

Bleeding risk in patients prescribed dual antiplatelet therapy and triple therapy after coronary interventions: the ADAPTT retrospective population-based cohort studies

Jessica Harris,¹ Koen B Pouwels,² Thomas Johnson,³
Jonathan Sterne,⁴ Christalla Pithara,⁵
Kalaivani Mahadevan,³ Barney Reeves,¹
Umberto Benedetto,⁶ Yoon Loke,⁷
Daniel Lasserson,⁸ Brett Doble,⁹
Noreen Hopewell-Kelly,¹⁰ Sabi Redwood,⁵
Sarah Wordsworth,² Andrew Mumford,⁶
Chris Rogers¹ and Maria Pufulete^{1*}

¹Bristol Trials Centre, University of Bristol, Bristol, UK

²Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK

³Department of Cardiology, Bristol Heart Institute, Bristol, UK

⁴National Institute for Health Research Biomedical Research Centre, Department of Population Health Sciences, University of Bristol, Bristol, UK

⁵National Institute for Health Research Applied Research Collaboration West (NIHR ARC West), Bristol, UK

⁶Bristol Medical School, University of Bristol, Bristol, UK

⁷Norwich Medical School, University of East Anglia, Norwich, UK

⁸Institute of Applied Health Research, University of Birmingham, Birmingham, UK

⁹Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK

¹⁰Health and Social Sciences, University of the West of England, Bristol, Bristol, UK

*Corresponding author maria.pufulete@bristol.ac.uk

Declared competing interests of authors: Thomas Johnson reports grants, personal fees and meeting sponsorship from AstraZeneca plc (Cambridge, UK) and Bayer AG (Leverkusen, Germany); personal fees and meeting sponsorship from Daiichi Sankyo Company Ltd (Tokyo, Japan); and personal fees from The Medicines Company (London, UK), outside the submitted work. Thomas Johnson has also received honoraria or consultation fees from Abbott Laboratories (Abbott Park, IL, USA), Bayer AG, Biosensors International Group Ltd (Singapore), Boston Scientific (Marlborough, MA, USA), Medtronic plc (Dublin, Ireland), Terumo Corporation (Tokyo, Japan) and Vascular Perspectives Ltd (Holme, UK); grants from AstraZeneca plc and Bayer AG for research support; and sponsorship for a speakers' bureau from Abbott Laboratories. Yoon Loke reports consultancy fees from Syri Ltd (Middlesex, UK) for regulatory review of drug treatments for peptic ulcer, outside the submitted work. Daniel Lasserson is a member of the

Health Technology Assessment (HTA) Clinical Evaluation and Trials Committee (April 2016–July 2021).
Chris Rogers is a member of the HTA Funding Committee Policy Group (2017–21) and the HTA
Commissioning Committee (2016–21).

Published May 2023
DOI: 10.3310/MNJY9014

Plain language summary

Bleeding risk in patients prescribed dual antiplatelet therapy
and triple therapy after coronary interventions: the ADAPTT
retrospective population-based cohort studies

Health Technology Assessment 2023; Vol. 27: No. 8
DOI: 10.3310/MNJY9014

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

Plain language summary

People who have a heart attack are treated with a stent to open up the blocked artery that caused the heart attack, with surgery to bypass the blocked artery or with medication only. Whatever the treatment, they are prescribed one or more antiplatelet drugs, either aspirin only or aspirin and an additional antiplatelet (clopidogrel, prasugrel or ticagrelor), for 12 months after the heart attack. Antiplatelets are given to prevent another heart attack, but increase the risk of bleeding.

We used a large general practice database and a database describing patients' attendances and admissions to hospital to determine how many people bleed with different antiplatelet combinations. We found that, overall, up to 1 in 10 people taking antiplatelets (rising to 2 in 10 if also taking an anticoagulant such as warfarin or dabigatran) reported a bleed. Among patients treated with surgery or medication only, we compared aspirin only (which is a less potent therapy) with aspirin and clopidogrel (a more potent therapy). Among patients treated with stents, we compared aspirin and clopidogrel (less potent therapy) with aspirin and prasugrel or ticagrelor (more potent therapy).

In all three populations, the more potent therapy increased the risk of bleeding by about one and a half times, but this was not offset by a reduced risk of having a subsequent heart attack. This may be explained by low adherence to the medication: between one-third and almost half of all patients did not adhere to their regimen, and non-adherence was generally higher among patients taking a more potent therapy. It may also be explained by bias inherent in the study, for example if the groups prescribed different antiplatelet regimens had different risks of having another heart attack. Nevertheless, the results show that doctors should be cautious about prescribing more potent antiplatelet therapy because it may increase serious bleeds without necessarily reducing the number of heart attacks.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.014

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 4.014 and is ranked 27th (out of 108 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2021 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), Embase (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

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.

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 14/192/89. The contractual start date was in April 2016. The draft report began editorial review in July 2020 and was accepted for publication in July 2021. 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 and Care 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, 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, the HTA programme or the Department of Health and Social Care.

Copyright © 2023 Harris et al. This work was produced by Harris 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 NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress, final files produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).

NIHR Journals Library Editor-in-Chief

Dr Cat Chatfield Director of Health Services Research UK

NIHR Journals Library Editors

Professor John Powell 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 (HSDR, PGfAR, PHR journals) and Editor-in-Chief of HSDR, 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 Consultant in Public Health, Delta Public Health Consulting Ltd, UK

Dr Peter Davidson Interim Chair of HTA and EME Editorial Board. Consultant Advisor, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Ms Tara Lamont Senior Adviser, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Dr Catriona McDaid Reader in Trials, 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, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Dr Rob Riemsma Consultant Advisor, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Professor Helen Roberts Professor of Child Health Research, Child and Adolescent Mental Health, Palliative Care and Paediatrics Unit, Population Policy and Practice Programme, UCL Great Ormond Street Institute of Child Health, London, 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