

# Cognitive-behavioural therapy for clozapine-resistant schizophrenia: the FOCUS RCT

Anthony P Morrison,<sup>1,2\*†</sup> Melissa Pyle,<sup>1,2†</sup>  
Andrew Gumley,<sup>3</sup> Matthias Schwannauer,<sup>4</sup>  
Douglas Turkington,<sup>5</sup> Graeme MacLennan,<sup>6</sup>  
John Norrie,<sup>7</sup> Jemma Hudson,<sup>6</sup> Samantha Bowe,<sup>1</sup>  
Paul French,<sup>1,8</sup> Paul Hutton,<sup>9</sup> Rory Byrne,<sup>1,2</sup>  
Suzy Syrett,<sup>3</sup> Robert Dudley,<sup>10</sup> Hamish J McLeod,<sup>3</sup>  
Helen Griffiths,<sup>4</sup> Thomas RE Barnes,<sup>11</sup> Linda Davies,<sup>12</sup>  
Gemma Shields,<sup>12</sup> Deborah Buck,<sup>12</sup> Sarah Tully<sup>1,2</sup>  
and David Kingdon<sup>13</sup>

<sup>1</sup>Psychosis Research Unit, Greater Manchester Mental Health NHS Foundation Trust, Prestwich, UK

<sup>2</sup>Division of Psychology and Mental Health, University of Manchester, Manchester, UK

<sup>3</sup>Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

<sup>4</sup>Department of Clinical Psychology, Edinburgh Medical School, University of Edinburgh, Edinburgh, UK

<sup>5</sup>Academic Psychiatry, Northumberland, Tyne and Wear NHS Foundation Trust, Centre for Ageing and Vitality, Newcastle General Hospital, Newcastle upon Tyne, UK

<sup>6</sup>Centre for Healthcare Randomised Trials, Health Services Research Unit, University of Aberdeen, Aberdeen, UK

<sup>7</sup>Clinical Trials Unit, Edinburgh Medical School, University of Edinburgh, Edinburgh, UK

<sup>8</sup>Institute of Psychology, Health and Society, University of Liverpool, Liverpool, UK

<sup>9</sup>School of Health and Social Care, Edinburgh Napier University, Edinburgh, UK

<sup>10</sup>School of Psychology, Newcastle University, Newcastle upon Tyne, UK

<sup>11</sup>Centre for Mental Health, Imperial College London, London, UK

<sup>12</sup>Division of Population Health, University of Manchester, Manchester, UK

<sup>13</sup>Department of Psychiatry, University of Southampton, Academic Centre, Southampton, UK

\*Corresponding author [tony.morrison@manchester.ac.uk](mailto:tony.morrison@manchester.ac.uk)

†First author

**Declared competing interests of authors:** Anthony P Morrison reports personal fees from the provision of training workshops in cognitive-behavioural therapy (CBT) for psychosis and royalties from books on the topic, outside the submitted work. Andrew Gumley reports grants from the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (grant number 13/15/04) outside the submitted work. Douglas Turkington reports personal fees from Insight-CBT partnership (Insight Healthcare, Newcastle upon Tyne), outside the submitted work. Gemma Shields reports grants from NIHR during the conduct of the study. Graeme MacLennan reports grants from the NIHR HTA programme during the conduct of the study. Hamish J MacLeod reports that he occasionally provides CBT for psychosis workshops and receives fees for this work. John Norrie reports personal fees from the NIHR Editors Board and grants from NIHR HTA General Board Deputy Chairperson, outside the submitted work, and has membership of the HTA Funding Boards Policy Group and Pre-Exposure Prophylaxis Impact Review Panel. Linda Davies reports grants from the NIHR HTA programme during the conduct of the study. Paul French has membership of the HTA prioritisation Panel. Paul Hutton reports that he sits on an Expert Steering Group for Professor Jill Stavert's Centre for Mental Health and Incapacity Law Rights and Policy at Edinburgh Napier University, and that he is a member of a committee developing National Institute for Health and Care Excellence (NICE) guidelines on supporting decision-making for people who may lack mental capacity. Robert Dudley reports receiving a NIHR Comprehensive Local Research Network Greenshoots award to fund time to support his contribution to the FOCUS (Focusing on Clozapine Unresponsive Symptoms) trial, royalties from Guilford Press and personal fees from Trinity College Dublin, outside the submitted work. Samantha Bowe reports personal fees from Pennine Care NHS Foundation Trust and personal fees from Cheshire & Wirral Partnership NHS Foundation Trust, outside the submitted work. Thomas RE Barnes reports personal fees from Sunovion (Marlborough, MA, USA) and Otsuka (Tokyo, Japan)/Lundbeck (Copenhagen, Denmark), outside the submitted work.

Published February 2019

DOI: 10.3310/hta23070

## Plain English summary

### The FOCUS RCT

Health Technology Assessment 2019; Vol. 23: No. 7

DOI: 10.3310/hta23070

NIHR Journals Library [www.journalslibrary.nihr.ac.uk](http://www.journalslibrary.nihr.ac.uk)

## Plain English summary

People who experience schizophrenia are usually prescribed antipsychotic medication. Some who take an antipsychotic continue to experience distressing and persistent symptoms; for these people the antipsychotic clozapine has been shown to be effective in reducing symptoms. About 30–40% of people who try clozapine experience persistent symptoms and there is little research to indicate what treatments are effective if clozapine has a poor impact. The Focusing on Clozapine Unresponsive Symptoms (FOCUS) trial was designed to test whether or not a talking treatment called cognitive–behavioural therapy (CBT) is clinically effective in reducing the symptoms of schizophrenia, and whether or not CBT is cost-effective. A total of 487 participants who met the criteria for a schizophrenia diagnosis and who had tried clozapine but experienced a poor response were recruited. Participants were randomly allocated to receive CBT plus treatment as usual (TAU) or TAU alone. CBT lasted for 9 months, and participants could have up to 30 hours of CBT. Participants were followed up at 9 and 21 months and it was found that those who had CBT experienced some small improvements in symptoms of schizophrenia at 9 months, but this did not last to 21 months. The data suggest that CBT was not cost-effective compared with TAU. Some benefits of CBT were evident at 21 months, such as feeling less emotional distress, a better understanding of ‘delusional’ beliefs and better self-rated recovery. The small benefit of CBT at 9 months is the same level of benefit people get from taking a second antipsychotic medication, but without the medication side effects. Although CBT cannot be recommended routinely for all people who have a poor response to clozapine, it may be helpful for some.

The results cannot answer questions about how helpful CBT is for people who have received a diagnosis of schizophrenia who have not tried clozapine. Better ways to help this population needed to be developed.



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/](http://www.publicationethics.org/)).

Editorial contact: [journals.library@nhr.ac.uk](mailto:journals.library@nhr.ac.uk)

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

## This report

The research reported in this issue of the journal was funded by the HTA programme as project number 10/101/02. The contractual start date was in December 2012. The final report began editorial review in August 2017 and was accepted for publication in February 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.

© Queen's Printer and Controller of HMSO 2019. This work was produced by Morrison *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.nhr.ac.uk](http://www.journalslibrary.nhr.ac.uk)), produced by Prepress Projects Ltd, Perth, Scotland ([www.prepress-projects.co.uk](http://www.prepress-projects.co.uk)).

## NIHR Journals Library Editor-in-Chief

**Professor Ken Stein** Chair of HTA and EME Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

## NIHR Journals Library Editors

**Professor Ken Stein** Chair of HTA and EME Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

**Professor Andrée Le May** Chair of NIHR Journals Library Editorial Group (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** Scientific Advisor, NETSCC, 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 John Powell** Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), 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 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](http://www.journalslibrary.nihr.ac.uk/about/editors)

**Editorial contact:** [journals.library@nihr.ac.uk](mailto:journals.library@nihr.ac.uk)