Study Title: Prospective Phenotyping for Genetic Subtypes of Early-onset Atrial Fibrillation
Version Date: May 16, 2024
PI: Benjamin Shoemaker MD, MSCI

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

This study seeks to learn about why patients, like you, have atrial fibrillation and if genetics can be used to improve how we treat atrial fibrillation. We will be enrolling 225 patients into this study. If you take part, we will perform genetic testing for atrial fibrillation to identify whether you have a change in your genetic code (sometimes called a "mutation") that may cause atrial fibrillation or related heart problems. You will come for an outpatient study visit that lasts about 4 hours. We will pay for the study visit and tests. You will undergo EKGs, bloodwork, a treadmill stress test, an MRI of your heart, and a 48-hour heart monitor. The amount of blood collected is about 3 tablespoons (45 milliliters). Within a few weeks after the study visit, our team of researchers and doctors will meet to review the results of your testing and decide if any changes to your medical care are recommended. We will then schedule to talk with you about the results of your testing and the experts' recommendations. A benefit to you for taking part in this study is we may make recommendations that improve your health.
Any changes to your care will be made by you and your doctors, not the research team. A risk of taking part in this study is we could discover a genetic problem that is potentially serious. This could potentially cause you anxiety, lead to you being started on new medicines, or undergoing procedures such as placement of a pacemaker (a device under your skin that can help your heartbeat more regularly) or implantable cardioverter defibrillator (ICD, a device under your skin that monitors your heart rhythm and can deliver electric shocks to fix abnormal rhythms). Once the study is completed you will be given a $200 gift card for participating and may be eligible to be reimbursed for your travel.

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Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have atrial fibrillation which was first diagnosed at a young age (< 65 years old) and you have undergone genetic testing for atrial fibrillation as either part of another research study or by one of your doctors in clinic. The purpose of this study is to learn more about the effect of genetics on the hearts of patients with atrial fibrillation and how that information can change your medical care. Specifically, we will ask you to come for a visit to the outpatient Vanderbilt Clinical Research Center and undergo tests that include: an interview, a routine physical exam, bloodwork, an electrocardiogram (EKG), measurement of hand strength, a treadmill exercise test, and a MRI of your heart. The amount of blood collected is about 3 tablespoons (45 milliliters). We will also send you home with a heart monitor to wear for 48 hours. If needed you will be given a prepaid shipping label to mail the monitor back to us. You should plan to be here about 4-5 hours to complete all the testing. If you have limited scheduling ability and we are unable to accommodate you with a same day testing or a cardiac MRI, you will be given the option to schedule testing on a separate day of the initial study visit. You will be given a $200 Amazon gift card after completion of the study and you may also paid for some of your travel expenses if you live far away.

If you have already undergone genetic testing as part of another research study; we will confirm the results of the prior genetic testing that was done for research. This will be done by sending your blood sample to a CLIA-approved genetic testing company.

About 4 weeks after the study visit, we will meet with you to tell you about the results of your testing and the recommendations from our panel of experts that reviewed your information. As part of being in this study, you agree to talk with us about the results of your tests and our recommendations. If you do not wish to know the results of your genetic and clinical testing, please do not enroll in this study. After these results are discussed, enrollment in this study will not otherwise affect your clinical care. Any future tests or procedures will be determined by your clinical care team.

Your medical and genetic data may be shared with others for research purposes, but this will not include your name, birthdate, social security number, or any other information that could be used to identify you. This is to protect your privacy. Your information may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

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Side effects and risks that you can expect if you take part in this study:

Many of the risks involved in this study are from the tests that are being performed. The risks of those tests are:

1. Collection of a blood sample and placement of an I.V.- a common risk is pain from the needle stick or a bruise. A rare side effect after an IV is the vein can become red and painful and sometimes require antibiotics. Rarely people faint from a blood draw or IV placement.
2. MRI- a common risk is anxiety or fear from being closed in the MRI machine. The MRI takes about 45 minutes to complete. In some cases, we can give you a medicine to make you more relaxed during the MRI. If you have any metal objects in your body, there is a rare risk of injury. If you have severe kidney disease, there is a risk of a skin reaction from the dye that is injected into the IV. If you have any metal objects or kidney disease, we will check to make sure it's safe and take all the necessary steps to perform the MRI safely. If it can't be done safely, we will perform an ultrasound (known as echocardiogram) instead of the MRI. Also, if you have an allergy to MRI dye (known as MRI contrast or gadolinium), we will perform an ultrasound instead of the MRI. There are no known risks of having an MRI while trying to become pregnant however there may be risks that are unknown. If you are trying to become pregnant, please let the study team know.
3. Electrocardiogram (EKG)- common risks for an EKG are skin irritation from the stickers.
4. Stress Treadmill Test- this is a test where you walk or run on a treadmill while EKGs are done. Common risks of this test are feeling tired and out of breath. You can stop when you are too tired to continue. Other common risks include abnormal heart rhythms due to exercise that are not life-threatening. Rare risks include dangerous heart rhythms. Other rare risks are physical injuries due to falling on the treadmill or straining your muscles or joints.

This study also carries risks related to the results of genetic testing. You may have already had a genetic test obtained for research. A patient may not wish to know the results of this genetic testing; as this study involves the discussion of those results with you, if you do not wish to know the results of your genetic testing, please do not consent to be in this study.

If your previous genetic testing that was done for research contained genetic information related to atrial fibrillation, we will confirm that result by sending a blood sample to a genetic testing company.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job. Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees, with the exception of government employers, and military, may not use your genetic information that comes from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

To prevent the release of your name and other private information, your information will be given a unique code. Only Dr. Shoemaker and members of the study team will know the code. The key to the code will be kept in a locked file or be placed into a password-protected computer database by study personnel.

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Risks that are not known:
There may be additional risks from participating in this study that are "not known at this time" since this is a research study and there may be unknown risks as a part of participation.

Good effects that might result from this study:

A) The benefit to science and humankind that might result from this study is that we may learn more about how atrial fibrillation occurs, whether patients like you with atrial fibrillation with early diagnosis have a genetic basis for their atrial fibrillation and whether there may be effective treatments for any genetic finding you may or may not have

B) We may find out new information about why you have atrial fibrillation and potentially your risk for other heart problems. Your results will be reviewed by a panel of experts, and we will share with you their recommendations for your medical care. You may decide to share this information with your doctor, and it may result in changes to your medical care.

Procedures to be followed:

1. You will be contacted by a member of the study team to tell you about the study. If you decide to take part in the study, your study visit will be scheduled.

2. The consent form and a questionnaire about your medical history and symptoms will be emailed or mailed to you. You will complete these prior to your study visit. If you have questions about them, you can call or email us.

3. You will come to the Vanderbilt Heart and Vascular Institute Outpatient Clinic on the morning of your study visit. A staff member will get you signed-in and take you to an exam room. A member of the study team will meet you. If you have not already done so, you will sign the consent form.

4. A blood sample will be collected and an IV will be placed. The blood sample will include a complete blood count, comprehensive metabolic panel, total creatine kinase, brain natriuretic peptide, and peripheral blood mononuclear cells (PBMCs). The PBMCs will be taken from the sample and frozen for storage.

5. Your hand grip strength will be measured by squeezing a device called a dynamometer. This takes less than a minute.

6. A member of the study team will talk with you about your medical history and perform a physical exam. This will be like a normal doctor's visit.

7. You will undergo a treadmill stress test. You will need to wear comfortable shoes for walking or running on the treadmill. Most people exercise for 5 to 10 minutes during the test. It can be more or less depending on your level of physical fitness. You stop when you are too tired to continue.

8. You will undergo a cardiac MRI. You will lay in the MRI scanner, which is closed tube. It will take about 45 minutes to complete. You will be able to listen to music and talk with research staff while in the MRI scanner.

9. You will go home with an EKG monitor to wear for 2-days (48 hours total). It will be placed at the end of the study visit, and you will be given instructions on how to mail or return it to the study team.

10. Your study visit is now complete, and you will be allowed to go home. If you needed to take medicine to relax for the MRI, you will need someone else to drive you home.

11. In about 4 weeks, we will meet with you to discuss the results of your testing and the recommendations of the experts who reviewed your information. We will arrange for this to be either by phone, a video conference such as Zoom, or in person. How we meet will depend on your preference and how far away you live.

12. You are now done with the study. If needed, information about the study, results, and expert recommendations can be shared with your doctors.

Payments for your time spent taking part in this study or expenses:
As a token of appreciation for taking part in this study, you will be given a $200 gift card.

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

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Version Date: April 11, 2022
PI: M. Benjamin Shoemaker MD, MSCI

Who to call for any questions or in case you are injured: If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please contact the study coordinator, Hollie Williams, nurse practitioner, at 615-875-0405**.** If you are unable to reach Hollie Williams, please contact Dr. Ben Shoemaker at 615-322-2318.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:

Your study doctor may choose to take you out of this study if they feel it is not in your best interest. You will not be removed from the study without being given a reason why.

What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Your standard heart health treatment will not change in any way if you choose not to be in this study. At any time, you may ask to have your samples destroyed if you request them to be. You should contact Dr. Ben Shoemaker in writing at 2525 West End Avenue Suite 300-A Nashville, TN 37203 or 615-322-2318 to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

Confidentiality:

Your study records and data will be stored in a secure database. The database will reside in a password-protected secure web site supported by Vanderbilt. Only study personnel will have access to the database. Information in the database that will identify you will only be available to study personnel.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Shoemaker and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study is supported by funding from the National Institutes of Health (NIH). Therefore, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:

Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Study Results:

As part of the study, Dr. Shoemaker may share the results of your study and/or non-study linked bloodwork, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, and the National Institutes of Health. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your protected health information (PHI) private.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use, or share the information?
The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed

by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?

You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in health plans or affect your ability to get benefits. You will get a copy of this form.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

Time: _____ _____
Printed Name and Title

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Consent for Genetic Research

The purpose of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment.

You are being asked to give a blood sample for genetic research. What we learn about you from this sample is not put in your health record. Your test results related to atrial fibrillation will be shared with you and your doctor. Genetic test results from non-cardiac genes will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results.

A single blood sample will be taken at the same time blood is being taken for the main part of the study. This will not take any additional time or require additional needle sticks.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only Dr. Shoemaker and members of their study team will have access to your name.

Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that comes from this research when planning to hire, promote, or fire you or when setting the terms of your employment.

Your sample will be used to make DNA that will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

Your samples may be used to make new products, tests, or findings. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Your samples and information about you may be shared with others to use for research. To protect your privacy, we will not release your name.

You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Giving samples for research is your free choice and you may be in the study even if you do not want your samples used or stored for gene research.

At any time, you may ask to have your sample destroyed. You should contact Dr. Ben Shoemaker at 2525 West End Avenue Suite 300-A Nashville, TN 37203/ #615-322-2318 to have your sample

destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

Please check Yes or No to the questions below:

My blood/tissue sample may be used for gene research in this study.

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future gene research in atrial fibrillation.

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future gene research for other health problems (such as cancer, heart disease, etc).

☐ Yes ☐ No

Signature: _____ Date: _____