

Very low-dose dexamethasone to facilitate extubation of preterm babies at risk of bronchopulmonary dysplasia: the MINIDEX feasibility RCT

Helen Yates,^{1*} Virginia Chiocchia,² Louise Linsell,² Nicolas Orsi,³ Edmund Juszczak,² Kathryn Johnson,⁴ Philip Chetcuti,⁴ Claire Illingworth,⁵ Pollyanna Hardy,⁶ Vaneesha Monk,⁷ Simon Newell^{8†} and Mark Turner⁹

¹Department of Neonatal Medicine, Women and Children's Hospital, Hull Royal Infirmary, Hull, UK

²NPEU Clinical Trials Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

³Women's Health Research Group, Leeds Institute of Cancer and Pathology, St James's University Hospital, Leeds, UK

⁴Leeds Neonatal Service, Leeds General Infirmary, Leeds, UK

⁵Patient and public involvement representative

⁶Birmingham Clinical Trials Unit, Institute of Applied Health Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

⁷Department of Paediatrics, University of Oxford, John Radcliffe Hospital, Oxford, UK

⁸Leeds Teaching Hospitals NHS Trust, Leeds, UK

⁹Neonatal Unit, Liverpool Women's Hospital, Liverpool, UK

*Corresponding author Helen.yates@hey.nhs.uk

†In memoriam

Declared competing interests of authors: Helen Yates reports personal fees from AbbVie Inc. (Lake Bluff, IL, USA) outside the submitted work.

Published August 2019

DOI: 10.3310/eme06080

Plain English summary

The MINIDEX feasibility RCT

Efficacy and Mechanism Evaluation 2019; Vol. 6: No. 8

DOI: 10.3310/eme06080

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

Plain English summary

Babies born prematurely who require prolonged support with breathing machines through a breathing tube (i.e. mechanical ventilation) are at an increased risk of developing long-term breathing problems because of a condition called bronchopulmonary dysplasia (BPD), sometimes called chronic lung disease. Babies with BPD have an increased risk of learning difficulties and cerebral palsy (CP).

Dexamethasone has been used to help babies get off mechanical ventilation. However, previous research shows that babies who are given large doses of dexamethasone and given dexamethasone in the first week of life have an increased risk of CP and learning difficulties. The benefits of the use of dexamethasone in babies with a low risk of developing BPD is outweighed by an increased risk of developmental delay.

Neonatologists now tend to use only low or very low doses of dexamethasone in babies older than 1 week of age, who are at high risk of developing BPD. There is no clear evidence to support this. To plan the research needed to inform practice, evidence was required to suggest that giving a very small dose of dexamethasone to a baby who is dependent on a ventilator will improve their lungs enough to allow the breathing tube to be removed.

This trial asked whether or not giving a very small dose of dexamethasone to a baby born at ≤ 30 weeks' gestation who is 'stuck' on a ventilator and at high risk of BPD will help the baby come off the ventilator. Babies were allocated randomly to receive dexamethasone or a dummy medicine (i.e. a placebo). Their breathing outcomes and side effects were compared. A few babies had assessments carried out on very small blood samples or breathing tube fluid samples to help to see what effects the dexamethasone has on the lungs.

There were fewer babies suitable to participate in the trial than anticipated, so recruitment was poor. The funder decided to stop recruitment. The study was not able to answer the research questions.

Efficacy and Mechanism Evaluation

ISSN 2050-4365 (Print)

ISSN 2050-4373 (Online)

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 EME archive is freely available to view online at www.journalslibrary.nihr.ac.uk/eme. 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 *Efficacy and Mechanism Evaluation* journal

Reports are published in *Efficacy and Mechanism Evaluation* (EME) if (1) they have resulted from work for the EME programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

EME programme

The Efficacy and Mechanism Evaluation (EME) programme was set up in 2008 as part of the National Institute for Health Research (NIHR) and the Medical Research Council (MRC) coordinated strategy for clinical trials. The EME programme is broadly aimed at supporting 'science driven' studies with an expectation of substantial health gain and aims to support excellent clinical science with an ultimate view to improving health or patient care.

Its remit includes evaluations of new treatments, including therapeutics (small molecule and biologic), psychological interventions, public health, diagnostics and medical devices. Treatments or interventions intended to prevent disease are also included.

The EME programme supports laboratory based or similar studies that are embedded within the main study if relevant to the remit of the EME programme. Studies that use validated surrogate markers as indicators of health outcome are also considered.

For more information about the EME programme please visit the website: <http://www.nets.nihr.ac.uk/programmes/eme>

This report

The research reported in this issue of the journal was funded by the EME programme as project number 13/158/48. The contractual start date was in November 2015. The final report began editorial review in November 2018 and was accepted for publication in February 2019. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The EME editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research. 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, the MRC, NETSCC, the EME 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 EME programme or the Department of Health and Social Care.

© Queen's Printer and Controller of HMSO 2019. This work was produced by Yates *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).

NIHR Journals Library Editor-in-Chief

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 Honorary Professor, University of Manchester, and Senior Clinical Researcher and Associate Professor, 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