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

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Manuscripts

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3 **1 Lateral Episiotomy versus No Episiotomy to Reduce**  
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6 **2 Obstetric Anal Sphincter Injury in Vacuum Assisted**  
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9 **3 Delivery in Nulliparous Women:**  
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14 **4 A Randomised Controlled Trial**  
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1  
2  
3 35 **Abstract**  
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5  
6 36 **Introduction**  
7

8 37 Obstetrical anal sphincter injury (OASIS) occurs in 5-7% of normal deliveries, and increases  
9  
10 38 with vacuum extraction (VE) to 12-14% in nulliparous women in Sweden.

11  
12 39 Lateral/mediolateral episiotomy may reduce the prevalence of OASIS at VE in nulliparous  
13  
14 40 women. The current use of episiotomy is restrictive, and the protective effect and  
15  
16 41 consequences are uncertain. The purpose of this trial is to investigate if lateral episiotomy can  
17  
18 42 reduce the prevalence of OASIS at VE in nulliparous women and to assess short- and long-  
19  
20 43 term effects.  
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22 44

23  
24  
25 45 **Methods and analysis**  
26

27 46 This is a randomised controlled trial of lateral episiotomy versus no episiotomy in nulliparous  
28  
29 47 women with a singleton, live fetus, after gestational week 34+0 with indication for VE. A  
30  
31 48 lateral episiotomy of 4 cm is cut at crowning, 1-3 cm from the midline, at a 60° angle. The  
32  
33 49 primary outcome is OASIS by clinical diagnosis analysed according to intention-to-treat. To  
34  
35 50 demonstrate a 50% reduction in OASIS prevalence (from 12.4% to 6.2%), 709 women will be  
36  
37 51 randomised at a 1:1 ratio. Secondary outcomes are pain, blood loss, other perineal injuries,  
38  
39 52 perineal complications, Apgar score, cord pH, and neonatal complications. Web-based  
40  
41 53 questionnaires at baseline, two months, one and five years, will be used to assess pain,  
42  
43 54 incontinence, prolapse, sexual function, quality of life, and childbirth experience. A subset of  
44  
45 55 women will receive follow-up by pelvic floor sonography and pelvic exam. Mode of delivery  
46  
47 56 and recurrence of OASIS/episiotomy in subsequent pregnancies will be assessed at five and  
48  
49 57 ten years using register data.  
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## 59 Ethics and dissemination

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

## 65 Trial registration

66 28 December 2015 at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02643108).

## 68 Article summary

### 69 *Strengths and limitations of this study*

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

## 79 Keywords

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

## 83 Background

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

90  
91 The use of episiotomy in Sweden is restrictive and was reported in approximately 10% of all  
92 vaginal deliveries and 30% of VE in 2016, with large regional variation (15% to 60%) (2).

93 The restrictive use of episiotomy spread in the 1990-ies, especially after Swedish publications  
94 reported little protective effect on severe perineal injury and increased early postpartum pain  
95 compared to spontaneous tears (4-6). The inability to reduce OASIS in normal delivery has  
96 been confirmed in repeated Cochrane meta-analyses and restrictive use is now generally  
97 recommended (7, 8). The restrictive approach has also influenced practice at operative vaginal  
98 delivery, supported by the uncertain effect of episiotomy in VE in the Swedish setting (9).

99 Following decades of restrictive use, midwives and doctors may have lost knowledge in  
100 correctly performing and repairing episiotomies. There is an inverse correlation between a  
101 nation's rate of episiotomy and rate of OASIS, and the optimal rate of episiotomy in operative  
102 vaginal delivery is not known (10).

103  
104 Several recent retrospective register studies have shown that nulliparous women who received  
105 a lateral or mediolateral episiotomy at VE had a reduced prevalence of OASIS compared to  
106 women without episiotomy (11-14). Lund et al compiled the outcome of 15 register studies in  
107 a meta-analysis published in 2016, and concluded that a mediolateral or lateral episiotomy

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2  
3 108 significantly reduced the risk of OASIS at VE in nulliparous women with aOR 0.53 (95%  
4  
5 109 Confidence Interval (CI) 0.37-0.77)(15). Numbers needed to treat was 18.3 (95%CI 17.7-  
6  
7 110 18.9). The protective effect of mediolateral or lateral episiotomy seemed most pronounced  
8  
9 111 when performed in more than 75% of VE with aOR 0.37 (95%CI 0.15-0.92). The results from  
10  
11 112 these studies were so promising that an official Swedish guideline and a new national  
12  
13 113 educational program launched in 2017 advocated to consider a mediolateral episiotomy at  
14  
15 114 operative vaginal deliveries in nulliparous women (16, 17).  
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18 115

19  
20 116 In register studies, despite controlling for several confounding factors, there is a risk of  
21  
22 117 selection bias, registering shortcomings, and confounding by indication. Furthermore, non-  
23  
24 118 measured variables, such as operator skills and tissue properties might result in residual  
25  
26 119 confounding. None of the register studies showing a protective effect of lateral/mediolateral  
27  
28 120 episiotomy have adjusted for tissue properties or taken the operator's experience or track  
29  
30 121 record of OASIS into account. Such factors may be balanced in a randomised controlled trial.  
31  
32 122 Hence, several authors and institutions, including the Cochrane Collaboration and the  
33  
34 123 Database of Uncertainties about the Effects of Treatments/National Institute for Health and  
35  
36 124 Care Excellence Evidence Search, state that the protective effect of a lateral/mediolateral  
37  
38 125 episiotomy at operative vaginal delivery should be investigated in an adequately sized  
39  
40 126 randomised controlled trial (RCT) (8, 15, 18-20).  
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42  
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44 127

45  
46 128 There is one published British pilot RCT on routine versus restrictive use of episiotomy  
47  
48 129 (undefined type) in operative vaginal delivery in 200 nulliparous women, but the trial was  
49  
50 130 underpowered mainly due to a fairly high rate of episiotomy (52%) in the restrictive group  
51  
52 131 and moderate prevalence of OASIS in both groups (routine 8.1% vs. restrictive 10.9%) (21).  
53  
54 132 The authors estimated that a sample size of 1600 women would have been necessary to  
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3 133 determine a difference at that level. Ethical concerns arise when a number of women will  
4  
5 134 sustain an iatrogenic perineal injury to perhaps avoid OASIS, which may heal well after  
6  
7 135 adequate suturing. Yet, only 4% of the women in the restrictive group in the British pilot trial  
8  
9 136 had an intact perineum after operative vaginal delivery.

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11 137

12  
13 138 Many earlier studies on the effects of episiotomy do not specify the type, although  
14  
15 139 mediolateral episiotomies are preferred in Europe, while lateral episiotomies are mainly used  
16  
17 140 in Finland (10, 21, 22). It is evident that mediolateral and lateral episiotomies often are  
18  
19 141 confused both in clinical practice and in research (15, 23, 24). In an effort to standardize  
20  
21 142 terminology, Kalis et al stated that a lateral episiotomy “begins in the vaginal introitus 1 or  
22  
23 143 2 cm lateral to the midline and directed downwards towards the ischial tuberosity”, while a  
24  
25 144 mediolateral episiotomy is more unclear with a suggested definition starting within 3 mm of  
26  
27 145 the midline and directed laterally at an angle of at least 60 degrees from the midline (25). In  
28  
29 146 the EPITRIAL, Sagi-Dain et al use “lateral/mediolateral” episiotomy, defined as an incision at  
30  
31 147 45-60 degrees and 3-4 cm long (24).

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37 149 We have decided to use lateral episiotomy in our RCT, defined further in the methods section.  
38  
39 150 The purpose of the lateral episiotomy is to cut the bulbocavernosus muscle, which is thought to  
40  
41 151 constitute the main restraining tissue in the vaginal opening at crowning. Lateral episiotomy  
42  
43 152 may affect the superficial transverse perineal muscle, but ideally not the levator muscle,  
44  
45 153 perineal body, or margins of the external anal sphincter muscle, which may be a risk at a  
46  
47 154 mediolateral episiotomy with an insufficient angle. Current evidence suggests little difference  
48  
49 155 between the techniques regarding bleeding, postpartum perineal pain, and sexual resumption  
50  
51 156 (26-30). A correlation between the extent of tissue damage and degree of pain has been  
52  
53 157 observed, but conflicting observations on pelvic floor function and pain after any episiotomy  
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3 158 versus spontaneous perineal injury call for a long-term follow-up to assess the optimal  
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5 159 treatment at delivery (31-34).  
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9 161 In all, to our knowledge, there is no published adequately sized RCT to assess the protective  
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11 162 effect of lateral episiotomy at VE in nulliparous women, nor sufficient published data on  
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13 163 long-term postpartum complications from episiotomy versus spontaneous perineal injury at  
14  
15 164 VE.  
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## 19 20 21 166 Methods and analysis

### 22 23 167 *Aim*

24  
25 168 The aim of this RCT is to investigate if routine lateral episiotomy can reduce the incidence of  
26  
27 169 OASIS at VE in nulliparous women, compared to a no-episiotomy-policy, and to assess short,  
28  
29 170 medium, and long-term effects on pelvic floor symptoms with the two different episiotomy  
30  
31 171 strategies.  
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34 172

### 35 36 173 *Study design and treatment allocation*

37  
38 174 We used the SPIRIT checklist when writing our report (35, 36). Randomisation is performed  
39  
40 175 on a 1:1 basis, based on computer-generated random permuted blocks provided by the  
41  
42 176 independent, non-profit Karolinska Trial Alliance. Treatment group is allocated using sealed  
43  
44 177 opaque envelopes placed on the VE equipment cart for immediate and easy access. When the  
45  
46 178 decision to perform a VE has been made by the attending physician and the patient's consent  
47  
48 179 has been verified, the envelope is opened by the assistant nurse or midwife. The allocated  
49  
50 180 treatment is confirmed by the attending physician, the midwife, and the woman in labour. The  
51  
52 181 allocated treatment cannot be blinded to women or investigators in the trial, nor at follow-up,  
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3 182 due to the design of intervention/no intervention. During analysis, group allocation will be  
4  
5 183 open to the investigators, to enable both intention-to-treat and per protocol analysis.  
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9 185 *Setting*

10  
11 186 All delivery wards in Sweden have been invited to participate in the trial. Presently, three  
12  
13 187 sites are recruiting; Danderyd, Falun, and Helsingborg. All sites are located within large  
14  
15 188 regional or university affiliated hospitals and have immediate access to a specialist  
16  
17 189 obstetrician or senior registrar, anaesthesiologist, operating theatre, and a neonatal intensive  
18  
19 190 care unit. Danderyd has approximately 6500 annual deliveries, of which 300 are VE in  
20  
21 191 nulliparous women, while Falun and Helsingborg each have approximately 3500 annual  
22  
23 192 deliveries, of which 150 are nulliparous VE.  
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28 194 *Characteristics of participants and informed consent*

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30  
31 195 All women expecting their first child, and  
32  
33 196 planning to deliver vaginally at the study sites,  
34  
35 197 are invited to participate. Written and oral  
36  
37 198 information is given by midwives and physicians  
38  
39 199 at regular visits to antenatal care from gestational  
40  
41 200 week 24. Women will also be approached at  
42  
43 201 visits to the hospital before delivery. Written  
44  
45 202 information is at present available in Swedish,  
46  
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48  
49 203 English, and Arabic. Signed informed consent forms are forwarded to the research midwife or  
50  
51 204 principal investigator at each site and documented in the woman's medical record. Women  
52  
53 205 who have contraindications to vacuum extraction will not be invited to participate in the trial,  
54  
55 206 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

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3 207 approval has been given to invite women in labour, if adequate pain relief has been given, and  
4  
5 208 there is enough time to obtain informed consent. The woman's consent is verified by the  
6  
7 209 attending physician before randomisation.  
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10 210

11 211 *Description of the intervention and comparison*

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13  
14 212 The decision to assist the delivery by vacuum extraction is made at the attending physician's  
15  
16 213 discretion. In all women, the urinary bladder should be emptied by catheterization and  
17  
18 214 adequate pain relief is recommended, prior to application of the vacuum cup. Pain relief may  
19  
20 215 consist of epidural anaesthesia, a pudendal block, or local infiltration.  
21

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24  
25 217 For women allocated to "lateral episiotomy", a lateral episiotomy is performed as follows.

26  
27 218 Local anaesthesia is recommended injecting Mepivacaine, Lidocaine, or similar local  
28  
29 219 anaesthetic in the hymeneal plane, 1 ml subcutaneously at the incision point and 9 ml in a fan-  
30  
31 220 like fashion from the incision point. The vacuum cup is then applied and the extraction is  
32  
33 221 performed synchronously with the contractions and pushing efforts, until the cup is visible in  
34  
35 222 the vaginal opening, which corresponds to the crowning head.  
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39  
40 224 Lateral episiotomy is then performed using specific episiotomy scissors, Mayo scissors, or  
41  
42 225 similar scissors.

- 43  
44 226
- 45 • Distance from incision point to the posterior fourchette: at least 1 cm, up to 3 cm.
  - 46
  - 47 227 • Angle from the sagittal or parasagittal plane: 60° (45-80°, aim at the ischiadic
  - 48
  - 49 228 tuberosity)
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  - 51 229 • Length of the incision: 4 cm (3-5 cm)
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3 231 For women allocated to “no episiotomy”, the perineum will possibly remain intact or tear  
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5 232 spontaneously. The operator may only perform episiotomy on fetal indication or on the  
6  
7 233 clinical judgement that extensive perineal injury cannot be avoided, which should comprise  
8  
9 234 less than 30% of the VE, if practice is unchanged. Any episiotomy should be lateral.  
10  
11 235 Episiotomy rates in trial participants and non-participants will be followed continuously by  
12  
13 236 the principal investigators.  
14

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18 238 All women will receive perineal protection using verbal guiding and manual support of the  
19  
20 239 perineum during the delivery of the fetal head and body. The third stage, examination and  
21  
22 240 diagnosis of perineal tears is managed according to clinical routine. The clinical diagnosis of  
23  
24 241 OASIS is our primary outcome. Adequate pain relief should again be offered to enable a  
25  
26 242 thorough clinical bi-digital rectal/vaginal exam to reveal any injury to the sphincter muscles  
27  
28 243 or rectum. The diagnosis is confirmed by a specialist gynaecologist/obstetrician or senior  
29  
30 244 registrar. Suturing of OASIS is performed by a specialist gynaecologist/obstetrician or senior  
31  
32 245 registrar and managed according to clinical routine or as suggested in the standard operating  
33  
34 246 procedures.  
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39 248 *Primary and secondary outcomes*

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41 249 The primary outcome is OASIS, also called third or fourth degree perineal tear, engaging the  
42  
43 250 external or internal anal sphincter muscles (International Classification of Diseases 10 code  
44  
45 251 O70.2 or O70.3). Diagnosis is made by clinical examination by a specialist  
46  
47 252 obstetrician/gynaecologist or senior registrar.  
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52 254 Short-term secondary outcomes are other degrees of perineal injury, blood loss postpartum,  
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54 255 complications to episiotomy or perineal injuries such as dehiscence or infection, Apgar score,  
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3 256 umbilical artery pH <7.05, shoulder dystocia, admission to the Neonatal ward, neonatal injury  
4  
5 257 (scalp trauma, obstetric brachial plexus palsy, cerebral injury, hypoxic ischemic  
6  
7 258 encephalopathy, respiratory distress, and fractures as diagnosed by the neonatologist),  
8  
9 259 duration of hospital stay after delivery, perineal pain, and childbirth experience 1-3 days after  
10  
11 260 delivery by Visual Analogue Scale. The data will be collected from the Swedish Pregnancy  
12  
13 261 Register and the National Quality Register for Neonatal Care. Information from maternal and  
14  
15 262 neonatal medical records is automatically forwarded to the registers when the medical records  
16  
17 263 are signed for archiving. The Swedish Pregnancy Register covers 90% of pregnancies in  
18  
19 264 Sweden and virtually all pregnancies at the study sites (37). The register consists of three  
20  
21 265 parts; the Swedish Maternal Health Care Register, launched in 1999, the Swedish National  
22  
23 266 Quality Register for Prenatal Diagnosis, with data from 2010, and the Obstetric Register,  
24  
25 267 which started in 2014. The three registers thus provide detailed information of pregnancies,  
26  
27 268 labours, and the postpartum period. The National Quality Register for Neonatal Care covers  
28  
29 269 all 37 neonatal wards and neonatal intensive care units in Sweden since 2012, and consists of  
30  
31 270 data from newborns admitted to hospital care from birth until 28 days of age. The primary  
32  
33 271 outcome OASIS and trial specific data not available from the registers will be collected in  
34  
35 272 electronic case report forms supplied and monitored by Karolinska Trial Alliance.  
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39 273  
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41 274 Medium-term secondary outcomes, to be assessed by clinical examination and sonographic  
42  
43 275 imaging six to 12 months after delivery, in at least one study site, are effects on the pelvic  
44  
45 276 floor anatomy. The OASIS diagnosis and the type of episiotomy will be quality controlled.  
46  
47 277 Descriptive data on pelvic floor muscle injury will be collected, specifically injuries to the  
48  
49 278 sphincters and the levator ani muscle. The women at this site will undergo a structured pelvic  
50  
51 279 exam performed by consultant gynaecologists in an independent Centre for Pelvic Floor  
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53 280 Disorders, including measurement of any scar, a clinical assessment of pelvic floor muscle  
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3 281 function by a six-point muscle strength score, prolapse staging by the pelvic organ prolapse  
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5 282 quantification system, and a high-resolution 2D perineal and 3D endovaginal and transrectal  
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7 283 ultrasound. Data from this follow-up will be collected using electronic case report forms  
8  
9 284 supplied and monitored by Karolinska Trial Alliance.  
10  
11 285  
12  
13 286 Medium- and long-term secondary outcomes, to be assessed by web-based questionnaires, are  
14  
15 287 duration of pain medication after delivery, symptoms regarding anal and urinary incontinence,  
16  
17 288 bowel function, prolapse, and sexual function at baseline, two months (up to six months), 12  
18  
19 289 months (up to 18 months), and five years (up to five years and six months) after delivery. The  
20  
21 290 questions are based on the questionnaires used by the Swedish Perineal Tear Register, and  
22  
23 291 will be distributed at identical intervals (baseline, two, and 12 months postpartum) as well as  
24  
25 292 after five years. Anal incontinence is assessed by Wexner score in these questionnaires (38).  
26  
27 293 Childbirth experience will be assessed at two months postpartum using the revised short form  
28  
29 294 of the Birth Satisfaction Scale and the Childbirth Experience Questionnaire (39, 40). The  
30  
31 295 questionnaires “Female Sexual Function Index” and “Female Sexual Distress Scale” will be  
32  
33 296 used for in-depth assessment of sexual function at baseline, one and five years (41-43).  
34  
35 297 Quality of life will be measured using the questionnaire Euro-QoL-5D at baseline, one and  
36  
37 298 five years (44). The questionnaires are administered by an independent provider of patient  
38  
39 299 surveys and data is forwarded to Karolinska Trial Alliance. We will also assess mode of  
40  
41 300 delivery, episiotomy, and OASIS in the subsequent pregnancy at five years and ten years after  
42  
43 301 the index delivery by using data from the Swedish Pregnancy Register. The schedule of all  
44  
45 302 follow-up assessments is illustrated in Figure 1. All collaborators have signed or are obliged  
46  
47 303 under law to keep data confidential during and after the trial.  
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54 305 *Adverse events, data collection and safety*

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3 306 All randomised women are offered a clinical (apart from the trial) follow-up at 6 months and  
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5 307 free and easy access to medical care in association with the episiotomy or perineal tear at the  
6  
7 308 study site during the study period of five years. All women will receive postpartum care as  
8  
9 309 individually needed. Serious adverse events, such as death, a life-threatening event, admission  
10  
11 310 to intensive care, persistent or significant disability or incapacity, or other medically  
12  
13 311 important event, will be reported in a separate form and evaluated by the sponsor and  
14  
15 312 principal investigators continuously. The Karolinska Trial Alliance will monitor the trial  
16  
17 313 conduct, as well as data collection and safety after start-up, midterm, and before closure at  
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19 314 each site, covering 20% of randomised women. Karolinska Trial Alliance will also manage  
20  
21 315 important study protocol modifications and communicate these to relevant parties.  
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26 317 *Statistical methods*

27  
28 318 Baseline data will be summarized by descriptive statistics as appropriate; mean and standard  
29  
30 319 deviation, median, upper and lower quartiles, minimum and maximum, or frequency tables,  
31  
32 320 stratified by the two arms.  
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36  
37 322 Data will be analysed by intention-to-treat and per protocol. The primary outcome variable,  
38  
39 323 clinical diagnosis of OASIS, will be presented in numbers as incidence rate in the two  
40  
41 324 allocation groups (intention-to-treat) and according to received treatment (per protocol). The  
42  
43 325 protective effect of lateral episiotomy will be calculated as a relative risk of OASIS with 95%  
44  
45 326 confidence intervals, adjusting for study site and other possible factors not balanced by  
46  
47 327 randomisation.  
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52 329 Further analyses will compare secondary outcomes using test of proportions, t-test and  
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54 330 logistic regression depending on variable characteristics. In the per protocol analysis of  
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3 331 OASIS, we will adjust for possible confounders/effect modifiers such as study site, country of  
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5 332 birth, maternal body mass index, operator experience, long duration of labor and second  
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7 333 stage, epidural, use of oxytocin, fetal birthweight, head circumference, station and position.  
8  
9 334 We also aim to create a prediction model of the protective effect of lateral episiotomy to aid  
10  
11 335 clinical decision.

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14  
15 337 Outcomes based on evaluation scores will be analysed by non-parametric tests and paired  
16  
17 338 analyses for change over time in the subgroups using Sign test. Details of the statistical  
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19 339 analysis will be supplied in the Statistical Analysis Plan, to be finalized in collaboration with  
20  
21 340 statisticians from the Karolinska Institute in a separate document before the data lock.

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24  
25 342 *Sample size calculation*

26  
27 343 The sample size has been calculated based on data from Lund et al, suggesting a 50%  
28  
29 344 reduction of OASIS in VE, when lateral/mediolateral episiotomy is performed (15). The  
30  
31 345 average rate of OASIS in VE in Sweden was 12.4% in 2016 according to the Swedish  
32  
33 346 Medical Birth Register. A reduction of OASIS from 12.4% to 6.2% can be detected with 80%  
34  
35 347 power and less than 5% risk of alpha-error ( $p$ -value  $<0.05$ ) with 354 women in each group  
36  
37 348 using Chi-square test comparing two independent proportions in a two-sided test (3% missing  
38  
39 349 outcome). A smaller reduction is clinically valuable, although the risk-benefit relationship  
40  
41 350 between receiving a prophylactic episiotomy and the chance of an intact perineum may limit  
42  
43 351 the feasibility of a larger trial in a setting with a restrictive episiotomy policy. We have  
44  
45 352 obtained ethical approval to randomise a total of 1400 women, which enables us to detect a  
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47 353 reduction in OASIS rate at VE from 12.4% to 7.8%.

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51 355 *Interim analyses*

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3 356 The Karolinska Trial Alliance will monitor primary outcome data using the electronic case  
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5 357 report forms, in which the diagnosis of OASIS is registered. We will perform a first interim  
6  
7 358 analysis after 350 randomised women, to detect a possible OASIS prevalence reduction from  
8  
9 359 12.4% to 2.5% with 80% power and p-value <0.01, in concordance with the pronounced  
10  
11 360 reduction observed in the Dutch register study by van Bavel et al (14). If a reduction of  
12  
13 361 OASIS is achieved at this level, the trial will be discontinued and modified, as the clinical  
14  
15 362 equipoise has been sufficiently disturbed. A second interim analysis will be performed after  
16  
17 363 709 randomised women, to detect a possible 50% reduction from 12.4% to 6.2% with 80%  
18  
19 364 power and p-value <0.05. Similarly, the trial will be stopped if a 50% reduction is detected. If  
20  
21 365 feasible, we will continue the trial until 1400 women have been randomised. Depending on  
22  
23 366 the size of the delivery ward, each site will contribute with approximately 5% of nulliparous  
24  
25 367 women giving birth vaginally (70-200 patients annually). Inclusion rate is expected to be two  
26  
27 368 to three patients per week at a site with 300 annual vacuum extractions in nulliparous women,  
28  
29 369 if 50% of women accept participation.  
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33 370

## 35 371 Ethics and dissemination

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38 372 Sweden has the potential for a perfect setting to perform a randomised controlled trial of  
39  
40 373 routine lateral episiotomy versus no episiotomy at VE in nulliparous women, since the  
41  
42 374 episiotomy rate is generally low and the prevalence of OASIS in nulliparous VE is relatively  
43  
44 375 high. We expect that adherence to non-intervention in the control group will be high,  
45  
46 376 facilitating the detection of any difference in OASIS incidence. The timing with new  
47  
48 377 guidelines for considering episiotomy further improves the setting of the study. It is crucial to  
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50 378 undertake and complete the trial now before new guidelines, advocating a liberal use of  
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52 379 episiotomy in VE in nulliparous women, are implemented despite low-grade evidence and  
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54 380 lack of long-term follow-up.  
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5 382 The low episiotomy rate may also limit the feasibility of the study. A survey regarding  
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7 383 episiotomy preferences and indications was performed in 2012 among 297 delegates at the  
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9 384 biennial Nordic obstetrical and gynaecological conference in Norway (23). Only 17% of the  
10  
11 385 54 Swedish senior consultants who participated perceived instrumental delivery as an  
12  
13 386 indication for episiotomy, while fetal distress was the most accepted indication.

14  
15 387 Consequently, 87% of the Swedish doctors never, seldom, or only sometimes performed an  
16  
17 388 episiotomy at VE. Thus, experience from episiotomy may be lacking and there is a need for  
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19 389 education and training at the sites when the study is being implemented.  
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24 391 Prior to the previously described British pilot RCT, Macleod and Murphy performed a survey  
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26 392 among 1631 obstetricians and specialist registrars in the United Kingdom and Ireland in 2006  
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28 393 with regard to operative vaginal delivery and the use of episiotomy (21, 45). The great  
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30 394 majority (72%) reported a restrictive attitude towards use of episiotomy in VE, although less  
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32 395 than 10% held the view that episiotomy increased the risk of OASIS. Over 65% of responders  
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34 396 said that they would be happy to participate in an RCT of restrictive versus routine use of  
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36 397 episiotomy at operative vaginal delivery. We estimate that a similar proportion of Swedish  
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38 398 physicians and midwives hold the same view, although hesitance to recruit women due to  
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40 399 private opinions on episiotomy may be another limitation.  
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46 401 The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2  
47  
48 402 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from  
49  
50 403 all participating women as described above. Pregnant women are generally curious about the  
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52 404 trial and the majority of approached women consent to participate, particularly motivated by a  
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54 405 thorough follow-up no matter what perineal injury. The interest from pregnant women is  
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3 406 consistent with the observation that 85% of invited women agreed to participate in the pilot  
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5 407 RCT by Murphy et al, although the rationale for participation may have been the chance to  
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7 408 avoid an episiotomy in their setting (21).  
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9 409  
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11 410 Considering the admitted knowledge gap regarding effectiveness and consequences of routine  
12  
13 411 lateral/mediolateral episiotomy in operative vaginal deliveries, we anticipate broad interest in  
14  
15 412 the results from this trial (8, 15, 18-20). Being a non-commercial academic study, the  
16  
17 413 investigators will author the results adhering to the authorship criteria recommended by the  
18  
19 414 International Committee of Medical Journal Editors. We intend to disseminate the results by  
20  
21 415 publication in peer-reviewed medical journals and public press, and by presentations at  
22  
23 416 national and international congresses. Data can be made available for future meta-analyses to  
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25 417 improve informed practice.  
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## 419 List of abbreviations

32  
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34 420 EVA – Episiotomy in Vacuum Assisted delivery  
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36 421 OASIS – Obstetrical anal sphincter injury/injuries  
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38 422 VE – Vacuum Extraction  
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41 423 RCT – Randomised Controlled Trial  
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43 424 OR – Odds ratio  
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3 427 **Declarations**  
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5 428 *Ethics approval and consent to participate*  
6

7 429 The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2  
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9 430 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from  
10  
11 431 all participating women.  
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16 433 *Consent for publication*  
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18 434 If case reports will be published, consent will be obtained from relevant parties.  
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23 436 *Availability of data and material*  
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25 437 The datasets generated and/or analysed are not publicly available due the possibility to extract  
26  
27 438 personal information, but may be made available from the corresponding author on request.  
28

29 439 All principal investigators will be given access to the final cleaned datasets and submissions  
30

31 440 for publication will be made in agreement. To ensure confidentiality, data dispersed to  
32

33 441 collaborators will be blinded of any identifying participant information.  
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36 442

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38 443 *Competing interests*  
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40 444 The authors have no competing interests to declare.  
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43 445

44 446 *Funding*  
45

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47  
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49 448

50  
51 449 *Author contributions*  
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53 450 Sandra Bergendahl and Victoria Ankarcrona are investigators and responsible for the  
54

55 451 implementation of the trial, and manuscript draft and revision. Åsa Leijonhufvud and Susanne  
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3 452 Hesselman are principal investigators at Helsingborg and Falun sites and responsible for  
4  
5 453 implementation of the trial, and manuscript draft and revision. Sofie Karlström is responsible  
6  
7 454 for the design, implementation, and investigations in the sub-study of pelvic floor anatomy at  
8  
9 455 six to 12 months after delivery. Helena Kopp Kallner is responsible for the manuscript  
10  
11 456 revision, funding, and study design. Sophia Brismar Wendel is overall responsible for the  
12  
13 457 implementation of the trial, manuscript draft and revision, funding, study design, and the  
14  
15 458 original idea of the study. All authors have participated in manuscript writing and have  
16  
17 459 approved the final version.  
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596 **Figure 1. Schedule of enrolment, interventions, and assessments in the EVA trial.**

TIME POINT	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					Close-out
	-4m	0	0m	2m	6m	1y	5y	10y
<b>ENROLMENT:</b>								
Information	x							
Informed consent	x							
Inclusion/exclusion criteria	x							
Randomisation		x						
<b>INTERVENTIONS:</b>								
Episiotomy		x						
No episiotomy		x						
<b>ASSESSMENTS:</b>								
Background variables	x <sup>1</sup>		x <sup>2</sup>					
Data from Pregnancy register (primary and secondary endpoints)			x <sup>3,4</sup>				x <sup>5</sup>	x <sup>6</sup>
Data from SNQ on neonatal outcome (secondary endpoints)			x					
Questionnaire BR 1 <sup>7</sup>			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 <sup>8</sup> (8 w)				x				
Questionnaire BR 3 <sup>9</sup> (1 y)						x	x	
Ultrasound evaluation					x			
POP-Q score					x			
Measurements of scar					x			
Questionnaire Q-SOPhIE					x			
Serious adverse events <sup>10</sup>		x	x	x	x	x	x	x

<sup>1</sup> maternal age, country of birth, weight and height at registration in the antenatal clinic

<sup>2</sup> 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

<sup>3</sup> perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH, and birth related diagnosis)

<sup>4</sup> birth experience, duration of hospital stay

<sup>5</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

<sup>6</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

<sup>7</sup> "Uppgifter om hälsa före graviditeten"

<sup>8</sup> "Din värdering av behandlingen av förlossningsbristningen (ca 8 veckor)"

<sup>9</sup> "Din värdering av behandlingen av förlossningsbristningen (ca 1 år)"

<sup>10</sup> 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.

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

598

### 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.

641 **How will we follow up?**

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

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

651 **Your integrity and safety**

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

657  
658 Your answers from the questionnaire are kept confidential. They will only be available to the  
659 research group (find details below) and will not be included in your medical records. The  
660 answers are anonymous and can only be linked to your personal data by the research group.  
661 An independent investigator may review the research and will in that case require access to  
662 the original data, including medical records and questionnaire answers. The investigator will  
663 treat all data as confidential information.

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

667  
668 If you wish, you can receive the result from the study when it is published. All data will be  
669 kept for 10 years before it is destroyed. Once per year you can request information about your  
670 personal data. Please contact us for more information. Your hospital is legally responsible for  
671 the personal data in this trial.

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

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3 676 **Informed Consent Form**

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6 678 **The EVA-trial:**  
7 679 **Lateral Episiotomy in**  
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9 680 **Vacuum Assisted Delivery**

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11 682 I agree to participate in the EVA-trial, if I would need a vacuum assisted delivery. I know that  
12 683 participation is voluntary and I can at any time change my mind. If I choose not to participate  
13 684 in any part of the follow-up, it will not affect the medical care I receive.  
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24 Name Place

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40 Signature of researcher/informer Date

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45 Name of researcher/informer Clinic/Place

46 690  
47 691  
48 692 Please hand the consent form to your midwife, who will send it to the responsible investigator  
49 693 at your hospital. The midwife will make a note in your Obstetrix record. You can also bring  
50 694 the consent form along to the delivery ward when it is time to give birth.  
51 695  
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# 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

1			trial, if applicable (see Item 21a for data monitoring committee)	
2	Background and	#6a	Description of research question and justification for undertaking the	5-8
3	rationale		trial, including summary of relevant studies (published and	
4			unpublished) examining benefits and harms for each intervention	
5				
6				
7	Background and	#6b	Explanation for choice of comparators	8-9
8	rationale: choice of			
9	comparators			
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11	Objectives	#7	Specific objectives or hypotheses	8
12				
13	Trial design	#8	Description of trial design including type of trial (eg, parallel group,	8-9
14			crossover, factorial, single group), allocation ratio, and framework	
15			(eg, superiority, equivalence, non-inferiority, exploratory)	
16				
17	Study setting	#9	Description of study settings (eg, community clinic, academic	9
18			hospital) and list of countries where data will be collected. Reference	
19			to where list of study sites can be obtained	
20				
21	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable,	9
22			eligibility criteria for study centres and individuals who will perform	
23			the interventions (eg, surgeons, psychotherapists)	
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26	Interventions:	#11a	Interventions for each group with sufficient detail to allow	10-11
27	description		replication, including how and when they will be administered	
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29	Interventions:	#11b	Criteria for discontinuing or modifying allocated interventions for a	10
30	modifications		given trial participant (eg, drug dose change in response to harms,	
31			participant request, or improving / worsening disease)	
32				
33	Interventions:	#11c	Strategies to improve adherence to intervention protocols, and any	10-11
34	adherence		procedures for monitoring adherence (eg, drug tablet return;	
35			laboratory tests)	
36				
37	Interventions:	#11d	Relevant concomitant care and interventions that are permitted or	11, 13
38	concomitant care		prohibited during the trial	
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40	Outcomes	#12	Primary, secondary, and other outcomes, including the specific	11-13
41			measurement variable (eg, systolic blood pressure), analysis metric	
42			(eg, change from baseline, final value, time to event), method of	
43			aggregation (eg, median, proportion), and time point for each	
44			outcome. Explanation of the clinical relevance of chosen efficacy	
45			and harm outcomes is strongly recommended	
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1	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
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6	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
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11	Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
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15	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
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25	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
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32	Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9
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36	Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
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41	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
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46	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
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56	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
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who discontinue or deviate from intervention protocols

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3	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
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9	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
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14	Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
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18	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
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24	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
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32	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
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37	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
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43	Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	14
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48	Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	17-18
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52	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
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59	Consent or assent	#26a	Who will obtain informed consent or assent from potential trial	9
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		participants or authorised surrogates, and how (see Item 32)	
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3	Consent or assent:	#26b Additional consent provisions for collection and use of participant	n/a
4	ancillary studies	data and biological specimens in ancillary studies, if applicable	
5			
6	Confidentiality	#27 How personal information about potential and enrolled participants	12-13
7		will be collected, shared, and maintained in order to protect	
8		confidentiality before, during, and after the trial	
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11	Declaration of	#28 Financial and other competing interests for principal investigators	19
12	interests	for the overall trial and each study site	
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15	Data access	#29 Statement of who will have access to the final trial dataset, and	19
16		disclosure of contractual agreements that limit such access for	
17		investigators	
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21	Ancillary and post	#30 Provisions, if any, for ancillary and post-trial care, and for	13
22	trial care	compensation to those who suffer harm from trial participation	
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24	Dissemination policy:	#31a Plans for investigators and sponsor to communicate trial results to	18
25	trial results	participants, healthcare professionals, the public, and other relevant	
26		groups (eg, via publication, reporting in results databases, or other	
27		data sharing arrangements), including any publication restrictions	
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31	Dissemination policy:	#31b Authorship eligibility guidelines and any intended use of	18
32	authorship	professional writers	
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35	Dissemination policy:	#31c Plans, if any, for granting public access to the full protocol,	19
36	reproducible research	participant-level dataset, and statistical code	
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39	Informed consent	#32 Model consent form and other related documentation given to	25-27
40	materials	participants and authorised surrogates	
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43	Biological specimens	#33 Plans for collection, laboratory evaluation, and storage of biological	n/a
44		specimens for genetic or molecular analysis in the current trial and	
45		for future use in ancillary studies, if applicable	
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48 The SPIRIT checklist is distributed under the terms of the Creative Commons Attribution License CC-BY-ND  
 49 3.0. This checklist was completed on 21. June 2018 using <http://www.goodreports.org/>, a tool made by the  
 50 [EQUATOR Network](#) in collaboration with [Penelope.ai](#)  
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# 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:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-025050.R1
Article Type:	Protocol
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<b>Primary Subject Heading</b>:	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

SCHOLARONE™  
Manuscripts

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3 1 **Lateral Episiotomy versus No Episiotomy to Reduce**  
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6 2 **Obstetric Anal Sphincter Injury in Vacuum Assisted**  
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26 34 **Protocol version** 3.0 date 18-08-24  
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3 35 **Abstract**  
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6 36 **Introduction**  
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8 37 Obstetric anal sphincter injury (OASIS) occurs in 5-7% of normal deliveries, and increases  
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10 38 with vacuum extraction (VE) to 12-14% in nulliparous women in Sweden.

11  
12 39 Lateral/mediolateral episiotomy may reduce the prevalence of OASIS at VE in nulliparous  
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14 40 women. The current use of episiotomy is restrictive. The protective effect and consequences  
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16 41 are uncertain. This trial will investigate if lateral episiotomy can reduce the prevalence of  
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18 42 OASIS and assess short- and long-term effects.  
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23 44 **Methods and analysis**  
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25 45 This is a randomised controlled trial of lateral episiotomy versus no episiotomy in nulliparous  
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27 46 women with a singleton, live fetus, after gestational week 34+0 with indication for VE. A  
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29 47 lateral episiotomy of 4 cm is cut at crowning, 1-3 cm from the midline, at a 60° angle. The  
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31 48 primary outcome is OASIS by clinical diagnosis analysed according to intention-to-treat. To  
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33 49 demonstrate a 50% reduction in OASIS prevalence (from 12.4% to 6.2%), 710 women will be  
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35 50 randomised at a 1:1 ratio. Secondary outcomes are pain, blood loss, other perineal injuries,  
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37 51 perineal complications, Apgar score, cord pH, and neonatal complications. Web-based  
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39 52 questionnaires at baseline, two months, one and five years, will be used to assess pain,  
40  
41 53 incontinence, prolapse, sexual function, quality of life, and childbirth experience. A subset of  
42  
43 54 women will receive follow-up by pelvic floor sonography and pelvic exam. Mode of delivery  
44  
45 55 and recurrence of OASIS/episiotomy in subsequent pregnancies will be assessed at five and  
46  
47 56 ten years using register data.  
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3 58 Ethics and dissemination

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5 59 The trial is open for enrolment. The trial has received ethical approval from the Regional

6  
7 60 Ethical Review Board of Stockholm and full funding from the Swedish Research Council.

8  
9 61 Women are interested in participation. The predominant restrictive view on episiotomy may

10  
11 62 limit recruitment. Results are of global interest and will be disseminated in peer-reviewed

12  
13 63 journals and at international congresses.

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16  
17 65 Trial registration

18  
19 66 28 December 2015 at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02643108).

20  
21 67

## 22 23 24 25 68 Article summary

### 26 27 69 *Strengths and limitations of this study*

- 28  
29  
30 70 • The main strength is the randomised trial design, which will provide evidence for
- 31  
32 71 routine or restrictive lateral episiotomy at VE in nulliparous women.
- 33  
34 72 • Another strength is the setting with relatively high OASIS rates and low episiotomy
- 35  
36 73 rates, enabling a realistic sample size.
- 37  
38 74 • One limitation is that the primary outcome, diagnosis of OASIS, is made by clinical
- 39  
40 75 examination, which may limit diagnostic accuracy.
- 41  
42 76 • Another limitation is the restrictive view on episiotomy, which may hamper trial
- 43  
44 77 feasibility.
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79 **Keywords**

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

For peer review only



## 83 Background

84 Obstetric anal sphincter injury (OASIS) is a serious complication to vaginal delivery. It is the  
85 most important cause of female anal incontinence, and therefore important to avoid (1).

86 OASIS occurs in 5-7% of spontaneous vaginal births and increases with operative vaginal  
87 delivery to 12-14% in nulliparous women in Sweden (2-4). In 2017, approximately 10% (6-  
88 17%) of nulliparous women were delivered by vacuum extraction (VE) depending on delivery  
89 site, and only a negligible number were delivered by forceps (4).

90  
91 The use of episiotomy in Sweden is restrictive and was reported in approximately 10% of all  
92 vaginal deliveries and 30% of VE in 2016, with large regional variation (10% to 79%) (4).

93 The restrictive use of episiotomy spread in the 1990-ies, especially after Swedish publications  
94 reported little protective effect on severe perineal injury and increased early postpartum pain  
95 compared to spontaneous tears (5-7). The inability to reduce OASIS in normal delivery has  
96 been confirmed in repeated Cochrane meta-analyses and restrictive use is now generally  
97 recommended (8, 9). The restrictive approach has also influenced practice at operative vaginal  
98 delivery, supported by the uncertain effect of episiotomy in VE in the Swedish setting (10).

99 Following decades of restrictive use, midwives and doctors may have lost knowledge in  
100 correctly performing and repairing episiotomies. There is an inverse correlation between a  
101 nation's rate of episiotomy and rate of OASIS, and the optimal rate of episiotomy in operative  
102 vaginal delivery is not known (11).

103

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

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3 108 significantly reduced the risk of OASIS at VE in nulliparous women with an adjusted odds  
4  
5 109 ratio (aOR) of 0.53 (95% Confidence Interval (CI) 0.37-0.77) (16). Numbers needed to treat  
6  
7 110 was 18.3 (95%CI 17.7-18.9). The protective effect of mediolateral or lateral episiotomy  
8  
9 111 seemed most pronounced when performed in more than 75% of VE with aOR 0.37 (95%CI  
10  
11 112 0.15-0.92). The results from these studies were so promising that an official Swedish  
12  
13 113 guideline and a new national educational program launched in 2017 advocated to *consider* a  
14  
15 114 mediolateral episiotomy at operative vaginal deliveries in nulliparous women (17, 18).  
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19  
20 116 In register studies, despite controlling for several confounding factors, there is a risk of  
21  
22 117 selection bias, registering shortcomings, and confounding by indication. Furthermore, non-  
23  
24 118 measured variables, such as operator skills and tissue properties might result in residual  
25  
26 119 confounding. None of the register studies showing a protective effect of lateral/mediolateral  
27  
28 120 episiotomy have adjusted for tissue properties or taken the operator's experience or track  
29  
30 121 record of OASIS into account. Such factors may be balanced in a randomised controlled trial.  
31  
32 122 Hence, several authors and institutions, including the Cochrane Collaboration and the  
33  
34 123 Database of Uncertainties about the Effects of Treatments/National Institute for Health and  
35  
36 124 Care Excellence Evidence Search, state that the protective effect of a lateral/mediolateral  
37  
38 125 episiotomy at operative vaginal delivery should be investigated in an adequately sized  
39  
40 126 randomised controlled trial (RCT) (9, 16, 19-21).  
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44 127

45  
46 128 There is one published British pilot RCT on routine versus restrictive use of episiotomy  
47  
48 129 (undefined type) in operative vaginal delivery in 200 nulliparous women, but the trial was  
49  
50 130 underpowered mainly due to a fairly high rate of episiotomy (52%) in the restrictive group  
51  
52 131 and moderate prevalence of OASIS in both groups (routine 8.1% vs. restrictive 10.9%) (22).  
53  
54 132 The authors estimated that a sample size of 1600 women would have been necessary to  
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3 133 determine a difference at that level. Ethical concerns arise when a number of women will  
4  
5 134 sustain an iatrogenic perineal injury to perhaps avoid OASIS, which may heal well after  
6  
7 135 adequate suturing. Yet, only 4% of the women in the restrictive group in the British pilot trial  
8  
9 136 had an intact perineum after operative vaginal delivery.  
10

11  
12 137

13 138 Many earlier studies on the effects of episiotomy do not specify the type, although  
14  
15 139 mediolateral episiotomies are preferred in Europe, while lateral episiotomies are mainly used  
16  
17 140 in Finland (11, 22, 23). It is evident that mediolateral and lateral episiotomies often are  
18  
19 141 confused both in clinical practice and in research (16, 24, 25). As surveyed at a Nordic  
20  
21 142 Congress of Obstetrics and Gynaecology, the majority of Nordic obstetricians declared to  
22  
23 143 perform a lateral episiotomy, but 64% called it a mediolateral episiotomy (24). Only 20%  
24  
25 144 performed a typical mediolateral episiotomy and one third drew an unclassifiable type. In an  
26  
27 145 effort to standardize terminology, Kalis et al stated that a lateral episiotomy “begins in the  
28  
29 146 vaginal introitus 1 or 2 cm lateral to the midline and directed downwards towards the ischial  
30  
31 147 tuberosity”, while a mediolateral episiotomy is more unclear with a suggested definition  
32  
33 148 starting within 3 mm of the midline and directed laterally at an angle of at least 60 degrees  
34  
35 149 from the midline (26). In the EPITRIAL, Sagi-Dain et al use “lateral/mediolateral”  
36  
37 150 episiotomy, defined as an incision at 45-60 degrees and 3-4 cm long (25).  
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43  
44 152 We have decided to use lateral episiotomy in our RCT, defined further in the methods section.  
45  
46 153 The purpose of the lateral episiotomy is to cut the bulbocavernosus muscle, which is thought to  
47  
48 154 constitute the main restraining tissue in the vaginal opening at crowning. Lateral episiotomy  
49  
50 155 may affect the superficial transverse perineal muscle, but ideally not the levator muscle,  
51  
52 156 perineal body, or margins of the external anal sphincter muscle, which may be a risk at a  
53  
54 157 mediolateral episiotomy with an insufficient angle, distance from the midline, and length (27-  
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3 158 31). Furthermore, current evidence suggests little difference between the techniques regarding  
4  
5 159 bleeding, postpartum perineal pain, and sexual resumption (32-35). A correlation between the  
6  
7 160 extent of tissue damage and degree of pain has been observed, but conflicting observations on  
8  
9 161 pelvic floor function and pain after any episiotomy versus spontaneous perineal injury call for  
10  
11 162 a long-term follow-up to assess the optimal treatment at delivery (32, 36-38).

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15  
16 164 In all, to our knowledge, there is no published adequately sized RCT to assess the protective  
17  
18 165 effect of lateral episiotomy at VE in nulliparous women, nor sufficient published data on  
19  
20 166 long-term postpartum complications from episiotomy versus spontaneous perineal injury at  
21  
22 167 VE.

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## 27 169 Methods and analysis

### 30 170 *Aim*

31  
32 171 The aim of this RCT is to investigate if routine lateral episiotomy can reduce the incidence of  
33  
34 172 OASIS at VE in nulliparous women, compared to a no-episiotomy-policy, and to assess short,  
35  
36 173 medium, and long-term effects on pelvic floor symptoms with the two different episiotomy  
37  
38 174 strategies.

39  
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### 43 176 *Study design and treatment allocation*

44  
45 177 We used the SPIRIT checklist when writing our report (Appendix 1) (39, 40). Randomisation  
46  
47 178 is performed on a 1:1 basis, based on computer-generated random permuted blocks provided  
48  
49 179 by the independent, non-profit Karolinska Trial Alliance. Treatment group is allocated using  
50  
51 180 sealed opaque envelopes placed on the VE equipment cart for immediate and easy access.

52  
53  
54 181 When the decision to perform a VE has been made by the attending physician and the  
55  
56 182 patient's consent has been verified, the envelope is opened by the assistant nurse or midwife.

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3 183 The allocated treatment is confirmed by the attending physician, the midwife, and the woman  
4  
5 184 in labour. The allocated treatment cannot be blinded to women or investigators in the trial, nor  
6  
7 185 at follow-up, due to the design of intervention/no intervention. During analysis, group  
8  
9 186 allocation will be open to the investigators, to enable both intention-to-treat and per protocol  
10  
11 187 analysis. The complete study protocol is available in Appendix 2.  
12

13 188

### 15 189 *Setting*

17  
18 190 All delivery wards in Sweden have been invited to participate in the trial. Presently, three  
19  
20 191 sites are recruiting; Danderyd, Falun, and Helsingborg. All sites are located within large  
21  
22 192 regional or university affiliated hospitals and have immediate access to a specialist  
23  
24 193 obstetrician or senior registrar, anaesthesiologist, operating theatre, and a neonatal intensive  
25  
26 194 care unit. Danderyd has approximately 6500 annual deliveries, of which 300 are VE in  
27  
28 195 nulliparous women, while Falun and Helsingborg each have approximately 3500 annual  
29  
30 196 deliveries, of which 150 are nulliparous VE.  
31

32 197

### 35 198 *Characteristics of participants and informed consent*

37  
38 199 All women expecting their first child, and planning to deliver vaginally at the study sites, are  
39  
40 200 invited to participate. Written and oral information is given and written consent is obtained by  
41  
42 201 midwives and physicians at regular visits to antenatal care from gestational week 24. Women  
43  
44 202 are also approached at visits to the hospital before delivery. Written information and consent  
45  
46 203 forms are at present available in Swedish and English (Appendix 3). Signed informed consent  
47  
48 204 forms are forwarded to the research midwife or principal investigator at each site and  
49  
50 205 documented in the woman's medical record. Women with contraindications to vacuum  
51  
52 206 extraction will not be invited to participate in the trial, neither will women with previous  
53  
54 207 surgery for incontinence or pelvic organ prolapse. Ethical approval has been given to invite  
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3 208 women in labour, if adequate pain relief has been given, and there is enough time to obtain  
4  
5 209 informed consent. Inclusion and exclusion criteria are listed in Table 1. Criteria to be verified  
6  
7 210 by the attending physician at randomisation include signed informed consent, indication for  
8  
9 211 VE, and a cephalic singleton live fetus, gestational week 34+0 or more, as well as the absence  
10  
11 212 of previous surgery for incontinence or prolapse.

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16 214 *Description of the intervention and comparison*

17  
18 215 The decision to assist the delivery by vacuum extraction is made at the attending physician's  
19  
20 216 discretion. In all women, the urinary bladder should be emptied by catheterization and  
21  
22 217 adequate pain relief is recommended, prior to application of the vacuum cup. Pain relief may  
23  
24 218 consist of epidural anaesthesia, a pudendal block, or local infiltration.

25  
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28  
29 220 For women allocated to "lateral episiotomy", a lateral episiotomy is performed as follows.

30  
31 221 Local anaesthesia is recommended, injecting Mepivacaine, Lidocaine, or similar local  
32  
33 222 anaesthetic in the hymeneal plane, 1 ml subcutaneously at the incision point and 9 ml in a fan-  
34  
35 223 like fashion from the incision point. The vacuum cup is then applied and the extraction is  
36  
37 224 performed synchronously with the contractions and pushing efforts, until the cup is visible in  
38  
39 225 the vaginal opening, which corresponds to the crowning head.

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43  
44 227 Lateral episiotomy is then performed using specific episiotomy scissors, Mayo scissors, or  
45  
46 228 similar scissors (Figure 1).

- 47  
48  
49 229
- Distance from incision point to the posterior fourchette: at least 1 cm, up to 3 cm.
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51 230
- Angle from the sagittal or parasagittal plane: 60° (45-80°, aim at the ischiadic
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53 231
- tuberosity)
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55 232
- Length of the incision: 4 cm (3-5 cm)
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5 234 For women allocated to “no episiotomy”, the perineum will possibly remain intact or tear  
6  
7 235 spontaneously. The operator may only perform episiotomy if severe fetal distress is suspected  
8  
9 236 or on the clinical judgement that extensive perineal injury cannot be avoided. These  
10  
11 237 exceptions should comprise ideally around 10%, but at the most 30% of the VE, if practice is  
12  
13 238 unchanged. Any episiotomy should be lateral. Episiotomy rates in trial participants and non-  
14  
15 239 participants will be followed continuously by the principal investigators.

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20 241 All women will receive perineal protection using verbal guiding and manual support of the  
21  
22 242 perineum during the delivery of the fetal head and body. The third stage, examination and  
23  
24 243 diagnosis of perineal tears is managed according to clinical routine. The clinical diagnosis of  
25  
26 244 OASIS is our primary outcome. Adequate pain relief should again be offered to enable a  
27  
28 245 thorough clinical bi-digital rectal/vaginal exam to reveal any injury to the sphincter muscles  
29  
30 246 or rectum. The diagnosis is confirmed by a specialist gynaecologist/obstetrician or senior  
31  
32 247 registrar. Suturing of OASIS is performed by a specialist gynaecologist/obstetrician or senior  
33  
34 248 registrar and managed according to clinical routine or as suggested in the standard operating  
35  
36 249 procedures.

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41 251 *Primary and secondary outcomes*

42  
43 252 The primary outcome is OASIS, including third and fourth degree perineal tears, engaging the  
44  
45 253 external or internal anal sphincter muscles, anal epithelium, or rectum (International  
46  
47 254 Classification of Diseases 10 code O70.2 or O70.3). Diagnosis is made by clinical  
48  
49 255 examination by a specialist obstetrician/gynaecologist or senior registrar.

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3 257 Short-term secondary outcomes are other degrees of perineal injury, blood loss postpartum,  
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5 258 complications to episiotomy or perineal injuries such as dehiscence or infection, Apgar score,  
6  
7 259 umbilical artery pH <7.05, shoulder dystocia, admission to the Neonatal ward, neonatal injury  
8  
9 260 (scalp trauma, obstetric brachial plexus palsy, cerebral injury, hypoxic ischemic  
10  
11 261 encephalopathy, respiratory distress, and fractures as diagnosed by the neonatologist),  
12  
13 262 duration of hospital stay after delivery, perineal pain, and childbirth experience 1-3 days after  
14  
15 263 delivery by Visual Analogue Scale. The data will be collected from the Swedish Pregnancy  
16  
17 264 Register and the National Quality Register for Neonatal Care. Information from maternal and  
18  
19 265 neonatal medical records is automatically forwarded to the registers when the medical records  
20  
21 266 are signed for archiving. The Swedish Pregnancy Register covers 90% of pregnancies in  
22  
23 267 Sweden and virtually all pregnancies at the study sites (41). The register consists of three  
24  
25 268 parts; the Swedish Maternal Health Care Register, launched in 1999, the Swedish National  
26  
27 269 Quality Register for Prenatal Diagnosis, with data from 2010, and the Obstetric Register,  
28  
29 270 which started in 2013. The three registers thus provide detailed information of pregnancies,  
30  
31 271 labours, and the postpartum period. The National Quality Register for Neonatal Care covers  
32  
33 272 all 37 neonatal wards and neonatal intensive care units in Sweden since 2012, and consists of  
34  
35 273 data from new-borns admitted to hospital care from birth until 28 days of age. The primary  
36  
37 274 outcome OASIS and trial specific data not available from the registers will be collected in  
38  
39 275 electronic case report forms supplied and monitored by Karolinska Trial Alliance.  
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46 277 Medium-term secondary outcomes, to be assessed by clinical examination and sonographic  
47  
48 278 imaging six to 12 months after delivery in at least one study site, are effects on the pelvic  
49  
50 279 floor anatomy. The OASIS diagnosis and the type of episiotomy will be quality controlled.  
51  
52 280 Descriptive data on pelvic floor muscle injury will be collected, specifically injuries to the  
53  
54 281 sphincters and the levator ani muscle. The women at this site will undergo a structured pelvic  
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3 282 exam performed by consultant gynaecologists in an independent Centre for Pelvic Floor  
4  
5 283 Disorders, including measurement of any scar, a clinical assessment of pelvic floor muscle  
6  
7 284 function by a six-point muscle strength score, prolapse staging by the pelvic organ prolapse  
8  
9 285 quantification system, and a high-resolution 2D perineal and 3D endovaginal and transrectal  
10  
11 286 ultrasound. Data from this follow-up will be collected using electronic case report forms  
12  
13 287 supplied and monitored by Karolinska Trial Alliance.  
14  
15 288  
16  
17 289 Medium- and long-term secondary outcomes, to be assessed by web-based questionnaires, are  
18  
19 290 duration of pain medication after delivery, symptoms regarding anal and urinary incontinence,  
20  
21 291 bowel function, prolapse, and sexual function at baseline, two months (up to six months), 12  
22  
23 292 months (up to 18 months), and five years (up to five years and six months) after delivery. The  
24  
25 293 questions are based on the questionnaires used by the Swedish Perineal Tear Register, and  
26  
27 294 will be distributed at identical intervals (baseline, two, and 12 months postpartum) as well as  
28  
29 295 after five years. Anal incontinence is assessed by Wexner score in these questionnaires (42).  
30  
31 296 Childbirth experience will be assessed at two months postpartum using the revised short form  
32  
33 297 of the Birth Satisfaction Scale and the Childbirth Experience Questionnaire (43, 44). The  
34  
35 298 questionnaires “Female Sexual Function Index” and “Female Sexual Distress Scale” will be  
36  
37 299 used for in-depth assessment of sexual function at baseline, one and five years (45-47).  
38  
39 300 Quality of life will be measured using the questionnaire Euro-QoL-5D at baseline, one and  
40  
41 301 five years (48). The questionnaires are administered by an independent provider of patient  
42  
43 302 surveys and data is forwarded to Karolinska Trial Alliance. We will also assess mode of  
44  
45 303 delivery, episiotomy, and OASIS in the subsequent pregnancy at five years and ten years after  
46  
47 304 the index delivery by using data from the Swedish Pregnancy Register. The schedule of all  
48  
49 305 follow-up assessments is illustrated in Table 2. All collaborators have signed or are obliged  
50  
51 306 under law to keep data confidential during and after the trial.  
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5 308 *Adverse events, data collection and safety*

6  
7 309 All randomised women are offered a clinical (apart from the trial) follow-up at 6 months and  
8  
9 310 free and easy access to medical care in association with the episiotomy or perineal tear at the  
10  
11 311 study site during the study period of five years. All women will receive postpartum care as  
12  
13 312 individually needed. Serious adverse events, such as death, a life-threatening event, admission  
14  
15 313 to intensive care, persistent or significant disability or incapacity, or other medically  
16  
17 314 important events, will be reported in a separate form and evaluated by the sponsor and  
18  
19 315 principal investigators continuously. The Karolinska Trial Alliance will monitor the trial  
20  
21 316 conduct, as well as data collection and safety after start-up, midterm, and before closure at  
22  
23 317 each site, covering 20% of randomised women. Karolinska Trial Alliance will also manage  
24  
25 318 important study protocol modifications and communicate these to relevant parties.  
26  
27

28  
29 319

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31 320 *Statistical methods*

32  
33 321 Baseline data will be summarized by descriptive statistics as appropriate; mean and standard  
34  
35 322 deviation, median, upper and lower quartiles, minimum and maximum, or frequency tables,  
36  
37 323 stratified by the two arms.  
38

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40 324

41  
42 325 Data will be analysed by intention-to-treat and per protocol. The primary outcome variable,  
43  
44 326 clinical diagnosis of OASIS, will be presented in numbers as incidence rate in the two  
45  
46 327 allocation groups (intention-to-treat) and according to received treatment (per protocol). The  
47  
48 328 protective effect of lateral episiotomy will be calculated as a relative risk of OASIS with 95%  
49  
50 329 confidence intervals, adjusting for study site and other possible factors not balanced by  
51  
52 330 randomisation.  
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3 332 Further analyses will compare secondary outcomes using test of proportions, t-test and  
4  
5 333 logistic regression depending on variable characteristics. In the per protocol analysis of  
6  
7 334 OASIS, we will adjust for possible confounders/effect modifiers such as study site, country of  
8  
9 335 birth, maternal body mass index, operator experience, long duration of labor and second  
10  
11 336 stage, epidural, use of oxytocin, fetal birthweight, head circumference, station and position.  
12  
13 337 We also aim to create a prediction model of the protective effect of lateral episiotomy to  
14  
15 338 support clinical decisions.  
16

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18 339

19  
20 340 Outcomes based on evaluation scores will be analysed by non-parametric tests and paired  
21  
22 341 analyses for change over time in the subgroups using Sign test. Details of the statistical  
23  
24 342 analysis will be supplied in the Statistical Analysis Plan, to be finalized in collaboration with  
25  
26 343 statisticians from the Karolinska Institute in a separate document before the data lock.  
27

28  
29 344

#### 30 31 345 *Sample size calculation*

32  
33 346 The sample size has been calculated based on data from Lund et al, suggesting a 50%  
34  
35 347 reduction of OASIS in VE, when lateral/mediolateral episiotomy is performed (16). The  
36  
37 348 average rate of OASIS in VE in Sweden was 12.4% in 2016 according to the Swedish  
38  
39 349 Medical Birth Register. A reduction of OASIS from 12.4% to 6.2% can be detected with 80%  
40  
41 350 power and less than 5% risk of alpha-error ( $p$ -value  $<0.05$ ) with 355 women in each group  
42  
43 351 using Chi-square test comparing two independent proportions in a two-sided test (3% missing  
44  
45 352 outcome). A smaller reduction is clinically valuable, although the risk-benefit relationship  
46  
47 353 between receiving a prophylactic episiotomy and the chance of an intact perineum may limit  
48  
49 354 the feasibility of a larger trial in a setting with a restrictive episiotomy policy. We have  
50  
51 355 obtained ethical approval to randomise a total of 1400 women, which enables us to detect a  
52  
53 356 reduction in OASIS rate at VE from 12.4% to 7.8%.  
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358 *Interim analyses*

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

375

376 *Patient and public involvement*

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

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3 382 motivated by a thorough follow-up no matter what perineal injury. The interest from pregnant  
4  
5 383 women is consistent with the observation that 85% of invited women agreed to participate in  
6  
7 384 the pilot RCT by Murphy et al, although the rationale for participation may have been the  
8  
9 385 chance to avoid an episiotomy in their setting (22). The burden of the intervention will be  
10  
11 386 assessed in the secondary outcomes. Results from this trial will be made available to study  
12  
13 387 participants through communication in public media.  
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## 17 18 389 Ethics and dissemination

19  
20 390 The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2  
21  
22 391 with addendums 2017/1005-32 and 2018/775-32). Previous register studies and guidelines all  
23  
24 392 point towards a reduction in OASIS if episiotomy is performed at VE in nulliparous women,  
25  
26 393 as described above. Reintroducing this routine demands a randomised trial and a thorough  
27  
28 394 follow-up to assess the consequences.  
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33 396 Swedish maternity wards should provide an excellent setting to perform a randomised trial of  
34  
35 397 routine lateral episiotomy versus no episiotomy at VE in nulliparous women, given the low  
36  
37 398 episiotomy rate and the relatively high prevalence of OASIS. We expect strong adherence to  
38  
39 399 non-intervention in the control group, facilitating the detection of any difference in OASIS  
40  
41 400 incidence. The timing with new guidelines to *consider* episiotomy further improves the  
42  
43 401 setting of the study (17, 18). The phrase “to consider” episiotomy is used deliberately to keep  
44  
45 402 recommendations weak. Yet, it is crucial to undertake and complete the trial before these new  
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47 403 guidelines are interpreted as recommendations despite low-grade evidence and lack of long-  
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49 404 term follow-up.  
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3 406 Then again, the low episiotomy rate may limit the feasibility of the study. A survey regarding  
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5 407 episiotomy preferences and indications was performed in 2012 among 297 delegates at the  
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7 408 biennial Nordic Congress of Obstetrics and Gynaecology (24). Only 17% of the 54  
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9 409 participating Swedish doctors perceived instrumental delivery as an indication for episiotomy,  
10  
11 410 while fetal distress was the most accepted indication. Consequently, 87% of the Swedish  
12  
13 411 doctors never, seldom, or only sometimes performed an episiotomy at VE. Thus, experience  
14  
15 412 from episiotomy may be lacking, which will require education and training at the sites when  
16  
17 413 the study is being implemented.  
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22 415 Prior to the previously described British pilot RCT, Macleod and Murphy performed a survey  
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24 416 among 1631 obstetricians and specialist registrars in the United Kingdom and Ireland with  
25  
26 417 regard to operative vaginal delivery and the use of episiotomy (22, 50). The great majority  
27  
28 418 (72%) reported a restrictive attitude towards use of episiotomy in VE and over 65% said that  
29  
30 419 they would be happy to participate in an RCT of restrictive versus routine use of episiotomy  
31  
32 420 at operative vaginal delivery. We estimate that a similar proportion of Swedish doctors and  
33  
34 421 midwives hold the same view, although personal preferences may hamper recruitment.  
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38 423 Considering the admitted knowledge gap regarding effectiveness and consequences of routine  
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40 424 lateral/mediolateral episiotomy in operative vaginal deliveries, we anticipate broad interest in  
41  
42 425 the results from the EVA trial (9, 16, 19-21). Being a non-commercial academic study, the  
43  
44 426 investigators will author the results adhering to the authorship criteria recommended by the  
45  
46 427 International Committee of Medical Journal Editors. We intend to disseminate the results by  
47  
48 428 publication in peer-reviewed medical journals and public press, and by presentations at  
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50 429 national and international congresses. Data can be made available for future meta-analyses to  
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52 430 improve informed practice.  
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3 431 List of abbreviations  
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5 432 EVA – Episiotomy in Vacuum Assisted delivery  
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7 433 OASIS – Obstetric anal sphincter injury/injuries  
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9 434 VE – Vacuum Extraction  
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11 435 RCT – Randomised Controlled Trial  
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13 436 OR – Odds ratio  
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3 437 **Declarations**

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6 438 *Ethics approval and consent to participate*

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8 439 The trial was approved by the Regional Ethical Review Board of Stockholm (2015/1238-31/2  
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10 440 with addendums 2017/1005-32 and 2018/775-32). Signed informed consent is obtained from  
11  
12 441 all participating women.

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16 443 *Consent for publication*

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18 444 If case reports will be published, consent will be obtained from relevant parties.

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20 445

21  
22 446 *Availability of data and material*

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25 447 The datasets generated and/or analysed are not publicly available due the possibility to extract  
26  
27 448 personal information, but may be made available from the corresponding author on request.

28  
29 449 All principal investigators will be given access to the final cleaned datasets and submissions  
30  
31 450 for publication will be made in agreement. To ensure confidentiality, data dispersed to  
32  
33 451 collaborators will be blinded of any identifying participant information.

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35 452

36  
37 453 *Competing interests*

38  
39 454 The authors have no competing interests to declare.

40  
41 455

42  
43 456 *Funding*

44  
45 457 This work is fully funded by the Swedish Research Council (grant number 2016-00526).

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47 458

48  
49 459 *Author contributions*

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51  
52 460 Sandra Bergendahl and Victoria Ankarcrona are investigators and responsible for the  
53  
54 461 implementation of the trial, and manuscript draft and revision. Åsa Leijonhufvud and Susanne



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2  
3 462 Hesselman are principal investigators at Helsingborg and Falun sites and responsible for  
4  
5 463 implementation of the trial, and manuscript draft and revision. Sofie Karlström is responsible  
6  
7 464 for the design, implementation, and investigations in the sub-study of pelvic floor anatomy at  
8  
9 465 six to 12 months after delivery. Helena Kopp Kallner is responsible for the manuscript  
10  
11 466 revision, funding, and study design. Sophia Brismar Wendel is overall responsible for the  
12  
13 467 implementation of the trial, manuscript draft and revision, funding, study design, and the  
14  
15 468 original idea of the study. All authors have participated in manuscript writing and have  
16  
17 469 approved the final version.  
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## 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**

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

For peer review only

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

TIME POINT	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation				Close-out	
	-4m	0	0m	2m	6m	1y	5y	10y
<b>ENROLMENT:</b>								
Information	x							
Informed consent	x							
Inclusion/exclusion criteria	x							
Randomisation		x						
<b>INTERVENTIONS:</b>								
Episiotomy		x						
No episiotomy		x						
<b>ASSESSMENTS:</b>								
Background variables	x <sup>1</sup>		x <sup>2</sup>					
Data from Pregnancy register (primary and secondary endpoints)			x <sup>3,4</sup>				x <sup>5</sup>	x <sup>6</sup>
Data from SNQ on neonatal outcome (secondary endpoints)			x					
Questionnaire BR 1 <sup>7</sup>			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 <sup>8</sup> (8 w)				x				
Questionnaire BR 3 <sup>9</sup> (1 y)						x	x	
Ultrasound evaluation					x			
POP-Q score					x			
Measurements of scar					x			
Questionnaire Q-SOPhIE					x			
Serious adverse events <sup>10</sup>		x	x	x	x	x		

<sup>1</sup> maternal age, country of birth, weight and height at registration in the antenatal clinic

<sup>2</sup> 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

<sup>3</sup> perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH, and birth related diagnosis)

<sup>4</sup> birth experience, duration of hospital stay

<sup>5</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

<sup>6</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

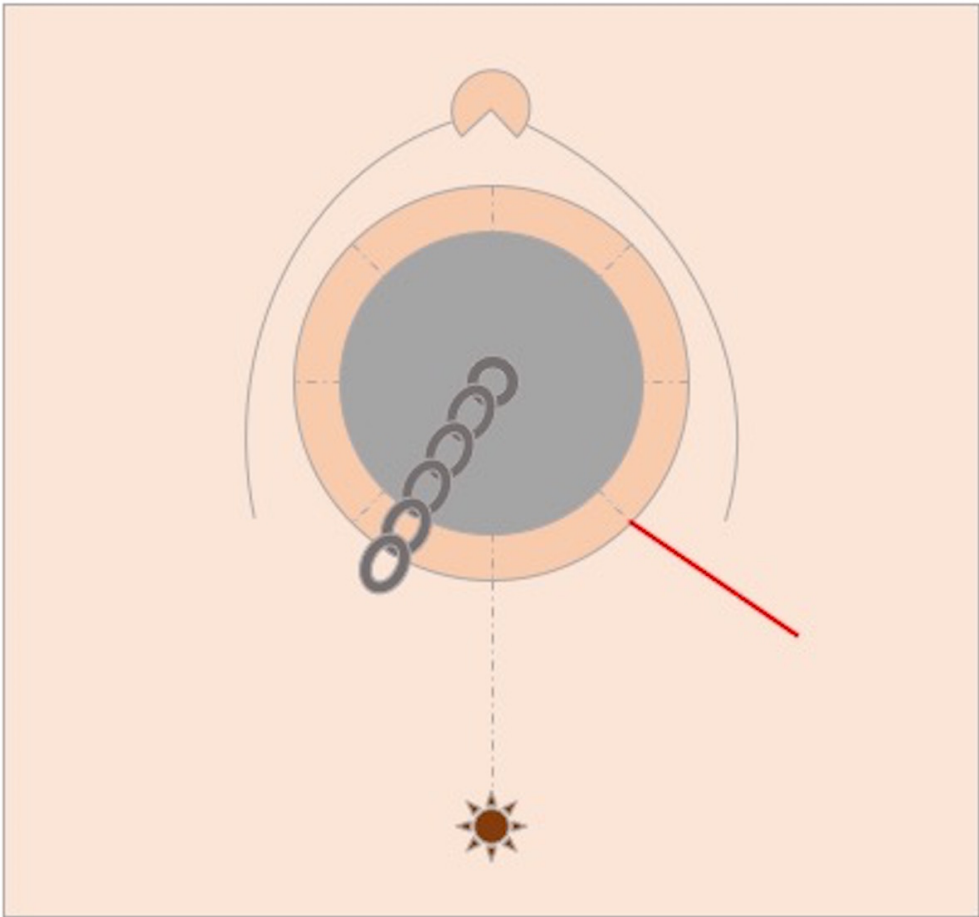
<sup>7</sup> "Information about your health before pregnancy"

<sup>8</sup> "Your evaluation of the treatment of perineal injury (approx. 8 weeks)"

<sup>9</sup> "Your evaluation of the treatment of perineal injury (approx. 1 year)"

<sup>10</sup> 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.

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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

1			management team, and other individuals or groups overseeing the	
2			trial, if applicable (see Item 21a for data monitoring committee)	
3				
4	Background and	#6a	Description of research question and justification for undertaking	6-9
5	rationale		the trial, including summary of relevant studies (published and	
6			unpublished) examining benefits and harms for each intervention	
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8				
9	Background and	#6b	Explanation for choice of comparators	8-9
10	rationale: choice of			
11	comparators			
12				
13				
14	Objectives	#7	Specific objectives or hypotheses	9
15				
16				
17	Trial design	#8	Description of trial design including type of trial (eg, parallel	9-10
18			group, crossover, factorial, single group), allocation ratio, and	
19			framework (eg, superiority, equivalence, non-inferiority,	
20			exploratory)	
21				
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24	Study setting	#9	Description of study settings (eg, community clinic, academic	10
25			hospital) and list of countries where data will be collected.	
26			Reference to where list of study sites can be obtained	
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28				
29	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable,	10-11
30			eligibility criteria for study centres and individuals who will	
31			perform the interventions (eg, surgeons, psychotherapists)	
32				
33				
34	Interventions:	#11a	Interventions for each group with sufficient detail to allow	11
35	description		replication, including how and when they will be administered	
36				
37				
38	Interventions:	#11b	Criteria for discontinuing or modifying allocated interventions for	12
39	modifications		a given trial participant (eg, drug dose change in response to	
40			harms, participant request, or improving / worsening disease)	
41				
42				
43	Interventions:	#11c	Strategies to improve adherence to intervention protocols, and	12
44	adherence		any procedures for monitoring adherence (eg, drug tablet return;	
45			laboratory tests)	
46				
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49	Interventions:	#11d	Relevant concomitant care and interventions that are permitted or	12
50	concomitant care		prohibited during the trial	
51				
52				
53	Outcomes	#12	Primary, secondary, and other outcomes, including the specific	12-14
54			measurement variable (eg, systolic blood pressure), analysis	
55			metric (eg, change from baseline, final value, time to event),	
56			method of aggregation (eg, median, proportion), and time point	
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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

1	Data collection plan:	#18b	Plans to promote participant retention and complete follow-up,	12-14
2	retention		including list of any outcome data to be collected for participants	
3			who discontinue or deviate from intervention protocols	
4				
5				
6	Data management	#19	Plans for data entry, coding, security, and storage, including any	12-14
7			related processes to promote data quality (eg, double data entry;	
8			range checks for data values). Reference to where details of data	
9			management procedures can be found, if not in the protocol	
10				
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12				
13	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary	15-16
14			outcomes. Reference to where other details of the statistical	
15			analysis plan can be found, if not in the protocol	
16				
17				
18	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and adjusted	16
19	analyses		analyses)	
20				
21				
22	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-	16
23	population and		adherence (eg, as randomised analysis), and any statistical	
24	missing data		methods to handle missing data (eg, multiple imputation)	
25				
26				
27	Data monitoring:	#21a	Composition of data monitoring committee (DMC); summary of	15, 17
28	formal committee		its role and reporting structure; statement of whether it is	
29			independent from the sponsor and competing interests; and	
30			reference to where further details about its charter can be found,	
31			if not in the protocol. Alternatively, an explanation of why a	
32			DMC is not needed	
33				
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37	Data monitoring:	#21b	Description of any interim analyses and stopping guidelines,	17
38	interim analysis		including who will have access to these interim results and make	
39			the final decision to terminate the trial	
40				
41				
42				
43	Harms	#22	Plans for collecting, assessing, reporting, and managing solicited	15
44			and spontaneously reported adverse events and other unintended	
45			effects of trial interventions or trial conduct	
46				
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48	Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and	15
49			whether the process will be independent from investigators and	
50			the sponsor	
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53	Research ethics	#24	Plans for seeking research ethics committee / institutional review	18
54	approval		board (REC / IRB) approval	
55				
56				
57	Protocol amendments	#25	Plans for communicating important protocol modifications (eg,	15
58			changes to eligibility criteria, outcomes, analyses) to relevant	
59				
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		parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	
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3			
4	Consent or assent	#26a Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10
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7			
8	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
9			
10			
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12			
13	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
14			
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18	Declaration of interests	#28 Financial and other competing interests for principal investigators for the overall trial and each study site	21
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22	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
23			
24			
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27	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
28			
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31	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
32			
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40	Dissemination policy: authorship	#31b Authorship eligibility guidelines and any intended use of professional writers	19
41			
42			
43	Dissemination policy: reproducible research	#31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	21
44			
45			
46			
47			
48			
49	Informed consent materials	#32 Model consent form and other related documentation given to participants and authorised surrogates	Appendix
50			
51			
52			
53	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
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2 3.0. This checklist was completed on 21. June 2018 using <http://www.goodreports.org/>, a tool made by the  
3 [EQUATOR Network](#) in collaboration with [Penelope.ai](#)  
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For peer review only

**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

<b>1</b>	<b>PROTOCOL SUMMARY</b>	<b>4</b>
<b>2</b>	<b>ABBREVIATIONS</b>	<b>6</b>
<b>3</b>	<b>ADMINISTRATIVE INFORMATION</b>	<b>7</b>
<b>4</b>	<b>BACKGROUND</b>	<b>7</b>
4.1	PURPOSE AND AIMS	7
4.2	SURVEY OF THE FIELD	7
<b>5</b>	<b>OBJECTIVES</b>	<b>8</b>
5.1	PRIMARY OBJECTIVE	8
5.2	SECONDARY OBJECTIVES	8
<b>6</b>	<b>ENDPOINTS</b>	<b>9</b>
6.1	PRIMARY ENDPOINT	9
6.2	SECONDARY ENDPOINTS	9
<b>7</b>	<b>DESIGN AND PROCEDURES</b>	<b>9</b>
7.1	OUTLINE	9
7.2	PROCEDURES	10
7.3	END OF STUDY	11
<b>8</b>	<b>SELECTION AND WITHDRAWAL OF SUBJECTS</b>	<b>11</b>
8.1	INCLUSION CRITERIA	11
8.2	EXCLUSION CRITERIA	11
8.3	SUBJECT LOG	11
<b>9</b>	<b>INTERVENTION</b>	<b>12</b>
9.1	DESCRIPTION OF THE INTERVENTION	12
9.2	RANDOMIZATION	12
<b>10</b>	<b>ASSESSMENTS</b>	<b>12</b>
10.1	PERINEAL INJURY	12
10.2	BLOOD LOSS	13
10.3	NEONATAL OUTCOME	13
10.4	ADMISSION TO THE NEONATAL WARD	13
10.5	SCALP TRAUMA AND OTHER NEONATAL TRAUMA	13
10.6	DURATION OF HOSPITAL STAY	13
10.7	PAIN AND BIRTH EXPERIENCE AFTER DELIVERY	13
10.8	QUESTIONNAIRES	13
10.9	PERINEAL EVALUATION WITH ULTRASOUND AND CLINICAL PELVIC EXAM	14
10.10	PREGNANCY REGISTER AND PATIENT REGISTER	14
<b>11</b>	<b>PROCEEDINGS FOR ADVERSE EVENTS</b>	<b>14</b>
11.1	DEFINITION OF ADVERSE EVENTS	14
11.2	ASSESSMENT OF ADVERSE EVENTS	14
11.3	METHODS FOR ELICITING ADVERSE EVENTS	15
11.4	REPORTING OF ADVERSE EVENTS	15



11.5	FOLLOW-UP OF ADVERSE EVENTS .....	15
<b>12</b>	<b>STATISTICS AND DATA MANAGEMENT .....</b>	<b>15</b>
12.1	DATA MANAGEMENT .....	15
12.2	STATISTICAL ANALYSIS .....	15
12.3	DETERMINATION OF SAMPLE SIZE .....	16
<b>13</b>	<b>QUALITY CONTROL AND QUALITY ASSURANCE .....</b>	<b>17</b>
13.1	SOURCE DATA .....	17
13.2	MONITORING .....	17
<b>14</b>	<b>DIRECT ACCESS TO SOURCE DOCUMENTS .....</b>	<b>17</b>
<b>15</b>	<b>ETHICS .....</b>	<b>17</b>
15.1	INDEPENDENT ETHICS COMMITTEE .....	17
15.2	ETHICAL CONDUCT OF THE STUDY .....	17
15.3	RISK - BENEFIT ASSESSMENT .....	18
15.4	SUBJECT INFORMATION AND INFORMED CONSENT .....	18
<b>16</b>	<b>DATA HANDLING AND RECORD KEEPING .....</b>	<b>18</b>
16.1	CASE REPORT FORMS .....	18
16.2	RECORD KEEPING .....	18
<b>17</b>	<b>FINANCING AND INSURANCE .....</b>	<b>19</b>
<b>18</b>	<b>PUBLICATION POLICY .....</b>	<b>19</b>
<b>19</b>	<b>SUPPLEMENTS .....</b>	<b>19</b>
19.1	AMENDMENTS .....	19
19.2	PERSONNEL INFORMATION .....	19
<b>20</b>	<b>REFERENCES .....</b>	<b>19</b>
<b>21</b>	<b>SIGNED AGREEMENT OF THE STUDY PROTOCOL .....</b>	<b>21</b>
<b>22</b>	<b>APPENDICES .....</b>	<b>22</b>
22.1	SCHEDULE OF INVESTIGATIONAL EVENTS .....	22
22.2	STANDARD OPERATING PROCEDURES .....	23
22.3	QUESTIONNAIRES .....	23

## 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:

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

Exclusion Criteria:

- 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

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### 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

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2  
3 implementation of a “Finnish” perineal support and lateral episiotomy, decreased anal sphincter injury  
4 from 4.0% to 1.2% in the total population and from 16.3% to 4.9% in vacuum extractions (5). In an  
5 American study, a change to mediolateral episiotomies in instrumental deliveries (commonly forceps)  
6 decreased the prevalence of sphincter tears from 41 to 26% (6). Similarly, a Dutch prospective study,  
7 showed a risk reduction at instrumental deliveries by 90% using mediolateral episiotomy (7). On the  
8 contrary, medial (midline) or too small episiotomies are associated with an increased risk of sphincter  
9 injury (8). In a British study comparing routine (93%) vs. restrictive (52%) use of episiotomy, there was a  
10 small non-significant difference in the rate of anal sphincter tears (8.1% routine versus 10.9% restrictive,  
11 OR 0.72, 95% CI 0.28-1.87) but the trial was underpowered (9). There is a recent randomized study  
12 comparing mediolateral and lateral episiotomy, finding equal although very low prevalence of sphincter  
13 injury (1.5 vs. 1.3%) (10). The objection that lateral incisions bleed more or causes more pain is  
14 contradicted by studies comparing incision techniques (11, 12). Little is known about chronic pain after  
15 episiotomy or spontaneous perineal injury, although there seem to be a correlation between the extent  
16 of tissue damage and degree of pain (13-15). An SBU report (Statens beredning för medicinsk och social  
17 utvärdering, www.sbu.se) published in April 2016 concludes that mediolateral episiotomy can protect  
18 against OASIS in operative vaginal deliveries in non-parous women based on two retrospective cohort  
19 studies (7, 8) although in Sweden, there is no correlation between a hospital’s rate of episiotomy and  
20 OASIS. The SBU report states that there is a knowledge gap regarding function and symptoms after  
21 episiotomy compared to moderate spontaneous tears/OASIS. Several others, including Cochrane and  
22 DUETS/NICE Evidence Search, state that the protective effect of lateral episiotomy at operative vaginal  
23 delivery should be investigated in an adequately sized randomized study (8, 16-18).  
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27

## 28 5 Objectives

### 29 5.1 Primary Objective

30  
31 The primary objective is to investigate if lateral episiotomy protects against obstetrical anal sphincter  
32 injury (OASIS) compared to no episiotomy in operative vaginal delivery by vacuum extraction, in term  
33 and late pre-term (gestational week 34+0 or more), non-parous women with one live fetus in cephalic  
34 presentation.  
35  
36

### 37 5.2 Secondary Objectives

38  
39 The secondary objectives are to investigate if lateral episiotomy compared to no episiotomy in the above  
40 specified group of patients can reduce:

- 41 • Prevalence of other degree of perineal injury, prevalence of postpartum hemorrhage, duration  
42 of hospital stay, pain, and duration of pain medication, compared to spontaneous perineal injury  
43 of different degrees (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> degree)
- 44 • Neonatal morbidity measured as prevalence of low Apgar score, metabolic acidosis, prevalence  
45 of admission to the Neonatal ward, and prevalence of scalp trauma/other birth trauma
- 46 • Prevalence of urinary, anal and fecal incontinence, prolapse symptoms, sexual dysfunction, or  
47 discontent with birthing experience after 2 months
- 48 • Prevalence of ultrasound evidence of extended pelvic floor injury at 6-12 months after delivery
- 49 • Prevalence of urinary, anal and fecal incontinence, prolapse symptoms, or sexual dysfunction  
50 after 1 and 5 years
- 51 • Prevalence of elective cesarean in a subsequent pregnancy/delivery, the prevalence of OASIS in  
52 a subsequent pregnancy/delivery, or of episiotomy in a subsequent pregnancy/delivery within 5  
53 and 10 years  
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57

## 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 förlösningensbristningen (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 förlösningensbristningen (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 Mepivacain (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

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3 tests (Mann-Whitney, Rank sum or Wilcoxon two unpaired samples) but also paired analyses for change  
4 over time (up to 5 years after delivery) in the subgroups using Sign test.  
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### 7 **12.3 Determination of Sample Size**

8 Primary outcome variable is prevalence of OASIS in the intervention group (lateral episiotomy)  
9 compared to the control group (no episiotomy). The average prevalence of OASIS in operative vaginal  
10 delivery in all women (not only non-parous women) was 12.4% in Sweden according to the [Medical Birth](#)  
11 [Register](#) in 2015. At Danderyd Hospital, the prevalence of OASIS has varied between 14 and 18% in  
12 primiparous women. In normal vaginal delivery, the prevalence of OASIS is 6-7% in primiparous women  
13 in Sweden. A reduction of OASIS from 12.4% to 6.2% ("normal delivery rate") can be detected with 80%  
14 power and 5% risk of alpha-error (p-value <0.05) with 350 women in each group using Chi-square test  
15 comparing two independent proportions in a two-sided test (1.5% loss of follow-up). A reduction to 7.8%  
16 is clinically valuable, thus a sample size of 694 women in each allocation group is needed. Total number  
17 of patients are 1400 women. We will perform a first interim analysis after 350 randomized women, to  
18 detect a possible reduction from 12.4% to 2.5% with 80% power and p-value <0.01, and a second interim  
19 analysis after 700 randomized women, to detect a possible reduction from 12.4% to 6.2% with 80%  
20 power and p-value <0.05. We are planning at least three sites. Depending on the size of the delivery  
21 ward, each site will contribute with approximately 5% of non-parous women giving birth vaginally (70-  
22 200 patients annually). Inclusion rate is expected to be 3 patients/week at a site with 300 annual vacuum  
23 extractions in non-parous women, if 50% of women accept participation.  
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## 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 2<sup>nd</sup> 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](http://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.

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## 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

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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 <sup>1</sup>	x <sup>2</sup>						
Data from Pregnancy register (primary and secondary endpoints)		x <sup>3</sup>	x <sup>4</sup>				x <sup>5</sup>	x <sup>6</sup>
Data from SNQ on neonatal outcome (secondary endpoints)			x					
Questionnaire BR 1 <sup>7</sup>			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 <sup>8</sup> (8 w)				x				
Questionnaire BR 3 <sup>9</sup> (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		

<sup>1</sup> maternal age, country of birth, weight at registration in the antenatal clinic and height

<sup>2</sup> 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

<sup>3</sup> perineal injury, blood loss, and neonatal outcomes (Apgar score, umbilical artery pH and birth related diagnosis)

<sup>4</sup> birth experience, duration of hospital stay

<sup>5</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

<sup>6</sup> mode of delivery, episiotomy, and OASIS in a subsequent pregnancy

<sup>7</sup> "Uppgifter om hälsa före graviditeten"

<sup>8</sup> "Din värdering av behandlingen av förlossningsbristningen (ca 8 veckor)"

<sup>9</sup> "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

1  
2  
3 regarding the delivery and if there were any complications to you or the baby. You will  
4 receive questionnaires on the postnatal ward, 2 months, and 1 year after delivery. The  
5 questions cover urine and bowel issues as well as sexual function, quality of life, and your  
6 childbirth experience. The questionnaires will take 5-10 minutes to complete. You will be  
7 offered a follow up visit at 6 months after the delivery. We will also contact you for a follow  
8 up at 5 years after delivery.  
9  
10  
11

### **Your integrity and safety**

12  
13 **Participation is voluntary.** It will not affect your care if you choose not to participate. If you  
14 decide to participate, your answers are important regardless of whether you experienced  
15 complications or not. We aim to improve care during childbirth, specifically during vacuum  
16 assisted delivery, and to improve the long-term health and wellbeing of women. Therefore,  
17 we need information about your experiences.  
18  
19  
20  
21

22 Your answers from the questionnaire are kept confidential. They will only be available to the  
23 research group (find details below) and will not be included in your medical records. The  
24 answers are anonymous and can only be linked to your personal data by the research group.  
25 An independent investigator may review the research and will in that case require access to  
26 the original data, including medical records and questionnaire answers. The investigator will  
27 treat all data as confidential information.  
28  
29  
30

31 **The medical data and questionnaire answers will be reported as a group so your**  
32 **participation will not be visible in the study results.**  
33  
34

35 If you wish, you can receive the result from the study when it is published. All data will be  
36 kept for 10 years before it is destroyed. Once per year you can request information about your  
37 personal data. Please contact us for more information. Your hospital is legally responsible for  
38 the personal data in this trial.  
39  
40  
41

42 *Thank you for your time and consideration to participate!*  
43

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66

## 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.