Nordic Randomized trial on laparoscopic versus vaginal cerclage

The NORACT trial

We hereby invite you to participate in a research project. Participation in the research project is voluntary, and you can withdraw your consent at any time. Withdrawal will have no consequences for your planned medical care.

TRIAL MANAGER:

Niels Uldbjerg, Professor in Obstetrics
Department of Clinical Medicine, Aarhus University & Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N
Phone: +45 20 67 94 20 | Email: uldbjerg@clin.au.dk

The research project is conducted by Lea Kirstine Hansen, MD, and PhD student (coordinating researcher), along with a NORACT Board consisting of experts in the field. The project is carried out in collaboration with several hospitals from the Nordic countries and England.

ABOUT THE PROJECT:

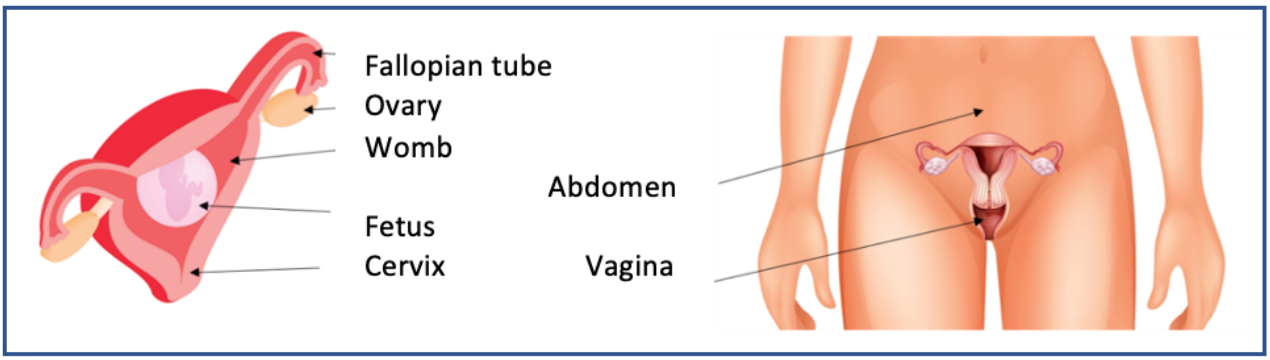
In women with an increased risk of premature birth due to a weak cervix, a supportive stitch of the cervix (cerclage) can be performed to try to prevent the cervix from opening prematurely and thus prevent premature birth.
The research project aims to compare the effect of two different surgical methods for performing the stitch and thereby prevent preterm birth.

In the enclosed patient information leaflet, you can read more about what the research project is about, what it means to participate and about your rights.

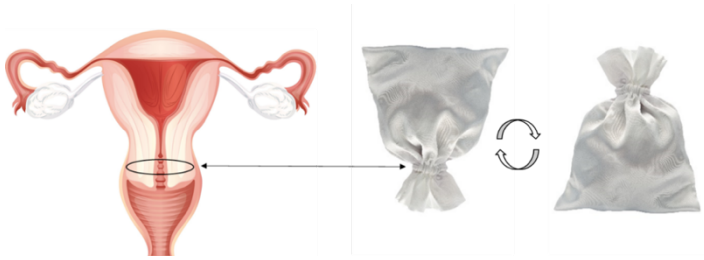
Before you decide whether you want to participate in the research project, you must fully understand what the project is about and why we are conducting it. We would therefore ask you to read the patient information leaflet carefully. You will be invited to have a personal conversation about the research project, where the information will be elaborated and where you can ask the questions you have about the project. You are welcome to bring a next of kin to the consultation.

PATIENT INFORMATION

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 to maintain the fetus inside the womb. 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 established in two ways:

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

PARTICIPATION:

We ask if you want to participate in the project because it has been assessed that you have a moderate or high risk of giving birth prematurely in your next pregnancy.

PARTICIPATION INVOLVES:

1. The type of cerclage you will be offered is chosen by chance (random allocation).
2. Before and during pregnancy, assessment of your cervix is performed with transvaginal ultrasound examination.
3. That we collect information from your health records about your surgery, your pregnancies and the babies you have after surgery. This has no effect on your or your children's further treatment.

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 weakened 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 project

PLAN FOR THE RESEARCH PROJECT:

A total of 210 women will participate in the research project from hospitals in Denmark, Sweden, Norway, Finland, Iceland and England. The research project has started in 2023 and is expected to last for up to 5 years. The first 18 months of the trial is carried out as a pilot study, to investigate if the research setup can be optimized during this time span. The results of the pilot study can lead to one of three scenarios: 1: The trial continues unchanged; 2) The trial continues with small alterations; 3) The trial is terminated.

During the trial, half of the participants will receive a vaginal cerclage and half a laparoscopic cerclage. It is by random allocation which of the two treatments is offered. Prior to participation in the trial, we will assess your previous pregnancies, perform a vaginal exam and a transvaginal ultrasound examination.

The vaginal 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 in spinal anesthesia, and you will not be fully anesthetized during the operation unless there are some special circumstances that make it necessary. The clinician will perform the surgery through your vagina, just like a gynaecological examination. The operation involves a small risk of bleeding, infection and pain.
Around or before week 37 of your pregnancy, the cerclage will be removed to allow for vaginal birth, if otherwise recommended.
The prenatal care you receive will be standard and like those who have a vaginal cerclage outside of the trial.

The laparoscopic cerclage

If the draw decides that you are offered the laparoscopic cerclage (keyhole surgery), it will be applied prior to your next pregnancy. In special circumstances, it can also be applied in very early pregnancy. The procedure takes place under general anesthesia, where you sleep during the operation. The surgeon will perform the surgery via small holes in your abdominal skin. The operation is associated with a small risk of bleeding, damage to the adjacent organs (bladder,

intestines or uterus) or infection. There is no known risk of the procedure affecting your fertility or risk of miscarriage.
The cerclage is permanent, i.e. it is not removed during or after your pregnancy. This means that you can only give birth by caesarean section. If you experience a missed miscarriage after weeks 9-10, it may be necessary to operate on you again to remove the cerclage to allow for medical management of the miscarriage. This happens very rarely.
Since the cerclage is not removed, it can be used again in subsequent pregnancies. The cerclage may cause discomfort outside of pregnancies. The nature and frequency of this is unknown, but experience tells us that it is limited. For some women, the laparoscopic cerclage is likely to prevent preterm birth more effectively than the vaginal cerclage, however, we do not know this for certain before this trial has been conducted.
The prenatal care you receive will be standard and like those who have a laparoscopic cerclage outside of the trial.

Ultrasound scans of the cervix

An ultrasound scan of the cervix is performed at the first examination, where it is assessed whether you can participate in the project. Ultrasound scans of the cervix may be performed shortly before and shortly after cerclage is inserted, in connection with a 20-week scan of the fetus, and possibly at later scans during your pregnancy. All scans of the cervix are performed transvaginally.

The treatment you will receive in connection with your pregnancy and childbirth will be the same as the women who have a vaginal or laparoscopic cerclage performed outside the framework of this project and follow usual local guidelines.

USEFULNESS AND IMPORTANCE OF THE STUDY

The research project will contribute to increase knowledge about the optimal surgical method to prevent premature birth in the event of a weakened cervix. This knowledge will benefit future patients and their babies.

RISKS, COMPLICATIONS AND DISADVANTAGES

How the pros and cons of the two types of surgery are weighted is not necessarily the same for everyone. Both interventions are described above. If you have any questions about the two surgeries, we encourage you to ask the doctor who informed you about this study. Below, we have summarized the pros, cons and risks. If we discover risks during the study period that we have not already informed you about, you will be informed. You can then decide whether you still wish to participate.

The vaginal cerclage	The laparoscopic cerclage
Performed in early pregnancy by vaginal access	Pre- pregnancy (or early pregnancy) keyhole surgery
Often performed at local hospital	Carried out in larger hospitals, which can result in increased transportation time
Spinal anesthesia	General anaesthesia
Small risk of infection, bleeding and pain	Small risk of bleeding, damage to the adjacent organs (bladder, intestines or uterus) or infection
Removed at pregnancy week 36/37	Not removed
Vaginal delivery is possible	Birth by caesarean section, vaginal delivery is not possible
To be re-established in case of new pregnancy	Can be used for subsequent pregnancies
	Potential discomfort from the material after pregnancy
	Potential need for new procedure due to late missed miscarriage
	Likely to be more effective than the vaginal cerclage, but this is not confirmed.

TERMINATION

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

INFORMATION ON ECONOMIC CONDITIONS

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.

YOUR INFORMATION

Consent to participate in the study includes access to disclosure and processing of necessary information about your surgery as well as other health information from your medical records and the records of your future newborn children. This means that the professionals working on the project (the independent monitoring staff, myself and project staff) can access information from the patient records. All data is stored and treated confidentially in accordance with Danish law. Anonymised data from the research project may be shared with other researchers in accordance with Danish law.

We will also ask you to consent to us contacting you again in the years after your birth with a view to whether you wish to participate in a follow-up investigation about how you and your child are doing. If you leave the study after you have given your consent, we will continue to collect and process information about you unless you specifically request this.

The results will be published in international scientific journals after the end of the project.

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.

Sincerely,

Lea Kirstine Hansen (coordinating researcher), Medical doctor, PhD student
Dept. of Obstetrics and Gynecology
Aarhus University Hospital
Palle Juul Jensens Boulevard 99
DK-8200 Aarhus N
Tel: 51910993, e-mail: lea.hansen@clin.au.dk

THE RESEARCH GROUP

Niels Uldbjerg, project sponsor and project manager, Professor, Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Denmark

Julie Glavind, Consultant, clinical associate professor, PhD, Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Denmark
Pernille Tine Jensen, Professor, Consultant, Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Denmark
Lise Qvirin Krogh, MD, PhD student, Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Denmark
Andrew Shennan, Professor, Department of Women and Children's Health, School of Life Course Sciences, FoLSM, King's College London, England
Oskari Heikinheimo, Professor, Department of Gynaecology and Obstetrics, Helsinki University Hospital, Finland
Hulda Hjartardóttir, MD, PhD, Department of Gynaecology and Obstetrics, Iceland University Hospital, Iceland
Kirsten Hald, Chief Physician, PhD, Department of Gynaecology and Obstetrics, Oslo University Hospital, Norway
Bo Jacobsson, Professor, Department of Gynaecology and Obstetrics, Gothenburg University Hospital, Sweden
Helena Karypidis, MD, PhD, Uppsala University Hospital, Sweden
Annie Lantto, MD, PhD student, Skånes University Hospital, Sweden