Official Title: Randomized controlled trial of varenicline for cessation of nicotine vaping in adolescent non-smokers
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Protocol Title: VARENICLINE FOR VAPING CESSATION IN NON SMOKER VAPER ADOLESCENTS

Principal Investigator: A. Eden Evins, MD/MPH

Site Principal Investigator: N/A

Description of Subject Population: Adolescents and young adults 16-25 years old

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Some of the people who are eligible to take part in this study may not be able to give consent because they are less than 18 years of age (a minor). Instead, we will ask their parent(s) to give permission for them to take part in the study and will ask them to agree (give their assent) to take part. Throughout the consent form, "you" always refers to the person who takes part in the study.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision will not change the medical care you get within Partners now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn more about how well varenicline, a medication that helps people quit smoking, will work to help young adults stop vaping.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 6 months to complete the study. During this time, we will ask you to take part in an enrollment visit, weekly individual behavioral vaping cessation sessions or study visits (virtual or in-person), and monthly assessment visits. In-person visits will be held at the Center for Addiction Medicine at 101 Merrimac St. Boston, MA, or in a private room at your school or local library.

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen: you will be asked about your medical and psychiatric history, complete questionnaires about your mood, vaping habits, smoking and substance use, and provide urine and saliva samples. If you are eligible and choose to participate, you will be randomly assigned to one of three groups. For two of the groups, you will take either the study medication (varenicline) or placebo (sugar pill), complete weekly in-person or virtual study visits, and attend brief weekly virtual behavioral vaping cessation sessions. If you are assigned to the third group (Enhanced Usual Care), you will complete weekly virtual or in-person study visits, but you will not take any medication or attend the vaping cessation sessions. All participants will complete monthly assessment visits, which can be in person or virtual. At the final study visit (week 24), all participants will have the option to provide contact information for three friends who will be invited to participate in a one-time virtual visit to answer some questionnaires about themselves. Providing contact information is voluntary and will not affect your participation in any way. Your information will remain confidential and private regardless of whether you provide your friends' contact information and they agree to participate.

Why might you choose to take part in this study?

We cannot promise you any benefits from taking part in this research study. However, for the group that is assigned to receive study medication, it is possible that you may have a good response to varenicline and/or the vaping cessation sessions and may be able to quit vaping. What we learn from this study may help other people quit vaping in the future.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

For the group assigned to receive varenicline, important risks and possible discomforts to know about include risks due to taking varenicline such as nausea, headache and dizziness. You may also experience withdrawal symptoms after stopping vaping or experience stress caused by behavioral vaping cessation sessions.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

What other treatments or procedures are available for your condition?

There are no FDA-approved medications for helping to quit vaping. There are, however, 7 FDA-approved medications to help people quit smoking: 5 nicotine replacement therapies (patches, gum, lozenges, inhaler, and nasal spray), bupropion (Zyban®), and varenicline (Chantix®). They may be available to you outside of this study. In addition, individual or group counseling is available outside this study and can be helpful in stopping vaping.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Eden Evins, MD, MPH is the person and physician in charge of this research study. You can call her at 617-643-4679, Monday through Friday 9AM to 5PM with questions about this research study. If you would like to speak with a clinician, you can contact Dr. Randi Schuster, PhD at 617-643-6673, Monday through Friday 9AM to 5PM. If you need to speak to someone

after office hours in an emergency, you can call 617-726-2000 and ask the operator to page Dr. Evins.

If you have questions about the scheduling of appointments or study visits, call our study staff at 617-643-3467.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:
- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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

Why is this research study being done?

The purpose of the study is to learn if varenicline, a medication to help people quit smoking, will work to help young adults stop vaping.

This research study will compare varenicline to placebo to enhanced usual care (EUC). The placebo looks exactly like varenicline but contains no varenicline. Placebos are used in research studies to see if the results are due to the study medication or due to other reasons. If you decide to participate in this study, you will be randomly assigned to one of three groups:

- **Varenicline Group (1):** You will receive varenicline, along with behavioral vaping cessation sessions, texting support, and daily smartphone assessments.
- **Placebo Group (2):** You will receive placebo (a sugar pill), along with behavioral vaping cessation sessions, texting support, and daily smartphone assessments.
- **Enhanced Usual Care (EUC) Group (3):** You will complete weekly study visits, but you will not take the study medication (varenicline or placebo), attend the vaping cessation sessions, or complete daily smartphone assessments. You will be advised to set a quit date and be introduced to a supportive texting program.

You will have a one in three chance of being assigned to one of the three groups. Neither you nor the study staff can choose your study group. If you are enrolled in this study, you must be willing to be randomized to any of the three groups. This is a blinded study. This means if you are assigned to the varenicline or placebo group, neither you nor the study team will know whether you received varenicline until after the study is over; however, your doctor or the study team can get this information quickly if needed.

The National Institute on Drug Abuse is paying for this study to be done.

Who will take part in this research?

We are asking you to take part in this research study because you are a healthy person between the ages of 16 and 25 who vapes nicotine daily or almost daily and you are willing to try varenicline to quit vaping. About 300 participants ages 16-25 will take part in this research study. We will enroll all of these subjects at Massachusetts General Hospital (MGH).

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. Even if you sign this consent form, you can change your mind at any time and stop taking part in the study. Vital signs and carbon monoxide will be collected only at in-person visits. If you complete all your visit virtually, these measures will not be collected at all, and we will ask you to self-report your height and weight. For virtual visits, drug and pregnancy screenings will be mailed to you will detailed instructions on how to complete each test on your own.

Enrollment Visit (in-person or virtual for all participants)

The enrollment visit will take about 2 hours. During this visit, we will do some tests and procedures to see if you qualify to take part in this research study. At this visit, we will:

- Ask you about your health, lifestyle, medical, and psychiatric history.
- Take your height, weight, and vital signs (blood pressure and heart rate).
- Ask you about current medications you are taking. This is important because if you are randomized to the varenicline group, some medications could have a bad reaction with the study medication.
- Measure the carbon monoxide in your breath using a small, hand-held machine to check for recent smoking activity. Carbon monoxide is produced by burning materials, like cigarettes and exhaust from cars. If this is done virtually, we will not collect this information.

- Test your urine for certain drugs, THC (marijuana), and illegal drugs. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.
- Test your urine for pregnancy if you are biologically female and able to become pregnant. Women who are currently pregnant or breastfeeding cannot take part in this research study.
- Test your saliva for cotinine. Cotinine is a substance that can be found in the body up to three days after someone has been exposed to tobacco products. Measuring cotinine in people's saliva is a good way to determine exposure to tobacco products for both smokers and nonsmokers. We will also teach you how to perform this test at home.
- Give you questionnaires to fill out about your general health and well-being, mental health, mood, vaping and smoking habits, substance use history, and cravings to vape.
- Ask you to fill out a form with information about your age, sex, race, marital status, employment, and occupation.

The study doctor will review the results of these tests and procedures to find out if you are eligible to continue in the study.

If you qualify to continue in the study, we will randomly assign you by chance (like a lottery chosen by a computer) to either the varenicline group, the placebo group, or the monitoring group. If you and another member of your household enroll, you will both be assigned to the same study group. Neither you nor the study staff can choose your study group. You will have a one in three chance of being assigned to one of the study groups. This is a blinded study. This means that if you are randomized to the varenicline or placebo group, you and the study team will not know which study group you are in, but the study team can find out if necessary.

If you qualify for the study, we will schedule you to attend weekly behavioral vaping cessation sessions (week 1 to week 12) and seven monthly assessment visits (weeks 0, 4, 8, 12, 16, 20, 24). All visits can be done virtually if necessary.

Visit Descriptions for Groups 1 and 2: Varenicline Group and Placebo Group

Week 0 (Baseline) to Week 12: Weekly Behavioral Vaping Cessation Sessions

At the week 0 (baseline, in-person or virtual visit) we will:

- Ask about any symptoms, illnesses, or injuries since your last visit.
- Ask about any medications you are taking or any non-drug treatment you are receiving.
- Ask you to complete questionnaires about your overall mental health and well-being, depression, aggression, and suicidal thoughts and feelings.

- Ask you about nicotine cravings and withdrawal symptoms.
- Ask you to take a saliva cotinine test (*see 'Saliva Testing for Cotinine' on page 12*).
- Test your urine for pregnancy if you are biologically female and able to become pregnant.
- Ask you to participate in weekly vaping cessation sessions to stop vaping.
- Teach you how to take the study medication. You will be asked to start the study medication the day after the week 0 (baseline) session.
- Collect vitals
- Set you up for daily REDCap surveys via emocha.. Daily REDCap surveys are estimated to take 1-5 minutes each.
- Teach you how to use emocha. The emocha Mobile Health app is a smartphone application that we will use to remind you about attending your vaping cessation sessions and study visits, as well as notify you to take your study medication. In this app, you will record yourself taking the study medication and record any side effects you may experience. You will receive daily micropayments for recording yourself taking your medication in the emocha app and completing your surveys ($1 per daily video and survey completion, up to $2 daily).
- Teach you how to use the "This is Quitting" (TIQ) text messaging program to quit vaping.

Week 1 to week 12 visits will be either in-person or virtual. During these visits, we will:

- Ask about any symptoms, illnesses, or injuries since your last visit.
- Ask about any medications you are taking or any non-drug treatment you are receiving.
- Ask you to complete questionnaires about your overall mental health and well-being, depression, aggression, and suicidal thoughts and feelings.
- Ask you about nicotine cravings and withdrawal symptoms.
- Ask you to take a saliva cotinine test if you report not using nicotine since the last visit.
- Ask you to count your unused study medication from the previous week. At the week 12 visit, you will stop taking the study medication.
- Ask you to report any recent vaping.

Weeks 0, 4, 8, 12, 16, 20, 24: Monthly Assessment Visits

The monthly assessment visits will take place <u>in-person or virtually</u> at weeks 0, 4, 8, 12, 16, 20, and 24. At these visits we will:

- Ask about any symptoms, illnesses, or injuries since your last visit.
- Ask about any medications you are taking or any non-drug treatment you are receiving.

- Ask you to complete questionnaires about your overall mental health and well-being, depression, aggression, and suicidal thoughts and feelings.
- Ask you about nicotine craving and withdrawal symptoms.
- Ask about your recent use of alcohol, marijuana, opioids, cigarettes and other tobacco products and vaping use.
- (Week 0) Test your saliva for cotinine (after week 0, we will only test your saliva for cotinine if you report not using nicotine).
- Ask you to provide a urine sample for a drug test.
- Collect your vitals.
- (Weeks 0, 4, 8 and 12) Ask you to provide a urine sample for a pregnancy test.
- (Weeks 0, 12, and 24) Collect your urine for THC (marijuana) and NNAL testing, a substance that identifies if you smoked tobacco products in the past 2 months.
- (Week 12) Ask you to bring all unused or empty study medication materials to the in-person visit.

Study Medication: Study staff will distribute and/or send via priority mail a 2-week or 4-week supply of varenicline or identical placebo according to the following schedule:

- Week 0: a 2-week supply
- Week 2: a 2-week supply
- Weeks 4 & 8: a 4-week supply

You will be instructed to start taking the study medication the day of your baseline visit (week 0) according to the following schedule:

If you are > 55kg (> 121 lbs; regardless of age)

- Week 1: For the first three days, you will take one 0.5 mg tablet every day in the evening. Then for the next 4 days, you will take one 0.5 mg tablet in the morning and one 0.5 mg tablet in the evening.
- Weeks 2-12: Starting at the beginning week 2, you will take one 1 mg tablet in the morning and one 1 mg tablet in the evening until the end of week 12.

If you are ≤ 55kg (≤ 121 lbs and between the ages of 16 and 17)

- Week 1: You will take one 0.5 mg tablet every day in the evening.
- Weeks 2-12: You will take one 0.5 mg tablet in the morning and one 0.5 mg tablet in the evening until the end of week 12.

Please make sure no one else uses your study medication and keep it out of reach of children. Please keep the study medication away from your other medication(s). The study medication should be stored at room temperature. Before taking your study medication, you should eat a small snack or meal. Swallow the pills whole with a full glass of water. Do not chew, crush, or split the pills. There should be at least 8 hours between your morning dose and your evening dose. It is important for you to follow our instructions about how to take the study medication.

QuitVaping Sessions (in-person or virtual): From week 1 to week 12 you will attend weekly individual QuitVaping behavioral therapy sessions. QuitVaping sessions will be video recorded for quality control. These sessions will last about 15 minutes. These sessions will teach you ways to become a "non-vaper," how to deal with cravings and withdrawal, how to deal with triggers in difficult situations, and how to help you stay quit. At each meeting, we will ask you about your vaping and ask you to take a saliva cotinine test to measure any exposure to nicotine.

Medication Adherence: During this study, you will use a smartphone application created by a company called emocha Mobile Health Inc. ("emocha").

Before using emocha, you will be instructed on how to set up the application to confirm your identity and register your preferred settings. You will also learn how to use it.

You may use your personal smartphone by downloading the app with assistance from the study staff. If you do not have a suitable smartphone, a device will be provided by the study site. If you are provided with a device, you will not be able to make general phone calls, respond to SMS (text) messages, or use the device to access the internet. You are required to return the device at the end of the study.

How you will interact with the application:

- The application will remind you when it is time to take your study medication. You will be required to use the application to record yourself taking each dose of study medication. The app is used to visually confirm that the same person uses the device each time, and that the study medication is properly administered. It is important that you use the application *every* time you take your study medication.
- The application will prompt you to report any side effects you may experience as a result of taking the study medication.
- You will receive micropayments for recording yourself taking the study medication in the emocha app and completing your REDCap surveys ($1 per daily emocha video and survey completion, up to $2 daily), for a maximum payment of $168.

During the registration process, you will be sent an email from noreply@emocha.com with the subject: "Welcome to emocha!" The email will house a link to create a username and password. Upon creation of your account, you will download the emocha app on the App Store or Google play. If you are registering on a computer, you will have an option to enter your phone number. The option to enter your personal telephone number(s), is voluntary. By submitting your number, you grant emocha permission to SMS (text) message or call you by phone if:

- You are not responding to the prompts or reminders in the application.
- The study staff needs to reach you regarding the study.
- The study device requires updates or alterations.

The information emocha will collect on or through their website or app may include:

- Information that you provide by filling in forms on their website or app. This includes information provided at the time of registering.
- Personally identifiable information such as: your name, password, age, gender, email address, and home/mobile telephone number that you may provide when you register for an account.
- Records and copies of your correspondence (including e-mail addresses) if you contact emocha.
- Your study ID and time-stamped videos of you (including audio) when you use the application to record yourself taking the study medication.

All of your video recordings and data are encrypted by the application and will be automatically forwarded to a secure server. The encrypted recordings are only accessible by authorized staff of emocha and study staff through a website that is password protected.

The video recordings and identifiable data will be deleted at the end of the study. If you withdraw from the study, your videos will be kept until the conclusion of the study.

The privacy of the individually identifiable health information emocha collects is protected by federal law (the Health Insurance Portability and Accountability Act or HIPAA).

Visit Descriptions for Group 3: EUC Group

At the week 0 (baseline, in-person or virtual visit) we will:

- Ask about any symptoms, illnesses, or injuries since your last visit.
- Ask about any medications you are taking or any non-drug treatment you are receiving.
- Ask you to complete questionnaires about your overall mental health and well-being, depression, aggression, and suicidal thoughts and feelings.

- Ask you about nicotine cravings and withdrawal symptoms.
- Collect vitals.
- Ask you to take a saliva cotinine test (*see 'Saliva Testing for Cotinine', pg 12*).
- Test your urine for pregnancy if you are biologically female and able to become pregnant.
- Ask about your recent use of alcohol, marijuana, opioids, cigarettes and other tobacco products, and vaping use.
- Teach you how to use the "This is Quitting" (TIQ) text messaging program to quit vaping.

Week 1 to week 12 visits will be either in-person or virtual and have the same procedures as week 0 (baseline), with the exception that we will:

- Ask about your recent vaping use **only**.

Weeks 0, 4, 8, 12, 16, 20, 24: Monthly Assessment Visits

The monthly assessment visits will take place <u>in-person</u> or virtually at weeks 0, 4, 8, 12, 16, 20, and 24. At these visits we will:

- Ask about any symptoms, illnesses, or injuries since your last visit.
- Ask about any medications you are taking or any non-drug treatment you are receiving.
- Ask you to complete questionnaires about your overall mental health and well-being, depression, aggression, and suicidal thoughts and feelings.
- Ask you about nicotine cravings and withdrawal symptoms.
- Ask about your recent use of alcohol, marijuana, opioids, cigarettes and other tobacco products and vaping use.
- Test your saliva for cotinine (after week 0, we will only test your saliva for cotinine if you report not using nicotine).
- Ask you to provide a urine sample for a drug test.
- Collect your vitals.
- (Weeks 0, 4, 8, and 12) Ask you to provide a urine sample for a pregnancy test.
- (Weeks 0, 12, and 24) Collect your urine for THC (marijuana) and NNAL testing, a substance that identifies if you smoked tobacco products in the past 2 months.

<u>For All Groups:</u>

At any time during the study, if your answers to the questions about mental health require more follow-up, you may be referred for a psychiatric evaluation.

"This is Quitting" Text Message Vaping Cessation Program (TIQ): "This is Quitting" is a free, publicly available text message vaping cessation program from Truth Initiative, designed specifically to help people quit vaping nicotine. As part of this program, you will receive messages for a week preceding your quit date and 30 days afterwards that include encouragement and support, skill and self-efficacy building exercises, coping strategies, and information about the risks of vaping, benefits of quitting, and cutting down to quit. Keywords "CRAVE," "STRESS," or "SLIP" provide on-demand support. You will be introduced to TIQ at your baseline visit (week 0), and be asked about your use of TIQ at each visit until week 12.

Texting: Text messages by mobile/cell phones are a common form of communication. This research study utilizes a third-party service, Google Voice, which we will use to send reminder de-identified text messages asking participants to confirm their appointments the day before the scheduled appointment.

Below are some important points about texting in this research study.

- Text messages are not encrypted, and therefore carry security risks. This research study and Partners Healthcare are not responsible for any interception of messages sent through unencrypted text message communications.
- You will be responsible for all fees charged by your carrier's service plan for text messaging. This research study and Partners Healthcare are not responsible for any increased charges, data usage against plan limits or changes to data fees from the research texts.
- You may decide to not send or receive text messages with staff associated with this research study at any time. You can do this in person or by sending the research email a message that says, "Stop Research Text."
- Your agreement applies to this research study only. Agreeing to other texts from Partners Healthcare, for example appointment reminders, is a separate process. Opting out of other texts from Partners Healthcare is a separate process as well.
- It is your responsibility to update your mobile/cell phone number with this research study in the event of a change.

Do we have your permission to send you text reminders to your cell phone?

☐ YES ☐ NO Initials_____

Urine Drug Screen: Before study procedures are initiated, we will perform a urine drug screen that will test for THC (marijuana) and illicit substances. The test will be administered by a trained research coordinator.

Urine Pregnancy Test: At the enrollment visit before any study procedures are initiated and at baseline, weeks 4, 8, and 12, we will perform a urine pregnancy test for females who are able to become pregnant. The test will be administered by a trained research coordinator.

Saliva Testing for Cotinine: At enrollment and Week 0, we will collect your saliva to see if you have cotinine in your body. We will collect saliva at each visit after Week 0 where you report not having used nicotine. For in-person sessions, we will collect saliva during the visit. For virtual sessions, we will give you a handout with instructions, materials, and barcoded kits unique to you to perform the test during the session.

Stopping the Study Early: Taking part in this research study is up to you. You may choose not to take part, or you can change your mind and withdraw (drop out) later. If you want to stop taking part in this study, you should tell us. We will make sure you end the study in the safest way. We will also talk to you about follow-up care, if needed.

The study doctor may take you out of the study without your permission if:

- You do not follow the directions of the study team.
- The study doctor decides that the study is not in your best interest.
- The study is stopped by the study sponsor, the institutional review board (IRB) or independent ethics committee.
- You become pregnant, want to become pregnant, or are nursing a child during this study.

If you no longer want to continue in the study, we may ask you to come in for a final clinic visit. The visit may take about 1.5 hours. During this final visit, the same procedures that are done at week 24 will happen.

During this study, it is important that you:

- Do not use tobacco products (including, cigarettes, pipe tobacco, cigars, snuff, chewing tobacco, and hookah).
- Do not use nicotine patches, bupropion and other aids used to quit smoking or vaping.
- Take the study medication as prescribed and return all unused pills and study medication packaging at the week 12 in-person visit.
- Use an appropriate form of birth control during the study if you are female and able to become pregnant.
- Do not take part in another research study.

If you turn 18 years of age while you are taking part in this study, we will ask you to sign a new consent form at that time.

Partners Alert System: Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study. A member of the study staff may contact you if they receive an alert to ensure your safety in continuing forward in our study.

Partners Medical Record Information: A notation that you are taking part in this research study may be made in your electronic medical record. **For this study, only a study number, and NOT the title of the study, will be in your record: for example, Study #123.** Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

(Optional) Saliva Samples for Genetic Testing: The collection of a saliva sample for genetic research is optional (not required). You can still take part in the main study even if you do not want to take part in the genetic study. Giving a DNA sample involves filling one small plastic container with your saliva. This will be done at your first visit and should take less than 5 minutes. Usually, researchers study just a few areas of genetic code that are linked to a disease or condition. Instead, we may perform a whole genome analysis on your DNA sample. In the whole genome analyses, all or most of the genes are looked at and used by researchers to study links to substance use and mental health. These whole genome analyses will be conducted by investigators at the Broad Institute. Samples shared with investigators at the Broad Institute will be labeled with a code number and not with your name or other identifying information. Research using whole genome information is important for the study of virtually all diseases and conditions. Therefore, the anonymized samples will provide study data for researchers working on any disease.

It is not intended to provide important genetic information about your health. We have no plan to return any research results to you or your doctor. The results of the genetic testing will not be placed in your medical record. Consenting to take part in this additional genetic study is voluntary, and you may decide to withdraw from the study at any time or decide not to join the study. If you change your mind and want to withdraw your saliva sample from further genetic research, you can do so at any time by contacting Dr. Evins (617-643-4679; AEEVINS@MGH.HARVARD.EDU) or Dr. Schuster (617-643-6673; RSCHUSTER@MGH.HARVARD.EDU). Any information obtained from the sample will also be withdrawn except to the extent to which the information has already been used in analyses.

All information and samples obtained for this study will be assigned a code number. No names or important numbers that could be used to identify you, like hospital medical record numbers or social security numbers, will be kept on samples. Only MGH study staff will keep the link between your subject number and your name on a computer protected by a personal password.

Would you like to provide a saliva sample to be used for genetic testing as described above? Please mark your choice below.

☐ YES ☐ NO Initials_____

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It will not be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

No. The research study we are doing is only a steppingstone in understanding how to help participants to quit vaping. Therefore, no information about the results of this research study or the results of your individual participation in the research study will be given to you or your doctor. Tests done for the research using your samples will not be useful in directing your medical treatment. The results of the tests will not be placed in your medical record.

What are the risks and possible discomforts from being in this research study?

All drugs have some risks and side effects. Some side effects may make you sick, make you feel uncomfortable, or hurt you. You will be watched carefully during the study for any side effects.

Risks of Varenicline

Common side effects:

Nausea: Nausea is the most common adverse reaction reported with varenicline treatment. Nausea is generally described as mild or moderate and often transient; however, for some patients, it is persistent over several months.

Other frequent side effects are:

- Headaches
- Sleep disturbances (difficulty in sleeping, abnormal dreams)
- Dizziness
- Constipation
- Flatulence (gas)
- Diarrhea
- Vomiting

Even though these side effects are expected to occur in some people, most people have not had to stop taking varenicline because of side effects.

Less common side effects are:

- Changes in mood (depression and mania)
- Agitation psychosis (loss of contact with reality)
- Hallucinations (seeing or hearing things that are not there)
- Paranoia (feeling people are against you)
- Delusions (false beliefs)
- Homicidal ideation (thoughts of killing others)
- Hostility (aggression)
- Changes in behavior
- Anxiety
- Panic (sudden fear that takes over or replaces normal thinking)
- Somnambulism (sleep walking)
- Suicidal ideation (suicidal thoughts)
- Suicide attempt
- Completed suicide

Smoking cessation with or without treatment is associated with nicotine withdrawal symptoms and the worsening of underlying psychiatric illness. Not all patients reporting these events had psychiatric illnesses before and not all had stopped smoking. The role of varenicline in these reports is not known.

Interaction with Alcohol: There have been postmarketing reports of patients experiencing increased intoxicating effects of alcohol while taking varenicline. Some cases described unusual and sometimes aggressive behavior and were often accompanied by amnesia for the events.

Accidental Injury: There have been postmarketing reports of traffic accidents, near-miss incidents in traffic, or other accidental injuries in patients taking varenicline. In some cases, the patients reported somnolence, dizziness, loss of consciousness or difficulty concentrating that

resulted in impairment, or concern about potential impairment, in driving or operating machinery. You should use caution driving or operating machinery or engaging in other potentially hazardous activities until you know how varenicline may affect you.

Rare (but serious) side effects:

- Hypersensitivity reactions (swelling of face, mouth, extremities [arms, legs], and neck that can make breathing difficult)
- Skin reactions (rash, swelling, redness)
- Peeling of the skin that can sometimes be life-threatening)
- Seizures**:** There have been reports of seizures in patients treated with varenicline. Some patients had no history of seizures, whereas others had a history of seizure disorder that was remote or well-controlled. In most cases, the seizure occurred within the first month of therapy. You should discontinue study medication and contact a healthcare provider immediately if you experience a seizure while on treatment.

If you have cardiovascular disease, taking varenicline may increase your risk of certain cardiovascular adverse events. You should contact your health care provider if you experience new or worsening symptoms of cardiovascular disease, such as chest pain, shortness of breath, calf pain when walking, or sudden onset of weakness, numbness, or difficulty speaking.

If there are any concerns that you are in need of clinical attention, the Physician Investigator (A. Eden Evins, MD, MPH) will be made aware of the issue immediately to determine appropriate steps. The Physician Investigator and another medically trained co-investigator will assess the needs of the subject and offer the subject either prompt treatment or medical referral, whichever is appropriate for the situation.

If you think you are having an allergic reaction and having trouble breathing, or other life-threatening events, call 911 immediately. It is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study medication.

Placebo Risk: You may receive a placebo. Taking a placebo may be similar to not taking any medication. If you receive a placebo, your vaping habit may stay the same or get worse, or you may spontaneously quit vaping just as you may have done without additional treatment.

Nicotine Withdrawal Symptoms: Decreased nicotine consumption, with or without treatment, may result in nicotine withdrawal symptoms (e.g., irritability, anxiety, restlessness, depressed mood, increased appetite, fatigue, insomnia/sleep problems, impatience, headache, difficulty

concentrating). Your withdrawal symptoms will be monitored throughout the study. The study doctors will help you to get appropriate treatment for any severe symptoms.

Pregnancy/Birth Control: The effects of varenicline on an embryo or fetus (developing baby still in the womb), or on a nursing infant are not known and may be harmful. If you are pregnant or breastfeeding, you cannot participate in this study. All female subjects must have a negative pregnancy test before starting the study drug. If your pregnancy test is positive at the visits it is collected at, then you cannot join the study. For this reason, we ask that women of child-bearing potential agree to use adequate contraception prior to study entry and during the study. Acceptable birth control methods include: birth control pill plus a condom, spermicide plus a condom, diaphragm plus spermicidal jelly, subcutaneous contraceptive medication (birth control medication).

If you are the parent of a 16- or 17-year-old subject, the results of your child's urine screen will not become part of your child's medical record, and the result will not be shared with you. However, if your daughter has a positive pregnancy test, we will inform her and encourage her to share those results with you, and she will be withdrawn from the study.

Risks of the Carbon Monoxide Test: The carbon monoxide test might cause only slight discomfort. The carbon monoxide test requires that you take a deep breath, hold it for 15 seconds and exhale (blow out) one large breath into a machine that will measure the amount of carbon monoxide in your lungs.

Saliva Collection: Using a collector to obtain saliva can be uncomfortable. We are going to give you all the tools and material such as gloves, etc.

Questionnaires: It is possible that some of the questions in the questionnaires may make you feel uncomfortable. You can skip any questions you do not want to answer. However, we hope that you will answer all questions.

Confidentiality and Loss of Privacy: Information collected from you will be stored in a password-protected research database on a password-protected computer. This information will not become part of your medical record. Your information may be kept for several decades.

We will assign all information a unique code. The key to the code will be kept on a password-protected computer. Only the researchers from our research study will be able to use the computer. The code linking test results to subject identity will only be accessible to study staff. We will not share your identity with anyone outside the Partners institutions. However, we cannot guarantee your confidentiality.

Confidentiality will be strictly enforced and is only limited in ways mandated by the law, which will be detailed below.

- Your research results will not be shared with you or entered into your medical record. This is because the research results cannot currently be used to guide your medical care.
- Through regular clinical interviews, questionnaires and conversations, we will monitor your mental health closely over the course of the study visits and you will meet regularly with Dr. Schuster who is a clinical psychologist at Massachusetts General Hospital/Harvard Medical School. If you indicate that you are having many feelings of depression or anxiety and/or we notice an elevation in symptoms during the study, we will tell you about these results and recommend that you get follow-up from a counselor, therapist, psychologist or psychiatrist. We have carefully collected the names and phone numbers of local mental health professionals who are trusted in the community and will provide you with their contact information. All study staff will be properly trained on assessment, monitoring and intervention of mental health issues and all study staff will be prepared to discuss counseling options.
- If you indicate concern about substance use, we will provide you with resources for local treatment/support options.
- We are obligated by law to report any suspicion of intention to cause harm to self or others. If at any time, any of the completed questionnaires or interviews reveal any such concerning information, we will notify you of our concerns and, if necessary, contact the appropriate officials. Specifically, if you tell us that you have intent and/or a plan to harm yourself or someone else, we will call 911.

There may be other risks that are currently unknown. Our study staff will update individuals of any new potential risks or discomforts as they arise.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this study. If you are assigned to the groups that receive study medications (Groups 1 and 2), you may have a good response to varenicline and/or the vaping cessation sessions may be able to quit vaping. However, there is no guarantee that you will benefit in any way. Information from this study may help other people quit vaping in the future.

What other treatments or procedures are available for your condition?

Your study doctor will discuss with you the good points and bad points of taking part in this study and your options for quitting vaping if you do not take part in this study.

There are no FDA-approved medications for helping to quit vaping. There are, however, 7 FDA-approved medications to help people quit smoking: 5 nicotine replacement therapies (patches, gum, lozenges, inhaler and nasal spray), bupropion (Zyban®), and varenicline (Chantix®). All reduce nicotine withdrawal symptoms. These treatments are often combined with individual or group counseling and some supportive intervention.

Varenicline is approved by the FDA for individuals aged 18 and older, but not for individuals under age 18 so it may not be available outside of a research study if you are 16 or 17 years of age.

In addition, individual or group counseling is available outside this study and can be helpful in stopping smoking. Talk with the study doctor if you have questions about any of these treatments or procedures.

Can you still get medical care within Partners if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

Independent of your group assignment, you will have the chance to earn $1188 by participating in our study. You will be paid for the completion of each study visit. You will be paid $30 for completing the enrollment visit and all subsequent weekly and follow-up visits. For each monthly assessment visit you will be paid $50 if you are in the varenicline or placebo group, and $100 if you are in EUC. If you complete all study visits from enrollment through week 24, you

will earn $738 if you are in the varenicline or placebo group, and $720 if you are in Enhanced Usual Care.

All participants who complete the study will have a chance to win a study completion bonus. For participants in the varenicline or placebo groups, the bonus is $450, and for the EUC group, it is $468. Including this bonus, all participants can make up to $1188 for participating in our study. For every ten people who complete the study (through week 24), one participant will be drawn as a winner.

If you are assigned to the varenicline or placebo group (Groups 1 and 2), you can receive micropayments of up to $2 per day for emocha medication adherence and REDCap survey completions, for a maximum of $168. If you are randomized to the EUC group (Group 3) you will not receive any micropayments.

If you come in for the enrollment visit but are found to be ineligible, you will still be paid for the enrollment only ($30). Payment will be provided in between visits. If you want to stop being in the study, you can stop at any time, but you will be paid only for the visits you have completed. Please refer to the table below for a complete breakdown of study payments:

Visit/Week	**Varenicline/Placebo**	**EUC**
Enrollment	30	30
Weeks 0, 1, 2, 3	30	30
Week 4	50	100
Weeks 5, 6, 7	30	30
Week 8	50	100
Weeks 9, 10, 11	30	30
Week 12	50	100
Week 16, 20, 24	30	30
Emocha + surveys	168	0
Total	**738**	**720**
Bonus	450	468
Grand Total	**1188**	**1188**

You will be reimbursed up to $15 for necessary travel for in-person visits.

We will use an approved, outside vendor (Advarra), or checks to make study visit payments to you via a reloadable credit card-based system, called Advarra Participant Payments. This secure system is similar to a gift card. You will be given an Advarra Payments Visa card when you enroll in the study. Once the card is activated, the study team will add your payment your card after you complete each visit. The payment should be available to you within a day, and you may

use the card anywhere Visa cards are accepted, such as at a grocery store. If you cannot be paid via Advarra or checks because you do not have a social security number or individual taxpayer identification number, we will pay you via gift card.

We will need to collect your Social Security number to make these payments, and it will be shared securely with Advarra, the company that runs the card-based system. If you are under 18 and would like to be paid through Advarra, you need to provide us with your parent or guardian's social security number, date of birth, and address to make these payments. Payments are considered taxable income. If you receive more than $600 a year from Partners HealthCare, Partners will issue a 1099 form to you and to the Internal Revenue Service for income reporting purposes. After you sign this consent form, you will be asked to sign an agreement form or provide a verbal agreement of Advarra procedures, acknowledging your understanding of the Advarra payment system.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

There is no cost to you for taking part in this study. The cost of all the tests and procedures done for research will be paid for by study funds.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Partners to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Partners researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other researchers within or outside Partners, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate,

unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Parent(s)/Guardian for Child:

I give my consent for my child to take part in this research study and agree to allow his/her identifiable information to be used and shared as described above.

_____	_____	_____
(Print) Parent(s)/Guardian for Child	Date	Time (optional)
_____	_____	_____
(Signature) Parent(s)/Guardian for Child	Date	Time (optional)

Relationship to Subject: _____

Assent

Statement of Person Giving Assent

- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions, and my questions have been answered.

Signature of Child:

I agree to take part in this research study and agree to allow my health information to be used and shared as described above.

Child, Ages 16-17	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version Date: 11/08/2023