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Reduced Fetal Movement Intervention Trial (ReMIT-2)

Submission date
04/09/2017

Recruitment status
No longer recruiting

Registration date
08/09/2017

Overall study status
Completed

Last Edited
18/02/2020

Condition category
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
In the UK, 1 in 220 babies are stillborn, which describes a baby born with no signs of life after 24 weeks of pregnancy. Forty percent of babies who are stillborn born die after 36 weeks of pregnancy and have no lethal structural abnormality. If these babies could be identified and delivered earlier, lives could be saved. The association between a woman's perception of a reduction in her baby's movement and stillbirth is well documented. Reduced fetal movement is thought to be a symptom of nutrient or oxygen restriction and is related to changes in placental structure and function. Other research suggests that adding a blood test to determine how well the placenta is working might help professionals make decisions about when to intervene to prevent complications. Currently, it is not known whether additional tests of the placenta can reduce the risk of pregnancy complications for both mothers and babies. This study involves women having an additional blood test to measure how well their placenta is working. The results of the blood test will help clinicians decide how to treat women with reduced fetal movement compared with standard care. This is a pilot trial to provide initial information about whether the blood test is helpful in making clinical decisions. A much larger research study will then be needed to assess this properly.

Who can participate?
Women aged between 16 and 50 who are between 36 to 41 weeks pregnant who have reduced fetal movement.

What does the study involve?
Participants are randomly allocated to one or two groups. All participants will have a blood sample taken. Those in the first group have their blood sample tested immediately and the result acted upon. Those in the second group do not have their blood sample tested immediately and so the result will not be available and therefore cannot be acted on. All participants are followed up with questionnaires.

What are the possible benefits and risks of participating?
There are no direct benefits with participating. There is a risk of discomfort when blood samples

are taken. For 1 in 8 cases in the first group, the blood test can suggest there is a complication even when the baby is OK. This could mean that early delivery of the baby was offered when it was not necessary although participants are free to choose not to accept the offer of delivery.

Where is the study run from?
This study is being run by University of Nottingham (UK) and takes place in hospitals in the UK.

When is the study starting and how long is it expected to run for?
July 2013 to October 2019 (updated 09/01/2020, previously: February 2019)

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
1. Prof. Alexander Heazell
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Protocol serial number
33384

Study information

Scientific Title
Reduced Fetal Movement Intervention Trial (ReMIT-2): a multicentre, randomised controlled pilot trial of standard care informed by results of an additional placental factor blood test versus standard care in women presenting with reduced fetal movement (RFM) at or after 36+0 weeks gestation

Acronym
ReMIT-2

Study objectives
The addition of a biochemical test of placental function will better identify pregnancies at high risk of complications after women present with reduced fetal movement at or after 36+0 weeks gestation. Therefore, intervention based upon a biochemical test is hypothesised to improve perinatal outcomes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West – Greater Manchester West Research Ethics Committee, 13/01/2017, ref: 17/NW /0014

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Diagnosis, Prevention, Management of Care

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied

Specialty: Reproductive health and childbirth, Primary sub-specialty: Maternal/ Fetal medicine; UKCRC code/ Disease: Reproductive Health and Childbirth/ Other disorders originating in the perinatal period

Interventions

Eligible participants are randomised in a 1:1 ratio to either the intervention arm or the control arm. Randomisation is stratified by site and number of weeks gestation when the participant first presents at hospital (<40 weeks gestation or ≥40 weeks gestation). The randomisation schedule is based on a computer generated pseudo-random code using random permuted blocks of randomly varying size, created by NCTU in accordance with their standard operating procedure (SOP) and held on a secure University of Nottingham server.

Intervention arm:
Participants in this arm receive the standard care. Participants provide an extra blood sample taken to measure the soluble-fms-like tyrosine kinase 1 (sFlt-1) to placental growth factor (PlGF) ratio. The sample is tested immediately and the results are acted upon by site staff.

Control arm:
Participants in this arm receive the standard care. Participants provide an extra blood sample taken to measure the sFlt-1/PlGF ratio but the sample is not tested immediately so the result is not be available to site staff or the participant and therefore cannot be acted on.

For participants not involved in the Midwife-Led Interview, the follow-up period from delivery to completion of the participant questionnaires is ~10 weeks. For the sub-group of participants involved in the Midwife-Led Interview, the follow-up period from delivery to completion of the interview is ~16 weeks.

Intervention Type

Other

Primary outcome(s)

ReMIT2 is a pilot feasibility trial and therefore does not have primary and secondary outcomes like a standard drug trial. There are feasibility outcomes which determine the feasibility of doing a large main trial based on results collected in ReMIT2 and there are proof of concept outcomes which address whether the intervention might have an effect on neonatal outcome or healthcare costs.

Current feasibility outcomes as of 23/04/2018:
1. Number of potentially eligible women at each site and number of women recruited at each site as collected from hospital records at the time women attend with RFM throughout recruitment period.
2. Proportion lost to follow-up after discharge from hospital and reasons for loss to follow-up as collected from hospital records at the time site confirms participant is lost to follow-up.
3. Spectrum of clinical characteristics of women at randomisation (frequency of small for gestational age (SGA) fetuses, obstetric history, nulliparous) as collected from patient medical records at randomisation.
4. Reasons for non-recruitment, if available as collected from hospital records of women who attend with RFM throughout recruitment period:
4.1. Views of women about reasons for not participating collected at point trial is offered using an Anonymous Survey

4.2. CI site only: Women will be offered short interview within 1 week of presenting with RFM to gain further insight into their reasons for not participating in the trial using a semi-structured interview guide
5. Compliance with the trial interventions and reasons for non-compliance as collected from patient medical records at the time the trial intervention is delivered.
6. Completeness of data collection for planned outcomes in the main trial including that needed for health economic analyses as measured using the SF12 questionnaires at baseline and ~6 weeks after birth, plus a Health Resource Questionnaire at ~ 6 weeks after birth.
7. CI site only: participants' views on sFlt-1/PlGF test collected at point results are given using scripted Test Performance questions.
8. Views of women about participation collected ~6 weeks after birth using a Participant Views questionnaire.
8.1. A sub-group of participants will be interviewed ~16 weeks after birth to gain further insight into their views of the trial using a semi-structured interview guide.
9. Views of clinicians on sFlt-1/PlGF test performance collected prior to recruiting first participant using a Health Professional Views questionnaire.
10. Views of clinicians on the trial collected prior to closing recruitment using a Health Professional Views questionnaire.

Previous feasibility outcomes:
1. Number of potentially eligible women at each site and number of women recruited at each site as collected from hospital records at the time women attend with RFM throughout recruitment period.
2. Proportion lost to follow-up after discharge from hospital and reasons for loss to follow-up as collected from hospital records at the time site confirms participant is lost to follow-up.
3. Spectrum of clinical characteristics of women at randomisation (frequency of small for gestational age (SGA) fetuses, obstetric history, nulliparous) as collected from patient medical records at randomisation.
4. Reasons for non-recruitment, if available as collected from hospital records of women who attend with RFM throughout recruitment period.
5. Compliance with the trial interventions and reasons for non-compliance as collected from patient medical records at the time the trial intervention is delivered.
6. Completeness of data collection for planned outcomes in the main trial including that needed for health economic analyses as measured using the SF12 questionnaires at baseline and ~6 weeks after birth, plus a Health Resource Questionnaire at ~ 6 weeks after birth.
7. Views of women about participation collected ~6 weeks after birth using a Participant Views questionnaire.
7.1. A sub-group of participants will be interviewed ~16 weeks after birth to gain further insight into their views of the trial using a semi-structured interview guide.
8. Views of clinicians on the trial collected 9-12 months after site initiation using a Health Professional Views questionnaire.

Key secondary outcome(s)

Proof of concept outcomes:
1. Frequency of induction of labour or planned caesarean and reasons for these procedures as collected from patient medical records at the time of the baby's birth
2. Neonatal outcome including:
2.1. Stillbirths and deaths before discharge as collected from patient medical records at the time of the baby's birth
2.2. Five minute Apgar score of <7 as collected from patient medical records at the time of the baby's birth

2.3. Umbilical artery pH <7.05 as collected from patient medical records at the time of the baby's birth
2.4. Admission to the neonatal unit for >48 hours as collected from patient medical records at the time the baby is discharged from the neonatal unit
2.5. SGA (<10th centile on neonatal birthweight standards) as collected from patient medical records at the time of the baby's birth
2.6. Use of therapeutic cooling as collected from patient medical records during the time the baby is on the neonatal unit
2.7. Length of stay in hospital. Collected from patient medical records at the time of the baby's discharge from hospital
2.8. Duration of respiratory support as collected from patient medical records during the time the baby is on the neonatal unit
2.9. Number of dependency days on neonatal unit as collected from patient medical records during the time the baby is on the neonatal unit
3. Maternal hypertensive disorders defined as development of gestational hypertension or pre-eclampsia as collected from patient medical records prior to baby's birth
4. Maternal deaths prior to discharge as collected from patient medical records prior to discharge from hospital
5. Maternal admissions to Intensive Care Unit (ICU) as collected from patient medical records prior to discharge from hospital
6. Change in Generalised Anxiety Disorder 2 (GAD-2) scale measured at enrolment and ~6 weeks after birth
7. Quantifiable impact on costs and outcomes incurred by delivering the intervention from an NHS perspective and as assessed by the SF-12™ Health Survey measured at enrolment and ~6 weeks after birth along with a Health Resource Use questionnaire measured ~6 weeks after birth
8. The diagnostic performance of the placental factor test in participants allocated to the control arm of the trial as measured by central laboratory analysis using a Roche Cobas plus sFlt-1 and PlGF kits

Completion date
29/10/2019

Eligibility

Key inclusion criteria
1. Women presenting with RFM before the onset of labour between 36+0 and 41+0 weeks gestation (assessment of gestation will be based on the best available information which will usually be the first or dating scan)
2. Viable singleton pregnancy on initial assessment
3. No indication for immediate delivery as assessed by CTG and ultrasound scan
4. Provision of written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
216

Key exclusion criteria
1. Maternal age < 16 years; added 23/04/2018: Maternal age >50 years
2. Fetus known to have any of the following congenital anomalies as per the Fetal Anomalies Screening Programme (FASP):
2.1. Anencephaly
2.2. Open spina bifida
2.3. Cleft lip
2.4. Diaphragmatic hernia
2.5. Gastrochisis
2.6. Exomphalos
2.7. Serious cardiac abnormalities
2.8. Bilateral renal agenesis
2.9. Lethal skeletal dysplasia
2.10. Edward's syndrome (trisomy 18)
2.11. Patau's syndrome (trisomy 13)
2.12. Any other severe structural abnormality
3. Multiple pregnancy
4. Women for whom it is their first attendance to ANY antenatal care e.g. "unbooked" women
5. Previous randomisation into the ReMIT-2 trial in this pregnancy
6. Concurrent participation in the intervention phase of another clinical trial which determined the timing or mode of delivery

Date of first enrolment
12/03/2018

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital
Hathersage Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Royal Preston Hospital
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
University Hospital Coventry
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
John Radcliffe Hospital
University of Oxford
Level 3 Women's Centre
Oxford
United Kingdom
OX3 9DU

Study participating centre
St George's Hospital
Fetal Medicine Unit
4th Floor
Lanesborough Wing
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
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London
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SW17 0QT

Study participating centre
Liverpool Women's Hospital
Department of Women's and Children's Health
Liverpool Women's Hospital
Crown Street

Liverpool
United Kingdom
L8 7SS

Study participating centre
Sunderland Royal Hospital
Maternity Unit
Kayll Road
Sunderland
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SR4 7TP

Study participating centre
James Cook University Hospital
Marton Road
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TS4 3BW

Study participating centre
Warwick Hospital
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Warwick
United Kingdom
CV34 5BW

Study participating centre
University Hospital of North Tees
Hardwick Road
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United Kingdom
TS19 8PE

Sponsor information

Organisation
The University of Manchester

ROR

https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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 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?
Results article	results	01/12/2020	17/02/2020	Yes	No
Protocol article	protocol	01/10/2018		Yes	No
HRA research summary			28/06/2023	No	No