPAA may be triggered. If either of these conditions is met, check "yes" to the HIPAA question in the PHIRST application.

2. If you plan to analyze human specimens or genetic/genomic data, provide details about the source of those specimens and whether they were collected using an informed consent document. If yes, explain whether your proposed use is "consistent with" the scope of the original consent, if it potentially introduces new analyses beyond the scope of the original consent, and/or if it introduces new sensitive topics (HIV/STDs, mental health, addiction) or cultural/community issues that may be controversial.

3. Explain whether (and how) you plan to return results to the participants either individually or as a group.

XII. Oversight Plan for Student-Initiated Studies:

A. For student-initiated studies, explain how the PI will monitor the student's adherence to the IRB-approved research plan, such as communication frequency and form, training, reporting requirements, and anticipated time frame for the research. Describe who will have direct oversight of the student for international studies if the PI will not personally be located at the study site, and their qualifications.

B. What is the data custody plan for student-initiated research? *(Note: Students may not take identifiable information with them when they leave the institution.)*

XIII. Creation of a Biospecimen Repository:

Explain the source of the biospecimens, if not described above, what kinds of specimens will be retained over time. Clarify whether the specimens will be obtained specifically for repository purposes, or will be obtained as part of the core study and then retained in a repository.

A. Describe where the biospecimens will be stored and who will be responsible for them.

B. Describe how long the biospecimens will be stored, and what will happen at the end of that period.

C. Explain whether the biospecimens will be shared with other investigators, inside and outside of JHU, how the decision to share will be made, and by whom. Include your plans, if any, for commercial use. Also explain how downstream use of the specimen will be managed, and what will happen to left-over specimens.

D. Describe whether future research using the biospecimens will include specimen derivation and processing (cell lines, DNA/RNA, etc.), genomic analyses, or any other work which could increase risk to participants. Explain what additional protections will be provided to participants.

E. If future research could yield unanticipated incidental findings (e.g., an unexpected finding with potential health importance that is not one of the aims of the study) for a participant, do you intend to disclose those findings to the study participant? Please explain your position.

F. Explain whether the specimens will be identifiable, and if so, how they will be coded, who will have access to the code, and whether the biospecimens will be shared in linked (identifiable) form.

G. Explain whether the repository will have Certificate of Confidentiality protections.

H. Explain whether a participant will be able to withdraw consent to use a biospecimen, and how the repository will handle a consent withdrawal request.

I. Describe data and/or specimen use agreements that will be required of users. Provide a copy of any usage agreement that you plan to execute with investigators who obtain biospecimens from you.

XIV. Data Coordinating Center:

Complete if JHSPH serves as the Data Coordinating Center.

A. How will the study procedures be developed?

B. How will the study documents that require IRB approval at each local site be developed? Will there be some sort of steering or equivalent committee that will provide central review and approval of study documents, or will template consent forms, recruitment materials, data collection forms, etc. be developed by and provided to the local sites by the coordinating center without external review?

C. Will each local clinical site be overseen by its own IRB with an FWA, or will a Single IRB review the study? State whether the coordinating center will collect IRB approvals and renewals from the clinical centers; if not, explain why.

D. How will the coordinating center provide each local site with the most recent version of the protocol and other study documents? What will be the process for requesting that these updates be approved by local clinical center IRBs?

E. What is the plan for collecting data, managing the data, and protecting the data at the coordinating center?

F. What is the process for reporting and evaluating protocol events and deviations from the local sites? Who has overall responsibility for overseeing subject safety: the investigators at the recruitment site, the Coordinating Center, the Steering Committee, or a Data and Safety Monitoring Board (DSMB)? Is there a DSMB that will evaluate these reports and provide summaries of safety information to all the

reviewing IRBs, including the coordinating center IRB? Please note that if there is a DSMB for the overall study, then the coordinating center PI does not have to report to the coordinating center IRB each individual adverse event/problem event that is submitted by the local site PIs.

G. Some FDA regulated studies have different AE reporting criteria than that required by the IRB (IRB Policy No. 103.06). How will you reconcile the different requirements, and who is responsible for this reconciliation?

H. Who is responsible for compliance with the study protocol and procedures and how will the compliance of the local sites be monitored and reviewed? How will issues with compliance be remedied?

XV. Drug Products, Vitamins, Food and Dietary Supplements:

Complete this section if your study involves a drug, botanical, food, dietary supplement or other product that will be applied, inhaled, ingested or otherwise absorbed by the study participants. If you will be administering drugs, please upload the product information.

A. List the name(s) of the study product(s), and the manufacturer/source of each product.

Name of Study Product	Manufacturer/Source

B. List each study product by name and indicate its approved/not approved status.

Approved by the FDA and Commercially Available	Approved by Another Gov't Entity (provide name)	Cleared for Use at Local Study Site

C. If your study product has an Investigational New Drug (IND) application through the U.S. Food and Drug Administration, provide the IND number, and the Investigators Brochure.

D. If your study product is a marketed drug, provide the package inserts or other product information. If the study product WILL NOT be used for its approved indication, dose, population, and route of administration, provide a detailed rationale justifying the off-label use of the study product.

E. If the study product does not require FDA approval (e.g., dietary supplements, botanicals, products not subject to the U.S. FDA, etc.), provide safety information (as applicable) and a certificate of analysis.

F. Explain who will be responsible for drug management and supply, labeling, dispensing, documentation and recordkeeping. Complete and upload into PHIRST the Drug Data Sheet available on the JHSPH IRB website at www.jhsph.edu/irb.

G. What drug monitoring and/or regulatory oversight will be provided as part of the study?

XVI. Medical Devices:

Complete this section if your study will involve an approved or investigational medical device (**diagnostic**, non-significant risk, significant risk).

A. List the name(s) of the study product(s), the manufacturer/source of each product, and whether or not it is powered (electric, battery). Provide product information. If it is electric, upload documentation of clinical engineering approval or its equivalent from a local authority, to ensure that the device is in good working order.

Name of Study Product	Manufacturer/Source	Powered?

B. List each study product by name and indicate its status as approved by a government authority or not approved.

Approved by the FDA and Commercially Available	Approved by Another Gov't Entity (provide name and approval information)	Not Approved

C. If your investigational device is Exempt from the FDA IDE regulations, explain which section of the code applies to your device and why it meets the criteria provided. If it is a **diagnostic device**, provide pre-clinical information about the sensitivity and specificity of the test and the anticipated failure rate. If you plan to provide the results to participants or their physicians, justify doing so, and explain how those results will validated (or not) against the current "gold standard".

D. If you believe the investigational device is not IDE exempt under 21CFR 812.2(c), but is a "Non-Significant Risk" device considered to have an approved IDE application, provide information from the manufacturer supporting that position.

E. If you are using an investigational device that is a Significant Risk Device, provide the IDE number given by the FDA, or if not under FDA jurisdiction, explain why it is appropriate to use this device in this study. Provide a description of the device, and upload a picture or manufacturing schematics into PHIRST. Provide any other information relevant to a determination of its safety to be used for the purposes outlined in this research plan.