

Tranexamic acid to reduce head injury death in people with traumatic brain injury: the CRASH-3 international RCT

Ian Roberts,^{1*} Haleema Shakur-Still,¹
Amy Aeron-Thomas,² Danielle Beaumont,¹
Antonio Belli,³ Amy Brenner,¹ Madeleine Cargill,¹
Rizwana Chaudhri,⁴ Nicolas Douglas,⁵
Lauren Frimley,¹ Catherine Gilliam,¹ Amber Geer,¹
Zahra Jamal,¹ Rashid Jooma,⁶ Raoul Mansukhani,¹
Alec Miners,⁵ Jason Pott,⁷ Danielle Prowse,¹
Temitayo Shokunbi⁸ and Jack Williams⁵

¹Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK

²RoadPeace, London, UK

³National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre, Queen Elizabeth Hospital, Birmingham, UK

⁴Department of Obstetrics and Gynaecology, Rawalpindi Medical University, Rawalpindi, Pakistan

⁵Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, London, UK

⁶Department of Surgery, The Aga Khan University Medical College, Karachi, Pakistan

⁷Emergency Department, Barts Health NHS Trust, The Royal London Hospital, London, UK

⁸Department of Anatomy and Surgery, University of Ibadan, Ibadan, Nigeria

*Corresponding author Ian.Roberts@lshtm.ac.uk

Declared competing interests of authors: Ian Roberts reports grants from the National Institute for Health Research (NIHR) Health Technology Assessment programme, the JP Moulton Charitable Trust, the Department of Health and Social Care, the Department for International Development, the Global Challenges Research Fund, the Medical Research Council and the Wellcome Trust (Joint Global Health Trials scheme) during the conduct of the study. Ian Roberts and Haleema Shakur-Still report membership of Clinical Trial Units (CTUs) funded by the NIHR CTU Management Committee.

Published April 2021

DOI: 10.3310/hta25260

Plain English summary

The CRASH-3 international RCT

Health Technology Assessment 2021; Vol. 25: No. 26

DOI: [10.3310/hta25260](https://doi.org/10.3310/hta25260)

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

Plain English summary

Traumatic brain injury is a leading cause of death and disability worldwide, with over 60 million new cases each year.

When the head is injured there is often bleeding inside the brain, which can continue for some time and worsen after hospital admission. This bleeding increases pressure inside the skull, causing further damage to the brain, which can be fatal or result in serious disability.

Tranexamic acid is a cheap drug that reduces bleeding in other conditions. A large trial of accident victims (other than those with head injury) found that it reduced the chances of bleeding to death. We wanted to find out if tranexamic acid would also reduce deaths among patients with head injuries.

We studied just under 13,000 patients with traumatic brain injury who did not have other major injuries to their bodies from 175 hospitals across 29 countries. Patients were assigned at random to receive either tranexamic acid or a dummy medicine called a placebo. Neither the clinical team nor the patient knew which medicine the patient received. All patients received the usual treatments given to head-injured patients.

Outcomes from 9127 participants were analysed. Among patients treated early, within 3 hours, the rate of head injury death was 18.5% (855/4613) in the tranexamic acid group and 19.8% (892/4514) in the placebo group. We found no evidence of an effect of tranexamic acid overall. However, in patients with mild or moderate traumatic brain injury, there was a 20% reduction in deaths. There were no side effects and no increase in disability in survivors when the drug was used. The economic analysis shows that tranexamic acid represents value for money for patients with mild or moderate traumatic brain injury.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.370

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and 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

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

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.

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 14/190/01. The contractual start date was in October 2014. The draft report began editorial review in February 2020 and was accepted for publication in July 2020. 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.

Copyright © 2021 Roberts *et al.* This work was produced by Roberts *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This is an Open Access publication distributed under the terms of the Creative Commons Attribution CC BY 4.0 licence, which permits unrestricted use, distribution, reproduction and adaptation in any medium and for any purpose provided that it is properly attributed. See: <https://creativecommons.org/licenses/by/4.0/>. For attribution the title, original author(s), the publication source – NIHR Journals Library, and the DOI of the publication must be cited.

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

NIHR Journals Library Editor-in-Chief

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

NIHR Journals Library Editors

Professor John Powell Chair of HTA and EME Editorial Board and Editor-in-Chief of HTA and EME journals. Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Professor of Digital Health Care, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals) and Editor-in-Chief of HS&DR, PGfAR, PHR journals

Professor Matthias Beck Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson Consultant Advisor, Wessex Institute, University of Southampton, UK

Ms Tara Lamont Senior Scientific Adviser (Evidence Use), Wessex Institute, University of Southampton, UK

Dr Catriona McDaid Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Emeritus Professor of Wellbeing Research, University of Winchester, UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

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