ISRCTN10651813 https://doi.org/10.1186/ISRCTN10651813

PRISM Follow-up: Child health review following progesterone in pregnancy

Submission date
30/09/2025

Recruitment status
Recruiting

Registration date
08/10/2025

Overall study status
Ongoing

Last Edited
06/10/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The PRISM trial (https://www.isrctn.com/ISRCTN14163439) was the largest ever study that tested whether vaginal progesterone treatment can prevent miscarriage in women with early pregnancy bleeding. The trial found that vaginal progesterone increased the live birth rate by 5% in comparison to placebo for women with early pregnancy bleeding and a history of one or more previous miscarriages.
The UK NICE Committee for the guideline 'Ectopic pregnancy and miscarriage: diagnosis and initial management (NG126)' reviewed this evidence and updated their guidance in November 2021 to recommend the use of vaginal micronised progesterone to treat women with the dual risk factors of a history of one or more previous miscarriages and early pregnancy bleeding.

Vaginal progesterone treatment has been routinely used in early pregnancy for women undergoing fertility treatment and early pregnancy bleeding complications over the last 40 years. However, data on long-term health outcomes of children born following early pregnancy progesterone treatment have not been routinely collected. For clinical trials conducted in pregnancy, it is good standard practice to check the health and development of children who were born during the trial. This information will give us assurances about the use of vaginal progesterone treatment during early pregnancy. The large cohort of children born in the PRISM trial provides a unique opportunity to conduct a follow-up study to assess the long-term health of children who were born to women with and without progesterone treatment. This study aims to compare the health outcomes of children born to women who took progesterone during early pregnancy with those who received a placebo.

Who can participate?
Adult women who previously participated in the PRISM trial and the children who were born. The women will complete information about their child. The central team will make all efforts, including verification using the NHS Spine, to ensure only appropriate participants are contacted.

What does the study involve?
The relevant participants will be contacted to:
1. Describe the PRISM Follow-up study
2. Provide a participant information sheet and, if willing, complete a consent form and a health

questionnaire on behalf of their child(ren).
To maximise the validity of this study, Confidentiality Advisory Group (CAG) approval will be used to check the electronic health record. This permission will support the existing ethically approved PRISM consent to follow up and trace the participants through the NHS database and GP records. The electronic health record will be used to check the mortality status of the woman and her child(ren) and to confirm their current contact information. If a participant does not reply, where available, some of the health data may be retrieved from the electronic health care record. This is a legal provision to temporarily release confidential patient information (CPI) without the need for "explicit" consent in line with section 251 of the National Health Service Act 2006. Section 251 allows the common law duty of confidentiality to be temporarily lifted for medical purposes and in the public interest.

What are the possible benefits and risks of participating?
Current evidence indicates that early pregnancy exposure to vaginal progesterone does not have long-term harmful effects during childhood. Data from this study may inform the evidence base and future practice.

Where is the study run from?
University of Birmingham, UK

When is the study starting and how long is it expected to run for?
August 2025 to December 2026

Who is funding the study?
NIHR Research for Patient Benefit (RfPB), UK

Who is the main contact?
prism@trials.bham.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
333342

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RG_23-147

Study information

Scientific Title
Long-term health assessment of children following first trimester progesterone treatment in the PRISM trial (PRISM Follow-up)

Acronym
PRISM FU

Study objectives
• To compare the Health Utilities Index (HUI3) score between the progesterone and placebo groups.
• To compare the EQ-5D-y3L score between the progesterone and placebo groups.
• To compare the incidence of Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity

Disorder (ADHD), dyslexia, dysgraphia, dyspraxia, dyscalculia, Obsessive-Compulsive Disorder (OCD), anxiety, and depression between the progesterone and placebo groups.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/08/2025, Seasonal REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8241; seasonal.rec@hra.nhs.uk), ref: 25/LO/0587

Study design
Prospective observational cohort study

Primary study design
Observational

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
A prospective observational study to follow up children born to women following first-trimester progesterone treatment who participated in the PRISM trial.

Interventions
This is a prospective observational study to follow up children born to women who participated in the PRISM trial (https://www.isrctn.com/ISRCTN14163439).

Health Utilities Index (HUI3) score of the children – a rating scale used to measure general health status and health-related quality of life (HRQoL).

The Health Utilities Index 3 (HUI3) is a generic, preference-based, comprehensive system for measuring health status and health-related quality of life. HUI3 was developed to apply to both clinical and general population studies, and to have structural independence among the attributes. Each HUI attribute (dimension) has 3–6 levels of classification and is very responsive to changes in health caused by treatment therapies or other influences. The questionnaire is validated and commonly used as an outcome measure in clinical studies and population health surveys.

The HUI3 classification system is comprised of 8 attributes – (i) Vision, (ii) Hearing, (iii) Speech, (iv) Ambulation, (v) Dexterity, (vi) Emotion, (vii) Cognition and (viii) Pain, each measuring 5 or 6 levels of ability (including low ability and disability).

EQ-5D-Y-3L score of the children:
The EQ-5D-Y-3L descriptive system comprises the five dimensions: (i) mobility, (ii) self-care, (iii) usual activities, (iv) pain/discomfort and (v) anxiety and depression. Within this validated questionnaire, each dimension has three levels: no problems, some problems, and extreme problems. The participant is asked to indicate their child(ren)'s health state by ticking the box next to the most appropriate statement in each of the five dimensions.

Additional secondary outcomes for the children:
1. Autism spectrum disorder (ASD) – a neurodevelopmental disorder characterised by deficits in

social communication and the presence of restricted interests and repetitive behaviours.
2. Attention deficit hyperactivity disorder (ADHD) – an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development.
3. Dyslexia – a learning difficulty that primarily affects the skills involved in accurate and fluent word reading and spelling.
4. Dysgraphia – a disorder of writing ability, including problems with letter formation/legibility, letter spacing, spelling, fine motor coordination, rate of writing, grammar, and composition.
5. Dyspraxia – a developmental co-ordination disorder (DCD) that affects movement and co-ordination.
6. Dyscalculia – a specific and persistent difficulty in understanding numbers, which can lead to a diverse range of difficulties with mathematics.
7. Obsessive-compulsive disorder (OCD) – a mental health condition where a person has obsessive thoughts and compulsive behaviours.
8. Anxiety – an emotion characterised by feelings of tension, worried thoughts, and associated physiological changes.
9. Depression – a mood disorder that causes a persistent feeling of sadness and loss of interest

These health conditions must have been formally diagnosed by a doctor or a relevant specialist. Most commonly, this will involve the child being referred for a formal assessment.

Intervention Type
Other

Primary outcome(s)
General health status and health-related quality of life (HRQoL) measured using the Health Utilities Index (HUI3) at one time point

Key secondary outcome(s))
1. Health-related quality of life measured using the EuroQol EQ-5D-Y-3L quality-of-life tool at one time point
2. Incidence of childhood health conditions (formally diagnosed by a doctor or relevant specialist) measured using University of Birmingham questions at one time point. The conditions investigated are autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), dyslexia, dysgraphia, dyspraxia, dyscalculia, obsessive-compulsive disorder (OCD), anxiety and depression.

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Participation in the PRISM Trial and had a live birth
2. Previously gave informed consent as part of the PRISM trial to be contacted about future follow-up studies
3. Willing and able to give informed consent for this study
4. Ability to confirm they wish to complete the parental follow-up questionnaire

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
Not meeting the key inclusion criteria

Date of first enrolment
01/11/2025

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
-
-
United Kingdom
-

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

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 and/or analysed during the current study will be available upon request from prism@trials.bham.ac.uk. The type of data that will be shared: Appropriate data-sharing requests will be considered by the study management group and the Tommy's National Centre for Miscarriage Research, based at the University of Birmingham. Any data shared will be anonymous. Data will be stored securely in a redcap database on servers at the University of Birmingham. Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the General Data Protection Regulation, 2018.

IPD sharing plan summary
Available on request