EVoLVeD (IRAS Project ID 196827)
PISCF (ECG only), version no. 5.0, 28 Jan 2020

Participant Information Sheet and Consent Form

The EvoLVed *Trial*

(Early Valve Replacement guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe Aortic Stenosis)

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?
We are doing this study to find out if replacing heart valves earlier in patients with heart valve narrowing (severe **aortic stenosis**) reduces the chance of the heart failing in the future and helps people to live longer.

Why have I been asked to take part?
You have been asked to take part as you have been previously diagnosed with severe aortic stenosis but do not have symptoms (such as shortness of breath, chest pain or fainting) related to your narrowed valve. At the moment, doctors aren't sure when the best time to replace your valve is – normally we would wait until you have symptoms from your valve before sending you to a surgeon for a valve replacement. Having these symptoms suggests that the heart is struggling to cope with the valve narrowing, but it can be hard to know if these symptoms are from your valve or for another reason.

Some doctors think we would get better results by operating earlier. By doing a heart scan (**MRI**) we can see if there is scarring in the heart, an early sign that the heart is struggling to work properly. Although we don't know yet, replacing the valve when there is scarring but before symptoms develop could lower the chance of the heart failing in the future and help people to live longer. This trial will see which is better - replacing the valve when you have no symptoms but have heart scarring, or replacing the valve when you start to have symptoms.

Do I have to take part?
No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?
If you decide to take part, you will be invited to confirm your consent in writing by a member of the research team and attend for **baseline assessments**. These assessments will take about 2 to 3 hours (including the MRI scan). We will first ask you to have an **ECG** (electrical tracing of the heart using sticky pads) if one was not done in the clinic recently. This is to see if you have an increased risk of heart scarring. If the ECG does not show any increased risk of heart

scarring you will not need any more tests as part of the study and you will continue to have your follow up with your cardiologist as you would normally.

If the ECG suggests that you are at higher risk of having heart scarring you will have the following tests:

Medical history. We will ask you about your medical history and any symptoms you have. We will also find out what medications you're on.

Blood pressure measurement. This will be performed three times with an automatic cuff.

Questionnaire and Assessment. We will ask you to fill in a short questionnaire and do a 5 minute assessment to get an idea of any symptoms you may have and if you are limited in your day-to-day life.

Blood tests. We will take up to approximately 50ml (10 teaspoons) of blood. Some of this will be used this to check if it is safe to give you the special dye we use in the MRI scan and we will keep a sample to measure **troponin**, a protein found in heart muscle. We would also like to freeze and store some of your blood for future research into heart disease, although you can decide that you would prefer us not to do this. *[delete if appropriate]*

Echocardiogram (heart ultrasound scan). This will need to be repeated if you have not had a recent scan in clinic.

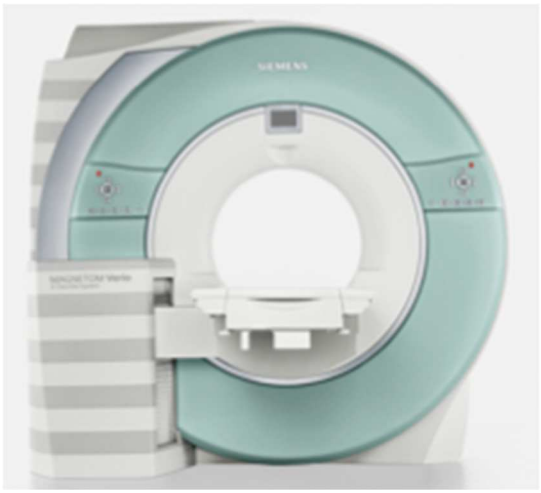
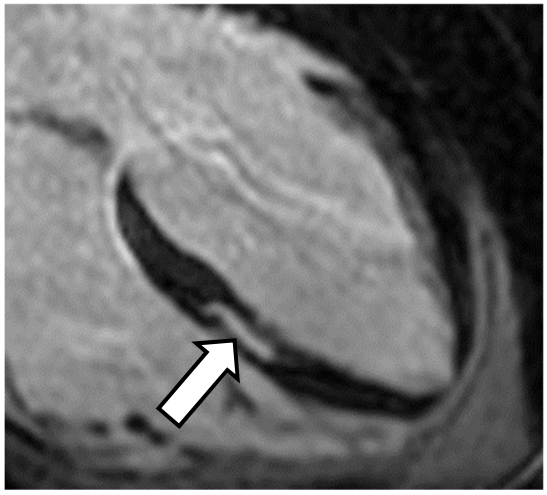
If you are safe to enter the study we will then perform a heart scan (**MRI**) to confirm the presence of heart scarring:

This will take place at **<insert local details here>.** We will do our best to perform this scan when you attend for your baseline assessments however if the scanner is particularly busy we may have to invite you back on a separate day for this scan.

The scanner itself involves a strong magnet and uses a combination of magnetic fields and radio waves to create extremely detailed pictures of the heart. No radiation is used and the scan is extremely safe. People who have certain types of metal in their bodies shouldn't enter the magnetic field (e.g. if you have previously had metal fragments in your eyes). It may mean you cannot take part in the study. Most orthopaedic implants (such as hip and knee replacements) are completely safe as are heart artery stents if they were implanted more than 6 weeks before the scan date. It is however usually unsafe to scan patients with pacemakers.

A small plastic tube (cannula) will be inserted into a vein in the arm and you will lie in the scanner for approximately 45 minutes. The scanning tunnel itself is relatively narrow, but you will be given headphones to listen to music during the scan if you wish, and you will also be able to directly speak to the radiographers performing the scan. If you suffer from severe claustrophobia you should discuss this with the research team before agreeing to take part in the trial. During the scan you will be asked to hold your breath for several seconds at a time in order to obtain better images. You will also receive an injection of a special dye (gadolinium contrast), which highlights if any heart scarring is present. The contrast itself is extremely safe.

Please let one of the research team know if you have any concerns regarding this scan.

	
Example MRI scanner	Heart MRI images with white area of heart scarring present (arrow) in the otherwise healthy black heart muscle

Following the baseline assessments, you will be allocated to one of 3 options:

Option 1: *Early Valve Intervention*

You will be referred to a heart surgeon who will assess you for early valve replacement surgery, either surgical aortic valve replacement (sAVR) or trans-catheter aortic valve implantation (TAVI). The surgeon will discuss in detail your options for surgery and any questions you may have. You will only be referred for early valve intervention if the MRI shows that you have heart scarring.

We will also contact you annually as part of the study (see the ***How will I be followed up?*** section).

Option 2: *Routine Clinical Care (with study follow up)*

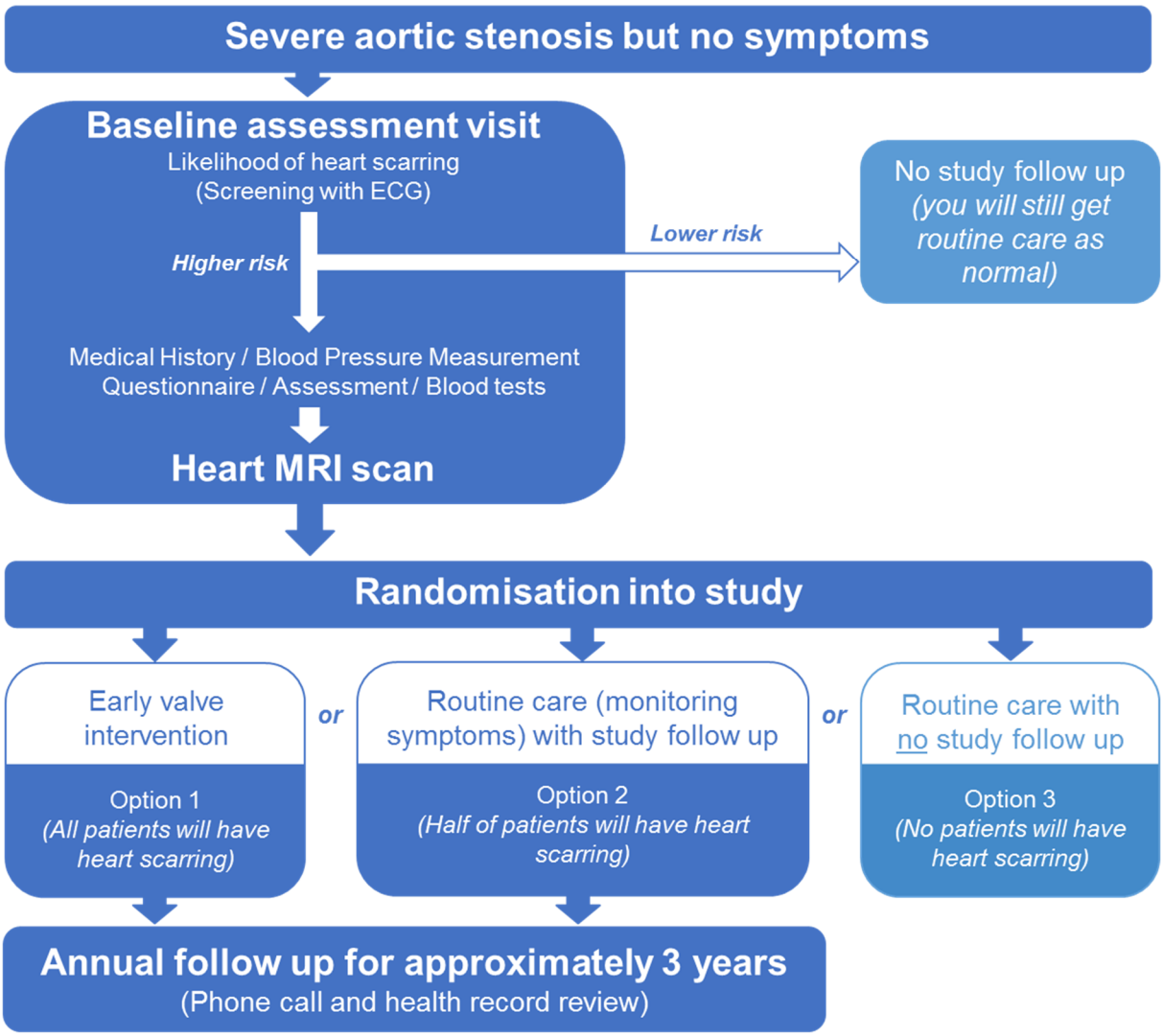
You will continue to undergo routine follow up with your regular cardiologist. Any decision for heart valve surgery in the future will be based on normal NHS guidelines. This option will contain a mix of people – some will have heart scarring and others will not.

We will also contact you annually as part of the study (see the ***How will I be followed up?*** section).

Option 3: *Routine Clinical Care (without study follow up)*

If allocated to this group, you will continue to be followed up by your regular clinical cardiology team as usual. However you will have no further follow up as part of the EVoLVeD study. Any decision for heart valve surgery in the future will be based on normal NHS guidelines.

You will only allocated this option if the MRI showed you have no heart scarring.



How will my treatment be decided?
Sometimes we don't know the best way to treat patients. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly).

In this study, if you have heart scarring you will be randomised to either option 1 or 2. You have an equal chance of getting either option.

If you don't have heart scarring you will be randomised to option 2 or 3.

If you are allocated option 2, neither you nor your doctor will know if you have scarring on your heart. This is known as **blinding**. This is used in all randomised trials wherever possible to make sure the study is fair.

If you are also taking part in the EASY-AS trial, your treatment will be decided by the EASY-AS trial. Which option you receive will not be affected by your heart scarring. *[delete if appropriate]*

How will I be followed up?
If you are allocated to option 1 or 2, we will phone you as part of the study every year until the end of the study (expected to be October 2024). This will involve a short discussion about your general health, any symptoms you may have had and we will complete a questionnaire with you. This should take about 10 minutes in total. We will also check your health records for any hospital admissions or new medical problems you may have developed.

If we have to contact you after 2024 we will discuss this at one of your study follow up visits and ask for your permission then.

What are the possible benefits of taking part?
You might benefit from the additional procedures and investigations that you will have as part of the study. This will include more contact with medical staff and heart imaging tests that might identify other important problems in the heart or outside the heart that were not previously known about.

What are the possible disadvantages and risks of taking part?
It is not thought that there are many disadvantages. The MRI scanner takes detailed images of a small area of your chest so there is a small chance that we will find another abnormality in this area. If these require further assessment we will let you and your GP know and arrange for you to see a specialist for any further tests that are required. Usually these abnormalities turn out to be of no significance to your health, but they may cause you stress and anxiety whilst they are being investigated.

Valve surgery is generally very successful but, like any other surgery, it is not risk-free. There is a small risk of having a heart attack or stroke, or dying, either during or soon after the operation. Your risk will depend on your age and your current state of health. There are also small risks of living with a replacement heart valve, such as infection, and some types of heart valve wear out gradually over time. If you are selected to have a TAVI the new valve will be implanted using x-ray guidance. The amount of radiation you will be exposed to for this is about the same as three years of the UK average background radiation. This is the same amount of radiation if you had a TAVI routinely. Before you agree to take part in the study you should discuss with the research team the risks of surgery for you. These risks will not be increased by taking part in the study but will be brought forward if you enter the study and are selected to have early heart valve surgery. The risk of complications from surgery might be slightly lower if the operation is performed earlier when you and your heart are healthier.

Taking part in a study might affect the insurance cover you get from your insurance provider. Always make sure you know what you need to tell your insurance company and what the insurance policy covers.

Will any genetic research be done?
With your permission, we may ask you to provide some blood for genetic research. This blood sample will be used to find out if certain genes are more common in people with aortic stenosis and for future research into heart disease. You will not know the type of future research your stored sample may be used for and you will not be told of the findings of this future research. You have the right to ask that your blood sample be destroyed at any time by contacting your study doctor. If you do not wish to have the genetic blood sample taken you may still take part in the main study. *[delete if appropriate]*

What if there is a problem?
If you have a concern about any aspect of this study please contact [*name and contact details*] who will do their best to answer your questions.

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against your hospital but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What happens when the study is finished?
If you have provided research blood samples we will continue to store these samples securely for up to 25 years. When we test these samples we may send them to other academic institutions or commercial companies to help us run those tests.

Your study data will be stored indefinitely in a secure manner with access restricted to the research team. With your consent, we will periodically ask central NHS registers to provide information on your health status (you will not be contacted directly for this). This is because it will enable us to find out about any longer-term consequences of aortic stenosis and heart scarring. To help us identify you correctly, we will need to collect your unique patient identifier (CHI number or NHS number) and store it at the University of Edinburgh.

At the end of the study we will make the study data available for other researchers to look at. Before we make it available we will make sure it does not contain any of your personal data.

What will happen to the results of the study?
Once we have completed the study and analysed the results, we will write a paper, which will be submitted for publication in one of the medical journals. You will not be identifiable in any published results. We do not routinely contact participants to inform them of the outcome of the research but once the study has been published a summary of the findings will be available on the Edinburgh Clinical Trials website (http://www.ed.ac.uk/edinburgh-clinical-trials).

Who is organising the research and why?
The study is being sponsored by the University of Edinburgh and NHS Lothian and is being funded by the Sir Jules Thorn Charitable Trust. Your doctors will not be paid for including you in this study.

Who has reviewed the study?
The study proposal has been reviewed by the funder and the Sponsor. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has been obtained from South East Scotland Research Ethics Committee. NHS management approval has also been obtained.

Will my taking part in the study be kept confidential?
All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. In the unlikely event that you lose capacity and cannot continue to give consent, no new data would be collected but we would keep any data we have already have.

Study researchers will need access to your medical records and data to carry out this research. Information will be stored on secure university/NHS computers, or locked away in secure rooms with restricted access. Access to personal identifiable information will be restricted to the research team. With your consent we will inform your GP that you are taking part.

To ensure that the study is being run correctly, we will ask your consent for responsible representatives from the Sponsor and NHS Institution to access your medical records and data collected during the study, where it is relevant to you taking part in this research. The Sponsor is responsible for overall management of the study and providing insurance and indemnity.

If you have any further questions about the study please contact <add local details> on <add contact details>.

If you would like to discuss this study with someone independent of the study please contact <add independent contact details> on <add contact details>.

If you wish to make a complaint about the study please contact <add local complaints contact>:

<add local complaints contact details>

Thank you for taking the time to read this information sheet.

The study visit schedule at a glance

Visit no.	What will happen
Screening & Baseline	✓ You will be asked to provide written consent to enter the study ✓ The study team will perform an ECG (if you've not had one recently) ✓ The study team will then ask you about your general health, ask you to complete a questionnaire and perform a brief assessment ✓ Your blood pressure will be taken ✓ An echocardiogram heart scan may be repeated if you've not had one recently ✓ We will take some blood
MRI scan	✓ The scan involves lying still inside a tunnel for approximately 45 minutes ✓ A small tube will be inserted into the arm vein to deliver a small amount of contrast needed to highlight heart scarring on the scan ✓ Both the contrast and scan itself are extremely safe
Valve surgery **(Option 1)**	✓ If the MRI scan shows heart scarring you may be randomised to early surgery ✓ The type of surgery that you get will be agreed between you and your local heart surgeon
Routine care **(Options 2 and 3)**	✓ If you are not randomised to early surgery you will continue to have follow up with your usual cardiology team ✓ You will be asked to tell your team if you get any symptoms and your heart will be checked periodically with ultrasound (echocardiogram) scans ✓ You may still receive an operation if or when it is recommended by your cardiologist
Annual contact	✓ The study team will contact you annually to check how you are feeling and will also complete a questionnaire about your symptoms ✓ They will also review your health records to see if you have had any complications or admissions to hospital ✓ This will continue until the end of the study (approximately 3 years but a maximum of 5 years) ✓ You will only be contacted by the study if you are allocated option 1 or 2

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CONSENT FORM FOR THE EVOLVED TRIAL

Name of Researcher (PI):	
Site:	
Patient Trial Number:	

Please **initial** each box

1. I confirm that I have read and understand the information sheet (as specified in this document header) for the above study and have had the opportunity to consider the information and ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Sponsor, from the NHS organisation or other authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I give permission for my Community Index (CHI) or NHS number to be collected and passed to the University of Edinburgh and its Clinical Trials Unit ☐
5. I understand that information held and managed by central UK NHS bodies and NHS Trusts may be used in order to provide information about my health status during and after the study. To do this, I understand that my information will be shared with those bodies. ☐
6. I agree to my data/tissue being used for future ethically approved studies ☐
7. I agree to my General Practitioner being informed of my participation in this study ☐

	Yes	No
8. I agree to give a blood sample which will be frozen and stored for future use (optional – initial the Yes or No box) *[delete if appropriate]*	☐	☐
9. I agree to give a blood sample which will be used for genetic (DNA) analysis (optional – initial the Yes or No box) *[delete if appropriate]*	☐	☐

10. I understand that my blood samples may be sent to other academic institutions or commercial companies for analysis ☐
11. I agree to take part in the above study ☐

Name of Patient	Signature	Date
Name of Person taking consent	Signature	Date

Original – to Investigator Site File. *First Copy – to participant.* *Second Copy – to hospital notes.*