Participant Name: _____ **Date**:_____

Title of Study: Genomic Medicine at VA (GenoVA) Study

Principal Investigator: Jason L. Vassy, MD, MPH, SM VA Facility: VA Boston Healthcare System

1. KEY SUMMARY INFORMATION ABOUT THIS STUDY

You are being invited to take part in a research study called GenoVA, funded by the US National Institutes of Health (NIH). The person in charge of the study is Dr. Jason Vassy at the VA Boston Healthcare System. Shortly after you receive this information, a staff member from the GenoVA study will call you to review this information with you, answer your questions, and ask if you are interested in participating in the study.

What is the study about and how long will it last?

By doing this study, we hope to learn whether informing patients about their genetic risk of certain common diseases will help them and their healthcare providers prevent, detect, or treat these diseases earlier.

Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks and benefits to you. Your participation is completely voluntary. You will not lose any services, benefits, or rights you would normally have if you choose not to volunteer.

Your participation in this research will last about 2 years and will include the following:

- A telephone survey at the beginning of the study, lasting about 15 minutes
- A saliva collection or blood draw at the beginning of the study
- Having your genetic results sent to you and your primary care provider
- A telephone survey at the end of the study (after 2 years), lasting about 20 minutes
- Review of your medical record

What are key reasons you might choose to volunteer for this study?

You might choose to volunteer to participate in this study if you are interested in learning more about your genetic risk for common diseases such as diabetes and colon cancer.

What are key reasons you might choose not to volunteer for this study?

You may choose not to volunteer for this study if you might find information about your risks for certain diseases emotionally distressing.

2. DETAILED INFORMATION ABOUT THE STUDY

Genes are made of DNA that we inherit from each of our parents, making us who we are. Our risks for some diseases are determined by our DNA, by our lifestyle factors (like the food we eat or the things in the environment we are exposed to), or by a combination of DNA and lifestyle factors. Scientists are now learning much more about the genetic factors that increase a person's risk for common diseases. Knowing about your risk for these diseases might help you and your healthcare provider take steps to lower your risk or detect and treat the diseases earlier.

What is the purpose of the study?

This research study will look at your genetic risk of 5 common diseases: coronary artery disease, atrial fibrillation, type 2 diabetes, colorectal cancer, prostate cancer (for participants with a prostate), and breast cancer (for participants born with female sex). If you choose to participate, we will test your blood or saliva sample for millions of genetic markers across all of your DNA. Using these markers, the researchers will be able to calculate your genetic risk of the 5 diseases. This test will not be able to tell you with 100% certainty whether you will or will not develop the disease. Instead, it will only be able to tell you whether you are at high genetic risk compared to the average person. Remember that other factors like diet, smoking, and physical activity also affect your risk of these diseases, and this genetic test will not take those factors into account.

These diseases are very common in the US population, and primary care providers are generally good at screening for these diseases in their patients. For example, patients can be screened for type 2 diabetes with a blood test, and they can be screened for colorectal cancer with a colonoscopy. This study will enroll about 1000 participants and look at whether learning about very high genetic risk for a disease might help patients and their healthcare providers prevent or detect these diseases even earlier than they might otherwise.

3. HOW LONG WILL I BE IN THE STUDY? WHAT WILL HAPPEN AND WHAT CAN I EXPECT IF I TAKE PART IN THE STUDY?

Your individual participation in the study will take approximately 2 years. If you agree to participate, you will complete the following steps:

- You will complete a telephone survey lasting approximately 15 minutes. You may skip any questions you prefer not to answer.
- You may choose to receive a "spit kit" for you to collect a saliva sample and return to us by mail. Or, you may choose to go to your local VA laboratory for a blood draw instead. In that case, the lab will draw 1 tube of blood.
- Your saliva or blood sample will be shipped to an external, VA-approved clinical genetics lab to perform the genetic test and calculate your genetic risk scores. This lab will send the results to the study team.
- You will be randomly assigned (like the flip of a coin) to receive your genetic results report at the beginning of the study (Immediate Results group) or at the end of the study, after 2 years (Delayed Results group). Comparing these groups will allow the researchers to see if the genetic risk scores help to improve disease prevention or detection.
- If you are in the Immediate Results group and are found to be at high genetic risk for any of the 5 conditions, you will receive a phone call from a member of the study team to let you know your results. A copy of your genetic results report will also be mailed to you, along with information about the disease for which you have high genetic risk. Your primary care provider will also be sent a copy of your report, along with some recommendations for what he/she might consider doing about the results.
- If you are in the Immediate Results group and are found to be at average genetic risk for all 5 conditions, the study team will send you a copy of your results.
- After 2 years, you will complete a follow-up telephone survey lasting about 20 minutes.
- After the follow-up survey, if you were in the Delayed Results group, you and your primary care provider will receive your results and recommendations in the same way the Immediate Results group did at the beginning of the study.
- The research team will review your medical records to collect data about your medical conditions and health care.
- Your genetic results report will be entered into your VA medical record.

During this study you will continue to receive medical care as usual from your primary care and other providers. The decision to use this genetic information in your medical care will be up to you and your healthcare providers. This study does not require you to take a new medication or have any other medical tests or procedures, except the blood draw or saliva collection at the beginning of the study.

While we are analyzing your DNA specimen, it is possible that we will uncover other genetic findings that are considered by experts to be "medically actionable" because they carry a higher risk for certain genetic diseases. This means that we believe these findings could be important for your health and that you and your healthcare providers should know about them so you can consider taking actions such as additional screening tests. Examples of diseases in this category include certain hereditary cancers and some types of cardiovascular disease, among other genetic conditions. Having one of these medically actionable genetic results does not necessarily mean you have one of these conditions. We estimate that 1-2% of participants will have one of these genetic results. If you are found to have one of these results, our genetic counselor will contact you immediately and give you the option to learn about the result and share it with your healthcare providers and family members. If you are found to have a medically actionable result, you will not be randomly assigned to receive your genetic risk scores for the 5 other common diseases (i.e. coronary artery diseases, atrial fibrillation, type 2 diabetes mellitus, colorectal cancer, and breast cancer (for biological female participants) or prostate cancer (for biological male participants)) either immediately or after 2 years. Instead, you will receive a report of your genetic risk scores for the 5 other common diseases along with a report of your medically actionable genetic results immediately.

4. WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

There is always a chance that any procedure can harm you. The procedures in this study are no different.

The blood draw in this study carries the possible risks of bleeding, bruising, or infection.

Learning about your genetic risk of a disease, including any unanticipated medically actionable findings, might cause you emotional distress. If you are in the 1-2% of participants with a medically actionable finding, that finding might also have implications for your blood relatives, since genes are shared in families. In that case, the genetic counselor will discuss those implications with you before you decide whether to learn about the finding.

You are not required to take a medication or undergo any procedures as a part of this study, other than the saliva collection or blood draw at the start of the study. However, if your healthcare provider recommends a medical procedure or a change to your medications based on the information you receive as a part of this study, including a medically actionable finding, he or she should discuss with you the potential benefits and harms of those interventions.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this document. You should talk with your health care providers if you have any questions about the risks of usual care. As described in Section 8 below, federal law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Also as described below in Section 8, if you are active-duty military, study-related information that is included in your VA medical record is subject to access by Department of Defense (DOD) personnel.

In addition to the risks described above, you may experience a previously unknown risk or side effect.

5. WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

There are no known direct benefits to you for being in this study. However, the results you receive about your genetic risk of certain diseases might help you and your healthcare providers make medical decisions to lower your risk.

6. DO I HAVE TO TAKE PART IN THE STUDY?

Participation is completely voluntary. Refusal to take part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you are a VA employee, refusal to take part in the study will in no way influence your employment, employment status, or ratings. As a VA employee, your supervisors will not have access to your research data, and in the event of a direct supervisory relationship, research staff other than your direct supervisor will obtain your consent to participate in this study.

You may discontinue taking part at any time without any penalty or loss of benefits. You will still receive the same medical care you would have received otherwise.

If you withdraw from the study, the research team may continue to review the data already collected for the study but cannot collect further information after you withdraw, except from public records, such as survival data. Specimens already used cannot be withdrawn.

7. WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

The only alternative to participating is to choose not to participate.

8. HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Information collected for the purpose of this research study will be kept confidential as required by law. The results of this study may be published for scientific purposes, but your records or identity will not be revealed unless required by law.

We will store your information in ways we think are secure. All data will be stored on secure, password-protected computers, accessible only to authorized research personnel.

Your saliva or blood sample will be sent to a VA-approved clinical laboratory for the purposes of genetic testing to calculate your genetic risk scores. Your specimen will be de-identified prior to being sent to the lab for genetic testing. This means personally identifying information (PII) such as your name, date of birth, and social security number will be removed from your specimen and replaced with a study identification (ID) code that only the research staff know and will not include your name or other identifiers. This laboratory will destroy your blood or saliva sample after the analysis is complete.

We have obtained a Certificate of Confidentiality from the Federal Government. This helps protect your privacy by allowing us to refuse to release your name or other information outside of the research study, even by a court order. The Certificate of Confidentiality will not be used to prevent disclosures to local authorities of child or elder abuse or neglect as defined by the Commonwealth of Massachusetts; or if you are deemed at immediate risk of suicide; or if you are deemed to be at risk of doing bodily harm to a specifically identifiable individual. The Certificate does not prevent you or a member of your family from releasing data about yourself or your involvement in this study.

We will record information from this study in your medical record, including a copy of your genetic results report, now or after two years, depending on your group assignment. Please ask us if you have any questions about what information will be included in your medical records. You should know that once information has been put into your medical records, it is not covered by the CoC. However, information in your medical records is protected in other ways. For active-duty military participants, a CoC only protects research information; it does NOT protect study-related information that is included in the VA medical record, which is subject to access by DOD personnel.

Your research records will be kept indefinitely or until the law allows their destruction per the VA Record Control Schedule. Records will be destroyed, when allowed, in the following ways. Paper records will be shredded. Electronic records will be destroyed in a manner in which they cannot be retrieved.

The research team may need to disclose your health information and the information it collects to others as part of the study progress. Others may include the National Institutes of Health, the Institutional Review Board at VA Boston, Research & Development Committee, Research Compliance Officers, Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability Office (GAO).

We will include information about your study participation in your medical record.

While this study is being conducted, you will not have access to your research-related health records. This will not affect your VA healthcare including your doctor's ability to see your records as part of your normal care.

A description of this clinical trial will be 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.

Does this study involve genetic research and how will my genetic information be protected?

Federal laws and policies provide you with protection from discrimination by health insurance companies, group health plans, and most employers based on your genetic information. A federal law called the Genetic Information Nondiscrimination Act (GINA) generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained from this study.
- Health insurance companies and group health plans may not use your genetic information obtained from this study when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information obtained from this study when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of already known genetic disease.

Future Use of Data and Re-Contact

You may be contacted in the future to determine your interest in participating in additional research. Your participation in additional research would be voluntary and would require additional consent at that time. De-identified study data will be entered into the following NIH and VA data repositories, and may be used for future studies approved by an IRB. This means personally identifying information (PII) such as your name, date of birth, social security number, or any other direct identifiers will not be entered into either data repository.

1. Your de-identified study data collected from this study will be submitted to the National Center for Biotechnology Information (NCBI) database of Genotypes and Phenotypes (dbGaP). VHA and external researchers may request access to these de-identified data through a Data Use Certification (DUC) Agreement on the dbGaP website.

2. Your de-identified study data will be stored in a GenoVA study data repository behind the VA firewall. These de-identified data will include individual-level trial data, including SNP array data, demographics, diagnoses, and survey data. VHA and external with an IRB-approved protocol and Data Use Agreement (DUA) may request access to these de-identified data.

9. WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

You will be told of any significant new findings that come to light during the course of this study and that may relate to your wanting to stay in the study. As described above, you and your primary care provider will be told at the beginning or end of the study whether you have high genetic risk for one the 6 conditions listed. If the researchers discover other potentially clinically relevant results about you over the course of the study, they will discuss with the Institutional Review Board about whether it would be appropriate to recontact you with this new information as well.

10. WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

A participant will not be required to pay for medical care and services received as a participant in an approved VA research study. Some participants are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services (including, but not limited to, dental services, supplies, medicines, orthopedic and prosthetic appliances, and domiciliary or nursing home care) provided by the VA that are not part of this research study.

Compensation for Study Participation

You will be compensated up to $60 for your time and effort taking part in this study.

You will receive a gift card worth $30 for completion of the baseline survey and blood or saliva collection at the beginning of your study participation. You will receive an additional $30 gift card upon completion of the end-of-study survey, 2 years later. If you choose to withdraw from the study before completion of the end-of-study survey, you will not receive the second gift card.

11. WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury is due to non-compliance by a study participant with study procedures or if the research is conducted for VA under contract with an individual or non-VA institution.

12. WHO COULD PROFIT FROM THE STUDY RESULTS?

Your study data and specimens will not be used for commercial profit.

13. WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

I understand that if I have any medical questions about this research study, I can call **Dr. Jason Vassy, the GenoVA Study principal investigator, at (857)-364-2561** during normal working hours.

Participant Name: _____ **Date**:_____

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Principal Investigator: Jason L. Vassy, MD, MPH, SM VA Facility: VA Boston Healthcare System

I understand that if I have any general questions about this research study, **I can call Ashley Antwi, the GenoVA Study project manager, at (857)-364-6037 or (617)-390-4637** during normal working hours.

If you have questions about your rights as a study participant or any other questions, complaints, concerns or suggestions about this study, you may contact the Institutional Review Board at (617)-637-3794. This is the Board that oversees all human research at VA Boston Healthcare Systems and has the responsibility to ensure the safety of human participants in this study.

14. AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

A study staff member has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it.

I agree to participate in this research study as has been explained in this form.		
_____ Participant's Name	_____ Participant's Signature	_____ Date