Triple versus guideline antiplatelet therapy to prevent recurrence after acute ischaemic stroke or transient ischaemic attack: the TARDIS RCT

Philip M Bath,[1,2]* Lisa J Woodhouse,[1]
Jason P Appleton,[1,2] Maia Beridze,[3]
Hanne Christensen,[4] Robert A Dineen,[5]
Katie Flaherty,[1] Lelia Duley,[6] Timothy J England,[7]
Diane Havard,[1] Stan Heptinstall,[1] Marilyn James,[8]
Chibeka Kasonde,[9] Kailash Krishnan,[1,2]
Hugh S Markus,[10] Alan A Montgomery,[6]
Stuart Pocock,[11] Marc Randall,[12] Annamarei Ranta,[13]
Thompson G Robinson,[14] Polly Scutt,[1]
Graham S Venables[15] and Nikola Sprigg[1,2]

[1]Stroke Trials Unit, Division of Clinical Neuroscience, University of Nottingham, Nottingham, UK
[2]Stroke, Nottingham University Hospitals NHS Trust, Nottingham, UK
[3]Department of Neurology, Hospital of War Veterans, Tbilisi, Georgia
[4]Department of Neurology, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark
[5]Radiological Sciences, Division of Clinical Neuroscience, University of Nottingham, Nottingham, UK
[6]Nottingham Clinical Trials Unit, University of Nottingham, Nottingham, UK
[7]Vascular Medicine, Division of Medical Sciences and Graduate Entry Medicine, University of Nottingham, Nottingham, UK
[8]Health Economics, Division of Rehabilitation and Ageing, University of Nottingham, Nottingham, UK
[9]Lowdham Medical Centre, Nottingham, UK
[10]Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
[11]Medical Statistics Unit, London School of Hygiene & Tropical Medicine, London, UK
[12]Department of Neurology, Leeds Teaching Hospitals NHS Trust, Leeds, UK
[13]Department of Neurology, Wellington Hospital and University of Otago, Wellington, New Zealand
[14]Department of Cardiovascular Sciences, University of Leicester, Leicester, UK
[15]Department of Neurology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

*Corresponding author philip.bath@nottingham.ac.uk

Declared competing interests of authors: Philip M Bath reports grants from the British Heart Foundation and National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme during the conduct of the study, and he is a shareholder in Platelet Solutions Ltd (Nottingham, UK). He also notes personal fees from Diamedica (Minneapolis, MN, USA), Nestlé (Vevey, Switzerland), Phagenesis Ltd (Manchester, UK), ReNeuron (Bridgend, UK), Athersys (Cleveland, OH, USA), and Covidien (Zurich, Switzerland) outside the submitted work. Robert A Dineen reports a grant from the British Heart Foundation during the conduct of the study. Hugh S Markus reports grants from the NIHR HTA programme during the conduct of the study. Alan A Montgomery is a member of the NIHR HTA Clinical Evaluation and Trials Funding Board.

Published August 2018
DOI: 10.3310/hta22480

Plain English summary

The TARDIS RCT

Health Technology Assessment 2018; Vol. 22: No. 48
DOI: 10.3310/hta22480

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Plain English summary

Brain damage due to a blood clot (stroke) is a common cause of disability in older adults. Mini-strokes are temporary damage to the brain that usually leave no long-term effect. Following a stroke or mini-stroke, there is an increased risk of having another one, especially over the next few hours. The risk of having another event can be reduced with blood-thinning drugs that reduce the formation of blood clots (e.g. aspirin, clopidogrel, dipyridamole). Typically, these are used alone (clopidogrel) or in combination (aspirin and dipyridamole). As one or two blood-thinning drugs are effective at reducing the risk of having another stroke, intensive treatment with all three might be even more beneficial, providing that excessive bleeding does not occur as a result.

The Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke (TARDIS) trial recruited patients who could start treatment within 48 hours of a stroke or brief mini-stroke caused by a blood clot blocking a blood vessel. Participants were randomised ('put into groups using chance') to either intensive treatment with combined aspirin, clopidogrel and dipyridamole, or routine treatment; these treatments were given for 30 days, after which routine treatment was taken. The main result was the occurrence of a repeat stroke or mini-stroke, and how severe they were, by 90 days. The key safety outcome was a count of bleeds (because of blood-thinning drugs) and their severity.

The trial was stopped early on the recommendation of the Data Monitoring Committee after recruitment of 3096 participants from 106 hospitals in four countries. Although there was no difference in the number and severity of repeat strokes and mini-strokes between the treatment groups, serious or fatal bleeding was increased in the group of participants receiving three blood-thinning drugs. There were no differences between the treatment groups in the number of deaths.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.513

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 10/104/24. The contractual start date was in October 2012. The draft report began editorial review in November 2017 and was accepted for publication in May 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).