

Planned delivery to improve postpartum cardiac function in women with preterm pre-eclampsia: the PHOEBE mechanisms of action study within the PHOENIX RCT

Fergus P McCarthy,^{1,2*} Jamie O'Driscoll,^{3,4} Paul Seed,¹
Anna Brockbank,¹ Alice Cox,⁵ Carolyn Gill,¹
Marcus Green,⁶ Mike Marber,⁷ Lucilla Poston,¹
Anna Placzek,⁸ Andrew Shennan,¹ Jenie Sparkes,¹
Paul Leeson,^{9†} Basky Thilaganathan^{10†}
and Lucy C Chappell^{1*†}

¹Department of Women and Children's Health, King's College London, London, UK

²Department of Obstetrics and Gynaecology, The INFANT Research Centre, University College Cork, Cork University Maternity Hospital, Cork, Ireland

³School of Human and Life Science, Canterbury Christ Church University, Kent, UK

⁴Department of Cardiology, St George's University Hospitals NHS Foundation Trust, London, UK

⁵Women's Services, University College London, London, UK

⁶Action on Pre-eclampsia, Evesham, UK

⁷Cardiovascular Division, King's College London British Heart Foundation Centre of Excellence, The Rayne Institute, St. Thomas' Hospital Campus, London, UK

⁸National Perinatal Epidemiology Unit (NPEU), Nuffield Department of Population Health, University of Oxford, Oxford, UK

⁹Oxford Cardiovascular Clinical Research Facility, Radcliffe Department of Medicine, University of Oxford, Oxford, UK

¹⁰Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust and Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK

*Corresponding authors Fergus.mccarthy@ucc.ie and lucy.chappell@kcl.ac.uk

†These authors contributed equally

Declared competing interests of authors: Lucy C Chappell is the chairperson of the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Clinical Evaluation and Trials Committee (January 2019 to present). Lucy C Chappell is funded by the NIHR Professorship, RP-2014-05-019, and has also been awarded the following NIHR funding: 12/164/16, 15/59/06, NIHR128721 and RP-2014-05-01. Lucy C Chappell declares that following the completion of this research project, she took up the role of Chief Scientific Adviser for the Department of Health and Social Care from 1 August 2021. Andrew Shennan is a member of the NIHR HTA Commissioning Committee. Mike Marber is named as an inventor on a patent (WO 2010/130985 A1) held by King's College London for the detection of cardiac myosin-binding protein C (cMyC) as a biomarker of myocardial injury.

Published September 2021

DOI: 10.3310/eme08120

Plain English summary

The PHOEBE RCT

Efficacy and Mechanism Evaluation 2021; Vol. 8: No. 12

DOI: 10.3310/eme08120

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

Plain English summary

Women who have a form of high blood pressure in pregnancy called pre-eclampsia may be at risk of heart disease later in life. When a woman becomes unwell with this type of high blood pressure in pregnancy we usually wait until she is 37 weeks pregnant before recommending delivery. We carried out a study to see if earlier delivery would lead to fewer complications for the woman and the baby, and to see if this would also reduce her risk of damage to her heart after pregnancy.

This study was part of a larger study called the Pre-eclampsia in HOspital: Early iNduction or eXpectant management (PHOENIX) study. In this study, women with pre-eclampsia between 34 and 37 weeks of pregnancy either had birth started within 48 hours (usually by induction of labour) or underwent usual care, waiting until the doctor thought that she needed delivery or she reached 37 weeks of pregnancy. In our study, we invited women back 6 months after having their baby, performed an ultrasound of their hearts and checked blood pressure. We then looked to see whether or not being delivered earlier caused less damage to the heart.

Between April 2016 and November 2018, 420 women in 28 hospitals in the England and Wales agreed to take part.

We showed that staying pregnant with pre-eclampsia for a few days longer did not cause more heart damage. However, 1 in 10 women in the study had ultrasound evidence of damage to their hearts. Over half of the women in the study did not have a normal ultrasound of their heart. Around 7 out of 10 of these women with pre-eclampsia still had high blood pressure 6 months after their pregnancy. These findings suggest that these women need more intensive monitoring and follow-up after their pregnancy. This might help reduce the long-term risks of heart disease.

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 funds ambitious studies evaluating interventions that have the potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies, EME supports research to improve the understanding of the mechanisms of both diseases and treatments.

The programme supports translational research into a wide range of new or repurposed interventions. These may include diagnostic or prognostic tests and decision-making tools, therapeutics or psychological treatments, medical devices, and public health initiatives delivered in the NHS.

The EME programme supports clinical trials and studies with other robust designs, which test the efficacy of interventions, and which may use clinical or well-validated surrogate outcomes. It only supports studies in man and where there is adequate proof of concept. The programme encourages hypothesis-driven mechanistic studies, integrated within the efficacy study, that explore the mechanisms of action of the intervention or the disease, the cause of differing responses, or improve the understanding of adverse effects. It funds similar mechanistic studies linked to studies funded by any NIHR programme.

The EME programme is funded by the Medical Research Council (MRC) and the National Institute for Health Research (NIHR), with contributions from the Chief Scientist Office (CSO) in Scotland and National Institute for Social Care and Health Research (NISCHR) in Wales and the Health and Social Care Research and Development (HSC R&D), Public Health Agency in Northern Ireland.

This report

The research reported in this issue of the journal was funded by the EME programme as project number 15/23/02. The contractual start date was in April 2016. The final report began editorial review in November 2019 and was accepted for publication in September 2020. 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 2021. This work was produced by McCarthy *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 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