

**Framingham Heart Study
Offspring Exam 10, Omni 1 Exam 5
RESEARCH CONSENT FORM**



Welcome Back to the Framingham Heart Study

Together we are helping to fight heart disease and other major diseases and health conditions through research.

Basic Information

Title of Project: Framingham Heart Study

IRB Number: H-32132

Sponsor: National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH)

Principal Investigator: Vasan S. Ramachandran, MD
fhs@bu.edu
73 Mount Wayte Avenue, Suite 2
Framingham, MA 01702

Study Phone Number: (508) 872-6562 or (800) 854-7582

PI Phone Number: (617) 358-1310 for Dr. Vasan S. Ramachandran

Why is the research study being done?

The Framingham Heart Study is a long-term research study. The purpose of the study is:

- (1) To help understand how heart and blood vessel diseases, lung and blood diseases, stroke, memory loss, cancer, and other major diseases and health conditions develop; and
- (2) To examine DNA and its relationship to the risks of developing these diseases and other health conditions.

The research examination that will be conducted as part of this study is not clinical care. The tests are for research purposes only. We do not provide medical services. This research examination does not take the place of medical care by your own health care provider.

About your consent

Please read this research consent form carefully. It tells you important information about the research study. Taking part in a research study is voluntary. The decision whether or not to take part in all or any part of the research exam is entirely up to you. If you choose to take part, you

can decide to stop at any time. Your decision will be honored and respected. There will be no penalty to you if you decide to stop or not to take part.

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

If you have any questions about the research or about this form, please ask us. You can call us with your questions or concerns. You can ask questions as often as you want.

You can call a study staff member directly at (508) 872-6562 or (800) 854-7582, or you can send an email to FHS@bu.edu.

The Framingham Heart Study is led by investigators from Boston University and the National Heart, Lung, and Blood Institute at the National Institutes of Health. Dr. Vasana S Ramachandran and Dr. Daniel Levy are in charge of the research study. You can contact Dr. Ramachandran at (617) 358-1310 Monday through Friday between 9am and 5pm or by email at vasan@bu.edu and Dr. Daniel Levy at (508) 935-3400 Monday to Friday between 9am and 5pm or by email at levyd@nih.gov.

You may also call 617-358-5372 or email medirb@bu.edu. You will be talking to someone at the Boston Medical Center and Boston University Medical Campus IRB. The IRB is a group that helps monitor research. You should call or email the IRB if you want to find out about your rights as a research subject. You should also call or email if you want to talk to someone who is not part of the study about your questions, concerns, or problems.

What will happen in this research study?

You will need to fast for 10 hours before you come to the study appointment for the blood draw. You can continue to drink water while fasting and take your usual medication on the morning of your visit.

Your research examination will take place at the FHS Research Center at 73 Mount Wayte Avenue, Framingham, MA, by phone or video conference (also referred to as a televisit), or in your home or other residence. The full onsite research exam will take around 4-5 hours to complete or the exam may also be split into multiple pieces: a 2-hour televisit and 2.5 hour in-person visit at the Research Center. Exam components that may be completed remotely will be included during the televisit and components that require in-person assessment will be conducted at the Research Center or offsite home or other residence.

As before, we will

- draw a sample of blood for genetic and laboratory tests to better understand risk factors for heart disease and other diseases under investigation (for example, the amount and function of different types of cholesterol in your blood). The total blood draw will be up to 80mL, which is about 5.4 tablespoons. The blood draw will occur soon after your arrival.
- collect a urine sample
- measure your height, weight, and waist
- measure grip strength
- complete an electrocardiogram (ECG)
- record your blood pressure
- update your medical history information

- complete a test of cardiac vascular function (tonometry) that examines heart function using ultrasound scanning (echocardiogram) and tests blood vessel (artery) stiffness by recording the blood pressure and flow waveforms
- ask you to sign a form to allow FHS to obtain copies of medical records, including Medicare records. The release form is valid to obtain these records unless canceled by you.
- contact you later by mail, email, or by phone (call or text) to obtain additional information or to invite you to participate in further FHS related studies. You may also be invited to return for another examination in the future.

Surveys

We will also be asking you to complete questionnaires such as physical function, diet, exercise, memory and mood, and your lifestyle habits, including whether you smoke or use alcohol. Some of the questionnaires you will have seen before and others will be new to you.

Some of your responses will be recorded using a digital audio recorder. Recordings will be analyzed in conjunction with other study information. We will also use recordings to make sure that your responses are accurately documented.

There are some new research activities.

1. Fibroscan: We are interested in improving our understanding of the factors that can help predict the development of liver fat and liver fibrosis (scarring) for this study, you will have a test called a Fibroscan. The Fibroscan measures the presence of fat or scarring in the liver. A painless pulse is generated on your skin that travels to the liver and measures how stiff your liver is.

What risks can I expect? There may be minor discomfort from the application of lubricating jelly and pressure on the skin from the Fibroscan probe. However, there are no known risks associated with the Fibroscan.

There are some conditions that may interfere with the ability of the device to obtain valid measures. They include being pregnant, having fluid in the abdominal cavity (ascites), and having implanted medical devices, such as a heart pacemaker. We will ask you to confirm if you have any of these conditions and if you do, we will not complete the Fibroscan.

2. Pain Assessment Study: We are interested in learning about pain people may be experiencing in their daily lives, and to better understand why some people have pain, more pain, or pain in more parts of their body, than other people do. We will ask some questions about pain and assess your sensitivity to pressure on your skin. To test your sensitivity to pressure, a small device will be pressed against a muscle on your shoulder to measure how much pressure is applied before you feel any discomfort.

What risks can I expect? Although rare, there is the potential for skin irritation and redness or bruising during testing. Bruising or discomfort could potentially result from application of the pressure meter during pressure pain threshold testing and/or blood pressure cuff inflation.

3. Brain Health Study: We are interested in finding a way to define brain health beyond the evaluation of cognitive testing. We will ask you to participate in a number of sensory

motor tests that capture your brain health, including testing your vision, hearing, and motor function. You will have eye testing (without dilatation); hearing testing (using an iPad and headphones); and physical function testing (includes gait speed assessment on an electronic gait mat, during normal walk and while doing a mental task like counting and timed chair stands).

What risk can I expect? There are no risks involved in eye and hearing testing. Gait testing has a minimal risk of falling. All precautions will be taken to prevent falls. A study staff member will stand near you to prevent you from falling and help you if needed.

4. Electronic FHS (eFHS) Study: If you live in the US, have an email account with access to a daily Internet connection or have a smartphone, we will invite you to take part in the eFHS study. Taking part requires that you visit a web platform, download apps and use wireless devices. The apps will require you to complete surveys regarding lifestyle and health, and the devices will measure heart rate, blood pressure, weight, and physical activity.

What risks can I expect? There are no known risks to taking part in this study.

5. Bone Scan: We are interested in learning about how the skeleton changes with aging. We will ask you to participate in two bone scans to examine the bone structure in your lower leg and lower arm. The scan is a non-invasive and painless test, and provides a detailed image of the “micro-architecture” inside the bone. Each scan takes about two minutes and requires that you keep as still as possible.

What risks can I expect? Bone scans involve the use of x-rays, a form of energy also called radiation. The radiation dose for the two scans together will be less than 10 μ Sv, which is equivalent to 2-3 days of background radiation that individuals experience in the U.S. Since the amount of radiation from the bone scans is so small, there are no known long-term effects of this radiation on your health.

Some of the study components described in this section “What will happen in this research study?” may not be administered during televisits, due to the need to take certain measurements in person. Also, some of the study components may not be administered during offsite examinations taking place at your home or care facility, due to large equipment that cannot be transported outside of the research center. For example, Fibroscan, Tonometry, and Computed Tomography.

Overall Examination Risks and Discomforts

General Risks: The research exam is time consuming and repetitive. Other discomforts include headaches, feeling hungry due to fasting, fatigue and chill during the visit.

CT bone scans involve exposure to radiation. Since the amount of radiation is so small, equivalent to 2-3 days of background radiation there are no known long-term effects of this radiation on your health. However due to potential risk to a fetus, pregnant women, as determined by self-report or by a positive pregnancy test, will be excluded from this test.

We do not expect any risk of injury as a result of your participation in the study. However, first aid will be available.

Unknown Risks: There may also be some risks that we are unable to determine at this time.

Genetic Studies

You may have already provided consent for the collection of biological samples for DNA research or the creation of Induced Pluripotent Stem Cells (iPS cells). We plan to continue to do genetic research on the DNA from your biological samples. The biological samples include blood cells, tissue cells, etc. DNA is the material that makes up your genes. Genes are passed from parent to child. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work and determine physical characteristics such as hair and eye color.

Also, if you agree, we will process white blood cells from a sample of your blood to become stem cells in the laboratory. The resulting cells are known as Induced Pluripotent Stem Cells (iPS cells), and they will be used in the laboratory to act like cells from other organs, such as liver cells, fat cells, heart cells, lung cells, vascular cells, gut cells, nerve cells, different types of blood cells, and many other engineered or naturally occurring cell types. These cells and the cell products that can be obtained from them such as RNA, proteins, and metabolites may be studied in laboratories to learn more about the causes of health and diseases of these organs.

Your cells will be stored indefinitely in a stem cell repository at Boston University. Your cells may also be stored in a central repository or bank.

If you agree, your stored tissues, cells and any resulting iPS cell lines or their derivatives could be used in future related and unrelated research studies including:

- Injecting or transplanting the stem cells or their derivatives into animals for research purposes. Your samples may be used in research that involves genetic manipulation but they will not be used to clone or to otherwise create an entire human being.
- Testing for genetic and DNA composition. Genes may be analyzed and/or manipulated to study normal function or development, and some of the DNA in the stem cells or their derivatives may be altered.
- Other uses involving research or development of commercial products for the diagnosis, prevention, or treatment of various diseases.
- Samples (blood cells, the iPS cells, or their derivatives) obtained from you in this study may be used in the development of one or more diagnostic or therapeutic products which could be patented and licensed by those involved in the research or development of such products. There are no plans to provide financial compensation to you should this occur.

How will I learn the results of this study?

The main way results of research from this study are reported is in scientific publications and presentations at scientific meetings. Summary findings are also sometimes described in our newsletters and on our study website.

We will also report some routine research test measurements to you and/or your health care provider at the time of the exam or after your visit. These may include, for example, blood pressure and cholesterol.

In some cases, if we determine it to be appropriate, we may report to you and/or your health care provider research findings as they relate to you, if you give your permission. This information, if it is reported, might be reported long after your visit for a number of reasons. As an example, it might take years of work to analyze information and arrive at research findings, possibly using newly developed scientific methods.

Our genetic research might generate findings that could be relevant to you and possibly your family members, such as information about a particular genetic variant that might put you at risk of a serious health condition. At this time, we believe that most of the genetic research findings do not have medical importance to individuals, but the field of genetics is changing rapidly.

We currently do not have specific plans to contact you or your health care provider about genetic or non-genetic research findings other than some routine research test measurements. In general, we cannot commit to providing any other research findings to you. In determining whether we share additional research information with you, we will take into account a number of considerations on a case-by-case basis. These might include whether the findings were based on tests that are clinically acceptable, accurate and reliable, whether the findings reveal a significant risk of a serious health condition, whether there is, at the relevant time, a recognized treatment or prevention intervention or other available actions that have the potential to change the clinical course of the health condition, whether reporting or not reporting the results is likely to increase the risk of harm to you, and other relevant factors that we might not be able to predict at this time. In the cases when genetic research findings are reported to you, a study investigator and genetic counselor will contact you to confirm your continued interest in hearing about genetic research results. If you confirm your interest, the study staff will inform you of the research results and recommend next steps such as obtaining confirmatory clinical testing and speaking with your personal healthcare provider.

Research test measurements and findings are not the same as clinical test results. As such, our research examination is not necessarily performed by individuals with clinical training and qualifications, and many parts of the examination do not meet the standards for certified clinical testing. For these reasons, our research tests should not be relied on to make any diagnosis, treatment, or health planning decisions. We do not provide health care or give medical advice or genetic testing or provide counseling. If you or your health care provider decides that follow-up tests or treatments are necessary, then you (or a third party such as a health insurance carrier or Medicare) will be responsible for the cost.

How are my samples and information shared with other researchers?

Samples and information will be kept indefinitely. If you agree, your data and donated blood, blood cells, resulting iPS cells or their derivatives, urine, and any other specimens may be shared with other researchers. These include other academic, non-profit, and for-profit entities, including but not limited to hospitals, universities, cell/tissue storage banks and repositories, databanks and data repositories and businesses, whether for related or unrelated research studies. The cell/tissue storage banks and repositories, databanks and data repositories, include but are not limited to, NIH repositories dbGaP and BioLINCC. Internal and external researchers may request data and materials for research. The repositories have standard operating procedures to protect your confidentiality. Your data and samples will not be labeled with your name or other direct personal identifiers, only a code.

Coded audio recording information will be analyzed by qualifying collaborators inside and outside of BUMC. Your name and other direct personal identifiers will not be shared with these entities.

You have the right to refuse to allow your data and samples to be used or shared for further research. Please check the appropriate box in the selection below.

If you give your permission to allow your data and biological samples to be used or shared for further research, you may withdraw your permission at any time by contacting the FHS investigators. However, if your data or samples have already been released to other researchers, we will not be able to instruct the other researchers to stop using them, to destroy them or products made from them. Your data and samples will not include your name or other direct identifiers.

What risks can I expect?

General risks and individual risks related to new activities are discussed above.

Participating in genetic research could have a negative impact on you, your family, and your loved ones. The genetic studies might result in research findings that relate to your risk of a serious health condition or other genetic information that we might consider to be appropriate to report to you and your health care provider, if you wish us to report them (see below). This could present you with some difficult decisions regarding the available information and the disease risks you and your family members might face. Knowledge of genetic research findings can provoke anxiety and influence decisions regarding marriage, family planning, and other matters. There is a potential risk that your genetic information could be used to your disadvantage. For example, if genetic research findings suggest a serious health problem, that could be used to make it harder for you to get or keep a job or insurance. Both Massachusetts state laws and federal laws, particularly the Genetic Information Nondiscrimination Act (GINA), generally make it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. These laws will generally protect you in the following ways:

1. Health insurance companies and group health plans may not request your genetic information that we get from this research.
2. Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
3. Massachusetts employers with 6 or more employees (or 15 or more employees in other states, under GINA) may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that neither Massachusetts law nor GINA protects you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Thus, life insurance, disability insurance, and long-term care insurance companies may legally ask whether you have had genetic testing and deny coverage for refusal to answer this question.

How is my information protected?

We will store your information in ways we think are secure. We label your samples and information with a code, and we keep the key to the code in a password protected database.

Only approved staff is given the password. We use other safeguards at our facilities and for our information technology and systems to protect the privacy and security of your information.

We do not sell, rent, or lease your contact information.

If information from this study is published or presented at scientific meetings, and when your samples and information are shared with other researchers and deposited in data and specimen banks and repositories, your name and other direct personal identifiers will not be used.

However, we cannot guarantee total privacy. We may provide access to your information in order to do the study and to make sure we do the study according to certain standards set by ethics, law, and quality groups. Information may be made available to researchers that are part of this study, the Institutional Review Board that oversees this research, research and non-research staff and organizations who need the information to do their jobs for the conduct and oversight of the study, people or groups that we hire to do work for us (such as data or biosample storage companies, insurers, and lawyers), and Federal and state agencies as required by law or if they are involved in the research or its oversight. In most cases, any information that is given out to others is identified by code and not with your name or other direct personal identifiers. Once information is given to outside parties, we cannot promise that it will be kept private. Please be aware that your personal information may be given out if required by law (e.g., to prevent possible injury to yourself or others).

This study is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. All studies funded by the National Institutes of Health that involve identifiable information or biological samples are covered by a CoC. The CoC provides how we can share research information or biological samples. Because we have a CoC, we cannot give out research information or biological samples that may identify you to anyone that is not involved in the research except as we describe below. Even if someone tries to get your information or biological samples in connection with a legal proceeding, we cannot give it to them. The CoC does not prevent you from sharing your own research information.

If you agree to be in the study and sign this form, we will share information and biological samples that may show your identity with the following groups of people:

- People who do the research or help oversee the research, including safety monitoring.
- People from Federal and state agencies who audit or review the research, as required by law. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and the Massachusetts Department of Public Health.
- Investigators who will get your data and your biological samples as we described in the section "*What will happen in this research study?*" These people are expected to protect your information and biological samples in the same way we protect it.
- Any people who you give us separate permission to share your information.

You should know that we are required to report information about child abuse or neglect; elder abuse; specific reportable diseases; or harm to others.

We will share research data where we have removed anything that we think would show your identity. There still may be a small chance that someone could figure out that the information is about you. Such sharing includes:

- Publishing results in a medical book or journal.

- Adding results to a Federal government database
- Using research data in future studies, done by us or by other scientists.
- Using biological samples in future studies, done by us or by other scientists.

Samples that are collected from you in this study will be analyzed to find out information about your genetic makeup. Your genetics and health information, without your name or other data that could easily identify you, will be put in a database run by the National Institutes of Health (NIH). This may include your whole genome information. Other researchers can ask the NIH to get your information from the database. You should know that it is possible that your genetics information might be used to identify you or your family, though we believe it is not too likely that this will happen. Once your information is given to the NIH database, you can ask to have NIH stop sharing it, but NIH cannot take back information that was already shared.

Patenting Discoveries

Research from this study may, one day, result in new tests to diagnose or predict diseases. It may also lead to the development of new ways to prevent or treat diseases. As is true of all federally-funded research, researchers and their employers are permitted by Federal law to patent discoveries from which they may gain financially. You and your heirs will not benefit financially.

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

While you will not receive any direct benefit as a result of your participation in this study; we hope that this study will help us better understand what causes heart disease and other diseases and conditions and how to better prevent and treat them.

What are the costs of taking part in the study?

Costs that you may incur on the day of your participation include, but are not limited to, loss of work and transportation costs (gas, tolls, etc.).

You will not be paid for your participation in this study.

No special arrangement will be made by the Framingham Heart Study for compensation or payment solely because of your participation in this study. If you think you have been injured by being in this study, please let the investigators know right away. Boston University and the sponsors do not offer a program to provide compensation for the cost of care for research related injury or other expenses such as lost wages, disability, pain, or discomfort. You will be sent a bill for the medical care you receive for research injury if your medical insurance does not pay for your medical care. This does not waive any of your legal rights.

How long will I be in the study?

FHS is a long-term study.

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.

Project Title: The Framingham Heart Study
Principal Investigator: Vasam S. Ramachandran, MD

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

The investigator may decide to discontinue your participation without your permission because he/she may decide that staying in the study will be bad for you, or the sponsor may stop the study.

Please read the following statements and check the appropriate box below:

- 1) I agree to participate in the FHS examination, including the collection of data, blood, urine samples, and various research tests and measurements. I agree to the use of all data, samples, and research materials for studies of the factors contributing to heart and blood vessel diseases, lung and blood diseases, stroke, memory loss, cancer, and other diseases and health conditions.

| YES | NO (*For Internal Use - Office Code 0*)

- 2) I agree to allow my data, blood, DNA and other genetic material, iPS cells and their derivatives, urine samples, and any other specimens to be used in genetic research, of factors contributing to heart and blood vessel diseases, lung and blood diseases, stroke, memory loss, cancer, and other diseases and health conditions.

| YES | NO (*For Internal Use - Office Code 3*)

- 3) I agree to allow researchers from commercial companies to have access to my data, blood, DNA and other genetic material, iPS cells and their derivatives, urine samples, and any other specimens for research. I understand that my data and specimens will be shared without my name or direct personal identifiers.

| YES | NO (*For Internal Use - Office Code 4*)

- 4) I agree to allow the FHS to release the findings of non-genetic research tests and examinations to me and/or my physician, clinic, hospital, or other health care provider.

| YES | NO (*For Internal Use - Office Code 30*)

- 5) I agree to allow the FHS to provide me, and with my permission, my physician, clinic, hospital, or other health care provider information relating to genetic research findings as they may relate to me.

| YES | NO (*For Internal Use - Office Code 31*)

Subject: _____
Printed name of subject

By signing this consent form, you are indicating that

- you have read this form (or it has been read to you)
- your questions have been answered to your satisfaction
- you voluntarily agree to participate in this research study
- you permit the use and sharing of information that may identify you as described, including your health information.

To be completed by subject if personally signing

Signature of subject

Date

To be completed by LAR if subject does not personally sign

I am providing consent on behalf of the subject.

Printed name of Legally Authorized Representative (LAR)

Relationship to Subject

Signature of Legally Authorized Representative

Date

Researcher: _____
Printed name of person conducting consent discussion

To be completed by researcher if subject personally signs

I have personally explained the research to the above-named subject and answered all questions. I believe that the subject understands what is involved in the study and freely agrees to participate.

Signature of person conducting consent discussion

Date

To be completed by researcher if subject does not personally sign

I have personally explained the research to the above-named subject's Legally Authorized Representative and answered all questions. I believe that the Legally Authorized Representative understands what is involved in the study and freely agrees to have the subject participate.

I consider that the above-named subject (check one):

- is capable of understanding what is involved in the study and freely agrees to participate.
- is not capable of understanding what is involved in the study.

Signature of person conducting consent discussion

Date