# Does progesterone prophylaxis to prevent preterm labour improve outcome?: a randomised, double-blind, placebo-controlled trial

Submission date	<b>Recruitment status</b>		
29/08/2008	No longer recruiting		
Registration date 21/11/2008	<b>Overall study status</b> Completed		
Last Edited	<b>Condition category</b>		
28/06/2018	Pregnancy and Childbirth		

[X] Prospectively registered

[X] Protocol

[] Statistical analysis plan

- [X] Results
- [] Individual participant data

### Plain English summary of protocol

### Background and study aims

A preterm birth is a birth that takes place more than three weeks before the baby is due (i.e., a birth before the start of the 37th week of pregnancy). There is now good evidence that the hormone progesterone prevents preterm birth in women at high risk. However, there is no evidence that preventing preterm birth with progesterone has any long-term beneficial effect on the baby. Given that we know that preterm birth is associated with intrauterine infection (infection within the womb) and inflammation, which itself is associated with brain damage for the newborn, it is possible that keeping the baby "in utero" (in the womb) when it would otherwise have been born preterm is harmful. The purpose of this study is to see if progesterone is beneficial to babies - we think it will be but this study is needed to check. The aim is to determine whether progesterone improves outcomes in women at high risk of preterm delivery. The outcomes we are interested in are those of women at delivery and babies from birth to the age of two.

#### Who can participate?

Women with risk factors for preterm birth (e.g., history of previous preterm birth).

### What does the study involve?

Women with risk factors for preterm birth are invited to have a fetal fibronectin test (a test for detecting premature labor). All those with a positive test result and women with selected risk factors but a negative test results are then randomly allocated to be treated with either progesterone or a placebo (dummy) treatment. Participants are followed up until after delivery, and their babies are followed up until the age of 2 years. Those just screened but not treated are also followed up until delivery.

What are the possible benefits and risks of participating? Not provided at time of registration. Where is the study run from? University of Edinburgh (UK).

When is the study starting and how long is it expected to run for? October 2008 to December 2015.

Who is funding the study? Medical Research Council (UK).

Who is the main contact?1. Sonia Whyte (Sonia.Whyte@ed.ac.uk)2. Lorraine Adamson (L.D.Adamson@ed.ac.uk)

### Study website

http://www.opptimum.org.uk

### **Contact information**

**Type(s)** Scientific

**Contact name** Prof Jane Norman

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### **Contact details**

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## Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

**Secondary identifying numbers** MRC ref: G0700452

# Study information

### Scientific Title

Does progesterone prophylaxis to prevent preterm labour improve outcome?: a randomised, double-blind, placebo-controlled trial

### Acronym

OPPTIMUM

### **Study objectives**

Primary objective: In women at high risk of preterm labour, does prophylactic vaginal natural progesterone, 200 mg daily from 22-34 weeks gestation, compared to placebo:

1. Improve obstetric outcome by lengthening pregnancy and thus reducing the incidence of preterm delivery (before 34 weeks gestation)?

2. Improve neonatal outcome by reducing a composite of death and major morbidity?

3. Lead to improved childhood cognitive and neurosensory outcomes at two years?

4. Represent cost effective management for women at high risk of preterm delivery?

More details can be found at: http://www.mrc.ac.uk/ResearchPortfolio/Grant/Record.htm? GrantRef=G0700452&CaseId=9676

Ethics approval required

Old ethics approval format

Ethics approval(s) Scotland MREC A, 19/02/2008, ref: 08/MRE00/6

**Study design** Randomised double-blind placebo-controlled trial

**Primary study design** Interventional

**Secondary study design** Randomised controlled trial

**Study setting(s)** Hospital

**Study type(s)** Prevention

### Participant information sheet

Patient information sheet can be found at: http://www.opptimum.org.uk/general-information. aspx

Health condition(s) or problem(s) studied Preterm labour

### Interventions

Prophylactic vaginal natural progesterone, 200 mg daily from 22-24 weeks gestation until 34 weeks gestation vs placebo.

### Intervention Type

Drug

**Phase** Not Applicable

### Drug/device/biological/vaccine name(s)

Progesterone

### Primary outcome measure

- 1. Primary obstetric outcome of the treatment phase is delivery <34 weeks of gestation (Yes/No)
- 2. Primary neonatal outcome is a composite of death or two markers of neonatal morbidity
- 3. Primary childhood outcome is developmental status at two years
- 4. Formal economic evaluation

### Secondary outcome measures

- 1. Gestational age at delivery
- 2. Death after trial entry or severe disability at two years of age
- 3. Incidence of the individual components of the primary neonatal outcome

4. Incidence of other major neonatal complications: need for and duration of respiratory support, surfactant administration, duration of oxygen therapy, necrotising enterocolitis, number of discrete episodes of infection (e.g., positive blood culture, cerebrospinal fluid [CSF] culture), daily level of care

5. Composite outcome of death or neurodevelopmental impairment at two years of age, the latter defined as one or more of:

5.1. Disabling cerebral palsy, defined as a score of 2 or higher on the Gross Motor Function Classification System, or 3 or higher on the Manual Ability Classification System, plus classified using the SCPE system

5.2. Developmental impairment (Cognitive standardised score <70)

5.3. Severe visual loss (legally certifiable as blind or partially sighted)

5.4. Profound/severe deafness (requiring hearing aids). Disability will be classified into domains according to professional consensus.

- 5.5. Brief Infant Toddler Social Emotional Assessment (BITSEA)
- 5.6. Women's perceptions of treatment

5.7. Maternal and child adverse events (e.g., operative delivery)

### Overall study start date

01/10/2008

### **Completion date**

31/12/2015

# Eligibility

### Key inclusion criteria

Screening Study: High risk for preterm birth as indicated by at least one of the following: 1. History of previous preterm birth (PTB)/second trimester loss

2. Previous preterm premature rupture of the foetal membranes

3. Short cervical length (<25 mm) on ultrasound at 18-22 weeks gestation

4. All women will have gestation established by scan at ¡Ü 16 weeks to ensure that the estimated date of delivery is accurate

5. Signed consent form

### Main Study:

All women fulfilling the above inclusion criteria and who have a positive screening (fFN) test at 22 weeks will be eligible for the main (treatment) phase of the study. Further consent must be obtained.

### Participant type(s)

Patient

### Age group

Adult

### Lower age limit

18 Years

**Sex** Female

### **Target number of participants** Planned sample size (randomised): 1125

### Key exclusion criteria

- 1. Known significant structural or chromosomal foetal anomaly
- 2. Known sensitivity, contraindication or intolerance to progesterone (including peanut allergy)
- 3. Suspected or proven rupture of the foetal membranes at the time of recruitment

4. Multiple pregnancy

5. Prescription or ingestion of medications known to interact with progesterone (e.g., ketoconazole and ciclosporin)

# Date of first enrolment 03/12/2008

# Date of final enrolment 31/03/2013

# Locations

**Countries of recruitment** Sweden

United Kingdom

Study participating centre

## Sponsor information

**Organisation** University of Edinburgh (UK)

Sponsor details Edinburgh Clinical Trials Unit The Queen's Medical Research Institute 47 Little France Crescent Edinburgh Scotland United Kingdom EH16 4TJ +44 (0)131 242 9461 researchgovernance@ed.ac.uk

**Sponsor type** University/education

Website http://www.ed.ac.uk

ROR https://ror.org/01nrxwf90

## Funder(s)

**Funder type** Government

**Funder Name** Medical Research Council (UK) (grant ref: G0700452)

Alternative Name(s) Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type** Government organisation

Funding Body Subtype

**Location** United Kingdom

# **Results and Publications**

### Publication and dissemination plan

To be confirmed at a later date Participant level data may be available on request from the CI (Jane Norman) after publication of papers arising from the study

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<u>Results article</u>	questionnaire results	01/08/2010		Yes	No
<u>Protocol article</u>	protocol	06/08/2012		Yes	No
<u>Results article</u>	results	21/05/2016		Yes	No
<u>Results article</u>	results	01/06/2018		Yes	No