Professional summary

REstart or STop Antithrombotics Randomised Trial

Primary research question	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 therapy result in a beneficial net reduction of all serious vascular events over two years compared with a policy of avoiding antiplatelet therapy?
Trial design	Investigator-led, multicentre, parallel group, prospective randomised open blinded end-point (PROBE) clinical trial of investigational medicinal products (CTIMP) comparing two treatment strategies that are widely used in the UK.
Setting	UK National Health Service (NHS) secondary care (inpatient and outpatient services in stroke, neurology and neurosurgery) and primary care.
Eligibility criteria	**Inclusion:** Patient age ≥18 years. Spontaneous primary or secondary ICH. Patient had taken antithrombotic drugs for the prevention of vaso-occlusive disease before ICH onset. Patient is approaching end of hospital admission for ICH. Patient and their doctor are uncertain about whether to start or avoid antiplatelet drugs. Patient is registered with a general practitioner (GP). Brain imaging that first diagnosed the ICH is available. Brain magnetic resonance imaging (MRI) performed after ICH but before randomisation (if in MRI sub-study). Participant consent (or representative if the patient is mentally incapacitated). **Exclusion:** ICH due to preceding trauma or haemorrhagic transformation of ischaemic stroke. Patient is pregnant, breastfeeding, or of childbearing age and not taking contraception. Patient is being treated or followed up in another CTIMP. Patient and carer unable to understand spoken or written English. Claustrophobia or contraindication to MRI (MRI sub-study).
Randomisation	Central, web-based randomisation system using a minimisation algorithm, with 1:1 treatment allocation to which central research staff are masked.
Interventions	Start *vs.* avoid antiplatelet drugs (drugs chosen at investigator's discretion).
Outcome measures	*Primary outcome measure:* recurrent symptomatic ICH. *Secondary outcome measures:* possible recurrent ICH; symptomatic non-fatal extracerebral haemorrhage, extracranial haemorrhage, and vaso-occlusive events; death; modified Rankin Scale score; adherence to antiplatelet drugs.
Follow up	*Central:* annual postal or telephone questionnaires to participants and their GPs. *Local:* medical records and any brain imaging relating to outcomes. *Administrative data:* Flagging and the GP Clinical Practice Research Datalink (CPRD).
Power	Given that the annual recurrence rate of ICH may be 1.8-7.4% and there may be a 1-4-fold relative increase in this risk on antiplatelet therapy, this trial will have 90% power to detect a doubling of an annual ICH rate of 4.5% or 93% power to detect a quadrupling of an annual rate of 1% over two years at the 5% level. This trial will also provide adequately precise estimates of the rates of all serious vascular events to inform the design of a trial with the power to assess net clinical benefit.
Statistical methods	Hazard ratio over two years after randomisation, adjusted for baseline covariates included in the minimisation algorithm.
Sample size	At least 720 participants in the main trial (at least 550 in the MRI sub-study).
Timetable	Regulatory approvals: 2012. Start up: 2013. Complete follow-up: 2017.