

# Progesterone in recurrent miscarriages (PROMISE) study

<b>Submission date</b> 10/03/2009	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 17/03/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 31/05/2016	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

This study was undertaken to test whether giving the hormone progesterone to pregnant women with a history of repeated unexplained early pregnancy losses could increase the number of pregnancies leading to live births after at least 24 weeks of gestation.

### Who can participate?

Women aged 18-39 with unexplained recurrent miscarriages (three or more consecutive or non-consecutive first trimester miscarriages). A pregnancy loss is considered to be unexplained if conditions known to increase the risk of miscarriage are absent.

### What does the study involve?

Participants were randomly allocated to one of two groups: one group received progesterone twice daily as vaginal pessaries and the other group received a placebo (dummy) with an identical appearance, from soon after a positive urinary pregnancy test, and no later than 6 weeks of pregnancy, until 12 completed weeks of pregnancy (or earlier if the pregnancy ended before 12 weeks).

### What are the possible benefits and risks of participating?

There is substantial evidence from IVF practice that progesterone supplementation is safe to the mother and fetus at the proposed dose. Moreover, recent studies of vaginal progesterone in the context of prevention of preterm birth have not shown any evidence of short-term safety concerns in the participants.

### Where is the study run from?

45 hospitals in the UK and the Netherlands

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

From May 2009 to September 2014

### Who is funding the study?

NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?

1. Dr Arri Coomarasamy (a.coomarasamy@bham.ac.uk)
2. Dr Rajendra Rai (r.rai@imperial.ac.uk)

**Study website**

<http://www.medscinet.net/promise>

## Contact information

**Type(s)**

Scientific

**Contact name**

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

HTA 08/38/01

## **Study information**

### **Scientific Title**

First trimester progesterone therapy in women with a history of unexplained recurrent miscarriages: a randomised double-blind placebo-controlled multi-centre trial (The PROMISE [PROgesterone in recurrent MIScarriage] Trial)

### **Acronym**

PROMISE

### **Study objectives**

1. In women with unexplained recurrent miscarriages, progesterone (400 mg pessaries, twice daily), started soon as possible after a positive pregnancy test (and no later than 6 weeks gestation) and continued to 12 weeks of gestation, compared to placebo, increases live births beyond 24 completed weeks by at least 10% (principal objective)
2. Progesterone improves secondary outcomes such as gestation at delivery, on-going pregnancy at 12 weeks, survival at 28 days of neonatal life
3. Progesterone, compared to placebo, does not incur substantial adverse effects to the mother or the neonate
4. Explore differential or subgroup effects of progesterone in prognostic subgroups
5. Perform an economic evaluation for cost-effectiveness

More details can be found at <http://www.nets.nihr.ac.uk/projects/hta/083801>

Protocol can be found at [http://www.nets.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0018/52911/PRO-08-38-01.pdf](http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0018/52911/PRO-08-38-01.pdf)

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

REC: West Midlands Research Ethics Committee, 19/10/2009, ref: 09/H1208/44

### **Study design**

Randomised double-blind placebo-controlled multi-centre trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

**Health condition(s) or problem(s) studied**

Unexplained recurrent miscarriages

**Interventions**

Intervention group: Progesterone pessaries (400 mg twice daily) started soon as possible after a positive pregnancy test (and no later than 6 weeks gestation) and continued to 12 weeks of gestation

Control group: Placebo

Total duration of follow-up per participant: 42 weeks

**Intervention Type**

Drug

**Phase**

Not Applicable

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

Progesterone

**Primary outcome measure**

Live births beyond 24 weeks

**Secondary outcome measures**

1. Gestation at delivery
2. Clinical pregnancy at 6-8 weeks
3. Ongoing pregnancy at 12 weeks (range 11-13 weeks)
4. Miscarriage rate
5. Survival at 28 days of neonatal life
6. Congenital abnormalities with specific examination for genital anomalies
7. Adverse events

**Overall study start date**

01/05/2009

**Completion date**

01/09/2014

**Eligibility****Key inclusion criteria**

1. Women with unexplained recurrent miscarriages (3 or more consecutive first trimester miscarriages)
2. Age 18-39 years at randomisation (likelihood of miscarriages due to chromosomal aberrations is higher in older women; such miscarriages are unlikely to be prevented by progesterone therapy)
3. Spontaneous conception (as confirmed by urinary pregnancy tests)
4. Willing and able to give informed consent

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

39 Years

**Sex**

Female

**Target number of participants**

790

**Key exclusion criteria**

1. Inability to conceive spontaneously within 1 year of recruitment
2. Antiphospholipid syndrome (lupus anticoagulant and/or anticardiolipin antibodies [IgG or IgM]); other recognised thrombophilic conditions (testing according to usual clinic practice)
3. Intrauterine abnormalities (as assessed by ultrasound, hysterosonography, hysterosalpingogram, or hysteroscopy)
4. Fibroids distorting uterine cavity
5. Abnormal parental karyotype
6. Other identifiable causes of recurrent miscarriages (tests initiated only if clinically indicated) e. g., diabetes, thyroid disease and systemic lupus erythematosus (SLE)

**Date of first enrolment**

01/06/2010

**Date of final enrolment**

01/10/2013

**Locations****Countries of recruitment**

Netherlands

United Kingdom

**Study participating centre**  
45 hospitals in the UK and the Netherlands

## **Sponsor information**

### **Organisation**

Imperial College London (UK)

### **Sponsor details**

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### **Sponsor type**

University/education

### **Website**

<http://www.imperial.ac.uk>

### **ROR**

<https://ror.org/041kmwe10>

## **Funder(s)**

### **Funder type**

Government

### **Funder Name**

Health Technology Assessment Programme

### **Alternative Name(s)**

NIHR Health Technology Assessment Programme, HTA

### **Funding Body Type**

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Publication and dissemination plan

Publication in the UK NIHR HTA library is anticipated before the end of 2015. Other publications may be produced but are not yet confirmed.

### Intention to publish date

01/11/2015

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	26/11/2015		Yes	No
<a href="#">Results article</a>	results	01/05/2016		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No