THE UNIVERSITY of EDINBURGH

Edinburgh Stroke Trials

Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage: main results of the REstart or STop Antithrombotics Randomised Trial (RESTART)

RESTART Collaboration

www.RESTARTtrial.org

@bleedingstroke

Adults ≥18y, taking antithrombotic (antiplatelet or anticoagulant) therapy for the prevention of occlusive vascular disease at ICH onset, who discontinued antithrombotic therapy, and survived ≥24h

Brain MRI before randomisation

Randomisation (central)

1:1

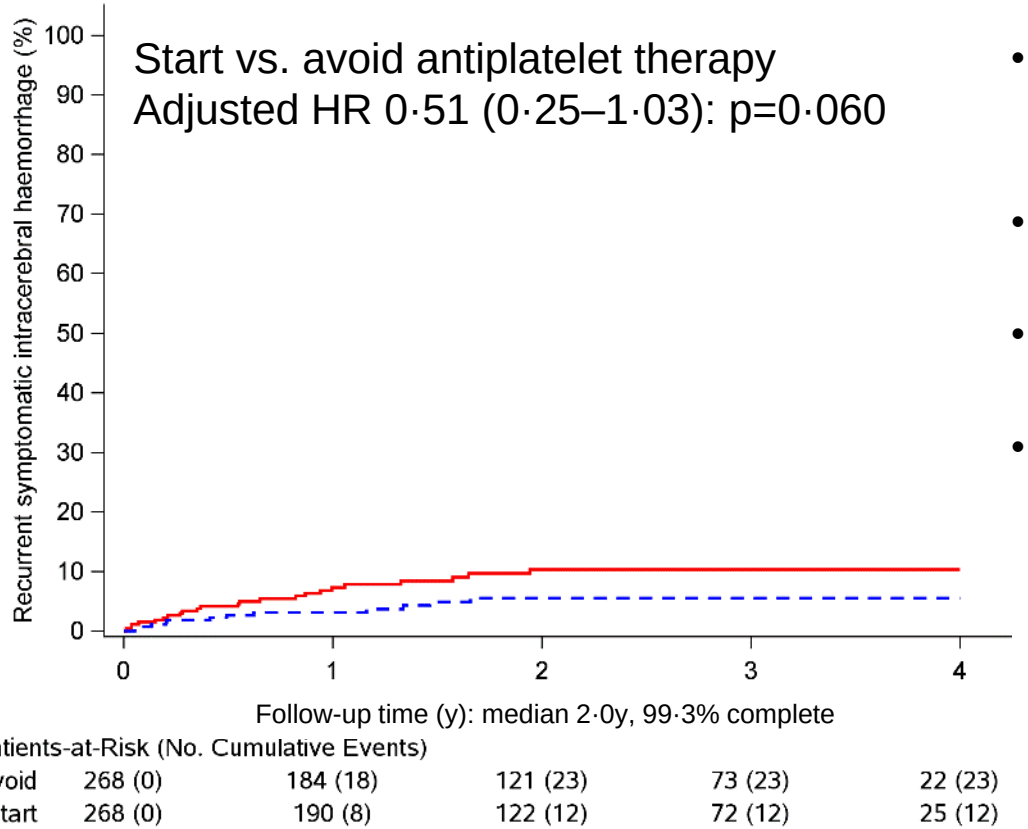
START antiplatelet therapy*

AVOID antiplatelet therapy

Follow-up (central, masked) for vascular events, death, mRS, adherence, BP control

* Aspirin or clopidogrel or dipyridamole (open, no placebo)

Primary outcome: recurrent ICH



- *Unchanged in unadjusted and adjusted models, and sensitivity analyses*
- *No heterogeneity in sub-group analyses*
- *Adherence 99% after randomisation, 82% @ 4y*
- *Median systolic BP 130mmHg throughout*

Avoid: n=23/268 (8·6%)

Start: n=12/268 (4·5%)

Starting antiplatelet therapy after ICH associated with antithrombotic drug use

- Reassuring effects on recurrent ICH
  - Lower than the increase in risk expected (RR=1·67 in ATT trials)
  - Antiplatelet therapy might reduce the risk of recurrent ICH
    - HR 0·51 (95% CI 0·25–1·03), p=0·060
  - Any possible increase in risk seems too small to exceed the established benefits of antiplatelet therapy
- No heterogeneity in sub-groups, but estimates imprecise
- Recruit to ongoing trials (RESTART-Fr, STATICH)

www.RESTARTtrial.org

@bleedingstroke

Thank you to everyone who helped…

- **Participants, relatives, and carers**
- **Primary care practitioners**
- **Collaborators:** at 122 hospitals in the UK
- **Trial management group:** K Innes (senior trial manager); L Dinsmore (imaging manager); J Drever (data manager); C Williams (centre coordinator); D Perry, C McGill, D Buchanan, A Walker, A Hutchison, C Matthews (database programmers); R Fraser, A McGrath, A Deary, R Anderson, A Maxwell, P Walker (trial support officers); J Stephen, C Holm Hansen, R Parker, A Rodriguez (unmasked independent statisticians)
- **Trial steering committee:** *Independent members:* C Baigent (chair), J Carrie (patient–public representative), D Lasserson, F Sullivan. *Others:* R Al-Shahi Salman (chief investigator), MS Dennis, GD Murray, DE Newby, PAG Sandercock, CLM Sudlow, WN Whiteley, N Sprigg, DJ Werring, PM White
- **Data monitoring committee:** J Bamford (chair), J Armitage, J Emberson, GJE Rinkel, G Lowe
- **Outcome event adjudicators:** WN Whiteley, MR Macleod (internal); T Gattringer (external)
- **Systematic Management, Archiving and Reviewing of Trial Images Service (SMARTIS):** JM Wardlaw (director), J Palmer, E Sakka, J Adil-Smith
- **Brain imaging assessors:** PM White, DP Minks, D Mitra, P Bhatnagar, JC du Plessis, Y Joshi
- **Funder:** British Heart Foundation (S Amoils)
- **Sponsor:** ACCORD (J Rojas)
- **Clinical research networks:** NIHR clinical research network, NRS Scottish Stroke Research Network, SINAPSE collaboration
- **Clinical trials unit:** Edinburgh Clinical Trials Unit
- **TICH-2 trial team:** co-enrolment
- **Peer reviewers:** ?
- **Editors and publisher…**

www.RESTARTtrial.org

@bleedingstroke

Get resources and share your opinion…


Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial

RESTART Collaboration*

Summary

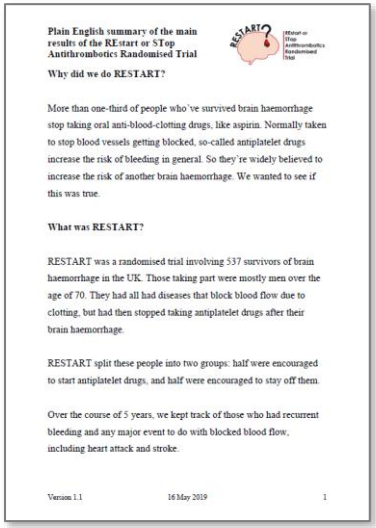
Background Antiplatelet therapy reduces the risk of major vascular events for people with occlusive vascular disease, although it might increase the risk of intracranial haemorrhage. Patients surviving the commonest subtype of intracranial haemorrhage, intracerebral haemorrhage, are at risk of both haemorrhagic and occlusive vascular events, but whether antiplatelet therapy can be used safely is unclear. We aimed to estimate the relative and absolute effects of antiplatelet therapy on recurrent intracerebral haemorrhage and whether this risk might exceed any reduction of occlusive vascular events.

Methods The REstart or STop Antithrombotics Randomised Trial (RESTART) was a prospective, randomised, open-label, blinded endpoint, parallel-group trial at 122 hospitals in the UK. We recruited adults (≥18 years) who were taking antithrombotic (antiplatelet or anticoagulant) therapy for the prevention of occlusive vascular disease when they developed intracerebral haemorrhage, discontinued antithrombotic therapy, and survived for 24 h. Computerised randomisation, incorporating minimisation, allocated participants (1:1) to start or avoid antiplatelet therapy. We


Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial

Summary

Background Findings from the RESTART trial suggest that starting antiplatelet therapy might reduce the risk of recurrent symptomatic intracerebral haemorrhage compared with avoiding antiplatelet therapy. Brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases (such as cerebral microbleeds) are associated with greater risks of recurrent intracerebral haemorrhage. We did subgroup analyses of the RESTART trial to explore whether these brain imaging features modify the effects of antiplatelet therapy.


Plain English summary of the main results of the REstart or STop Antithrombotics Randomised Trial

Why did we do RESTART?

More than one-third of people who've survived brain haemorrhage stop taking oral anti-blood-clotting drugs, like aspirin. Normally taken to stop blood vessels getting blocked, so-called antiplatelet drugs increase the risk of bleeding in general. So they're widely believed to increase the risk of another brain haemorrhage. We wanted to see if this was true.

What was RESTART?

RESTART was a randomised trial involving 537 survivors of brain haemorrhage in the UK. Those taking part were mostly men over the age of 70. They had all had diseases that block blood flow due to clotting, but had then stopped taking antiplatelet drugs after their brain haemorrhage.

RESTART split these people into two groups: half were encouraged to start antiplatelet drugs, and half were encouraged to stay off them.

Over the course of 5 years, we kept track of those who had recurrent bleeding and any major event to do with blocked blood flow, including heart attack and stroke.

Version 1.1 16 May 2019 1