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What is the best type of blood-thinning medication to be used after a heart valve operation in people with an irregular heart beat.

Submission date 21/12/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 31/01/2025	**Overall study status** Ongoing	
Last Edited 31/01/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Mitral regurgitation is where the mitral valve doesn't close properly allowing some blood to flow the wrong way in the heart, causing a number of symptoms, including dizziness, breathlessness, and chest pain. Mitral valve repair (MVr) surgery is the gold standard treatment for it. After MVr surgery there are risks of complications such as blood clots and stroke, and this risk is greater for people who also have an irregular heartbeat (called atrial fibrillation). A blood-thinning medication (an anti-coagulant) is usually prescribed to prevent these complications and one of these drugs is called Warfarin, which is a type of drug called a vitamin K antagonist (VKA). Using Warfarin/VKAs brings with it other risks, including increased bleeding and bruising; it is also difficult to get the dosing correct for individual patients, needing them to regularly visit their GP to measure their blood levels. In older (2017) European guidelines, VKAs were the recommended therapy, but this was based on scant evidence. A newer type of anti-coagulant medicine called Direct Oral Anti-Coagulants (DOACs) are also effective in preventing complications such as stroke, are easier to dose, and in other conditions have shown to have lower risks of bleeding. DOACs are more expensive but the more recent 2024 European guidelines suggest DOACs are a reasonable alternative to VKAs. This means that both types of anticoagulants are routinely used, but there is still very limited data on the best therapy. Therefore, the purpose of this study is to see which of the two types of anti-coagulants work best, in stopping complications such as stroke and causing fewer complications such as bleeding. We will compare how much each costs the National Health Service (NHS) overall.

Who can participate?

Patients aged 18 years old or over with confirmed pre-op Atrial Fibrillation (AF) which should be persistent or permanent, who have undergone mitral valve repair surgery and require prolonged anticoagulation

What does the study involve?

Participants will be randomly allocated (randomised) to one of the two types of anti-coagulants with an equal chance of being allocated to each group. Participants will be followed up for a period of up to 4 years from randomisation.

What are the possible benefits and risks of participating?
At screening, baseline assessments will be conducted and recorded. These include capturing data from routine care on the medical history of the participant, vital signs and laboratory assessments. There should be no additional burden to the patient for these procedures. Any patients of child-bearing potential who are found to be pregnant at the time eligibility is assessed will be excluded.
Once the patient is randomised, they will be provided with study medication. All of the drugs used in this study are used routinely in treating patients with atrial fibrillation to prevent blood clots and all have some degree of risk of bleeding. There may be differences between the two groups compared in this trial, one group of participants may receive a less effective treatment or possibly have more side effects than the other group. There are no direct benefits expected other than what would be received as standard clinical treatment. The risk associated with taking part in this trial is expected to be comparable to that of standard medical care. As marketed drugs, the side effects and risks of all the medications used in this study are well-documented and subject to the MHRA Yellow Card Scheme for reporting additional incidents. All the medications may increase the risk of serious bleeding. Signs of bleeding include bruising, black or red stools, bleeding gums, nosebleeds, blood in urine, cuts in the skin that won't stop bleeding, feeling dizzy or very tired or headaches. Study participants will be informed of the potential of the most common adverse events and these are described in the accompanying participant information sheet. For some of the treatments (e.g., Warfarin) routine blood testing will be required, and this will follow the routine primary care pathways (usually INR clinics). The participants' GPs will be informed of their participation in the study. Participants will be asked to call their GP or the local research study team should they experience any adverse incidents. Any 'out-of-hours' situations should be treated through normal emergency care pathways. After hospital discharge, participants will also be regularly followed over the course of this study, they will be called at 3 months and 1 year post-randomisation and thereafter annually. There are no planned 'in-person' reviews for trial data collection but there may be routine care post-surgical review visits; discharge back to the primary care provider will also occur as per standard of care. The 3-month, 1-year and annual time point data collection requires the site to contact the patient via telephone (or video) call, the burden of each contact is expected to be in the region of 30-60 minutes, where questionnaires will be completed with participant responses. Participants may also choose to complete the questionnaires electronically; we will be using an electronic Patient Reported Outcomes (ePRO) system to enable this. This means that if a participant provides a personal email address, they can use technology to reduce the time spent in the call. Some people feel uncomfortable when answering questions about their health or healthcare in person, the ePRO facility may assist with this. Participants are also under no obligation to complete any questions that make them feel uncomfortable. The collection of data and personal identifiers will be limited as much as possible, restricted to the needs of the trial. We will be requesting demographics such as date of birth, sex assigned at birth, ethnicity, and postcode. Some of these categories (including postcode) will help us to understand the reach of the trial and may help us to meet the study aims for diversity and inclusion (including income deprivation) in our patient population and are part of the funder requirements.
This data along with that from study assessments will be entered in a pseudo-anonymised (coded) format in a study-specific database. Personal identifiers such as dates of birth are further encrypted in the study database. The study database will be within an established secure environment, compliant with industry standards, in line with Good Clinical Practice requirements. The data will be hosted on UK or EU servers.
Participant data with direct identifiers (names and addresses) will only be kept at the hospital site and will be kept confidentially in accordance with local Trust research policies, which usually include restricted access and lockable storage.

What are the possible disadvantages and risks of taking part?
One group of participants may receive a less effective treatment or possibly have more side effects than the other group. There are no direct benefits expected other than what would be received as standard clinical treatment. The risk associated with taking part in this trial is expected to be comparable to that of standard medical care.
Individual patients will be reviewed by participating consultant surgeons for all the potential side effects of the medications that maybe prescribed in this study. All drugs used in this study are used routinely but may increase the risk of heavy bleeding which could be serious.
Participants are advised of the signs of of bleeding including bruising, black or red stools, bleeding gums, nosebleeds, vomiting that looks like coffee grounds, blood in the urine, cuts in the skin that won't stop bleeding, feeling dizzy or very tired or a very bad headache. Participants are advised they should take care while shaving or any other activity that could lead to injury.
Participants are advised that they maybe randomised to a group where the treatment is not their preference and that there may be unknown risks associated with their participation in the research.
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 is prescribed in this study, participants are advised they need routine blood testing. If participants are prescribed warfarin, they may need to limit their intake of some types of foods containing vitamin K (e.g., green leafy vegetables like kale, spinach, etc) and avoid cranberry juice, grapefruit juice and pomegranate juice.
All participants are advised to contact their doctor immediately if they notice any signs of bleeding, they fall, hurt themselves, or hit their head while taking this therapy, they become pregnant, or they are planning any medical procedures.
Participants are asked to inform their healthcare providers they are taking part in this trial (including pharmacists, nurses, and doctors). Participants are advised not to stop taking the drugs prescribed in this trial without consulting their doctor.
The collection of personal data for the purposes of the study raises a risk that confidentiality might be breached, despite measures in place to ensure safe and secure storage of this. Participants are informed in the Participant Information leaflet of how the information we collect in relation to them, will be handled.

Where is the study run from?
James Cook University Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2024 to May 2030

Who is funding the study?
NIHR Health Technology Assessment Programme, HTA (UK)

Who is the main contact?
AFFECT Trial Team, stees.affecttrial@nhs.net

Contact information

Type(s)
Scientific

Contact name
Mrs Sarah Kiddell

Contact details
The James Cook University Hospital
Middlesbrough
United Kingdom
TS4 3BW
-
stees.affecttrial@nhs.net

Type(s)
Scientific, Principal Investigator

Contact name
Prof Enoch Akowuah

ORCID ID
https://orcid.org/0000-0002-2429-3579

Contact details
Cardiovascular Clinical Research Facility
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW
+44 (0)1642 850850
stees.affecttrial@nhs.net

Type(s)
Public

Contact name
Dr AFFECT Trial Team

Contact details
South Tees NHS Foundation Trust
Cardiovascular Clinical Research Facility
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW
+44 (0)1642 850850
stees.affecttrial@nhs.net

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009448

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
23/165

Study information

Scientific Title
Optimum therapy for those with Atrial Fibrillation aFtEr Completing miTral valve repair surgery - The AFFECT trial

Acronym
AFFECT

Study objectives
To compare the effectiveness and safety of two types of oral anticoagulation (OAC) after mitral valve repair surgery, in participants with a history of an abnormal heartbeat (atrial fibrillation). Both types of OAC: vitamin K antagonists (VKAs) and direct oral anticoagulants (DOACs) are in routine use, but there is no clear evidence which is better. This study will look at the difference in time to a number of complications, including death, major cardiovascular events or major bleeding between the two different types of blood thinning medications. The time period will be a minimum of 1 year and up to 4 years, after participants are randomly allocated to one of the two types of OAC.
We will also compare the cost-effectiveness of the two types of medications after a year.

We will compare a range of other outcomes across the two medication types at timepoints up to 4 years after allocation. These include patient and clinical effectiveness, safety and health economic outcomes. To do this we will look at how patients feel (using a standard health questionnaire), clinical complications experienced (e.g., bleeding, strokes, deaths, and heart failure), both individually and in combination, and costs to the NHS and patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/01/2025, Harrow Research Ethics Committee (2 Redman Place, Stratford, London , E20 1JQ, United Kingdom; 020 3080 6456; clintrialhelpline@mhra.gov.uk), ref: 25/LO/0066

Study design
Randomized controlled open-label study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Patients with a history of atrial fibrillation undergoing mitral valve repair surgery for mitral regurgitation, requiring anti-coagulation after surgery

Interventions
Intervention arm: Direct Oral Anti-Coagulants (DOACs)
Participants allocated to the intervention arm will be prescribed any commercially available DOAC (e.g., apixaban, edoxaban, dabigatran, rivaroxaban). The DOACs are all oral medications and dosing should be prescribed in accordance with the label guidance.

Control arm: Vitamin K Antagonists (VKAs)
Participants allocated to the control arm will be prescribed any commercially available VKA (e.g., warfarin, phenindione, acenocoumarol). The VKAs are oral medications and dosing should be prescribed in accordance with the label guidance and local practice.

Participants are required to remain on the allocated treatment arm for at least 12 months and the duration of their active participation in the study, which could be for up to 4 years. Participants will be followed up at 3 months and 12 months after their allocation, and thereafter annually for the duration of the trial.

All participants should receive their randomised strategy medication before discharge and within 7 days of the date of index surgery.

Once eligibility has been confirmed, randomisation will be undertaken by the research team using a validated web-based system. The randomisation system will use permuted random blocks of variable length and will allocate participants on a 1:1 ratio to either of the two arms. Randomisation will be stratified by (1) whether the participant has undergone any ablation surgery, (2) a participant's stroke risk score, and (3) whether the participant has undergone any other concomitant surgery.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacoeconomic, Prophylaxis

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Apixaban, rivaroxaban, edoxaban, dabigatran, warfarin, phenindione, acenocoumarol

Primary outcome measure
Primary Outcome Measures:
All-cause mortality, major cardiovascular events or major bleeding events will be measured through the collection of patient-reported outcomes and medical record data capture of each of these events, at 3 months, 12 months and then annually for up to 4 years, from the date of randomisation until the end of the trial.

Primary Economic Outcome Measures:
The incremental cost per quality-adjusted life year (QALY) gained based on responses to the EQ-5D-5L at 1 year post-randomisation.

Secondary outcome measures
Secondary Economic Outcome Measures:
1. Costs to NHS, patients, and lifetime cost-effectiveness measured by a Health Resource Usage Questionnaire at 3 months, 1 year, and annually, up to 4 years from randomisation.
2. Health status at baseline, 3 months, 1 year, and annually, up to 4 years from randomisation, measured by the EQ-5D-5L questionnaire.

Secondary Outcomes Measures:
1. Safety outcomes defined as any bleeding up to 4 years post-randomisation, measured by the collection of data from patient-reported outcomes and medical records at 3 months, 1 year, and annually, up to 4 years from randomisation.
2. Clinical effectiveness outcomes defined as a composite of cardiovascular deaths and systemic thromboembolic complications/events for the duration of the trial, measured by the collection of data from patient-reported outcomes and medical records at 3 months, 1 year, and annually, up to 4 years from randomisation.
3. Adverse events of special interest (neurological events, non-CNS emboli, venous thromboembolic events, heart failure, major bleeding, non-major bleeding, cardiovascular mortality), measured by the collection of data from patient-reported outcomes and medical records, at 3 months, 1 year, and annually, up to 4 years from randomisation.
4. Adherence with therapeutic strategies up to 4 years post-randomisation, measured by the collection of data from patient-reported outcomes and medical records at 3 months, 1 year, and annually, up to 4 years from randomisation.

Overall study start date
19/12/2024

Completion date
31/05/2030

Eligibility

Key inclusion criteria

1. Adults aged 18 years old or over
2. Confirmed pre-op Atrial Fibrillation (AF) which should be persistent or permanent
3. Undergone Mitral Valve repair surgery*
4. Require prolonged anticoagulation after MVr surgery e.g. for permanent or persistent AF
5. Provided written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1282

Key exclusion criteria
1. Received a mitral valve replacement or any other valve replacement.
2. Anticoagulation contraindicated
3. Already taking long-term anticoagulation unrelated to an atrial arrhythmia
4. Antiphospholipid syndrome with triple positive antibodies
5. Patients who are pregnant or breastfeeding at the time eligibility is confirmed.
6. Patients with severe renal impairment (defined as creatinine clearance <15 ml/min)

Date of first enrolment
31/03/2025

Date of final enrolment
31/08/2028

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
South Tees Hospitals NHS Foundation Trust

Sponsor details
Academic Cardiovascular Unit
Middlesbrough
England
United Kingdom
TS4 3BW
+44 (0)1642 850850 ext 1
stees.tvra.projects@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.southtees.nhs.uk/hospitals/james-cook/

ROR
https://ror.org/02js17r36

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Any journal publications will be accompanied by datasets as required to verify the analysis and results. The study will be registered with ISRCTN and a final report will be submitted following the conclusion of the study,

Intention to publish date
31/05/2031

Individual participant data (IPD) sharing plan
Aggregated coded datasets will be available to be shared upon request, following the publication of the main findings, from the Academic Cardiovascular Unit, South Tees Hospitals NHS Foundation Trust (stees.affecttrial@nhs.net). The data will be available, as described in the participant information leaflet, and according to the consent provided by the participant. Requesters must provide an outline of their analysis plans and agree to adhere to UK data privacy laws as a minimum, access will be granted after consideration of the plan by the study chief investigator, trials unit and sponsor.

IPD sharing plan summary
Available on request