

# The effect of doxycycline on live birth rates in women with chronic endometritis suffering from recurrent miscarriage

<b>Submission date</b> 27/08/2019	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/09/2019	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 27/01/2025	<b>Condition category</b> 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

A healthy lining of the womb is important for conception and the support of the developing foetus. An imbalance of the bacteria that occupy this space can cause inflammation of the womb (endometritis) which can cause miscarriage. Antibiotics can reduce this inflammation, this treatment is available at private clinics in some European countries but there is no confirming evidence to support this approach. Therefore, this study aims to determine if the antibiotic (doxycycline), taken before conception, improves pregnancy outcome in women with recurrent miscarriage associated with chronic endometritis.

### Who can participate?

Women aged 18-41 and have had 2 or more consecutive first trimester miscarriages and have no apparent cause for these miscarriages.

### What does the study involve?

The study involves you having a biopsy to determine if you have chronic endometritis. The results from this will determine if you are eligible to be randomised.

If the biopsy results indicate you do not have chronic endometritis, you will be contacted every 3 months for follow-up to see if you have become pregnant. If you do become pregnant, we will continue to follow you up every 3 months and will gain some more information from you once your pregnancy is complete. Once this is completed, you are longer part of the trial. If you do not become pregnant, you will be followed up for a maximum of one year.

If the results indicate you do have chronic endometritis, you can be randomised into the controlled trial and will either have the antibiotic or the placebo. Once you have completed your course of capsules and had your next menstrual period, you can begin trying to conceive again. You will be contacted after you have completed your capsules. You will then be contacted every 3 months to see if you have become pregnant. If you do become pregnant, we will continue to follow you up every 3 months and will gain some more information from you regarding your scans. Upon completion of your pregnancy, we will collect the outcome information and any

information regarding complications and infections approx. 8 weeks after you have had your baby. If you do not become pregnant, we will continue to contact you for follow-up every 3 months until the end of the trial.

What are the possible benefits and risks of participating?

Taking part could help to determine the cause of your miscarriages. The results will help us provide advice on treatment options for women who have recurrent miscarriage. Some women find the endometrial biopsy is painful and may get cramping at the time of the biopsy, some women may have vaginal bleeding (spotting) after the biopsy is taken but this will stop quickly on its own.

If you enter the randomised trial then a drug pack will be given to you, side effects are possible from taking these, however, there is a small chance you will experience this. There is also the chance of having an allergic reaction to the drug, however, this is a small chance once again. You will also be required to avoid pregnancy for approx. 3 months.

Where is the study run from?

Warwick Clinical Trials Unit (UK)

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

June 2019 to March 2024

Who is funding the study?

The study received funding from the National Institute for Health Research, Efficacy and Mechanism Evaluation programme (UK)

Who is the main contact?

The trial manager, based at Warwick Clinical Trials Unit, can be contacted by emailing: CERM@warwick.ac.uk

**Study website**

<https://warwick.ac.uk/cerm>

## Contact information

**Type(s)**

Public

**Contact name**

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## Additional identifiers

**EudraCT/CTIS number**

2019-000585-38

**IRAS number****ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 42757

## Study information

**Scientific Title**

## Chronic Endometritis and Recurrent Miscarriage (CERM)

### Acronym

CERM

### Study objectives

Does doxycycline given prior to conception (conceiving a child) improve the number of on-going pregnancies and total live births in women with recurrent miscarriage associated with chronic endometritis (inflamed lining of the womb)?

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 20/08/2019, Research Ethics Committee: North West – Haydock (3rd Floor Barlow House, 4 Minshull Street, Manchester, M1 3DZ; cwow.admin@nhs.uk; 0207 1048 024), ref: 19/NW/0462

### Study design

Randomized; Interventional; Design type: Treatment, Screening, Diagnosis, Drug

### 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 to request a patient information sheet

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

Recurrent miscarriage

### Interventions

Current interventions as of 17/08/2021:

CERM A

Pre-Screening

Potential participants for the CERM trial will be identified by one of two ways:

1. Women on the Tommy's 'Recurrent Miscarriage' database. These women have had investigations for a treatable cause of their miscarriage and have given consent to be contacted for research purposes.
2. Women referred to a recurrent miscarriage clinic

Women will be sent an invitation letter and CERM Trial Screening participant information sheet by post or email. In the invitation email/letter, women on the Tommy's 'Recurrent Miscarriage' database will be contacted by the hospital research team via telephone as described in the invitation email/letter. Women referred to a recurrent miscarriage clinic are asked to contact the hospital research team if they are interested in taking part in the trial.

In the telephone conversation, a member of the hospital research team will explain what the trial is about and what participation in the research trial will mean. The woman will have chance to ask questions over the phone. If a woman agrees to consider the trial they will be offered a continuation of the phone consultation or offered a face to face appointment.

The next step either by phone or face to face is that a member of the hospital research team will ask if the woman potentially meets the specific criteria to participate. These specific criteria will include their age, number of previous miscarriages and general medical history.

If investigations for the cause of recurrent miscarriage haven't been carried out this will be done when a woman attends the clinic. All women will be made aware that an important part of the eligibility is to ensure that they are willing to use condoms, during sexual intercourse for up to four menstrual cycles.

If a woman is deemed potentially eligible over the phone/face to face, the woman will be required to give verbal consent for a 'biopsy preparation kit' to be sent/given to them. The kit contains instructions, period tracker, condoms, and ovulation testing kit. At this point the participant will be assigned a screening identification number (ID).

The biopsy needs to be taken 10 days (+/- 4) after the participant has ovulated. The period tracker and ovulation testing kit helps to track when this is. When the ovulation test indicates ovulation or on day 23 of the cycle (+/- 3 days) if the kit does not indicate ovulation, the woman will need to contact the clinic (hospital research team) to arrange an appointment to attend for their biopsy.

### Screening

When a woman attends hospital for their biopsy, they will be asked to bring along their period tracker. In the clinic a member of the hospital research team will explain the biopsy procedure to the woman and check eligibility, the woman will be able to ask any questions. A set of assessments will be taken to determine eligibility. These assessments will include the collection of medical history (including obstetric and pregnancy history), smoking history, a review of any medication they are taking a review of the period tracker and checks to ensure they do not suffer from any condition or illness that would make the trial medication unsuitable for them. If the woman is eligible and would like to take part she will need to sign a consent form. The woman will also be required to take a pregnancy test, if the test indicates she is pregnant the biopsy cannot be taken and the woman will be referred to her GP. If the pregnancy test indicates the woman is not pregnant, a clinician will explain the procedure. At this point the women will be registered into the trial and given a participant trial ID number.

The procedure involves a vaginal examination to find out the position of the womb to take the biopsy. The procedure usually takes a couple of minutes. The biopsy is taken by passing a thin plastic tube through the cervix and into the uterus. A small sample of the lining of the womb is taken and sent to the laboratory at the University Hospitals Coventry and Warwickshire NHS Trust (UHCW) for analysis under the microscope. The sample will be labelled with participant's

assigned trial ID number. With the participants permission any tissue left over following analysis will be stored in the Tommy's National Reproductive Health Biobank and used in future ethically approved research.

During the biopsy procedure, every effort will be made to ensure that enough endometrial tissue is collected for analysis. In a few cases this may not be possible. If the clinician is unable to obtain a sample or not enough tissue for analysis they will discuss with the participant the following options:

1. The same clinician will repeat the biopsy at the same sitting
2. A different clinician will take the biopsy at the same sitting
3. A biopsy will be arranged for the next menstrual cycle
4. The biopsy will be taken at UHCW permitting that the participant is willing to travel to this site

Participants will be reminded that it is important that while they wait for the biopsy results they continue to use condoms during sexual intercourse. Biopsy results are usually available within four weeks. When they are available, participants will be contacted and if positive, participants will be invited to attend an appointment to come to the clinic.

If results indicate that the participant does not have endometritis they will continue on the usual care pathway. The hospital trial team will keep in touch and phone participants at three, six, nine and 12 months. If a participant gets pregnant within the 12 months the hospital team will keep in touch to record the pregnancy outcome.

#### Randomisation

Women who screen positive for CE will be randomised into the randomised controlled trial of doxycycline versus placebo (N=1,500).

If results indicate endometritis, participants may then be eligible to take part in the randomised controlled trial. At this point the participants will be given another information sheet explaining further what participation would involve and a member of the hospital research team will answer any questions.

The hospital research team will perform additional assessments to assess eligibility for the randomised controlled trial. These assessments will include a review of the period tracker, a review of any medication they are taking and review of any signs of hepatic failure. If hepatic failure is suspected liver function tests will be taken. If a participant is eligible and would like to take part in the randomised controlled trial they will be asked to verbally reaffirm their consent. After the participant has verbally reaffirmed their consent, they will be asked to take a pregnancy test. If the test indicates they are pregnant they will not be able to participate in the randomised controlled trial and will be referred to their GP who will arrange for their care. If the pregnancy tests indicates they are not pregnant, they will be randomly selected to have either a two week course of doxycycline, an antibiotic (the intervention group) or two weeks of placebo (the control group). No one can influence which treatment a participant receives; a computer will make this decision. As this is a double blind trial neither the participant nor the trial team will know which treatment the participant is taking, but it will be possible to access this information should it become necessary for the participants clinical care.

The hospital team will give participants a prescription for the capsules (antibiotic/placebo) these need to be collected from the hospital pharmacy. Participants will be given a guidance leaflet 'Taking my capsules on the CERM trial' this contains full instructions on how to take the capsules, participants will be encouraged to read this carefully. Participants need to take one capsule twice a day 12 hours apart for 14 days, participants will be provided with a treatment

diary to write down every time they have taken a capsule. Participants will also be informed of the importance of carrying their CERM Trial Participant Card at all times. If participants have unprotected sexual intercourse or a condom failure during the time they are taking the capsules they should stop taking them and contact the hospital research team.

Participants will be encouraged to try and conceive from the first day of their menstrual cycle after they have completed taking the capsules.

Participants will be contacted by the hospital team within six weeks of being prescribed the capsules and asked if they have taken the capsules as per the instructions given. Participants will also be expected to return the treatment diary they have completed which shows when they took their medication. The participant will also be asked:

1. If they have had unprotected sexual intercourse or a condom failure during the menstrual cycle you were on whilst taking the capsules.
2. If the participant has experienced any side effects from the capsules
3. If they are taking any other medication
4. If the participant has become pregnant.

The hospital team will then phone participants every 3 months from the point of the treatment completion phone call, this will be to check if the participant has become pregnant. Participants will be asked to contact the hospital trial team if they become pregnant in-between contact from the hospital trial team. At each contact a member of the hospital research team will check if participants are trying to conceive, their pregnancy status and pregnancy outcome.

If the randomised participant confirms that they are pregnant then the hospital research team will phone participants and trial data will be collected at 12 (+/-2 weeks) and 20-24 weeks gestation which follows standard UK practice. Data will also be collected for any additional scans taken between 6 – 20 weeks gestation as part of standard practice. Ultrasound scans will be performed as per standard practice. Information on the current pregnancy status, any complications and their current medication will be collected at these standard visits from hospital notes and from the patients themselves. Patients will be reminded to provide their participant treatment diary and bring back any unused medication if applicable.

The participant will then be contacted 6-8 weeks following delivery (>24 weeks gestation). The hospital research team will phone the participant and collect information on pregnancy outcome, any pregnancy complications, any medication that the participant is taking and the participant and infants health. If a participant delivers a baby over 24 weeks gestation then the trial will conclude 6-8 weeks after delivery. This will be the participant's last follow-up for the purposes of the trial and a participant's normal care will resume afterwards.

If a participant loses their baby before 24 weeks gestation then they will remain in the trial and the hospital team will then phone participants every 3 months from the point of pregnancy loss, this will be to check if the participant has become pregnant again. If a participant confirms that they are pregnant again then trial data will be collected again at the time points stated above.

## CERM B

Within CERM a subset of patients will be recruited to CERM B to determine if doxycycline treatment improves CE and microbiota compositions (the name given to the microbes that live in our and on our bodies - it is mostly made up of bacteria and everyone's microbiome is unique.) CERM B patients will all be recruited at University Hospital Coventry and Warwickshire NHS Trust. CERM B patients will follow the same pathway as CERM A patients but will have the following additional assessments:

1. Patients will be registered into the screening study, consented to the CERM B trial and have a vaginal, endometrial and cervical swab at the same examination as the screening biopsy.
2. Women who screen positive for CE and are randomised into CERM B will have a second endometrial biopsy with concurrent vaginal, endometrial and cervical swabs following treatment completion.

For CERM B participants there will not be any results from the swabs, because a test is not clinically validated, instead the research team look at the microbiome to see what microbes are present. Women will not receive the results of the second endometrial biopsy but this will be used to determine the effect of the capsules

Previous interventions:

CERM A

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The procedure involves a vaginal examination to find out the position of the womb to take the biopsy. The procedure usually takes a couple of minutes. The biopsy is taken by passing a thin plastic tube through the cervix and into the uterus. A small sample of the lining of the womb is taken and sent to the laboratory at the University Hospitals Coventry and Warwickshire NHS Trust (UHCW) for analysis under the microscope. The sample will be labelled with participant's assigned trial ID number. With the participants permission any tissue left over following analysis will be stored in the Tommy's National Reproductive Health Biobank and used in future ethically approved research.

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Participants will be reminded that it is important that while they wait for the biopsy results they continue to use condoms during sexual intercourse. Biopsy results are usually available within four weeks. When they are available, participants will be contacted and if positive, participants will be invited to attend an appointment to come to the clinic.

If results indicate that the participant does not have endometritis they will continue on the usual care pathway. The hospital trial team will keep in touch and phone participants at three, six, nine and 12 months. If a participant gets pregnant within the 12 months the hospital team will keep in touch to record the pregnancy outcome.

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failure is suspected liver function tests will be taken. If a participant is eligible and would like to take part in the randomised controlled trial they will be asked to sign a consent form. After the participant has signed the consent form they will be asked to take a pregnancy test. If the test indicates they are pregnant they will not be able to participate in the randomised controlled trial and will be referred to their GP who will arrange for their care. If the pregnancy tests indicates they are not pregnant, they will be randomly selected to have either a two week course of doxycycline, an antibiotic (the intervention group) or two weeks of placebo (the control group). No one can influence which treatment a participant receives; a computer will make this decision. As this is a double blind trial neither the participant nor the trial team will know which treatment the participant is taking, but it will be possible to access this information should it become necessary for the participants clinical care.

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3. If they are taking any other medication
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The hospital team will then phone participants every 3 months from the point of the treatment completion phone call, this will be to check if the participant has become pregnant. Participants will be asked to contact the hospital trial team if they become pregnant in-between contact from the hospital trial team. At each contact a member of the hospital research team will check if participants are trying to conceive, their pregnancy status and pregnancy outcome.

If the randomised participant confirms that they are pregnant then the hospital research team will phone participants and trial data will be collected at 12 (+/-2 weeks) and 20-24 weeks gestation which follows standard UK practice. Data will also be collected for any additional scans taken between 6 – 20 weeks gestation as part of standard practice. Ultrasound scans will be performed as per standard practice. Information on the current pregnancy status, any complications and their current medication will be collected at these standard visits from hospital notes and from the patients themselves. Patients will be reminded to provide their participant treatment diary and bring back any unused medication if applicable.

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outcome, any pregnancy complications, any medication that the participant is taking and the participant and infants health. If a participant delivers a baby over 24 weeks gestation then the trial will conclude 6-8 weeks after delivery. This will be the participant's last follow-up for the purposes of the trial and a participant's normal care will resume afterwards.

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#### **CERM B**

Within CERM a subset of patients will be recruited to CERM B to determine if doxycycline treatment improves CE and microbiota compositions (the name given to the microbes that live in our and on our bodies - it is mostly made up of bacteria and everyone's microbiome is unique.) CERM B patients will all be recruited at University Hospital Coventry and Warwickshire NHS Trust. CERM B patients will follow the same pathway as CERM A patients but will have the following additional assessments:

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#### **Intervention Type**

Other

#### **Phase**

Phase II

#### **Primary outcome measure**

1. Ongoing pregnancy at 12 weeks, measured by ultrasound completed at approximately 12 weeks gestation.
2. Total live births plus ongoing pregnancies, measured by a cumulative of live births at the end of the trial as well as the total no. of ongoing pregnancies (as defined in outcome 1) at the end of the trial.

#### **Secondary outcome measures**

1. No. of CD138+ cells in the endometrium, measured by endometrial biopsy, the first taken at registration, the second taken after the 14 day course of capsules.
2. Time to first conception is determined by calculating the difference between date of positive pregnancy test and date of first tablet taken post randomisation.
3. Anticipated time to first live birth is determined by date of first tablet taken to the date of pregnancy outcome if gestation >24weeks post randomisation.
4. Live births, the proportion of women with a live birth after 24 weeks of gestation in their first pregnancy after randomisation.
5. Pregnancy complications, in first pregnancy following randomisation lasting greater than 12

weeks gestation; second trimester miscarriage intrauterine death, preterm delivery, small for gestational age and placental abruption is determined by reviewing patient notes at pregnancy outcome.

6. Early pregnancy complications are determined by reviewing patient notes at pregnancy outcome and pregnancy review (12 weeks and 20-24 weeks gestation)

7. Type of miscarriage, biochemical, gestational sac, foetal, karyotype of miscarried tissue are determined by reviewing patients notes at pregnancy outcome.

8. A reassessment of the ability of the CD138+ cell test to detect which patients will benefit from doxycycline will be undertaken. This analysis will use on-going pregnancy and live births per patient in women excluded from randomisation by having low CD138+ cell scores. And those randomised to placebo.

9. Termination for social reasons is determined by reviewing patient notes at pregnancy outcome.

### **Overall study start date**

01/06/2019

### **Completion date**

07/03/2024

## **Eligibility**

### **Key inclusion criteria**

Inclusion criteria - screening

1. Age  $\geq 18$  to  $< 42$  years
2. Two or more consecutive first-trimester miscarriages
3. Women who agree to use barrier methods of contraception during the following cycles: biopsy preparation, screening-biopsy, waiting for the results and during the intervention

Inclusion criteria - RCT

1. Women with  $\geq 5$  CD138+ cells/10mm<sup>2</sup>

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Upper age limit**

42 Years

### **Sex**

Female

### **Target number of participants**

Planned Sample Size: 3062; UK Sample Size: 3062

## Total final enrolment

737

### Key exclusion criteria

Current participant exclusion criteria as of 17/08/2021:

Exclusion criteria– screening:

1. Known treatable cause(s) of RM. Participants may not have undergone tests for treatable causes of RM prior to registration. If a treatable cause for RM is identified after registration, the participant cannot be randomised.
  - 1.1. Antiphospholipid antibody syndrome
  - 1.2. Thyroid disease
  - 1.3. Parental karyotypical abnormalities.
2. Known sub-septate uterus.
3. Poorly controlled diabetes (HbA1c >48 mmol/mol)
4. Allergy to doxycycline or its excipients
5. Doxycycline contraindicated
6. Antibiotics in the current menstrual cycle
7. Taking a medication that may interact with doxycycline
8. Myasthenia Gravis.
9. Systemic lupus erythematosus (SLE)
10. Immunodeficiency disorder
11. Known serious liver disease as judged by a medically qualified doctor assessing trial eligibility informed by referral letter from GP and hospital records
12. Alcohol dependency as judged by a medically qualified doctor assessing trial eligibility informed by referral letter from GP and hospital records
13. Long-term antibiotic(s) use.
14. Menstrual cycle  $\leq 21$  or  $\geq 42$  days
15. Any co-morbid disease or condition that would make the patient unsuitable for the trial as judged by a medically qualified doctor assessing trial eligibility informed by referral letter from GP and hospital records
16. Unable to give informed consent.
17. Participation in another clinical trial of an investigational medicinal product (CTIMP) within the last 90 days.
18. Breast feeding
19. Pregnancy

Exclusion criteria– RCT:

1. Treatable cause(s) of RM
2. A course of antibiotics between screening registration and randomisation to RCT. If a woman has a course of antibiotics between screening registration and randomisation they will not be eligible for trial randomisation at the time but should be given the option to re-screen and have another biopsy to confirm eligibility for randomisation.
3. A delay of longer than three months between biopsy result and randomisation to RCT. If a woman was registered for screening over three months before randomisation to the RCT they will not be eligible for trial randomisation at the time but should be given the option to re-screen and have another biopsy to confirm eligibility for randomisation.
4. Known serious liver disease as judged by a medically qualified doctor assessing trial eligibility informed by referral letter from GP and hospital records
5. Taking a medication that may interact with doxycycline
6. Any co-morbid disease or condition that would make the patient unsuitable for the trial as judged by a medically qualified doctor assessing trial eligibility informed by referral letter from

GP and hospital records

## 7. Pregnancy

If a clinician has doubts about a participants' suitability for the trial because of a long-term medical condition they should undertake a Full Blood Count (FBC) and Liver function tests (LFTs); in order for a woman to be included in the trial the following should apply and all required additional checks must be documented in the patients' medical notes:

1. WBC  $>3 \times 10^9/l$
2. Neutrophils  $>1.5 \times 10^9/l$
3. Platelets  $>75 \times 10^9/l$  and hemoglobin (Hb)  $>100 \text{ g/l}$
4. Bilirubin  $<1.5 \times$  upper limit of normal (ULN)
5. AST/ALT  $<3 \times$  ULN
6. Albumin  $>30 \text{ g/dl}$

Previous participant exclusion criteria:

Exclusion criteria – screening

1. Treatable cause(s) of RM for example:

- 1.1. Antiphospholipid antibody syndrome
- 1.2. Thyroid disease
- 1.3. Parental karyotypical abnormalities.

2. Known sub-septate uterus.

3. Poorly controlled diabetes (HbA1c  $> 48\text{mmol/mol}$ )

4. Allergy to doxycycline or its excipients.

5. Doxycycline contraindicated

6. Antibiotics in the current menstrual cycle

7. Taking a medication that may interact with doxycycline

8. Myasthenia Gravis.

9. Systemic lupus erythematosus (SLE).

10. Immunodeficiency disorder.

11. Alcohol dependency\*

12. Long-term antibiotic(s) use.

13. Menstrual cycle  $\leq 21 - \geq 42$  days.

14. Unable to give informed consent.

15. Participation in another clinical trial of an investigational medicinal product (CTIMP) within the last 90 days.

16. Women who are breast feeding.

17. Pregnancy

Exclusion criteria – RCT

1. A course of antibiotics between screening registration and randomisation to RCT\*\*

2. A delay of longer than three months between biopsy result and randomisation to RCT\*\*

3. Known serious liver disease\*1

4. Taking a medication that may interact with doxycycline

5. Any co-morbid disease or condition that would make the patient unsuitable for the trial\*1

6. Pregnancy

\*As judged by a medically qualified doctor assessing trial eligibility informed by referral letter from GP and hospital records

**\*\*If a woman has a course of antibiotics between screening registration and randomisation or was registered for screening over three months before randomisation to the RCT they will not be eligible for trial randomisation at the time. These women should be given the option to re-screen and have another biopsy to confirm eligibility for randomisation.**

**1If a clinician has doubts about a participants' suitability for the trial because of a long-term medical condition they should undertake a Full Blood Count (FBC) and Liver function tests (LFTs); in order for a woman to be included in the trial the following should apply:**

- 1. WBC >  $3 \times 10^9/L$ ,**
- 2. Neutrophils >  $1.5 \times 10^9/L$ ,**
- 3. Platelets >  $75 \times 10^9/L$ , Hb > 100g/L**
- 4. Bilirubin < 1.5XULN\***
- 5. AST/ALT < 3xULN\***
- 6. Albumin > 30g/dL).**

**\* ULN = Upper Limit of Normal**

**All required additional checks must be documented in the patients' medical notes**

**Date of first enrolment**

01/10/2019

**Date of final enrolment**

31/10/2022

## **Locations**

**Countries of recruitment**

England

United Kingdom

Wales

**Study participating centre**

**Walsgrave General Hospital**

Clifford Bridge Road

Coventry

United Kingdom

CV2 2DX

**Study participating centre**

**John Radcliffe Hospital**

Headley Way

Headington

Oxford

United Kingdom

OX3 9DU

**Study participating centre**  
**Liverpool Womens Hospital**  
Crown Street  
Liverpool  
United Kingdom  
L8 7SS

**Study participating centre**  
**Burnley General Hospital**  
Casterton Avenue  
Burnley  
United Kingdom  
BB10 2PQ

**Study participating centre**  
**Worthing Hospital**  
Lyndhurst Road  
Worthing  
United Kingdom  
BN11 2DH

**Study participating centre**  
**St Richard's Hospital**  
Spitalfield Lane  
Chichester  
United Kingdom  
PO19 6SE

**Study participating centre**  
**Singleton Hospital**  
Sketty Lane  
Sketty  
Swansea  
United Kingdom  
SA2 8QA

**Study participating centre**  
**The James Cook University Hospital**  
Marton Road



Middlesbrough  
United Kingdom  
TS4 3BW

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

**Study participating centre**  
**Ipswich Hospital**  
Heath Road  
Ipswich  
United Kingdom  
IP4 5PD

**Study participating centre**  
**Darlington Memorial Hospital**  
Hollyhurst Road  
Darlington  
United Kingdom  
DL3 6HX

**Study participating centre**  
**University Hospital of North Durham**  
North Road  
Durham  
United Kingdom  
DH1 5TW

**Study participating centre**  
**Norfolk and Norwich University Hospital**  
Colney Lane  
Colney  
Norwich  
United Kingdom  
NR4 7UY

**Study participating centre**  
**King's College Hospital**  
Denmark Hill  
London  
United Kingdom  
SES 9RS

**Study participating centre**  
**University College London Hospital**  
235 Euston Road  
London  
United Kingdom  
NW1 2BU

**Study participating centre**  
**Queen Alexandras Hospital**  
Southwick Hill Road  
Cosham  
Portsmouth  
United Kingdom  
PO6 3LY

**Study participating centre**  
**Royal London Hospital**  
Whitechapel  
London  
United Kingdom  
E1 1BB

**Study participating centre**  
**Royal Albert Edward Infirmary**  
Wigan Lane  
Wigan  
United Kingdom  
WN1 2NN

**Study participating centre**  
**Heartlands Hospital**  
Bordesley Green East  
Bordesley Green

Birmingham  
United Kingdom  
B9 5ST

**Study participating centre**  
**Southampton General Hospital**  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Princess Royal Hospital**  
Apley Castle,  
Grainger Drive  
Apley  
Telford  
United Kingdom  
TF1 6TF

**Study participating centre**  
**Sunderland Royal Hospital**  
Kayll Road  
Sunderland  
United Kingdom  
SR4 7TP

**Study participating centre**  
**Aberdeen Maternity Hospital**  
Foresterhill  
Aberdeen  
United Kingdom  
AB25 2ZL

**Study participating centre**  
**Calderdale Royal Hospital**  
Godfrey Road  
Salterhebble  
Halifax  
United Kingdom  
HX3 0PW

**Study participating centre**

**Addenbrookes**

Addenbrookes Hospital  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**West Middlesex University Hospital**

Twickenham Road  
Isleworth  
United Kingdom  
TW7 6AF

**Study participating centre**

**Dumfries & Galloway Royal Infirmary**

Cargenbridge  
Dumfries  
Dumfries and Galloway  
United Kingdom  
DG2 8RX

**Study participating centre**

**Chelsea & Westminster Hospital**

369 Fulham Road  
London  
United Kingdom  
SW10 9NH

**Study participating centre**

**Princess of Wales Hospital**

Coity Road  
Bridgend  
Bridgend County Borough  
United Kingdom  
CF31 1RQ

**Study participating centre****Birmingham Women's NHS Foundation Trust**

Birmingham Womens Hospital  
Metchley Park Road  
Birmingham  
United Kingdom  
B15 2TG

**Study participating centre****The Royal Glamorgan Hospital**

Ynysmaerdy  
Pontyclun  
United Kingdom  
CF72 8XR

## **Sponsor information**

**Organisation**

University Hospitals Coventry and Warwickshire NHS Trust

**Sponsor details**

Research & Development  
ADA40007  
4th Floor Rotunda  
University Hospital Coventry  
Clifford Bridge Road  
Coventry  
England  
United Kingdom  
CV2 2DX

**Sponsor type**

Hospital/treatment centre

**Website**

<https://www.uhcnhs.uk/leading-research/about-us/>

**ROR**

<https://ror.org/025n38288>

## **Funder(s)**

**Funder type**

Government

## Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 17/60/22

## Results and Publications

### Publication and dissemination plan

The chief investigator will submit a final report to the required authorities with the results, including any publications within one year of the declared end of trial.

The results will be reported first to trial collaborators. The main report will be drafted by the WCTU CERM Trial team and the final version will be agreed by the wider trial management group before submission for publication.

The results will be available to women, their partners, health care professionals and policy makers via the Tommy's website (<https://www.tommys.org>), social media, publications in open access journals, clinical practice guidelines (e.g. Royal College of Obstetricians and Gynaecologists, European Society of Human Reproduction and Endocrinology, National Institute for Health and Care Excellence (NICE)), conference presentations and via a trial webpage to be hosted on Warwick Medical School (<https://warwick.ac.uk/cerm>).

### Intention to publish date

01/07/2025

### Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

### IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		01/12/2023	04/12/2023	Yes	No