

The PIONEER Study - A study to investigate whether taking the medication Pravastatin reduces the number of babies born too early (preterm, i.e., before 37 weeks of pregnancy) and, if so, how it works in the body to do this.

Submission date 17/02/2024	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 18/04/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 09/12/2025	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Around 7 out of every 100 UK babies are born too early (preterm, i.e., before 37 weeks of pregnancy). Being born preterm is the most common cause of babies dying before the age of one year in the UK; 1 in 3 of those who survive are diagnosed with cerebral palsy. This study will test whether the medicine Pravastatin reduces the number of babies born preterm. It is not fully understood why some babies are born early, and there are few effective treatments to prevent this from happening. Research shows it is likely that early labour may occur because of types of inflammation in the mother's body. Taking a medication which reduces inflammation, such as Pravastatin, could therefore reduce the number of babies being born preterm. Pravastatin has been tested for the treatment and prevention of other pregnancy problems, with no safety concerns for women or their babies, and some studies suggest that it may reduce the number of babies born preterm. This study will test whether taking one tablet of Pravastatin once a day, from between 16-20 weeks of pregnancy until 37 weeks, reduces the number of babies born too early.

Who can participate?

Young and adult women aged 16 years old and over who attend Preterm Birth Prevention clinics

What does the study involve?

Participants will be asked if they would like to join the study. If they join, half will be given Pravastatin and half will be given a placebo (a dummy tablet which looks like Pravastatin but does not contain Pravastatin). Neither the women nor the researchers will know which tablets they are taking until the end of the study. The study will record how many weeks of pregnancy their babies are born and compare this between the two groups of women. The study will also measure levels of certain bacteria and markers of inflammation, which may be related to babies being born early, by collecting blood, fluid produced in the vagina and stool samples. Any

complications the women or their babies have will be recorded and the babies' development will be assessed at two years of age.

What are the possible benefits and risks of participating?

There is a possibility that participants who receive Pravastatin will have a lower chance of preterm birth, but we cannot be certain. This is what this study will help us to find out. If Pravastatin does have this effect, the research could help us to improve the options for pregnant women who are at risk of preterm birth in the future. Participants may also benefit from the increased contact that comes with being a part of a clinical study.

The potential risks and burdens for the trial are summarised in the Participant Information Sheet (PIS), which has been reviewed and approved by our public contributors.

- Possible side effects from the trial medication. These are explained in the PIS, including how likely they are to occur, with clarity that side effects relate to the participant and not their baby.
- Discomfort or pain when having a blood sample taken. Localised bruising and discomfort can occur at the site of venipuncture. Infrequently fainting may occur. Blood samples must be taken from all participants to confirm eligibility and at 28 weeks to assess liver transaminase levels (ALT or AST) - additional blood samples will be taken from all participants at sites taking part in the mechanistic sub-study. Samples will be taken by trained phlebotomists and every effort will be made to reduce pain or discomfort.
- Mild discomfort when having a vaginal swab taken (only participants in the mechanistic sub-study). This will be done by trained clinical staff who are experienced in taking these swabs and will be conducted in such a manner as to maintain privacy and dignity.
- Loss of participant's time to attend research visits at the hospital, take part in qualitative interviews or complete follow-up at home. Trial activities will be integrated into usual care visits where possible to reduce the burden of participation, and researchers will make efforts to arrange visits/calls for convenient times. Participants will also be reimbursed for some expenses.

Where is the study run from?

University Hospitals Bristol and Weston NHS Foundation Trust

When is the study starting and how long is it expected to run for?

February 2024 to February 2028

Who is funding the study?

National Institute for Health and Care Research (NIHR)

Who is the main contact?

pioneer-trial@bristol.ac.uk

Contact information

Type(s)

Scientific, Principal investigator

Contact name

Dr Katherine Birchenall

ORCID ID

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Contact details

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Type(s)

Public

Contact name

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Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

1007563

Protocol serial number

OG/2022/7409, IRAS 1007563, CPMS 60531

Study information

Scientific Title

Pravastatin to prevent preterm birth (PIONEER): a parallel group randomised placebo-controlled trial

Acronym

PIONEER

Study objectives

We are interested to find out whether treatment with a statin, Pravastatin, reduces the chance a person will have a preterm birth by extending the length of pregnancy and so reducing the risks associated with babies being born too soon.

We would also like to find out how Pravastatin might work to reduce preterm birth by looking at blood samples, vaginal swabs and stool samples taken from some of the pregnant people who

take part in the trial.

We will also see whether Pravastatin has an effect on a number of outcomes which have been selected as being important to this population. Some of these relate to the mother, for example whether they had an infection after birth, and some relate to the child, for example did they need to go to intensive care after birth.

Finally, we will ask some of the people who take part in the trial to complete a questionnaire when their child is 2 years old, to look at the child's development.

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 16/04/2024, North West - Greater Manchester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None provided; gmcentral.rec@hra.nhs.uk), ref: 24/NW/0074

Study design

Interventional double-blind randomized parallel group placebo-controlled trial

Primary study design

Interventional

Study type(s)

Efficacy, Safety

Health condition(s) or problem(s) studied

Intermediate or high risk for preterm birth

Interventions

Participants will be randomised in a 1:1 ratio to receive either Pravastatin or placebo.

Randomisation will be performed via the trial database using Sealed Envelope.

Participants randomised to the intervention group will receive Pravastatin 20mg and participants randomised to the placebo group will receive a matched tablet with no active substance. Both will be taken orally once daily by participants, from between 16+0 and 20+0 weeks gestation until 37+0 weeks gestation. Treatment may be stopped earlier (reasons are detailed in the protocol).

All participants will be followed up until birth or loss of pregnancy. Participants recruited in the first 18 months of the trial will be asked to complete a questionnaire when their child is two years old.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Pravastatin

Primary outcome(s)

Gestational age, in days, at birth, measured using patient records.

Key secondary outcome(s)

1. Maternal and neonatal secondary outcomes:

Maternal secondary outcomes: maternal mortality; antenatal infection requiring antibiotics; intrapartum infection requiring antibiotics; development of pre-eclampsia; PPRM; harm to mother from intervention; cervical cerclage; progesterone use; shortest cervical length measured.

Neonatal secondary outcomes: Premature birth (categorising <37 weeks' gestation, and <34 weeks gestation); Apgar scores at 1, 5, and 10 minutes of age; admission to Neonatal Intensive Care Unit (NICU); birthweight; early neurodevelopmental morbidity; gastrointestinal and respiratory morbidity; neonatal mortality; infection requiring antibiotics; need for respiratory support; harm to offspring from intervention. Collected from hospital databases following birth and discharge from hospital admission.

2. Mechanism of action of Pravastatin, evaluated using mechanistic studies to assess maternal:

2.1. Cervicovaginal fluid concentrations of inflammatory markers of interest, including IL-8, IL-6, IL-2, MBL, IgG1, IgG3, C3b and C5a;

2.2. Vaginal microbiota profile;

2.3. Serum lipid profile: very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) assessed via NMR metabolomics; and,

2.4. Stool microbiota profile and metabolomics profile.

2.5. Maternal blood inflammatory profile.

Samples collected as baseline, 24 weeks' gestation and 28 weeks' gestation.

3. For the offspring of pregnancies for those participants recruited during the first 18 months of the trial only. Assessment of child's cognitive and language development using the Parent Report of Children's Abilities-Revised (PARCA-R) questionnaire. Questionnaire completed at 2 years corrected age for child.

Completion date

29/02/2028

Eligibility

Key inclusion criteria

1. Pregnant people with a singleton pregnancy identified as being at high or intermediate risk for PTB according to criteria detailed in the Saving Babies' Lives Care Bundle (V3), where:

1.1. High risk - at least one of the following:

1.1.1. Previous mid-trimester loss >16 weeks' gestation;

1.1.2. Previous PTB <34 week's gestation;

1.1.3. Previous Preterm Premature Rupture of Membranes (PPROM) <34 weeks' gestation;

1.1.4. Previous use of cervical cerclage;

1.1.5. Known uterine structural variant;

1.1.6. Intrauterine adhesions;

1.1.7. History of trachelectomy (for cervical cancer).

OR

1.2. Intermediate risk - at least one of the following:

1.2.1. Previous birth by caesarean section at full dilatation;

1.2.2. History of significant excision of cervical cells (e.g., Large Loop Excision of Transformation Zone (LLETZ) where >15mm depth removed, or >1 LLETZ procedure carried out or cone biopsy).

2. Between 16+0- and 20+0 weeks' gestation at randomisation.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

16 years

Upper age limit

60 years

Sex

Female

Total final enrolment

0

Key exclusion criteria

1. Multiple pregnancy
2. <16 years of age
3. Hypersensitivity to Pravastatin (active substance or any of the excipients)
4. Personal or first-degree relative with heritable muscle disorder
5. Participating in the active phase of another CTIMP
6. Lactose intolerance
7. >14 units alcohol/week
8. Past/current liver disease
9. ALT or AST above upper limit of normal (as set by local laboratories), to be taken at the time of screening*
10. Bilirubin above upper limit of normal (as set by local laboratories), to be taken at the time of screening*
11. Creatine Kinase (CK) concentration >5 times upper limit of normal (as set by local laboratories), to be taken at the time of screening
12. Currently breastfeeding
13. Unable to provide informed consent
14. Previously participated in PIONEER
15. Currently taking medicines or groups of medicines that are contraindicated for concomitant use with pravastatin§

* It is acknowledged that the Liver Function Test may include different assessments at different sites, therefore for the purpose of the screening blood test, the term "Liver Function Test" at screening should include measurement of Bilirubin and at least one of ALT or AST. If any of these are above the upper limit of the normal, the person would not be eligible for inclusion in PIONEER, and should have ongoing follow-up according to local policy.

§ Those taking macrolides should be excluded from PIONEER, however, if a limited course of macrolides are prescribed with the course due to complete prior to 20+0 weeks' gestation, then it may be possible to recruit to PIONEER following completion of the course of antibiotics (if completion of the course of antibiotics is prior to 20+0).

Date of first enrolment

18/12/2024

Date of final enrolment

31/03/2027

Locations**Countries of recruitment**

United Kingdom

England

Scotland

Study participating centre**Birmingham Womens Hospital**

Womens Health Care

Mindelsohn Way

Birmingham

England

B15 2TG

Study participating centre**St Michaels Hospital**

Southwell Street

Bristol

England

BS2 8EG

Study participating centre**Southmead Hospital**

Southmead Road

Westbury-on-trym

Bristol

England

BS10 5NB

Study participating centre**St James's University Hospital**

Gledow Wing

Beckett Street

Leeds
England
LS9 7TF

Study participating centre
University Hospital (coventry)
Clifford Bridge Road
Coventry
England
CV2 2DX

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
Hammersmith Hospital
Du Cane Road
Hammersmith
London
England
W12 0HS

Study participating centre
The Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh
Scotland
EH16 4SA

Study participating centre
West Cumberland Hospital
Homewood
Hensingham
Whitehaven
England
CA28 8JG

Study participating centre
Birmingham Heartlands Hospital
Bordesley Green East
Bordesley Green
Birmingham
England
B9 5SS

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
Exeter
England
EX2 5DW

Study participating centre
Cumberland Infirmary
Newtown Road
Carlisle
England
CA2 7HY

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
England
TS4 3BW

Study participating centre
Burnley General Hospital
Casterton Avenue
Burnley
England
BB10 2PQ

Study participating centre

St Marys Hospital
Oxford Road Site
Manchester
England
M13 9WL

Study participating centre
University College London Hospital
235 Euston Road
London
England
NW1 2BU

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
Wales
CF14 4XW

Study participating centre
Royal Cornwall Hospital (treliske)
Treliske
Truro
England
TR1 3LJ

Study participating centre
Royal United Hospital Bath
Combe Park
Bath
England
BA1 3NG

Study participating centre
Broomfield Hospital
Court Road
Broomfield
Chelmsford
England
CM1 7ET

Study participating centre
Mid Yorkshire Teaching NHS Trust
Pinderfields Hospital
Aberford Road
Wakefield
England
WF1 4DG

Study participating centre
Musgrove Park Hospital
Musgrove Park
Taunton
England
TA1 5DA

Study participating centre
Maidstone
Maidstone Hospital
Hermitage Lane
Maidstone
England
ME16 9QQ

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
England
NE9 6SX

Study participating centre
The Princess Royal Maternity Unit
16 Alexandra Parade
Glasgow
Scotland
G31 2ER

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
NE1 4LP

Study participating centre
United Lincolnshire Teaching Hospitals NHS Trust
Lincoln County Hospital
Greetwell Road
Lincoln
England
LN2 5QY

Study participating centre
Worcestershire Acute Hospitals NHS Trust
Worcestershire Royal Hospital
Charles Hastings Way
Worcester
England
WR5 1DD

Sponsor information

Organisation
University Hospitals Bristol and Weston NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during the current trial will be available upon request after publication of the main results of the trial. The trial team intends to share underpinning research data to maximise reuse and evidence findings. The datasets will be deposited at the University of Bristol Research Data Repository (<https://data.bris.ac.uk/data/>) where, once published, they will be assigned a doi. A metadata record will be published openly by the repository and this record will clearly state how data can be accessed by bona fide researchers. The consent form for the trial includes the optional statement: "I agree to my information being stored securely and used for future research and training purposes. I understand that information shared will not include personally identifiable data." As such, data will only be deposited from participants who agree to this statement.

IPD sharing plan summary

Available on request, Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website		11/11/2025	11/11/2025	No	Yes