AFFECT- PARTICIPANT INFORMATION LEAFLET

Study Title:	Optimum therapy for those with Atrial Fibrillation aFtEr Completing miTral valve repair surgery - The AFFECT trial
IRAS ID:	1009448
Study Doctor:	If you have any questions about this study, please talk to your study team. *<Full name of principal investigator, title, institutional affiliation, address, phone number>*
Study Sponsor & Data Controller:	*South Tees Hospitals NHS Foundation Trust*
Participant ID:	*<INSERT, IF AVAILABLE>*

SUMMARY

You are being invited to take part in a research study. This section provides an overview of this research. It describes the key information to help you to decide whether or not you want to take part in this study. Thank you for taking the time to read this.

WHY IS THIS RESEARCH BEING DONE?	You are scheduled to have, or have had, surgery to repair a valve in your heart, called the mitral valve. This mitral valve repair surgery is to fix leakiness around the valve that has been allowing blood to flow the wrong way (called mitral regurgitation), which has been causing you to feel unwell, for example, you might have been feeling breathless or dizzy. After mitral valve repair surgery, there are risks of certain complications, such as blood clots and stroke. These risks are greater for people who also have an irregular heartbeat (called atrial fibrillation). To try and prevent such complications, we have traditionally given a blood-thinning medication called warfarin, which is a type of drug called a vitamin K antagonist (VKA). Using a VKA brings with it other risks, including increased risks of bleeding and bruising, it is also inconvenient in that you need to visit your GP clinic regularly for blood tests to make sure you're taking the right dose. There is another type of blood thinner called a Direct Oral Anti-Coagulants (DOAC), this is a newer type of medicine and lots of people are safely being given them by their surgeons before and after heart surgery. DOACs also carry risks of complications such as bleeding. Being an older type of medication, warfarin is less expensive, but needing to

	go for regular blood tests increases the cost of using warfarin; whereas DOACs cost slightly more, but there's no need for regular clinic visits. With the AFFECT study we want to see which of these two types of blood thinner work best, in terms of reducing complications (such as blood clots and stroke) and causing fewer additional complications such as bleeding. We will also look at how much each compares in costs to the National Health Service (NHS) overall.
WHAT HAPPENS TO ME IF I AGREE TO TAKE PART IN THIS RESEARCH?	If you agree to take part in this research study and your clinical team confirm that you are eligible; then you will be randomly allocated to one of two groups by a computer (like tossing a coin). One group will receive VKAs and one group will receive DOACs. There is equal chance of being allocated to each group and you will be prescribed the medicine to take at that point,before you leave hospital. You should continue to take the same medicine for as long as you are taking part in the trial, which could be for up to 4 years. Once you leave hospital we will monitor your health for between 1 and 4 years. During this time, you will be contacted at 3 months, 12 months and then yearly over the phone and asked about your health and to complete questionnaires. If you provide an e-mail address then you will be contacted every 3 months between visits, directly from the trial database to complete a simple online questionnaire.
COULD BEING IN THIS RESEARCH HARM ME?	This study is aiming to find out whether, after mitral valve repair surgery, taking one drug or the other is better for reducing blood clots and stroke, whilst not causing more complications, such as bleeding. Both of the drugs used in this study are already used routinely in treating patients after heart surgery and so there is no additional risk to taking part. We won't know the differences between the drugs until we analyse all the results at the end of the study.
YOUR PERSONAL DATA	We will use information from you and your medical records, including from your GP or other hospitals where you receive any care. We will only use information that we need for the research study. Very few people will know your name or contact details, and only if they really need it for the purpose of this study. Everyone involved in this study must keep your data safe and secure. We will follow all privacy laws. We are required to save all personal data for 5 years after the study has ended in case we need to check it, after which it will be destroyed. but it might also be used in future research on this topic. All the data collected will be coded, meaning that no one will identify you. When we write the reports about the trial, any data will be coded, meaning no one will be able to identify you.
Thank you for reading this summary. The information on the following pages provides more information about this study for you to read if you are interested in taking part in AFFECT.	

1. WHY AM I RECEIVING THIS INFORMATION LEAFLET?

You are being asked to take part in this clinical research study because you are soon to have (or have had) mitral valve repair surgery to fix your mitral regurgitation and you have a history of an irregular heartbeat (atrial fibrillation). Joining the study is entirely up to you. Before you decide if you want to join, you should understand why the study is being done and what it would mean for you.
This information leaflet tells you about the study. Please take your time to read it carefully, and a member of the research team will also go through this with you. Then ask your doctor or nurse if anything is not clear or if you would like more information. If you decide to join the study and later change your mind, you will be able to stop at any time without giving a reason.

If you decide not to take part in this study, you will still get your usual medical care.

2. WHY IS THE STUDY BEING DONE?

Mitral valve regurgitation is a condition where the mitral valve does not close properly and some of the blood then flows the wrong way in the heart. It is the most common heart valve disorder in the USA and Europe, and your symptoms might include dizziness, breathlessness or chest pain. To treat it, surgery to repair the mitral valve is often carried out. After surgery, there is a risk of complications from blood clots, causing conditions such as stroke. If you also have a history of atrial fibrillation (AF), which causes an irregular and often abnormally fast heart rate, then your risks of such complications are almost 2 times higher than if you didn't have AF.

To prevent blood clots, medicines called anti-coagulants are used; they work by interrupting the process involved with forming a blood clot. They are also known as blood-thinners. However, as they reduce the ability of your blood to clot, they increase the chances of heavy bleeding. This heavy (major) bleeding can also increase the risk of complications, including heart attacks and death.

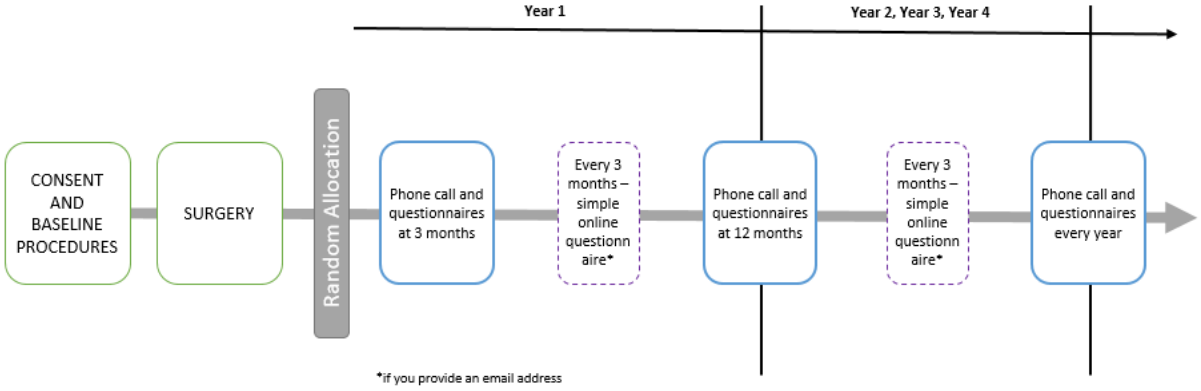
Older guidelines recommend a type of anti-coagulant drug called a Vitamin K Antagonist (VKA), of which Warfarin is most common example. VKAs work well, but may take a while to act, finding the right dosages can take a long time and involve regular visits to a clinic for blood tests, and they can cause major bleeding.

There is another, newer, type of anti-coagulant called a Direct Oral Anti-Coagulant (DOAC); these are widely used for the prevention of strokes and blood clots in patients with AF outside of surgery (and you might also have been prescribed these before your surgery). Under these circumstances, they have been shown to have a lower risk of major bleeding. For this reason, as well being faster-acting and not needing a regular clinic visit to find the right dosage, DOACs are increasingly being prescribed after mitral valve repair surgery. However, DOACs are not yet formally recommended for use in patients with AF after mitral valve surgery, and in some other heart conditions they have not been as good as VKAs.

Therefore, the purpose of this study is to compare the two different types of anti-coagulant medication to find the best way to stop blood clots whilst minimising the risk of major bleeding. We will also look at how much each treatment pathway costs the health service overall.
There will be 1282 participants in this study, 641 in each group. One group will be allocated to take VKAs, the other group will be prescribed DOACs. Both groups will be followed-up for up to about 4 years after their treatment starts.

It is entirely up to you to decide whether you want to take part in this trial or not. Your choice will not affect your ongoing care or any future medical care. If you choose not to participate in the research study, you may be prescribed either VKAs or DOACs as part of your after-surgery care, as both types of medication are routinely prescribed for patients with AF after mitral valve surgery.

3. WHAT HAPPENS TO ME IF I TAKE PART IN THE STUDY?



Consent and baseline procedures

If you choose to take part, we will ask you to confirm this by signing a consent form and we then need to check that you meet the eligibility criteria for the study. To do this we will collect a set of baseline data from you and your medical records, and ask you to complete a set of questionnaires. The questionnaires will cover aspects of your quality of life, current medications usage, your medical history, and use of healthcare resources. If you are able to do so, we would prefer you to do this online; we'll need a personal email address from you to do this, and we would send you a link that would take you through to a secure questionnaire.

Surgery and confirmation of eligibility

Once you have your mitral valve repair surgery, the team will check again that you meet the eligibility criteria for the study whilst you are still in hospital following your surgery.

Allocation

If you are eligible, the group you will be allocated to will be decided by chance (like tossing a coin), the chance that you are allocated to be prescribed VKAs or DOACs will be 50% or 1 in 2. You will be told as soon as possible which group you have been allocated to, and the hospital team will then start giving you this treatment before you leave hospital.

At hospital discharge

For whichever group you are allocated to, you will be given about one month's supply of medicine before you leave hospital. Your GP will be told that you are taking part in this trial and which medicine you should be given when you need a repeat prescription.

As part of your usual care, you'll likely be asked to return to the hospital where you have had surgery at around 6-8 weeks after surgery for a check-up. Some hospitals now have these appointments on-line or over the phone.

For the VKA group only

As mentioned above, finding the right dose of VKA for you might take some time and you will need to visit your GP or local clinic to measure your blood to adjust your dose. The clinic will test how long it takes for your blood to clot (known as the international normalised ratio, INR), and they will be aiming for an INR of between around 2.0 and 3.0. It's likely that you will have the test more frequently at the start and once your blood test results are stable then you might only need tests every few months. We will ask you to keep a record of your INR values and dosage.

At 3 months and 1 year after you have started treatment

The research team at the hospital that you had your surgery will get in touch with you to ask you about the medications that you are taking, to complete questionnaires about your quality of life, how often you might have been to see your GP or to the hospital, and any complications (like bleeding) you might have had. If you have agreed to complete questionnaires online then some of these will be sent to you via an email link, and you will also be contacted by the research team.

*Every 3 months

Every 3 months, between the times that you speak with the hospital research team, if you provide us with an email address, we will send you an online questionnaire to complete, asking you if you are still taking your allocated treatment, whether you have had any complications (like bleeding), if you have been admitted to hospital, or if your health has changed and to enter your INR results (if you are taking a VKA).

Every year thereafter

Every year until the end of the trial, for a maximum of up to about 4 years, the hospital research team will get in touch with you, ask you some questions about your health and you will be asked to complete the same (online) questionnaires.

If you see another doctor or health care professional, please tell them you are taking part in this study and that they can contact the study team for information.

Please speak to your study team right away if you have any concerns or questions.

4. ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

There is no direct benefit expected other than what you would receive as your usual clinical treatment. It may be that you are in a group that has fewer complications, but we will not know this until the very end of the study when the results are analysed.

The results of this study should provide important information for the medical treatment for future patients undergoing mitral valve surgeries similar to yours. Patients who participate in research studies like this may indirectly benefit from the additional observation they receive from study personnel.

5. WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART? WILL THERE BE ANY COMPLICATIONS?

The doctor will review with you all of the potential side effects of the medication you may be prescribed in this study. All of the drugs used in this study are used routinely, but may increase your risk of heavy bleeding which could be serious. Signs of bleeding include bruising, black or red stools, bleeding gums, nosebleeds, vomiting what looks like coffee grounds, blood in your urine, cuts in the skin that won't stop bleeding, feeling dizzy or very tired or a very bad headache. You should take care while shaving or any other activity that may lead to injury. There may be unknown risks from your participation in this research. You may be randomised to a group where the treatment is not your preference.
The most common risks of DOACs such as apixaban, rivaroxaban, edoxaban, dabigatran are increased bleeding or easy bruising, nose bleeds, bleeding gums, shortness of breath, stomach pain, or muscle spasms. These risks affect between 1 in 100 people and 1 in 10 people (between 1 and 10%).

The most common risks of VKAs like warfarin are increased bleeding, red or brown urine, black or bloody (red) stools, headache, stomach pain, vomiting or coughing up blood, and joint pain. These risks affect between 1 in 100 people and 1 in 10 people (between 1 and 10%).
Depending on which treatment you are prescribed in this study, you may need routine blood testing. If you are prescribed warfarin, you may need to limit your intake of some types of foods containing vitamin K (e.g., green leafy vegetables like kale, spinach, etc) and also avoid cranberry juice, grapefruit juice and pomegranate juice.

Call your doctor immediately if:

- you notice any signs of bleeding
- you fall, hurt yourself, or hit your head while taking this therapy
- you become pregnant
- you are planning any medical procedures

You should tell all of your health care providers you taking part in this trial (including pharmacists, nurses and doctors). Do not stop taking the drugs prescribed in this trial without consulting your doctor.

We will be collecting your personal data, with this there is a risk your confidentiality might be breached, despite us keeping it as safe and secure as we can. In Section 7 of this information leaflet we tell you more about how we handle information we collect about you.

Important information about pregnancy

Pregnant and breastfeeding women are not eligible to take part in the study, therefore women of childbearing age will be asked to perform a pregnancy test as part of standard care prior to surgery. If you become pregnant during the study, please inform your study doctor immediately. Information about your pregnancy and the outcome will be collected.

6. WHAT PROCEDURES WILL BE DONE IN THIS STUDY?

Study Procedures(s) Glossary	Description text	Risks
Questionnaires 	You will be asked to complete up to 6 questionnaires at regular intervals during the course of the study. The questionnaires will be about: - Your quality of life – including how well you get about doing daily activities - What health services you have recently used and how much time and money you have spent using them - If you are still taking your allocated medications - If you are allocated to take VKAs, then we will ask you to note down your blood test values - If you have had any complications We would prefer if you could complete these questionnaires online, but you would also be able to complete these directly with a study team member, either when you see them or over the phone.	No risks
General health interview 	You'll be asked at each follow-up generally about your health, medications you are taking and any complications or additional hospital visits that you might have had since the last time the team contacted you. Some of this will be through the questionnaire pack that you receive, but the study team will also contact you over the phone.	No risks

7. WHAT ARE MY RIGHTS AS A STUDY PARTICIPANT?

What if something goes wrong?

If you think there has been damage to your health as a direct result of participating in this study, you must tell your study team as soon as possible. In the event that something does go 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 South Tees Hospitals NHS Foundation Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

You will be told if any new information becomes available that may affect your decision to continue to take part in the study. You will be asked to sign a form if you agree to continue with your participation. Some new information may also mean that you will no longer be able to continue in this study. If this happens, one of your study team will discuss this with you.

If you want to complain about how researchers have handled your information, you should contact the research team. If you are not happy after that, you can contact the Data Protection Officer. The research team can give you details of the right Data Protection Officer. If you are not happy with their response or believe they are processing your data in a way that is not right or lawful, you can complain to the Information Commissioner's Office (ICO) (www.ico.org.uk or 0303 123 1113).

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

You can completely stop study participation at any time, without giving a reason, but we will keep information about you that we already have.

You can also choose to only partly withdraw, for example, where you might not want direct contact with the study team, but are happy with completing questionnaires online.

How will we use information about you and how will it be kept confidential?

We will need to use information from you and your medical records and from routine data collected by the NHS) for this research project, this will include your personal data.
The following types of personal data collected in the study, will include:

- Information to arrange your participation in the study such as your name, address, telephone number, email address.
- Information such as your date of birth, sex at birth, postcode, ethnicity, NHS number *(or equivalent, if applicable).*
- Health information such as medical history, medical conditions.

Data collected for the study is "coded". This means any information that could directly identify you, like your name, is removed by your hospital study team and replaced by a code. This code is usually a number. A separate list that matches the code to who you are is kept by your hospital study team (separate from coded data). If you choose to use the online electronic system to answer the questionnaires, then we will need to keep your email address with the study data.

Your records at your hospital will remain "un-coded" and contain data that can directly identify you.

Apart from the hospital study teams, only a small group of people from the sponsor and research team can see your un-coded data and part of their role is to make sure the study is being done properly. These people must keep your data private. People who do not need to know who you are will not be able to see your name, NHS number *(or equivalent, if applicable)* or contact details.

Your data are protected by UK data privacy laws (UK GDPR and the Data Protection Act 2018). As the Sponsor of this study, South Tees Hospitals NHS Foundation Trust is the data controller for this study. This means that we, as South Tees Hospitals NHS Foundation Trust researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible.
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.

We will keep identifiable information about you for 5 years after the study has finished, unless you provide your additional consent to a longer-term follow-up after the end of the study. If you do agree to the longer-term follow-up, then we will keep your information for another 5 years after the end of the follow-up period. The study data will then be de-identified and securely archived or destroyed.

Part of this project will also involve us collecting data about you from routine NHS data sources . We will be using this to compare the information to the trial data during and at the end of the trial. This will help us to understand if using routine data is helpful in this and in future mitral valve repair trials. When we obtain data from national sources, we will need to use an 'NHS Research Secure Data Environment (SDE)' platform to store and analyse the data securely. This data may be under the joint data control of both South Tees Hospitals and the SDE. You will be able to find further information about how we handle your data in our Privacy Notice, which will be available on our study website

https://www.southtees.nhs.uk/about/strive/research-team/academic-cardiovascular-unit/acu-trials/the-affect-trial/.

Who receives my coded data?

The coded data will be provided to the research team, who include people at other NHS institutions and UK universities. We may also share coded data about you outside the UK for research-related purposes to:

- Be able to bring together data from other research or from patients who may take part in this trial who are not in the UK.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Other healthcare researchers based at hospitals and universities

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing

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, or your GP. If you do not want this to happen, tell us and we will stop.
- You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- 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:

- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- our website: https://www.southtees.nhs.uk/about/strive/research-team/academic-cardiovascular-unit/acu-trials/the-affect-trial/
- by asking one of the research team
- by sending an email to stees.affecttrial@nhs.net

Will I receive any financial reimbursement, expenses or compensation?

You will not be paid for taking part in this study and your surgery and medical care will not cost you anything. However, should you need to visit the hospital after your surgery to help us collect information for the study, we are able to offer travel reimbursements of up to £40 per visit.

Who is organising and funding the study?

In the UK, funding has been provided by the National Institute for Health and Care Research Health Technology Assessment (HTA) Programme. South Tees Hospitals NHS Foundation Trust is organising this study and known as the 'Sponsor'.

Who has approved the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee which is there to protect your safety, rights, wellbeing and dignity. This project has been reviewed and was given a favourable review by the ***London - Harrow Research Ethics Committee***

What happens with the study results?

A description of this study is available on www.isrctn.com (ref: ISRCTN13146458)

No information will be published that can identify you.

After the whole study is finished and the data have been analysed, we will report our findings to the funder, to the National Institute for Health and Care Excellence (NICE) and to a number of professional surgical societies and present at surgical conferences. We may also show the results and use coded data at educational events. We will also work with our Patient Advisory Group (PAG) and the patient representatives on the research team to decide on the best way to let patients and the public know about the results.

How have patients and the public been involved in this study?

There are patient representatives on the funding application team and they will continue to remain involved with the study. They have helped to develop the question and how we might answer it in the design of the study, with the two treatment groups, the assessments and the follow-up periods.

The patient representatives have also been involved with reviewing this Participant Information Sheet.

Will my General Practitioner (GP) be informed of my participation?

Your GP will be notified that you are taking part in this study. Your GP may be approached to provide further information about your health during the course of this study, this might be in asking for results of blood tests or the results of other tests.

8. FURTHER INFORMATION AND CONTACT DETAILS:

Please contact *stees.affecttrial@nhs.net*

Thank you for reading this information and considering taking part in this study.