Participant Information Sheet/Consent Form

Non-Interventional Study - *Adult providing own consent*

Healthy Volunteers

Title:	**Inter-organ cross talk in heart failure: A multisite biomarker sampling study**
Short Title:	Multisite biomarker sampling in heart failure
HREC Protocol Number:	HREC/80653/Alfred-2021
Local Project Number:	633/21
Project Sponsor:	Alfred Health
Principal Investigator:	Professor David Kaye, Department of Cardiology, Alfred Hospital
Associate Investigators:	Assoc Prof Justin Mariani, Dr Shane Nanayakkara, Dr Hitesh Patel, Dr Jason Bloom, Ms Donna Vizi, Ms Liz Dewar, Ms Jia Tang, Mr Nicholas Hemsley, Dr Waled Shihata, Assoc Prof Bing Wang, Mr Duncan Horlock

This document is 12 pages long. Please make sure you have all the pages.

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project as a Healthy Volunteer subject. This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether you take part or not.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- understand what you have read;
- consent to continue to take part in the research project;
- consent to have the tests that are described;
- consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

Our study is investigating the way in which the body responds during heart failure. In trying to understanding this process, it is important to understand the way in which relevant systems operate in normal health. When the heart fails to function normally, either due to reduced pumping capacity or increased muscle stiffness, it adapts in various ways. One of these appears to be the release of various hormones and chemicals by the heart muscle. For example, it is already known that the heart secretes some proteins (e.g. brain natriuretic peptide: BNP) in high levels of heart failure, and the measurement of BNP levels in blood is now a routine test for heart failure patients. In conjunction, it is increasingly understood that the levels of many other chemicals (such as small molecules, proteins and nucleic acids) change during the heart failure process. Whilst some of these are released by the heart, others likely originate in other organs including the lungs, kidneys and liver which are also major potential contributors to the symptoms, progression and outcomes in heart failure. Much less is known about the release of the various types of chemicals from these other organs in the setting of heart failure. The objective of this study is to better understand the level of these chemicals released in heart failure, with a view to developing better tests and treatments for heart failure patients.

Professor David Kaye has designed this study and the study is supported by a research grant from the National Health and Medical Research Council of Australia. Prof Kaye and his team have conducted several studies over the past 25 years, using the techniques outlined in this study.

3 What does participation in this research involve?

You must meet certain requirements and have certain test results in order to take part. We will need to check that you are free from heart disease. This will involves taking a detailed medical history, a physical examination and several investigations as described below.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

You may be reimbursed for any reasonable travel, parking and other expenses associated with the research project visit.

It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research project

What will happen to me during the study?
If you agree to take part in this study, you will first sign this Study Participant Informed Consent Form before any study-related procedures are performed. Before you sign, you will need to read the information in this form. The research staff will explain the study to you and you are free to ask questions from the research staff before you decide you want to participate. You will be given a copy of this signed form.

Study Procedures Summary
This will give you information about what taking part in the study will mean to you, for example, how often you have to come to see the study centre, how long each visit will take, how much blood will be taken and when tests and procedures will be performed.

The duration of the visits shown below is if all the procedures are done on the same day. The study team will discuss with you the scheduling of the different procedures, and these may be done on more than one day within the study visit window, if needed.

Visit 1 Approximately 1.5 hours

At this visit, the following procedures will take place:

- Informed consent, a full physical examination and medical history and check of all medications you are taking.
- Height and weight measurements
- Heart rate and blood pressure will be measured
- An electrocardiogram (ECG) will be performed
- Non-fasting blood samples (approximately 4 teaspoons or 20 mL) to assess kidney and liver function, blood count and thyroid function tests. (A pregnancy test will be done if you are a woman of childbearing potential).
- You will perform a 6-minute walk test. This will measure the distance you can walk for six minutes on a hard, flat surface.
- Questionnaire*:* You will be asked to complete two questionnaires related to heart failure symptoms (the Kansas City Cardiomyopathy Questionnaire & EQ-5D).

Visit 2 Approximately 4 hours

You will have had a light meal at least 3 hours before attending for the study visit.

Echocardiogram: This is a heart ultrasound scan, you have probably had these performed before. You will be asked to lie on a bed, as relaxed as possible, whilst the technician takes pictures of the heart for approximately 30 minutes. You will be asked by the technician to roll on your side and various positions in order to obtain different views of the heart. A water-based gel is applied to the skin of your chest to allow soundwaves to be conducted from the ultrasound probe. The ultrasound itself is painless; at times there may be some firm pressure applied to the chest from the ultrasound probe. The echocardiogram is safe; it has no side effects. Three sticky electrodes on your shoulders will record your ECG during the test. You may hear whooshing noises for some of the time, when blood flow is measured.

Heart catheter study: You will be awake during the test; 2 separate tubes will be placed into blood vessels. After injection of local anaesthetic into the skin, a doctor will insert a catheter (a thin plastic tube) into a large vein usually in the arm but sometimes in the right side of the neck (jugular vein) using ultrasound to identify the correct placement. Through this tube a smaller tube will be advanced step by step to the heart, lungs, kidney and liver using x-ray guidance to measure the blood pressure and to collect a blood sample from each location. A fine tube will also be placed into an artery located at the wrist or elbow under local anaesthetic to measure your blood pressure and to collect blood samples.

The amount of blood that will be collected during the heart catheter test will be about 150mL. This procedure will take approximately 1-1.5 hours to complete. After the test, you will stay for a further 1 hour for observation and then be allowed to go home. Avoid bending, heavy lifting or straining for the next 24 hours.

Follow up contact

We will contact you by telephone 1 week after the heart catheter study to check in on your well-being.

VISIT SUMMARY TABLE:

	Screening Visit (Visit 1)	Randomisation (Visit 2)	Follow up (Phone call)
Day of study & visit window	**Day -7 (±7)**	**Day 0**	**Day 7**
Informed Consent	**X**		
Inclusion/exclusion criteria check	**X**		
Physical examination	**X**		
Electrocardiogram (ECG)	**X**		
Medication Review	**X**		
Vital Signs	**X**		
Peripheral blood test	**X**		
Questionnaires (KCCQ & EQ-5D)	**X**		
6-minute walk test	**X**		
Trans-thoracic echocardiogram (TTE) (if not one available within 3 months)		**X**	
Catheterisation & multisite sampling		**X**	
Adverse Event report		**X**	**X**
Study review and close			**X**

4 What do I have to do?

There are no specific lifestyle restrictions during your participation in this study. You can take all other regular medications, unless specifically advised by the study researchers. Your ability to donate blood will not be affected by your participation in this study.

5 Other relevant information about the research project

This project will collect samples from 100 participants who have been diagnosed with heart failure and another 25 healthy control subjects.

This project is a single-site study and Alfred hospital is the only site. This study will be conducted at Baker Heart and Diabetes Institute and the Alfred Hospital. The project involves researchers from the Baker Heart and Diabetes Institute and the Heart Failure Research Group at the Alfred Hospital working in collaboration.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part you are not obliged to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Alfred Health.

Before you make your decision, a member of the research team will be available so that you can ask any questions you have about the research project. You can ask for any information you want. Sign the Consent Form only after you have had a chance to ask your questions and have received satisfactory answers.

If you decide to withdraw from this project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to inform you if there are any health risks or special requirements linked to withdrawing.

7 What are the alternatives to participation?

Your alternative is not to participate in this study. This research project is not providing a treatment option to you. If you decide not to participate in the study, this will not affect your treatment at the Alfred Hospital.

8 What are the possible benefits of taking part?

There will be no clear immediate benefit to you from your participation in this research.

9 What are the possible risks and disadvantages of taking part?

Venepuncture (Taking Blood Samples): Having a blood sample taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel. Some people may feel faint when having blood taken, and may occasionally faint. Rarely, there could be bleeding or a minor infection. If this happens, it can be easily treated.

Catheterisation of the wrist/elbow artery is a commonly performed procedure. We will apply local anaesthesia at the puncture site, the local anaesthesia or the puncture may cause some discomfort or bruising. Minor possible side effects related to this procedure are bruising or bleeding at the puncture side which can be treated by compression of the artery after removal of the catheter. More serious complications including closure of the vessel requiring surgery, or infection at the puncture site are rare (2-10 in 10,000 procedures). If untreated these could lead to permanent damage of the hand.

Right heart catheterisation is also commonly performed. After using local anaesthetic on the skin of the neck or arm, the tube is directed towards the chambers of the right side of the heart, to the main artery feeding your lung or to the veins draining the heart. Moving the tube to different parts of the body is painless and you will generally be unaware of its location.

The risk of death or serious disability resulting from this procedure is extremely small. Amongst thousands of these research procedures performed at The Alfred, we are yet to encounter any serious problem leading to long term disability. There is a slight risk of damaging the vein or wall of the heart with the catheter causing internal bruising or bleeding. Generally, this will quickly stop of its own accord and all that would be required is a period of observation. On very rare occasions (so rare that we have not encountered it) it might be necessary to repair the damage with an operation. It is not uncommon to experience some bleeding and bruising where the catheter was inserted in the arm or neck. This can generally be prevented by firm pressure over the area for at least 5 minutes and like other bruises it will resolve over the next week or so. The advancement of the catheter through the heart may cause an abnormal heart rhythm which may cause some thumping in your chest. This can be alleviated by removal of the catheter or by giving appropriate medication. Occasionally, rhythm disturbances may last a day or two, and require admission to hospital for a controlled shock to restore normal heart rhythm (cardioversion). Rarely, there could be blockage of the vein causing swelling of the relevant limb.

The whole procedure generally lasts 1-2 hours and it may be uncomfortable lying horizontally for this period.

X-rays/Radiation: This research study involves exposure to a small amount of radiation. We will use an X-ray camera to help guide the catheters into the correct location. You may have had a similar test previously (angiogram or right heart catheter test). As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is about 2 mSv. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. The risk is believed to be low.

If you have been involved in any other research studies that involve radiation please tell us. Please keep information contained within the Patient Information and Consent Form about your exposure to radiation in this study, including the radiation dose, for at least five years. You will be required to provide this information to researchers of any future research projects involving exposure to radiation.

10 What will happen to my test samples?

The collection of the blood samples will be split into two parts. One component will be processed and handled via the Alfred Pathology department and then destroyed after analysis in accordance with hospital policy.

The second part will be processed at the Baker Heart and Diabetes Institute and at our partner laboratories. Prof Kaye and his team have a specialised laboratory, that allow us to measure the levels of various chemicals in your blood samples. These blood samples will be stored in a re-identifiable manner (by Professor Kaye only). These samples will be coded with a study number, of which a study log is kept, linking your study sample and your identity. This log is kept in secure area only accessible by Prof Kaye and his research team. Laboratory staff and any external partners will not know the identity of the samples. This means that samples will be collected and labelled with a study identification number and will not contain any personal identifying information. Blood samples will be kept for a maximum of 10 years and will be destroyed thereafter using medical waste service.

The following component of future research is optional.
It is possible that during the period your samples will be stored in the Baker laboratory that we may develop collaborations with other research partners that have access to techniques or treatments of mutual research interest. As new techniques and information emerge in the future we would like to be able to reanalyse your blood samples to understand more about the mechanisms of heart failure. We would like your permission to store your samples for future research. The blood samples left over from our initial studies will be frozen down and will be stored in Professor Kaye's laboratory at the Baker Heart and Diabetes Institute, in a -80°C freezer. There is no possibility that you could be identified from the samples. In the event of such a collaboration we would first obtain approval from the Alfred Hospital Ethics Committee and also arrange for the necessary agreements between researchers.

By signing the Consent Form for tissue sample storage and use, you consent to the future use of the blood samples. These samples for future research will be kept for a maximum period of 10 years and will be destroyed thereafter using medical waste service.

11 What if new information arises during this research project?

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information.

12 Can I have other treatments during this research project?

The study does not require any change to your usual medication. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project.

13 What if I withdraw from this research project?

If you decide to withdraw from this research project, please notify a member of the research team before you withdraw. A member of the research team will inform you if there are any special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly. This may include the possibility of unexpected and unacceptable side effects becoming evident during the course of the study.

15 What happens when the research project ends?

The study results will be presented at national and international meetings, and published in medical journals.

Any personal information will be removed and you will not be identifiable from the results presented or published.

We will also put the results of the study on the Heart Centre website located on this link www.alfredheartcentre.org.au

Part 2 How is the research project being conducted?

16 What will happen to information about me?

In accordance with relevant Australian and/or Victoria privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information gathered during this research study that can identify you will remain confidential and will used for the purpose of this research study and future research related to heart failure, including the use of your stored samples. In accordance with applicable laws, every effort will be made to keep all information about you private. The information gathered will be stored in re-identifiable format with a study number. There is, however, a screening log kept by the study staff to connect the study number to your true identity, in order to perform data verification. The re-identifiable information will only be shared with your permission, except as required by law. At the end of this study it is possible that the information collected for all patients, including you, may be presented at a local or international scientific conference or published in a scientific journal. All information will be presented in such a way that neither you nor any other patient may be identified. By signing the consent form you give permission for your re-identifiable data to be used in this way.

A de-identified database will be created. Basic demographic data (age, sex, diagnosis), and cardiovascular data (echocardiographic and haemodynamic/catheter data) and basic clinic pathology data (including kidney function) will be recorded to correlate with blood tests. All

study data for this trial will be kept indefinitely as per Alfred Research Ethics policy guidelines. Only members of the study team will have access to the data and all the information will either be securely locked in a storeroom, or protected by electronic encryption.

If you consent to future research, these data will also be used.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Information about your participation in this research project may be recorded in your health records.

The samples and the data for this research project will be stored at the Alfred Hospital and Baker Heart Failure Group Laboratory.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. You need to be eligible for Medicare to participate in the study as a requirement at Alfred Health. Medicare will allow you to receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research project is being conducted by Professor David Kaye, who has designed this study and is supported by a research grant from the National Health and Medical Research Council of Australia

19 Who has reviewed the research project?

An independent group of people called a Human Research Ethics Committee (HREC) reviews all research projects in Australia involving humans. The HREC of Alfred Health – the Alfred Hospital Ethics Committee has approved the ethical aspects of this research project.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 03 *9076 3263* or any of the following people

Clinical contact person

Name	Ms Donna Vizi, Ms Jia Tang or Mr Nik Hemsley
Position	Research Coordinators
Telephone	03 9076 2948, 03 9076 6519
Email	hfresearch@alfred.org.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Position	Complaints Officer
Telephone	03 9076 3619
Email	research@alfred.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Local HREC Office contact (Single Site - Research Governance Officer)

HREC name	Alfred Hospital Ethics Committee
Position	HREC Executive Officer
Telephone	03 9076 3619
Email	research@alfred.org.au

theAlfred

Consent Form - *Adult providing own consent*

Title	**Inter-organ cross talk in heart failure: A multisite biomarker sampling study**
Short Title	Multisite biomarker sampling in heart failure
HREC Protocol Number:	HREC/80653/Alfred-2021
Local Project Number:	633/21
Project Sponsor	Alfred Health
Principal Investigator	Professor David Kaye
Associate Investigator(s)	Assoc Prof Justin Mariani, Dr Shane Nanayakkara, Dr Hitesh Patel, Dr Jason Bloom, Ms Donna Vizi, Ms Liz Dewar, Ms Jia Tang, Mr Nicholas Hemsley, Dr Waled Shihata, Assoc Prof Bing Wang, Mr Duncan Horlock
Location	Alfred Hospital

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 give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Alfred Hospital concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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 study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher†

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

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

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

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

Consent Form for Blood Sample Storage and Use

Adult providing own consent

Title	**Inter-organ cross talk in heart failure: A multisite biomarker sampling study**
Short Title	Multisite biomarker sampling in heart failure
HREC Protocol Number:	HREC/80653/Alfred-2021
Local Project Number:	633/21
Project Sponsor	Alfred Health
Principal Investigator	Professor David Kaye
Associate Investigator(s)	Assoc Prof Justin Mariani, Dr Shane Nanayakkara, Dr Hitesh Patel, Dr Jason Bloom, Ms Donna Vizi, Ms Liz Dewar, Ms Jia Tang, Mr Nicholas Hemsley, Dr Waled Shihata, Assoc Prof Bing Wang, Mr Duncan Horlock
Location	Alfred Hospital

I consent to the storage and use of blood samples taken from me for use in further research as described in this Participant Information by ***Professor David Kaye***.

Yes ☐ ***No*** ☐

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher†

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

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

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

Form for Withdrawal of Participation - *Adult providing own consent*

Title	**Inter-organ cross talk in heart failure: A multisite biomarker sampling study**
Short Title	Multisite biomarker sampling in heart failure
HREC Protocol Number:	HREC/80653/Alfred-2021
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Project Sponsor	Alfred Health
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Location	Alfred Hospital

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Alfred Health

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 Researcher† (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.