BMJ Open

# Lateral Episiotomy versus No Episiotomy to Reduce Obstetric Anal Sphincter Injury in Vacuum Assisted Delivery in Nulliparous Women: A Randomised Controlled Trial



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2018-025050 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 27-Jun-2018 |
| Complete List of Authors: | Bergendahl, Sandra; Karolinska Institutet, Department of Clinical Sciences<br>Ankarcrona, Victoria; Karolinska Institutet, Department of Clinical Sciences<br>Leijonhufvud, Åsa; Lunds Universitet, Department of Clinical Sciences Lund/Clinical Science Helsingborg<br>Hesselman, Susanne; Uppsala Universitet, Department of Women's and Children´s Health, Centre for Clinical Research Dalarna, Falu Hospital<br>Karlström, Sofie ; Karolinska Institutet, Department of Clinical Science, Intervention and Technology<br>Kopp-Kallner, Helena; Karolinska Institutet, Department of Women's and Children's Health<br>Brismar Wendel, Sophia; Karolinska Institutet, Department of Clinical Sciences |
| Keywords: | OBSTETRICS, Obstetric anal sphincter injury, Lateral episiotomy, Vacuum extraction, Pelvic floor ultrasound, Randomised controlled trial |
| | |

# Lateral Episiotomy versus No Episiotomy to Reduce Obstetric Anal Sphincter Injury in Vacuum Assisted Delivery in Nulliparous Women: A Randomised Controlled Trial

Sandra Bergendahl, MD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: sandra.bergendahl@sll.se

Victoria Ankarcrona, MD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: victoria.liversedge-ankarcrona@sll.se

Åsa Leijonhufvud, MD, PhD. Department of Clinical Sciences Lund/Clinical Science Helsingborg. Helsingborgs Lasarett, Svartbrödragränd 3-5, 251 87 Helsingborg, Sweden. E-mail: asa.leijonhufvud@skane.se

Susanne Hesselman, MD, PhD. Department of Women's and Children´s Health, Uppsala University and Centre for Clinical Research Dalarna, Falu Hospital, Sweden. E-mail: susanne.hesselman@ltdalarna.se

Sofie Karlström, MD. Department of Clinical Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden. E-mail: sofie.karlstrom@sll.se.

Helena Kopp Kallner, MD, PhD, Ass Prof. Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital Solna, 17176 Stockholm, Sweden. E-mail: helena.kopp-kallner@ki.se

Sophia Brismar Wendel*, MD, PhD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: sophia.brismar-wendel@sll.se

*Corresponding author

**Word count** 3738 words (main text)

**Protocol version** 2.1 date 180619

# Abstract

## Introduction

Obstetrical anal sphincter injury (OASIS) occurs in 5-7% of normal deliveries, and increases with vacuum extraction (VE) to 12-14% in nulliparous women in Sweden. Lateral/mediolateral episiotomy may reduce the prevalence of OASIS at VE in nulliparous women. The current use of episiotomy is restrictive, and the protective effect and consequences are uncertain. The purpose of this trial is to investigate if lateral episiotomy can reduce the prevalence of OASIS at VE in nulliparous women and to assess short- and long-term effects.

## Methods and analysis

This is a randomised controlled trial of lateral episiotomy versus no episiotomy in nulliparous women with a singleton, live fetus, after gestational week 34+0 with indication for VE. A lateral episiotomy of 4 cm is cut at crowning, 1-3 cm from the midline, at a 60° angle. The primary outcome is OASIS by clinical diagnosis analysed according to intention-to-treat. To demonstrate a 50% reduction in OASIS prevalence (from 12.4% to 6.2%), 709 women will be randomised at a 1:1 ratio. Secondary outcomes are pain, blood loss, other perineal injuries, perineal complications, Apgar score, cord pH, and neonatal complications. Web-based questionnaires at baseline, two months, one and five years, will be used to assess pain, incontinence, prolapse, sexual function, quality of life, and childbirth experience. A subset of women will receive follow-up by pelvic floor sonography and pelvic exam. Mode of delivery and recurrence of OASIS/episiotomy in subsequent pregnancies will be assessed at five and ten years using register data.

Ethics and dissemination

The trial is open for enrolment. We have formal ethical approval, full funding, and support from the national clinical research network. Women are interested in participation. The predominant restrictive view on episiotomy may limit recruitment. Results are of global interest and will be disseminated in peer-reviewed journals and at international congresses.

Trial registration

28 December 2015 at www.clinicaltrials.gov (NCT02643108).

## Article summary

*Strengths and limitations of this study*

- The main strength is the randomised trial design, which will provide evidence for routine or restrictive episiotomy at VE in nulliparous women.
- Another strength is the setting with relatively high OASIS rates and low episiotomy rates, enabling a realistic sample size.
- One limitation is that the primary outcome, diagnosis of OASIS, is made by clinical examination, which may limit diagnostic accuracy.
- Another limitation is the restrictive view on episiotomy, which may hamper trial feasibility.

## Keywords

Randomised controlled trial, lateral episiotomy, obstetric anal sphincter injury, vacuum extraction, operative vaginal delivery, nulliparous women, anal incontinence, sexual function, pelvic floor ultrasound.

# Background

Obstetric anal sphincter injury (OASIS) is considered to be a serious complication to vaginal delivery. It is the most important cause of female anal incontinence, and therefore important to avoid (1). OASIS occurs in 5-7% of spontaneous vaginal births and increases with operative vaginal delivery to 12-14% in nulliparous women in Sweden (2, 3). In 2016, approximately 10% (6.9-17.8%) of nulliparous women were delivered by vacuum extraction (VE) depending on delivery site, and only a negligible number were delivered by forceps (2).

The use of episiotomy in Sweden is restrictive and was reported in approximately 10% of all vaginal deliveries and 30% of VE in 2016, with large regional variation (15% to 60%) (2). The restrictive use of episiotomy spread in the 1990-ies, especially after Swedish publications reported little protective effect on severe perineal injury and increased early postpartum pain compared to spontaneous tears (4-6). The inability to reduce OASIS in normal delivery has been confirmed in repeated Cochrane meta-analyses and restrictive use is now generally recommended (7, 8). The restrictive approach has also influenced practice at operative vaginal delivery, supported by the uncertain effect of episiotomy in VE in the Swedish setting (9). Following decades of restrictive use, midwives and doctors may have lost knowledge in correctly performing and repairing episiotomies. There is an inverse correlation between a nation's rate of episiotomy and rate of OASIS, and the optimal rate of episiotomy in operative vaginal delivery is not known (10).

Several recent retrospective register studies have shown that nulliparous women who received a lateral or mediolateral episiotomy at VE had a reduced prevalence of OASIS compared to women without episiotomy (11-14). Lund et al compiled the outcome of 15 register studies in a meta-analysis published in 2016, and concluded that a mediolateral or lateral episiotomy

significantly reduced the risk of OASIS at VE in nulliparous women with aOR 0.53 (95% Confidence Interval (CI) 0.37-0.77)(15). Numbers needed to treat was 18.3 (95%CI 17.7-18.9). The protective effect of mediolateral or lateral episiotomy seemed most pronounced when performed in more than 75% of VE with aOR 0.37 (95%CI 0.15-0.92). The results from these studies were so promising that an official Swedish guideline and a new national educational program launched in 2017 advocated to consider a mediolateral episiotomy at operative vaginal deliveries in nulliparous women (16, 17).

In register studies, despite controlling for several confounding factors, there is a risk of selection bias, registering shortcomings, and confounding by indication. Furthermore, non-measured variables, such as operator skills and tissue properties might result in residual confounding. None of the register studies showing a protective effect of lateral/mediolateral episiotomy have adjusted for tissue properties or taken the operator's experience or track record of OASIS into account. Such factors may be balanced in a randomised controlled trial. Hence, several authors and institutions, including the Cochrane Collaboration and the Database of Uncertainties about the Effects of Treatments/National Institute for Health and Care Excellence Evidence Search, state that the protective effect of a lateral/mediolateral episiotomy at operative vaginal delivery should be investigated in an adequately sized randomised controlled trial (RCT) (8, 15, 18-20).

There is one published British pilot RCT on routine versus restrictive use of episiotomy (undefined type) in operative vaginal delivery in 200 nulliparous women, but the trial was underpowered mainly due to a fairly high rate of episiotomy (52%) in the restrictive group and moderate prevalence of OASIS in both groups (routine 8.1% vs. restrictive 10.9%) (21). The authors estimated that a sample size of 1600 women would have been necessary to

determine a difference at that level. Ethical concerns arise when a number of women will sustain an iatrogenic perineal injury to perhaps avoid OASIS, which may heal well after adequate suturing. Yet, only 4% of the women in the restrictive group in the British pilot trial had an intact perineum after operative vaginal delivery.

Many earlier studies on the effects of episiotomy do not specify the type, although mediolateral episiotomies are preferred in Europe, while lateral episiotomies are mainly used in Finland (10, 21, 22). It is evident that mediolateral and lateral episiotomies often are confused both in clinical practice and in research (15, 23, 24). In an effort to standardize terminology, Kalis et al stated that a lateral episiotomy "begins in the vaginal introitus 1 or 2 cm lateral to the midline and directed downwards towards the ischial tuberosity", while a mediolateral episiotomy is more unclear with a suggested definition starting within 3 mm of the midline and directed laterally at an angle of at least 60 degrees from the midline (25). In the EPITRIAL, Sagi-Dain et al use "lateral/mediolateral" episiotomy, defined as an incision at 45-60 degrees and 3-4 cm long (24).

We have decided to use lateral episiotomy in our RCT, defined further in the methods section. The purpose of the lateral episiotomy is to cut the bulbocavernous muscle, which is thought to constitute the main restraining tissue in the vaginal opening at crowning. Lateral episiotomy may affect the superficial transverse perineal muscle, but ideally not the levator muscle, perineal body, or margins of the external anal sphincter muscle, which may be a risk at a mediolateral episiotomy with an insufficient angle. Current evidence suggests little difference between the techniques regarding bleeding, postpartum perineal pain, and sexual resumption (26-30). A correlation between the extent of tissue damage and degree of pain has been observed, but conflicting observations on pelvic floor function and pain after any episiotomy

versus spontaneous perineal injury call for a long-term follow-up to assess the optimal treatment at delivery (31-34).

In all, to our knowledge, there is no published adequately sized RCT to assess the protective effect of lateral episiotomy at VE in nulliparous women, nor sufficient published data on long-term postpartum complications from episiotomy versus spontaneous perineal injury at VE.

## Methods and analysis

*Aim*

The aim of this RCT is to investigate if routine lateral episiotomy can reduce the incidence of OASIS at VE in nulliparous women, compared to a no-episiotomy-policy, and to assess short, medium, and long-term effects on pelvic floor symptoms with the two different episiotomy strategies.

*Study design and treatment allocation*

We used the SPIRIT checklist when writing our report (35, 36). Randomisation is performed on a 1:1 basis, based on computer-generated random permuted blocks provided by the independent, non-profit Karolinska Trial Alliance. Treatment group is allocated using sealed opaque envelopes placed on the VE equipment cart for immediate and easy access. When the decision to perform a VE has been made by the attending physician and the patient's consent has been verified, the envelope is opened by the assistant nurse or midwife. The allocated treatment is confirmed by the attending physician, the midwife, and the woman in labour. The allocated treatment cannot be blinded to women or investigators in the trial, nor at follow-up,

due to the design of intervention/no intervention. During analysis, group allocation will be open to the investigators, to enable both intention-to-treat and per protocol analysis.

*Setting*

All delivery wards in Sweden have been invited to participate in the trial. Presently, three sites are recruiting; Danderyd, Falun, and Helsingborg. All sites are located within large regional or university affiliated hospitals and have immediate access to a specialist obstetrician or senior registrar, anaesthesiologist, operating theatre, and a neonatal intensive care unit. Danderyd has approximately 6500 annual deliveries, of which 300 are VE in nulliparous women, while Falun and Helsingborg each have approximately 3500 annual deliveries, of which 150 are nulliparous VE.

*Characteristics of participants and informed consent*

All women expecting their first child, and planning to deliver vaginally at the study sites, are invited to participate. Written and oral information is given by midwifes and physicians at regular visits to antenatal care from gestational week 24. Women will also be approached at visits to the hospital before delivery. Written information is at present available in Swedish, English, and Arabic. Signed informed consent forms are forwarded to the research midwife or principal investigator at each site and documented in the woman's medical record. Women who have contraindications to vacuum extraction will not be invited to participate in the trial, neither will women with previous surgery for incontinence or pelvic organ prolapse. Ethical

Inclusion criteria

- Nulliparous woman
- Singleton, live fetus in cephalic presentation
- Gestational week 34+0 or more
- Indication for vacuum extraction
- Signed informed consent

Exclusion criteria

- Previous surgery for incontinence or prolapse

approval has been given to invite women in labour, if adequate pain relief has been given, and there is enough time to obtain informed consent. The woman's consent is verified by the attending physician before randomisation.

*Description of the intervention and comparison*

The decision to assist the delivery by vacuum extraction is made at the attending physician's discretion. In all women, the urinary bladder should be emptied by catheterization and adequate pain relief is recommended, prior to application of the vacuum cup. Pain relief may consist of epidural anaesthesia, a pudendal block, or local infiltration.

For women allocated to "lateral episiotomy", a lateral episiotomy is performed as follows. Local anaesthesia is recommended injecting Mepivacaine, Lidocaine, or similar local anaesthetic in the hymeneal plane, 1 ml subcutaneously at the incision point and 9 ml in a fan-like fashion from the incision point. The vacuum cup is then applied and the extraction is performed synchronously with the contractions and pushing efforts, until the cup is visible in the vaginal opening, which corresponds to the crowning head.

Lateral episiotomy is then performed using specific episiotomy scissors, Mayo scissors, or similar scissors.

- Distance from incision point to the posterior fourchette: at least 1 cm, up to 3 cm.
- Angle from the sagittal or parasagittal plane: 60° (45-80°, aim at the ischiadic tuberosity)
- Length of the incision: 4 cm (3-5 cm)

For women allocated to "no episiotomy", the perineum will possibly remain intact or tear spontaneously. The operator may only perform episiotomy on fetal indication or on the clinical judgement that extensive perineal injury cannot be avoided, which should comprise less than 30% of the VE, if practice is unchanged. Any episiotomy should be lateral. Episiotomy rates in trial participants and non-participants will be followed continuously by the principal investigators.

All women will receive perineal protection using verbal guiding and manual support of the perineum during the delivery of the fetal head and body. The third stage, examination and diagnosis of perineal tears is managed according to clinical routine. The clinical diagnosis of OASIS is our primary outcome. Adequate pain relief should again be offered to enable a thorough clinical bi-digital rectal/vaginal exam to reveal any injury to the sphincter muscles or rectum. The diagnosis is confirmed by a specialist gynaecologist/obstetrician or senior registrar. Suturing of OASIS is performed by a specialist gynaecologist/obstetrician or senior registrar and managed according to clinical routine or as suggested in the standard operating procedures.

*Primary and secondary outcomes*

The primary outcome is OASIS, also called third or fourth degree perineal tear, engaging the external or internal anal sphincter muscles (International Classification of Diseases 10 code O70.2 or O70.3). Diagnosis is made by clinical examination by a specialist obstetrician/gynaecologist or senior registrar.

Short-term secondary outcomes are other degrees of perineal injury, blood loss postpartum, complications to episiotomy or perineal injuries such as dehiscence or infection, Apgar score,

umbilical artery pH <7.05, shoulder dystocia, admission to the Neonatal ward, neonatal injury (scalp trauma, obstetric brachial plexus palsy, cerebral injury, hypoxic ischemic encephalopathy, respiratory distress, and fractures as diagnosed by the neonatologist), duration of hospital stay after delivery, perineal pain, and childbirth experience 1-3 days after delivery by Visual Analogue Scale. The data will be collected from the Swedish Pregnancy Register and the National Quality Register for Neonatal Care. Information from maternal and neonatal medical records is automatically forwarded to the registers when the medical records are signed for archiving. The Swedish Pregnancy Register covers 90% of pregnancies in Sweden and virtually all pregnancies at the study sites (37). The register consists of three parts; the Swedish Maternal Health Care Register, launched in 1999, the Swedish National Quality Register for Prenatal Diagnosis, with data from 2010, and the Obstetric Register, which started in 2014. The three registers thus provide detailed information of pregnancies, labours, and the postpartum period. The National Quality Register for Neonatal Care covers all 37 neonatal wards and neonatal intensive care units in Sweden since 2012, and consists of data from newborns admitted to hospital care from birth until 28 days of age. The primary outcome OASIS and trial specific data not available from the registers will be collected in electronic case report forms supplied and monitored by Karolinska Trial Alliance.

Medium-term secondary outcomes, to be assessed by clinical examination and sonographic imaging six to 12 months after delivery, in at least one study site, are effects on the pelvic floor anatomy. The OASIS diagnosis and the type of episiotomy will be quality controlled. Descriptive data on pelvic floor muscle injury will be collected, specifically injuries to the sphincters and the levator ani muscle. The women at this site will undergo a structured pelvic exam performed by consultant gynaecologists in an independent Centre for Pelvic Floor Disorders, including measurement of any scar, a clinical assessment of pelvic floor muscle

function by a six-point muscle strength score, prolapse staging by the pelvic organ prolapse quantification system, and a high-resolution 2D perineal and 3D endovaginal and transrectal ultrasound. Data from this follow-up will be collected using electronic case report forms supplied and monitored by Karolinska Trial Alliance.

Medium- and long-term secondary outcomes, to be assessed by web-based questionnaires, are duration of pain medication after delivery, symptoms regarding anal and urinary incontinence, bowel function, prolapse, and sexual function at baseline, two months (up to six months), 12 months (up to 18 months), and five years (up to five years and six months) after delivery. The questions are based on the questionnaires used by the Swedish Perineal Tear Register, and will be distributed at identical intervals (baseline, two, and 12 months postpartum) as well as after five years. Anal incontinence is assessed by Wexner score in these questionnaires (38). Childbirth experience will be assessed at two months postpartum using the revised short form of the Birth Satisfaction Scale and the Childbirth Experience Questionnaire (39, 40). The questionnaires "Female Sexual Function Index" and "Female Sexual Distress Scale" will be used for in-depth assessment of sexual function at baseline, one and five years (41-43). Quality of life will be measured using the questionnaire Euro-QoL-5D at baseline, one and five years (44). The questionnaires are administered by an independent provider of patient surveys and data is forwarded to Karolinska Trial Alliance. We will also assess mode of delivery, episiotomy, and OASIS in the subsequent pregnancy at five years and ten years after the index delivery by using data from the Swedish Pregnancy Register. The schedule of all follow-up assessments is illustrated in Figure 1. All collaborators have signed or are obliged under law to keep data confidential during and after the trial.

*Adverse events, data collection and safety*

All randomised women are offered a clinical (apart from the trial) follow-up at 6 months and free and easy access to medical care in association with the episiotomy or perineal tear at the study site during the study period of five years. All women will receive postpartum care as individually needed. Serious adverse events, such as death, a life-threatening event, admission to intensive care, persistent or significant disability or incapacity, or other medically important event, will be reported in a separate form and evaluated by the sponsor and principal investigators continuously. The Karolinska Trial Alliance will monitor the trial conduct, as well as data collection and safety after start-up, midterm, and before closure at each site, covering 20% of randomised women. Karolinska Trial Alliance will also manage important study protocol modifications and communicate these to relevant parties.

*Statistical methods*

Baseline data will be summarized by descriptive statistics as appropriate; mean and standard deviation, median, upper and lower quartiles, minimum and maximum, or frequency tables, stratified by the two arms.

Data will be analysed by intention-to-treat and per protocol. The primary outcome variable, clinical diagnosis of OASIS, will be presented in numbers as incidence rate in the two allocation groups (intention-to-treat) and according to received treatment (per protocol). The protective effect of lateral episiotomy will be calculated as a relative risk of OASIS with 95% confidence intervals, adjusting for study site and other possible factors not balanced by randomisation.

Further analyses will compare secondary outcomes using test of proportions, t-test and logistic regression depending on variable characteristics. In the per protocol analysis of

OASIS, we will adjust for possible confounders/effect modifiers such as study site, country of birth, maternal body mass index, operator experience, long duration of labor and second stage, epidural, use of oxytocin, fetal birthweight, head circumference, station and position. We also aim to create a prediction model of the protective effect of lateral episiotomy to aid clinical decision.

Outcomes based on evaluation scores will be analysed by non-parametric tests and paired analyses for change over time in the subgroups using Sign test. Details of the statistical analysis will be supplied in the Statistical Analysis Plan, to be finalized in collaboration with statisticians from the Karolinska Institute in a separate document before the data lock.

*Sample size calculation*

The sample size has been calculated based on data from Lund et al, suggesting a 50% reduction of OASIS in VE, when lateral/mediolateral episiotomy is performed (15). The average rate of OASIS in VE in Sweden was 12.4% in 2016 according to the Swedish Medical Birth Register. A reduction of OASIS from 12.4% to 6.2% can be detected with 80% power and less than 5% risk of alpha-error (p-value <0.05) with 354 women in each group using Chi-square test comparing two independent proportions in a two-sided test (3% missing outcome). A smaller reduction is clinically valuable, although the risk-benefit relationship between receiving a prophylactic episiotomy and the chance of an intact perineum may limit the feasibility of a larger trial in a setting with a restrictive episiotomy policy. We have obtained ethical approval to randomise a total of 1400 women, which enables us to detect a reduction in OASIS rate at VE from 12.4% to 7.8%.

*Interim analyses*

The Karolinska Trial Alliance will monitor primary outcome data using the electronic case report forms, in which the diagnosis of OASIS is registered. We will perform a first interim analysis after 350 randomised women, to detect a possible OASIS prevalence reduction from 12.4% to 2.5% with 80% power and p-value <0.01, in concordance with the pronounced reduction observed in the Dutch register study by van Bavel et al (14). If a reduction of OASIS is achieved at this level, the trial will be discontinued and modified, as the clinical equipoise has been sufficiently disturbed. A second interim analysis will be performed after 709 randomised women, to detect a possible 50% reduction from 12.4% to 6.2% with 80% power and p-value <0.05. Similarly, the trial will be stopped if a 50% reduction is detected. If feasible, we will continue the trial until 1400 women have been randomised. Depending on the size of the delivery ward, each site will contribute with approximately 5% of nulliparous women giving birth vaginally (70-200 patients annually). Inclusion rate is expected to be two to three patients per week at a site with 300 annual vacuum extractions in nulliparous women, if 50% of women accept participation.

## Ethics and dissemination

Sweden has the potential for a perfect setting to perform a randomised controlled trial of routine lateral episiotomy versus no episiotomy at VE in nulliparous women, since the episiotomy rate is generally low and the prevalence of OASIS in nulliparous VE is relatively high. We expect that adherence to non-intervention in the control group will be high, facilitating the detection of any difference in OASIS incidence. The timing with new guidelines for considering episiotomy further improves the setting of the study. It is crucial to undertake and complete the trial now before new guidelines, advocating a liberal use of episiotomy in VE in nulliparous women, are implemented despite low-grade evidence and lack of long-term follow-up.

The low episiotomy rate may also limit the feasibility of the study. A survey regarding episiotomy preferences and indications was performed in 2012 among 297 delegates at the biennial Nordic obstetrical and gynaecological conference in Norway (23). Only 17% of the 54 Swedish senior consultants who participated perceived instrumental delivery as an indication for episiotomy, while fetal distress was the most accepted indication. Consequently, 87% of the Swedish doctors never, seldom, or only sometimes performed an episiotomy at VE. Thus, experience from episiotomy may be lacking and there is a need for education and training at the sites when the study is being implemented.

Prior to the previously described British pilot RCT, Macleod and Murphy performed a survey among 1631 obstetricians and specialist registrars in the United Kingdom and Ireland in 2006 with regard to operative vaginal delivery and the use of episiotomy (21, 45). The great majority (72%) reported a restrictive attitude towards use of episiotomy in VE, although less than 10% held the view that episiotomy increased the risk of OASIS. Over 65% of responders said that they would be happy to participate in an RCT of restrictive versus routine use of episiotomy at operative vaginal delivery. We estimate that a similar proportion of Swedish physicians and midwives hold the same view, although hesitance to recruit women due to private opinions on episiotomy may be another limitation.

The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from all participating women as described above. Pregnant women are generally curious about the trial and the majority of approached women consent to participate, particularly motivated by a thorough follow-up no matter what perineal injury. The interest from pregnant women is

consistent with the observation that 85% of invited women agreed to participate in the pilot RCT by Murphy et al, although the rational for participation may have been the chance to avoid an episiotomy in their setting (21).

Considering the admitted knowledge gap regarding effectiveness and consequences of routine lateral/mediolateral episiotomy in operative vaginal deliveries, we anticipate broad interest in the results from this trial (8, 15, 18-20). Being a non-commercial academic study, the investigators will author the results adhering to the authorship criteria recommended by the International Committee of Medical Journal Editors. We intend to disseminate the results by publication in peer-reviewed medical journals and public press, and by presentations at national and international congresses. Data can be made available for future meta-analyses to improve informed practice.

## List of abbreviations

EVA – Episiotomy in Vacuum Assisted delivery

OASIS – Obstetrical anal sphincter injury/injuries

VE – Vacuum Extraction

RCT – Randomised Controlled Trial

OR – Odds ratio

## Declarations

*Ethics approval and consent to participate*

The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from all participating women.

*Consent for publication*

If case reports will be published, consent will be obtained from relevant parties.

*Availability of data and material*

The datasets generated and/or analysed are not publicly available due the possibility to extract personal information, but may be made available from the corresponding author on request. All principal investigators will be given access to the final cleaned datasets and submissions for publication will be made in agreement. To ensure confidentiality, data dispersed to collaborators will be blinded of any identifying participant information.

*Competing interests*

The authors have no competing interests to declare.

*Funding*

This work is fully funded by the Swedish Research Council (grant number 2016-00526).

*Author contributions*

Sandra Bergendahl and Victoria Ankarcrona are investigators and responsible for the implementation of the trial, and manuscript draft and revision. Åsa Leijonhufvud and Susanne

Hesselman are principal investigators at Helsingborg and Falun sites and responsible for implementation of the trial, and manuscript draft and revision. Sofie Karlström is responsible for the design, implementation, and investigations in the sub-study of pelvic floor anatomy at six to 12 months after delivery. Helena Kopp Kallner is responsible for the manuscript revision, funding, and study design. Sophia Brismar Wendel is overall responsible for the implementation of the trial, manuscript draft and revision, funding, study design, and the original idea of the study. All authors have participated in manuscript writing and have approved the final version.

# References


1. Bols EM, Hendriks EJ, Berghmans BC, Baeten CG, Nijhuis JG, de Bie RA. A systematic review of etiological factors for postpartum fecal incontinence. Acta obstetricia et gynecologica Scandinavica. 2010;89(3):302-14.
2. Annual report 2016, Swedish Pregnancy Register (in Swedish) [Internet]. MedSciNet. 2016 [cited 18 dec 2017]. Available from: https://www.medscinet.com/gr/uploads/hemsida/dokumentarkiv/GR_Årsrrapport_2016_2.1.pdf.
3. Waldenstrom U, Ekeus C. Risk of obstetric anal sphincter injury increases with maternal age irrespective of parity: a population-based register study. BMC pregnancy and childbirth. 2017;17(1):306.
4. Rockner G, Fianu-Jonasson A. Changed pattern in the use of episiotomy in Sweden. British journal of obstetrics and gynaecology. 1999;106(2):95-101.
5. Rockner G, Henningsson A, Wahlberg V, Olund A. Evaluation of episiotomy and spontaneous tears of perineum during childbirth. Scand J Caring Sci. 1988;2(1):19-24.
6. Rockner G, Wahlberg V, Olund A. Episiotomy and perineal trauma during childbirth. J Adv Nurs. 1989;14(4):264-8.
7. Carroli G, Mignini L. Episiotomy for vaginal birth. Cochrane database of systematic reviews (Online). 2009(1):CD000081.
8. Jiang H, Qian X, Carroli G, Garner P. Selective versus routine use of episiotomy for vaginal birth. Cochrane database of systematic reviews (Online). 2017;2:CD000081.
9. Simic M, Cnattingius S, Petersson G, Sandstrom A, Stephansson O. Duration of second stage of labor and instrumental delivery as risk factors for severe perineal lacerations: population-based study. BMC pregnancy and childbirth. 2017;17(1):72.
10. Blondel B, Alexander S, Bjarnadottir RI, Gissler M, Langhoff-Roos J, Novak-Antolic Z, et al. Variations in rates of severe perineal tears and episiotomies in 20 European countries: a study based on routine national data in Euro-Peristat Project. Acta obstetricia et gynecologica Scandinavica. 2016;95(7):746-54.
11. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. BJOG : an international journal of obstetrics and gynaecology. 2008;115(1):104-8.
12. Raisanen S, Vehvilainen-Julkunen K, Cartwright R, Gissler M, Heinonen S. Vacuum-assisted deliveries and the risk of obstetric anal sphincter injuries-a retrospective register-based study in Finland. BJOG : an international journal of obstetrics and gynaecology. 2012;119(11):1370-8.
13. de Vogel J, van der Leeuw-van Beek A, Gietelink D, Vujkovic M, de Leeuw JW, van Bavel J, et al. The effect of a mediolateral episiotomy during operative vaginal delivery on the risk of developing obstetrical anal sphincter injuries. American journal of obstetrics and gynecology. 2012;206(5):404 e1-5.
14. van Bavel J, Hukkelhoven C, de Vries C, Papatsonis DNM, de Vogel J, Roovers JWR, et al. The effectiveness of mediolateral episiotomy in preventing obstetric anal sphincter injuries during operative vaginal delivery: a ten-year analysis of a national registry. International urogynecology journal. 2017.
15. Lund NS, Persson LK, Jango H, Gommesen D, Westergaard HB. Episiotomy in vacuum-assisted delivery affects the risk of obstetric anal sphincter injury: a systematic review and meta-analysis. European journal of obstetrics, gynecology, and reproductive biology. 2016;207:193-9.
16. Anal Sphincter Injuries: A Systematic Review and Assessment of Medical, Social and Ethical Aspects. SBU Systematic Review Summaries. Stockholm2016.

17. Bäckenbottenutbildning. Stockholm, Sweden: LÖF Landstingens Ömsesidiga Försäkring; 2017. Available from: http://backenbottenutbildning.se/index.php.
18. Revicky V, Nirmal D, Mukhopadhyay S, Morris EP, Nieto JJ. Could a mediolateral episiotomy prevent obstetric anal sphincter injury? European journal of obstetrics, gynecology, and reproductive biology. 2010;150(2):142-6.
19. Sagi-Dain L, Sagi S. Morbidity associated with episiotomy in vacuum delivery: a systematic review and meta-analysis. BJOG : an international journal of obstetrics and gynaecology. 2015;122(8):1073-81.
20. Verghese TS, Champaneria R, Kapoor DS, Latthe PM. Obstetric anal sphincter injuries after episiotomy: systematic review and meta-analysis. International urogynecology journal. 2016.
21. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. BJOG : an international journal of obstetrics and gynaecology. 2008;115(13):1695-702; discussion 702-3.
22. Raisanen SH, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Lateral episiotomy protects primiparous but not multiparous women from obstetric anal sphincter rupture. Acta obstetricia et gynecologica Scandinavica. 2009;88(12):1365-72.
23. Fodstad K, Staff AC, Laine K. Episiotomy preferences, indication, and classification--a survey among Nordic doctors. Acta obstetricia et gynecologica Scandinavica. 2016;95(5):587-95.
24. Sagi-Dain L, Bahous R, Caspin O, Kreinin-Bleicher I, Gonen R, Sagi S. No episiotomy versus selective lateral/mediolateral episiotomy (EPITRIAL): an interim analysis. International urogynecology journal. 2017;2017 Sep 20. doi: 10.1007/s00192-017-3480-7. [Epub ahead of print].
25. Kalis V, Laine K, de Leeuw JW, Ismail KM, Tincello DG. Classification of episiotomy: towards a standardisation of terminology. BJOG : an international journal of obstetrics and gynaecology. 2012;119(5):522-6.
26. Fodstad K, Staff AC, Laine K. Effect of different episiotomy techniques on perineal pain and sexual activity 3 months after delivery. International urogynecology journal. 2014;25(12):1629-37.
27. Fodstad K, Laine K, Staff AC. Different episiotomy techniques, postpartum perineal pain, and blood loss: an observational study. International urogynecology journal. 2013;24(5):865-72.
28. Karbanova J, Rusavy Z, Betincova L, Jansova M, Necesalova P, Kalis V. Clinical evaluation of early postpartum pain and healing outcomes after mediolateral versus lateral episiotomy. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2014;127(2):152-6.
29. Karbanova J, Rusavy Z, Betincova L, Jansova M, Parizek A, Kalis V. Clinical evaluation of peripartum outcomes of mediolateral versus lateral episiotomy. Int J Gynaecol Obstet. 2014;124(1):72-6.
30. Necesalova P, Karbanova J, Rusavy Z, Pastor Z, Jansova M, Kalis V. Mediolateral versus lateral episiotomy and their effect on postpartum coital activity and dyspareunia rate 3 and 6 months postpartum. Sex Reprod Healthc. 2016;8:25-30.
31. De Souza A, Dwyer PL, Charity M, Thomas E, Ferreira CH, Schierlitz L. The effects of mode delivery on postpartum sexual function: a prospective study. Bjog. 2015;122(10):1410-8.
32. Fodstad K, Staff AC, Laine K. Sexual activity and dyspareunia the first year postpartum in relation to degree of perineal trauma. Int Urogynecol J. 2016;27(10):1513-23.

33. Signorello LB, Harlow BL, Chekos AK, Repke JT. Postpartum sexual functioning and its relationship to perineal trauma: a retrospective cohort study of primiparous women. Am J Obstet Gynecol. 2001;184(5):881-8; discussion 8-90.
34. Dogan B, Gun I, Ozdamar O, Yilmaz A, Muhcu M. Long-term impacts of vaginal birth with mediolateral episiotomy on sexual and pelvic dysfunction and perineal pain. J Matern Fetal Neonatal Med. 2017;30(4):457-60.
35. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krle AJK, et al. SPIRIT 2013 Statement: defining standard protocol items for clinical trials. Rev Panam Salud Publica. 2015;38(6):506-14.
36. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krleza-Jeric K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-7.
37. Stephansson O, Petersson K, Bjork C, Conner P, Wikstrom AK. The Swedish Pregnancy Register - for quality of care improvement and research. Acta obstetricia et gynecologica Scandinavica. 2017.
38. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Diseases of the colon and rectum. 1993;36(1):77-97.
39. Hollins Martin CJ, Martin CR. Development and psychometric properties of the Birth Satisfaction Scale-Revised (BSS-R). Midwifery. 2014;30(6):610-9.
40. Dencker A, Taft C, Bergqvist L, Lilja H, Berg M. Childbirth experience questionnaire (CEQ): development and evaluation of a multidimensional instrument. BMC pregnancy and childbirth. 2010;10:81.
41. Derogatis LR, Rosen R, Leiblum S, Burnett A, Heiman J. The Female Sexual Distress Scale (FSDS): initial validation of a standardized scale for assessment of sexually related personal distress in women. J Sex Marital Ther. 2002;28(4):317-30.
42. Ryding EL, Blom C. Validation of the Swedish version of the Female Sexual Function Index (FSFI) in women with hypoactive sexual desire disorder. J Sex Med. 2015;12(2):341-9.
43. Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther. 2005;31(1):1-20.
44. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-43.
45. Macleod M, Murphy DJ. Operative vaginal delivery and the use of episiotomy--a survey of practice in the United Kingdom and Ireland. European journal of obstetrics, gynecology, and reproductive biology. 2008;136(2):178-83.

**Figure 1. Schedule of enrolment, interventions, and assessments in the EVA trial.**

| | STUDY PERIOD | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Enrolment** | **Allocation** | **Post-allocation** | | | | | **Close-out** |
| **TIME POINT** | ***-4m*** | **0** | ***0m*** | ***2m*** | ***6m*** | ***1y*** | ***5y*** | ***10y*** |
| **ENROLMENT:** | | | | | | | | |
| Information | x | | | | | | | |
| Informed consent | x | | | | | | | |
| Inclusion/exclusion criteria | x | | | | | | | |
| Randomisation | | x | | | | | | |
| **INTERVENTIONS:** | | | | | | | | |
| Episiotomy | | x | | | | | | |
| No episiotomy | | x | | | | | | |
| **ASSESSMENTS:** | | | | | | | | |
| Background variables | x[1] | | x[2] | | | | | |
| Data from Pregnancy register (primary and secondary endpoints) | | | x[3,4] | | | | x[5] | x[6] |
| Data from SNQ on neonatal outcome (secondary endpoints) | | | x | | | | | |
| Questionnaire BR 1[7] | | | x | | | | | |
| Questionnaires FSFI+FSDS | | | x | | | x | x | |
| Questionnaire Euro-Qol-5D | | | x | | | x | x | |
| Questionnaire BSS-R | | | | x | | | | |
| Questionnaire CEQ 2.0 | | | | x | | | | |
| Questionnaire BR 2[8] (8 w) | | | | x | | | | |
| Questionnaire BR 3[9] (1 y) | | | | | | x | x | |
| Ultrasound evaluation | | | | | x | | | |
| POP-Q score | | | | | x | | | |
| Measurements of scar | | | | | x | | | |
| Questionnaire Q-SOPhIE | | | | | x | | | |
| Serious adverse events[10] | | x | x | x | x | x | x | x |

[1] maternal age, country of birth, weight and height at registration in the antenatal clinic
[2] use of oxytocin, use of regional or local anaesthesia, birthweight, head circumference, neonatal length, second stage duration, indication for vacuum extraction, fetal position and station, operator skills, number of pulls, use of sequential instruments
[3] perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH, and birth related diagnosis)
[4] birth experience, duration of hospital stay
[5] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[6] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[7] "Uppgifter om hälsa före graviditeten"
[8] "Din värdering av behandlingen av förlossningsbristningen (ca 8 veckor)"
[9] "Din värdering av behandlingen av förlossningsbristningen (ca 1 år)"
[10] Serious adverse events (death, intensive care, disability or other important serious medical event) will be reported continuously from allocation until close-out in a separate form.

**Appendix.** Patient information and informed consent form

## Invitation to first-time mothers

# The EVA-trial: Lateral Episiotomy in Vacuum Assisted Delivery

Hello first-time mother!

**In this leaflet, you are invited to participate in a medical research trial investigating how to avoid large perineal tears during vacuum assisted delivery.**

Sometimes it is necessary to assist the delivery by using a ventouse suction cup (vacuum assisted delivery). During this type of delivery, it is slightly more common to experience larger tears in the area between the vagina and anus (the perineum), which can involve the anal muscles.

EVA stands for Episiotomy in Vacuum Assisted delivery.

The purpose of this trial is to investigate if it is better to proactively cut (lateral episiotomy), or to leave the perineum to possibly tear spontaneously. The overall aim is to study how larger tears involving the anal muscles can be avoided during vacuum assisted delivery.

***What will we be doing?***

**By intentionally cutting we aim to redirect the tear away from the anal muscles. However, a cut can be more painful than a spontaneous tear whilst healing. Therefore, we would like to ask you, if you require a vacuum assisted delivery, would you consider joining a trial in which you would be randomly selected to undergo a lateral episiotomy (a cut) or a delivery with no cut, but the potential of a spontaneous tear?**

Random selection is a scientific method used to avoid selection errors when dividing patients into separate treatment groups.

If you do require a vacuum assisted delivery you will always receive pain relief. Before a cut an additional local pain relief is given to numb the area around the vagina. If you are randomly selected for a lateral episiotomy this will be performed as the baby's head is being delivered by making a small diagonal cut from the vagina and out to one side. Most women do not feel the cut and do not experience any difference compared to having a spontaneous tear.

All patients will receive the same perineal support to avoid tearing. This means we will manually support the perineum and guide you during your contractions. After delivery, everyone will be properly examined and any cut or tear will be repaired. Larger tears are always repaired in the operating theatre by an experienced doctor.

***How will we follow up?***

**Regardless of which group you belong to, you will receive equal care and follow up.** During the follow up we will collect data from your medical records and from registers regarding the delivery and if there were any complications to you or the baby. You will receive questionnaires on the postnatal ward, 2 months, and 1 year after delivery. The questions cover urine and bowel issues as well as sexual function, quality of life, and your childbirth experience. The questionnaires will take 5-10 minutes to complete. You will be offered a follow up visit at 6 months after the delivery. We will also contact you for a follow up at 5 years after delivery.

***Your integrity and safety***

**Participation is voluntary.** It will not affect your care if you choose not to participate. If you decide to participate, your answers are important regardless of whether you experienced complications or not. We aim to improve care during childbirth, specifically during vacuum assisted delivery, and to improve the long-term health and wellbeing of women. Therefore, we need information about your experiences.

Your answers from the questionnaire are kept confidential. They will only be available to the research group (find details below) and will not be included in your medical records. The answers are anonymous and can only be linked to your personal data by the research group. An independent investigator may review the research and will in that case require access to the original data, including medical records and questionnaire answers. The investigator will treat all data as confidential information.

**The medical data and questionnaire answers will be reported as a group so your participation will not be visible in the study results.**

If you wish, you can receive the result from the study when it is published. All data will be kept for 10 years before it is destroyed. Once per year you can request information about your personal data. Please contact us for more information. Your hospital is legally responsible for the personal data in this trial.

*Thank you for your time and consideration to participate!*

**Susanne Hesselman**
Senior Consultant, PhD
Falun Hospital
susanne.hesselman@ltdalarna.se
023-49 2000

**Åsa Leijonhufvud**
Senior Consultant, PhD
Helsingborg Hospital
asa.leijonhufvud@skane.se
042-406 2227

**Helen Fagraeus**
Research midwife
Danderyd Hospital
helen.fagraeus@sll.se
070-737 4988, 08-123 570 22

**Sophia Brismar Wendel**
Senior Consultant, PhD
Danderyd Hospital
sophia.brismar-wendel@sll.se
08-123 585 64

**Informed Consent Form**

# The EVA-trial: Lateral Episiotomy in Vacuum Assisted Delivery

I agree to participate in the EVA-trial, if I would need a vacuum assisted delivery. I know that participation is voluntary and I can at any time change my mind. If I choose not to participate in any part of the follow-up, it will not affect the medical care I receive.

| | |
|---|---|
| Signature | Date |
| Name | Place |
| ”Personnummer” | E-mail (also after delivery) |
| | Mobile number (also after delivery) |
| Signature of researcher/informer | Date |
| Name of researcher/informer | Clinic/Place |

Please hand the consent form to your midwife, who will send it to the responsible investigator at your hospital. The midwife will make a note in your Obstetrix record. You can also bring the consent form along to the delivery ward when it is time to give birth.

# Reporting checklist for protocol of a clinical trial

Based on the SPIRIT guidelines. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | #2a | Trial identifier and registry name. If not yet registered, name of intended registry | 4 |
| Trial registration: data set | #2b | All items from the World Health Organization Trial Registration Data Set | 4 |
| Protocol version | #3 | Date and version identifier | 2 |
| Funding | #4 | Sources and types of financial, material, and other support | 19 |
| Roles and responsibilities: contributorship | #5a | Names, affiliations, and roles of protocol contributors | 1-2 |
| Roles and responsibilities: sponsor contact information | #5b | Name and contact information for the trial sponsor | 2 |
| Roles and responsibilities: sponsor and funder | #5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 19 |
| Roles and responsibilities: committees | #5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the | 19 |

| | | | |
|---|---|---|---|
| | | trial, if applicable (see Item 21a for data monitoring committee) | |
| Background and rationale | #6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 5-8 |
| Background and rationale: choice of comparators | #6b | Explanation for choice of comparators | 8-9 |
| Objectives | #7 | Specific objectives or hypotheses | 8 |
| Trial design | #8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory) | 8-9 |
| Study setting | #9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 9 |
| Eligibility criteria | #10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 9 |
| Interventions: description | #11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 10-11 |
| Interventions: modifications | #11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease) | 10 |
| Interventions: adherance | #11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) | 10-11 |
| Interventions: concomitant care | #11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 11, 13 |
| Outcomes | #12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 11-13 |

| | | | |
|---|---|---|---|
| Participant timeline | #13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 24 |
| Sample size | #14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 15 |
| Recruitment | #15 | Strategies for achieving adequate participant enrolment to reach target sample size | 9 |
| Allocation: sequence generation | #16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 8 |
| Allocation concealment mechanism | #16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 8 |
| Allocation: implementation | #16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 8-9 |
| Blinding (masking) | #17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 9 |
| Blinding (masking): emergency unblinding | #17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | n/a |
| Data collection plan | #18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 11-13 |
| Data collection plan: retention | #18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants | 11-13 |

| | | | |
|---|---|---|---|
| | | who discontinue or deviate from intervention protocols | |
| Data management | #19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 11-13 |
| Statistics: outcomes | #20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 14-16 |
| Statistics: additional analyses | #20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 14 |
| Statistics: analysis population and missing data | #20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 14-15 |
| Data monitoring: formal committee | #21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 15-16 |
| Data monitoring: interim analysis | #21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 15-16 |
| Harms | #22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 13-14 |
| Auditing | #23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 14 |
| Research ethics approval | #24 | Plans for seeking research ethics committee / institutional review board (REC / IRB) approval | 17-18 |
| Protocol amendments | #25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) | 14 |
| Consent or assent | #26a | Who will obtain informed consent or assent from potential trial | 9 |

| | | | |
|---|---|---|---|
| | | participants or authorised surrogates, and how (see Item 32) | |
| Consent or assent: ancillary studies | #26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | n/a |
| Confidentiality | #27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 12-13 |
| Declaration of interests | #28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 19 |
| Data access | #29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | 19 |
| Ancillary and post trial care | #30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 13 |
| Dissemination policy: trial results | #31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 18 |
| Dissemination policy: authorship | #31b | Authorship eligibility guidelines and any intended use of professional writers | 18 |
| Dissemination policy: reproducible research | #31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | 19 |
| Informed consent materials | #32 | Model consent form and other related documentation given to participants and authorised surrogates | 25-27 |
| Biological specimens | #33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | n/a |

BMJ Open

# Lateral Episiotomy versus No Episiotomy to Reduce Obstetric Anal Sphincter Injury in Vacuum Assisted Delivery in Nulliparous Women: Study Protocol on a Randomised Controlled Trial



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2018-025050.R1 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 26-Sep-2018 |
| Complete List of Authors: | Bergendahl, Sandra; Karolinska Institutet, Department of Clinical Sciences<br>Ankarcrona, Victoria; Karolinska Institutet, Department of Clinical Sciences<br>Leijonhufvud, Åsa; Lunds Universitet, Department of Clinical Sciences Lund/Clinical Science Helsingborg<br>Hesselman, Susanne; Uppsala Universitet, Department of Women's and Children´s Health, Centre for Clinical Research Dalarna, Falu Hospital<br>Karlström, Sofie ; Karolinska Institutet, Department of Clinical Science, Intervention and Technology<br>Kopp-Kallner, Helena; Karolinska Institutet, Department of Women's and Children's Health<br>Brismar Wendel, Sophia; Karolinska Institutet, Department of Clinical Sciences |
| Primary Subject Heading: | Obstetrics and gynaecology |
| Secondary Subject Heading: | Evidence based practice, Medical management, Reproductive medicine, Sexual health |
| Keywords: | OBSTETRICS, Obstetric anal sphincter injury, Lateral episiotomy, Vacuum extraction, Pelvic floor ultrasound, Randomised controlled trial |
| | |

# Lateral Episiotomy versus No Episiotomy to Reduce Obstetric Anal Sphincter Injury in Vacuum Assisted Delivery in Nulliparous Women:

# Study protocol on a Randomised Controlled Trial

Sandra Bergendahl, MD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: sandra.bergendahl@sll.se

Victoria Ankarcrona, MD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: victoria.liversedge-ankarcrona@sll.se

Åsa Leijonhufvud, MD, PhD. Department of Clinical Sciences Lund/Clinical Science Helsingborg. Helsingborgs Lasarett, Svartbrödragränd 3-5, 251 87 Helsingborg, Sweden. E-mail: asa.leijonhufvud@skane.se

Susanne Hesselman, MD, PhD. Department of Women's and Children´s Health, Uppsala University and Centre for Clinical Research Dalarna, Falu Hospital, Sweden. E-mail: susanne.hesselman@ltdalarna.se

Sofie Karlström, MD. Department of Clinical Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden. E-mail: sofie.karlstrom@sll.se.

Helena Kopp Kallner, MD, PhD, Ass. Professor. Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital Solna, 17176 Stockholm, Sweden. E-mail: helena.kopp-kallner@ki.se

Sophia Brismar Wendel*, MD, PhD. Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 18288 Stockholm, Sweden. E-mail: sophia.brismar-wendel@sll.se

*Corresponding author

**Word count** 3960 words (main text)

**Protocol version** 3.0 date 18-08-24

# Abstract

## Introduction

Obstetric anal sphincter injury (OASIS) occurs in 5-7% of normal deliveries, and increases with vacuum extraction (VE) to 12-14% in nulliparous women in Sweden. Lateral/mediolateral episiotomy may reduce the prevalence of OASIS at VE in nulliparous women. The current use of episiotomy is restrictive. The protective effect and consequences are uncertain. This trial will investigate if lateral episiotomy can reduce the prevalence of OASIS and assess short- and long-term effects.

## Methods and analysis

This is a randomised controlled trial of lateral episiotomy versus no episiotomy in nulliparous women with a singleton, live fetus, after gestational week 34+0 with indication for VE. A lateral episiotomy of 4 cm is cut at crowning, 1-3 cm from the midline, at a 60° angle. The primary outcome is OASIS by clinical diagnosis analysed according to intention-to-treat. To demonstrate a 50% reduction in OASIS prevalence (from 12.4% to 6.2%), 710 women will be randomised at a 1:1 ratio. Secondary outcomes are pain, blood loss, other perineal injuries, perineal complications, Apgar score, cord pH, and neonatal complications. Web-based questionnaires at baseline, two months, one and five years, will be used to assess pain, incontinence, prolapse, sexual function, quality of life, and childbirth experience. A subset of women will receive follow-up by pelvic floor sonography and pelvic exam. Mode of delivery and recurrence of OASIS/episiotomy in subsequent pregnancies will be assessed at five and ten years using register data.

Ethics and dissemination

The trial is open for enrolment. The trial has received ethical approval from the Regional Ethical Review Board of Stockholm and full funding from the Swedish Research Council. Women are interested in participation. The predominant restrictive view on episiotomy may limit recruitment. Results are of global interest and will be disseminated in peer-reviewed journals and at international congresses.

Trial registration

28 December 2015 at www.clinicaltrials.gov (NCT02643108).

## Article summary

*Strengths and limitations of this study*

- The main strength is the randomised trial design, which will provide evidence for routine or restrictive lateral episiotomy at VE in nulliparous women.
- Another strength is the setting with relatively high OASIS rates and low episiotomy rates, enabling a realistic sample size.
- One limitation is that the primary outcome, diagnosis of OASIS, is made by clinical examination, which may limit diagnostic accuracy.
- Another limitation is the restrictive view on episiotomy, which may hamper trial feasibility.

## Keywords

Randomised controlled trial, lateral episiotomy, obstetric anal sphincter injury, vacuum extraction, operative vaginal delivery, nulliparous women, anal incontinence, sexual function, pelvic floor ultrasound.

# Background

Obstetric anal sphincter injury (OASIS) is a serious complication to vaginal delivery. It is the most important cause of female anal incontinence, and therefore important to avoid (1). OASIS occurs in 5-7% of spontaneous vaginal births and increases with operative vaginal delivery to 12-14% in nulliparous women in Sweden (2-4). In 2017, approximately 10% (6-17%) of nulliparous women were delivered by vacuum extraction (VE) depending on delivery site, and only a negligible number were delivered by forceps (4).

The use of episiotomy in Sweden is restrictive and was reported in approximately 10% of all vaginal deliveries and 30% of VE in 2016, with large regional variation (10% to 79%) (4). The restrictive use of episiotomy spread in the 1990-ies, especially after Swedish publications reported little protective effect on severe perineal injury and increased early postpartum pain compared to spontaneous tears (5-7). The inability to reduce OASIS in normal delivery has been confirmed in repeated Cochrane meta-analyses and restrictive use is now generally recommended (8, 9). The restrictive approach has also influenced practice at operative vaginal delivery, supported by the uncertain effect of episiotomy in VE in the Swedish setting (10). Following decades of restrictive use, midwives and doctors may have lost knowledge in correctly performing and repairing episiotomies. There is an inverse correlation between a nation's rate of episiotomy and rate of OASIS, and the optimal rate of episiotomy in operative vaginal delivery is not known (11).

Several recent retrospective register studies have shown that nulliparous women who received a lateral or mediolateral episiotomy at VE had a reduced prevalence of OASIS compared to women without episiotomy (12-15). Lund et al compiled the outcome of 15 register studies in a meta-analysis published in 2016, and concluded that a mediolateral or lateral episiotomy

significantly reduced the risk of OASIS at VE in nulliparous women with an adjusted odds ratio (aOR) of 0.53 (95% Confidence Interval (CI) 0.37-0.77) (16). Numbers needed to treat was 18.3 (95%CI 17.7-18.9). The protective effect of mediolateral or lateral episiotomy seemed most pronounced when performed in more than 75% of VE with aOR 0.37 (95%CI 0.15-0.92). The results from these studies were so promising that an official Swedish guideline and a new national educational program launched in 2017 advocated to *consider* a mediolateral episiotomy at operative vaginal deliveries in nulliparous women (17, 18).

In register studies, despite controlling for several confounding factors, there is a risk of selection bias, registering shortcomings, and confounding by indication. Furthermore, non-measured variables, such as operator skills and tissue properties might result in residual confounding. None of the register studies showing a protective effect of lateral/mediolateral episiotomy have adjusted for tissue properties or taken the operator's experience or track record of OASIS into account. Such factors may be balanced in a randomised controlled trial. Hence, several authors and institutions, including the Cochrane Collaboration and the Database of Uncertainties about the Effects of Treatments/National Institute for Health and Care Excellence Evidence Search, state that the protective effect of a lateral/mediolateral episiotomy at operative vaginal delivery should be investigated in an adequately sized randomised controlled trial (RCT) (9, 16, 19-21).

There is one published British pilot RCT on routine versus restrictive use of episiotomy (undefined type) in operative vaginal delivery in 200 nulliparous women, but the trial was underpowered mainly due to a fairly high rate of episiotomy (52%) in the restrictive group and moderate prevalence of OASIS in both groups (routine 8.1% vs. restrictive 10.9%) (22). The authors estimated that a sample size of 1600 women would have been necessary to

determine a difference at that level. Ethical concerns arise when a number of women will sustain an iatrogenic perineal injury to perhaps avoid OASIS, which may heal well after adequate suturing. Yet, only 4% of the women in the restrictive group in the British pilot trial had an intact perineum after operative vaginal delivery.

Many earlier studies on the effects of episiotomy do not specify the type, although mediolateral episiotomies are preferred in Europe, while lateral episiotomies are mainly used in Finland (11, 22, 23). It is evident that mediolateral and lateral episiotomies often are confused both in clinical practice and in research (16, 24, 25). As surveyed at a Nordic Congress of Obstetrics and Gynaecology, the majority of Nordic obstetricians declared to perform a lateral episiotomy, but 64% called it a mediolateral episiotomy (24). Only 20% performed a typical mediolateral episiotomy and one third drew an unclassifiable type. In an effort to standardize terminology, Kalis et al stated that a lateral episiotomy "begins in the vaginal introitus 1 or 2 cm lateral to the midline and directed downwards towards the ischial tuberosity", while a mediolateral episiotomy is more unclear with a suggested definition starting within 3 mm of the midline and directed laterally at an angle of at least 60 degrees from the midline (26). In the EPITRIAL, Sagi-Dain et al use "lateral/mediolateral" episiotomy, defined as an incision at 45-60 degrees and 3-4 cm long (25).

We have decided to use lateral episiotomy in our RCT, defined further in the methods section. The purpose of the lateral episiotomy is to cut the bulbocavernous muscle, which is thought to constitute the main restraining tissue in the vaginal opening at crowning. Lateral episiotomy may affect the superficial transverse perineal muscle, but ideally not the levator muscle, perineal body, or margins of the external anal sphincter muscle, which may be a risk at a mediolateral episiotomy with an insufficient angle, distance from the midline, and length (27-

31). Furthermore, current evidence suggests little difference between the techniques regarding bleeding, postpartum perineal pain, and sexual resumption (32-35). A correlation between the extent of tissue damage and degree of pain has been observed, but conflicting observations on pelvic floor function and pain after any episiotomy versus spontaneous perineal injury call for a long-term follow-up to assess the optimal treatment at delivery (32, 36-38).

In all, to our knowledge, there is no published adequately sized RCT to assess the protective effect of lateral episiotomy at VE in nulliparous women, nor sufficient published data on long-term postpartum complications from episiotomy versus spontaneous perineal injury at VE.

## Methods and analysis

*Aim*

The aim of this RCT is to investigate if routine lateral episiotomy can reduce the incidence of OASIS at VE in nulliparous women, compared to a no-episiotomy-policy, and to assess short, medium, and long-term effects on pelvic floor symptoms with the two different episiotomy strategies.

*Study design and treatment allocation*

We used the SPIRIT checklist when writing our report (Appendix 1) (39, 40). Randomisation is performed on a 1:1 basis, based on computer-generated random permuted blocks provided by the independent, non-profit Karolinska Trial Alliance. Treatment group is allocated using sealed opaque envelopes placed on the VE equipment cart for immediate and easy access. When the decision to perform a VE has been made by the attending physician and the patient's consent has been verified, the envelope is opened by the assistant nurse or midwife.

The allocated treatment is confirmed by the attending physician, the midwife, and the woman in labour. The allocated treatment cannot be blinded to women or investigators in the trial, nor at follow-up, due to the design of intervention/no intervention. During analysis, group allocation will be open to the investigators, to enable both intention-to-treat and per protocol analysis. The complete study protocol is available in Appendix 2.

*Setting*

All delivery wards in Sweden have been invited to participate in the trial. Presently, three sites are recruiting; Danderyd, Falun, and Helsingborg. All sites are located within large regional or university affiliated hospitals and have immediate access to a specialist obstetrician or senior registrar, anaesthesiologist, operating theatre, and a neonatal intensive care unit. Danderyd has approximately 6500 annual deliveries, of which 300 are VE in nulliparous women, while Falun and Helsingborg each have approximately 3500 annual deliveries, of which 150 are nulliparous VE.

*Characteristics of participants and informed consent*

All women expecting their first child, and planning to deliver vaginally at the study sites, are invited to participate. Written and oral information is given and written consent is obtained by midwives and physicians at regular visits to antenatal care from gestational week 24. Women are also approached at visits to the hospital before delivery. Written information and consent forms are at present available in Swedish and English (Appendix 3). Signed informed consent forms are forwarded to the research midwife or principal investigator at each site and documented in the woman's medical record. Women with contraindications to vacuum extraction will not be invited to participate in the trial, neither will women with previous surgery for incontinence or pelvic organ prolapse. Ethical approval has been given to invite

women in labour, if adequate pain relief has been given, and there is enough time to obtain informed consent. Inclusion and exclusion criteria are listed in Table 1. Criteria to be verified by the attending physician at randomisation include signed informed consent, indication for VE, and a cephalic singleton live fetus, gestational week 34+0 or more, as well as the absence of previous surgery for incontinence or prolapse.

*Description of the intervention and comparison*

The decision to assist the delivery by vacuum extraction is made at the attending physician's discretion. In all women, the urinary bladder should be emptied by catheterization and adequate pain relief is recommended, prior to application of the vacuum cup. Pain relief may consist of epidural anaesthesia, a pudendal block, or local infiltration.

For women allocated to "lateral episiotomy", a lateral episiotomy is performed as follows. Local anaesthesia is recommended, injecting Mepivacaine, Lidocaine, or similar local anaesthetic in the hymeneal plane, 1 ml subcutaneously at the incision point and 9 ml in a fan-like fashion from the incision point. The vacuum cup is then applied and the extraction is performed synchronously with the contractions and pushing efforts, until the cup is visible in the vaginal opening, which corresponds to the crowning head.

Lateral episiotomy is then performed using specific episiotomy scissors, Mayo scissors, or similar scissors (Figure 1).

- Distance from incision point to the posterior fourchette: at least 1 cm, up to 3 cm.
- Angle from the sagittal or parasagittal plane: 60° (45-80°, aim at the ischiadic tuberosity)
- Length of the incision: 4 cm (3-5 cm)

For women allocated to "no episiotomy", the perineum will possibly remain intact or tear spontaneously. The operator may only perform episiotomy if severe fetal distress is suspected or on the clinical judgement that extensive perineal injury cannot be avoided. These exceptions should comprise ideally around 10%, but at the most 30% of the VE, if practice is unchanged. Any episiotomy should be lateral. Episiotomy rates in trial participants and non-participants will be followed continuously by the principal investigators.

All women will receive perineal protection using verbal guiding and manual support of the perineum during the delivery of the fetal head and body. The third stage, examination and diagnosis of perineal tears is managed according to clinical routine. The clinical diagnosis of OASIS is our primary outcome. Adequate pain relief should again be offered to enable a thorough clinical bi-digital rectal/vaginal exam to reveal any injury to the sphincter muscles or rectum. The diagnosis is confirmed by a specialist gynaecologist/obstetrician or senior registrar. Suturing of OASIS is performed by a specialist gynaecologist/obstetrician or senior registrar and managed according to clinical routine or as suggested in the standard operating procedures.

*Primary and secondary outcomes*

The primary outcome is OASIS, including third and fourth degree perineal tears, engaging the external or internal anal sphincter muscles, anal epithelium, or rectum (International Classification of Diseases 10 code O70.2 or O70.3). Diagnosis is made by clinical examination by a specialist obstetrician/gynaecologist or senior registrar.

Short-term secondary outcomes are other degrees of perineal injury, blood loss postpartum, complications to episiotomy or perineal injuries such as dehiscence or infection, Apgar score, umbilical artery pH <7.05, shoulder dystocia, admission to the Neonatal ward, neonatal injury (scalp trauma, obstetric brachial plexus palsy, cerebral injury, hypoxic ischemic encephalopathy, respiratory distress, and fractures as diagnosed by the neonatologist), duration of hospital stay after delivery, perineal pain, and childbirth experience 1-3 days after delivery by Visual Analogue Scale. The data will be collected from the Swedish Pregnancy Register and the National Quality Register for Neonatal Care. Information from maternal and neonatal medical records is automatically forwarded to the registers when the medical records are signed for archiving. The Swedish Pregnancy Register covers 90% of pregnancies in Sweden and virtually all pregnancies at the study sites (41). The register consists of three parts; the Swedish Maternal Health Care Register, launched in 1999, the Swedish National Quality Register for Prenatal Diagnosis, with data from 2010, and the Obstetric Register, which started in 2013. The three registers thus provide detailed information of pregnancies, labours, and the postpartum period. The National Quality Register for Neonatal Care covers all 37 neonatal wards and neonatal intensive care units in Sweden since 2012, and consists of data from new-borns admitted to hospital care from birth until 28 days of age. The primary outcome OASIS and trial specific data not available from the registers will be collected in electronic case report forms supplied and monitored by Karolinska Trial Alliance.

Medium-term secondary outcomes, to be assessed by clinical examination and sonographic imaging six to 12 months after delivery in at least one study site, are effects on the pelvic floor anatomy. The OASIS diagnosis and the type of episiotomy will be quality controlled. Descriptive data on pelvic floor muscle injury will be collected, specifically injuries to the sphincters and the levator ani muscle. The women at this site will undergo a structured pelvic

exam performed by consultant gynaecologists in an independent Centre for Pelvic Floor Disorders, including measurement of any scar, a clinical assessment of pelvic floor muscle function by a six-point muscle strength score, prolapse staging by the pelvic organ prolapse quantification system, and a high-resolution 2D perineal and 3D endovaginal and transrectal ultrasound. Data from this follow-up will be collected using electronic case report forms supplied and monitored by Karolinska Trial Alliance.

Medium- and long-term secondary outcomes, to be assessed by web-based questionnaires, are duration of pain medication after delivery, symptoms regarding anal and urinary incontinence, bowel function, prolapse, and sexual function at baseline, two months (up to six months), 12 months (up to 18 months), and five years (up to five years and six months) after delivery. The questions are based on the questionnaires used by the Swedish Perineal Tear Register, and will be distributed at identical intervals (baseline, two, and 12 months postpartum) as well as after five years. Anal incontinence is assessed by Wexner score in these questionnaires (42). Childbirth experience will be assessed at two months postpartum using the revised short form of the Birth Satisfaction Scale and the Childbirth Experience Questionnaire (43, 44). The questionnaires “Female Sexual Function Index” and “Female Sexual Distress Scale” will be used for in-depth assessment of sexual function at baseline, one and five years (45-47). Quality of life will be measured using the questionnaire Euro-QoL-5D at baseline, one and five years (48). The questionnaires are administered by an independent provider of patient surveys and data is forwarded to Karolinska Trial Alliance. We will also assess mode of delivery, episiotomy, and OASIS in the subsequent pregnancy at five years and ten years after the index delivery by using data from the Swedish Pregnancy Register. The schedule of all follow-up assessments is illustrated in Table 2. All collaborators have signed or are obliged under law to keep data confidential during and after the trial.

*Adverse events, data collection and safety*

All randomised women are offered a clinical (apart from the trial) follow-up at 6 months and free and easy access to medical care in association with the episiotomy or perineal tear at the study site during the study period of five years. All women will receive postpartum care as individually needed. Serious adverse events, such as death, a life-threatening event, admission to intensive care, persistent or significant disability or incapacity, or other medically important events, will be reported in a separate form and evaluated by the sponsor and principal investigators continuously. The Karolinska Trial Alliance will monitor the trial conduct, as well as data collection and safety after start-up, midterm, and before closure at each site, covering 20% of randomised women. Karolinska Trial Alliance will also manage important study protocol modifications and communicate these to relevant parties.

*Statistical methods*

Baseline data will be summarized by descriptive statistics as appropriate; mean and standard deviation, median, upper and lower quartiles, minimum and maximum, or frequency tables, stratified by the two arms.

Data will be analysed by intention-to-treat and per protocol. The primary outcome variable, clinical diagnosis of OASIS, will be presented in numbers as incidence rate in the two allocation groups (intention-to-treat) and according to received treatment (per protocol). The protective effect of lateral episiotomy will be calculated as a relative risk of OASIS with 95% confidence intervals, adjusting for study site and other possible factors not balanced by randomisation.

Further analyses will compare secondary outcomes using test of proportions, t-test and logistic regression depending on variable characteristics. In the per protocol analysis of OASIS, we will adjust for possible confounders/effect modifiers such as study site, country of birth, maternal body mass index, operator experience, long duration of labor and second stage, epidural, use of oxytocin, fetal birthweight, head circumference, station and position. We also aim to create a prediction model of the protective effect of lateral episiotomy to support clinical decisions.

Outcomes based on evaluation scores will be analysed by non-parametric tests and paired analyses for change over time in the subgroups using Sign test. Details of the statistical analysis will be supplied in the Statistical Analysis Plan, to be finalized in collaboration with statisticians from the Karolinska Institute in a separate document before the data lock.

*Sample size calculation*

The sample size has been calculated based on data from Lund et al, suggesting a 50% reduction of OASIS in VE, when lateral/mediolateral episiotomy is performed (16). The average rate of OASIS in VE in Sweden was 12.4% in 2016 according to the Swedish Medical Birth Register. A reduction of OASIS from 12.4% to 6.2% can be detected with 80% power and less than 5% risk of alpha-error (p-value <0.05) with 355 women in each group using Chi-square test comparing two independent proportions in a two-sided test (3% missing outcome). A smaller reduction is clinically valuable, although the risk-benefit relationship between receiving a prophylactic episiotomy and the chance of an intact perineum may limit the feasibility of a larger trial in a setting with a restrictive episiotomy policy. We have obtained ethical approval to randomise a total of 1400 women, which enables us to detect a reduction in OASIS rate at VE from 12.4% to 7.8%.

*Interim analyses*

The Karolinska Trial Alliance will monitor primary outcome data using the electronic case report forms, in which the diagnosis of OASIS is registered. When 100 women have been randomised, we will perform a safety analysis to verify adherence to protocol and collate serious adverse events. We will perform a first interim analysis when 350 women have been randomised, to detect a possible OASIS prevalence reduction from 12.4% to 2.5% with 80% power and p-value <0.01, in concordance with the pronounced reduction observed in the Dutch register study by van Bavel et al (15). If a reduction of OASIS is achieved at this level, the trial will be discontinued and modified, as the clinical equipoise has been sufficiently disturbed. A second interim analysis will be performed when 710 women have been randomised, to detect a possible 50% reduction from 12.4% to 6.2% with 80% power and p-value <0.05. Similarly, the trial will be stopped if a 50% reduction is detected. If feasible, we will continue the trial until 1400 women have been randomised. Depending on the size of the delivery ward, each site will contribute with approximately 5% of nulliparous women giving birth vaginally (70-200 patients annually). Inclusion rate is expected to be two to three patients per week at a site with 300 annual vacuum extractions in nulliparous women, if 50% of women accept participation.

*Patient and public involvement*

There is no applicable Swedish patient organization, but prevention of maternal birth injuries has been ranked the most important area of research by patients and unbiased professionals (49). Ethical approval was obtained from a board composed of professionals and lay men and women, also considering non-professional opinions. Pregnant women are generally curious about the trial and the majority of approached women consent to participate, particularly

motivated by a thorough follow-up no matter what perineal injury. The interest from pregnant women is consistent with the observation that 85% of invited women agreed to participate in the pilot RCT by Murphy et al, although the rational for participation may have been the chance to avoid an episiotomy in their setting (22). The burden of the intervention will be assessed in the secondary outcomes. Results from this trial will be made available to study participants through communication in public media.

## Ethics and dissemination

The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2 with addendums 2017/1005-32 and 2018/775-32). Previous register studies and guidelines all point towards a reduction in OASIS if episiotomy is performed at VE in nulliparous women, as described above. Reintroducing this routine demands a randomised trial and a thorough follow-up to assess the consequences.

Swedish maternity wards should provide an excellent setting to perform a randomised trial of routine lateral episiotomy versus no episiotomy at VE in nulliparous women, given the low episiotomy rate and the relatively high prevalence of OASIS. We expect strong adherence to non-intervention in the control group, facilitating the detection of any difference in OASIS incidence. The timing with new guidelines to *consider* episiotomy further improves the setting of the study (17, 18). The phrase "to consider" episiotomy is used deliberately to keep recommendations weak. Yet, it is crucial to undertake and complete the trial before these new guidelines are interpreted as recommendations despite low-grade evidence and lack of long-term follow-up.

Then again, the low episiotomy rate may limit the feasibility of the study. A survey regarding episiotomy preferences and indications was performed in 2012 among 297 delegates at the biennial Nordic Congress of Obstetrics and Gynaecology (24). Only 17% of the 54 participating Swedish doctors perceived instrumental delivery as an indication for episiotomy, while fetal distress was the most accepted indication. Consequently, 87% of the Swedish doctors never, seldom, or only sometimes performed an episiotomy at VE. Thus, experience from episiotomy may be lacking, which will require education and training at the sites when the study is being implemented.

Prior to the previously described British pilot RCT, Macleod and Murphy performed a survey among 1631 obstetricians and specialist registrars in the United Kingdom and Ireland with regard to operative vaginal delivery and the use of episiotomy (22, 50). The great majority (72%) reported a restrictive attitude towards use of episiotomy in VE and over 65% said that they would be happy to participate in an RCT of restrictive versus routine use of episiotomy at operative vaginal delivery. We estimate that a similar proportion of Swedish doctors and midwives hold the same view, although personal preferences may hamper recruitment.

Considering the admitted knowledge gap regarding effectiveness and consequences of routine lateral/mediolateral episiotomy in operative vaginal deliveries, we anticipate broad interest in the results from the EVA trial (9, 16, 19-21). Being a non-commercial academic study, the investigators will author the results adhering to the authorship criteria recommended by the International Committee of Medical Journal Editors. We intend to disseminate the results by publication in peer-reviewed medical journals and public press, and by presentations at national and international congresses. Data can be made available for future meta-analyses to improve informed practice.

# List of abbreviations

EVA – Episiotomy in Vacuum Assisted delivery

OASIS – Obstetric anal sphincter injury/injuries

VE – Vacuum Extraction

RCT – Randomised Controlled Trial

OR – Odds ratio

## Declarations

*Ethics approval and consent to participate*

The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from all participating women.

*Consent for publication*

If case reports will be published, consent will be obtained from relevant parties.

*Availability of data and material*

The datasets generated and/or analysed are not publicly available due the possibility to extract personal information, but may be made available from the corresponding author on request. All principal investigators will be given access to the final cleaned datasets and submissions for publication will be made in agreement. To ensure confidentiality, data dispersed to collaborators will be blinded of any identifying participant information.

*Competing interests*

The authors have no competing interests to declare.

*Funding*

This work is fully funded by the Swedish Research Council (grant number 2016-00526).

*Author contributions*

Sandra Bergendahl and Victoria Ankarcrona are investigators and responsible for the implementation of the trial, and manuscript draft and revision. Åsa Leijonhufvud and Susanne

Hesselman are principal investigators at Helsingborg and Falun sites and responsible for implementation of the trial, and manuscript draft and revision. Sofie Karlström is responsible for the design, implementation, and investigations in the sub-study of pelvic floor anatomy at six to 12 months after delivery. Helena Kopp Kallner is responsible for the manuscript revision, funding, and study design. Sophia Brismar Wendel is overall responsible for the implementation of the trial, manuscript draft and revision, funding, study design, and the original idea of the study. All authors have participated in manuscript writing and have approved the final version.

# References


1. Bols EM, Hendriks EJ, Berghmans BC, Baeten CG, Nijhuis JG, de Bie RA. A systematic review of etiological factors for postpartum fecal incontinence. Acta obstetricia et gynecologica Scandinavica. 2010;89(3):302-14.
2. Annual report 2016, Swedish Pregnancy Register (in Swedish) [Internet]. MedSciNet. 2016 [cited 18 dec 2017]. Available from: https://www.medscinet.com/gr/uploads/hemsida/dokumentarkiv/GR_Årsrrapport_2016_2.1.pdf.
3. Waldenstrom U, Ekeus C. Risk of obstetric anal sphincter injury increases with maternal age irrespective of parity: a population-based register study. BMC pregnancy and childbirth. 2017;17(1):306.
4. Annual report 2017, Swedish Pregnancy Register (in Swedish) [Internet]. MedSciNet. 2017 [cited 22 September 2018]. Available from: https://www.medscinet.com/GR/uploads/hemsida/dokumentarkiv/GR_Årsrrapport_2017_4.0.pdf.
5. Rockner G, Fianu-Jonasson A. Changed pattern in the use of episiotomy in Sweden. British journal of obstetrics and gynaecology. 1999;106(2):95-101.
6. Rockner G, Henningsson A, Wahlberg V, Olund A. Evaluation of episiotomy and spontaneous tears of perineum during childbirth. Scand J Caring Sci. 1988;2(1):19-24.
7. Rockner G, Wahlberg V, Olund A. Episiotomy and perineal trauma during childbirth. J Adv Nurs. 1989;14(4):264-8.
8. Carroli G, Mignini L. Episiotomy for vaginal birth. Cochrane database of systematic reviews (Online). 2009(1):CD000081.
9. Jiang H, Qian X, Carroli G, Garner P. Selective versus routine use of episiotomy for vaginal birth. Cochrane database of systematic reviews (Online). 2017;2:CD000081.
10. Simic M, Cnattingius S, Petersson G, Sandstrom A, Stephansson O. Duration of second stage of labor and instrumental delivery as risk factors for severe perineal lacerations: population-based study. BMC pregnancy and childbirth. 2017;17(1):72.
11. Blondel B, Alexander S, Bjarnadottir RI, Gissler M, Langhoff-Roos J, Novak-Antolic Z, et al. Variations in rates of severe perineal tears and episiotomies in 20 European countries: a study based on routine national data in Euro-Peristat Project. Acta obstetricia et gynecologica Scandinavica. 2016;95(7):746-54.
12. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. BJOG: an international journal of obstetrics and gynaecology. 2008;115(1):104-8.
13. Raisanen S, Vehvilainen-Julkunen K, Cartwright R, Gissler M, Heinonen S. Vacuum-assisted deliveries and the risk of obstetric anal sphincter injuries-a retrospective register-based study in Finland. BJOG: an international journal of obstetrics and gynaecology. 2012;119(11):1370-8.
14. de Vogel J, van der Leeuw-van Beek A, Gietelink D, Vujkovic M, de Leeuw JW, van Bavel J, et al. The effect of a mediolateral episiotomy during operative vaginal delivery on the risk of developing obstetrical anal sphincter injuries. American journal of obstetrics and gynecology. 2012;206(5):404 e1-5.
15. van Bavel J, Hukkelhoven C, de Vries C, Papatsonis DNM, de Vogel J, Roovers JWR, et al. The effectiveness of mediolateral episiotomy in preventing obstetric anal sphincter injuries during operative vaginal delivery: a ten-year analysis of a national registry. International urogynecology journal. 2018;29(3):407-13.
16. Lund NS, Persson LK, Jango H, Gommesen D, Westergaard HB. Episiotomy in vacuum-assisted delivery affects the risk of obstetric anal sphincter injury: a systematic

review and meta-analysis. European journal of obstetrics, gynecology, and reproductive biology. 2016;207:193-9.
17. Anal Sphincter Injuries: A Systematic Review and Assessment of Medical, Social and Ethical Aspects. SBU Systematic Review Summaries. Stockholm 2016.
18. Bäckenbottenutbildning. Stockholm, Sweden: LÖF Landstingens Ömsesidiga Försäkring; 2017. Available from: http://backenbottenutbildning.se/index.php.
19. Revicky V, Nirmal D, Mukhopadhyay S, Morris EP, Nieto JJ. Could a mediolateral episiotomy prevent obstetric anal sphincter injury? European journal of obstetrics, gynecology, and reproductive biology. 2010;150(2):142-6.
20. Sagi-Dain L, Sagi S. Morbidity associated with episiotomy in vacuum delivery: a systematic review and meta-analysis. BJOG: an international journal of obstetrics and gynaecology. 2015;122(8):1073-81.
21. Verghese TS, Champaneria R, Kapoor DS, Latthe PM. Obstetric anal sphincter injuries after episiotomy: systematic review and meta-analysis. International urogynecology journal. 2016;27(10):1459-67.
22. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. BJOG: an international journal of obstetrics and gynaecology. 2008;115(13):1695-702; discussion 702-3.
23. Raisanen SH, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Lateral episiotomy protects primiparous but not multiparous women from obstetric anal sphincter rupture. Acta obstetricia et gynecologica Scandinavica. 2009;88(12):1365-72.
24. Fodstad K, Staff AC, Laine K. Episiotomy preferences, indication, and classification-a survey among Nordic doctors. Acta obstetricia et gynecologica Scandinavica. 2016;95(5):587-95.
25. Sagi-Dain L, Bahous R, Caspin O, Kreinin-Bleicher I, Gonen R, Sagi S. No episiotomy versus selective lateral/mediolateral episiotomy (EPITRIAL): an interim analysis. International urogynecology journal. 2018;29(3):415-23.
26. Kalis V, Laine K, de Leeuw JW, Ismail KM, Tincello DG. Classification of episiotomy: towards a standardisation of terminology. BJOG: an international journal of obstetrics and gynaecology. 2012;119(5):522-6.
27. Andrews V, Thakar R, Sultan AH, Jones PW. Are mediolateral episiotomies actually mediolateral? BJOG : an international journal of obstetrics and gynaecology. 2005;112(8):1156-8.
28. Naidu M, Kapoor DS, Evans S, Vinayakarao L, Thakar R, Sultan AH. Cutting an episiotomy at 60 degrees: how good are we? International urogynecology journal. 2015;26(6):813-6.
29. Ma K, Byrd L. Episiotomy: What angle do you cut to the midline? European journal of obstetrics, gynecology, and reproductive biology. 2017;213:102-6.
30. Stedenfeldt M, Pirhonen J, Blix E, Wilsgaard T, Vonen B, Oian P. Episiotomy characteristics and risks for obstetric anal sphincter injuries: a case-control study. BJOG: an international journal of obstetrics and gynaecology. 2012;119(6):724-30.
31. Ginath S, Elyashiv O, Weiner E, Sagiv R, Bar J, Menczer J, et al. The optimal angle of the mediolateral episiotomy at crowning of the head during labor. International urogynecology journal. 2017;28(12):1795-9.
32. Fodstad K, Staff AC, Laine K. Effect of different episiotomy techniques on perineal pain and sexual activity 3 months after delivery. International urogynecology journal. 2014;25(12):1629-37.

33. Fodstad K, Laine K, Staff AC. Different episiotomy techniques, postpartum perineal pain, and blood loss: an observational study. International urogynecology journal. 2013;24(5):865-72.
34. Karbanova J, Rusavy Z, Betincova L, Jansova M, Necesalova P, Kalis V. Clinical evaluation of early postpartum pain and healing outcomes after mediolateral versus lateral episiotomy. International journal of gynaecology and obstetrics. 2014;127(2):152-6.
35. Necesalova P, Karbanova J, Rusavy Z, Pastor Z, Jansova M, Kalis V. Mediolateral versus lateral episiotomy and their effect on postpartum coital activity and dyspareunia rate 3 and 6 months postpartum. Sex Reprod Healthc. 2016;8:25-30.
36. De Souza A, Dwyer PL, Charity M, Thomas E, Ferreira CH, Schierlitz L. The effects of mode delivery on postpartum sexual function: a prospective study. BJOG: an international journal of obstetrics and gynaecology. 2015;122(10):1410-8.
37. Signorello LB, Harlow BL, Chekos AK, Repke JT. Midline episiotomy and anal incontinence: retrospective cohort study. BMJ (Clinical research ed). 2000;320(7227):86-90.
38. Dogan B, Gun I, Ozdamar O, Yilmaz A, Muhcu M. Long-term impacts of vaginal birth with mediolateral episiotomy on sexual and pelvic dysfunction and perineal pain. J Matern Fetal Neonatal Med. 2017;30(4):457-60.
39. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krle AJK, et al. SPIRIT 2013 Statement: defining standard protocol items for clinical trials. Rev Panam Salud Publica. 2015;38(6):506-14.
40. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krleza-Jeric K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-7.
41. Stephansson O, Petersson K, Bjork C, Conner P, Wikstrom AK. The Swedish Pregnancy Register - for quality of care improvement and research. Acta obstetricia et gynecologica Scandinavica. 2018;97(4):466-76.
42. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Diseases of the colon and rectum. 1993;36(1):77-97.
43. Hollins Martin CJ, Martin CR. Development and psychometric properties of the Birth Satisfaction Scale-Revised (BSS-R). Midwifery. 2014;30(6):610-9.
44. Dencker A, Taft C, Bergqvist L, Lilja H, Berg M. Childbirth experience questionnaire (CEQ): development and evaluation of a multidimensional instrument. BMC pregnancy and childbirth. 2010;10:81.
45. Derogatis LR, Rosen R, Leiblum S, Burnett A, Heiman J. The Female Sexual Distress Scale (FSDS): initial validation of a standardized scale for assessment of sexually related personal distress in women. J Sex Marital Ther. 2002;28(4):317-30.
46. Ryding EL, Blom C. Validation of the Swedish version of the Female Sexual Function Index (FSFI) in women with hypoactive sexual desire disorder. J Sex Med. 2015;12(2):341-9.
47. Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther. 2005;31(1):1-20.
48. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-43.
49. SBU. Prioritised research areas within the fields of prevention, diagnosis, and treatment of maternal birth injuries 2018. Accessed 22 September 2018. Available from: https://www.sbu.se/291e.
50. Macleod M, Murphy DJ. Operative vaginal delivery and the use of episiotomy--a survey of practice in the United Kingdom and Ireland. European journal of obstetrics, gynecology, and reproductive biology. 2008;136(2):178-83.

# Legend of tables, figures and appendices

Table 1. Inclusion and exclusion criteria

Table 2. Schedule of enrolment, interventions, and assessments

Figure 1. Schematic illustration of a lateral episiotomy in the EVA trial

Appendix 1. Completed SPIRIT checklist

Appendix 2. Study protocol EVA Version 3.0 2018-08-24

Appendix 3. Patient information and informed consent form

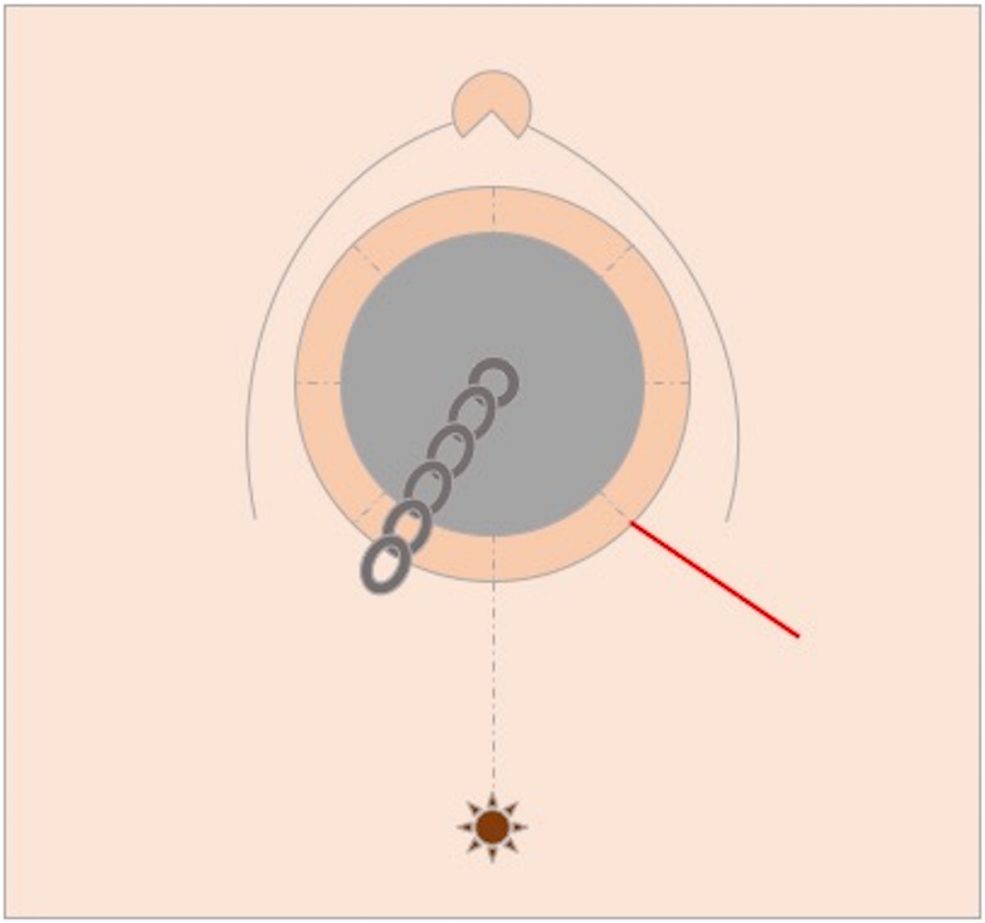
**Table 1. Inclusion and exclusion criteria**

| Inclusion criteria | Exclusion criteria |
|---|---|
| Nulliparous woman<br>Singleton, live fetus in cephalic presentation<br>Gestational week 34+0 or more<br>Indication for vacuum extraction<br>Signed informed consent | Previous surgery for incontinence or prolapse |

**Table 2. Schedule of enrolment, interventions, and assessments**

| | STUDY PERIOD | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Enrolment** | **Allocation** | **Post-allocation** | | | | | **Close-out** |
| **TIME POINT** | ***-4m*** | **0** | ***0m*** | ***2m*** | ***6m*** | ***1y*** | ***5y*** | ***10y*** |
| **ENROLMENT:** | | | | | | | | |
| Information | x | | | | | | | |
| Informed consent | x | | | | | | | |
| Inclusion/exclusion criteria | x | | | | | | | |
| Randomisation | | x | | | | | | |
| **INTERVENTIONS:** | | | | | | | | |
| Episiotomy | | x | | | | | | |
| No episiotomy | | x | | | | | | |
| **ASSESSMENTS:** | | | | | | | | |
| Background variables | x[1] | | x[2] | | | | | |
| Data from Pregnancy register (primary and secondary endpoints) | | | x[3,4] | | | | x[5] | x[6] |
| Data from SNQ on neonatal outcome (secondary endpoints) | | | x | | | | | |
| Questionnaire BR 1[7] | | | x | | | | | |
| Questionnaires FSFI+FSDS | | | x | | | x | x | |
| Questionnaire Euro-Qol-5D | | | x | | | x | x | |
| Questionnaire BSS-R | | | | x | | | | |
| Questionnaire CEQ 2.0 | | | | x | | | | |
| Questionnaire BR 2[8] (8 w) | | | | x | | | | |
| Questionnaire BR 3[9] (1 y) | | | | | | x | x | |
| Ultrasound evaluation | | | | | x | | | |
| POP-Q score | | | | | x | | | |
| Measurements of scar | | | | | x | | | |
| Questionnaire Q-SOPhIE | | | | | x | | | |
| Serious adverse events[10] | | x | x | x | x | x | | |

[1] maternal age, country of birth, weight and height at registration in the antenatal clinic
[2] use of oxytocin, use of regional or local anaesthesia, birthweight, head circumference, neonatal length, second stage duration, indication for vacuum extraction, fetal position and station, operator skills, number of pulls, use of sequential instruments
[3] perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH, and birth related diagnosis)
[4] birth experience, duration of hospital stay
[5] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[6] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[7] "Information about your health before pregnancy"
[8] "Your evaluation of the treatment of perineal injury (approx. 8 weeks)"
[9] "Your evaluation of the treatment of perineal injury (approx. 1 year)"
[10] Serious adverse events (death, intensive care, disability or other important serious medical event) will be reported continuously from allocation until close-out in a separate form.



Schematic illustration of lateral episiotomy in the EVA trial

102x95mm (300 x 300 DPI)

# Reporting checklist for protocol of a clinical trial

Based on the SPIRIT guidelines. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | #2a | Trial identifier and registry name. If not yet registered, name of intended registry | 4 |
| Trial registration: data set | #2b | All items from the World Health Organization Trial Registration Data Set | 4 |
| Protocol version | #3 | Date and version identifier | 2 |
| Funding | #4 | Sources and types of financial, material, and other support | 21 |
| Roles and responsibilities: contributorship | #5a | Names, affiliations, and roles of protocol contributors | 1-2, 21-22 |
| Roles and responsibilities: sponsor contact information | #5b | Name and contact information for the trial sponsor | 2 |
| Roles and responsibilities: sponsor and funder | #5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 21-22 |
| Roles and responsibilities: committees | #5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data | 21-22 |

| | | | |
|---|---|---|---|
| | | management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | |
| Background and rationale | #6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 6-9 |
| Background and rationale: choice of comparators | #6b | Explanation for choice of comparators | 8-9 |
| Objectives | #7 | Specific objectives or hypotheses | 9 |
| Trial design | #8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory) | 9-10 |
| Study setting | #9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 10 |
| Eligibility criteria | #10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 10-11 |
| Interventions: description | #11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 11 |
| Interventions: modifications | #11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease) | 12 |
| Interventions: adherance | #11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) | 12 |
| Interventions: concomitant care | #11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 12 |
| Outcomes | #12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point | 12-14 |

| | | | |
|---|---|---|---|
| | | for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | |
| Participant timeline | #13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | Appendix |
| Sample size | #14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 16 |
| Recruitment | #15 | Strategies for achieving adequate participant enrolment to reach target sample size | 10 |
| Allocation: sequence generation | #16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 9 |
| Allocation concealment mechanism | #16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 9 |
| Allocation: implementation | #16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 9-10 |
| Blinding (masking) | #17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 10 |
| Blinding (masking): emergency unblinding | #17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | n/a |
| Data collection plan | #18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 12-14 |

| | | | |
|---|---|---|---|
| Data collection plan: retention | #18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 12-14 |
| Data management | #19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 12-14 |
| Statistics: outcomes | #20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 15-16 |
| Statistics: additional analyses | #20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 16 |
| Statistics: analysis population and missing data | #20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 16 |
| Data monitoring: formal committee | #21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 15, 17 |
| Data monitoring: interim analysis | #21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 17 |
| Harms | #22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 15 |
| Auditing | #23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 15 |
| Research ethics approval | #24 | Plans for seeking research ethics committee / institutional review board (REC / IRB) approval | 18 |
| Protocol amendments | #25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant | 15 |

| | | | |
|---|---|---|---|
| | | parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) | |
| Consent or assent | #26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 10 |
| Consent or assent: ancillary studies | #26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | n/a |
| Confidentiality | #27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 13-14 |
| Declaration of interests | #28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 21 |
| Data access | #29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | 21 |
| Ancillary and post trial care | #30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 15 |
| Dissemination policy: trial results | #31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 19 |
| Dissemination policy: authorship | #31b | Authorship eligibility guidelines and any intended use of professional writers | 19 |
| Dissemination policy: reproducible research | #31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | 21 |
| Informed consent materials | #32 | Model consent form and other related documentation given to participants and authorised surrogates | Appendix |
| Biological specimens | #33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | n/a |

# EVA

## Episiotomy in Vacuum Assisted delivery

A randomized controlled trial of lateral episiotomy vs. no episiotomy in vacuum assisted delivery in non-parous women



Sponsor: Sophia Brismar Wendel

Coordinating Investigator: Sophia Brismar Wendel

# Table of Contents

# 1 Protocol Summary

| **PROTOCOL IDENTITY AND OBJECTIVES** | |
|---|---|
| Protocol Title: | EVA – Episiotomy in Vacuum Assisted delivery. A randomized controlled trial of lateral episiotomy vs. no episiotomy in vacuum assisted delivery in non-parous women. |
| Study Objectives: | The aims are to investigate if lateral episiotomy can reduce the prevalence of obstetrical anal sphincter injury (OASIS) in operative vaginal delivery, notably vacuum extraction, in non-parous women, and to investigate secondary outcomes such as immediate maternal complications like post-partum haemorrhage and hospital stay, medium term effects like prolapse symptoms, incontinence, sexual dysfunction, birthing experience, and aspects of neonatal care. In a long-term follow-up, we will investigate if episiotomy/spontaneous tear is associated with caesarean section, episiotomy or OASIS in a subsequent pregnancy/childbirth. We will also re-evaluate symptoms of incontinence, prolapse and sexual function after 5 years. |

| **METHODOLOGY** | |
|---|---|
| Study Design: | The study is a randomized controlled trial with parallel groups. |
| Intervention: | The effect of lateral episiotomy vs. no episiotomy in vacuum assisted delivery in non-parous women in Sweden will be studied. Women with a singleton, live fetus in cephalic presentation, after week 34+0 requiring vacuum assisted vaginal delivery will be randomized to lateral episiotomy or no episiotomy. At least three sites are planned to participate. |
| Primary Endpoint: | The primary endpoint is third or fourth degree perineal tear (OASIS, ICD-10 code O70.2 or O70.3). |

| **POPULATION OF STUDY SUBJECTS** | |
|---|---|
| Description of Study Subjects: | Inclusion Criteria:<br>• Non-parous woman<br>• Singleton, live fetus in cephalic presentation<br>• Gestational week 34+0 or more<br>• Requiring vacuum assisted vaginal delivery<br>• Signed informed consent<br>Exclusion Criteria:<br>• Previous surgery for incontinence or prolapse |
| Number of Subjects: | 1400 subjects |

| **STUDY TIMETABLE** | |
|---|---|
| First Subject In: | June 2017 |
| Last Subject In: | June 2021 |
| Last Subject Out: | Sept 2031 |

## 2 Abbreviations

| Abbreviation | Explanation |
|---|---|
| AE | Adverse Event |
| BMI | Body Mass Index |
| BSS-R | Birth Satisfaction Scale-Revised |
| CEQ | Child Experience Questionnaire |
| CRF | Case Report Form |
| FSDS | Female Sexual Distress Scale |
| FSFI | Female Sexual Function Index |
| GCP | Good Clinical Practice |
| ICD-10 | International Statistical Classification of Diseases and Related Health Problems - Tenth Revision |
| ICH | International Conference of Harmonization |
| IEC | Independent Ethics Committee |
| NICU | Neonatal Intensive Care Unit |
| OASIS | Obstetric Anal Sphincter Injury |
| PDB | Pudendal Block |
| POP-Q | Pelvic Organ Prolapse Quantification |
| SAE | Serious Adverse Event |
| SBU | Statens Beredning för Medicinsk och Social Utvärdering |
| SNQ | Swedish Neonatal Quality Register |
| SOP | Standard Operating Procedure |
| VAS | Visual Analogue Scale |
| WMA | World Medical Association |

# 3 Administrative Information

| | |
|---|---|
| **Sponsor** | Sophia Brismar Wendel<br>MD, PhD, senior consultant<br>Dept of Women's Health, Danderyd Hospital<br>182 88 Stockholm<br>Telephone: +46-(0)8-123 58564, +46-(0)72-2024895<br>Email: sophia.brismar-wendel@sll.se<br>Email: sophia.brismar@ki.se |
| **Coordinating Investigator** | Sophia Brismar Wendel<br>MD, PhD, senior consultant<br>Dept of Women's Health, Danderyd Hospital<br>182 88 Stockholm<br>Telephone: +46-(0)8-123 58564, +46-(0)72-2024895<br>Email: sophia.brismar-wendel@sll.se<br>Email: sophia.brismar@ki.se |

# 4 Background

## 4.1 Purpose and aims

The purpose is to improve obstetrical care in Sweden by making the second stage safer, specifically to reduce obstetric anal sphincter injury (OASIS) in operative vaginal delivery. OASIS prevalence in all vaginal deliveries is 5-7% in Sweden. The prevalence of perineal tears increases with operative vaginal delivery, and the frequency of OASIS is 12-14% in vacuum extractions in Sweden.

The aims are to investigate if lateral episiotomy can reduce the rate of OASIS in operative vaginal delivery, notably vacuum extraction, in non-parous women, and to investigate secondary outcomes such as immediate maternal complications like postpartum hemorrhage and hospital stay, medium term effects like prolapse symptoms, incontinence, sexual dysfunction, birthing experience, and aspects of neonatal care (cord pH, Apgar score, subcutaneous hemorrhage, birth trauma). In a long-term follow-up, we will investigate if episiotomy/spontaneous tear is associated with cesarean section, episiotomy or OASIS in a subsequent pregnancy/childbirth. We will also re-evaluate symptoms of incontinence, prolapse and sexual function after 5 years.

The proposed study is a randomized controlled trial of lateral episiotomy vs. no episiotomy in vacuum assisted delivery in non-parous women in Sweden. Women with a singleton, live fetus in cephalic presentation, after week 34+0 requiring vacuum assisted vaginal delivery will be randomized to lateral episiotomy or no episiotomy.

## 4.2 Survey of the field

A third or fourth degree tear (OASIS) is considered to be the most important cause of anal incontinence in women, and therefore important to avoid. In Finland, the prevalence has been very low since several decades, probably due to a different technique (no pushing) at delivery of the fetal head and an effective perineal support, as well as a longstanding tradition of lateral episiotomy (1-3). A lateral episiotomy involves an incision at least 1 cm from the midline and at least at 30 degrees angle from the midline, as measured after healing (4). In Norway, a national prospective multi-center study during 2000-2010, with

implementation of a "Finnish" perineal support and lateral episiotomy, decreased anal sphincter injury from 4.0% to 1.2% in the total population and from 16.3% to 4.9% in vacuum extractions (5). In an American study, a change to mediolateral episiotomies in instrumental deliveries (commonly forceps) decreased the prevalence of sphincter tears from 41 to 26% (6). Similarly, a Dutch prospective study, showed a risk reduction at instrumental deliveries by 90% using mediolateral episiotomy (7). On the contrary, medial (midline) or too small episiotomies are associated with an increased risk of sphincter injury (8). In a British study comparing routine (93%) vs. restrictive (52%) use of episiotomy, there was a small non-significant difference in the rate of anal sphincter tears (8.1% routine versus 10.9% restrictive, OR 0.72, 95% CI 0.28-1.87) but the trial was underpowered (9). There is a recent randomized study comparing mediolateral and lateral episiotomy, finding equal although very low prevalence of sphincter injury (1.5 vs. 1.3%) (10). The objection that lateral incisions bleed more or causes more pain is contradicted by studies comparing incision techniques (11, 12). Little is known about chronic pain after episiotomy or spontaneous perineal injury, although there seem to be a correlation between the extent of tissue damage and degree of pain (13-15). An SBU report (Statens beredning för medicinsk och social utvärdering, www.sbu.se) published in April 2016 concludes that mediolateral episiotomy can protect against OASIS in operative vaginal deliveries in non-parous women based on two retrospective cohort studies (7, 8) although in Sweden, there is no correlation between a hospital's rate of episiotomy and OASIS. The SBU report states that there is a knowledge gap regarding function and symptoms after episiotomy compared to moderate spontaneous tears/OASIS. Several others, including Cochrane and DUETS/NICE Evidence Search, state that the protective effect of lateral episiotomy at operative vaginal delivery should be investigated in an adequately sized randomized study (8, 16-18).

# 5 Objectives

## 5.1 Primary Objective

The primary objective is to investigate if lateral episiotomy protects against obstetrical anal sphincter injury (OASIS) compared to no episiotomy in operative vaginal delivery by vacuum extraction, in term and late pre-term (gestational week 34+0 or more), non-parous women with one live fetus in cephalic presentation.

## 5.2 Secondary Objectives

The secondary objectives are to investigate if lateral episiotomy compared to no episiotomy in the above specified group of patients can reduce:

- Prevalence of other degree of perineal injury, prevalence of postpartum hemorrhage, duration of hospital stay, pain, and duration of pain medication, compared to spontaneous perineal injury of different degrees (1st, 2nd, 3rd and 4th degree)
- Neonatal morbidity measured as prevalence of low Apgar score, metabolic acidosis, prevalence of admission to the Neonatal ward, and prevalence of scalp trauma/other birth trauma
- Prevalence of urinary, anal and fecal incontinence, prolapse symptoms, sexual dysfunction, or discontent with birthing experience after 2 months
- Prevalence of ultrasound evidence of extended pelvic floor injury at 6-12 months after delivery
- Prevalence of urinary, anal and fecal incontinence, prolapse symptoms, or sexual dysfunction after 1 and 5 years
- Prevalence of elective cesarean in a subsequent pregnancy/delivery, the prevalence of OASIS in a subsequent pregnancy/delivery, or of episiotomy in a subsequent pregnancy/delivery within 5 and 10 years

# 6 Endpoints

## 6.1 Primary Endpoint

The primary endpoint is third or fourth degree perineal tear (OASIS, ICD-10 code O70.2 or O70.3). The diagnosis is made clinically. Clinical diagnosis is quality controlled in a sub-study in one site by ultrasound of the pelvic floor muscles at 6-12 months after delivery.

## 6.2 Secondary Endpoints

The secondary endpoints are:

- other degree of perineal injury (O70.0, O70.1, O71.4 or O71.7)
- blood loss postpartum (ml)
- neonatal outcome (prevalence of Apgar score <7 at 1 min, 5 min and 10 min, umbilical artery pH <7.05)
- admission to the Neonatal ward (hours of stay and prevalence)
- fetal trauma (clinical diagnosis of hematoma/fracture/obstetric brachial plexus palsy/hypoxic ischemic encephalopathy by neonatologist)
- duration of hospital stay after delivery (days)
- pain and birth experience after delivery (Visual Analog Scale (VAS))
- duration of pain medication after delivery (days)
- symptoms regarding anal incontinence (Wexner score) (19) at 2 months, 12 months and 5 years after delivery
- symptoms regarding urinary incontinence at 2 months, 12 months and 5 years after delivery
- sexual function, prolapse and bowel symptoms at 2 months, 12 months and 5 years after delivery
- birthing experience and satisfaction 2 months after delivery
- ultrasound evidence of OASIS or levator ani muscle injury at 6-12 months after delivery
- mode of delivery, episiotomy, and OASIS in a subsequent pregnancy at 5 years and 10 years after index delivery
- quality of life at 12 months and 5 years after delivery

# 7 Design and Procedures

## 7.1 Outline

The study is a randomized controlled trial with parallel groups. The effect of lateral episiotomy vs. no episiotomy in vacuum assisted delivery in non-parous women in Sweden will be studied. Women with a singleton, live fetus in cephalic presentation, after week 34+0 requiring vacuum assisted vaginal delivery will be randomized to lateral episiotomy or no episiotomy. Lateral episiotomy will be performed after local anesthesia at crowning. After delivery routine care is given.

Primary outcome is obstetrical anal sphincter injury (OASIS) diagnosed clinically. In at least one center, transperineal, endovaginal and transrectal ultrasound validation of the clinical diagnosis and effects on pelvic floor will be made at 6-12 months after delivery.

Follow-up will be performed at 2 months, 12 months and 5 years using web-based questionnaires and at 5 years and 10 years through the Pregnancy Register.

## 7.2 Procedures

The procedures at each time point are described below and can also be found in Appendix 21.1 Schedule of Investigational Events.

### *7.2.1 At the maternity clinic*

#### 7.2.1.1 Before delivery

After admission to the clinic the women will be given information about the study and asked to participate. Before any screening and study related activities take place, written informed consent must be obtained from the subject. The Investigator will review the inclusion and exclusion criteria for eligibility. If all the inclusion criteria and none of the exclusion criteria are met the subject will be included in the study.

Included subjects are randomized to lateral episiotomy at crowning or no episiotomy. Randomization and lateral episiotomy is performed as described in 9.1 and 9.2. Lateral episiotomy is also described in the study specific Standard Operating Procedure (SOP), see Appendix 21.2 Standard Operating Procedures.

Background and explanatory variables to be recorded are maternal age, country of birth, weight at registration in the antenatal clinic and height.

#### 7.2.1.2 Shortly after delivery

Perineal incisions and tears are sutured according to the clinical routine or as suggested by the study specific SOP, see Appendix 21.2 Standard Operating Procedures.

Perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH and birth related diagnosis) are recorded.

Background and explanatory variables to be recorded are use of Oxytocin, use of regional or local anesthesia, birthweight, head circumference, neonatal length, second stage duration, indication for vacuum extraction, fetal position and station, operator skills, number of pulls, and use of sequential instruments.

#### 7.2.1.3 On the maternity ward

Pain after delivery (VAS, included in the questionnaires), birth experience (VAS), duration of hospital stay, and admission to the Neonatal ward will be recorded.

Assessment of baseline data on pelvic floor function will be performed using the questionnaire “Uppgifter om hälsa före graviditeten”. The questionnaires “Female Sexual Function Index” (FSFI) and “Female Sexual Distress Scale” (FSDS) will be used for in depth assessment of sexual function. Quality of life will be measured using the questionnaire Euro-QoL-5D.

### *7.2.2 Follow up 2 months (up to 6 months after delivery)*

Assessment of duration of pain medication, pelvic floor and sexual function will be performed using the questionnaire “Din värdering av behandlingen av förlossningsbristningen (ca 8 veckor)”. Assessment of birth satisfaction will be performed using the Birth Satisfaction Scale (BSS-R) and the Child Experience Questionnaire (CEQ 2.0).

#### *7.2.3 Follow up 6 months (up to 12 months after delivery)*

(In at least one site) The scar after tears/episiotomy will be measured using a ruler and a protractor, pelvic organ prolapse will be quantified using a specific score (POP-Q), and transperineal, endovaginal and transrectal 2D/3D ultrasound will be used to evaluate occult OASIS and other injuries to the muscles of the pelvic floor. In the other sites, an individual clinical follow-up will be offered at six months after delivery, without any planned data entry points.

#### *7.2.4 Follow up 12 months (up to 18 months after delivery)*

Assessment of pelvic floor and sexual function will be performed using the questionnaire "Din värdering av behandlingen av förlossningsbristningen (ca 1 år)". The questionnaires "Female Sexual Function Index" (FSFI) and "Female Sexual Distress Scale" (FSDS) will be used for in depth assessment of sexual function. Quality of life will be measured using the questionnaire Euro-QoL-5D.

#### *7.2.5 Follow up 5 years (up to 5 years and 6 months after delivery)*

Assessment of pelvic floor and sexual function will be performed using the questionnaire "Din värdering av behandlingen av förlossningsbristningen (ca 1 år)". *The questionnaires "Female Sexual Function Index" (FSFI) and "Female Sexual Distress Scale" (FSDS) will be used for in depth assessment of sexual function. Quality of life will be measured using the questionnaire Euro-QoL-5D.*

Data on mode of delivery, episiotomy, and OASIS in a subsequent pregnancy will be collected from the Pregnancy Register.

#### *7.2.6 Follow up 10 years*

Data on mode of delivery, episiotomy, and OASIS in a subsequent pregnancy will be collected from the Pregnancy Register.

### 7.3 End of Study

The end of study is defined as the last follow up for the last subject.

## 8 Selection and Withdrawal of Subjects

### 8.1 Inclusion Criteria

- Non-parous woman
- Singleton, live fetus in cephalic presentation
- Gestational week 34+0 or more
- Requiring vacuum assisted vaginal delivery
- Signed informed consent

### 8.2 Exclusion Criteria

- Previous surgery for incontinence or prolapse

### 8.3 Subject Log

Investigators must keep a record, a screening log, of all patients that were considered for enrolment even if they were not subsequently enrolled. In this study, this applies to all women who have given consent to participation. This information is necessary to verify that the patient population was selected

without bias. The reasons for non-eligibility are to be defined in terms of one or more of the eligibility criteria.

Investigators must also keep a Subject identification log of all patients enrolled (equals to randomized) which includes sufficient information to link records, i.e. the Case Report Form (CRF) and clinical records.

# 9 Intervention

## 9.1 Description of the intervention

Intervention: Lateral episiotomy
Comparison: No episiotomy

In all women, the urinary bladder should be emptied by catheterization before application of the vacuum cup. For pain relief, a pudendal block (PDB) can be administered using for example Mepivakain (Carbocain) 10 mg/ml 5-10 ml. The anesthetic substance is injected using a Kobak needle on each side localizing the ischiadic spines bilaterally.

For women randomized to the intervention group, lateral episiotomy is performed as follows.
Local anesthesia is administered using for example Mepivacaine (Carbocain) or Lidocaine (Xylocain) in the hymeneal plane, 1 ml subcutaneously at the incision point and 9 ml in a fan-like fashion from the incision point. The vacuum cup is then applied and the extraction is performed until the fetal head is crowning, i.e. the cup is visible in the vaginal opening.

Lateral episiotomy is then performed using specific episiotomy scissors, Mayo scissors, or similar.

- Distance from incision point to the posterior fourchette: at least 1 cm, up to 3 cm.
- Angle from the sagittal or parasagittal plane: 60° (45-80°, aim at the ischiadic tuberosity)
- Length of the incision: 4 cm (3-5 cm)

All women will receive perineal support using verbal guiding and manual support of the perineum during the delivery of the head and body. The third stage, examination and diagnosis of perineal tears is managed according to clinical routine. Suturing is managed according to clinical routine or as suggested in the study specific SOP, see appendix 21.2 Standard Operating Procedures.

## 9.2 Randomization

The physician in charge of the operative delivery is responsible for randomization. Women included in the study will be randomized to lateral episiotomy or no episiotomy using opaque envelopes on the vacuum extractor equipment wagon.

# 10 Assessments

## 10.1 Perineal injury

A physician specialist or a senior registrar physician will make the diagnosis clinically. In a subgroup, diagnosis will be confirmed by transperineal and transrectal ultrasound at six to 12 months after delivery. This will be performed in a participating site where the method is established for the diagnosis

of OASIS. Any degree of perineal injury will be recorded. Data will be entered manually and collected from the Pregnancy register.

### 10.2 Blood loss

Postpartum hemorrhage is measured in milliliters. Data will be collected from the Pregnancy register.

### 10.3 Neonatal outcome

Assessment of Apgar score is performed according to clinical routine. The score at 1, 5, and 10 min is recorded for the study. Umbilical cord blood is sampled routinely in all operative deliveries. Arterial and venous blood gases are analyzed using regular equipment in the ward. Data will be collected from the Pregnancy register.

### 10.4 Admission to the Neonatal ward

Admission to the Neonatal ward (duration of stay and prevalence) will be collected from the Swedish Neonatal Quality Register (SNQ).

### 10.5 Scalp trauma and other neonatal trauma

Clinical diagnosis of cephalic hematoma/subgaleal hematoma/intracranial hemorrhage as well as diagnosis of fractures, obstetric brachial plexus palsy and hypoxic ischemic encephalopathy by neonatologist. These variables will be collected from the Pregnancy register and the SNQ.

### 10.6 Duration of hospital stay

Duration of hospital stay (days) after delivery will be collected from the Pregnancy register.

### 10.7 Pain and birth experience after delivery

Pain after delivery will be assessed using a simplified VAS (0-10) and this assessment will be included in the questionnaires.

Birth experience after delivery will be assessed using a simplified VAS (1-10). This variable will be collected from the Pregnancy register.

### 10.8 Questionnaires

The questionnaires ”Uppgifter om hälsa före graviditeten” and “Din värdering av behandlingen av förlossningsbristningen” will be used for assessment of pelvic floor and sexual function. The questionnaire is identical to the baseline questionnaire used in ”Bristningsregistret”, a national register of perineal injuries in obstetric care. The questionnaire consists of a set of questions regarding pelvic floor function, i.e. urinary and anal continence, symptoms of vaginal prolapse, sexual function, and bowel function.

The questionnaires “Female Sexual Function Index” (FSFI) and “Female Sexual Distress Scale” (FSDS) will be used for in depth assessment of sexual function. Both contain questions on sexual arousal, lubrication, pain, and orgasm.

The Birth Satisfaction Scale (BSS-R) (20, 21) and The Childbirth Experience Questionnaire (CEQ 2.0)(22) will be used for assessment of the birthing experience and satisfaction. The questionnaires contain questions regarding self-empowerment, fear, and overall satisfaction with care.

Euro-QoL-5D will be used for assessment of quality of life. The questionnaire contains 5 questions on mobility, personal hygiene, anxiety, and an over-all health evaluation using a VAS scale (23).

All the questionnaires will be managed by the patient survey company ImproveIT AB, with extensive experience in web-based questionnaires. Data will be encrypted and kept confidential and forwarded to the research team for clinical follow-up.

### 10.9 Perineal evaluation with ultrasound and clinical pelvic exam

In a subgroup of patients at specific sites, a structured clinical pelvic exam at 6-12 months after delivery will be done. The scar after tears/episiotomy will be measured, a pelvic organ prolapse quantification (POP-Q) score will be applied, and transperineal, endovaginal and transrectal 2D/3D ultrasound will be used to evaluate different parts of the pelvic floor. This exam will be accompanied by a questionnaire under development called (Q-SOPhIE, Questionnaire on Symptoms of Obstetric Perineal tears).

### 10.10 Pregnancy register and patient register

Data on several background variables, a number of outcome variables, and mode of delivery, episiotomy, and OASIS in a subsequent pregnancy will be collected from the Pregnancy Register. Data on outcomes regarding pelvic floor function may be collected from the Patient register in a later sub-study.

## 11 Proceedings for Adverse Events

### 11.1 Definition of Adverse Events

#### *11.1.1 Definition of Adverse Events*

An Adverse Event (AE) is any untoward medical occurrence in a subject and which does not necessarily have a causal relationship with the allocated treatment. An AE can be any unfavourable and unintended sign, abnormal laboratory finding, symptom or disease temporally associated with the subject participating in the clinical study, whether or not related to the allocated treatment.

#### *11.1.2 Definition of Serious Adverse Events*

Each AE is to be classified by the investigator as serious or non-serious. Seriousness is not defined by a medical term; it is a result or an outcome. An AE is defined as a Serious Adverse Event (SAE) if it:

- results in death
- is life-threatening
- requires admission to an intensive care unit
- results in persistent or significant disability/incapacity
- other medically important event

### 11.2 Assessment of Adverse Events

#### *11.2.1 Assessment of Intensity*

Each AE is to be classified by the investigator as mild, moderate or severe.
**Mild:** Acceptable. The subject is aware of symptoms or signs, but these are easily tolerated.
**Moderate:** Disturbing. The AE is discomforting enough to interfere with usual daily activities.
**Severe:** Unacceptable. The subject is incapable of working or performing usual daily activities.

#### *11.2.2 Assessment of Causality*

**Unlikely:** The event is most likely related to an aetiology other than the allocated treatment.
**Possible:** A causal relationship is conceivable and cannot be dismissed.
**Probably:** Good reason and sufficient documentation to assume a causal relationship.

### 11.3 Methods for Eliciting Adverse Events

AEs are spontaneously reported by subject, or reported by subject to study personnel during study visit or other visits at the participating the clinic, or by laboratory test results. Events will be registered when reported in the CRF AE form by date, time, symptoms and course of events.

### 11.4 Reporting of Adverse Events

All AEs will be rated as serious or non-serious and the causality will be assessed. Only AEs classified as serious (SAEs) will be recorded in the CRF. AEs reported in the questionnaire at 2 months' follow-up do not need separate recording in the CRF. SAEs will be reported by the investigator to the sponsor within 72 hours after the SAE has been communicated to the investigator. Follow-up information describing the outcome of the SAE and actions taken will be reported as soon as available.

### 11.5 Follow-up of Adverse Events

For all AEs, the subject will be followed until either the AE has ceased or until the subject is under professional medical care and a potential causality between the study treatment and the AE has been assessed.

## 12 Statistics and Data Management

### 12.1 Data Management

Data will be entered electronically from the Pregnancy register and from the questionnaires into the database. Data from the CRF will be entered manually into the database, until an eCRF has been developed.

### 12.2 Statistical Analysis

Descriptive statistics will be used to characterize the groups of individuals recruited to the study to investigate comparability of the two groups at baseline. T-tests and Chi-square tests will be used depending on variable characteristics.

Data will be analysed both by intention to treat and per protocol. The primary analysis will comprise intention-to-treat comparisons between the intervention group and the control group for both primary and secondary maternal and fetal outcomes. Results will be presented as absolute prevalence (rate of OASIS) or measurement (post-partum haemorrhage in millilitres), and after univariable and multivariable logistic regression analysis as odds ratios with 95% confidence intervals. The multivariable logistic regression models will adjust for possible confounders/effect modifiers such as maternal Body Mass Index (BMI) (>30), operator skills (specialist or not), long duration of labour >12 hours, epidural and use of oxytocin expressed as binary variables.

Secondary analyses will compare secondary outcomes using comparison of test of proportions, t-test and logistic regression depending on variable characteristics in the research questions. Outcomes based on evaluation scores (Wexner score and Birth Satisfaction Scale) will be analysed by non-parametric

tests (Mann-Whitney, Rank sum or Wilcoxon two unpaired samples) but also paired analyses for change over time (up to 5 years after delivery) in the subgroups using Sign test.

### 12.3 Determination of Sample Size

Primary outcome variable is prevalence of OASIS in the intervention group (lateral episiotomy) compared to the control group (no episiotomy). The average prevalence of OASIS in operative vaginal delivery in all women (not only non-parous women) was 12.4% in Sweden according to the Medical Birth Register in 2015. At Danderyd Hospital, the prevalence of OASIS has varied between 14 and 18% in primiparous women. In normal vaginal delivery, the prevalence of OASIS is 6-7% in primiparous women in Sweden. A reduction of OASIS from 12.4% to 6.2% ("normal delivery rate") can be detected with 80% power and 5% risk of alpha-error (p-value <0.05) with 350 women in each group using Chi-square test comparing two independent proportions in a two-sided test (1.5% loss of follow-up). A reduction to 7.8% is clinically valuable, thus a sample size of 694 women in each allocation group is needed. Total number of patients are 1400 women. We will perform a first interim analysis after 350 randomized women, to detect a possible reduction from 12.4% to 2.5% with 80% power and p-value <0.01, and a second interim analysis after 700 randomized women, to detect a possible reduction from 12.4% to 6.2% with 80% power and p-value <0.05. We are planning at least three sites. Depending on the size of the delivery ward, each site will contribute with approximately 5% of non-parous women giving birth vaginally (70-200 patients annually). Inclusion rate is expected to be 3 patients/week at a site with 300 annual vacuum extractions in non-parous women, if 50% of women accept participation.

# 13 Quality Control and Quality Assurance

## 13.1 Source Data

The requirements regarding information in the medical records follows the "Patientdatalagen" (SFS 2008:355) and the coming General Data Protection Regulation (from May 2018). Information that is of importance for the wellbeing and care of the patient, must be recorded in the medical records. The following study specific information should also be recorded:

- Study title and a brief description of the study in terms of intervention and assessments
- Date when patient information was given and when signed Informed Consent was obtained
- Subject randomization number
- Medically responsible study doctor, with contact details

Details and information that is study specific and of no interest for the medical care of the subject can be recorded in the CRF and other documents and may be considered as source data. Prior to study start the expected location of source data (e.g. medical record notes, CRF, work sheets), must be identified and documented. This will be done by completing a site-specific Source Data List.

## 13.2 Monitoring

The Sponsor will appoint an independent monitor for quality control of the study. Monitoring will be performed before, during and after study completion in accordance with the International Conference of Harmonization Good Clinical Practice (ICH GCP) guidelines. The extent of monitoring will be described in a monitoring plan, which will be approved by the Sponsor. Study conductance, source data, adherence to the study protocol and ICH GCP will be monitored.

# 14 Direct Access to Source Documents

The Investigator(s) will permit study-related monitoring, providing direct access to source data/hospital records. The Investigator verifies that each patient has consented in writing to direct access to the original source data/hospital records using written patient information and signed Informed Consent. During the monitoring, the data recorded in the CRFs by the Investigator will be controlled for consistency with the source data/hospital records by the study monitor (source data verification). The monitor will sign a secrecy agreement.

# 15 Ethics

## 15.1 Independent Ethics Committee

It is the responsibility of the Investigator to obtain approval of the study protocol/protocol amendments, the subject information and the Informed Consent from the Independent Ethics Committee (IEC) before enrolment of any subject into the study.

## 15.2 Ethical Conduct of the Study

The study will be performed in accordance with the protocol, ICH GCP, and the ethical principles of the World Medical Association (WMA) Declaration of Helsinki (as amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013).

### 15.3 Risk - benefit assessment

Childbirth is associated with pain and discomfort, which may increase with an episiotomy as well as with a perineal injury. An estimated 80% of women sustain at least a 2nd degree perineal injury in operative vaginal delivery, which is similar in size to a lateral episiotomy. Thus, the risk of pain and discomfort is similar in both allocation groups. Negative sensations are reduced by routine local anesthesia. The risk of long term pain is not known, and will be assessed.

The questions in the questionnaires in follow-up are private in nature and can be perceived as psychologically disturbing or intrusive. Information about the importance of the answers before distribution may reduce discomfort.

Benefits of study participation could be a standardized anesthetic routine before the vacuum extraction, a standardized perineal support, and a standardized follow-up including a contact person at the research clinic, and an optional follow-up visit at 6 months after delivery. In clinical routine, there is only follow-up of third-fourth degree tears.

### 15.4 Subject Information and Informed Consent

It is the responsibility of the Investigator, or a person designated by the Investigator, to provide each subject with full and adequate verbal and written information about the objectives, procedures and possible risks and benefits of the study. All subjects should be given the opportunity to ask questions about the study and should be given sufficient time to decide whether to participate in the study or not.

The subjects will be notified of their voluntary participation and of their freedom to withdraw from the study at any time and without giving any reason. Subjects must also be informed that withdrawing from the study will not affect their future medical care, treatment or benefits to which the subject is otherwise entitled.

The Investigator, or a person designated by the Investigator, is responsible for obtaining written Informed Consent from all subjects prior to enrolment in the study. The Informed Consent Form must be signed and dated before any study-specific procedures are performed. The Investigator should file the signed Informed Consent Forms in the Investigator's File for possible future audits and inspections. A copy of the subject information and the Informed Consent Form should be given to the subject.

## 16 Data Handling and Record Keeping

### 16.1 Case Report Forms

Case Report Forms (CRF) will be provided for the recording of all data. The Investigator is responsible for ensuring the accuracy, completeness, legibility and timeliness of the data recorded in the CRFs.

### 16.2 Record Keeping

To enable audits and evaluations by the Sponsor, the Investigator shall keep records (essential documents) of the study for at least 10 years after end of the study. This includes any original source data related to the study, the subject Identification log (with subject numbers, full names and addresses) and the original signed Informed Consent Forms.

The Sponsor is also, as per ICH GCP-requirements, responsible for archiving their part of the study documentation.

## 17 Financing and Insurance

This is a non-commercial study financed by research grants. Subjects in the study are covered by the Patient Insurance (LÖF).

## 18 Publication Policy

The results from the study will be published in peer reviewed medical journals. Furthermore, information about the study will be publicly accessible in a clinical trial registry (www.clinicaltrials.gov).

## 19 Supplements

### 19.1 Amendments

No change in the study procedures shall be effected without the mutual agreement of the Investigator and the Sponsor (except where necessary to eliminate an immediate hazard to subjects). All changes of the final study protocol must be documented by signed protocol amendments. Any substantial changes to the design or procedures of the study should be reviewed and approved by the IEC before implementation.

### 19.2 Personnel Information

It is the responsibility of the Investigator to ensure that all personnel involved in the study are fully informed of all relevant aspects of the study, including detailed knowledge of and training in all procedures to be followed.

## 20 References

1. Pirhonen JP, Grenman SE, Haadem K, Gudmundsson S, Lindqvist P, Siihola S, et al. Frequency of anal sphincter rupture at delivery in Sweden and Finland--result of difference in manual help to the baby's head. Acta Obstet Gynecol Scand. 1998;77(10):974-7.
2. Laine K, Gissler M, Pirhonen J. Changing incidence of anal sphincter tears in four Nordic countries through the last decades. Eur J Obstet Gynecol Reprod Biol. 2009;146(1):71-5.
3. Raisanen SH, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Lateral episiotomy protects primiparous but not multiparous women from obstetric anal sphincter rupture. Acta Obstet Gynecol Scand. 2009;88(12):1365-72.
4. Stedenfeldt M, Pirhonen J, Blix E, Wilsgaard T, Vonen B, Oian P. Episiotomy characteristics and risks for obstetric anal sphincter injuries: a case-control study. BJOG. 2012;119(6):724-30.
5. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal sphincter tears during delivery. Obstet Gynecol. 2008;111(5):1053-7.
6. Hirsch E, Haney EI, Gordon TE, Silver RK. Reducing high-order perineal laceration during operative vaginal delivery. Am J Obstet Gynecol. 2008;198(6):668 e1-5.
7. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. BJOG. 2008;115(1):104-8.
8. Revicky V, Nirmal D, Mukhopadhyay S, Morris EP, Nieto JJ. Could a mediolateral episiotomy prevent obstetric anal sphincter injury? Eur J Obstet Gynecol Reprod Biol. 2010;150(2):142-6.

9. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. BJOG. 2008;115(13):1695-702; discussion 702-3.
10. Karbanova J, Rusavy Z, Betincova L, Jansova M, Parizek A, Kalis V. Clinical evaluation of peripartum outcomes of mediolateral versus lateral episiotomy. Int J Gynaecol Obstet. 2014;124(1):72-6.
11. Fodstad K, Laine K, Staff AC. Different episiotomy techniques, postpartum perineal pain, and blood loss: an observational study. Int Urogynecol J. 2012.
12. Fodstad K, Staff AC, Laine K. Effect of different episiotomy techniques on perineal pain and sexual activity 3 months after delivery. Int Urogynecol J. 2014.
13. De Souza A, Dwyer PL, Charity M, Thomas E, Ferreira CH, Schierlitz L. The effects of mode delivery on postpartum sexual function: a prospective study. Bjog. 2015;122(10):1410-8.
14. Fodstad K, Staff AC, Laine K. Sexual activity and dyspareunia the first year postpartum in relation to degree of perineal trauma. Int Urogynecol J. 2016;27(10):1513-23.
15. Signorello LB, Harlow BL, Chekos AK, Repke JT. Postpartum sexual functioning and its relationship to perineal trauma: a retrospective cohort study of primiparous women. Am J Obstet Gynecol. 2001;184(5):881-8; discussion 8-90.
16. Sagi-Dain L, Sagi S. Morbidity associated with episiotomy in vacuum delivery: a systematic review and meta-analysis. Bjog. 2015;122(8):1073-81.
17. Verghese TS, Champaneria R, Kapoor DS, Latthe PM. Obstetric anal sphincter injuries after episiotomy: systematic review and meta-analysis. Int Urogynecol J. 2016.
18. Jiang H, Qian X, Carroli G, Garner P. Selective versus routine use of episiotomy for vaginal birth. Cochrane Database Syst Rev. 2017;2:Cd000081.
19. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993;36(1):77-97.
20. Hollins Martin CJ, Martin CR. Development and psychometric properties of the Birth Satisfaction Scale-Revised (BSS-R). Midwifery. 2014;30(6):610-9.
21. Martin CH, Fleming V. The birth satisfaction scale. Int J Health Care Qual Assur. 2011;24(2):124-35.
22. Dencker A, Taft C, Bergqvist L, Lilja H, Berg M. Childbirth experience questionnaire (CEQ): development and evaluation of a multidimensional instrument. BMC Pregnancy Childbirth. 2010;10:81.
23. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-43.

## 21 Signed Agreement of the Study Protocol

*"I agree to the terms of this trial protocol. I will conduct the study in accordance with the procedures specified in the protocol, the ethical principles in the latest version of the Declaration of Helsinki and ICH GCP."*

**Principal Investigator**

Name

Signature Date

**Coordinating Investigator**
Sophia Brismar Wendel, MD PhD
Department of Women's Health, Danderyd Hospital

Signature Date

**Sponsor**
Sophia Brismar Wendel, MD PhD
Department of Women's Health, Danderyd Hospital

Signature Date

# 22 Appendices

## 22.1 Schedule of Investigational Events

| | Before delivery | Shortly after delivery | At the maternity ward | Follow up 2 months | Follow up 6 months | Follow up 12 months | Follow up 5 years | Follow up 10 years |
|---|---|---|---|---|---|---|---|---|
| Information | x | | | | | | | |
| Informed consent | x | | | | | | | |
| Inclusion/exclusion criteria | x | | | | | | | |
| Randomization | x | | | | | | | |
| Episiotomy/no episiotomy | x | | | | | | | |
| Background variables | x[1] | x[2] | | | | | | |
| Data from Pregnancy register (primary and secondary endpoints) | | x[3] | x[4] | | | | x[5] | x[6] |
| Data from SNQ on neonatal outcome (secondary endpoints) | | | x | | | | | |
| Questionnaire BR 1[7] | | | x | | | | | |
| Questionnaire FSFI+FSDS | | | x | | | x | x | |
| Questionnaire Euro-Qol-5D | | | x | | | x | x | |
| Questionnaire BSS-R | | | | x | | | | |
| Questionnaire CEQ 2.0 | | | | x | | | | |
| Questionnaire BR 2[8] (8 w) | | | | x | | | | |
| Questionnaire BR 3[9] (1 y) | | | | | | x | x | |
| Ultrasound evaluation | | | | | x | | | |
| POP-Q score | | | | | x | | | |
| Measurements of scar | | | | | x | | | |
| Questionnaire Q-SOPhIE | | | | | x | | | |
| Serious adverse events | | x | x | x | x | x | | |

[1] maternal age, country of birth, weight at registration in the antenatal clinic and height
[2] use of Oxytocin, use of regional or local anesthesia, birth weight, head circumference, birth length, second stage duration, indication for vacuum extraction, fetal position and station, operator skills, number of pulls, use of sequential instruments
[3] perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH and birth related diagnosis)
[4] birth experience, duration of hospital stay
[5] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[6] mode of delivery, episiotomy, and OASIS in a subsequent pregnancy
[7] ”Uppgifter om hälsa före graviditeten”
[8] ”Din värdering av behandlingen av förlossningsbristningen (ca 8 veckor)”
[9] ”Din värdering av behandlingen av förlossningsbristningen (ca 1 år)”

### 22.2 Standard Operating Procedures

Lateral episiotomi vid sugklocka
Primär suturering av bristningar och klipp

### 22.3 Questionnaires

Uppgifter om hälsa före graviditeten
Din värdering av behandlingen av förlossningsbristningen
Female Sexual Function Index (FSFI)
Female Sexual Distress Scale (FSDS)
Birth Satisfaction Scale (BSS-R)
Childbirth Experience Questionnaire (CEQ 2.0)
Euro-QoL-5D
Questionnaire Q-SOPhIE

**Invitation to first-time mothers**

# The EVA-trial: Lateral Episiotomy in Vacuum Assisted Delivery

Hello first-time mother!

**In this leaflet, you are invited to participate in a medical research trial investigating how to avoid large perineal tears during vacuum assisted delivery.**

Sometimes it is necessary to assist the delivery by using a ventouse suction cup (vacuum assisted delivery). During this type of delivery, it is slightly more common to experience larger tears in the area between the vagina and anus (the perineum), which can involve the anal muscles.

EVA stands for Episiotomy in Vacuum Assisted delivery.

The purpose of this trial is to investigate if it is better to proactively cut (lateral episiotomy), or to leave the perineum to possibly tear spontaneously. The overall aim is to study how larger tears involving the anal muscles can be avoided during vacuum assisted delivery.

***What will we be doing?***

**By intentionally cutting we aim to redirect the tear away from the anal muscles. However, a cut can be more painful than a spontaneous tear whilst healing. Therefore, we would like to ask you, if you require a vacuum assisted delivery, would you consider joining a trial in which you would be randomly selected to undergo a lateral episiotomy (a cut) or a delivery with no cut, but the potential of a spontaneous tear?**

Random selection is a scientific method used to avoid selection errors when dividing patients into separate treatment groups.

If you do require a vacuum assisted delivery you will always receive pain relief. Before a cut an additional local pain relief is given to numb the area around the vagina. If you are randomly selected for a lateral episiotomy this will be performed as the baby's head is being delivered by making a small diagonal cut from the vagina and out to one side. Most women do not feel the cut and do not experience any difference compared to having a spontaneous tear.

All patients will receive the same perineal support to avoid tearing. This means we will manually support the perineum and guide you during your contractions. After delivery, everyone will be properly examined and any cut or tear will be repaired. Larger tears are always repaired in the operating theatre by an experienced doctor.

***How will we follow up?***

**Regardless of which group you belong to, you will receive equal care and follow up.**

During the follow up we will collect data from your medical records and from registers

regarding the delivery and if there were any complications to you or the baby. You will receive questionnaires on the postnatal ward, 2 months, and 1 year after delivery. The questions cover urine and bowel issues as well as sexual function, quality of life, and your childbirth experience. The questionnaires will take 5-10 minutes to complete. You will be offered a follow up visit at 6 months after the delivery. We will also contact you for a follow up at 5 years after delivery.

***Your integrity and safety***

**Participation is voluntary.** It will not affect your care if you choose not to participate. If you decide to participate, your answers are important regardless of whether you experienced complications or not. We aim to improve care during childbirth, specifically during vacuum assisted delivery, and to improve the long-term health and wellbeing of women. Therefore, we need information about your experiences.

Your answers from the questionnaire are kept confidential. They will only be available to the research group (find details below) and will not be included in your medical records. The answers are anonymous and can only be linked to your personal data by the research group. An independent investigator may review the research and will in that case require access to the original data, including medical records and questionnaire answers. The investigator will treat all data as confidential information.

**The medical data and questionnaire answers will be reported as a group so your participation will not be visible in the study results.**

If you wish, you can receive the result from the study when it is published. All data will be kept for 10 years before it is destroyed. Once per year you can request information about your personal data. Please contact us for more information. Your hospital is legally responsible for the personal data in this trial.

*Thank you for your time and consideration to participate!*

**Susanne Hesselman**
Senior Consultant, PhD
Falun Hospital
susanne.hesselman@ltdalarna.se
023-49 2000

**Åsa Leijonhufvud**
Senior Consultant, PhD
Helsingborg Hospital
asa.leijonhufvud@skane.se
042-406 2227

**Helen Fagraeus**
Research midwife
Danderyd Hospital
helen.fagraeus@sll.se
070-737 4988, 08-123 570 22

**Sophia Brismar Wendel**
Senior Consultant, PhD
Danderyd Hospital
sophia.brismar-wendel@sll.se
08-123 585 64

**Informed Consent Form**

# The EVA-trial: Lateral Episiotomy in Vacuum Assisted Delivery

I agree to participate in the EVA-trial, if I would need a vacuum assisted delivery. I know that participation is voluntary and I can at any time change my mind. If I choose not to participate in any part of the follow-up, it will not affect the medical care I receive.

| | |
|---|---|
| Signature | Date |
| Name | Place |
| ”Personnummer” | E-mail (also after delivery) |
| | Mobile number (also after delivery) |
| Signature of researcher/informer | Date |
| Name of researcher/informer | Clinic/Place |

Please hand the consent form to your midwife, who will send it to the responsible investigator at your hospital. The midwife will make a note in your Obstetrix record. You can also bring the consent form along to the delivery ward when it is time to give birth.