

REstart or SToP Antithrombotics Randomised Trial

Submission date 24/04/2013	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 25/04/2013	Overall study status Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 19/11/2024	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

More than one third of the adults with a stroke due to bleeding into the brain - known as brain haemorrhage - are taking drugs to prevent clotting when they have a brain haemorrhage. These patients had previously suffered illnesses like angina, heart attack, or stroke due to blood vessel blockage, which is why they are treated with drugs to prevent further clots occurring. These drugs are usually stopped when the brain haemorrhage occurs. But when patients recover from brain haemorrhage, they and their doctors are often uncertain about whether to restart these drugs to prevent further clots occurring, or whether to avoid them in case they increase the risk of brain haemorrhage happening again. We will study the potentially beneficial effects of three antiplatelet drugs (aspirin, clopidogrel, or dipyridamole) on the risks of heart attack, stroke and other clotting problems as well as their effect on the risk of a brain haemorrhage happening again. This information will help us to decide whether antiplatelet drugs are a promising treatment. If they are, we will recruit a much larger number of patients so that we can determine really reliably whether the beneficial effects of antiplatelet drugs on the risk of clotting outweigh any risks of a repeat brain haemorrhage for such people.

Who can participate?

We aim to recruit 720 men and women in the UK aged 18 years or more who survive a brain haemorrhage. If participants are unable to provide fully informed consent a relative or other legal representative may be approached for their consent.

What does the study involve?

Research staff will collect baseline information about each participant. Some participants may also have an additional MRI scan. Participants will be randomly allocated to either start or avoid antiplatelet medication. Over a period of at least two years we will collect information about participants progress, any medical problems and their adherence to the randomised treatment allocation (start or avoid antiplatelet medication). This follow up information will be obtained from participants, relatives and General Practitioners.

What are the possible benefits and risks of participating?

We do not know whether taking or avoiding antiplatelet medication is best, but participants have a chance to be exposed to the benefit of one or other strategy by participating. Some

people find it beneficial to be part of a research study and to be under regular follow-up. The results of this study will help us to treat patients better in future. Participants may find the time spent completing one questionnaire each year inconvenient. Participants, who have agreed to have an MRI scan, may become claustrophobic in the MRI scanner - if this happens the scan would be stopped. Because MRI scans are so detailed, there is also a 1 in 37 chance of finding an abnormality on your MRI scan that is completely incidental to your brain haemorrhage.

Where is the study run from and how long will it last?

RESTART is run by a team at the Division of Clinical Neurosciences at the University of Edinburgh, UK and it will last for at least five years.

When is the study starting and how long is it expected to run for?

Recruitment started on the 2nd May 2013 and will continue until 31st May 2018. Follow-up of these participants will be at least 6 months.

Who is funding the study?

RESTART is funded by the British Heart Foundation

Who is the main contact?

The UK Chief Investigator is Rustam Al-Shahi Salman and the Trial Manager is Karen Innes, and they can be contacted via RESTART.trial@ed.ac.uk.

Study website

<http://www.restarttrial.org>

Contact information

Type(s)

Scientific

Contact name

Mrs Karen Innes

Contact details

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Additional identifiers

EudraCT/CTIS number

2012-003190-26

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

14297

Study information

Scientific Title

REstart or STop Antithrombotics Randomised Trial

Acronym

RESTART

Study objectives

For adults surviving spontaneous (non-traumatic) intracerebral haemorrhage (ICH) who had taken an antithrombotic (i.e. anticoagulant or antiplatelet) drug for the prevention of vaso-occlusive disease before the ICH, does a policy of starting antiplatelet drugs result in a beneficial net reduction of all serious vascular events over at least two years compared with a policy of avoiding antiplatelet drugs?

More details can be found at: www.restarttrial.org

Ethics approval required

Old ethics approval format

Ethics approval(s)

Scotland A Research Ethics Committee, 02/11/2012, ref: 12/SS/0138

Study design

Interventional multicentre parallel group prospective randomised open blinded end-point (PROBE) clinical trial, Design type: Treatment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

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

Health condition(s) or problem(s) studied

Intracerebral haemorrhage

Interventions

1. Patients will be randomised to either 'start antiplatelet medication' (restricted to the use of one or more of aspirin, dipyridamole or clopidogrel at the investigator's discretion) or 'avoid antiplatelet medication'.
2. Additional pre-randomisation brain MRI (for patients participating in the MRI sub-study)

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Aspirin, dipyridamole, clopidogrel

Primary outcome measure

Current primary outcome measures as of 26/06/2017:

1. Recurrent symptomatic ICH
2. Fatal or non-fatal radiographically- or pathologically-proven recurrent symptomatic

Measured at least 6 months after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Previous primary outcome measures:

1. Recurrent symptomatic ICH
2. Fatal or non-fatal radiographically- or pathologically-proven recurrent symptomatic

Measured over 2 years after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Secondary outcome measures

1. Possible recurrent ICH
2. Symptomatic non-fatal extracerebral haemorrhage, extracranial haemorrhage, and vaso-occlusive events
3. Death
4. Modified Rankin Scale score
5. Adherence to antiplatelet drug(s)

1. Fatal events (i.e. followed by death within 30 days): complication of qualifying ICH; symptomatic extradural/subdural/subarachnoid/intraventricular haemorrhage; symptomatic major extracranial haemorrhage; symptomatic vaso-occlusive events; cardiac death with symptoms suggestive of myocardial ischaemia (type 3) or evidence of arrhythmia; deaths from any other known cause; rapidly fatal stroke, consistent with the clinical manifestations of ICH, but without radiographic or pathological confirmation; unwitnessed deaths without a clear cause and without further investigation.
2. Non-fatal events (i.e. not followed by death within 30 days): symptomatic extradural/subdural/subarachnoid/intraventricular haemorrhage; symptomatic major extracranial haemorrhage; symptomatic vaso-occlusive events; non-fatal stroke, with brain imaging performed too late to distinguish ICH from cerebral infarction.

Timepoint: over 2 years after baseline, detected using annual general practitioner and participant follow-up, with independent, blinded adjudication of the clinical information and investigations relating to every reported outcome

Annual ratings of participant function:

Simplified modified Rankin Scale postal questionnaire or Structured telephone interview with non-responders to the postal questionnaire, completed by the participant or their carer.

Overall study start date

01/04/2013

Completion date

28/02/2021

Eligibility

Key inclusion criteria

1. Patient age 18 years or over, either sex
2. Spontaneous intracerebral haemorrhage (ICH) not attributable to preceding traumatic brain injury, on the basis of:
 - 2.1. A history from the patient/witness of spontaneous symptom onset without preceding head trauma (head trauma occurring subsequent to ICH symptom onset is permissible)
 - 2.2. brain imaging appearances consistent with spontaneous ICH (which may be accompanied by the brain/bone/soft tissue appearances of trauma occurring subsequently)
 - 2.3. Either 'secondary' to an underlying structural cause (e.g. aneurysm, tumour, arteriovenous malformation, or intracranial venous thrombosis), or 'primary' (if the investigator either does not suspect an underlying structural cause, or it is not detected by further radiographic investigation)
3. Patient had taken an antithrombotic (i.e. anticoagulant or antiplatelet) drug for the prevention of vaso-occlusive disease for any length of time before the onset of the qualifying ICH.
4. Patient is at least 24 hours after ICH symptom onset (randomisation is expected to usually occur when they are approaching the end of their hospital admission/assessment for the qualifying ICH).
5. Patient and their doctor are both uncertain about whether to start or avoid antiplatelet drugs.
6. Patient is registered with a general practitioner (GP).
7. Brain imaging study that first diagnosed the qualifying ICH is available.
8. Consent to randomisation from the patient (or personal / legal / professional representative if the patient does not have mental capacity).
9. If eligible for the brain MRI sub-study, the MRI must be performed after the ICH but before randomisation.

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 720; UK Sample Size: 720

Total final enrolment

537

Key exclusion criteria

1. ICH due to traumatic brain injury, in the opinion of the investigator
2. ICH due to haemorrhagic transformation of an ischaemic stroke, in the opinion of the investigator
3. Patient is taking an anticoagulant drug following ICH
4. Patient is pregnant, breastfeeding, or of childbearing age and not taking contraception
5. Patient is being treated or followed up in another Clinical Trial of an Investigational Medicinal Product (CTIMP)
6. Patient and carer unable to understand spoken or written English (local translator is not available)
7. Patients are ineligible for the brain MRI sub-study if they are claustrophobic or they have a contraindication to MRI

Date of first enrolment

02/05/2013

Date of final enrolment

31/05/2018

Locations**Countries of recruitment**

Scotland

United Kingdom

Study participating centre

122 Sites in the United Kingdom

United Kingdom

EH4 2XU

Sponsor information**Organisation**

University of Edinburgh (UK) and NHS Lothian

Sponsor details

ACCORD
QMRI
47 Little France Crescent
Edinburgh
Scotland
United Kingdom
EH16 4TJ

Sponsor type

University/education

Website

www.accord.ed.ac.uk

ROR

<https://ror.org/03q82t418>

Funder(s)**Funder type**

Charity

Funder Name

British Heart Foundation (BHF) (UK)

Alternative Name(s)

the_bhf, The British Heart Foundation, BHF

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Results and Publications**Publication and dissemination plan**

The final results, following 2-year extended follow-up, will be presented and submitted for publication before the end of 2021.

Intention to publish date

28/02/2022

Individual participant data (IPD) sharing plan

A fully anonymised version of the dataset used for analysis of the main results and the final results with individual participant data and a data dictionary will be available on Datashare for other researchers to apply to use, via <https://datashare.is.ed.ac.uk/handle/10283/3265>. Written proposals will be assessed by members of the RESTART trial steering committee and a decision made about the appropriateness of the use of data. A data-sharing agreement will be put in place before any data are shared.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	05/03/2018		Yes	No
Statistical Analysis Plan	statistical analysis plan	25/03/2019	27/03/2019	No	No
Results article	results	29/06/2019	29/05/2019	Yes	No
Other publications	subgroup analyses	01/07/2019	17/02/2021	Yes	No
Results article		08/06/2021	10/06/2021	Yes	No
Results article	Extended Follow-up	03/09/2021	06/09/2021	Yes	No
Abstract results	Results abstract of extended follow-up European Stroke Organisation Conference 2021	03/09/2021	29/03/2023	No	No
HRA research summary			28/06/2023	No	No
Other publications	Healthcare systems data accuracy compared with adjudicated questionnaire follow-up	16/11/2024	19/11/2024	Yes	No