

Fluoxetine to improve functional outcomes in patients after acute stroke: the FOCUS RCT

Martin Dennis,^{1*} John Forbes,² Catriona Graham,³
Maree Hackett,⁴ Graeme J Hankey,⁵ Allan House,⁶
Stephanie Lewis,⁷ Erik Lundström,^{8,9}
Peter Sandercock¹ and Gillian Mead¹ on behalf of the
FOCUS Trial Collaboration[†]

¹Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

²Health Research Institute, University of Limerick, Limerick, Ireland

³Edinburgh Clinical Research Facility, University of Edinburgh, Edinburgh, UK

⁴The George Institute for Global Health, University of New South Wales, Sydney, NSW, Australia

⁵Medical School, University of Western Australia, Crawley, WA, Australia

⁶Institute of Health Sciences, University of Leeds, Leeds, UK

⁷Edinburgh Clinical Trials Unit, University of Edinburgh, Edinburgh, UK

⁸Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

⁹Department of Neuroscience, Neurology, Uppsala University, Uppsala, Sweden

*Corresponding author martin.dennis@ed.ac.uk

[†]See *Appendix 1* for membership and contributions

Declared competing interests of authors: Martin Dennis, Maree Hackett, Graeme J Hankey, Gillian Mead and Erik Lundström report grants from the National Health and Medical Research Council (Australia) and funding from the Swedish Research Council Framework grant in clinical therapy research during the conduct of the study. Maree Hackett also reports grants from The Stroke Association (London, UK), grants from the National Institute for Health Research (NIHR) Stroke Research Network and a grant in clinical therapy research during the conduct of the study, and grants from the National Heart Foundation of Australia outside the submitted work. She also held a National Health and Medical Research Council (Australia) Career Development Fellowship, level 2 (reference APP1141328) (2018–21). Stephanie Lewis reports being a member of the NIHR Health Technology Assessment General Committee (2016 to present). Peter Sandercock reports lecture fees from Bayer AG (Leverkusen, Germany) paid to his department, outside the submitted work.

Published May 2020

DOI: 10.3310/hta24220

Plain English summary

The FOCUS RCT

Health Technology Assessment 2020; Vol. 24: No. 22

DOI: [10.3310/hta24220](https://doi.org/10.3310/hta24220)

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

Plain English summary

Fluoxetine, sometimes referred to by the drug company name Prozac, has been used for many years to treat people who are depressed, including after a stroke. However, studies have suggested that treatment with fluoxetine started soon after a stroke might improve patients' physical recovery. The Fluoxetine Or Control Under Supervision (FOCUS) trial recruited 3127 volunteers who had had a stroke within the previous 2 weeks from 103 UK hospitals between 2012 and 2017. Participants were randomly allocated to take a 6-month course of fluoxetine or an identical placebo capsule containing no fluoxetine. They were followed up at 6 months and 12 months after recruitment. Patients completed questionnaires that indicated how much they had recovered, and also measured their mood, fatigue and quality of life. The results of the trial showed that the physical recovery of patients was very similar in both groups. This indicates that fluoxetine does not improve physical outcomes of stroke patients. However, participants receiving fluoxetine were less likely to develop depression after the stroke but once the fluoxetine was stopped these effects on mood disappeared. Unfortunately, patients on fluoxetine were slightly more likely to fall and fracture a bone than those on placebo. The FOCUS trial is the first of three large randomised controlled trials testing fluoxetine in stroke patients to be completed. The FOCUS trial results suggest that patients with stroke should not routinely be treated with fluoxetine.

The other two trials will give us further information about the effects of fluoxetine after stroke and whether or not its effects differ between countries or ethnic groups.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

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 13/04/30. The contractual start date was in October 2014. The draft report began editorial review in May 2019 and was accepted for publication in November 2019. 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.

© Queen's Printer and Controller of HMSO 2020. This work was produced by Dennis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

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

Editor-in-Chief of *Health Technology Assessment* and NIHR Journals Library

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 Senior Clinical Researcher, 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 Director, NIHR Dissemination Centre, 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 Professor of Wellbeing Research, University of Winchester, UK

Professor John Norrie Chair in Medical Statistics, University of Edinburgh, 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

Professor Martin Underwood Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

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

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