Mar 30, 2021

The effects of long-term oral antithrombotic agents after intracranial haemorrhage: protocol for a prospective individual participant data meta-analysis of randomised controlled trials

Rustam Al-Shahi Salman[1], Craig S. Anderson[2], Oscar R. Benavente[3], Barbara Casolla[4], Chen Chen[5], Xin Cheng[6], Stuart J. Connolly[7], Charlotte Cordonnier[8], Eva-Lotta Glader[9], Graeme J. Hankey[10], Peter U. Heuschmann[11], Jeannette Hofmeijer[12], Hooman Kamel[13], Henk Kerkhoff[14], Catharina J.M. (Karin) Klijn[15], Christina Kruuse[16], Kristin Tveitan Larsen[17], Steff Lewis[18], Santosh Murthy[19], Johanna Pennlert[9], Roz Pollock[18], Ole Morten Rønning[20], Floris Schreuder[15], Kevin Sheth[21], Ashkan Shoamanesh[7], Lily Song[5], Jayne F. Tierney[22], Roland Veltkamp[23], H Bart van der Worp[24]

[1]University of Edinburgh; [2]The George Institute for Global Health, Sydney. Australia;

[3]Department of Medicine (Neurology), University of British Columbia, Vancouver. Canada;

[4]Stroke Unit, University Hospital of Nice, Université Côte d'Azur (UCA), Nice. France;

[5]The George Institute for Global Health at Peking University Health Science Center, Shanghai. China;

[6]Department of Neurology, Huashan Hospital, Fudan University, Shanghai. China;

[7]Department of Medicine (Neurology), McMaster University / Population Health Research Institute, Hamilton. Canada;

[8]Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille. France;

[9]Department of Public Health and Clinical Medicine, Umeå University. Sweden;

[10]University of EdinburghMedical School, Faculty of Medical & Health Sciences, The University of Western Australia, Perth. Australia;

[11]Institute of Clinical Epidemiology and Biometry, University of Würzburg, Würzburg. Germany;

[12]Department of Neurology / Clinical Neurophysiology, Rijnstate Hospital / University of Twente, Arnhem. The Netherlands;

[13]Clinical and Translational Neuroscience Unit, Department of Neurology and Feil Family Brain and Mind Research Institute, Weill Cornell Medicine, New York. USA;

[14]Department of Neurology, Albert Schweitzer Hospital, Dordrecht. The Netherlands;

[15]Department of Neurology, Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Center, Nijmegen. The Netherlands;

[16]Department of Neurology, Copenhagen University Hospital Herlev and Gentofte. Institute of Clinical Medicine, University of Copenhagen, Copenhagen. Denmark;

[17]Department of Geriatric Medicine, Oslo University Hospital/Department of Neurology, Akershus University Hospital, Oslo. Norway;

[18]Edinburgh Clinical Trials Unit, Usher Institute, University of Edinburgh, Edinburgh. UK;

[19]Clinical and Translational Neuroscience Unit, Department of Neurology, Weill Cornell Medicine, New York. USA;

[20]Department of Medicine (neurology), Akershus University Hospital, Institute of Clinical Medicine, University of Oslo, Oslo. Norway;

[21]Department of Neurology, Yale University School of Medicine, New Haven. USA;

[22]MRC Clinical Trials Unit at UCL, Institute of Clinical Trials & Methodology, London. UK;

[23]Department of Brain Sciences, Imperial College, London. UK;

[24]Department of Neurology and Neurosurgery, Brain Center, University Medical Center Utrecht, Utrecht. The Netherlands

1 *Works for me* dx.doi.org/10.17504/protocols.io.bttdnni6

Rustam Al-Shahi Salman
University of Edinburgh

SUBMIT TO PLOS ONE

Citation: Rustam Al-Shahi Salman, Craig S. Anderson, Oscar R. Benavente, Barbara Casolla, Chen Chen, Xin Cheng, Stuart J. Connolly, Charlotte Cordonnier, Eva-Lotta Glader, Graeme J. Hankey, Peter U. Heuschmann, Jeannette Hofmeijer, Hooman Kamel, Henk Kerkhoff, Catharina J.M. (Karin) Klijn, Christina Kruuse, Kristin Tveitan Larsen, Steff Lewis, Santosh Murthy, Johanna Pennlert, Roz Pollock, Ole Morten RÃÂ¸nning, Floris Schreuder, Kevin Sheth, Ashkan Shoamanesh, Lily Song, Jayne F. Tierney, Roland Veltkamp, H Bart van der Worp (03/30/2021). The effects of long-term oral antithrombotic agents after intracranial haemorrhage: protocol for a prospective individual participant data meta-analysis of randomised controlled trials. https://dx.doi.org/10.17504/protocols.io.bttdnni6

ABSTRACT

Introduction – Randomised controlled trials (RCTs) have shown that antiplatelet and anticoagulant (antithrombotic) agents reduce the risk of stroke and other major vascular events for a variety of patients despite increasing the risk of bleeding. However, patients with intracranial haemorrhage were not included in these RCTs, so the risks and benefits of antithrombotic agents after intracranial haemorrhage are uncertain.

Methods and analysis – The Collaboration Of Controlled Randomised trials of long-term Oral Antithrombotic drugs after spontaneous intraCranial Haemorrhage (COCROACH) aims to perform an individual participant data meta-analysis (IPDMA) in order to provide reliable information about the effects of antithrombotic agents on the risks of major vascular events after spontaneous intracranial haemorrhage overall, and in clinically important sub-groups. The protocol of the corresponding Cochrane Review (8 April 2016) specified the methods used by this IPDMA for searching the Cochrane Stroke Group Trials Register, the Cochrane Central Register of Controlled Trials, Ovid MEDLINE, Ovid Embase, and online registries of RCTs. RCTs are eligible for inclusion in this IPDMA if they are registered with a trial registry, include participants with spontaneous intracranial haemorrhage who are allocated at random to long-term use of any oral antithrombotic agent(s) or to placebo, open control, another antithrombotic agent, or another intervention for the prevention of major vascular events, and their chief investigator agrees to share participant-level de-identified data. COCROACH was initiated at the European Stroke Organisation Conference on 17 May 2017 before the results of any RCTs were known. This protocol was agreed after the publication of one RCT of antiplatelet agents (RESTART ISRCTN71907627) and the presentation of one trial of an oral anticoagulant agent (NASPAF-ICH NCT02998905), but before the majority of RCT results were known. We will perform two-step IPDMA of included RCTs using their intention-to-treat datasets using fixed effects models as the primary analysis. We will conduct separate IPDMAs, grouping RCTs into distinct dyads of intervention (antithrombotic agent class) and comparator, as allocated by randomisation. The primary outcome for each IPDMA will be a composite outcome of major vascular events that are appropriate to the intervention-comparator dyad. Secondary outcomes will include major ischaemic events and major haemorrhagic events. We will assess interactions with the effects of antithrombotic agents on the primary outcome in demographic, clinical, imaging, and treatment-related sub-groups.

Ethics and dissemination – All participant data will be shared with the University of Edinburgh by included RCTs with the intention of addressing the same research question for which they were acquired. Participant-level data will be de-identified and shared unless forbidden by individual participants or regulatory authorities. We will disseminate the results of this IPDMA in peer-reviewed journals.

ATTACHMENTS

COCROACH IPDMA protocol v1.0 30 March 2021.pdf

DOI

dx.doi.org/10.17504/protocols.io.bttdnni6

PROTOCOL CITATION

Rustam Al-Shahi Salman, Craig S. Anderson, Oscar R. Benavente, Barbara Casolla, Chen Chen, Xin Cheng, Stuart J. Connolly, Charlotte Cordonnier, Eva-Lotta Glader, Graeme J. Hankey, Peter U. Heuschmann, Jeannette Hofmeijer, Hooman Kamel, Henk Kerkhoff, Catharina J.M. (Karin) Klijn, Christina Kruuse, Kristin Tveitan Larsen, Steff Lewis, Santosh Murthy, Johanna Pennlert, Roz Pollock, Ole Morten Rønning, Floris Schreuder, Kevin Sheth, Ashkan Shoamanesh, Lily Song, Jayne F. Tierney, Roland Veltkamp, H Bart van der Worp 2021. The effects of long-term oral antithrombotic agents after intracranial haemorrhage: protocol for a prospective individual participant data meta-analysis of randomised controlled trials. **protocols.io** https://dx.doi.org/10.17504/protocols.io.bttdnni6

Citation: Rustam Al-Shahi Salman, Craig S. Anderson, Oscar R. Benavente, Barbara Casolla, Chen Chen, Xin Cheng, Stuart J. Connolly, Charlotte Cordonnier, Eva-Lotta Glader, Graeme J. Hankey, Peter U. Heuschmann, Jeannette Hofmeijer, Hooman Kamel, Henk Kerkhoff, Catharina J.M. (Karin) Klijn, Christina Kruuse, Kristin Tveitan Larsen, Steff Lewis, Santosh Murthy, Johanna Pennlert, Roz Pollock, Ole Morten RÃÂ¸nning, Floris Schreuder, Kevin Sheth, Ashkan Shoamanesh, Lily Song, Jayne F. Tierney, Roland Veltkamp, H Bart van der Worp (03/30/2021). The effects of long-term oral antithrombotic agents after intracranial haemorrhage: protocol for a prospective individual participant data meta-analysis of randomised controlled trials. https://dx.doi.org/10.17504/protocols.io.bttdnni6

CREATED

Mar 30, 2021

LAST MODIFIED

Mar 30, 2021

PROTOCOL INTEGER ID

48709

Citation: Rustam Al-Shahi Salman, Craig S. Anderson, Oscar R. Benavente, Barbara Casolla, Chen Chen, Xin Cheng, Stuart J. Connolly, Charlotte Cordonnier, Eva-Lotta Glader, Graeme J. Hankey, Peter U. Heuschmann, Jeannette Hofmeijer, Hooman Kamel, Henk Kerkhoff, Catharina J.M. (Karin) Klijn, Christina Kruuse, Kristin Tveitan Larsen, Steff Lewis, Santosh Murthy, Johanna Pennlert, Roz Pollock, Ole Morten RÃÂ¸nning, Floris Schreuder, Kevin Sheth, Ashkan Shoamanesh, Lily Song, Jayne F. Tierney, Roland Veltkamp, H Bart van der Worp (03/30/2021). The effects of long-term oral antithrombotic agents after intracranial haemorrhage: protocol for a prospective individual participant data meta-analysis of randomised controlled trials. https://dx.doi.org/10.17504/protocols.io.bttdnni6