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ABOVE: Cerclage after Caesarean

Submission date
17/05/2024

Recruitment status
Recruiting

Registration date
17/05/2024

Overall study status
Ongoing

Last Edited
17/05/2024

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Recent studies have shown that if a woman has had a caesarean section in labour (when the cervix is opening) she is more likely to have a premature baby in a future pregnancy. In women who have had an in-labour caesarean section there is a 5-10% chance of a preterm birth in a subsequent pregnancy.
For women who have had an in-labour caesarean section, which was then followed by a preterm birth or mid-trimester loss, early birth is even more likely in subsequent pregnancies. Currently it is not known which treatments are most effective to stop this happening.
These women should be referred to specialist preterm clinics, which will offer them ultrasound monitoring of the length of their cervix, and they may or may not also be offered a cervical cerclage, although there are currently no national guidelines about this. This is a small surgical procedure where a stitch is placed around the cervix through the vagina (transvaginal cerclage). A cerclage can also be placed higher up, through an abdominal procedure involving a cut in the tummy (transabdominal cerclage). This procedure is a longer operation with more recovery time and means that any future babies will need to be born by caesarean section.
Both types of cerclage are offered as standard care to women at high risk of preterm birth. Although transvaginal cerclages are more straightforward, transabdominal cerclages might be more effective because they are above any damage that might have been caused during a previous caesarean section.

Who can participate?
Women who have had a preterm birth or mid-trimester loss (a loss between 14 and 24 weeks of pregnancy) after a previous caearean section in labour

What does the study involve?
Participants will be allocated to one of two treatments: a vaginally-placed cervical stitch or an abdominally-placed cervical stitch, performed before 14 weeks of pregnancy. Some women will join the study before pregnancy, in this group the abdominally-placed stitch will be sited before they get pregnant and the vaginal stitch before 14 weeks in the next pregnancy.
With both stitches participants are followed up in a prematurity clinic with regular transvaginal scanning. If the cervix becomes short participants may be admitted to hospital or offered other treatments (such as a steroid injection to help the baby's lungs mature, and/or putting in an additional stitch if the cervix opens). These may be offered if there is a high chance the baby may be born very early.

The researchers will ask your permission to look at participants' medical notes after delivery to find out what happened. They may also save some scan images of the cervix taken in the prematurity clinic.

What are the possible benefits and risks of participating?
Taking part in the study may not have any direct benefit to participants now. However, the results of this study might help to improve care in any future pregnancies as well as other women, and to reduce the number of babies being born too early.
Having a cervical stitch inserted is a relatively common procedure and is known to help some women. Risks of both treatments include post-operative pain, infection and bleeding. The uncommon risks (occurring in 1 out of 1000) include tearing of the cervix or bladder. The obstetrician would generally be able to repair any tearing to the cervix immediately. A tear to the bladder would require another operation by a urologist (a medical doctor with specialist training in problems of the urinary tract). Both would require a few extra days in hospital. If the doctor is worried about infection, a swab may be taken from the vagina and, if there is evidence of infection, participants may be given a course of antibiotics. While it is likely that either of the cerclages will reduce the chance of miscarriage or preterm birth, they will not entirely eliminate the possibility.

Where is the study run from?
St Thomas' Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2023 to October 2026

Who is funding the study?
1. Action Research Medical (UK)
2. Borne (UK)

Who is the main contact?
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Contact information

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Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
327879

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 59777, IRAS 327879

Study information

Scientific Title
Cerclage after Caesarean: a randomised controlled trial to assess the optimal preventative management for preterm birth secondary to caesarean section damage (ABOVE)

Acronym
ABOVE

Study objectives
Transabdominal cerclage (TAC) will be more effective than transvaginal cerclage (TVC) in reducing mid-trimester pregnancy loss (MTL) and spontaneous preterm birth (PTB) in women with experience of MTL/spontaneous preterm birth (sPTB) after in-labour caesarean section (CS).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval 15/05/2024, North West - Preston Research Ethics Committee (2 Redman Place Stratford, London, E20 1JQ, UK; +44 (0)2071048364; preston.rec@hra.nhs.uk), ref: 24 /NW/0093

Study design
Randomized; Interventional; Design type: Treatment, Surgery

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Preterm birth secondary to caesarean section

Interventions
ABOVE is a multi-centre randomized controlled trial comparing TAC or TVC as a preventative strategy for sPTB in women with a history of sPTB or MTL after an in-labour caesarean section.

Participants will be allocated to either Group A or Group B depending on whether they are already pregnant or planning a pregnancy. The trial is separately powered for these two groups; Group A: in pregnancy and Group B: pre-conception.

160 participants with complete data in total (80/group) with a history of term CS in labour, followed by a subsequent pregnancy loss or sPTB (defined as MTL between 14+0-23+6 weeks or sPTB <30 weeks), either planning a pregnancy, or <14 weeks pregnant <14 weeks pregnant (Group A) or planning a pregnancy (Group B), will be recruited. To allow for loss to follow up, and Group B participants not becoming pregnant within the 18 recruitment period.

Eligible women referred to specialist preterm birth services, either for pre-pregnancy counselling or pregnancy surveillance, will be offered the opportunity to take part in this trial. Pregnant participants (<14 weeks gestation) will be allocated to Group A, while women planning a pregnancy will be allocated to Group B.

Participants will be randomised (1:1) through the ABOVE trial database, which will be hosted within the Medscinet PCN Database (https://www.medscinet.net/ukpcn; REC reference 22/ES /01; IRAS 308157). Women will be randomised to one of the two preventative treatments: 1) TAC, or 2) TVC

It is important to separately evaluate pre-conception and in-pregnancy TACs. The suture can be placed higher pre-conception and this may provide better support around scar weakness. Efficacy could therefore be different in these populations so separately powered trials are planned.

Once randomisation has occurred, the allocated procedure will be arranged. A cervical cerclage will be inserted. The choice of cerclage insertion technique and anaesthesia will be at the local clinician’s discretion with all details recorded on the trial database. Participants in Group A will have the cerclage (TAC or TVC) inserted prior to 14 weeks’
gestation, usually under regional anaesthetic. Group B participants allocated to TAC will have the procedure placed pre-conceptually and those allocated to TVC will have it placed before 14 weeks' gestation (depending on the time point at study entry and randomisation). TACs are performed as as an open or laparoscopic procedure under either regional or general anaesthetic, requiring an inpatient stay of up to 3 days. TVCs will be performed at the participant’s local maternity unit with the insertion technique and anaesthesia according to the clinician’s discretion and local practices. TACs will usually remain in-situ (to support any future pregnancies) while TVCs are removed at around 37 weeks’ gestation. TACs are more specialised procedures and so, if unavailable locally, they may be carried out in tertiary specialist units. The time frame between randomisation and study procedure is flexible from site to site, depending on theatre list availability, although all procedures must be carried out before 14 weeks’ gestation.

There will be no additional research visits, and all preterm care will continue according to local participating site protocols.

Demographic, ongoing preterm surveillance (including cervical length measurements) and outcome data will be collected by recruiting sites from hospital electronic records and entered directly into the study database. Participant identifiers (initials, date of birth, hospital and NHS number) are kept on a separate but linked Medscinet database which is only accessible to authorised site users.

Intervention Type

Procedure/Surgery

Primary outcome measure
The occurrence of mid-trimester pregnancy loss or spontaneous preterm birth before 30 weeks of gestation, collected from the patient's medical records

Secondary outcome measures
Maternal:
1. Admission to hospital for symptoms of threatened preterm labour
2. Administration of antenatal corticosteroids for fetal lung maturation
3. Administration of magnesium sulphate for fetal cerebral protection.
4. Transfer to other hospitals for neonatal cot availability (in-utero transfer)
5. Time between intervention and delivery
6. Requirement for additional emergency/rescue cerclage
7. Serious complications occurring as a result of trial intervention: bladder injury, bowel injury, intraoperative rupture of membranes, cervical tear, hysterectomy
8. Maternal sepsis
9. Admission to ITU
10. Maternal death

Neonatal:
1. Gestation at birth
2. Birthweight
3. Apgar scores (if available)
4. Days before discharge home (up to 28 days)
5. Admission to neonatal unit
6. Neonatal infection
7. In utero fetal death after 14 weeks
8. Stillbirth
9. Neonatal death

Collected from the patient's medical records at time of birth unless stated otherwise

Overall study start date
01/10/2023

Completion date
01/10/2026

Eligibility

Key inclusion criteria
Women will be eligible for the trial if they are:
1. Willing and able to give informed consent
2. Aged 16 years or above
3. Have had a previous term in-labour caesarean section (between 4 and 10 cm dilated) followed by an MTL (> 14 weeks) or preterm birth (<30 weeks)
4. Pregnant, but will be less than 14+0 weeks’ gestation at the time of the allocated intervention (Group A) OR
5. Not yet pregnant but considering a further pregnancy (Group B)

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Female

Target number of participants
Planned Sample Size: 243; UK Sample Size: 243

Key exclusion criteria
Potential participants will not be eligible for the trial if:
1. They are more than 14+0 weeks pregnant at the time of randomisation (as insertion of TAC is associated with higher risk beyond this gestation)
2. They already have a cerclage or (Arabin) pessary in situ
3. They are not planning another pregnancy
4. They have a history of preterm birth (spontaneous/iatrogenic) prior to the term emergency section
5. They are pregnant and expecting more than one baby (multiple pregnancy)

Date of first enrolment
01/07/2024

Date of final enrolment
01/01/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre

Uclh
250 Euston Road
London
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NW1 2PQ

Study participating centre
Rosie Hospital
Robinson Way
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Study participating centre
Liverpool Womens Hospital
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L8 7SS

Study participating centre
Leicester General Hospital
Gwendolen Road
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LE5 4PW

Study participating centre
The Royal Victoria Infirmary
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TS1 4LP

Study participating centre
Chelsea and Westminster Hospital
Chelsea & Westminster Hospital
369 Fulham Road
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SW10 9NH

Study participating centre
West Middlesex University Hospital
Twickenham Road
Isleworth
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TW7 6AF

Study participating centre
Sunderland Royal Hospital
Kayll Road
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SR4 7TP

Study participating centre
Heartlands Hospital
Bordesley Green East
Bordesley Green
Birmingham
United Kingdom
B9 5ST

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Birmingham Womens Hospital
Metchley Park Road
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B15 2TG

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LS9 7TF

Study participating centre
Leeds General Infirmary
Great George Street

Leeds
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LS1 3EX

Study participating centre
Royal Hampshire County Hospital
Romsey Road
Winchester
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SO22 5DG

Study participating centre
St Richards Hospital
Spitalfield Lane
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Study participating centre
John Radcliffe Hospital
Headley Way
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Ethelbert Road
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University Hospital Coventry
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Study participating centre
Barnet Hospital
Wellhouse Lane
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Study participating centre
Royal London Hospital
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Study participating centre
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Action Medical Research; Grant Codes: GN2967

Alternative Name(s)
actionmedres, action medical research for children, AMR

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Borne

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer-reviewed journal
2. Presentation at local and regional conferences

Intention to publish date
01/07/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available and will be stored in a non-publicly available repository. Data will be stored on the ABOVE Trial Database, which is hosted within the already established PCN Database (https://www.medscinet.net/ukpcn). This is a secure web-based platform containing standardised clinical information regarding women at high risk of spontaneous preterm birth. Participant identifiers are kept on a secure separate but linked Medscinet “Patient Details” database, which is only accessible to authorised site users and the PCN Database Project Manager (where the ABOVE study database is hosted) for providing user access and assistance in resolving queries.

IPD sharing plan summary

Stored in non-publicly available repository, Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Group A version 3.0		17/05/2024	No	Yes
Participant information sheet	Group B version 3.0		17/05/2024	No	Yes