

# The use of aspirin or clopidogrel for people who survive stroke due to bleeding in the brain

<b>Submission date</b> 07/06/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 15/07/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/07/2024	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Stroke due to bleeding into the brain, known as brain haemorrhage, affects more than 3 million people in the world each year. There are more than 20 million brain haemorrhage survivors in the world. People who survive brain haemorrhage are at risk of suffering another major vascular event. These events include heart attacks, strokes, and death due to clotting or bleeding problems. The risk of having a major vascular event remains high after brain haemorrhage. Antiplatelet medicines (like aspirin and clopidogrel) thin the blood and are used in standard practice to protect people from blood clotting problems, even though they increase the risk of bleeding slightly. Doctors aren't sure whether antiplatelet medicines can be used for people who have had a brain haemorrhage. A pilot study in the UK with survivors of brain haemorrhage found that fewer people who started antiplatelet medicines had another brain haemorrhage compared to people who kept off these medicines over 2 years. Antiplatelet medicines also seemed to cause fewer major vascular events. This study will be the largest randomised study of antiplatelet medicines after brain haemorrhage.

### Who can participate?

Brain haemorrhage survivors aged 18 years and over

### What does the study involve?

Participants will be randomly allocated to start or avoid the antiplatelet medicines aspirin or clopidogrel, and will be followed up for major vascular events for 1-5 years.

### What are the possible benefits and risks of participating?

This study will provide the most reliable information about whether antiplatelet medicines help after brain haemorrhage. If it shows that antiplatelet medicines work, they could prevent another major vascular event for more than 150,000 brain haemorrhage survivors worldwide. The study team will explain to patients or their representatives that the potential risks of the antiplatelet drugs used in this study are the same as in standard medical practice. The common side effects of aspirin are an increased bleeding tendency and indigestion. The common side effect of clopidogrel is an increased bleeding tendency. Participants will have access to all other treatments; if a patient has atrial fibrillation and they prefer to take an oral anticoagulant drug (in either standard medical care or a randomised controlled trial), they will not take part in this

study. The risks will be minimised by checking participants' medical histories and the other medications that they are prescribed. Participants' outcomes' will be monitored on a regular basis, and the risk of major bleeding events will be monitored by the Data Monitoring Committee. Additionally each site involved will be taught to record all adverse events that they become aware of and promptly report them to the study Sponsor. Participants may find the time they spend taking part inconvenient, so before deciding to take part we encourage them or their representatives to consider this and if participation will affect any insurance they have and encourage them to seek advice if necessary.

Where is the study run from?  
University of Edinburgh (UK)

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

Who is funding the study?  
1. British Heart Foundation (UK)  
2. Canadian Institutes of Health Research (Canada)  
3. Hartstichting (The Netherlands)  
4. National Health and Medical Research Council (Australia)

Who is the main contact?  
ASPIRING.study@ed.ac.uk

**Study website**  
<http://ASPIRING.ed.ac.uk>

## Contact information

**Type(s)**  
Public

**Contact name**  
Ms Claire Cochran

**Contact details**  
Usher Building  
BioQuarter  
Gate 5-7  
3 Little France Road  
Edinburgh  
United Kingdom  
EH16 4UX  
-  
ASPIRING.study@ed.ac.uk

**Type(s)**  
Scientific, Principal Investigator

**Contact name**  
Prof Rustam Al-Shahi Salman

## Contact details

Centre for Clinical Brain Sciences  
Chancellor's Building  
49 Little France Crescent  
Edinburgh  
United Kingdom  
EH16 4SB  
+44 (0)131 537 2944  
Rustam.Al-Shahi@ed.ac.uk

## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

1009845

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

AC24035, IRAS 1009845

## Study information

### Scientific Title

Antiplatelet Secondary Prevention International Randomised study after INtracerebral haemorrhage (ASPIRING): an investigator-initiated, multicentre, pragmatic, prospective, randomised, parallel group, open clinical trial of an investigational medicinal product

### Acronym

ASPIRING

### Study objectives

The primary objective is to determine if starting one oral antiplatelet drug is superior to avoiding antiplatelet drugs, in addition to standard care, for increasing the time to first major adverse cardiovascular/cerebrovascular event (MACE) for survivors of stroke due to intracerebral haemorrhage (ICH).

The secondary objectives are to determine the effects of one oral antiplatelet drug on:

1. Ischaemic major adverse cardiovascular/cerebrovascular events (efficacy)
2. Haemorrhagic major adverse cardiovascular/cerebrovascular event (safety)
3. Individual components of the major adverse cardiovascular/cerebrovascular event composite outcome
4. All/ischaemic/haemorrhagic major adverse cardiovascular/cerebrovascular events in clinically important sub-groups
5. Non-cardiovascular death, and
6. Generalisability of the effect on the primary outcome between countries

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

Approved 12/07/2024, Scotland A REC (South East Scotland Research Ethics Service, 2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; -; sesres@nhslothian.scot.nhs.uk), ref: 24/SS/0056

## **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**

Stroke due to intracerebral haemorrhage (ICH)

## **Interventions**

The intervention is oral daily antiplatelet drug monotherapy (with aspirin or clopidogrel) in addition to standard care for secondary prevention after ICH at the participating hospital. Aspirin or clopidogrel, if they are available in standard clinical practice at the site where a participant is recruited, may be used within the terms of their marketing authorisation. There is no specific trial drug manufacturer. There is no specific marketing authorisation holder. The antiplatelet drug that was pre-specified at the time of randomisation must be prescribed with a single loading dose as described in the Summary of Product Characteristics. After the loading dose, participants should receive antiplatelet drug monotherapy at a daily dose that is authorised for secondary prevention against MACE. The comparator is standard care at the participating site for secondary prevention after ICH, without any oral antiplatelet drugs. There is no placebo. At the time of randomisation, there should be no intention to use concomitant full therapeutic dose oral anticoagulation. The computerised randomisation application randomly assigns the participant 1:1 to intervention or comparator (stratified by country of recruitment and the pre-specified intended antiplatelet drug).

## **Intervention Type**

Drug

## **Pharmaceutical study type(s)**

Prophylaxis, Therapy

## **Phase**

Phase IV

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

Acetylsalicylic acid, clopidogrel

## **Primary outcome measure**

The first occurrence of any MACE, defined as:

1. Hospitalisation due to stroke (ischaemic, haemorrhagic [i.e. ICH or spontaneous subarachnoid haemorrhage (SAH)], or unknown pathological type), or
2. Hospitalisation due to myocardial infarction, or
3. Cardiovascular death (due to any vascular cause, including pulmonary embolism, haemorrhage, sudden death or death of unknown cause)

Measured using record linkage to healthcare systems data, telephone interview, or postal /telephone questionnaires between 1 year (minimum) and 5 years (maximum) for each participant according to their time of randomisation before the end of study follow-up

## **Secondary outcome measures**

1. MACE condition groups (ischaemic MACE and haemorrhagic MACE)
2. MACE components (hospitalisation due to stroke, hospitalisation due to myocardial infarction, and cardiovascular death)
3. Non-cardiovascular death

Any additional secondary outcomes are specified in the country-specific national addendum

Measured using record linkage to healthcare systems data, telephone interview, or postal /telephone questionnaires between 1 year (minimum) and 5 years (maximum) for each participant according to their time of randomisation before the end of study follow-up

## **Overall study start date**

01/02/2024

## **Completion date**

31/07/2030

# **Eligibility**

## **Key inclusion criteria**

1. Stroke due to ICH, diagnosed by brain imaging, with symptom onset at least 24 hours before randomisation (i.e. there is no upper limit on the time since ICH onset)
2. Age  $\geq 18$  years at the time of first imaging diagnosis of ICH
3. Radiological text report of the brain imaging study that first diagnosed the ICH is available
4. Consent obtained from the participant (or their representative if the participant lacks mental capacity)

## **Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

4148

**Key exclusion criteria**

1. ICH due to specific causes:
  - 1.1. Head injury, exclusively, or
  - 1.2. Secondary to aneurysm, angiitis, arteriovenous malformation/fistula, cavernous malformation, coagulopathy, intracranial venous thrombosis, moyamoya disease, or tumour at the time of consent, or
  - 1.3. Haemorrhagic transformation of cerebral infarction at the time of consent.
2. Systolic BP  $\geq 160$  mmHg at randomisation.
3. Antithrombotic drug use:
  - 3.1. Oral antiplatelet or oral anticoagulant drug, or aspirin over the counter, were taken within 24 hours before randomisation.
  - 3.2. Investigator believes that prescription of a daily oral antiplatelet drug is required at the time of randomisation.
  - 3.3. Use of all permitted antiplatelet drugs is contraindicated according to their representative Summary of Product Characteristics (SPC) provided with the protocol's national addendum.
4. Follow-up:
  - 4.1. Death appears imminent (very unlikely to survive 1 year after randomisation)
  - 4.2. Follow-up will not be possible for the primary and secondary outcomes
5. Pregnant, breastfeeding, or of childbearing potential and not using highly effective contraception. Birth control methods which may be considered as highly effective include combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation, progestogen-only hormonal contraception associated with inhibition of ovulation, intrauterine device, intrauterine hormone-releasing system, bilateral tubal occlusion, vasectomised partner, or sexual abstinence
6. Previously enrolled in ASPIRING
7. Enrolled in a study that precludes co-enrolment with ASPIRING

**Date of first enrolment**

01/03/2025

**Date of final enrolment**

28/02/2029

**Locations****Countries of recruitment**

Australia

Belgium

Canada

England

Netherlands

Scotland

United Kingdom

Wales

**Study participating centre**

**Royal Infirmary of Edinburgh**

Centre for Clinical Brain Sciences

Chancellor's Building

49 Little France Crescent

Lothian

United Kingdom

EH16 4SB

## **Sponsor information**

**Organisation**

University of Edinburgh

**Sponsor details**

Usher Building

BioQuarter

Gate 5-7

3 Little France Road

Edinburgh

England

United Kingdom

EH16 4UX

+44 (0)131 242 6476

resgov@accord.scot

**Sponsor type**

University/education

**Website**

<https://www.accord.scot/>

**ROR**

<https://ror.org/01nrxf90>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

British Heart Foundation

**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

**Funder Name**

Canadian Institutes of Health Research

**Funder Name**

Hartstichting

**Funder Name**

National Health and Medical Research Council (Australia)

## **Results and Publications**

**Publication and dissemination plan**

1. Peer-reviewed scientific journals
2. Conference presentation

3. Publication on website
4. Other publications (e.g. video abstract, social media posts)
5. Submission to regulatory authorities

**Intention to publish date**

31/07/2031

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study will be available on request from [ECTUdatashare@ed.ac.uk](mailto:ECTUdatashare@ed.ac.uk). A de-identified version of the dataset used for analysis with individual participant data and a data dictionary will be available for other researchers to apply to use one year after publication. Written proposals will be assessed by members of the ECTU data-sharing 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**

Available on request