The Arabin pessary to prevent preterm birth in women with a twin pregnancy and a short cervix: the STOPPIT 2 RCT

Jane E Norman,1* John Norrie,2 Graeme MacLennan,3 David Cooper,3 Sonia Whyte,4 Sushila Chowdhry,5 Sarah Cunningham-Burley,5 Aileen R Neilson,5 Xue W Mei,6 Joel BE Smith,6 Andrew Shennan,7 Stephen C Robson,8 Steven Thornton,9 Mark D Kilby,10 Neil Marlow,11 Sarah J Stock,5 Philip R Bennett12 and Jane Denton13 on behalf of the STOPPIT collaborative group

1Faculty of Health Sciences, University of Bristol, Bristol, UK
2Edinburgh Clinical Trials Unit, University of Edinburgh, Edinburgh, UK
3Centre for Healthcare Randomised Trials, University of Aberdeen, Aberdeen, UK
4Tommy’s Centre for Maternal and Fetal Health, MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK
5Usher Institute, University of Edinburgh, Edinburgh, UK
6Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK
7Tommy’s London Research Centre, King’s College London, London, UK
8Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK
9Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK
10Fetal Medicine Centre, Birmingham Women’s and Children’s NHS Foundation Trust and College of Medical and Dental Science, University of Birmingham, Birmingham, UK
11Institute for Women’s Health, University College London, London, UK
12Department of Surgery and Cancer, Imperial College London, London, UK
13The Multiple Births Foundation, London, UK

*Corresponding author jane.e.norman@bristol.ac.uk

Declared competing interests of authors: Jane E Norman has received grants from government and charitable bodies for research into understanding the mechanism of term and preterm labour and understanding treatments. Within the last 3 years, Jane E Norman has acted on a Data Safety and Monitoring Board for a study involving a preterm birth therapeutic agent for GlaxoSmithKline plc (GlaxoSmithKline plc, Brentford, UK) and has provided consultancy for a small pharmaceutical company (Dilafor AB, Solna, Sweden) on drugs to alter labour progress. She was on the Health Technology Assessment (HTA) Maternal Neonatal and Child Health Panel (2013–18) and she was a member of the National Institute for Health Research (NIHR) HTA and Efficacy and Mechanism Evaluation (EME) Editorial Board (2012–14). John Norrie reports grants from the University of Edinburgh (Edinburgh, UK)
during the conduct of the study, and declares that he is or has been a member of the following: HTA Commissioning Sub-Board (EOI) (2012–16), NIHR CTU Standing Advisory Committee (2017–present), NIHR HTA and EME Editorial Board (2014–19), Pre-Exposure Prophylaxis Impact Review Panel (2017–present), EME Strategy Advisory Committee (2019–present), EME – Funding Committee Members (2019–present), EME Funding Committee Sub-Group Remit & Comp Check (2019–present), HTA General Committee (2016–19), HTA Funding Committee Policy Group (formerly Clinical Studies Group) (2016–19), HTA Commissioning Committee (2010–16) and was a member of the HTA and EME Editorial Board between 2014 and 2019. Sarah Cunningham-Burley reports personal fees and other from the Wellcome Trust (London, UK), other from the University of Copenhagen (Copenhagen, Denmark), other funding from NIHR Global Health Research, personal fees from the French National Cancer Institute (Paris, France) and personal fees from the Health Research Board (Dublin, Ireland), outside the submitted work. Andrew Shennan is a member of the NIHR HTA Commissioning Committee (2018–22).

Stephen C Robson was a member of the NIHR EME Funding Committee (2012–15). Steven Thornton is a trustee of a number of charities, including those that fund related research. He reports personal fees from GlaxoSmithKline plc, during the conduct of the study and outside the submitted work, and personal fees from Johnson & Johnson (Johnson & Johnson, Brunswick, NJ, USA) for consulting services. He holds positions in the Royal College of Obstetricians and Gynaecologists (London, UK) and other organisations. He was a member of the NIHR EME Strategy Advisory Committee (2018–19), EME – Funding Committee Members (2015–19), EME Funding Committee Sub-Group Remit & Comp Check (2018–19) and the Medical Research Council Multimorbidity Board (2020). Neil Marlow reports personal fees from Shire-Takeda (London, UK), Novartis Pharmaceuticals UK Ltd (London, UK) and GlaxoSmithKlein plc, outside the submitted work. Sarah J Stock declares that she is a member of the NIHR HTA General Committee (2016–22).

In addition, Sarah J Stock received other research funding from the NIHR (14/32/01 QUIDS), Wellcome Trust (209560/Z/17/Z) and Chief Scientist Office (Edinburgh, UK), during the course of the study. Philip R Bennett reports personal fees and membership of a scientific panel from ObsEva (Plan-les-Ouates, Switzerland), outside the submitted work. In addition, Philip R Bennett has a patent PCT/GB1997/000529 WO1997031631 A1 ‘COX-2 selective inhibitors for managing labour and uterine contractions’ issued, a patent PCT/GB2004/001380 WO2005053705 A1 ‘Use of a cyclopentenone prostaglandin for delaying the onset and/or preventing the continuation of labour’ (priority date 2 December 2003) issued, a patent PCT/GB2016/050618 ‘Circulating miRNAs predictive of cervical shortening and preterm birth’ (pending UK filing 6 March 2015/full international filing completed 7 March 2016) issued, a patent PCT/GB2016/050621 ‘Rapid evaporative ionisation mass spectroscopy (REIMS) and desorption electrospray ionisation mass spectroscopy (DESI-MS) analysis of swabs and biopsy samples’ (pending UK filing 6 March 2015/full international filing completed 7 March 2016) pending, a patent PCT/GB2019 ‘Desorption electrospray ionisation mass spectroscopy (DESI-MS) analysis of swabs to predict vaginal microbiota’ (pending UK filing March 2019) pending, and a patent PCT/GB2019/’Circulating miRNAs predictive of IUGR’ (pending UK filing March 2019) pending.

Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.
Plain English summary

The STOPPIT 2 RCT
Health Technology Assessment 2021; Vol. 25: No. 44
DOI: 10.3310/hta25440

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Plain English summary

Women who are pregnant with twins have a much higher risk of going into labour early and having an early (preterm) birth than women who are pregnant with only one baby. For this reason, babies who are twins are much more likely to die or to have serious health complications in the first months of life.

Although we know that women with twin pregnancy are at risk, there are no treatments that are recommended to prevent early births.

Some studies have suggested that the Arabin pessary can help. The Arabin pessary is a silicone ring that fits around the cervix (neck of the womb). The pessary can be put in place in a clinic without any need for an anaesthetic.

Some studies have suggested that the Arabin pessary helps and others have suggested that it does not. It appears to be most helpful when the cervix (neck of the womb) is already shortening. Shortening of the neck of the womb is a sign that early birth is even more likely.

We asked women with twin pregnancy to take part in STOPPIT 2. Women who agreed had an ultrasound scan of the neck of the womb, which measured its length. Those with a short cervix were randomised to be offered the Arabin pessary (in addition to standard care) or standard care alone. This allocation was carried out ‘at random’ by a computer.

We followed women up until the end of their pregnancy and collected information on the babies’ health after birth.

We found that the Arabin pessary did not reduce the risk of an early birth; nor did it reduce the risk of health complications for the baby. We conclude that the Arabin pessary should not be used for this purpose.
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