

Consent to Participate in a Research Study
Longitudinal Pulmonary Vascular Disease Phenomics Program (L-PVDOMICS) Consent

Study title: Pulmonary Vascular Disease Phenomics Program (PVDOMICS)
Sponsor: National Institutes of Health (NIH), Heart, Lung and Blood Institute, (NHLBI)
PI: XXX
Study Coordinator: XXX

You are being asked to join in the Longitudinal, or follow-up, study called L-PVDOMICS Study to the previous parent NIH PVDOMICS study in which you have already participated.

This study will enhance the findings of the PVDOMICS study by having additional follow-up data. There are 3 levels of participation depending on your ability and/or willingness to be seen again at the clinical center where you were enrolled into the parent PVDOMICS Study. The purpose of this consent form is to provide a written review of the discussion of research information you had with the research team. It is also for use as a reference during the L-PVDOMICS study.

Please note:

- **You are being asked to join in a follow-up to the parent PVDOMICS study you participated in provided this has been at least 6 months ago.**
- **You can ask as many questions as needed so you can make an informed decision.**
- **Carefully consider the risks and benefits of the research.**
- **Your decision to join is completely voluntary and will have no effect on your medical care if you choose not to join. You can also stop doing the study at any time.**

INFORMATION ON THE RESEARCH

Why is the research study being done?

As you know, doctors from medical centers across the U.S. have formed a research group to study pulmonary hypertension (high pressures in the blood tubes of the lungs). These medical centers are Mayo Clinic, Vanderbilt University, Johns Hopkins University, Columbia University, Cornell University, University of Arizona, Brigham and Women's Hospital (Boston) and Cleveland Clinic.

The goal of this study is to gain a better understanding of this illness and problems in the right side of the heart, based on traits from the cells of the body and clinical tests. This is the first time that this research has been done and as such, we would like to see if there are any changes over time in the special blood tests ("OMICS") by analyzing repeat blood specimens along with a minimum number of noninvasive tests to compare to prior testing. The initial PVDOMICS aims of relooking at the current pulmonary hypertension (PH) classification system to see if improvements can be made remain as does the desire to identify new ways to prevent, detect and treat pulmonary hypertension.

Why are you being asked to take part in this research?

You are being asked to take part in this study because you have previously participated in the parent PVDOMICS study.

How many people will take part in the study?

About 400 participants (including participants with PH, comparators and controls) will take part in this follow-up study at the centers listed above.

What is involved if you decide to take part in this research study?

The 3 levels of participation are described below.

a) Level 1 Participation

The Level 1 testing and data collection can occur during a follow-up visit to the clinical center as a standard of care visit in addition to a review of your medical record. Data collection will include a review of: medical history inclusive of medications, both prescription and over-the-counter (OTC) lists, assessment of interim health history (i.e., whether you have been the same, better or worse since your last visit for the parent PVDOMICS study). It will also include whether there have been any hospitalizations for heart or lung related events. You will be asked to answer questions on the quality of life questionnaires. You will be asked to perform the 6-minute walk test with or without oxygen as you have previously done, undergo a non-invasive echocardiogram test which will be explained later in this document and have a physical exam including determination of your body mass index.

You will be asked to provide fasting blood and urine.

An echocardiogram (ultrasound of the heart) will be done for participants who have pulmonary hypertension and comparators (which for some may be clinical standard of care and billed to insurance) and controls considered to be done for research purposes only and not billed to insurance.

You can still take part in L-PVDOMICS study Level 1 participation if you have had a corneal transplant.

b) Level 2 Participation. If you cannot or do not want to come into the center for the L-PVDOMICS study, you will be asked on a phone call to provide health history including medications, prescription and over-the-counter drug lists, assessment of interim medical history (i.e., whether there have been changes in your health since the parent study). You will be asked about any hospitalizations for heart or lung related events. Also, you will be asked to answer quality of life questionnaires. We will ask for your permission to review your electronic health record and extract available information for the study.

c) Level 3 Participation

The Level 3 participation is for any individual not agreeing to participate at Level 1 or 2.

We will review your medical record and extract available information for the study.

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During the course of the L-PVDOMICS Study, if the medical tests or other research analyses find an abnormality or a potential health problem, we will contact you if you give permission and want to know. We can also contact your doctor, if you would like us to. The results of many of the medical tests you undergo for this study will be automatically put in your medical record which means they will be available to your healthcare providers.

Medical History:

We will ask you about your interim medical history including prescription and over-the-counter medicines you are taking now. We will also look at your medical record and gather results from other tests that you may have had since the parent PVDOMICS study. These tests may have included an echocardiogram(s), right heart catheterization(s) (pressure measurements in your heart and lung vessels) exercise and lung function tests, and radiology reports. If you had a medical test that was done at another hospital, we would like to have the results from this test with your permission.

Physical Exam:

You will have a limited physical exam that will include measuring your height, weight, and vital signs such as heart rate, blood pressure, breaths per minute and oxygen saturation (a measurement of the amount of oxygen in your blood).

Quality of Life Questionnaires:

During the study you will be asked to fill out three questionnaires regarding your pulmonary hypertension symptoms, health, and quality of life. These are the same three questionnaires you may have completed in the parent PVDOMICS study.

Echocardiogram:

An echocardiogram will be done to look at your heart function. This test is an ultrasound of your heart. It is done by a trained person by holding a device (shaped like a microphone) on the skin of your chest with some pressure to look at the heart and surrounding larger blood vessels. The test will take about 30-45 minutes. An intravenous (IV) line may be placed in order to use an ultrasound enhancing agent (under physician supervision) to improve the pictures of your heart. The echocardiogram may be done as part of your routine care or just for this research study.

Blood Collection:

Fasting blood will be collected once during the study, unless you are having a routine right heart catheterization and are willing to have another sample collected at that time. Approximately 90 milliliters of blood (7.5 tablespoons) will be collected. Some of the blood will be used to check your general health. The rest of the blood will be stored and used for the "OMICS" portion of the study (including DNA, RNA). Any blood not used in this study will be stored in a biobank for later, if you agree to this.

The research samples will be labeled with a study code and not your name or medical record number. Some of this blood will be sent to the L-PVDOMICS study Data Coordinating Center at the Cleveland Clinic for storage and other protein testing by researchers in this study.

Urine Collection:

We will collect urine to learn more about pulmonary hypertension.

Six Minute Walk Test:

You will be asked to walk as far as possible in six minutes. You may self-pace and rest as needed as you walk back and forth along a marked walkway. If you use oxygen, you can use it during the walk.

Sleep Study

Based upon investigator discretion, you may be asked to have an overnight sleep monitoring test. In this case, you will be given a small device to take home, and at bedtime you will wear straps around your chest and abdomen, a small clip on your finger, sensors on your chest for heart monitoring (electrocardiogram) and small plastic prongs in your nose. These will monitor your breathing and oxygen levels while you sleep. We will have you fill in a brief questionnaire asking about your sleep. The following morning you will remove the equipment and return it to the study team.

Follow-Up

We may look at your medical records for the study. You may be contacted by the study team by phone and/or mail during the study. Investigators may contact you in the future if there are new research studies being done that you may be a candidate for. If the investigator is not part of L-PVDOMICS (your PVDOMICS site will provide your contact information to the investigator if you give permission). You have no obligation to participate in any additional studies and may simply decline, if contacted.

Please initial below to indicate whether or not you give permission for your L-PVDOMICS investigator to give other investigators your contact information so that you can be asked to join other research studies:

_____ (initials) I agree to have my contact information given to other investigators.

_____ (initials) I do NOT agree to have my contact information given to other investigators.

RISKS

What are the possible risks or discomforts from being in this research study?

Blood Draw Risks:

The risks of drawing blood are small and may include pain, bruising, dizziness, and/or passing out, or infection at the site of the blood draw.

Quality of Life Questionnaires Discomforts:

It may be uncomfortable for you to answer personal or difficult questions about your pulmonary hypertension and how it affects your activities of daily living but there is no pain expected with completing the forms.

Echocardiogram:

This test uses sound waves to look at your heart. The person doing the test will press on your chest with a machine to obtain the pictures. The pressure may be uncomfortable. An ultrasound enhancing agent (UEA) is sometimes used to improve the view of the heart. Possible side effects of the UEA may include headache, flushing, a drop in blood pressure, back or chest pain, nausea, dizziness, or injection site reactions (such as infection or fever), and very rarely an allergic reaction including itching, rash/hives or difficulty breathing.

6-Minute Walk Test Risk:

During the 6-minute walk test you may feel short of breath, dizzy or tired.

Genetic Research:

These studies might uncover a genetic or inborn abnormality that you did not previously know about. Some genetic changes may be clinically relevant, meaning they could affect your risks for future health related problems and change the recommendations for your health care. They might also show that you have a genetic risk factor for pulmonary hypertension that could be shared by other members of your family.

You can decide whether or not you want to be told about this type of genetic result. This information may cause you and family members to be worried and have many questions. Therefore, if you choose to be told about these results, you will be recommended to talk to a genetic counselor who can explain the meaning of the results. The central core laboratory that is doing genetic testing is a research facility and does not have the ability to provide genetic test results directly to you. Therefore, the study investigator at your site will send the information to the genetic counselor and the results will need to be confirmed in a clinical testing laboratory before they are given to you. The cost of genetic counseling and clinical genetic testing is not covered under this research protocol.

To help prevent disclosure, the results of the genetic research will not be placed in your medical record. While every effort will be made to protect the privacy of your results, this cannot be certain. Because your genetic information is unique to you, there is a chance that someone could trace it back to you even without having your name or other personal information in the study database. The risk of this happening is very small.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), effective May 21, 2010, makes it against the law for health insurance companies, group health plans, and most employers to discriminate against you based on genetic information. This law will protect you by:

(1) Health insurance companies and group health plans may not ask for 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) Employers with 15 or more employees may not use your genetic information from this research when making a decision to hire, promote, or fire you or when setting terms of your employment. This federal law does not apply to companies that sell life insurance, disability insurance, or long-term care insurance and does not protect you against use of this information for an already diagnosed genetic condition or disease.

Please initial below to indicate whether or not you would like to be notified about clinically relevant genetic results.

_____ (initials) I would like to be contacted if clinically relevant genetic results become available during this study. I would like to receive results related to (initial one option below):

_____ (initials) ONLY results related to pulmonary hypertension risk

_____ (initials) ONLY results related to risks for other serious health conditions

_____ (initials) ANY results related to pulmonary hypertension or other diseases

OR

_____ (initials) I do not want to be contacted about any abnormal genetic results.

Confidentiality Risk:

The information and samples that researchers are going to collect includes your DNA and information on your medical history. Before your information is sent to the study database, your name and other identifiers will be removed and replaced with a study code. We will keep your identity private but there is a small risk that someone could identify you from the information in the study database.

Tests performed at your center, such as laboratory tests, echocardiogram, sleep study results and 6-minute walk test are likely to be placed into your medical record which can be accessed by healthcare providers other than study physicians.

At the conclusion of this study your medical information collected during the study will be transferred to a biobank at the National, Heart, Lung and Blood Institute. Your name and other identifiers will be removed before the transfer. A biobank is a database that has medical information available to researchers so that more can be learned about this disease. **We cannot include you in this study without your permission to have your information transferred to the biobank. You do not have to give us this permission. If you do not, then you may not join this study.**

Certificate of Confidentiality

To further protect your identifiable data and/or identifiable bio-specimens (for example, blood or tissue) collected and used under this research, a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS) and the National Institutes of Health (NIH) has been obtained.

This added protection to your privacy, limits the re-disclosure of your private identifiable data by the researchers without your permission in any federal, state, or administrative proceedings.

The Certificate will not prevent the researchers from notifying the appropriate authorities when there is a federal, state or local law that requires reporting, such as reporting communicable diseases or child/elderly abuse. The Certificate cannot be used during required auditing or evaluation of federally-funded projects or when required by the Federal Food and Drug Administration (FDA).

This Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer or employer learns about your participation, and obtains your consent to receive research information, we may not use the Certificate of Confidentiality to withhold this information. This means you must actively protect your own privacy.

If you have any questions about what this notice means and would like to speak to someone, you may call the study's Principal Investigator, [Insert name and phone], or Study Coordinator, [Insert name and phone], or the Institutional Review Board (Insert phone number). If you would like to read more about Certificate of Confidentiality, the NIH has a website you can visit online at: <https://grants.nih.gov/policy/humansubjects/coc.htm>.

BENEFITS

What are possible benefits of participating in the research?

There is no direct benefit for your participation in this study. Your participation in this study may provide information that may help other people who have a similar medical problem in the future.

COSTS

Are there any costs to you if you participate in this study?

The study related tests, procedures, and visits will be provided at no cost to you. The cost for echocardiogram and services that would normally be performed even if you don't participate in the study will be billed to you or your insurance provider. You will be responsible for your usual co-pays and deductibles that you would pay when you have a medical test or see your doctors for a regularly scheduled visit. If you have recently had an echocardiogram with your non-study center physicians, then the echocardiogram that is being done will be considered a study related test and you will not be billed. If there is no clinical indication for doing the test, then it will be considered a study related test.

Will I be paid for taking part in this study?

You will receive reimbursement for travel costs if you are coming only for the study purposes and we will cover costs and time related to the study. By law, payments to subjects may be considered taxable income. You will not receive any financial benefits from future use of your samples or information.

RESEARCH RELATED INJURY

What will happen if you are injured as a result of taking part in the research?

In the event you are injured as a result of participation in this research, medical care is available to you. The costs of such medical care will be billed to you or your insurance company. There are no plans to provide compensation for lost wages, direct or indirect losses. The XXX will not voluntarily provide compensation for research related injury. You are not waiving any legal rights by signing this form. Further information about research related injury is available by contacting the Institutional Review Board at XXX.

PRIVACY AND CONFIDENTIALITY

Your name and participation in these studies will be held strictly confidential. Your research samples will be identified only by a study code (not your name). Any identifying data will be kept in a locked drawer or in a password protected computer file. Only the Principal Investigator, XXX, of this study and his or her study coordinator will have access to the numeric code, which identifies you by name. No group health companies or insurance companies will ever be allowed access to the genetic results.

These are some things to remember:

Although the genetic information about you is shared with other investigators in the study, the information will be anonymous: other investigators will be unable to link the results with you.

Results from the research using your samples may be presented in publications and meetings but individual names will not be identified. As part of the publication process, genetic results may be placed in databases that are available to other researchers outside the study, but no personal identifying information will be included.

However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your study data may be reviewed by the following groups (as applicable to the research):

- The U.S. Department of Health and Human Services
- The XXX Institutional Review Board or Human Subjects Protection Program
- The National Institutes of Health (NIH), their agents or study monitors

Tests, such as laboratory tests, 6-minute walk, sleep study results and imaging tests like echocardiogram or lung CT scan, are likely to be placed into your medical record at the site of your testing. Placement into your medical record means that healthcare providers outside of the L-PVDOMICS Study, and insurers, will have access to those test results. Placement in medical records also means that any abnormal findings from those tests can be seen by your healthcare providers.

Protected Health Information

The XXX has rules to protect information about you. Federal and state laws also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it. Generally, only people on the research team will know that you are in the research study and will see your information. However, there are a few exceptions that are listed in this section of the consent form.

The people working on the study will collect information about you. This includes things learned from the procedures described in this consent form or collected by reviewing your electronic health record. They may collect other information including your name, address, date of birth, and other details.

Health information may be collected about you from:

- Your electronic health record, including the management of your pulmonary hypertension.
- Research procedures including interviews, questionnaires, lab results, and other exams explained above.

Why will this information be used and/or given to others?

- To do the research
- To report the results
- To see if the research was done correctly
- To create a National Institutes of Health Global Unique Identifier (GUID) to be able to identify a person who participates in more than one research study. Your GUID will be a random number and does not include any of your protected health information.

If the results of this study are made public, information that identifies you will not be used.

Who may use or share your health information?

- XXX research staff involved in this study
- The XXX Institutional Review Board that oversees the research
- Researchers involved in this study at other institutions
- The National Institutes of Health (NIH)
- The Data Coordinating Center (at the Cleveland Clinic)
- The Observational Safety and Monitoring Board (OSMB) for this study
- Future researchers may request study data from the National Heart, Lung and Blood Institute Biological Specimen and Data Repository Information Coordinating Center (BioLINCC) repository where the study data will be stored when the study is over.

We cannot include you in this study without your permission to use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form; however, people outside the XXX who receive your information may not be covered by this promise. We try

to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee this.

The use and disclosure of your information has no time limit.

QUESTIONS

Who do you call if you have any questions or problems?

- XXX contact information for PI (required) and primary SC (optional) which must be 24/7 number(s)
- XXX If the study involves the Clinical Research Unit (CRU),
- XXX IRB Contact Information

VOLUNTARY PARTICIPATION

What Are Your Rights As A Participant?

Taking part in this study is voluntary. You will be told of any new, relevant information from the research that may affect your health, welfare, or willingness to continue in this study. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled. Your samples and any study data collected will be destroyed at the time, if you decide to withdraw consent. If you decide to withdraw, contact the study PI, XXX at XXX.

There are certain circumstances that would result in stopping further L-PVDOMICS testing without your approval. For example, if you develop conditions that might make continued participation harmful.

SIGNATURES

Statement of Participant

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

Printed name of Participant

Participant Signature

Date

Statement of Person Conducting Informed Consent Discussion

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I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

Printed name of person obtaining consent

Signature of person obtaining consent

Date

CONSENT FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

Printed Name of Impartial Witness

Signature of Impartial Witness*

Date

*Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the subject.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance