

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

<b>Submission date</b> 28/08/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 28/10/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 10/06/2025	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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](mailto:restart.trial@liverpool.ac.uk)

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Public

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# Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

1008878

**ClinicalTrials.gov number**

NCT06322953

**Secondary identifying numbers**

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

**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**

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

**Pharmaceutical study type(s)**

Not Applicable

**Phase**

Phase III

**Drug/device/biological/vaccine name(s)**

Apixaban, dabigatran etexilate mesilate, edoxaban tosilate, rivaroxaban

**Primary outcome measure**

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

**Secondary outcome measures**

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

**Overall study start date**

23/08/2024

**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  $\geq 18$  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  $\geq 2$  in men and  $\geq 3$  in women) OR patients taking long-term OAC for deep vein thrombosis (DVT) / pulmonary embolism (PE)

Previous participant inclusion criteria:

1. Informed consent obtained from participant/participants' legal representative/participants' Consultee and ability to comply with the requirements of the trial
2. Adult  $\geq 18$  years with traumatic intracranial haemorrhage (tICrH) in the past 1 week who were taking oral anticoagulants (OAC) prior to admission
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  $\geq 2$  in men and  $\geq 3$  in women)

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

**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)

Previous participant exclusion criteria:

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
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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)
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11. Indication to stay on VKA (Warfarin) rather than switching to DOAC (e.g. severe renal impairment)

**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

## Sponsor details

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## Sponsor type

Hospital/treatment centre

# 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. Submission to regulatory authorities

Requests for data sharing will be reviewed by the study team led by the Chief Investigator. If a request is approved then data will be shared securely with the researcher requesting access. Data shared will be anonymised.

**Intention to publish date**

31/05/2029

**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