The NORACT study: Participant information Sheet

Prevention of premature birth – comparison of two surgical methods

UK Chief Investigator: Professor Andrew Shennan

You are invited to take part in the NORACT research study. Before you decide, it is important that you understand the purpose of the research and what it will involve. Please take time to read the following information carefully and discuss with friends and family if you wish. It is voluntary to participate in the research project, and you can withdraw your consent at any time. Withdrawing will have no consequences for your planned medical care. Please ask the study team if you would like more information and take time to decide whether you wish to take part.

In this research study we will use information from you and your medical records. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study.

Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules.

At the end of the study, we will save some of the data in case we need to check it and to contact you about for future research.

We will make sure no-one can work out who you are from the reports we write.

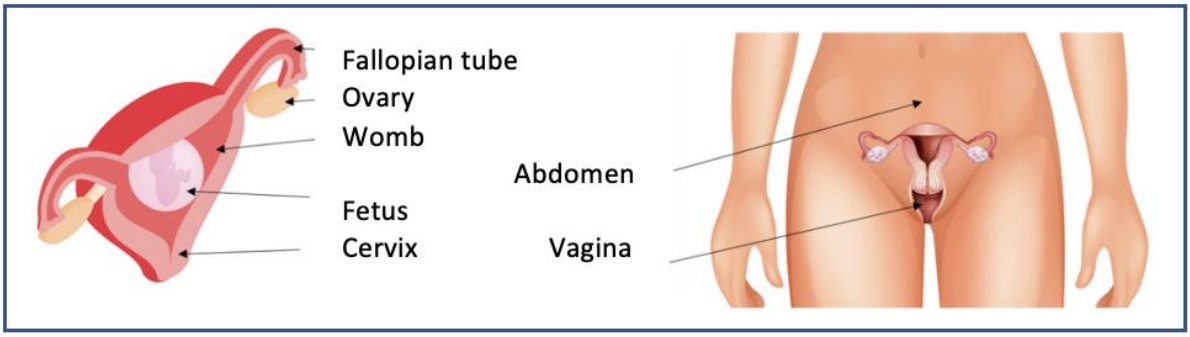
The information pack tells you more about this.

BACKGROUND

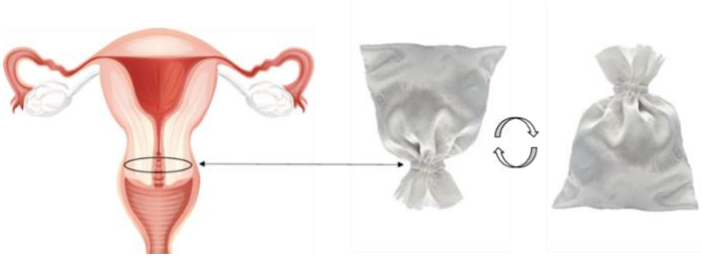
In some women who have an increased risk of premature birth, (delivery before 37 weeks) due to a short cervix (the neck of the womb), you can place a supportive stitch of the cervix (cerclage), to try and prevent the cervix from opening early and preventing premature birth.

We would like to compare the effect of two different surgical methods to perform the stitch and thereby prevent premature birth.

WHAT IS A CERVICAL STITCH (A CERCLAGE)?



A cerclage is a supportive stitch that is applied around the cervix. The purpose is to keep the cervix closed during pregnancy and prevent preterm birth. You can think of it, in the same way as a bag that is tightened around the opening with a drawstring to hold the contents.



The cerclage can be inserted in different ways, in this study, there are two options:

1. An operation performed via the vagina (a Transvaginal cerclage).
2. A keyhole surgery performed via the abdomen (a laparoscopic cerclage).

WHY HAVE I BEEN ASKED TO TAKE PART?

You have been asked to take part because you are planning a future pregnancy and have a risk factor or factors for preterm birth. You are suitable for the study if your doctor is unsure which procedure is a better choice for you to prevent future preterm birth.

WHO CAN PARTICIPATE

You can participate if:

- You wish to become pregnant.
- You are estimated by your doctor to be at moderate to high risk of giving birth prematurely in your next pregnancy due to a problem with your cervix.
- It is uncertain which type of cerclage is the better choice for you to prevent preterm birth.
- You are 18 years or older.
- You can read and understand the information about the study.

WHAT DO I HAVE TO DO IF I TAKE PART?

You will be seen by a member of the research team who will answer questions you may have. Once you have agreed to take part you will be asked to sign a consent form- you will be given a copy of this to keep.

The type of cerclage you will be offered is chosen by random allocation before you become pregnant, and the timing of the surgery will depend on which procedure you are allocated. If you decline having random allocation you can still take part in the trial, by consenting to your data being collected only, while you continue care as recommended by your local care team.

Before and during your pregnancy, your cervix will be assessed with a transvaginal ultrasound (TVUS) in a preterm surveillance clinic. This involves a probe with a sterile cover being placed inside the vagina and measurements of the cervix being taken. The scan usually takes 3-5 minutes.

We will ask for your consent to collect relevant information from your health records about your surgery, medical, surgical, and obstetric history, your future pregnancies, and the children you have after surgery. This has no effect on you or your children's further treatment.

We will also inform your General Practitioner (GP) or referring doctor that you have consented to take part in the study, and which surgery we will perform.

Any participation in the trial is completely voluntary, and you are free to say no to taking part. This will not affect how you are treated by the team looking after you, and you will still receive care according to the guidelines of your department or country.

WHAT DO THE SURGERIES INVOLVE?

During the research study, half of the participants will have a vaginal cerclage, and half will have a laparoscopic cerclage. It is randomly allocated which of the two treatments is offered, which means if you take part, a computer will assign the type of surgery to you.

The Transvaginal cerclage

If the draw determines that you are offered vaginal cerclage surgery, this will be performed early in your next pregnancy. The procedure is usually performed under spinal anaesthesia, where you are numbed from the waist down, but are awake, unless there are some special circumstances that make general anaesthetic (being put to sleep) necessary. There is no known risk of the procedure affecting your chances of future pregnancy or the risk of miscarriage.

The clinician will perform the surgery through your vagina, where they will place a stitch around the outside of the cervix. The operation involves a small risk of bleeding (most women will experience some spotting), and pain. The risk of infection is small (less than 5%). There is also a very small risk of injury to the bladder or cervix (less than 1%) which may require repair, or an additional stay in hospital. Women often go home the same day.

After week 36 of your pregnancy, the cerclage will be removed so how you give birth is not impacted. Less than 5% of women will need anaesthetic for removal.
Transvaginal cerclage insertion is not associated with an increased risk of preterm prelabour rupture of membranes, chorioamnionitis, or caesarean section.

The likelihood of delivery at term with a transvaginal cerclage varies depending on risk factors. However, studies have reported the likelihood of delivery after 32 weeks to be over 90%.

The laparoscopic cerclage

If you are allocated to the laparoscopic cerclage (keyhole surgery), it will be inserted before your next pregnancy. In special circumstances, it can also be inserted in very early pregnancy, before 10 weeks. The procedure takes place under general anaesthesia, where you are asleep during the operation.

The surgeon will perform the surgery via small holes in your abdomen ("keyhole"). The operation is associated with a small risk of bleeding, damage to the organs nearby or infection. There is no known risk of the procedure affecting your chances of pregnancy or the risk of miscarriage. Usually after the procedure patients go home after 24-48 hours, or when pain is adequately controlled with tablet pain relief.

Like all surgery, transabdominal cerclage carries a small risk of bleeding and infection. Very rarely (less than 1%) damage to the bowel or bladder may occur during the operation, which may require further repair. In some situations, changing the operation to an open cut (laparotomy) may be necessary.
The cerclage is permanent, i.e. it is not removed during or after your pregnancy. It can remain in place forever or be removed later once your family is complete. This means that you can only give birth by caesarean section. This may also impact management of miscarriage or pregnancy loss in future pregnancies, which may require surgical management. However, looking your baby after 12 weeks once you have a transabdominal cerclage is rare, less than 1 in 20 (5%) chance.

FOLLOW UP

With both stitches, follow in the prematurity clinic in pregnancy will be arranged, with transvaginal ultrasound scans (TVUS). This will also be performed at your initial visit, as part of the assessment as to whether you can be invited to participate in the study.

Ultrasound scans of the cervix are then performed shortly before and shortly after cerclage is inserted, and during your second trimester of pregnancy. All scans of the cervix are transvaginal.

If the cervix becomes short, we may consider advising you to stay in hospital or offering you other treatments (such as a steroid injection to help your baby's lungs mature, and/or putting in an additional stitch if the cervix opens). These may be offered if we think there is a high chance you will have your baby very early.

Your care will be the same as it would if you do not take part in this study, apart from the addition of one of the two cerclages.

SCHEDULE OF VISITS

Schedule of Visits Timepoints	**Transvaginal Cerclage**	**Laparoscopic Abdominal Cerclage**
Eligibility Check **Consent** **Randomisation** **Allocation** **Baseline data collection**	Pre-pregnancy Less than 10 weeks' gestation	Pre-pregnancy Less than 10 weeks' gestation
Intervention	In Pregnancy, before 16 weeks' gestation	Pre-pregnancy Less than 10 weeks' gestation
In Pregnancy Monitoring	As per local policy (no additional study visits)	As per local policy (no additional study visits)
Delivery	Removal of cerclage at 37 weeks unless indicated earlier	Caesarean at term unless indicated earlier
28 Days after delivery	Collection of delivery and neonatal data from baby chart up to 28 days after birth.	Collection of delivery and neonatal data from baby chart up to 28 days after birth.
42 days after end of pregnancy	Remote Collection of medical data	Remote Collection of medical data *DATA COLLECTION FROM FIRST POST CERCLAGE PREGNANCY ONLY*

WHAT WILL HAPPEN TO MY INFORMATION

We will ask your permission to look at your medical notes and those of your baby for the first 28 days after delivery so that we can find out what happened to you both. If you don't have your baby in this hospital, we may contact your GP, or the hospital where you have the baby.

Although there is no study follow up visits, we will collect information about the care you receive during pregnancy, which may include scan images of your cervix taken in

prematurity clinic. We will only collect information about your current pregnancy, or the first pregnancy after you have consented to take part.
42 days after your pregnancy has ended, we will complete collection of your data, and you will no longer be enrolled in the study.

DO I HAVE TO TAKE PART

Whether you decide to take part or not is entirely up to you. Your decision will not affect the care you receive. Your obstetrician will offer you the treatment prescribed in the usual local guidelines.

WHAT IF I CHANGE MY MIND?

You are free to withdraw at any time from the trial, by contacting the local study team (details on page 10). If you withdraw before a cerclage is placed, you can discuss your care options with your obstetrician. If you change your mind after the cerclage is placed, you will continue you post operative care with the preterm surveillance pathway of your local unit, however we will not collect any further information.

WHAT ARE THE BENEFITS OF TAKING PART

Having either of the two cerclages will reduce your chance of having an early baby. However, taking part in the study may not have any direct benefit for your current pregnancy.
The research study will contribute to knowledge about the best surgical method to prevent premature birth in the event of a weakened cervix. This knowledge will benefit future patients and their children.

ARE THERE POTENTIAL SIDE EFFECTS TO TAKING PART

How the pros and cons of the two types of surgery are weighted is not necessarily the same for everyone. If you have any questions about the two surgeries, we encourage you to ask the doctor who spoke to you about this study.

Below, we have summarized the differences between the two procedures. If we discover risks during the study period that we have not already informed you about, you will be updated. You can then decide whether you still wish to participate.

	Transvaginal Cerclage	Laparoscopic cerclage
How the procedure is performed	Performed in early pregnancy. Vaginal surgery. Spinal anaesthesia. Removed after 36 completed weeks of pregnancy. Performed as a day case procedure (home within 24 hours, usually without an overnight stay)	Pre- pregnancy (or early pregnancy). Keyhole surgery. General anaesthesia. Performed as an inpatient procedure (admission for 24-48 hours, or until pain adequately controlled) Not removed- permanent cerclage which can be used in future pregnancies. Birth by caesarean section, vaginal delivery is not possible
Benefits	Often performed at local hospital. Vaginal delivery is possible Place of birth not affected	Can be used for subsequent pregnancies

	Transvaginal Cerclage	Laparoscopic cerclage
Risks	Bleeding (usually light spotting post procedure) Infection (<5%) Damage to surrounding structures (bowel, bladder, cervix) (<1%) Some cerclages require additional anaesthetic for removal (depends on type of cerclage). To be re-inserted in future pregnancies. Requires removal after 36 completed weeks of pregnancy, or sooner if clinically indicated.	The overall risk of serious complications from laparoscopy is approximately 2 women in every 1000 (uncommon) Damage to bowel, bladder, uterus or major blood vessels which would require immediate repair by laparoscopy or laparotomy(uncommon). However up to 15% of bowel injuries might not be diagnosed at the time of laparoscopy Failure to gain entry to abdominal cavity and to complete intended procedure 3–8 women in every 100 000 undergoing laparoscopies die because of complications (very rare) Hernia at site of entry **Frequent risks:** Bruising Shoulder-tip pain Wound gaping Wound infection Birth by caesarean section, vaginal delivery is not possible Carried out in larger hospitals, which can result in increased transportation time. Some local hospitals may also refer to larger units for delivery. Potential discomfort from the material after pregnancy Potential need for additional surgery if future pregnancy loss.

TERMINATION OF THE INVESTIGATION

If unforeseen circumstances arise during your pregnancy or childbirth, we will assess whether it is necessary to interrupt your participation in the study. The research study is under the supervision of an independent committee, which may propose to stop the study if there are unacceptable risks in continuing.

ADDITIONAL SUPPORTS

High Risk Pregnancy, and Pregnancy after loss can be difficult, especially if there are complications. Staff in the preterm birth clinic have experience working with people after loss and ensuring access to appropriate supports and counselling services in your local area. Other available supports include Tommys (www.tommys.org), The Miscarriage association (www.miscarriageassociation.org.uk) , SANDS (www.sands.org.uk) and Petals (www.petalscharity.org).

WHAT MEDICAL CARE WILL ME AND MY CHILD RECEIVE AT THE END OF THE RESEARCH STUDY?

Once you and your child's involvement in the study is over, they will continue to receive their usual birth and postpartum care.

YOUR INFORMATION

We will need to use information from you, from your medical records and your GP records for this research project.
This information will include:

- Initials
- NHS number
- Name
- Contact details
- Hospital Number

People will use this information to do the research or to check your records to make sure that the research is being done properly.
People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.
Aarhus University, Denmark is the sponsor of this research and is responsible for looking after your information. We will share your information related to this research project with the following types of organisations:

- **Kings College London**
- **Aarhus University Denmark**

We will keep all information about you safe and secure by:

- Information will be stored on a password protected database, with a unique study participant number used
- Only members of the study team will have access to the database.
- Only members of the local study/direct care team will have access to hospital records or identifying details.

INTERNATIONAL TRANSFERS

We may share or provide access to data about you outside the UK for research related purposes, as this is an international study and the sponsor of the study is **Aarhus University, Denmark**. This may include the type of surgery you had, details of your pregnancy, and you and your baby's outcome. We will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations: Universities or Research collaborators participating in this or similar studies where the research question or goal is aligned.
We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- Countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/uk-gdpr-guidance-and-resources/international-transfers/
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- We have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when this is legally required. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach

How will we use information about you after the study ends?

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Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for a maximum of **25** years. The study data will then be fully anonymised and securely archived or destroyed.s

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. If you wish to withdraw, please contact your local team using the contact details below.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records / your hospital / your GP. If you do not want this to happen, tell us and we will stop.
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- If you agree to take part in this study, and consent to your information being stored, we may contact you to invite you to take part in future studies.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED?

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK:

- Health Research Authority: (HRA) leaflet:

www.hra.nhs.uk/patientdataandresearch

- by asking one of the research team

by sending an email to leakha@rm.dk.

- by ringing us on Tel: +45 51910993
- by contacting our UK representative at Nicole.moriarty@nhs.net or 020 718 83634

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

The results will be published in international scientific journals after the end of the project. You will not be identified in any report/publication.

WHO IS ORGANISING AND FUNDING THE STUDY?

The study is supported by the Novo Nordisk Foundation (DKK 10,026,229).

The researchers have no financial interest in the contributing organisations. Additional funding may be applied for from private funds on an ongoing basis.

This study does not provide any additional financial support or reimbursement. All travel or transport costs associated with attending study-related appointments, procedures, or receiving care will remain your personal responsibility

WHAT IF THERE IS A PROBLEM?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact information below).

If you remain unhappy and wish to complain formally, you can do this through the Guy's and St Thomas'(GSTT) Patient Advice and Liason Service (PALS) on 020 7188 8801, pals@gstt.nhs.uk. The PALS team are based in the main entrance wing on the ground floor at St Thomas' Hospital and on the ground floor at Guy's Hospital in the Tower Wing.

If something does go wrong and you are harmed during the research, and this is due to someone's negligence then you may have grounds for a legal action for compensation against Guy's and St. Thomas' Hospital, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). If you are harmed due to the way the study has been set up or run, you may have grounds for legal action against Aarhus University, who are liable for any harm caused by the way the study has been arranged.

If at any time you have any unanswered questions, concerns, or a complaint about the study, please contact the study team (see below):

YOUR RIGHTS

We encourage you to read about your rights in the attached material; *"Rights of the subject in a health science research project"* before deciding on participation.

Where can you find out more about how my information is used?

You can find out more about how we use your information:

- www.hra.nhs.uk/information-about-patients/
- our leaflet available from:

www.guysandstthomas.nhs.uk/research/patients/use-of-data.aspx (For GSTT)

and https://www.kcl.ac.uk/research/research-environment/rgei/research-ethics/use-of-personal-data-in-research (for King's College London (KCL))

- by asking one of the research team (contact details included below)
- by contacting the Data Protection Officer:

For GSTT: Nick Murphy-O'Kane DPO@gstt.nhs.uk

For KCL: Olenka Cogias info-compliance@kcl.ac.uk)

FURTHER INFORMATION AND CONTACT

We hope that with this information you feel able to decide whether you want to participate. If you want to know more about the research project or have questions for the research group, please feel free to contact us.

Local Study Team:
-Coordinator: Nicole Moriarty nicole.moriarty@nhs.net
-Preterm Birth Surveillance clinic: Phone 020 7188 3634
-Address: Fetal Medicine Unit, 8th Floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, SE1 7EH London

For PALS (Patient Advice and Liaison Service):
Email: pals@gstt.nhs.uk
Phone: 020 7188 8801
Address: Westminster Bridge Road, SE1 7EH, London

WHO HAS REVIEWED THE STUDY?

This research has been reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by: West of Scotland REC 1.

THE RESEARCH GROUP

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