The effect of statins on muscle symptoms in primary care: the StatinWISE series of 200 N-of-1 RCTs

Emily Herrett,1 Elizabeth Williamson,2 Kieran Brack,3 Alexander Perkins,4 Andrew Thayne,4 Haleema Shakur-Still,4 Ian Roberts,4 Danielle Prowse,4 Danielle Beaumont,4 Zahra Jamal,4 Ben Goldacre,5 Tjeerd van Staa,6 Thomas M MacDonald,7 Jane Armitage,8 Michael Moore,9 Maurice Hoffman10 and Liam Smeeth1*

1Department of Non-communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK
2Department of Medical Statistics, London School of Hygiene & Tropical Medicine, London, UK
3Liver Research, King’s College Hospital, London, UK
4Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK
5Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
6Division of Informatics, Imaging and Data Sciences, University of Manchester, Manchester, UK
7Medicines Monitoring Unit, School of Medicine, University of Dundee, Dundee, UK
8Medical Research Council Population Health Research Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK
9School of Primary Care and Population Sciences, University of Southampton, Southampton, UK
10London, UK

*Corresponding author Liam.smeeth@lshtm.ac.uk

Declared competing interests of authors: Liam Smeeth reports grants from the Wellcome Trust, the Medical Research Council (MRC), the National Institute for Health Research (NIHR), GlaxoSmithKline plc (Brentford, UK), British Heart Foundation and Diabetes UK outside the submitted work. Liam Smeeth is also a trustee of the British Heart Foundation. Thomas M MacDonald reports grants and personal fees from Novartis International AG (Basel, Switzerland), Pfizer Inc. (New York, NY, USA) and Menarini (Florence, Italy), grants from Ipsen (Paris, France) and personal fees from Takeda (Tokyo, Japan) outside the submitted work. Jane Armitage reports grants from the UK MRC, the British Heart Foundation and Cancer Research UK during the conduct of the study, and grants from The Medicines Company (Parsippany-Troy Hills, NJ, USA) outside the submitted work. Ian Roberts reports grants from NIHR during the conduct of the study and membership of the clinical trials units funded by NIHR. Haleema Shakur-Still reports grants from the NIHR Health Technology Assessment (HTA) programme during the conduct of
the study and membership of the clinical trials units funded by NIHR. Ben Goldacre has received research funding from the Laura and John Arnold Foundation, the Wellcome Trust, the NIHR Oxford Biomedical Research Centre, the NHS NIHR School of Primary Care Research, the Mohn Westlake Foundation, Health Data Research UK, the Good Thinking Foundation, the Health Foundation and the World Health Organization. He also receives personal income from speaking and writing for lay audiences on the misuse of science and is writing a book for lay readers summarising the evidence on statins. Michael Moore was the chairperson of the Trial Steering Committee, which was an unpaid position ratified by the funder to provide independent advice to the trial team and to the funder. There was no expectation of authorship resulting from this position. The study team has invited authorship following completion of data collection and analysis based on the input of the chairperson into the study design, conduct and evaluation of the study findings.

Published March 2021
DOI: 10.3310/hta25160

Plain English summary

The StatinWISE series of 200 N-of-1 RCTs
Health Technology Assessment 2021; Vol. 25: No. 16
DOI: 10.3310/hta25160

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Statins are one of the most commonly prescribed drugs in the UK. There is strong evidence that they are effective in safely reducing heart disease; however, there is some doubt about whether or not statins cause muscle pain, stiffness or weakness. This research has been carried out to understand the effect of statins on muscle symptoms.

To answer our question, we asked 200 volunteers from across England and Wales to participate in the study. Patients who joined the study either had recently stopped taking statins because of muscle symptoms or were considering stopping because of muscle symptoms. Patients who participated were randomly assigned to a sequence of six 2-month treatment periods during which they received either statins or a placebo. Neither patients nor their general practitioner knew which tablet they were receiving. This helped to reduce bias in the data. At the end of each treatment period, patients were asked to report any muscle symptoms, or any other symptoms, that they experienced.

The key result of this work is that patients reported no difference, on average, in their muscle symptoms between periods of taking a statin and periods of taking a placebo. We also assessed the impact on the patient’s quality of life by looking at how statins affected the following areas: general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life. As with muscle symptoms, there was no evidence of a difference between statin and placebo periods. The majority of patients who finished the trial decided to continue using statins after the trial. Future research should be carried out to assess different statin doses, as higher doses are often used following a heart attack. In addition, further work is needed to see how the approach we used could be adopted into everyday clinical care.
Health Technology Assessment

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 14/49/159. The contractual start date was in April 2016. The draft report began editorial review in October 2019 and was accepted for publication in March 2020. 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 2021. This work was produced by Herrett 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).
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 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 (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  Senior Scientific Adviser (Evidence Use), Wessex Institute, University of Southampton, 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  Emeritus Professor of Wellbeing Research, University of Winchester, 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

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

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