COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY
YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Impact of cigarette and e-cigarette flavors on adult smoking behavior
Principal Investigator: Krysten Bold, Ph.D.
Funding Source: National Institute of Health

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to look at the effects of cigarette and e-cigarette flavors on smoking behavior among adults who currently smoke cigarettes.
- Study procedures will include: an intake appointment to determine eligibility, then follow-up visits. Research visits will include questionnaires and breath and urine samples. You will be provided with cigarettes and e-cigarettes that you may use during the study.
- 6 visits are required and may occur remotely or at a convenient location.
- These visits will take 3-4 hours total.
- There are some risks from participating in this study: completing research rating scales, potential loss of confidentiality, and cigarettes and e-cigarettes contain nicotine which is addictive.
- The study may have no benefits to you. This study is not designed to help you quit smoking. If you do wish to quit smoking, please inform the research assistant and he/she will give you referrals regarding treatment options. Study results may help us understand better understand smoking behavior and the impact of flavors in tobacco products.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.
- We care about your safety as a research participant. Because participating in this study may involve travel outside of your home and exposure to others during a pandemic, we will discuss ways to minimize risks related to COVID-19. Before you decide whether to participate in this study, talk to your study doctor or the researcher about anything you do not understand or any concerns you may have.

Why is this study being offered to me?

You are invited to participate in a research study designed to look at the effects of cigarette and e-cigarette flavors on smoking behavior. You have been asked to participate because you are at least 21 years old, report use of cigarettes in the past 30 days, and do not want to quit smoking. About 50 subjects will be enrolled into this study.

What is the study about?

The purpose of this research study is to look at the effects of cigarette and e-cigarette flavors on smoking behavior among adults who currently smoke cigarettes. If you take part in this research study, you will be asked to complete 6 research appointments. Research appointments can be completed remotely, at our office, or a location that is convenient to you, such as a public place.

What are you asking me to do and how long will it take?

If you agree to take part in this study, this is what will happen:

1. Intake appointment: At the initial screening appointment which may take place remotely, you will speak with our research staff by phone or video call. You will be asked to complete a number of questionnaires that will ask you about your smoking, mood, and psychological characteristics. These questionnaires will be completed through the Yale Qualtrics system, a secure online survey system. In addition, we will ask for demographic information including age, sex, ethnic/racial identity, and educational activities. We will ask you questions about your medical history and any recent concerns or problems with your health.

2. If you appear to be eligible for the study after this intake appointment, we will schedule you for a brief (5-10 minute) in-person screening before proceeding with the study. At this screening, you will be asked to provide a urine sample to test for pregnancy (if female), cotinine (which is a byproduct of nicotine), menthol (which is a flavor additive in certain tobacco products), and to verify that you are not currently using other drugs. You will be asked not to use any drugs while you are participating in this study. If you test positive for any drugs, you will not be paid for the visit and will have the opportunity to reschedule this appointment one time. If you are pregnant or are trying to become pregnant, you will not be enrolled in the study. You will also be asked to complete a breath carbon monoxide (CO) test to help us understand your current use of tobacco products. We will measure your blood pressure and heart rate. We will measure your pulse oximetry, which measures how well oxygen is being sent through the body, using a clip-like device on your finger that is quick and painless. If you are eligible for the study based on the screening visit, you will be enrolled in the study and scheduled to return for research visits.

3. COVID-19 screening and safety measures: For your safety, if you are eligible and choose to enroll in the study, we will ask that you monitor yourself daily for symptoms of COVID-19 and alert the research team if you have any symptoms or concerns. We will ask about the following symptoms: a) cough, b) shortness of breath, c) difficulty breathing, d) fatigue, e) fever greater than 99.9 F, f) repeated shaking with chills, g) muscle aches or pain, h) body aches, i) headache, j) sore throat or k) congestion or runny nose, l) nausea or vomiting, m) diarrhea, n) *new* loss of taste or smell. We will ask you to report on any COVID-19 symptoms using an online questionnaire every 72 hours and prior to in-person study visits. This questionnaire will be sent to you via an online link to your cell phone or email. Depending on your symptoms, we may need to call you to follow up on your symptoms. You will not be allowed to attend in-person visits until your COVID-19 symptom questionnaires are completed. If you are not able to fill out the questionnaire online, study staff can administer the questionnaire by phone.

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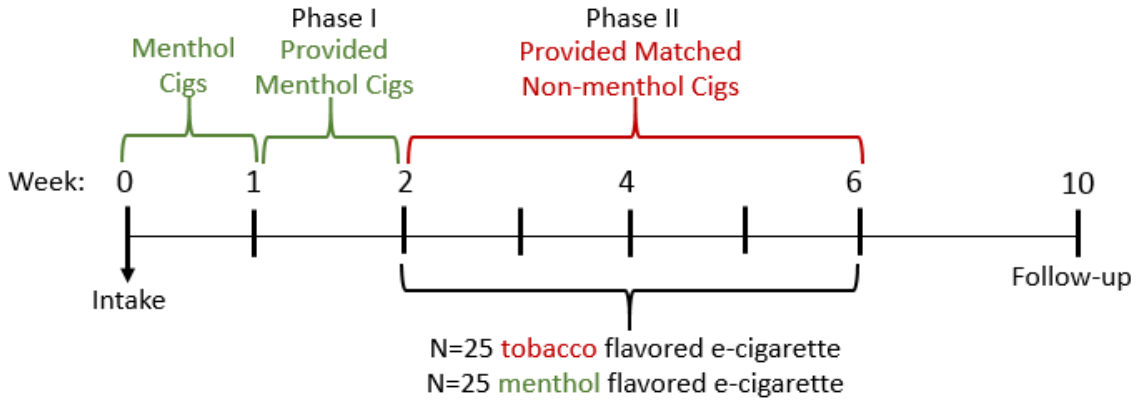
If you develop symptoms for COVID-19 or have known or suspected exposure, please self-isolate, monitor your symptoms, and contact your healthcare provider to discuss obtaining a test for COVID-19. Please inform research staff if you develop any of these symptoms or have known/suspected exposure to COVID-19. Please review the CDC guidelines for up to date information about COVID-19:
https://www.cdc.gov/coronavirus/2019-ncov/index.html

For your safety, at all in-person appointments, you will be asked to wear a mask and study staff will wear masks and gloves. If you do not have a mask, one will be provided to you by the study staff. For your safety, best practice health and safety measures will be used for any in-person contact including sanitizing and disinfecting all devices before and after use, maintaining social distancing, using hand sanitizer and frequent hand washing, and use of masks and gloves by staff and all participants.

4. Research appointments: Research visits will occur at weeks 1, 2, 4, 6, 10. Visits will last about 30 minutes each. You will be asked to complete research assessments including surveys which can be done remotely online or by phone or video contact. We will ask you about your use of cigarettes and e-cigarettes. We will ask you about how you are feeling and if you have any recent changes or problems with your health. At follow-up in-person visits we will conduct a brief (5-10 minute) evaluation where you will be asked to provide breath samples for carbon monoxide (CO), and you will be asked to provide urine samples to monitor cotinine and menthol levels and test for pregnancy (if female). If you become pregnant at any point in the study, we will stop study procedures and will not give you cigarettes/e-cigarettes to use. You can still participate in the end of study assessment to complete survey questionnaires. We will also measure your blood pressure and heart rate at follow-up appointments as recommended by the study physician.

5. Cigarette/e-cigarette use: During the study, you will be provided with cigarettes and e-cigarettes to understand your smoking behavior and preference for various products. During the first week, you may smoke your own usual cigarettes. We will provide cigarettes for the remaining time in the study, menthol cigarettes for 1 week, and non-menthol cigarettes for 4 weeks. We will collect any remaining menthol cigarettes from you before switching you to non-menthol cigarettes. If you choose to smoke cigarettes, we will ask you to smoke the cigarettes provided and collect and return all spent cigarette filters. We will also provide you a JUUL e-cigarette device and prefilled e-liquid pods/cartridges to use for 4 weeks. We will randomly assign you, like with a flip of a coin, to receive either a tobacco or menthol-flavored e-cigarette. If you choose to use an e-cigarette, we ask that you only use the device and e-liquid pods provided and collect and return all used e-liquid pods at each visit. We ask that you do not use any other tobacco products during the study and you should not attempt to modify the e-cigarette device in any way. We will ask you to return the JUUL device at the last visit, week 10.

Study Timeline:



What are the risks and discomforts of participating?

The potential risks in this study are related to 1) use of cigarettes/e-cigarettes, 2) urine and breath collections, 3) rating scales and assessments, 4) potential loss of confidentiality.

1) Use of cigarettes/e-cigarettes:

You were asked to participate because you are currently a daily smoker, therefore reducing the risk to experience any kind of adverse reaction to nicotine-containing tobacco products. The e-cigarette delivers nicotine much in the same way that a regular cigarette does. As a current cigarette smoker, you are already self-administering nicotine and already have experience with tobacco products with flavors such as menthol.

People who use any nicotine product may experience adverse reactions if they use too much nicotine (e.g., nausea, vomiting, headache, diarrhea, rapid heartbeat, hearing and vision problems, syncope, seizure, hypotension, and irregular pulse). You can decide how often you use the cigarettes and e-cigarettes in this study. If you experience these or other symptoms, we recommend you reduce your cigarette and/or e-cigarette use. Please let us know of any symptoms you experience.

There have been recent reported cases of severe pulmonary illness linked to “vaping” or e-cigarette use. These cases included symptoms such as coughing, shortness of breath, chest pain, fever, fatigue, nausea, vomiting, diarrhea, and/or abdominal pain. Some patients reported symptoms to have occurred over a few days and some reported to have occurred over a few weeks. Deaths have occurred. The CDC identified that vitamin E acetate was a chemical found in the e-liquids associated with these lung injury cases. In most cases, people experiencing these symptoms were using cannabidiol (CBD) or marijuana (THC) e-liquids, and/or were using e-cigarette devices and e-liquids that were mixed at home or purchased off market (such as purchasing an e-liquid or device on the street, not from a licensed retailer).

The e-cigarettes and e-liquid pods that we use in the current study are purchased only from a licensed retailer and do not contain CBD or THC, and are tested to ensure they do not contain vitamin E acetate. Additionally, the JUUL device used in this study is a “closed” e-cigarette system meaning that the pods and e-liquids cannot be hacked or tampered with in any way. The pods we are giving you contain nicotine, solvents, and flavorings. At this time, we do not know much about the risks associated with the use of e-liquid flavors used in this study (such

as allergic reactions). If you choose to use the e-cigarette in this study, you should only use the e-cigarette pods provided and should not hack or modify the e-cigarette device in any way. **However, despite these safety measures it is possible that you could still be affected.**

We will assess your health at the intake to make sure you are healthy prior to participating and will continue to monitor your health closely during the study. If you experience any side effects or concerns during the study, (such as abdominal pain, nausea, vomiting, diarrhea, cough, shortness of breath, chest pain) or other concerns, please let us know and let your doctor know promptly (right away). Go to the emergency room if your symptoms increase. You can stop the study at any point. If you feel any discomfort or need to stop for any reason, please let the research team know. The CDC requires the hospital to report to the State Health Department and the CDC cases of illness after using e-cigarettes. The report will contain the name and address of the person who is ill.

E-cigarettes contain other chemicals besides nicotine including propylene glycol/vegetable glycol/vegetable glycerin. At this time, we do not know the risks associated with the propylene glycol/ vegetable glycerin that may in the fillers in the liquids used in this study.

It is important to note that there may be unforeseen risks (such as allergic reactions). We will be using e-liquids that are freely available for purchase and the propylene glycol/vegetable glycerin doses will be what is available in these e-liquids. Some research has indicated that in large doses propylene glycol and vegetable glycerin can be harmful. All levels of e-liquids administered in this research study are below any potentially harmful levels. However, if you experience any side effects, you can stop the study at any point. If you feel any discomfort or need to stop for any reason, please let the researcher know.

The CDC has warned against vaping e-cigarettes
The CDC (www.cdc.gov) has issued the below recommendations for e-cigarette use:

- CDC and FDA recommend that people not use THC-containing e-cigarette, or vaping, products, particularly from informal sources like friends, family, or in-person or online dealers.
- Vitamin E acetate should not be added to any e-cigarette, or vaping, products. Additionally, people should not add any other substances not intended by the manufacturer to products, including products purchased through retail establishments.
- Adults using nicotine-containing e-cigarette, or vaping, products as an alternative to cigarettes should not go back to smoking; they should weigh all available information and consider using FDA-approved smoking cessation medications. If they choose to use e-cigarettes as an alternative to cigarettes, they should completely switch from cigarettes to e-cigarettes and not partake in an extended period of dual use of both products that delays quitting smoking completely. They should contact their healthcare professional if they need help quitting tobacco products, including e-cigarettes, as well as if they have concerns about EVALI. We will provide you with referral sources to quit smoking if you are interested.
- E-cigarette, or vaping, products (nicotine- or THC-containing) should never be used by youths, young adults, or women who are pregnant.
- Adults who do not currently use tobacco products should not start using e-cigarette, or vaping, products.

- THC use has been associated with a wide range of health effects, particularly with prolonged frequent use. The best way to avoid potentially harmful effects is to not use THC-containing e-cigarette, or vaping, products.

  Although the science on the relationship between tobacco use such as cigarettes and e-cigarettes is still unclear, you should remember that using tobacco products like cigarettes can lead to respiratory conditions like COPD. Therefore, if you use tobacco products and become infected with COVID-19, there is a potential that you could have worse health outcomes. We recommend you follow the CDC guidelines for the most up to date information about ways to reduce your risk for exposure to COVID-19. https://www.cdc.gov/coronavirus/2019-ncov/index.html

  If you develop symptoms for COVID-19 (fever, cough, shortness of breath, difficulty breathing, muscle aches, sore throat, congestion or runny nose, nausea or vomiting, diarrhea, new loss of taste or smell) or have known or suspected exposure, please self-isolate and contact your healthcare provider to discuss obtaining a test for COVID-19. Please inform research staff if you develop any of these symptoms or have known/suspected exposure to COVID-19. If you become infected with COVID-19, we recommend you stop using all tobacco products.

2) Urine and breath collections: Urine and breath sample collections will be done at your intake appointment and each research visit as a way to understand more about your tobacco product and drug use. Urine and breath sample collection does not pose any physical risks. Only trained research staff will know the results of these tests, and results will not be disclosed to others. Any obtained results will only be recorded with a study ID number and not your name.

3) Rating scales and assessments: These are all noninvasive and should add no risk. The major disadvantages are the time taken to complete them, and possible breach of confidentiality. We have done our best to make the assessment schedule in this study as brief as possible. Also, our past experience with these measures indicates that they are acceptable to participants. All answers you provide will only be recorded with a study ID number and not your name.

4) Potential loss of confidentiality: We do not reveal any personal information collected as part of the research procedures, including your reported tobacco use and other substance use history. Careful efforts aimed at maintaining confidentiality will be made.

How will I know about new risks or important information about the study?

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

How can the study possibly benefit me? How can the study possibly benefit other people?

There are no direct benefits to you for your participation. We expect that the results of the study, however, will benefit science and others by helping us learn more about how tobacco product flavors affect smoking behavior.

Are there any costs to participation?

You will not be charged for any aspects of the study.

Will I be paid for participation?
You will be paid $30 for the baseline intake appointment and will receive $20 for visits at weeks 1, 2, and 4, and $30 cash for visits at weeks 6 and 10. You will receive a $20 bonus for returning the JUUL device and charger at the last visit, week 10. You have the chance to earn an additional $50 bonus through weekly bonus payments for returning the spent cigarette filters and e-liquid cartridges ($10). Maximum earnings for completing all study procedures is $220. We will use a Bank of America pre-paid debit card to provide the payment for taking part in the study. We will have to share your name, address, and telephone number with Bank of America for ePayments. You will receive a card in the mail with the first payment. You will need to activate the card over the phone. Each additional payment will be automatically added to your card.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.

What are my choices if I decide not to take part in this study?
Instead of participating in this study, you have other choices. You could take part in another study. This is not a treatment study. If you are currently interested in quitting tobacco product use, we will provide you with a treatment referral and you will not be eligible to participate in this study. If you would like access to treatment resources at any point during the study, you must let a study staff member know.

What are my responsibilities as a participant?
You should be aware that as a participant in a research study, you have certain requirements and responsibilities. Your requirements/responsibilities during the study are to:

1. Not use any drugs including marijuana during your participation in the study.

2. Report all changes in your physical or mental condition during the course of the study to the study staff whether or not they are related to study procedures.

3. If you need to have any emergency medical procedures while you are participating in this study, please let the research staff know immediately.

4. Tell the research staff immediately if you have:
   - A side effect (including shortness of breath, chest pain, fever, fatigue, nausea, vomiting, diarrhea, and/or abdominal pain)
   - An injury
   - Any symptom or complaint

If you have questions, an injury or any symptom or complaint, you should contact the Principal Investigator for this study, Dr. Bold (203-974-7603 or 203-530-1724).

How will you keep my data safe and private?
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or

biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse or neglect, or harm to self or others.

If you decide to be in this study, the researcher will have information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and street number and date of birth. This information will be kept for 7 years. After that time it will be destroyed or de-identified, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, but this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this study.
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Laboratory, and other test results
    - Questionnaires
    - Use of tobacco products and other drugs

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study
- Bank of America for processing payments

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to ***Krysten Bold, Ph.D., 34 Park Street CMHC,*** at the Yale University, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?
If you are injured as a result of your participation in this study, you or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this consent form.

What if I want to refuse or end participation before the study is over?
Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. The study team may decide to take you out of the study without your agreement if:

- You do not follow the directions of the study team;
- The study team decides that the study is not in your best interest;
- You become pregnant, intend to become pregnant or are nursing a child during this study.

What will happen with my data if I stop participating?
When you withdraw from the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Who should I contact if I have questions?
Please feel free to ask about anything you don't understand. If you have questions later or if you have a research-related problem, you can call the Principal Investigator at **203-974-7603.**

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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 Web site will include a summary of the results. You can search this Web site at any time.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study. We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Consent to Recontact

The research team may wish to contact you in the future, to clarify questions from the questionnaires or interviews, or to invite you to participate in other studies. Therefore, we ask your permission to contact you in the future. Giving your permission for the research team to contact you does not obligate you to answer any future questions, or to participate in any future research – you always have the right to decline further participation in research. Please indicate your preference about future contact by writing your initials in one of the spaces below:

Initials: _____ I give the research team permission to contact me in the future.
Initials: _____ I DO NOT give the research team permission to contact me in the future.

Consent for Forwarding Address

Please provide the names of two friends or relatives that we can contact in case we cannot reach you. We will contact these individuals only if we are unable to reach you directly, and we will only ask for a forwarding address or updated phone number. Research staff will only identify themselves as calling from Yale University and will not share any information about the research study or your participation.

Name: _____

Relation: _____

Phone Number: _____

Name: _____

Relation: _____

Phone Number: _____

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