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

Submission date
27/08/2019

Recruitment status
No longer recruiting

Registration date
12/09/2019

Overall study status
Completed

Last Edited
27/01/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-000585-38

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Treatment

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 women 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 be 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

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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

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
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.

Key secondary outcome(s))
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.

Completion date
07/03/2024

Eligibility

Key inclusion criteria
Inclusion criteria - screening
1. Age > = 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 > = 5 CD138+ cells/10mm2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
42 years

Sex
Female

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 ≤21 or ≥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 $x10^9$/l
2. Neutrophils >1.5 $x10^9$/l
3. Platelets >75 $x10^9$/l and hemoglobin (Hb) >100 g/l
4. Bilirubin <1.5 x upper limit of normal (ULN)
5. AST/ALT <3 x ULN
6. Albumin >30 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 > 48mmol/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 < = 21 - > = 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 > 3x10^9/L,
2. Neutrophils > 1.5x10^9/L,
3. Platelets > 75x10^9/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
United Kingdom

England

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

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

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?
Protocol article		01/12/2023	04/12/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes