Official Title: Genetic Testing to Understand and Address Renal Disease Disparities Across the United States - Pharmacogenetic Substudy

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DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
ADULT
Genetic testing to Understand and Address Renal Disease Disparities across the United States (GUARDD-US)

SUMMARY

The purpose of this study is to find out if a genetic test can help improve blood pressure in people with controlled or uncontrolled high blood pressure. Certain genes can increase the risk for kidney disease and kidney failure in people with African ancestry. Other genes can affect whether some commonly used blood pressure medications work well or cause side effects.

Your genetic test may help you and your health care provider learn if your blood pressure puts you at risk for serious kidney problems. The test may also help your provider pick the best dose or type of blood pressure medicine for you.

We will meet you at a location agreed upon between you and our research team for three study visits over a 6-month period. During each visit, a trained person from our study team will measure your blood pressure and ask you survey questions. During the first visit, a trained person will also collect some blood or swab the inside of your cheek for genetic testing.

Risks of the study include things related to getting your blood drawn such as pain, bruising, infection, dizziness or fainting during or after a blood draw. You may feel discomfort when the blood pressure cuff inflates to measure your blood pressure. Results of the genetic tests may cause you to feel anxious or distressed. In research, there is always a risk of loss of private information, but we have procedures in place to reduce this risk.

If you are interested in learning more about this study, please continue to read below.

I am asking if you would like to take part in this research study because you told me you are African-American, Black or have African ancestry and you have high blood pressure**.** Research studies like this only include people who choose to take part. I would like to read you this form, or you may read it yourself. You can take your time to decide whether or not to take part. Please feel free to ask me to explain anything you do not understand. You can speak with your health care provider, a genetic counselor, family and friends before you decide to take part.

This study is funded by a grant from the National Human Genome Research Institute (NHGRI), a part of the National Institutes of Health (NIH). The NIH is a part of the US government that supports health research. This grant pays parts of the salaries of the researchers and their team.

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During the study, you will continue to see your regular doctor. Dr. Neil Calman will oversee the study where you get your health care.

WHY ARE WE DOING THIS STUDY?
We aim to learn more about how people and their healthcare providers respond to getting the results of two genetic tests related to their blood pressure. One test shows whether people like you with high blood pressure, which may or may not be controlled, have an increased risk for kidney failure. The other test may help your health care provider figure out the best dose or type of blood pressure medicine for you. Your health care provider may also use your genetic test result to make better decisions about your health care. The test results may change how you care for yourself. To be part of the study, you must be between 18-70 years old, identify as having African ancestry, and have high blood pressure, which may or may not be controlled.

Chronic kidney disease affects millions of people. Over time, people with chronic kidney disease can develop kidney failure, which can make people ill and means people will need dialysis or a kidney transplant to survive. People of African ancestry are more likely to develop chronic kidney disease and kidney failure than people of European ancestry. There are many reasons for this difference. One has to do with our genetic makeup.

Genes are tiny threads made of DNA found in most cells in our bodies. They carry instructions for how our bodies work. Changes in genes can cause health problems. We all inherit genes from our parents. If we have children, we pass half our genes on to them. That is why most of us look like our parents! Hundreds of years ago, racial and ethnic groups tended to live in very separate areas. In some areas, genes changed (mutated) to protect people against common diseases where they lived. These changes, (also called variations) were passed on because people who had them lived longer and had more children than those who did not. Sometimes the variations protected people against one health problem, but caused another one.

This is what happened with a gene called *APOL1*. Hundreds of years ago, some people in Africa developed variations in *APOL1* that stopped them from dying from sleeping sickness. But, if we inherit this variation in *APOL1* from both of our parents, and we have high blood pressure, we have a 5-10 times increased risk for kidney failure. Because only people in Africa were exposed to sleeping sickness, only people with African ancestors have this high-risk genetic variation. So while 1 in 7 people with African-ancestry have this risk, it is very rare in persons with European ancestry. For this reason, our study only includes people with African ancestry. We now have a test to see which people with African ancestry and high blood pressure have the high-risk variant, and we will offer this test to people in the study.

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There are also genetic tests that can help identify which blood pressure medicines might work best for you. These tests check for genes that affect how well certain blood pressure medicines may work for you so you and your health provider can choose medicines that can best improve your blood pressure and avoid medicines that either won't help that much, or cause side effects. We call this type of test a *pharmacogenetics* test- a word that includes "pharmaco"- like a pharmacy, meaning medicines, and the word "genetics" referring to genetic testing. In other words, this type of test tells us whether differences in genes influence how medicines act on our bodies. We will also be offering this test to people in the study.

If you choose to be part of this study, we will take a sample of your blood or cheek swab to test you for these variations. If you have gene variations that put you at higher risk for kidney failure, you and your provider may take some actions to control your blood pressure and keep your kidneys as healthy as possible. If you have gene variations related to blood pressure medicines, you and your provider may choose different medicines or different doses. Any changes in your care are up to you and your provider.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Over 6,000 people will take part in this study at about 50 different hospitals and practices across the United States. About 900 people will take part where you get your care.

WHAT IS INVOLVED IN THE STUDY?
If you agree to take part, we will ask you to sign and date this consent form. If you do not sign this consent form, you will not be part of this study. Either way, you will still get your regular medical care.

If you agree to take part, we will ask you to do several things:
First Study Visit (This should last about 1½ hours):

- We will ask you some questions in a survey about your medical and family history and your thoughts on high blood pressure, kidney disease, and genes.
- We will measure your blood pressure.
- We will assign you by chance (using a process like drawing numbers from a hat) to one of three groups:

Group 1: You will get both genetic test results as soon as they are available.

- At your first study visit, we will ask you survey questions, measure your blood pressure and take a sample of your blood or cheek swab to test for the *APOL1* gene variations for kidney failure risk and those related to blood pressure medicines (pharmacogenetics testing). When the results are ready, a member of our team will call you to go over them, explain what they mean, and mail

or securely email you a letter with the results. We will also give the results of both tests to your provider, who can decide, with you, whether to make any changes in your healthcare.

- About 3 months after your first visit, we will meet you at a location agreed upon between you and our research team for a follow-up visit, complete a survey like the one you did during the first visit and check your blood pressure. This visit should take about 45 minutes.

- About 6 months after the first study visit, we will meet you at a location agreed upon between you and our research team for a final visit, complete a final survey and check your blood pressure. This visit should also take about 45 minutes.

Group 2: You will get the *APOL1* genetic test result as soon as it is ready and you will get your pharmacogenetics test results in about 6 months

- At your first study visit, we will ask you survey questions, measure your blood pressure and take a sample of your blood or cheek swab to test for the *APOL1* gene related to kidney failure. When the results are ready, a member of our team will call you to go over them, explain what they mean, and mail or securely email you the results. We will also share the results with your provider who can decide, with you, whether to make any changes in your healthcare.

- We will also begin to process your blood or cheek swab for the pharmacogenetics test at the same time as the *APOL1* test, but no one, including the lab staff, research team or your provider, will know the results of the pharmacogenetics test until after your final study visit (6 to 7 months after your first visit).

- About 3 months after your first visit, we will meet you at a location agreed upon between you and our research team, complete a survey like the one you did during the first visit, and measure your blood pressure. This visit should take about 45 minutes.

- About 6 months after your first study visit, we will meet you at a location agreed upon between you and our research team for a final visit, complete a final survey and check your blood pressure. This visit should also take about 45 minutes. After the final visit, the lab will finish running the pharmacogenetics test and as soon as the results are ready, you will get a phone call from a member of our study team to go over your test results, explain what they mean, and mail or securely email you the results. We will share these results with your provider who can decide, with you, whether to make any changes in your blood pressure medicine.

Group 3: You will get the *APOL1* and pharmacogenetics test results in about 6 months

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- At your first study visit, we will ask you survey questions, measure your blood pressure and take a sample of your blood or cheek swab. We will store your sample, but will not do any testing and no one will know the results of the tests until after you complete the final visit of the study.

- About 3 months your first visit, we will meet you at a location agreed upon between you and our research team, complete a survey like the one you did during the first visit and measure your blood pressure. This visit should take about 45 minutes.

- About 6 months after your first study visit, we will meet you at a location agreed upon between you and our research team, complete a final survey and check your blood pressure. This visit should also take about 45 minutes. After the final visit, the lab will do the genetic testing. As soon as your results are ready, we will call you to go over the results related to both kidney risk and blood pressure medicines, explain what they mean and mail or securely email you a letter with the results. We will also share the result of your tests with your provider who can decide, with you, whether to make any changes in your healthcare.

All Groups

- We will send your blood or cheek swab sample to a lab for testing. The lab will have your information so they can send your results to your provider. They will do no other tests without your permission. Once you are done with the study, they will destroy whatever is left of your sample.

- Everyone in all 3 groups will have their sample tested for kidney disease risk and for choice of blood pressure medicines. We will share the results of these tests with you and your provider. When your sample is tested and when you and your provider receive the results will be determined by which group you are randomly assigned to. This way we can compare people who are tested right away and those who are not.

- A positive *APOL1* test result means that you have a higher risk for developing kidney disease and kidney failure. We will call you to go over your results, explain what they mean, and mail or securely email you a letter explaining the results, and a booklet with more information. You can share these with your provider or whoever you would like. We will share the results with your provider and they will become part of your medical record, like other tests you get, so your provider can act on them if he/she wants. You can speak with study staff or your provider about your test results. You will be able to speak by phone with a genetic counselor who is part of our research team, at no cost to you, if you have more questions.

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You may be asked if you want to take part in another study and to provide additional data or biological samples. This will require your permission. You can still be in this study if you decide not to do that.

HOW LONG WILL I BE IN THIS STUDY?
The study lasts ~6 months and includes 3 study visits. We will also review your medical record information related to this study (such as blood pressure, lab tests and medical diagnoses) up to 24 months before you join the study and up to about 12 months after you complete the final visit so we can compare the information before and after you take part.

WHAT ARE THE RISKS OF THE STUDY?
Taking part in a research study can involve certain risks. These can include:

Blood Pressure: You may feel some arm pressure when the blood pressure cuff is briefly inflated.

Blood Draw: Risks associated with drawing blood from your arm include slight pain or bruising. Rarely, people get an infection, bleed a lot, or faint due to a blood draw.

Survey: Some questions may make you feel uncomfortable. You may refuse to answer them or take a break at any time.

Getting your test results: Some people may feel upset if they learn they carry a gene that puts them at a higher risk of developing kidney problems or if their tests show they may do better on different blood pressure medicine or at a different dose. Please let the research staff know if you are upset.
There is always a risk of loss of private information, but we have procedures in place to reduce this risk.

Genetic Information: There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people 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.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
You may not get any benefit from taking part. However, you and your provider may be able to make better decisions about your healthcare. We hope that in the future the information learned from this study will benefit other people with high blood pressure.

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WILL MY INFORMATION BE KEPT CONFIDENTIAL OR PRIVATE?
Taking part in research involves some loss of privacy. We will do our best to keep your information private, but we cannot guarantee this. We will do everything we can to reduce the risk and we will share only the minimum amount needed to conduct the research.

We have to connect your information to your samples because your test results will be returned to your provider and filed in your medical record.

Researchers involved in this study, including those funding, and overseeing the study may also see your personal healthcare information.

To protect your privacy, a part of the government, the Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality. Study members may not share research information that may identify you to any other person or group unless you have written down that you approve for them to do this. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your privacy may no longer apply to the things you have shared.
The only reason we may share your information with someone else if we learn of possible harm to yourself or others, or if you need medical help.

HOW LONG DO YOU KEEP MY DATA?
The study results will stay in your research record for at least six years after the study is completed. At that time, we will either destroy the research information not already in your medical record, or remove any information about you from the study results.

Some information, like your genetic information, age, sex, ethnic background, diagnosis and disease history, may be entered into one or more scientific databases available to other researchers such as "dbGAP" that stores medical information from many studies done at many different places. Researchers can then study the combined information to learn even more about health and many different diseases. Your data will only be in databases for which researchers must apply for permission to use the data, and will not have any information that can identify you such as your name, address, telephone number, or social security number. Because your genetic information is unique to you, there is a chance that someone could trace it back to you. The risk of this happening is very small. Researchers will always have a duty to protect your privacy and to keep your information confidential.

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We will put a description of the study and a summary of the results on https://clinicaltrials.gov/. This website will not include information that can identify you or anyone else in the study. You can search this website at any time.

After this study ends, we would like to keep collecting information about how your kidneys are doing. We do not yet know enough about how high blood pressure and genes affect people's kidneys over a long period of time. We could get this from your medical record by looking at lab test results and a list of new health problems related to kidneys. We could also get it through the United States Renal Data System that has information about people in the United States with kidney problems. Finally, if you have Medicare or Medicaid, we could get information from them about whether they are being billed to pay for kidney-related health problems. We would want to get this information for up to the next 10 years so we could learn about these effects. We would not need to speak with you and would not ask you to do any more tests or surveys. You can still be in the study if you do not want us to do this. Would it be OK with you if we did continue to get this information?

_____ Yes _____ No
Initial here Initial here

After this study ends, would it be OK with you if we stored and shared your data for future related studies without the study team asking you for additional permission. Your data will only be shared with members of the GUARDD-US study team. You can still be in the study if you do not want us to do this.

_____ Yes _____ No
Initial here Initial here

WHAT ARE THE COSTS TO YOU?
The research team and study sponsor, will pay for the genetic test, study services and procedures. Neither you, nor your insurer will be charged or billed for the tests. They are free for you.
Taking part in this research study may lead to added costs to you such as transportation to come to study visits.

All costs related to your routine medical care, including copayments and deductibles will be billed to you or your insurance provider as normal, just as they would if you had not been part of the study.

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WHAT ELSE WILL I GET?
If you agree to take part in this research study, we will pay you up to a total of $120 in gift cards; $40 after you complete each of the three study visits at baseline, 3 and 6 month follow up.

WHAT ABOUT RESEARCH RELATED INJURIES OR OTHER PROBLEMS OR QUESTIONS I MIGHT HAVE?
If you are injured as a result of taking part, we will get you immediate medical care at *the Institute for Family.*

If you have any questions about the study or research-related injury, contact Dr. Neil Calman at (212) 633-0800 x1255. For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

CAN I REFUSE TO TAKE PART OR WITHDRAW?
You do not have to take part at all. You can stop taking part at any time without losing any benefits. Your decision not to take part or to withdraw will not affect your access to health care at your institution. If you decide to stop taking part in the study, we ask that you tell a study staff member.

If you withdraw from the study, we will not collect any new data about you other than data needed to keep track of your withdrawal. All data that have already been collected for study purposes will be sent to the study sponsor. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. The people, agencies or institutions funding and overseeing this study may stop this study at any time without your consent. This could happen if there are problems with the way the study is being done, if the investigator believes it is in your best interest, or for any other reason. If this occurs, we will notify you and discuss other options with you.

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STATEMENT OF CONSENT
"A study member has explained the purpose of this study, what will be done, the risks and benefits. I have been allowed to ask questions, and all my questions have been answered in a way I understand. I was told who to contact if I have questions, problems, concerns, or suggestions about the research. I have read, or someone read me this consent form and I agree to be in this study. I understand I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____
Printed Name of Subject

_____ _____ _____
Signature of Subject Date Time

_____
Printed Name of Person Obtaining Consent

_____ _____ _____
Signature of Person Obtaining Consent Date Time

(Optional)

_____ _____ _____
Signature of Principal Investigator **Date** **Time**

(If applicable – under the circumstance where the participant is unable to read the consent or unable to make a signature)

_____
Printed Name of Witness

_____ _____ _____
Signature of Witness Date Time