A randomised trial of the effect and cost-effectiveness of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with screen-detected type 2 diabetes: the Anglo–Danish–Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION-Europe) study

Rebecca K Simmons,1 Knut Borch-Johnsen,2,3 Torsten Lauritzen,3 Guy EHM Rutten,4 Annelli Sandbæk,3 Maureen van den Donk,4 James A Black,1 Libo Tao,1 Edward CF Wilson,5 Melanie J Davies,6 Kamlesh Khunti,6 Stephen J Sharp,1 Nicholas J Wareham1 and Simon J Griffin1*

1Medical Research Council Epidemiology Unit, School of Clinical Medicine, University of Cambridge, Cambridge, UK
2Holbæk Hospital, Holbæk, Denmark
3School of Public Health, Department of General Practice, University of Aarhus, Aarhus, Denmark
4Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands
5Department of Public Health and Primary Care, Cambridge Centre for Health Services Research, University of Cambridge, School of Clinical Medicine, Cambridge, UK
6Diabetes Research Centre, Leicester Diabetes Centre, University of Leicester, Leicester General Hospital, Leicester, UK

*Corresponding author
Declared competing interests of authors: Torsten Lauritzen reports unrestricted grants from Novo Nordisk, AstraZeneca, Pfizer, GlaxoSmithKline, Servier and HemoCue during the conduct of the study. Torsten Lauritzen also owns stock/shares in Novo Nordisk. Guy EHM Ruttem reports grants from Novo Nordisk, GlaxoSmithKline and Merck during the conduct of the study and personal fees from Novo Nordisk and AstraZeneca outside the submitted work. Melanie J Davies has acted as a consultant, advisory board member and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Eli Lilly and Company, Merck Sharp & Dohme, Boehringer Ingelheim and Roche. Melanie J Davies has also received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Eli Lilly and Company, Pfizer, Merck Sharp & Dohme and GlaxoSmithKline. Kamlesh Khunti has acted as a consultant and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Eli Lilly and Company and Merck Sharp & Dohme and has received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Eli Lilly and Company, Pfizer, Boehringer Ingelheim and Merck Sharp & Dohme. Simon J Griffin reports grants from the Wellcome Trust, the Medical Research Council, NHS Research and Development, the National Institute for Health Research and the University of Aarhus (Denmark) and non-financial support from Bio-Rad Laboratories during the conduct of the study. Simon J Griffin has also received personal fees from Eli Lilly and Company, the Royal College of General Practitioners and AstraZeneca outside the submitted work.
Diabetes is a common chronic condition associated with an increased risk of heart attack, stroke, amputation, eye disease and kidney damage. Many people have symptoms or a complication when diagnosed with diabetes; however, the true onset of the disease occurs several years earlier. Although it seems logical to propose that earlier detection would be beneficial, this has not been clearly established. We aimed to discover whether or not intensive treatment of people who have their diabetes detected early using preventative medication and lifestyle advice leads to health benefits at 5 years and in the longer term.

A total of 343 general practices in England, Denmark and the Netherlands took part. Following invitation to a screening programme, 3057 people were diagnosed with diabetes. General practices were allocated by chance to deliver either intensive treatment (a combination of medication and advice on lifestyle changes, e.g. diet and physical activity) or standard care according to national guidelines. After 5 years we re-examined participants to see whether or not intensive treatment reduced the risk of diabetes-related complications such as heart attack and stroke.

After 5 years, people receiving intensive treatment had slightly lower cholesterol levels, blood pressure and blood glucose levels than those receiving routine care. However, we cannot be sure that the small reductions in the number of heart attacks, strokes and premature deaths and in the level of visual impairment and kidney damage between the groups were not due to chance. Participants in both groups reported similar levels of well-being and quality of life and were equally satisfied with the treatment that they received. Intensive treatment is likely to be cost-effective only if it can be delivered at a reduced cost.
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 08/116/300. The contractual start date was in July 2010. The draft report began editorial review in August 2014 and was accepted for publication in December 2015. 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 Simmons 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 Elaine McColl**  Director, Newcastle Clinical Trials Unit, Institute of Health and Society, Newcastle University, 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