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A study to test different times for starting direct oral anticoagulants again after someone has had bleeding in their brain due to an injury

Submission date
28/08/2024

Recruitment status
Recruiting

Registration date
28/10/2024

Overall study status
Ongoing

Last Edited
10/06/2025

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Older people falling from a standing height is the most common cause of hospital admission for head injury. Up to 1 in 3 patients admitted are taking a tablet medication which thins the blood, known as an oral anticoagulant. This type of medication can increase the likelihood of bleeding in the brain. Many patients are taking oral anticoagulation due to having an irregular heartbeat (called atrial fibrillation) or because of having a previous stroke or blood clots. When a scan shows blood in the brain, oral anticoagulation is nearly always stopped. However, this leaves the question of when it is safe to restart them. The risk of making the bleeding in the brain worse must be balanced against the risk of having a stroke or blood clots.
There is no clear evidence on the safest time to restart oral anticoagulation, but most neurosurgeons advise restarting them 1-4 weeks after head injury. The number of people who have a bleed on their brain after a head injury is increasing and further brain bleeding or a stroke can have a serious effect on patients' lives and their ongoing healthcare needs.
The main purpose of the trial is to determine when is the most beneficial time for people to start or restart a direct oral anticoagulant (DOAC) after their head injury.

Who can participate?
Patients aged 18 years and over admitted to hospital with a bleed on the brain caused by a head injury who were taking oral anticoagulation before their head injury and have been prescribed a DOAC for a previously diagnosed medical condition (e.g., atrial fibrillation). Patients on other oral anti-coagulants such as warfarin may also be able to take part.

What does the study involve?
People will be asked to start the medication either 1 week or 4 weeks after their head injury. This will be randomly assigned by a computer. They will be then followed closely for 26 weeks and any major bleeding events or blood clots (thrombotic events) such as a stroke or heart attack will be recorded.

What are the possible benefits and risks of participating?
Both timepoints for restarting oral anticoagulants have been shown to improve symptoms but it

is not known which timescale is best. In normal clinical care patients will restart oral anticoagulants 1-4 weeks after head injury so this study will not put participants at any additional risk. Participants will receive only CT or MRI scans as they would normally for standard of care so there is not expected to be any additional risk for participants.

Where is the study run from?
Liverpool Clinical Trials Centre (UK)

When is the study starting and how long is it expected to run for?
August 2024 to May 2028

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

Who is the main contact?
Dr Laura Wright, restart.trial@liverpool.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Laura Wright

Contact details
Block C
Waterhouse Building
1-5 Brownlow Street
Liverpool
United Kingdom
L12 2AP
+44 (0)151 795 0600
restart.trial@liverpool.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Dr Catherine McMahon

Contact details
Mayo Building
Salford Royal
Stott Lane
Salford
United Kingdom
M6 8HD
+44 (0)161 789 7373
catherine.mcmahon@nca.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
1008878

ClinicalTrials.gov (NCT)
NCT06322953

Protocol serial number
RG442-21, CPMS 65417

Study information

Scientific Title
Restart tICrH: a randomised trial of timing to restart direct oral anticoagulants after traumatic intracranial haemorrhage

Acronym
RESTART tICrH

Study objectives
Primary objective:
To compare the clinical effectiveness of restarting/starting direct oral anticoagulant (DOAC) early (1 week) versus late (4 weeks) following traumatic intracranial haemorrhage (tICrH).

Secondary objectives:
1. To evaluate the safety of treating patients restarting/starting DOAC early (1 week) in comparison to late (4 weeks)
2. To evaluate functional status and quality of life for patients restarting/starting DOAC early (1 week) in comparison to late (4 weeks)
3. To determine patient/carer attitudes to restarting/starting DOAC post-traumatic intracranial haemorrhage (tICrH)
4. To estimate the cost-effectiveness of restarting/starting DOAC early (1 week) in comparison to late (4 weeks)

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/10/2024, South Central – Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8178; berkshire.rec@hra.nhs.uk), ref: 24/SC/0298

Study design
Open randomized controlled parallel-group trial

Primary study design
Interventional

Study type(s)

Safety, Efficacy

Health condition(s) or problem(s) studied
Traumatic intracranial haemorrhage

Interventions
Participants will be randomised to one of the two arms using an online randomisation system:

Start/Restart DOAC at 1 week – Participants will be restarted/started on DOAC 1 week post-traumatic intracranial haemorrhage

Start/Restart DOAC at 4 weeks – Participants will be restarted/started on DOAC 4 weeks post-traumatic intracranial haemorrhage

DOACs prescribed with dose, frequency and duration as per local standard practice. DOACs commonly used are apixaban, dabigatran etexilate mesilate, edoxaban and rivaroxaban. These are to be restarted at either 1 or 4 weeks post tICrH.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Apixaban, dabigatran etexilate mesilate, edoxaban tosilate, rivaroxaban

Primary outcome(s)
The proportion of patients with critical haemorrhagic or thrombotic events within 12 weeks following traumatic intracranial haemorrhage (tICrH), measured using case report form

Key secondary outcome(s))
1. Time to first haemorrhagic or thrombotic event within 12 weeks, measured using case report form
2. Time to first haemorrhagic event within 12 weeks, measured using case report form
3. Time to first thrombotic event within 12 weeks, measured using case report form
4. Time to death measured at 12 and 26 weeks, measured using case report form
5. Functional outcome measured using modified Rankin Scale (mRS), Barthel Index and extended Glasgow Outcome Scale (GOS-E) at 12 and 26 weeks
6. Quality of life measured with EQ-5D-5L at 6, 12 and 26 weeks
7. Patient and caregiver attitudes to recommencing DOAC following tICrH within the first 9 months of recruitment start, collected using a semi-structured interview
8. Incremental cost per quality-adjusted life year (QALY) gained, measured using case report form and routine data at 6, 12 and 26 weeks

Completion date
31/05/2028

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 06/06/2025:
1. Informed consent obtained from participant/participants' legal representative and the ability to comply with the requirements of the trial
2. Adult ≥18 years with traumatic intracranial haemorrhage (tICrH) in the past 1 week who were taking oral anticoagulants (OAC) prior to admission (Oral anticoagulants include any DOAC or Vitamin K antagonist (e.g. Warfarin), prescribed for atrial fibrillation (AF) or venous thromboembolism (VTE) prior to admission for tICrH)
3. At high risk for thromboembolic complications (CHA2DS2-VASc ≥2 in men and ≥3 in women) OR patients taking long-term OAC for deep vein thrombosis (DVT) / pulmonary embolism (PE)

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3. Oral anticoagulants include any DOAC or Vitamin K antagonist (e.g. Warfarin), prescribed for atrial fibrillation (AF) or venous thromboembolism (VTE) prior to admission for tICrH
4. At high risk for thromboembolic complications (CHA2DS2-VASc ≥2 in men and ≥3 in women)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current participant exclusion criteria as of 06/06/2025:
1. Patients whose traumatic intracranial haemorrhage is a chronic subdural haematoma only
2. Patients with a mechanical heart valve
3. Patients with a plan to start/restart anti-platelet therapy within 12 weeks of tICrH
4. Abbreviated Injury Scale other than head with a score >3
5. Pregnant or nursing female
6. For participants of reproductive potential (males and females), not willing to use a reliable means of contraception*
7. Participants with a hypersensitivity or contraindication to Direct Oral Anticoagulant (DOAC) as detailed in each IMP SmPC
8. Participant with bleeding where it would be unsafe to restart DOAC at 1 week
9. Participant with clinical reason to restart DOAC before 4 weeks or complete within 12 weeks
10. Concomitant p-gp and CYP3A4 inducers/inhibitors
11. Indication to stay on VKA (Warfarin) rather than switching to DOAC (e.g. severe renal impairment)

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Date of first enrolment
01/03/2025

Date of final enrolment
30/06/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
Not provided at time of registration
United Kingdom
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Sponsor information

Organisation
The Walton Centre NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name

Health Technology Assessment Programme

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date