

Mini-combined test compared with NICE guidelines for early risk-assessment for pre-eclampsia: the SPREE diagnostic accuracy study

Liona C Poon,¹ David Wright,² Steve Thornton,³
Ranjit Akolekar,⁴ Peter Brocklehurst⁵ and
Kypros H Nicolaides^{1*}

¹Fetal Medicine Research Institute, King's College Hospital, King's College London, London, UK

²Institute of Health Services Research, University of Exeter, Exeter, UK

³Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK

⁴Department of Obstetrics and Gynaecology, Medway Maritime Hospital, Kent, UK

⁵Comprehensive Clinical Trials Unit, University College London, London, UK

*Corresponding author kypros@fetalmedicine.com

Declared competing interests of authors: Steve Thornton reports grants from the National Institute for Health Research (NIHR), the British Heart Foundation (BHF) and Barts Charity during the conduct of the study. Outside the submitted work, he was a member of the NIHR Efficacy and Mechanism Evaluation Editorial Board (2016–19), a trustee of Wellbeing of Women until 2019 (London, UK), MedCity (London, UK) and the William Harvey Research Institute (London, UK). He provides consultancy advice for commercial organisations [i.e. GlaxoSmithKline plc (Brentford, UK), Hologic, Inc. (Bedford, MA, USA), and Ferring Pharmaceuticals (Saint-Prex, Switzerland)]. He is a non-executive director of the NHS Trust (2016 to present). Ranjit Akolekar and Kypros H Nicolaides are trustees of the Fetal Medicine Foundation. Peter Brocklehurst reports grants and personal fees from the Medical Research Council (London, UK), grants from the NIHR Services and Delivery Research programme, the NIHR Health Technology Assessment (HTA) programme and the Wellcome Trust (London, UK) outside the submitted work. He was chairperson of the NIHR HTA Maternal, Neonatal and Child Health Panel and the Medical Research Council Methodology Research Programme Panel between 2014 and 2018.

Published November 2020

DOI: 10.3310/eme07080

Plain English summary

The SPREE diagnostic accuracy study

Efficacy and Mechanism Evaluation 2020; Vol. 7: No. 8

DOI: [10.3310/eme07080](https://doi.org/10.3310/eme07080)

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

Plain English summary

Pre-eclampsia is a medical condition characterised by high blood pressure and the presence of protein in the urine of a pregnant woman. There could also be impaired function in organs such as the liver, kidneys and brain. It occurs in 2–3% of all pregnancies. The effects of pre-eclampsia can be serious for both the mother and the baby, especially when the disease is severe and requires delivery of the baby before 37 weeks' gestation (i.e. preterm pre-eclampsia).

There is evidence that in high-risk women their risk for preterm pre-eclampsia can be reduced substantially by taking low-dose aspirin (i.e. 150 mg) every day from the 12th to the 36th week of pregnancy. There is a need for accurate prediction of preterm pre-eclampsia in early pregnancy.

The National Institute for Health and Care Excellence has issued guidelines recommending that the way to determine whether or not a woman is at high risk for developing pre-eclampsia depends on her characteristics and medical history. Alternatively, we have developed a new method of screening that combines the information from maternal characteristics and medical history with the results from measurements of blood pressure, blood flow that supplies the uterus and levels of two placental proteins in the mother's blood to calculate the individual risk for developing preterm pre-eclampsia.

In this study of 16,747 women, 473 (2.8%) developed pre-eclampsia, including 142 (0.8%) women with preterm pre-eclampsia. The proportion of women considered as high risk by the National Institute for Health and Care Excellence method was \approx 10%. The proportions of all pre-eclampsia and preterm pre-eclampsia cases with a high-risk result were 32% and 43%, respectively. We found that only 23% of high-risk women identified by the National Institute for Health and Care Excellence method actually received aspirin. The proportion of preterm pre-eclampsia cases with a high-risk result based on the combined test was 67%, which was much higher than that of the National Institute for Health and Care Excellence method (i.e. 44%). We conclude that our method of screening by a combination of maternal factors and various tests is superior to that achieved by current National Institute for Health and Care Excellence guidelines.

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 14/01/02. The contractual start date was in February 2016. The final report began editorial review in September 2018 and was accepted for publication in June 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 2020. This work was produced by Poon *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).

Editor-in-Chief of *Efficacy and Mechanism Evaluation* and NIHR Journals Library

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 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