UW HS-IRB #2017-1090

UNIVERSITY OF WISCONSIN-MADISON

Subject CONSENT to Participate in Research
and
AUTHORIZATION to Use and/or Disclose Identifiable Health Information for Research

Title of the Study: E-cigarette Effects on Markers of Cardiovascular and Pulmonary Disease Risk Study (aka CLUES - Cardiac and Lung Ecig Smoking study)

Principal Investigator: James H. Stein, MD
600 Highland Avenue, MC 3248
Madison, Wisconsin 53792
Phone: (608) 262-2075

Study Funding: National Heart, Lung and Blood Institute

INVITATION

You are invited to participate in a research study about the health effects of using electronic cigarettes ("e-cigarettes") and conventional cigarettes. You are being invited because you expressed an interest as someone who uses cigarettes, e-cigarettes, or because you never used either product. Approximately 440 people will participate in this study.

Optional study: On a subset of 100 participants, some of the tests we will perform on your blood will be genetic testing, which is done on your DNA. DNA, or deoxyribonucleic acid, carries the genetic instructions for the cells that make up your body. Genes tell your body how to do things like form your spine, or what color your eyes should be.

Your participation in this research study is voluntary. If you decide not to participate, the health care that may be provided to you by the University of Wisconsin-Madison (UW-Madison) and its affiliates (UW Health, the University of Wisconsin Hospital and Clinics, and the University of Wisconsin Medical Foundation) will not be affected in any way.

A. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this research is to compare the health effects of using e-cigarettes and conventional cigarettes or their combination on the heart, lung, and blood vessel function.

B. WHAT WILL MY PARTICIPATION INVOLVE?

IRB Approval Date: 5/5/2021
University of Wisconsin – Madison

If you decide to take part in this research study, you will be asked to attend another visit within 1-2 weeks after today's orientation visit, only under exceptional circumstances the second visit could be up to one month from today. In total, you will attend 2 visits. For your next visit you will start your appointment at the UW Center for Tobacco Research and Intervention (CTRI) office and finish the visit at UW Hospital (600 Highland Avenue, Room K6/319).

Today, for this Orientation and screening visit (V1) you will:

1. Complete several surveys. The surveys will include questions about your health history and your smoking and e-cigarette use (when and how often you smoke, vape, or Juul), how dependent you are on nicotine, your mood, your thoughts about cigarettes and e-cigarettes, your health, and basic information about you (such as your age and gender). These will take approximately 30 minutes to complete.
2. We will measure your height, weight, and waist circumference
3. You will be asked to provide a urine sample to test for nicotine and its breakdown in the urine
4. You will provide breath samples to measure carbon monoxide (a substance contained in cigarette smoke) to measure how much you smoke. After inhaling deeply and holding your breath for 15 seconds, you will breathe out into a disposable straw that will be placed over a sensor.

Things to accomplish **at home** between V1 and V2 visits (this applies to users only, not for controls).

1. At this office visit we will give you a smartphone to carry until next appointment. For a week before your next appointment, you will be asked to press a button every time you smoke or vape/Juul. Every night the smartphone app will ask you to answer a few questions about your smoking or vaping/Juuling. These responses help us collect real-time data to assess smoking behaviors and environments.
   a. The ap does not collect any information about you, or data on it – only study related research information.
   b. You will not be responsible for the cost of the study smartphone data plan.

   A few days before your final appointment we will send you an email and text your cell phone with location information and instructions

Your second (and final visit, V2) will start at the UW Center for Tobacco Research and Intervention, located at 1930 Monroe St, Suite 200, Madison, WI 53711.

You will be asked to:

1. Come in the morning after fasting from food, refraining from caffeine and not smoking or vaping/Juuling or using any nicotine-containing products for 8 hours.
2. Return the phone.
3. Bring your smoking/vaping or Juuling products.
4. We will repeat the carbon monoxide tests and the urine tests described above.
5. We will perform an ultrasound study of the carotid arteries in the neck. The ultrasound scan takes about 20 minutes. Gel will be applied to your neck and images the carotid artery will be obtained using gentle application of an ultrasound wand. Most people experience no discomfort with this test.

6. We will detect the pulse in your right wrist and will gently rest a small cylinder shaped sensor (a tonometer) on it to record the waveforms of your pulsations in a laptop computer

During this visit, you will complete a few tests before and after smoking/vaping your own cigarette/e-cigarette. If you are part of the never-smoker group, we will repeat the tests 30 minutes apart, but you will not be exposed to smoke. The procedures that we will perform before and after smoking/vaping/Juuling challenge include:

1. Placement of a small needle in your arm to draw blood before and after smoking. Four to six small tubes of blood will be taken in total.
2. Left upper arm blood pressure measurements repeated every 5 minutes with an automated blood pressure monitor.
3. Heart rate monitoring by applying 3 sticky patches to your chest and connecting them to a computer with software that can monitor heart rate variations.
4. Ultrasound scan of your arm. We will use an ultrasound wand and gel to take images of your brachial (upper arm) artery. We first measure the artery size and blood flow, then we inflate a small pressure cuff on your forearm and release it after 5 minutes. Some people find the cuff inflation to be mildly uncomfortable because it is tight. When we release the cuff, the blood flow to your hand will increase. We will record changes on brachial artery size and flow after we release the cuff in order to see the natural response of your artery to this increased flow. This test will take about 10 minutes.
5. Lung function tests where you will be asked to hold your breath and then breathe out as quickly and for as long as you can into a tube. This will measure the health of your lungs.
6. You may have a 12-lead electrocardiogram (ECG or EKG) that uses 12 sticky patches to record the electrical pattern of your heart.

Following these baseline tests, you will be allowed to smoke or vape your own cigarettes/e-cigarette/Juul as you normally would for up to 20 minutes while we electronically record (videotape) you to assess how you smoke/vape. Never-smokers will not need to smoke or vape but will wait around for 30 minutes before performing the second round of tests. Never-smokers will not be videotaped.

We then will ask smokers some questions about their smoking/vaping experience and have all subjects complete another blood draw, blood pressure measurements, heart rate monitor, upper arm ultrasound test, and lung function tests. Video recordings will be destroyed after they have been analyzed.

You will be able to have a light snack before driving to the UW Hospital (600 Highland Avenue, Room K6/319), but asked not to smoke or vape during the drive, before the treadmill stress test (your final assessment):

1. For the stress test, we will apply sticky patches to your chest for an electrocardiogram to monitor the electrical activity of your heart at rest while laying down, then standing-up before we start the treadmill, while you walk or jog on the

treadmill, and after you return to the bed. For better contact of the stickers with the skin, we might need to shave the spots where we place the patches, and thoroughly clean the area for better adhesion.

2. After 5 minutes of resting electrocardiogram recordings, you will walk on a treadmill adjusted to your pace and fitness level. The incline of the treadmill will be increased every 2 minutes. Some participants will reach their peak exercise while walking briskly, while others might need to jog to reach the desired heart rate. Your blood pressure and electrocardiogram will be monitored at all times. You will exercise until one of three things happens:
    - You feel unable to continue, usually because you are too tired;
    - You develop severe shortness of breath or chest discomfort; or
    - We stop you if there are concerns about your medical condition in response to the exercise.
3. After a few minutes of a cool down walk on the treadmill, you will return to the bed. Your blood pressure and electrocardiogram will be monitored until you are back to baseline. Blood pressure measurements are obtained from your upper arm every 2-4 minutes during the test using a manual or automated blood pressure monitor.

Your participation during these 2 visits will last about 90 minutes today and up to 4 hours for the last visit. The smartphone assessments should take about 5 minutes per day. This should result in about 6 hours of total participation time over the next 2 weeks.

To summarize, we will collect the following health information about you for this research study:

1. From you:
    - Information about you, such as your birth date, sex, race, initials, appointments dates/time, height, weight and waist circumference
    - home address, home phone number, and alternative phone number to contact you during the study
    - Information about your health, and your use of tobacco products.
2. From tests or other procedures done for this study:
    - Results from the following medical tests: blood work, urine test, carbon monoxide tests, carotid and brachial artery ultrasounds, stress test, ECG tracings, blood pressure measurements and tracings, and lung function tests

3. Optional Genomic Study:

From some of the blood drawn, some blood cells will be separated and used to obtain DNA and RNA and to do other types of research to help us learn more about the causes of cardiovascular disease, the effects of smoking or vaping. These samples will be sent to Duke University for processing de-identified. The samples shipped outside the UW will be labeled using a code number that is linked to your name, but this link will never be shared outside the UW.

Any remaining cell samples sent to Duke University will be destroyed, and never sent back to us or used for any future analyses. The team that collaborates with us on this

optional genomic study is from Duke University School of Medicine, Duke Molecular Physiology Institute, Immunogenomics Program under the direction of Dr Yongmei Liu, M.D., Ph.D., within the Department of Medicine, Division of Cardiology, Room 50-102, Carmichael Building, 300 N Duke St, Durham, NC 27701-2047

By signing this form, you are giving us permission to collect the information described above.

C. ARE THERE ANY BENEFITS TO ME?

You are not guaranteed any benefits from participating in this study. Your participation in this research may benefit other people in the future by helping us learn more about cigarettes and e-cigarettes, and how they may influence cardiac and pulmonary health.

D. WILL I BE PAID FOR MY PARTICIPATION?

You will receive up to $200 over the course of this 2-week study:

- $50 for attending this orientation visit (visit 1)
- $50 for completing at home the EMA prompts (smart phone app questions)
  - $2 for each evening report for up to $14,
  - $36 for returning the smartphone
- $100 for completing visit 2 ($60 for part one at CTRI, and $40 for the stress test at UW Hospital)
- For participants that drive more than 1 hour for the visit, they will be compensated for mileage
- Parking is covered at all locations
- In case we find out that you do not qualify to participate in the study during the first in-person visit, we will reimburse you $20 for attending

You will receive a check after you complete your last visit.

E. ARE THERE ANY COSTS TO ME?

The study tests will be provided at no cost to you. Any costs related to your medical care will be your responsibility.

F. WILL THE RESULTS OF ANY OF THESE RESEARCH TESTS BE REPORTED TO ME?

As part of this study, you will be given the results of your heart rate, blood pressure, white blood cell count, hemoglobin concentration, lipid (blood cholesterol and fats) and hemoglobin A_1C (a measurement of 3-month blood sugar control) values, pulmonary function test, and stress test that may improve the understanding of your health. We will not provide an interpretation of these results and will not provide these results to your physician, though you are encouraged to discuss them with your primary medical care provider. If you have concerns about these test results, please contact your primary medical care provider directly.

For Optional Study Participants: Genetic information will not be reported to you.

G. ARE THERE ANY SIDE EFFECTS OR RISKS TO ME?

The main risk of taking part in this study is that your study information could become known to someone who is not involved in performing or monitoring this study, known as a breach of confidentiality. You may find that completing the surveys is time-consuming. Some people may experience temporary unpleasant withdrawal symptoms during the 8 hours they have to abstain from using any nicotine products prior to the study visits. Some people may also experience slight discomfort during the lung function test when they are asked to blow as long and as hard as they can into the tube. A blood draw is mildly uncomfortable because of the needle stick. In rare cases, people become light headed and may pass out, or get a bruise or infection at the site of the blood draw. For the stress test, trained personnel will attach several sticky patches to your chest and connect wires to them. We may have to shave off some chest hair so the patches will stick to your skin and for females, we will provide gowns to maintain your privacy as you walk on the treadmill. As you walk on a treadmill your legs might feel tired or your breathing become more rapid as you exert yourself.

Whenever medical testing is done, there is the chance of finding something unexpected. Unexpected findings can have clear clinical significance, or uncertain clinical significance. Clear clinical significance means that the results show a problem that may be treatable and we generally know what the risks are of not treating the problem. Uncertain clinical significance means that the test shows something unusual, but we do not know if it might affect your health, and treatment may not be appropriate or possible.

You will be informed of any findings of clear clinical significance that may be discovered during the imaging procedures, but you will not be informed if there are findings of uncertain clinical significance. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate). The images we are collecting for this research study are not the same quality as images that you may have as part of your health care and will not be included in your medical record. If you believe you are having symptoms that may require clinical imaging, you should contact your primary care physician or health care provider.

Optional Study Participants: The DNA/RNA samples and information sent to other researchers will not include personal information like your name or your birthdate. However, even without your name or other identifiers, your genetic information is unique to you, like a fingerprint. Scientists expect that over the next few years, researchers will be able to look at your genetic information and be able to trace the data back to you (and potentially also to your blood relatives). The collaborators at Duke will not run a full genome sequence, therefore the risk of identification will be minimized.

There may be other risks related to genetic testing that we don't know about right now. This is because the field of genetics is moving forward very quickly.

H. WILL THERE BE COMPENSATION FOR INJURY?

If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency medical problems, contact your regular health care provider.
- Call the Principal Investigator, Dr James H. Stein at (608) 262-2075 to report your sickness or injury.

Here are some things you need to know if you get sick or are injured because of this research:

- If the sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.

I. HOW WILL MY PRIVACY BE PROTECTED AND WHO WILL USE MY HEALTH INFORMATION?

We will protect your confidentiality by storing your data, including video recordings, on a secure, password-protected data server accessible only by study staff. Your data will be identified by a subject identification number, not by name. This informed consent document (which contains your name) will be stored apart from other study data in a locked cabinet. All research records will be treated confidentially. Your name will not appear in any publication of the results of this study.

The information collected from you during this study will be used by the researchers and research staff of the UW-Madison and its affiliates (UW Health) for this study. It may also be shared with others at the UW-Madison and outside the UW-Madison. Whenever possible your health information will be kept confidential.

Others at UW-Madison and its affiliates who may need to use your health information in the course of this research:

- UW-Madison regulatory and research oversight boards and offices
- Accounting and billing personnel at the UW-Madison and UW Health
- Research support services at the UW-Madison and its affiliates

Others <u>outside</u> of UW-Madison and its affiliates who may receive your health information in the course of this research:

- The National Heart, Lung and Blood Institute (the study sponsor)

- Duke University, Department of Medicine – Cardiology Division, Immunogenomics Program.

People outside the UW-Madison and its affiliates who receive your health information may not be covered by privacy laws and may be able to share your health information with others without your permission. Usually when we share information from research studies with others outside the UW-Madison and its affiliates it is not shared in a way that can identify an individual.

If you share with your physician study results that we reported directly to you, those results could end up in your medical record.

A description of this clinical research study is available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website 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.

J. IS MY PERMISSION VOLUNTARY AND MAY I CHANGE MY MIND?

Your decision to participate in this research study is voluntary. You may choose not to participate. You do not have to sign this form and you may refuse to do so. If you refuse to sign this form, however, you cannot take part in this research study. You may completely withdraw from the study at any time. You also may choose to stop participating or skip any questions that you do not feel comfortable answering.

If you decide not to participate in this study or if you stop while the study is underway, the health care you receive from the UW-Madison and its affiliates and your primary care clinic will not be affected in any way.

K. HOW LONG WILL MY PERMISSION TO USE MY HEALTH INFORMATION LAST?

By signing this form you are giving permission for your health information to be used by and shared with the individuals, companies, or institutions described in this form. Unless you withdraw your permission in writing to stop the use of your health information, there is no end date for its use for this research study. You may withdraw your permission at any time by writing to the person whose name is listed below:

James H. Stein, MD
600 Highland Avenue, MC 3248
Madison, Wisconsin 53792
Phone: (608) 262-2075

Beginning on the date you withdraw your permission, no new information about you will be used. Any information that was shared before you withdrew your permission will continue to be used. If you withdraw your permission, you can no longer actively take part in this research study.

L. WHO SHOULD I CONTACT IF I HAVE QUESTIONS?

If you have questions about this research, please contact the Lead Researcher, Dr. James H. Stein at (608) 262-2075. If you have any questions about your rights as a research subject or have complaints about the research study or study team, contact UW Health Patient Relations at 608-263-8009. The Patient Relations Representatives work with research subjects to address concerns about research participation and assist in resolving problems.

AGREEMENT TO PARTICIPATE IN THIS STUDY AND
PERMISSION TO USE AND/OR DISCLOSE MY HEALTH INFORMATION

You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study.

If you sign the line below, it means that:

- You have read this consent and authorization form.
- You have had a chance to ask questions about the research study, and the research team has answered your questions.
- You want to be in this study.
- You give authorization for your protected health information to be used and shared as described in this form.

YOU WILL RECEIVE A COPY OF THIS FORM AFTER SIGNING IT.

_____ _____
Printed Name of Participant Date

_____ _____
Signature of Participant Date

_____ _____
Printed Name of Person Obtaining Consent Date

_____ _____
Signature of Person Obtaining Consent Date

AGREEMENT TO PARTICIPATE IN THE OPTIONAL GENOMIC STUDY

_____ _____
Printed Name of Participant Date

_____ _____
Signature of Participant Date

_____ _____
Printed Name of Person Obtaining Consent Date

_____ _____
Signature of Person Obtaining Consent Date