NSW HEARTS: The NSW Inherited Cardiomyopathy Cohort Study
Participant Information Sheet

The information statement describes the research project and is divided into three sections:

Section 1: Information about the research project

Section 2: Understanding genomic testing

Section 3: What will happen to my sample and data?

Section 1: Information about the research project

We would like to invite you to participate in a research study gathering information about individuals living in NSW with an inherited cardiomyopathy. We wish to better understand the underlying causes of inherited cardiomyopathies and ultimately provide better care to families. You have been asked to participate in this study because you have an inherited cardiomyopathy, or a close family member does.

NSW HEARTS: The NSW Inherited Cardiomyopathy Study is an NHMRC-funded study. We seek to identify individuals who live in NSW between 2021 to 2023, who have a diagnosis of an inherited cardiomyopathy. We will collect a lot of baseline information and will keep in touch with you into the future to update our information. This follow-up information allows us to answer some really important questions that otherwise wouldn't be possible to investigate.

The study is being conducted by A/Prof Jodie Ingles, Clinical Genomics Laboratory, Centre of Population Genomics, The Garvan Institute of Medical Research, in conjunction with other health professionals and research staff across several NSW centres:

- Royal Prince Alfred Hospital
- St Vincent's Hospital Sydney
- Westmead Hospital Sydney

If you would like to take part in the research project, you will be asked to sign and return the consent form. You will be given a copy of this Participant Information Sheet and the Consent Form to keep.

As a future direction, we are interested in moving to an online consent model. This will allow participants to complete consent online and to customise and change your consent preferences over the course of the study. This platform is still under development; however, we may contact you in the future to move your consent to an online portal when it becomes available.

What does participation in this research involve?

If you consent, we will collect information about you and request you to have a blood sample collected, described in more detail below:

a) Surveys

You will be asked to complete some online surveys about your health: The first three surveys are to be completed when you join the study, and additional surveys will be sent every 1-3 years. Each survey will take approximately 15-20 mins to complete. These surveys will help us to gather important clinical and family history information.

b) Blood sample

You will be asked to provide a 20ml blood sample from a vein in your arm. Some of this will be used to perform a type of genetic test called whole genome sequencing. Your sample will be stored as serum, plasma and DNA at the *NSW Health Statewide Biobank*. These are described below:

- **Genome testing**

  A portion of your blood sample will be sent to an accredited sequencing at laboratory such as the Kinghorn Centre for Clinical Genomics at the Garvan Institute of Medical Research, for DNA extraction and research-based genomic sequencing such as whole-genome sequencing. This is a research test; however, we will provide a report to all participants which will also be sent to their nominated health professional.

- **Biobanking**

  Your sample will be stored at the NSW Health Statewide Biobank. See “Biobanking” on page 3 for further details on blood sample storage.

c) Access to Medical records

Providing your consent and personal details such as name, address, date of birth and the hospital site where you are enrolled in this study, will give us access to your medical record for the purposes of the research project.

We will gather the results of any heart tests you have had with your cardiologist. This may include your medical history, clinical examination by the cardiologist, results of your electrocardiogram (ECG), echocardiogram, cardiac magnetic imaging (CMR) and exercise testing.

If you have been to a genetics clinic in the past, we will also request any genetic testing reports.

Any information not related to the research study will not be requested from any of your doctors.

d) Additional investigations

We will invite eligible participants to undertake other tests that you may not have previously had:

- **Sleep apnoea monitor** is a device that you take home and wear for 1 night. There is a chest strap and a tube that sits under your nose to measure your breath rate. The device will measure the oxygen in your blood, which is an indicator of sleep apnoea. If there is any indication you are at risk of having sleep apnoea, we will feedback to your

nominated health professional and you may be referred to a sleep physician. You will receive written instructions on how to use the equipment. You will receive it by Express Post and be provided with an Express Post envelope to send it back to us in.

- **Charlson comorbidity index** is a series of questions we can use to give a score to how many other health conditions you have. This will be discussed with a study investigator in the clinic setting and will take no more than 5 minutes.
- **Cardiac magnetic resonance imaging (MRI)** is a type of heart scan. It involves laying on a bed in a large tube that is a magnet, for approximately 45 minutes. Cardiac MRIs are not painful, involve no radiation, and have a low risk of side-effects, but are noisy. These tests provide us with useful information about the heart. We will check that you are eligible to have a cardiac MRI (i.e. if you do not have tattoos, permanent body piercings, or an implanted device) If you are eligible, you may be invited to have a cardiac MRI by the study coordinators who will give you more information and a separate consent form.

e) What are the possible risks of taking part?

Blood collection involves some discomfort at the site from which the blood is taken. There is also a risk of some minor bruising at the site, which may last one to two days. Most other tests that we will perform are those performed routinely because of your heart condition and are safe and non-invasive.

f) What are the potential benefits of taking part?

While we intend that this research study furthers medical knowledge about inherited cardiomyopathies and may improve treatment in the future, it may not be of direct benefit to you.

g) Costs

Participation in this study will not cost you anything, nor will you be paid.

h) Voluntary Participation and Withdrawal

Participation in this study is entirely voluntary. You do not have to take part. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be assured that it will not affect your relationship with the staff who are caring for you and your family.

If you decide to withdraw from this research study or from part of this study, you can choose whether you wish to have 'no further contact' from the research team or 'no further contact *and* no further use of your data' by indicating on the *Participant Withdrawal of Consent Form.* If you choose 'no further contact', the research team will not contact you again in the future, but you are happy for your blood sample(s) and information that has already been collected to remain part of the study.

If you also choose the 'no further use of data' option, this means that the blood sample(s) you donated would be removed from storage at the NSW Health Statewide Biobank and safely destroyed. However, in some cases, some or all of your sample might have already been given to a researcher and used for a study, and it might not be possible to trace all the remnants of

your sample. Your health information will also be deleted. However, in some cases, it might not be possible to remove information from analyses that have already been undertaken.

To withdraw from this study, please complete the *Participant Withdrawal of Consent Form* and return it to A/Prof Jodie Ingles at the address on the form.

i) Who is funding this research project?

This study is funded by the National Health and Medical Research Council (NHMRC).

Section 2 – Understanding genomic testing

a) About the test

Our bodies contain billions of cells. Most cells contain a complete copy of all of our genetic information, called the genome. Each of us has about 20,000 genes in our genome. Each gene consists of DNA, which contains instructions for our body's growth and development. New technology has recently allowed us to test all of our genes at once, by using genomic testing. Each person's genome contains many genetic changes (variants) and most of these are harmless because they do not change how the gene works in the body. Genomic testing is done to find the genetic variants that do change how a gene works that result in health conditions. For this study, genomic testing will be used to find genetic variants that change how heart genes work, and may help us learn more about how these genetic variants result in cardiomyopathies.

Genetic counselling is an important part of the genomic testing process. We will ensure that you have access appropriate genetic counselling and can answer any questions that you may have about the testing.

b) Potential outcomes of genomic testing

Your doctor or genetic counsellor can discuss the outcomes of genetic testing with you. If you have not had previous genetic testing, possible outcomes of having the genomic testing include:

- Finding a variant that is the cause of the condition.
- Finding a variant of unknown significance (VUS). The effect of a VUS is unknown, but medical understanding of the VUS may change over time.
- No gene variants found that could explain a genetic condition. Reasons for this include:
    - The variant causing the condition cannot be found by the test.
    - The gene causing the condition was not tested.
    - The gene causing the condition is not yet known.
    - The condition may not have a genetic cause.

If you have had a previous genetic test, possible outcomes of having the genomic testing include:

- Finding a genetic variant related to your cardiac condition that was not found on your previous genetic test.
- Confirmation of your previous genetic testing results.
- Being informed that the variant(s) you are already aware of has/have changed classifications, i.e. if we now know it to be disease-causing, or if it is no longer known to be disease-causing, in the time since you had your previous test.

Since there might be a delay in returning this gene result to you, if you have not had genetic testing in the past and would like your genetic result sooner, we can help you find a local genetics service who can do this with a faster turnaround time.

c) Potential benefits of genomic testing

Some people wish to have genomic testing to find a genetic diagnosis to help them understand their condition. A genetic diagnosis can help families to access support and services that they need and to plan for the future, and a genetic diagnosis may also help health professionals manage their patients' conditions.

A genetic diagnosis may provide families with information about the chance of having another child. Sometimes, the genomic test result for one family member may also be important in helping to identify the same variant in another relative, and in the health care plans for their relatives.

If a genetic diagnosis for your cardiomyopathy doesn't happen through genomic testing we are able to offer, the data will be looked at again in the future as our understanding improves.

d) Potential risks of genomic testing

- **Incidental findings**

  Genomic testing looks at many genes at once, so there is a small chance of unintentionally finding a variant that is not related to your cardiomyopathy that may have serious and significant health implications for you (and your genetic relatives). This is called an incidental finding.

  There is a small chance that now, or in the future, we may identify a variant in a gene that is not related to your cardiomyopathy, i.e. an incidental finding. We will only return these to you if we believe they are clinically important. You are consenting to be notified of any incidental findings and then you can decide whether or not you would like to receive the details of the findings.

  Incidental findings will be returned to you by a doctor or healthcare professional when the following 3 criteria are met:

  - The finding indicates a potentially life-threatening condition or affects your reproductive health;
  - There are specific established and therapeutic interventions or other available actions, and;
  - The finding has been checked and confirmed as accurate and/or valid, as far as reasonably possible in a research context.

  If medical follow-up is required as a result of an incidental finding, your doctor or genetic counsellor will assist you by making appropriate referrals as necessary.

Section 3 – What will happen to my sample and data?

Biobanking (long term storage of samples)

A biobank is a stored collection of human biological samples such as blood and/or their products (e.g. DNA, serum and plasma). Biobanks are an important resource for medical researchers to improve the understanding of diseases and to help find better ways to prevent or treat them. A person from the NSW Health Statewide Biobank may contact you by phone to confirm that you have given consent. This phone call will be recorded and kept as a legal record.

Blood sample storage

All blood samples will be stored indefinitely in the NSW Statewide Biobank Facility in Camperdown, NSW, and from time to time, at the location of the sequencing provider(s) such as the Garvan Institute of Medical Research in Darlinghurst, NSW. The samples and associated health information are stored securely, and used for medical and health-related research projects. Any projects must be approved by a Human Research Ethics Committee, which is an independent committee that has ethical oversight of research involving humans. This committee will be required to meet Australian ethical standards.

Genomic testing

Your blood sample will be sent to the laboratory for DNA extraction and research-based genomic testing will be performed. During this process, your sample will be identifiable as a requirement of sample tracking. They will only be identifiable to laboratory personnel and approved study researchers.

Data linkage

By consenting to biobanking, you are also consenting for researchers to access and link information held by NSW Health. This may include your clinical records and hospital admission details. Name, date of birth and address will not be stored with this information. The information will be stored in a secure, password-protected database. Researchers involved in your clinical care will not have access to your NSW Health linked data.

Study data storage and usage

All study data will be stored in secure, controlled-access databases managed and housed at the Garvan Institute of Medical Research, that meet international security standards and Australian laboratory accreditation requirements. During the course of the study, we may need to transfer your data to another location secure and ethically approved location. Only the study doctors, researchers, coordinators and personnel working directly with this study will have access to the databases. Research data will be stored for a minimum of 15 years after the completion of the study.

Your “re-identifiable” information and sample may be requested to be used by current or future health and medical researchers. All requests will be stringently reviewed and discussed by the study team before access is granted. Access will only be granted to ethically approved health and medical research studies, and your data will only be shared when safeguards are in place to help protect your privacy. Personal identifiers will be removed (including your name, date of birth and address) and replaced with a study code. Stringent security measures will help prevent

unauthorised access or misuse. These safeguards make it difficult to know whether the information is about you or other people; however, there is always a very small chance that it might be linked back to you.

Providing consent for genomic testing also allows for the sharing of your sample, genomic data and related health information to advance scientific knowledge. Your information will be shared in a way that protects your privacy ("anonymised"). This may include sharing on large databases to help improve understanding of related conditions by comparing your results to those from other people.

Confidentiality

All of the information collected from you for the study will be treated confidentially. All data will be stored on a secure, password protected database, housed at the Garvan Institute of Medical research, or in locked, filing cabinets at your recruitment site.

All data will be stored for at least 15 years in accordance with NSW law.

These data may be used in a de-identified way in other larger studies, but your information will not be identifiable in any way. Should any breach of privacy occur, the lead investigator (A/Prof Jodie Ingles) will ensure the situation is dealt with in accordance with existing privacy laws and guidelines.

The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Future research studies

Information and samples collected as part of this study may be used in larger national or international studies. In some cases, we require very large datasets to be able to answer really important questions, and combining information among research groups is a powerful way to advance our knowledge. Any data or sample we send will be de-identified and treated confidentially.

Further Information

When you have read this information, a study coordinator will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact us on XXXX XXXX.

<u>This information sheet is for you to keep.</u>

Ethics Approval and Complaints

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District and given the protocol number X20-0450. Any concerns or complaints about the ethical conduct of this study can be directed to the Executive Officer on 02 9515 6766.

The conduct of this study at the {name of site} has been authorised by {name of LHD). Any person with concerns or complaints about the conduct of this study may also contact the Research Governance Officer on 02 XXXX XXXX and quote Protocol number {insert local protocol number}.

NSW HEARTS: The NSW Inherited Cardiomyopathy Cohort Study

Participant Consent Form

Tissue bank and genetic study – Adult providing their own consent

Title	The NSW Inherited Cardiomyopathy Cohort Study
Short Title	NSW HEARTS
Protocol Number	X20-0450
Project Sponsor	Sydney Local Health District
Coordinating Principal Investigator/ Principal Investigator	A/Prof Jodie Ingles
Location	{insert site name}

Declaration by Participant

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.
- I understand that I will be given a signed copy of this document to keep.
- I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information concerning my condition and treatment for the purposes of this project. I understand that such information will remain confidential.

Biobank

- I understand that my data will be linked to health and personal information held by NSW and Commonwealth governments and by researchers. This will be coded any my identity will be protected.
- I understand that my blood sample will be stored safely at the NSW Health Statewide Biobank and will be linked with my health and personal information (data). My privacy will be secure and protected. My sample and records will not include my name or contact details when sent to researchers.

- I understand that my sample and data may be held indefinitely. It will be kept under strict security and privacy conditions in line with the law.

- I understand that other researchers (in NSW, Australia, and internationally) may request to use my sample and data stored at the NSW Health Statewide Biobank for health or medical research studies, now and in the future. I understand that my sample and data can only be used in ethically approved research studies that have been approved by a registered Human Research Ethics Committee.

- I understand that all requests to use my sample or data in ethically approved research studies will be individually reviewed by the NSW HEARTS research team, who will decide to accept or reject the request. I understand that I won't be told what research studies my sample is used for, but we will keep people updated about overall study findings via our website.

- I understand that, although rare, it is possible that other ethically approved research studies using my sample or data could make discoveries that have potentially serious and important health consequences for me or my family. I understand that I will be contacted by a healthcare professional in this event and can decide whether I would like to know the details of the findings.

- I understand that present and future research with my DNA may reveal clinically relevant findings relating to me or my family for which treatment is available or pending, and that I will be notified of this.

- I would like to be emailed a copy of the study results: Yes □ No □

If yes, my email address is: _____

- I understand that my nominated healthcare professional will be notified of any study findings relevant to my health.

  My health professional to be informed of any clinically relevant findings relating to my health. The details of my healthcare provider are:

  Cardiologist's name: _____

  Address: _____

- I understand that I can withdraw my consent to participate in this research project by completing a "Withdrawal of Consent" form. I can also specify whether I wish to have my blood, which has already been collected and stored, to remain part of the study, or deleted, destroyed or returned to me if it is still identifiable as mine.

Name of Participant _____

(Please Print)

Signature _____ **Date** _____

Name of Witness* _____

(Please Print)

Signature _____ **Date** _____

** A witness is not to be the investigator, a member of the study team or their delegate. A participant's interpreter cannot act as a witness. A witness must be over 18 years old.*

Declaration by Study Doctor/Senior Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe the participant has understood that explanation.

Name of Study Doctor/ Senior Research _____

(Please Print)

Signature _____ **Date** _____

NSW HEARTS: The NSW Inherited Cardiomyopathy Cohort Study

Participant Withdrawal of Consent Form

Title	The NSW Inherited Cardiomyopathy Cohort Study
Short Title	NSW HEARTS
Protocol Number	X20-0450
Project Sponsor	Sydney Local Health District
Coordinating Principal Investigator/ Principal Investigator	A/Prof Jodie Ingles
Location	{insert site name}

Declaration by Participant

Please tick your withdrawal of consent option(s):

☐ I wish to not be contacted again by the research team about the above research project in the future. *(No further contact)*

☐ I agree to my data and blood sample(s) that have already been collected to remain part of this study.

☐ I request that my data and blood sample(s) collected and banked be deleted, destroyed or returned to me if it is still identifiable. I understand that it might not be possible to trace all the remnants of my sample that have already been given to a researcher and used for a study. I also understand that it might not be possible to remove all my data from analyses that have already been undertaken. *(No further use of data)*

- I understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with {insert site name]

Name of Participant _____

(Please Print)

Signature _____ **Date** _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher*

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Research _____ (Please Print)

Signature _____ **Date** _____

* *A senior member of the research team must provide the explanation of, and information concerning, withdrawal from the research project.*

Note: All parties signing the consent section must date their own signature.

Mail this page to: **A/Prof Jodie Ingles**

Clinical Genomics Laboratory, Centre of Population Genomics
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Darlinghurst NSW 2010
Sydney Australia