Imperial College London

NHS Royal Brompton and Harefield hospitals

Participant Information Form

A randomised trial examining therapy to maintain remission in dilated cardiomyopathy

Chief / Principal Investigator
Dr Brian Halliday
Senior Clinical Lecturer in Cardiomyopathy and CMR
Consultant Cardiologist
National Heart and Lung Institute, Imperial College London
Royal Brompton and Harefield Hospitals, London
Ext: 02073528121 Ext 82928

IRAS reference:

We would like to invite you to take part in a research study. Your participation is entirely voluntary. The following information is designed to help you understand why the research is being done and help you decide whether or not you wish to take part. Please take time to read the following information carefully and contact us if you have any questions. Thank you for reading this.

What is the purpose of the study?

The aim of the study is to determine if it is safe and feasible for patients, with a prior diagnosis of dilated cardiomyopathy that is now in remission, to reduce the number of medications they take from 3 or 4 to 2.

Why have I been invited?

You have previously been diagnosed with dilated cardiomyopathy (DCM) and your doctor thinks that you may be suitable to enter our study.

DCM is the most common disease of the heart muscle and can be caused by many different things including spelling mistakes in genes, infections and excess alcohol consumption. It is characterised by a reduction in function and increase in size of the heart's pumping chambers. In 2 out of 3 patients, the heart function improves with medications. In around 1 in 3 patients, the heart function returns to normal and symptoms resolve – we call this remission of DCM. A question we are often asked by patients is whether they need to continue their medications after their DCM has entered remission.

Our previous study of patients in remission showed that around 4 out of 10 of them had a deterioration in their heart function if all medications for heart failure were stopped in quick succession. We detected this at an early stage and after restarting medications, patients heart function improved again.

We have held workshops with patients with DCM and they emphasised the desire to take part in further studies investigating which of the 4 conventional heart failure therapies were most important to maintain DCM remission. They felt it was important to investigate whether we could reduce the number of medications that patients with DCM remission needed to take in the long-term.We aim to carry out a study which answers this important question.

What is the drug or intervention that is being tested?

We will study 50 patients with DCM who now have remission and assess whether it is safe for participants to stop mineralocorticoid receptor antagonists (MRA, eg. spironolactone or eplerenone)

and sodium glucose co-transporter 2 inhibitors (SGLT2i, eg. empagliflozin or dapagliflozin) in a slow and supervised fashion, whilst continuing beta-blockers (eg, bisoprolol) and renin-angiotensin system inhibitors (eg, ramipril or sacubitril valsartan). We will follow participants very closely by seeing the in clinic and performing blood tests and cardiac magnetic resonance (CMR) scans to ensure the risk from reducing medications is minimised.

If the study demonstrates that it is safe and feasible to stop the 2 medications, we will go on to perform a larger study looking at the risks and benefits of withdrawing heart failure medications in the long-term.

Do I have to take part?

No. Your participation is entirely voluntary. To check whether you are suitable to take part in the study, we may ask you to provide consent for us to contact your doctors and find out more information about you. If it appears that you are suitable and you decide to take part, you will be invited to visit or speak with the research team. They will talk to you about the study and if you are happy to take part, they will ask you to sign a consent form.

You are free to leave the study at any time if you do choose to take part. If you decide to leave the study, we will pass on the results of the investigations performed, to your GP and your usual cardiology team. We will also contact them to update them on your progress since entering the study. Your future care will be planned by your regular doctors. We will use the data that we have collected up until this point for the research. We may also speak to usual doctors to gather information about you.

If your GP wishes to seek specialist advice after you have left the study, this can be facilitated through referral to a cardiology service, such as our Adult Cardiomyopathy Clinic, at the Royal Brompton Hospital (RBH). If you choose to withdraw from the study, your future medical care will not be affected. You will be informed of any significant new findings that may affect your willingness to continue to participate.

What will happen to me if I take part?

If you decide to take part, you will attend a visit at Royal Brompton Hospital. After completing the consent form, the research team will ask you some questions and you will complete some questionnaires about your symptoms. Your responses will be entered using a computer. The research team will assist you if needed. You will then undergo a CMR scan, a heart tracing known as an electrocardiogram (ECG) and blood tests. Women of childbearing age will have a pregnancy test. You will then be randomly assigned to the treatment withdrawal group or the control group (see diagram). This means that participants will be put into groups and their progress compared during the study. The groups are selected by a computer which has no information about the individual – i.e. by chance. Participants in each group will have a different treatment. These groups will be compared over the following 8 months. Participants will have 5-7 visits in total to monitor their progress.

Those participants in the treatment de-escalation group will stop their SGLT2i first and then their MRA 8 weeks later. If patients are only taking one of these 2 medications, they will stop that medication first. Those patients in the control arm will continue their medications as usual.

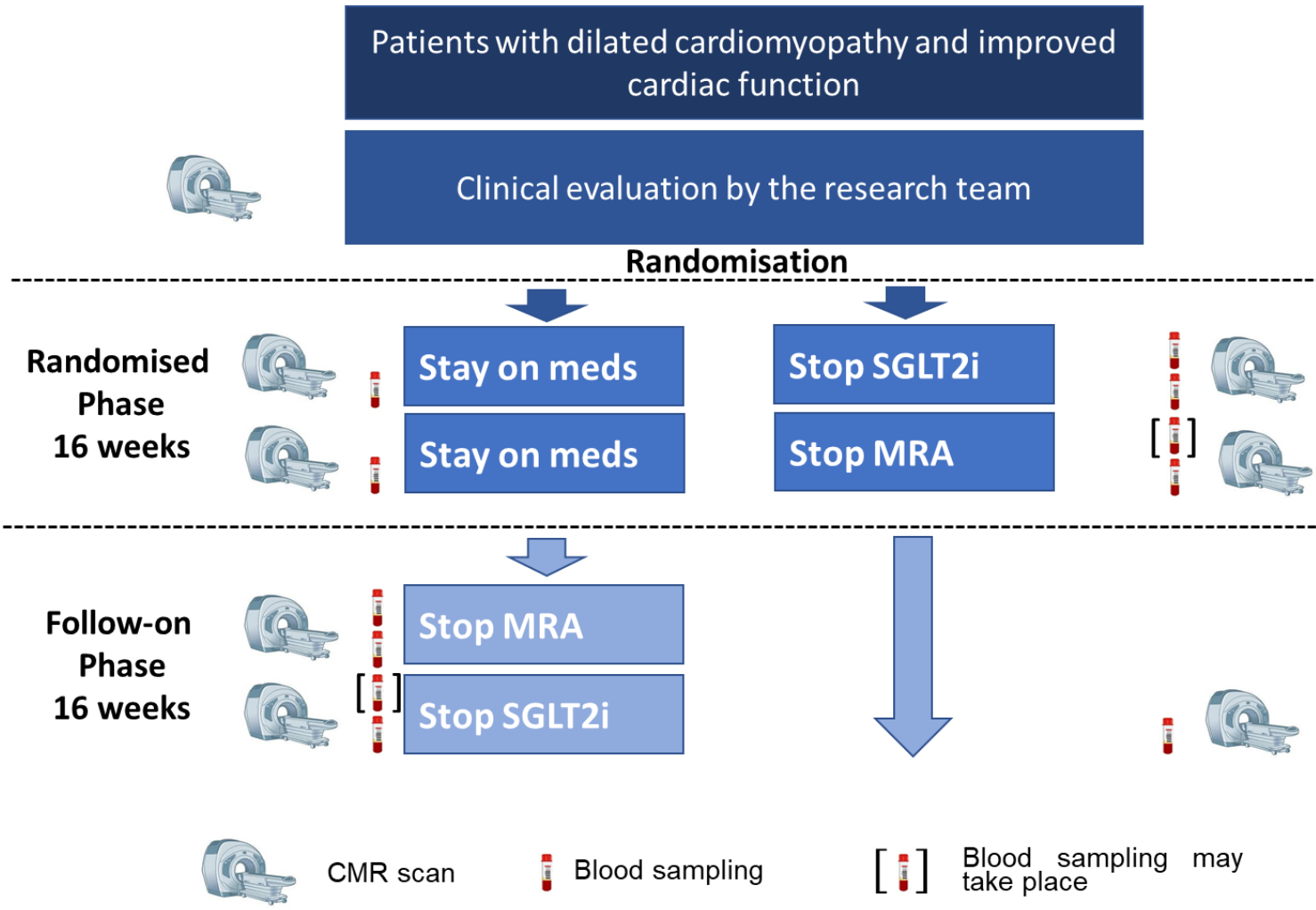
All participants will be seen in clinic and have a CMR scan after 8 and 16 weeks. Two weeks after stopping a medication, participants in the treatment de-escalation arm will have a telephone call with the research team to check progress. Four weeks after stopping a medication, participants will have a clinic visit with the research team. Visits will be more frequent for participants as they stop medications.

After 16 weeks, those patients who continued all medications in the first half of the study will be given the opportunity to stop the medications in the same supervised fashion over the following 16 weeks. The only difference is that they will stop their MRA first and their SGLT2i second. **All patients in the study will therefore get an opportunity to stop their medications.** Visits and scans will be repeated as described for those undergoing therapy withdrawal in the initial phase of the study.

After 16 weeks, those patients who have stopped SGLT2i and MRA in the first phase of the study will have the opportunity to continue off their treatment for the following 16 weeks. They will have a repeat CMR scan and blood test at the end of the study, 16 weeks later.

If patients meet any of the criteria for a relapse of DCM (reduction in heart function, a rise in the heart failure biomarker [NT-pro-BNP], or develops signs or symptoms of heart failure), they will restart all heart failure therapy as quickly as possible.

This study gives participants the opportunity to come off medications in a supervised, monitored fashion, not ordinarily available otherwise. If there is any sign of worsening heart function, patients will be put back on medications at the earliest opportunity, reducing the chances of coming to any harm as a result of stopping medications to the smallest possible level.



MRI Scans

As part of the study, participants will undergo 4 or 5 MRI scans. Magnetic resonance imaging (MRI) is a technique which produces detailed images (pictures) of the body without using radiation (X-rays). We will use MRI to examine your heart and muscles. It allows us to look at the heart and muscles in detailed ways that other imaging techniques such as ultrasound are unable to replicate. This is achieved by using a body scanner consisting of a strong magnet which generates a magnetic field. A combination of this magnetic field, together with radio-waves is used to produce images.

It is necessary to remove all metallic objects and clothing with metal fastenings before a scan. You will then be asked to lie on a couch which is moved into the open-ended scanner. During the examination you will be asked to hold your breath for a few seconds while the images are being taken. The scanner makes quite a loud noise when it is operating so you will be given headphones to wear. The headphones also enable the staff to speak to you during the scan. If at any stage you are feeling uncomfortable, you can ask to be taken out of the scanner. The scan will take between 20-40 minutes. Some people find the scanner claustrophobic.

Extra information can be gained by the use of a "contrast agent" called gadolinium. We will use this for 1-3 scans. This is a dye which is injected into the bloodstream via a small tube called a cannula that is inserted into a vein in your arm. The role of the contrast agent is to show up any areas of scarring in

the heart. It only remains in the bloodstream for a short time and does not usually have any side-effects. Very occasionally people may complain of a headache, metallic taste, dizziness or feeling sick. Gadolinium is routinely used in clinical practice. It is not possible to give gadolinium to patients with severe kidney disease.

Patients with pacemaker or defibrillator devices will be scanned using special protocols with all necessary precautions taken. Studies have shown that it is safe to scan patients with pacemakers or defibrillators provided these special protocols are used. The Royal College of Radiologists has approved these protocols and this practice.

Blood Tests and Genetic Tests

Patients will undergo 6-9 blood tests during the study. We aim to take the blood sample at the same time as putting your cannula in (if required for the MRI scan), thereby minimizing the number of needles used. The samples will look at markers of heart function, scarring of the heart muscle, markers of metabolism (the processes used to promote growth and make energy) and spelling mistakes in genes (changes in DNA) that are known to cause cardiomyopathy or changes in heart function. It is possible that a spelling mistake in a gene is unique to the individual in whom it is found. If a spelling mistake is unique to you, it is possible that this could be used to track information back to you. It will only be possible for others to track information back to you if other information linking the spelling mistake to you is available. We will ensure such information is protected.

We will take 2-3 tablespoons of blood on each occasion, which is around 30-50mls. Some of the blood sample will be analysed immediately for tests and some will be stored in our Biobank for future analysis. This will look for changes in genes known to be associated with cardiovascular disease, including dilated cardiomyopathy. Whenever we analyse these tests, we look for spelling mistakes in genes associated with dilated cardiomyopathy.

In the future, we may collaborate with colleagues who specialise in MRI image or blood sample analysis to make the best use of the scan images and blood samples that we have collected. This may allow us to identify features that can be used to select which therapies individual patients need. This may be done as part of the study or as part of future, ethically approved research projects. All data sent to outside institutions will have your name removed. This means that images and samples will be labelled with a unique code. Your name and personal details linked to the unique code will be held confidentially on password protected computers at Royal Brompton Hospital. Your personal details will only be accessible to researchers at the Royal Brompton Hospital. When we send the images and samples we will ask the researcher at the collaborating centre to sign a letter confirming that they will treat the samples as confidential, will not disclose the information to outside sources and destroy them following analysis.

Symptom Questionnaires

At visits, we will ask you to fill in questionnaires assessing your symptoms and quality of life.

We will also ask your permission to contact your specialist, general practitioner and local hospital to gather some information regarding any possible hospital admissions or adverse health that may occur over the next five years. We will contact you (phone, fax, post) on an annual basis for 5 years, to ask about your general health and to forward you the questionnaire.

Will I be reimbursed for my expenses?

A contribution to cover reasonable travel expenses (up to £35 per visit) to the Royal Brompton Hospital for visits related to the study will be offered. This will include reimbursement of bus, tube, taxi and rail fares. You will not receive any other monetary compensation for taking part in the study.

Are there any restrictions on what I can do during the study?

Apart from the things outlined above, there are no additional things you need to do as a result of taking part in this study. Involvement in this study should not impose restrictions on your lifestyle. There are no specific dietary restrictions. You can drive, drink small to moderate amounts of alcohol, take part in sport or indeed do anything that is within the usual advice given by your regular doctors.

What are the alternatives for diagnosis or treatment?

You can continue to take your medications. You could also speak to your usual doctor about stopping your medications under their supervision. Your usual doctor, however, may not be able to provide the level of supervision and monitoring offered within this study.

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

There is a risk that there will be a reduction in heart function after stopping your heart failure medications. Our previous trial suggested that 4 in 10 patients similar to those we will study in this trial had a relapse of their DCM after stopping **all** of their medications. All patients' heart function improved after restarting medications and none were admitted to hospital for heart failure. In this study, we will investigate a more conservative pathway, where all patients will continue at least 2 of the 4 usual medications – the two that we predict may be the most important for maintaining remission.

Nevertheless, there is still a risk that we will see a reduction in heart function. We will monitor participants closely to mitigate the risk associated with this. During the withdrawal of treatment, we will closely monitor participants using the latest techniques to identify any change in heart function at the earliest possible stage. If we do see a reduction in heart function, your participation in the study will stop and we will restart your usual medications immediately. We will provide close care, along with your usual doctor, until your heart function returns back to normal.

Signs and symptoms of reduced heart function, that you may experience and should be aware of, include shortness of breath on exertion or on lying flat, swollen ankles and increasing fatigue. If you choose to participate in the study we will educate you regarding the symptoms and signs of reduced heart function. If you develop any of these during the study you should contact the research team as soon as possible and we will arrange appropriate review.

If you have private medical insurance you should to check with the company before agreeing to take part in the trial to see if taking part in the trial affects the policy.

It is possible that we will find an 'incidental finding' during the study. This is something 'extra' found on one of the tests, such as a cyst in the liver or kidney on MRI. If this is the case, we will notify your GP and ask them to consider further tests and treatment if necessary.

Pregnancy and contraception:
Current guidelines for the use of MRI in clinical settings recommends that MRI studies be delayed until after the pregnancy when possible. It is also possible that some of the medications may be harmful to babies as they develop during a pregnancy. Consequently, we request that women who are pregnant, or think that they might be pregnant, not participate in this research study.

Women of child-bearing potential are required to use a highly effective form of contraception. This includes some hormonal forms of contraception, intrauterine devices and previous sterilisation – please speak to the research team about which form of contraception are suitable. Women of child-bearing potential must have a negative pregnancy test at the start of the study, before each MRI scan and at the end of the study. A repeat pregnancy test will be done if women miss any periods or their cycle becomes very irregular. If a woman becomes pregnant whilst participating in this study, they will stop participating in the study due to the possible harmful effects of some of the medications. Pregnancies occurring in a female participant or in a female partner of a male participant will be reported to the Sponsor of the study, Imperial College London.

Are there any benefits to me if I participate in the study?

We cannot promise that the study will you however, we recognise the negative impact that taking medications can have on a person's wellbeing, including the risk of side effects. This study offers participants the chance to stop medications reducing this risk.

What are the side effects of any investigations when taking part?

On the whole the MRI scan is a very safe procedure and seldom causes problems. Some patients experience claustrophobia but this is often prevented by reassurance and other simple measures like

an eye mask. Anytime a needle or cannula is put into a vein for taking blood or administering a contrast agent or drug there is a risk of slight pain, bruising, or irritation of the vein. We aim to take the blood at the same time as putting your cannula in thereby minimizing the number of needles used.

As with any medication or contrast agent, there is also a possibility of different side effects including an allergic reaction which has not been seen before. However, our experience is that people rarely experience any side-effects at all except for mild nausea and headache. You will be closely monitored throughout the course of this study for any such side-effects.

What happens when the research study stops?

At the end of the study we will provide your GP and, if you see one, your regular cardiologist with the results of all of the investigations performed during the study. We will contact them in writing, and if appropriate by telephone to update them on your progress during your time in the study. Your future care can then be planned by your regular doctors. They will make a decision with you about whether you go back on the medications that were withdrawn during the study or not. This may be influenced by the results of the study. We will inform you and your doctors of the results so that this information can be used to help inform decisions as appropriate. If you have stopped your medications and you decide, with your doctors, that you wish to continue off them, we will recommend that your doctors monitor your condition using blood tests and imaging investigations. If at any stage, you experience symptoms such as shortness of breath or develop signs such as ankle swelling, you should seek medical attention.

At the end of the study, we will send you a summary of the results so that you can be kept informed.

Are there any reasons why I should not participate in the study?

You should only take part in the trial if you want to try to stop some of your medications. You should not take part in this study if you are pregnant or if you are planning to become pregnant. You will also not be able to take part if you have kidney failure. You will not be able to participate in any other trial for the entire period you are participating in this trial. There may be other reasons why you should not take part in this study which have been explained to you in more detail by the research team.

What if relevant new information becomes available?

Sometimes during the course of a research study, new information becomes available about the condition that is being studied. If this happens, we will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, we will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

What will happen if I don't want to carry on with the study?

If you do not want to take part in this study, you will receive usual care as determined by your doctor. Your participation in this study is voluntary and you may withdraw from the study at any time without prejudice to your future medical care. If you decide to leave the study at any time, we will contact your doctors to update them on your progress during the study, as outlined above (in section 'Do I have to take part?'), so that they can plan your future care appropriately. Should you decide to withdraw from the study for any reason, you are asked to contact Dr Brian Halliday (0207 352 8121 Ext 82928).

What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Insert name and contact details). The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

What will happen to information about you?

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms as well contact details and other identifiers.
- 10 years after the study has completed in relation to primary research data.

The study is expected to finish in April 2026.
For more information regarding the end date please contact the study team, see 'Where you can find out more information about how my data is used?' for contact information.

We will need to use information from you, your medical records and your usual doctors for this research project. This information will include your:

- Name and initials
- NHS number
- Contact details
- Date of birth

People within the College and study team (see section sharing your information with others) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Some of your information may be sent abroad for specialised analysis that cannot be performed in the UK. They must follow our rules about keeping your information safe. A code number will be used rather than your name.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Legal Basis
As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

Imperial College London - "performance of a task carried out in the public interest"); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

International transfers
There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

Sharing your information with others
For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third-party service providers are

required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

- the following Research Collaborators / Partners in the study
    - Our trial statisticians at the London School of Hygiene and Tropical Medicine – they will have access to data to perform statistical analysis. Your name, date of birth, postcode, hospital and NHS numbers will be removed. You will only be able to be identified by a unique trial number.

Potential use of study data for future research

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

Commercialisation

Samples and data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records, your hospital and your GP. If you do not want this to happen, tell us and we will stop.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to b.halliday@imperial.ac.uk, or
- by ringing us on 02073528121 ext 82928

Complaints

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to b.halliday@rbht.nhs.uk, or by ringing us on 02073528121 ext 82928.

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO)- via www.ico.org.uk.

Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

Will my General Practitioner / Family doctor (GP) and Specialist be informed of my involvement?

Your GP and, if you see one, your specialist will be notified of your participation in the study. They will be kept informed of your progress and will be provided with the results of the investigations performed as part of the study, so that we can plan your future care as best and as safely as possible. Otherwise, all information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital, other than that which is passed on to your GP and specialist, will have your name, address and personal details removed so that you cannot be recognised from it.

What will happen to the results of the research study?

At the end of the project all the research results are gathered together and analysed. The researchers have a professional responsibility to publish their findings, however your identity will not be revealed. Most research is published in the medical press – if you are interested in knowing the overall results of the study, please ask the researchers about this. You are entitled to see any results or information about you under the Freedom of Information Act. At the end of the study, we will send you a summary of the results so that you can be kept informed.

Who is organising and funding the research?

The study is organised by the Cardiovascular Research Centre at the Royal Brompton Campus of the National Heart and Lung Institute, Imperial College London. Imperial College London will act as the sponsor. The study is funded by the British Heart Foundation. Your doctor will not be paid for including you in this study.

Who has reviewed the study?

This study has been given a favourable ethical opinion by XXX, REC reference XXX.

Contact for Further Information

If you would like any further information about the study, either now or at a time during the course of the study, please ask a member of the Research Team. You may contact Dr Brian Halliday, Senior Clinical Lecturer, Royal Brompton Hospital on telephone 0207 352 8121 Ext 82928.

Thank you for taking the time to consider this study. If you do choose to participate, you will be given a copy of this information sheet to keep and also a copy of the consent form that you will be asked to sign.