## Modelling disease progression in relapsing-remitting onset multiple sclerosis using multilevel models applied to longitudinal data from two natural history cohorts and one treated cohort

Kate Tilling,<sup>1</sup>\* Michael Lawton,<sup>1</sup> Neil Robertson,<sup>2</sup> Helen Tremlett,<sup>3</sup> Feng Zhu,<sup>3</sup> Katharine Harding,<sup>2</sup> Joel Oger<sup>3</sup> and Yoav Ben-Shlomo<sup>1</sup>

 <sup>1</sup>School of Social and Community Medicine, Bristol University, Bristol, UK
<sup>2</sup>Department of Neurology, Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, Cardiff, UK
<sup>3</sup>Faculty of Medicine, Department of Medicine, Division of Neurology, University of British Columbia, Vancouver, BC, Canada

### \*Corresponding author

Declared competing interests of authors: Kate Tilling has received non-financial support from the Multiple Sclerosis (MS) Trust during the conduct of the study, and had her expenses paid by the MS Trust to attend meetings of the UK MS risk-sharing scheme (RSS) scientific advisory group in order to outline the plan for these analyses. Michael Lawton has had his expenses paid by the MS Trust to attend meetings of the UK MS RSS scientific advisory group in order to outline the plan for these analyses, and also his travel and accommodation expenses for visiting Vancouver to analyse the British Columbia MS data set. Neil Robertson has received travel grants and honoraria from Biogen, Novartis, Serono, Sanofi, Genzyme and Bayer and holds grants for unrelated work from Genzyme and Novartis. Helen Tremlett is funded by the MS Society of Canada (Don Paty Career Development Award), Michael Smith Foundation for Health Research and is the Canada Research Chair for Neuroepidemiology and MS. She has received research support from the National MS Society, the Canadian Institutes of Health Research and the UK MS Trust; and speaker honoraria and/or travel expenses to attend conferences from the Consortium of MS Centres (2013), the National MS Society (2012, 2014), Bayer Pharmaceuticals (2010), Teva Pharmaceuticals (2011), European Committee for Treatment and Research in MS (2011, 2012, 2013 and 2014), UK MS Trust (2011), the Chesapeake Health Education Program, US Veterans Affairs (2012), Novartis Canada (2012), Biogen Idec (2014) and the American Academy of Neurology (2013, 2014 and 2015). Unless otherwise stated, all speaker honoraria are either donated to a MS charity or to an unrestricted grant for use by her research group. Yoav Ben-Shlomo has had his expenses paid by the MS Trust to attend meetings of the UK MS RSS Scientific Advisory Group in order to outline the plan for these analyses, and has a relative with MS who is currently on treatment for the disease. He is a member of the UK MS RSS Scientific Advisory Group.

Published October 2016 DOI: 10.3310/hta20810

# **Plain English summary**

Predicting disease progression in patients with MS

Health Technology Assessment 2016; Vol. 20: No. 81 DOI: 10.3310/hta20810

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

# **Plain English summary**

Multiple sclerosis (MS) is a disorder of the brain and spinal cord in which presentation (initial symptoms) and progression (disability and quality of life) vary widely between individuals. There are a number of drugs that are thought to slow down disease progression, although randomised trials have only shown evidence of short-term benefit. To establish the longer-term benefit, a large cohort of patients [UK MS risk-sharing scheme (RSS)] was followed up over 10 years after treatment with four different products. Here, we developed a model for natural history of MS by modelling patterns of disability change with age in two groups of people with MS who were not treated with these drugs (one group from Wales, UK, and one from British Columbia, Canada). We used the Expanded Disability Status Scale (EDSS) to measure disability, which ranges from 0 (no disability) to 10 (death from MS). We showed that the model from one group could be used to predict disability in the other group with reasonable accuracy. We then used this natural history model to predict disability in people whose MS was treated under the UK MS RSS. The average EDSS score in the treated cohort was slightly lower than that expected if they had not been treated. This provides some evidence that treatment may be associated with a small slowing in progression of disability up to 6 years post treatment. However, this was not a randomised controlled trial, so conclusions about the efficacy or effectiveness of the treatments cannot be made.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Tilling *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. 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.

## **Health Technology Assessment**

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.058

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI 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: nihredit@southampton.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**

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.nihr.ac.uk/programmes/hta

#### This report

The research reported in this issue of the journal was funded by the HTA programme as project number 10/55/01. The contractual start date was in August 2011. The draft report began editorial review in August 2015 and was accepted for publication in May 2016. 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. 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.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Tilling *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. 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).

## Health Technology Assessment Editor-in-Chief

**Professor Hywel Williams** Director, HTA Programme, UK and Foundation Professor and Co-Director of the Centre of Evidence-Based Dermatology, University of Nottingham, UK

### **NIHR Journals Library Editor-in-Chief**

Professor Tom Walley Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

### **NIHR Journals Library Editors**

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

Professor Andree Le May Chair of NIHR Journals Library Editorial Group (EME, HS&DR, PGfAR, PHR journals)

Dr Martin Ashton-Key Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

**Professor Matthias Beck** Chair in Public Sector Management and Subject Leader (Management Group), Queen's University Management School, Queen's University Belfast, UK

**Professor Aileen Clarke** Professor of Public Health and Health Services Research, Warwick Medical School, University of Warwick, UK

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Ms Tara Lamont Scientific Advisor, NETSCC, UK

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

**Professor Geoffrey Meads** Professor of Health Sciences Research, Health and Wellbeing Research and Development Group, University of Winchester, UK

Professor John Norrie Health Services Research Unit, University of Aberdeen, 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 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** Director, Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of members of the NIHR Journals Library Board: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: nihredit@southampton.ac.uk