



Assessing the risk of oxytocin augmentation on obstetric anal sphincter injury in nulliparous women

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4 **ASSESSING THE RISK OF OXYTOCIN AUGMENTATION ON OBSTETRIC ANAL**
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ABSTRACT

Objective: To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.

Design: Cross-sectional, population-based study.

Setting: Primary and secondary teaching hospital serving a Norwegian region.

Population: 15 493 nulliparous women with spontaneous start of labour, single cephalic presentation, and gestation ≥ 37 weeks delivering vaginally between 1999 and 2012.

Methods: Based on the presence or absence of oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (< 4000 g vs. ≥ 4000 g), we did stratified analysis of all 16 combinations to assess the risk of anal sphincter injury. Within a modified model, we tested for possible confounding, and interactions between maternal age, ethnicity, occiput posterior position, and epidural analgesia.

Main outcome measure: Obstetric anal sphincter injury.

Results: Oxytocin augmentation was associated with an increased risk of obstetric anal sphincter injuries in women giving spontaneous birth to infants weighing < 4000 g (OR 1.7; 95% CI: 1.4–2.1). Episiotomy did not influence the risk during spontaneous deliveries, but was protective in operative vaginal deliveries. Spontaneous delivery of infants weighing ≥ 4000 g was associated with a 3-fold increased risk of obstetric anal sphincter injuries, and epidural analgesia reduced the risk by 30%.

Conclusions: Oxytocin augmentation was associated with an increased risk of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants. We observed a considerable effect modification between the most important risk factors involved in the active second stage of labour.

ARTICLE SUMMARY

Strengths and limitations of this study

- Stratifying by the main risk factors that are active during the expulsive phase of labour and testing for confounders is a strength of the study.
- We reveal how oxytocin augmentation interacts with other major risk factors active in the expulsive phase of labour.
- The study is based on prospectively collected data from a large unselected population, which make bias unlikely.
- The study design is a limitation, as we cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study, however a randomized, controlled study would not be feasible.

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- There are possible risk modifiers that were unavailable in our database.

For peer review only

INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Primiparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} ethnicity other than Caucasian,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11-13} is debated. However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} The current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to explore the effect of oxytocin augmentation on the occurrence of obstetric anal sphincter injuries in a dynamic model of main risk factors in the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4 500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period (15 May 1999 to 15 May 2012), 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department. Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 52 women with no estimated day of delivery, this cross-sectional study comprised 15 493 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries. Throughout the study period, episiotomy was performed either medio-laterally or laterally.

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3 According to our routines and national guidelines, operative vaginal delivery was indicated if
4 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
5 with a Malmstrøm metal cup as the preferred procedure for operative vaginal delivery.
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9 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
10 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Caucasian or
11 non-Caucasian.
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16 We analysed our dataset using the Chi-squared test and forward stepwise logistic
17 regression analyses with $p < 0.05$ as significance level. We applied a stratified approach to
18 investigate the impact of oxytocin augmentation on the outcome across the presence (+) or
19 absence (-) during labour of episiotomy, operative vaginal delivery, and birth weight (<4000
20 g or ≥ 4000 g). We displayed all 16 possible combinations of the four variables, with absence
21 of oxytocin augmentation, episiotomy, and operative vaginal delivery, and birth weight <4000
22 g set as the reference value. From these stratified analyses, we collapsed strata that were non-
23 significant, taking the order of occurrence and the clinical impact of the risk factor into
24 consideration. In this modified model, we tested for possible confounding effects and
25 interactions from maternal age, ethnicity, occiput posterior position, and epidural analgesia in
26 forward stepwise logistic regression analyses. Confounders were tested one by one and set to
27 at least 10% change in any estimate of combinations of the modified target variables on
28 obstetric anal sphincter injuries. Interaction terms were significant at $p < 0.05$. Statistical
29 analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM
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49 The Regional Committee for Medical and Health Research Ethics, Western Norway,
50 approved the protocol as a quality assurance study in obstetric care, and fulfilling the
51 requirements for data protection procedures (REK 2011-1247).
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RESULTS

The study population comprised 15 493 (27%) of the 57 036 women giving birth during the study period, including 1014 (54%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury

Factor	Obstetric anal sphincter injury		In total N=15 493	Prevalence %	p Value
	No N=14 479 %	Yes N=1014 %			
Time period					<0.001
1999–2000	11.1	16.9	1781	9.6	
2001–2003	19.7	30.6	3169	9.8	
2004–2006	22.9	29.6	3611	8.3	
2007–2009	25.5	14.3	3833	3.8	
2010–2012	20.8	8.6	3099	2.8	
Maternal factors					
Age (years)					<0.001
Younger than 25	26.6	19.3	4041	4.9	
25–29	33.5	37.6	5241	7.3	
30–34	17.8	20.9	2788	7.6	
35 and older	22.1	22.2	3423	6.6	
Origin					0.12
Caucasian	90.5	92.0	14 039	6.6	
Non-Caucasian	9.5	8.0	1454	5.6	
Obstetric factors					
Epidural analgesia					0.77
No	58.1	57.6	8997	6.5	
Yes	41.9	42.4	6496	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.8	8507	5.3	
Yes	44.4	55.2	6986	8.0	
Active second stage of labour (min)					<0.001
0–14	11.4	7.1	1723	4.2	
15–29	26.8	18.4	4066	4.6	
30–59	40.1	37.8	6188	6.2	
>59	21.7	36.7	3516	10.6	
Episiotomy					0.24
No	67.1	65.3	10 376	6.4	
Yes	32.9	34.7	5117	6.9	
Operative vaginal delivery					<0.001

No	77.5	60.1	11 829	5.1	
Yes	22.5	39.9	3664	11.1	
Fetal factors					
Birth weight (g)					<0.001
<4000	88.3	74.8	13 543	5.6	
≥4000	11.7	25.2	1950	13.1	
Occiput posterior position					0.28
No	95.5	94.8	14 787	6.5	
Yes	4.5	5.2	706	7.5	

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.1% vs. 5.1%), and in those who gave birth to an infant weighing ≥ 4000 g (13.1% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour. In the subsequent analysis, missing data (Table 1) for birth weight (n=3), maternal age (n=2), fetal position at delivery (n=8), and duration of the second stage of labour (n=92) were re-coded into the reference category of each variable.

The results of the stratified analysis are presented in Table 2.

Table 2 Stratified analyses of the risk of obstetric anal sphincter injury by the presence (+) or absence (-) of risk factors: oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (strata 1–16; risk group 1 as reference). Crude odds ratio (OR) and 95% confidence intervals (95%CI)

Risk group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95%CI
1	-	-	-	-	5353	201 (3.8)	1.0	
2	-	+	-	-	1444	60 (4.2)	1.11	0.8–1.5
3	+	-	-	-	2633	147 (5.6)	1.52	1.2–1.9
4	+	+	-	-	1055	60 (5.7)	1.55	1.2–2.1
5	-	+	+	-	539	44 (8.2)	2.3	1.6–3.2
6	+	+	+	-	1291	93 (7.2)	2.0	1.5–2.6
7	-	-	+	-	319	48 (15.0)	4.5	3.2–6.4
8	+	-	+	-	909	105 (11.6)	3.4	2.6–4.3
9	-	-	-	+	517	56 (10.8)	3.1	2.3–4.3
10	+	-	-	+	424	45 (10.6)	3.0	2.2–4.3
11	-	+	-	+	195	20 (10.3)	2.9	1.8–4.8
12	+	+	-	+	208	20 (9.6)	2.7	1.7–4.4
13	-	+	+	+	100	11 (11.0)	3.2	1.7–6.0
14	+	+	+	+	285	44 (15.4)	4.7	3.3–6.7
15	-	-	+	+	40	14 (35.0)	13.8	7.1–26.8

16 + - + + 181 46 (25.4) 8.7 6.1–12.6

We found a strong effect modification between episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight on obstetric anal sphincter injuries. Oxytocin augmentation was associated with an increased risk of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants, and was independent of episiotomy (risk groups 3 and 4). Episiotomy had no influence on anal sphincter injuries when the other risk factors were absent (risk groups 1 and 2). Oxytocin augmentation did not influence the risk of anal sphincter injury during instrumental deliveries of normal-sized infants without episiotomy (risk groups 7 and 8), which was similar to the risk associated with infants weighing ≥ 4000 g delivered spontaneously without episiotomy (risk groups 9 and 10). Furthermore, oxytocin use did not influence the risk of anal sphincter injuries in spontaneous (risk groups 11 and 12) or operative vaginal deliveries (risk groups 13 and 14) of infants weighing ≥ 4000 g when episiotomy was applied. Operative vaginal delivery of an infant weighing ≥ 4000 g without episiotomy represented the group with the highest risk of injury (risk groups 15 and 16) and was not influenced by oxytocin use. Episiotomy appeared to have a protective effect in operative vaginal deliveries regardless of the birth weight and the use of oxytocin (risk groups 5-8 and 13-16).

In the modified model (Table 3), we collapsed the groups shown in Table 2 that had similar risks of obstetric anal sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–16) from Table 2 into new strata (A–G). Unadjusted Odds Ratios (OR), Adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Risk group (Risk group from Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women n	Obstetric anal sphincter injury n (%)	OR	aOR (95% CI)
A (1,2)	-	±	-	-	6797	261 (3.8)	1.0	1.0
B (3,4)	+	±	-	-	3368	207 (5.6)	1.5	1.7 (1.4–2.1)

C (5,6)	±	+	+	-	1830	137 (7.5)	2.0	2.3 (1.8–2.9)
D (7,8)	±	-	+	-	1228	153 (12.5)	3.6	4.1 (3.3–5.1)
E (9-12)	±	±	-	+	1344	141 (10.5)	2.9	3.2 (2.4–3.9)
F (13,14)	±	+	+	+	385	55 (14.3)	4.2	4.8 (3.5–6.5)
G (15,16)	±	-	+	+	221	60 (27.5)	9.3	10.7 (7.7–14.9)

Age, origin of the mother, and occiput posterior position did not change the estimates of obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (subgroups A to G in Table 3). The unadjusted odds ratio (OR) for the presence or absence of an epidural was 1.02; however, the adjusted OR for epidural analgesia was 0.7, i.e. an epidural reduced the risk of obstetric anal sphincter injury by 30%.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all time periods (1999-2000, 2001-03, 2004-06, 2007-09, and 2010-12) from an average of 32% in <30 minutes, 46% in 30–59 minutes, and 66% (range 49–76%) in ≥60 minutes during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45–48% when the active part of the second stage of labour lasted ≥60 minutes vs. 11–22% for durations of the second stage of labour of <60 minutes. We did not enter duration of second stage of labour into our modified model because of colinearity between oxytocin augmentation and duration of second stage, and colinearity between operative delivery and duration of second stage.

DISCUSSION

We found that oxytocin augmentation during active labour was associated with a 70% increased risk of obstetric anal sphincter injury in women in TGCS group 1 giving

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3 spontaneous birth to an infant weighing <4000 g. We also found that an episiotomy did not
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5 influence the risk of tears during spontaneous deliveries, but was protective in all operative
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7 vaginal deliveries.
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10 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
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12 However, a Cochrane review concluded that a reduction of labour by two hours was the only
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14 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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16 the entire concept of active management of labour to be associated with a slightly reduced
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18 risk of caesarean delivery.²¹ As in other studies, we found that approximately 50% of
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20 nulliparous women received oxytocin augmentation.^{16, 17, 22} There is reason to believe that
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22 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
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24 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
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26 progress of the expulsive phase of labour, leading to rushed situations, impaired
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28 communication with the mother, and less focus on protecting the perineum and controlling
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30 delivery of the head. Recent studies from Norway indicate that focus on these elements are
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32 important to reduce the risk of perineal injuries.^{23, 24}
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37 Many authors have used logistic regression analysis to identify risk factors for
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39 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
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41 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found that oxytocin augmentation was
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43 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
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45 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
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47 which is a methodological weakness since the true effect of other factors is concealed by the
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49 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
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51 women, entering oxytocin augmentation, duration of active second stage of labour, and
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53 instrumental delivery into the same model.¹⁵
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3 Our study shows strong colinearity between a prolonged active second stage of labour
4 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
5 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
6 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Consequently, we
7 omitted this factor from our analyses.
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14 Jander et al. conducted a single institution, retrospective, case-control study of 214
15 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
16 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
17 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
18 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
19 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
20 for induction or augmentation purposes.²⁵⁻²⁷ Three large population-based studies on the risk
21 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.^{1, 7,}
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34 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
35 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhede found epidural
36 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
37 by parity and found a significantly increased risk associated with epidural analgesia in
38 nulliparous women.²⁸ In our study, epidural analgesia was associated with a significantly
39 reduced risk of sphincter tears.
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47 Our study takes into account four risk factors that exert their effect on the anal
48 sphincter during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both
49 operative vaginal delivery and high birth weight to be strongly associated with obstetric anal
50 sphincter injuries. We found episiotomy to be protective against sphincter tears in operative
51 vaginal deliveries, but not in spontaneous births. This is consistent with a large national
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3 registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 29, 30} In our study, neither
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5 oxytocin augmentation nor episiotomy influenced the risk of obstetric anal sphincter injuries
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7 during spontaneous delivery of infants weighing ≥ 4000 g.
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10 Our methodological approach, stratifying by the main risk factors that are active
11 during the expulsive phase of labour and testing for confounders, is a strength. This approach
12 leads to a more detailed understanding of how oxytocin augmentation interacts with other
13 major risk factors. Without testing for possible interactions, multivariable regression models,
14 e.g. entering all variables simultaneously, would fail to reveal this information. This cross-
15 sectional study is based on prospectively collected data from a large unselected population,
16 and represents all deliveries meeting the inclusion criteria that occurred during the study
17 period, which make bias unlikely. Our department has a high proportion of vaginal deliveries.
18 The overall caesarean delivery rate in our institution was 12.5% over the study period. For
19 women in TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to
20 7.5% in 2012. Accordingly, the study population includes both high- and low-risk
21 pregnancies, which adds to the external validity of our results.
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36 However, some limitations apply. We cannot prove causality between oxytocin
37 augmentation and obstetric anal sphincter injuries in an observational study. On the other
38 hand, for practical and ethical reasons this is not a research question that can be addressed in a
39 randomized controlled trial. Furthermore, body mass index, maternal delivery positions,
40 perineal support technique, and the birth attendant's experience level may be possible risk
41 modifiers not registered in our database.
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49 Our findings have some important implications. Birth attendants should be aware of
50 oxytocin augmentation as an important risk factor for obstetric anal sphincter injuries in the
51 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
52 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
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3 of evidence-based guidelines for using oxytocin augmentation should be encouraged, and use
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5 of a partogram with an action line defining failure to progress could be helpful.³¹ Moreover,
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7 our study supports restricted use of episiotomy during normal births, and as a
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9 recommendation for operative vaginal deliveries. Birth weight is an important risk factor, but
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11 is not known prior to delivery. Fetal weight estimation by ultrasound may be considered when
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13 macrosomia is suspected.
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Contributorship

All four authors have contributed to the idea and design of the research project. ABR, TME managed the dataset and the statistical analyses were performed by FES. All four authors have contributed to the interpretation of the results and the writing of the manuscript.

Competing interests

None

Data Sharing

No additional data

References

1. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;116:25-34.
2. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;90:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;247:224-37.
4. Sultan AH, Thakar R, Fenner DE. Perineal and anal sphincter trauma : diagnosis and clinical management. New York; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;80:229-34.
6. Hornemann A, Kamischke A, Luedders DW, Beyer DA, Diedrich K, Bohlmann MK. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;281:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;98:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, Wallenburg HC. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;108:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;29:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;85:1252-8.

11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;206:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;115:1695-702; discussion 702-3.
13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009:CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, Gareberg B, Nyberg K, Hagberg H. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;107:926-31.
15. Prager M, Andersson KL, Stephansson O, Marchionni M, Marions L. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;87:209-15.
16. Blix E, Pettersen SH, Eriksen H, Royset B, Pedersen EH, Oian P. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;122:1359-62.
17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;85:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011:CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;15:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.

- 1
2
3 21. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active
4 management in labour for reducing caesarean section rates in low-risk women. *Cochrane*
5 *Database Syst Rev* 2013;9:CD004907.
6
7
- 8
9 22. Selin L, Almstrom E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation
10 of labor. *Acta Obstet Gynecol Scand* 2009;88:1352-7.
11
12
- 13 23. Hals E, Oian P, Pirhonen T, Gissler M, Hjelle S, Nilsen EB, et al. A multicenter
14 interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol*
15 2010;116:901-8.
16
17
- 18 24. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal
19 sphincter tears during delivery. *Obstet Gynecol* 2008;111:1053-7.
20
21
- 22 25. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with
23 complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;71:520-4.
24
25
- 26 26. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter
27 rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol*
28 1988;27:27-32.
29
30
- 31 27. Legino LJ, Woods MP, Rayburn WF, McGoogan LS. Third- and fourth-degree
32 perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;33:423-6.
33
34
- 35 28. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third
36 degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy.
37 *Br J Obstet Gynaecol* 1997;104:563-6.
38
39
- 40 29. Hartmann K, Viswanathan M, Palmieri R, Gartlehner G, Thorp J, Jr., Lohr KN.
41 Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;293:2141-8.
42
43
- 44 30. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces
45 the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;115:104-8.
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31. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;7:CD005461.

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(R) In abstract; a cross sectional study, analyzed as case-control study.</p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>(R) Fulfilled</p>
Introduction		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>(R) Recent studies have shown the importance of the perineal protection technique in preventing perineal tears. Oxytocin augmentation could impair the control of the perineum during the delivery by causing too fast progress in the last minutes of labour. Oxytocin augmentation is widely used (50% of births). Guidelines for its use are often deficient and the evidence for its positive effect is challenged. Therefore, oxytocin augmentation as a risk factor for obstetric anal sphincter injuries, and should be explored in a study taking other relevant risk factors into account.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>(R) To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.</p>
Methods		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>(R) Present in Abstract and Methods.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>(R) Setting: Tertiary teaching hospital.</p> <p>Location: Delivery department of Stavanger University Hospital, serving the total obstetric population of the region of South Rogaland.</p> <p>Dates 15 May 1999 – 15 May 2012.</p> <p>Data were collected consecutively.</p>
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants.</p> <p>(R) Nulliparous women with spontaneous start of labour, single, cephalic pregnancy and ≥ 37 weeks gestation who delivered vaginally, where we had access to complete information on the main exposure and the explanatory variables. The source population was the entire obstetric population of the region.</p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect</p>

1		modifiers. Give diagnostic criteria, if applicable
2		(R) Outcome: Obstetric anal sphincter injury; that is grade 3 and 4 perineal tears as
3		defined by International Society of Incontinence.
4		Exposure: Oxytocin augmentation in active labour, that is oxytocin intravenous
5		infusion (5 international units (0.01mg) oxytocin in 500 ml saline) used in incremental
6		doses during active labour.
7		Predictors: NA
8		Effect modifiers: Episiotomy, operative vaginal delivery, birth weight <4000 g vs
9		≥4000 g.
10		Potential confounders: maternal age, ethnicity, occiput posterior position, duration of
11		second stage of labour and epidural analgesia.
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18	Data sources/ measurement	8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. (R) All variables are precisely defined in the obstetric databases of Stavanger University Hospital. The grade of perineal injury was assessed during operative repair and plotted directly into the database.
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26	Bias	9 Describe any efforts to address potential sources of bias. (R) In this cross-sectional study all women giving births and who fulfil the inclusion criteria are included. There were very few cases with missing data. We may have missed some cases of perineal injury due to underreporting. The variables are hard variables with clear definitions: Use of oxotocin (yes/no), episiotomy (yes/no), mode of delivery (spontaneous/operative vaginal), birth weight categorized <4000/ ≥4000 g.
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34	Study size	10 Explain how the study size was arrived at (R) The study size is given by the number of women fulfilling the eligibility criteria and who delivered at Stavanger University Hospital from 15 May 1999 to 15 May 2012.
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40	Quantitative variables	11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. (R) Birth weight was categorized into < 4000/ ≥4000 g.
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44	Statistical methods	12 (a) Describe all statistical methods, including those used to control for confounding (R) Chi-square test and stepwise forward logistic regression using IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp. (b) Describe any methods used to examine subgroups and interactions (R) We applied a stratified approach to control for interaction between the main variables (oxytocin augmentation, episiotomy, instrumental delivery and birth weight). Then we tested for confounding and interaction to a modified model by entering one variable at time. (c) Explain how missing data were addressed (R) Cases with missing data for estimated date of delivery were excluded. Cases with
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other missing data were recoded to the reference value in the logistic regression analyses. Very few cases with missing data (n=52).

(d) If applicable, describe analytical methods taking account of sampling strategy

(R) NA

(e) Describe any sensitivity analyses

(R) NA

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(R) Potentially eligible: 15 545 Confirmed eligible: 15 493 Included/analyzed: 15 493</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(R) Cases with missing data for estimated date of delivery were excluded (n=52)</p> <p>(c) Consider use of a flow diagram</p> <p>(R) Not useful in this study.</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(R) Given in Table 1.</p> <p>The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(R) Cases with missing data for estimated date of delivery were excluded from the study population (n=52)</p> <p>Recoded to the reference category of the variable and included in the analyses:</p> <p>Birth weight 3 cases. Maternal age 2 cases. Lie at delivery 8 cases. Duration of second stage of labour 92 cases.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>(R) Table 1.</p> <p>Outcome event, the dependant variable, anal sphincter injury: 1014 cases.</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(R) Table 2 and 3. Confounders: paragraph 4 in Material and Methods.</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(R) Table 1</p>

1		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
2		meaningful time period
3		(R) NA
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6	Other analyses	17 Report other analyses done—eg analyses of subgroups and interactions, and
7		sensitivity analyses
8		(R) NA
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10	Discussion	
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12	Key results	18 Summarise key results with reference to study objectives
13		(R) Fulfilled.
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15	Limitations	19 Discuss limitations of the study, taking into account sources of potential bias or
16		imprecision. Discuss both direction and magnitude of any potential bias
17		(R) Bias regarding main outcome: We do not know the magnitude of underreporting
18		of anal sphincter tear grade 3 and 4, however believe this to be low.
19		Bias regarding main exposure: The quality system of the department relies on honest
20		reporting by midwives and obstetricians, and has been a cornerstone in the systematic
21		interdisciplinary work towards better clinical outcomes since 1996. We have reason to
22		believe that ownership to the concept has resulted in good adherence to the reporting
23		routines, and we believe the reporting of oxytocin augmentation to be a robust
24		measure of what was actually practised. The midwives plotting the information were
25		not aware of any research issue related to oxytocin augmentation.
26		We consider the other main exposure variables to be robust: It is unlikely that reports
27		of episiotomy, instrumental delivery and birth weight are skewed in any direction. The
28		same applies to the possible confounders age, ethnicity, occiput posterior position and
29		epidural analgesia.
30		We believe that the reporting of these variables reflects the actual practice. Therefore
31		we consider the estimates for risks related to anal sphincter tear grade 3 and 4 to be
32		precise with little bias. Our stratified approach, modified model, takes care of the
33		interaction problems between episiotomy, operative vaginal delivery, birth weight and
34		oxytocin augmentation.
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43	Interpretation	20 Give a cautious overall interpretation of results considering objectives, limitations,
44		multiplicity of analyses, results from similar studies, and other relevant evidence
45		(R) Fulfilled.
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47	Generalisability	21 Discuss the generalisability (external validity) of the study results.
48		(R) The study participants represent the total population of women fulfilling the
49		inclusion criteria in a Norwegian region of 320 000 people. The study population is
50		heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%),
51		social status and ethnicity. This adds value to the external validity of the study results.
52		We encourage other study groups to make research on the effect of oxytocin
53		augmentation on anal sphincter injury in other populations.
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57	Other information	
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59	Funding	22 Give the source of funding and the role of the funders for the present study and, if
60		

applicable, for the original study on which the present article is based
(R) No specific funding.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women – a population-based, case-control study

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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Epidemiology
Keywords:	Maternal medicine < OBSTETRICS, EPIDEMIOLOGY, Colorectal surgery < SURGERY

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3 **ASSESSING THE ASSOCIATION OF OXYTOCIN AUGMENTATION WITH**
4 **OBSTETRIC ANAL SPHINCTER INJURY IN NULLIPAROUS WOMEN – A**
5 **POPULATION-BASED, CASE CONTROL-STUDY**
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29 Oxytocin augmentation and anal sphincter injury
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32 *Key words:* anal sphincter injury, oxytocin, episiotomy, operative vaginal delivery, birth
33 weight,
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35 Word Count: 2619
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ABSTRACT

Objective: To assess the association of oxytocin augmentation with obstetric anal sphincter injury among nulliparous women.

Design: A population-based, case-control study.

Setting: Primary and secondary teaching hospital serving a Norwegian region.

Population: 15 476 nulliparous women with spontaneous start of labour, single cephalic presentation, and gestation ≥ 37 weeks delivering vaginally between 1999 and 2012.

Methods: Based on the presence or absence of oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (< 4000 g vs. ≥ 4000 g), we did stratified analysis of all 16 combinations to assess the odds ratios (OR) of anal sphincter injury. Within a modified model, we tested for possible confounding, and interactions between maternal age, ethnicity, occiput posterior position, and epidural analgesia.

Main outcome measure: Obstetric anal sphincter injury.

Results: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries in women giving spontaneous birth to infants weighing < 4000 g (OR 1.8; 95% CI: 1.5–2.2). Episiotomy was not associated with sphincter injuries in spontaneous births, but with a lower OR in operative vaginal deliveries. Spontaneous delivery of infants weighing ≥ 4000 g was associated with a 3-fold higher OR, and epidural analgesia was associated with a 30% lower OR in comparison to no epidural analgesia.

Conclusions: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants. We observed a

1
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3 considerable effect modification between the most important factors involved in the active
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5 second stage of labour when anal sphincter injuries occur.
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11 12 13 **ARTICLE SUMMARY**

14 15 **Strengths and limitations of this study**

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17 • Stratifying by the main risk factors that are active during the expulsive phase of labour
18 and testing for confounders are strengths of the study.
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21 • We reveal how oxytocin augmentation interacts with the major factors active in the
22 expulsive phase of labour.
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25 • The study is based on prospectively collected data from a large, unselected population,
26 which makes bias unlikely.
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29 • The study design is a limitation, as we cannot prove causality between oxytocin
30 augmentation and obstetric anal sphincter injuries in an observational study.
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INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} Asian or African ethnicity,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of >300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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3 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
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5 According to our routines and national guidelines, operative vaginal delivery was indicated if
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7 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
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9 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
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11 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
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13 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
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15 originating from Europe or North America, or non-Western.
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18 We analysed our dataset using the Chi-squared test and forward stepwise logistic
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20 regression analyses with $p < 0.05$ as significance level. We applied a stratified approach to
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22 investigate the association of oxytocin augmentation and the outcome across the presence (+)
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24 or absence (–) during labour of episiotomy, operative vaginal delivery, and birth weight
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26 (<4000 g or ≥ 4000 g). We displayed all 16 possible combinations of the four variables, with
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28 absence of oxytocin augmentation, episiotomy, and operative vaginal delivery, and birth
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30 weight <4000 g set as the reference value. From these stratified analyses, we collapsed strata
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32 that were non-significant, taking the order of occurrence and the clinical impact of the
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34 variable into consideration. In this modified model, we tested for possible confounding effects
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36 and interactions from maternal age, ethnicity, occiput posterior position, and epidural
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38 analgesia in forward stepwise logistic regression analyses. Confounders were tested one by
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40 one and set to at least 10% change in any estimate of combinations of the modified target
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42 variables on obstetric anal sphincter injuries. Interaction terms were significant at $p < 0.05$.
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44 Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk,
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46 NY: IBM Corp.
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52 The Regional Committee for Medical and Health Research Ethics, Western Norway,
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54 approved the protocol as a quality assurance study in obstetric care, and fulfilling the
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56 requirements for data protection procedures (REK 2011-1247).
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RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					
Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	

30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The results of the stratified analysis are presented in Table 2.

Table 2 Stratified analyses of the prevalence of obstetric anal sphincter injury by the presence (+) or absence (–) of: oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (strata 1–16; group 1 as reference). Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	+	-	-	-	2621	148 (5.6)	1.5	1.3-1.9
4	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
5	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
6	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
7	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
8	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
9	-	-	-	+	539	59 (10.9)	3.2	2.4-4.3
10	+	-	-	+	438	45 (10.3)	3.0	2.1-4.2

11	-	+	-	+	203	20 (9.9)	2.8	1.7-4.6
12	+	+	-	+	215	20 (9.3)	2.7	1.6-4.3
13	-	+	+	+	101	11 (10.9)	3.2	1.7-6.0
14	+	+	+	+	292	44 (15.1)	4.6	3.2-6.5
15	-	-	+	+	42	15 (35.7)	14.4	7.5-27.5
16	+	-	+	+	192	47 (24.5)	8.4	5.9-12.0

We found a strong effect modification between episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight on obstetric anal sphincter injuries. Oxytocin augmentation was associated with an increased odds ratio of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants, and was independent of episiotomy (groups 3 and 4). Episiotomy was not associated with anal sphincter injuries when the other factors were absent (groups 1 and 2). Oxytocin augmentation was not associated with anal sphincter injury during instrumental deliveries of normal-sized infants without episiotomy (groups 7 and 8), nor in spontaneous deliveries of infants weighing ≥ 4000 g without episiotomy (groups 9 and 10). Furthermore, oxytocin use was not associated with anal sphincter injuries in spontaneous (groups 11 and 12) or operative vaginal deliveries (groups 13 and 14) of infants weighing ≥ 4000 g when episiotomy was applied. Operative vaginal delivery of an infant weighing ≥ 4000 g without episiotomy represented the group with the highest prevalence of injury (groups 15 and 16) and was not associated with oxytocin use. Episiotomy appeared to be negatively associated with sphincter rupture in operative vaginal deliveries regardless of the birth weight and the use of oxytocin (groups 5-8 and 13-16).

In the modified model (Table 3), we collapsed the groups from Table 2 that had odds ratios of similar magnitude for obstetric anal sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–16) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (3,4)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (5,6)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (7,8)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-12)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.4-3.9)
F (13,14)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (15,16)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

Age, origin of the mother, and occiput posterior position had no confounding effect on odds ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3). The use of oxytocin augmentation was restricted in the department from 2010 onwards, however, we observed a significant association between oxytocin augmentation and anal sphincter injuries through all time periods (1999-2003, 2004-2006, 2007-2009, 2010-2012). The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural analgesia was associated with a 30% lower odds ratio of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30–59 minutes group, and 65% (range 49–76%) in the ≥60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45–49% when the active part of the second stage of labour lasted ≥60

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3 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
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5 strong associations between oxytocin augmentation and the duration of second stage, and
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7 between operative delivery and the duration of second stage (collinearity), which means that
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9 the duration of second stage is measured through operative delivery and oxytocin
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11 augmentation.
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13 14 15 16 **DISCUSSION**

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18 We found that oxytocin augmentation during active labour was associated with a 70%
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20 increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving
21
22 spontaneous birth to an infant weighing <4000 g. We did not find an association between
23
24 episiotomy and tears during spontaneous deliveries, but a significantly reduced association in
25
26 all operative vaginal deliveries.
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30 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
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32 However, a Cochrane review concluded that a reduction of labour by two hours was the only
33
34 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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36 the entire concept of active management of labour to be associated with a slightly reduced
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38 risk of caesarean delivery.²¹ As in other studies, we found that approximately 50% of
39
40 nulliparous women received oxytocin augmentation.^{16, 17, 22} There is reason to believe that
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42 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
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44 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
45
46 progress of the expulsive phase of labour, leading to rushed situations, impaired
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48 communication with the mother, and less focus on protection of the perineum and a controlled
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50 delivery of the head. Recent studies from Norway indicate that focus on these elements is
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52 important in preventing perineal injuries.^{23, 24}
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3 Many authors have used logistic regression analysis to identify risk factors for
4 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
5 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
6 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
7 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
8 which is a methodological weakness since the true effect of other factors is concealed by the
9 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
10 women, entering oxytocin augmentation, duration of active second stage of labour, and
11 instrumental delivery into the same model.¹⁵

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14 Our study shows strong collinearity between a prolonged active second stage of labour
15 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
16 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
17 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
18 second stage is a time related event before the expulsion of the head. During this latency the
19 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
20 during the expulsive phase. Consequently, we do not consider the duration of the active
21 second stage as a risk factor for anal sphincter injuries.

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23
24 Jander et al. conducted a single institution, retrospective, case-control study of 214
25 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
26 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
27 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
28 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
29 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
30 for induction or augmentation purposes.²⁵⁻²⁷ Three large population-based studies on the risk
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3 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.^{1, 7,}
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7 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
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9 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhed found epidural
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11 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
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13 by parity and found a significantly increased odds ratio associated with epidural analgesia in
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15 nulliparous women.²⁸ In our study, epidural analgesia was associated with a significantly
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17 reduced odds ratio for sphincter tears.
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21 Our study takes into account four factors that exert their effect on the anal sphincter
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23 during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both operative
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25 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
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27 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
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29 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
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31 national registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 29, 30} In our study,
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33 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
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35 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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39 Our methodological approach, stratifying by the factors that are active during the
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41 expulsive phase of labour and testing for confounders, is considered a strength of the study.
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43 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
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45 with these major risk factors. Stepwise, forward multivariable regression analyses, without
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47 testing for possible interactions, would fail to reveal this information. This case-control study
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49 is based on prospectively collected data from a large unselected population, and represents all
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51 deliveries meeting the inclusion criteria that occurred during the study period, which make
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53 bias unlikely. Our department has a high proportion of vaginal deliveries. The overall
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55 caesarean delivery rate in our institution was 12.5% over the study period. For women in
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3 TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012.
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5 Accordingly, the study population includes both high- and low-risk pregnancies, which adds
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7 to the external validity of our results.
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10 However, some limitations apply. We cannot prove causality between oxytocin
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12 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
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14 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
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16 support technique, and the birth attendant's experience level may be possible risk modifiers
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18 not included in our database. Finally, single institution studies, also when based on unselected
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20 populations, should be interpreted with caution.
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23 Our findings have some important implications. Birth attendants should be aware of
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25 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
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27 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
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29 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
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31 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
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33 World Health Organization recommends the use of a partogram with an action line defining
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35 failure to progress. However, a recent Cochrane review could not confirm that such a
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37 partogram was beneficial in high resource settings.³¹ Given the doubtful benefits from
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39 augmentation of labour, randomized controlled trials are strongly needed, and we propose
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41 anal sphincter injury as one of the most important endpoints.
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46 Moreover, our study supports restricted use of episiotomy during normal births and as
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48 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
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50 unpredictable risk factor as weight estimation of a large fetus is unreliable.³²
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Contributorship Statement

All four authors have contributed to the idea and design of the research project. ABR, TME managed the dataset and the statistical analyses were performed by FES. All four authors have contributed to the interpretation of the results and the writing of the manuscript.

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Competing interests

None

Data Sharing Statement

There is no additional data material to be shared.

References

1. Baghestan E, Irgens LM, Bordahl PE, et al. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;**116**:25-34.
2. Laine K, Skjeldestad FE, Sanda B, et al. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;**90**:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;**247**:224-37.
4. Sultan AH, Thakar R, Fenner DE. *Perineal and anal sphincter trauma : diagnosis and clinical management*. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;**80**:229-34.
6. Hornemann A, Kamischke A, Luedders DW, et al. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;**281**:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;**98**:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, et al. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;**108**:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;**29**:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;**85**:1252-8.

- 1
2
3 11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, et al. Hospital-based lateral
4
5 episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register
6
7 study. *Am J Obstet Gynecol* 2012;**206**:347 e1-6.
8
- 9
10 12. Murphy DJ, Macleod M, Bahl R, et al. A randomised controlled trial of routine versus
11
12 restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG*
13
14 2008;**115**:1695-702; discussion 702-3.
15
- 16
17 13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev*
18
19 2009:CD000081.
20
- 21
22 14. Samuelsson E, Ladfors L, Wennerholm UB, et al. Anal sphincter tears: prospective
23
24 study of obstetric risk factors. *BJOG* 2000;**107**:926-31.
25
- 26
27 15. Prager M, Andersson KL, Stephansson O, et al. The incidence of obstetric anal
28
29 sphincter rupture in primiparous women: a comparison between two European delivery
30
31 settings. *Acta Obstet Gynecol Scand* 2008;**87**:209-15.
32
- 33
34 16. Blix E, Pettersen SH, Eriksen H, et al. [Use of oxytocin augmentation after
35
36 spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;**122**:1359-62.
37
- 38
39 17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, et al. Outcome in obstetric care related
40
41 to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;**85**:1094-8.
42
- 43
44 18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment
45
46 for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*
47
48 2011:CD007123.
49
- 50
51 19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet*
52
53 *Gynaecol* 2001;**15**:179-94.
54
- 55
56 20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors.
57
58 *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
59
60

- 1
2
3 21. Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management
4 in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst*
5 *Rev* 2013;**9**:CD004907.
6
7
- 8
9 22. Selin L, Almstrom E, Wallin G, et al. Use and abuse of oxytocin for augmentation of
10 labor. *Acta Obstet Gynecol Scand* 2009;**88**:1352-7.
11
- 12 23. Hals E, Oian P, Pirhonen T, et al. A multicenter interventional program to reduce the
13 incidence of anal sphincter tears. *Obstet Gynecol* 2010;**116**:901-8.
14
- 15 24. Laine K, Pirhonen T, Rolland R, et al. Decreasing the incidence of anal sphincter tears
16 during delivery. *Obstet Gynecol* 2008;**111**:1053-7.
17
- 18 25. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with
19 complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;**71**:520-4.
20
- 21 26. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter
22 rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol*
23 1988;**27**:27-32.
24
- 25 27. Legino LJ, Woods MP, Rayburn WF, et al. Third- and fourth-degree perineal tears. 50
26 year's experience at a university hospital. *J Reprod Med* 1988;**33**:423-6.
27
- 28 28. Poen AC, Felt-Bersma RJ, Dekker GA, et al. Third degree obstetric perineal tears: risk
29 factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol*
30 1997;**104**:563-6.
31
- 32 29. Hartmann K, Viswanathan M, Palmieri R, et al. Outcomes of routine episiotomy: a
33 systematic review. *JAMA* 2005;**293**:2141-8.
34
- 35 30. de Leeuw JW, de Wit C, Kuijken JP, et al. Mediolateral episiotomy reduces the risk
36 for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;**115**:104-8.
37
- 38 31. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in
39 spontaneous labour at term. *Cochrane Database Syst Rev* 2013;**7**:CD005461.
40
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32. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;**43**:3-10.

For peer review only

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7 Assessing the **association** of oxytocin augmentation **with** obstetric anal sphincter injury
8 in nulliparous women – a population-based, **case-control** study

Comment [ar1]: Title changed acc. to Editor and rev. comm.

ARTICLE SUMMARY

Strengths and limitations of this study

- Stratifying by the main risk factors that are active during the expulsive phase of labour and testing for confounders are strengths of the study.
- We reveal how oxytocin augmentation interacts with the major factors active in the expulsive phase of labour.
- The study is based on prospectively collected data from a large, unselected population, which makes bias unlikely.
- The study design is a limitation, as we cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study.

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INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1, 3, 5} high birth weight,^{1, 3, 5, 6} operative vaginal delivery,^{1, 3, 5} advanced maternal age,^{1, 5, 6} Asian or African ethnicity,^{1, 7} and prolonged second stage of labour^{3, 7, 8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9, 10} and episiotomy^{1, 11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5, 14, 15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16, 17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was [to assess the association between](#) oxytocin augmentation [and obstetric anal sphincter injuries](#) in a dynamic model [related to](#) the active second stage of labour.

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MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded.

The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification

System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

Comment [ar6]: Gissler 1 on missing cases

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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Throughout the study period, episiotomy was performed either medio-laterally or laterally. According to our routines and national guidelines, operative vaginal delivery was indicated if delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction with a Malmström metal cup as the preferred procedure for operative vaginal delivery. Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e. originating from Europe or North America, or not.

Comment [ar7]: Steer minor comm. 2, Gissler minor comm. 1

We analysed our dataset using the Chi-squared test and forward stepwise logistic regression analyses with $p < 0.05$ as significance level. We applied a stratified approach to investigate the association of oxytocin augmentation and the outcome across the presence (+) or absence (-) during labour of episiotomy, operative vaginal delivery, and birth weight (<4000 g or ≥ 4000 g). We displayed all 16 possible combinations of the four variables, with absence of oxytocin augmentation, episiotomy, and operative vaginal delivery, and birth weight <4000 g set as the reference value. From these stratified analyses, we collapsed strata that were non-significant, taking the order of occurrence and the clinical impact of the variable into consideration. In this modified model, we tested for possible confounding effects and interactions from maternal age, ethnicity, occiput posterior position, and epidural analgesia in forward stepwise logistic regression analyses. Confounders were tested one by one and set to at least 10% change in any estimate of combinations of the modified target variables on obstetric anal sphincter injuries. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

Comment [ar8]: Steer 3, birth weight as dichotomous variable was needed for the stratified model

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					
Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Not Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	

Comment [ar9]: Throughout Results we have replaced terminology indicating causality, complying with Steers remark 4.

Comment [ar10]: 27% is still correct

Comment [ar11]: Now corrected to 53%

Comment [ar12]: New analyses

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30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The results of the stratified analysis are presented in Table 2.

Table 2 Stratified analyses of the prevalence of obstetric anal sphincter injury by the presence (+) or absence (-) of: oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (strata 1–16; group 1 as reference). Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Comment [ar13]: new analysis

Risk Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth_weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.13	0.8-1.5
3	+	-	-	-	2621	148 (5.6)	1.53	1.3-1.9
4	+	+	-	-	1039	61 (5.9)	1.62	1.2-2.2
5	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
6	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
7	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
8	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
9	-	-	-	+	539	59 (10.9)	3.2	2.4-4.3
10	+	-	-	+	438	45 (10.3)	3.0	2.1-4.2

11	-	+	-	+	203	20 (9.9)	2.8	1.7-4.6
12	+	+	-	+	215	20 (9.3)	2.7	1.6-4.3
13	-	+	+	+	101	11 (10.9)	3.2	1.7-6.0
14	+	+	+	+	292	44 (15.1)	4.6	3.2-6.5
15	-	-	+	+	42	15 (35.7)	14.4	7.5-27.5
16	+	-	+	+	192	47 (24.5)	8.4	5.9-12.0

We found a strong effect modification between episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight on obstetric anal sphincter injuries. Oxytocin augmentation was associated with an increased [odds ratio](#) of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants, and was independent of episiotomy (groups 3 and 4). Episiotomy was not associated with anal sphincter injuries when the other factors were absent (groups 1 and 2). Oxytocin augmentation was not associated with anal sphincter injury during instrumental deliveries of normal-sized infants without episiotomy (groups 7 and 8), [nor in spontaneous deliveries of](#) infants weighing ≥ 4000 g without episiotomy (groups 9 and 10). Furthermore, oxytocin use was not associated with anal sphincter injuries in spontaneous (groups 11 and 12) or operative vaginal deliveries (groups 13 and 14) of infants weighing ≥ 4000 g when episiotomy was applied. Operative vaginal delivery of an infant weighing ≥ 4000 g without episiotomy represented the group with the highest prevalence of injury (groups 15 and 16) and was not associated with oxytocin use. Episiotomy appeared to be negatively associated with sphincter rupture in operative vaginal deliveries regardless of the birth weight and the use of oxytocin (groups 5-8 and 13-16).

In the modified model (Table 3), we collapsed the groups from Table 2 that had [odds ratios of similar magnitude for](#) obstetric anal sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–16) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Comment [ar14]: new analysis

Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (3,4)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (5,6)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (7,8)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-12)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.4-3.9)
F (13,14)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (15,16)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

Age, origin of the mother, and occiput posterior position [had no confounding effect on odds](#)

[ratios for](#) obstetric anal sphincter injury across combinations of episiotomy, oxytocin

augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3). **The**

use of oxytocin augmentation was restricted in the department from 2010, however, we

observed a significant association between oxytocin augmentation and anal sphincter injuries

Comment [ar15]: Comment Steer 2

through all time periods (1999-2003, 2004-2006, 2007-2009, 2010-2012). The unadjusted

odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the

adjusted OR for epidural analgesia was **0.73, (95% CI 0.63-0.84)** i.e. epidural analgesia was

Comment [ar16]: New analysis

associated with a 30% lower [odds ratio](#) of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30–59 minutes group, and 65% (range 49–76%) in the ≥ 60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45–49% when the active part of the second stage of labour lasted ≥ 60

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7 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
8 [strong associations](#) between oxytocin augmentation and the duration of second stage, and
9 between operative delivery and the duration of second stage (colinearity), which [means that](#)
10 [the duration of second stage is measured through operative delivery and oxytocin](#)
11 [augmentation.](#)
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17 18 **DISCUSSION**

19
20 [We found that oxytocin augmentation during active labour was associated with a 70%](#)
21 [increased odds ratio](#) of obstetric anal sphincter injury in women in TGCS group 1 giving
22 [spontaneous birth to an infant weighing <4000 g. We did not find an association between](#)
23 [episiotomy and tears during spontaneous deliveries, but a significantly reduced association in](#)
24 [all operative vaginal deliveries.](#)
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Comment [ar17]: Steer 4

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30 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
31 However, a Cochrane review concluded that a reduction of labour by two hours was the only
32 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
33 the entire concept of active management of labour to be associated with a slightly reduced
34 risk of caesarean delivery.²¹ As in other studies, we found that approximately 50% of
35 nulliparous women received oxytocin augmentation.^{16, 17, 22} There is reason to believe that
36 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
37 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
38 progress of the expulsive phase of labour, leading to rushed situations, impaired
39 communication with the mother, and less focus on protection of the perineum and a controlled
40 delivery of the head. Recent studies from Norway indicate that focus on these elements is
41 important in preventing perineal injuries.^{23, 24}
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7 Many authors have used logistic regression analysis to identify risk factors for
8 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
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10 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
11
12 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
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14 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
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16 which is a methodological weakness since the true effect of other factors is concealed by the
17
18 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
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20 women, entering oxytocin augmentation, duration of active second stage of labour, and
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22 instrumental delivery into the same model.¹⁵
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24 Our study shows strong colinearity between a prolonged active second stage of labour
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26 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
27
28 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
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30 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
31
32 second stage is a time related event before the expulsion of the head. During this latency the
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34 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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36 during the expulsive phase. Consequently, we do not consider the duration of the active
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38 second stage as a risk factor for anal sphincter injuries.

Comment [ar18]: Gissler 3

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40 Jander et al. conducted a single institution, retrospective, case-control study of 214
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42 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
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44 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
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46 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
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48 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
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50 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
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52 for induction or augmentation purposes.²⁵⁻²⁷ Three large population-based studies on the risk
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6 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.^{1,7,}
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10 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
11 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhede found epidural
12 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
13 by parity and found a significantly increased [odds ratio](#) associated with epidural analgesia in
14 nulliparous women.²⁸ In our study, epidural analgesia was associated with a significantly
15 reduced [odds ratio for](#) sphincter tears.
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22 Our study takes into account four factors that exert their effect on the anal sphincter
23 during the final minutes of delivery. As in previous studies,^{1,3,5} we found both operative
24 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
25 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
26 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
27 national registry study from Norway,¹ but differs from other studies.^{8,11,13,29,30} In our study,
28 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
29 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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37 Our methodological approach, stratifying by the factors that are active during the
38 expulsive phase of labour and testing for confounders, is [considered](#) a strength [of the study](#).
39 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
40 with these major risk factors. [Stepwise, forward multivariable regression analyses, without](#)
41 [testing for possible interactions, would fail to reveal this information.](#) [This case-control study](#)
42 is based on prospectively collected data from a large unselected population, and represents all
43 deliveries meeting the inclusion criteria that occurred during the study period, which make
44 bias unlikely. Our department has a high proportion of vaginal deliveries. The overall
45 caesarean delivery rate in our institution was 12.5% over the study period. For women in
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Comment [ar19]: Steer 3

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TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012. Accordingly, the study population includes both high- and low-risk pregnancies, which adds to the external validity of our results.

However, some limitations apply. We cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study. Furthermore, socioeconomic status, smoking, body mass index, maternal delivery positions, perineal support technique, and the birth attendant's experience level may be possible risk modifiers not included in our database. Finally, single institution studies, also when based on unselected populations, should be interpreted with caution.

Our findings have some important implications. Birth attendants should be aware of the association between oxytocin augmentation and obstetric anal sphincter injuries in the large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation of evidence-based guidelines for using oxytocin augmentation should be encouraged. The World Health Organisation recommends the use of a partogram with an action line defining failure to progress. However, a recent Cochrane review could not confirm that such a partogram was beneficial in high resource settings.³¹ Given the doubtful benefits from augmentation of labour, randomized controlled trials are strongly needed, and we propose anal sphincter injury as one of the most important endpoints.

Moreover, our study supports restricted use of episiotomy during normal births and as a recommendation for operative vaginal deliveries. Birth weight is an important, albeit unpredictable risk factor as weight estimation of a large fetus is unreliable.³²

Comment [ar20]: Gissler, Steer 1

Comment [ar21]: Gissler 4

Comment [ar22]: Gissler 4

Comment [ar23]: Gissler 1 and Steer 4:
Risk replaced by association

Comment [ar24]: On Steer 7, WHO vs
Cochrane

Comment [ar25]: Steer 1, we agree.

Comment [ar26]: Steer 8, we have added a
reference to emphasize this

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Competing interests

None

Funding

No specific

References

1. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;**116**:25-34.
2. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;**90**:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;**247**:224-37.
4. Sultan AH, Thakar R, Fenner DE. *Perineal and anal sphincter trauma : diagnosis and clinical management*. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;**80**:229-34.
6. Hornemann A, Kamischke A, Luedders DW, Beyer DA, Diedrich K, Bohlmann MK. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;**281**:59-64.

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7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;**98**:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, Wallenburg HC. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;**108**:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;**29**:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;**85**:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;**206**:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;**115**:1695-702; discussion 702-3.
13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009:CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, Gareberg B, Nyberg K, Hagberg H. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;**107**:926-31.
15. Prager M, Andersson KL, Stephansson O, Marchionni M, Marions L. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;**87**:209-15.
16. Blix E, Pettersen SH, Eriksen H, Royset B, Pedersen EH, Oian P. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;**122**:1359-62.

17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;**85**:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011:CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;**15**:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev* 2013;**9**:CD004907.
22. Selin L, Almstrom E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation of labor. *Acta Obstet Gynecol Scand* 2009;**88**:1352-7.
23. Hals E, Oian P, Pirhonen T, Gissler M, Hjelle S, Nilsen EB, et al. A multicenter interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;**116**:901-8.
24. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal sphincter tears during delivery. *Obstet Gynecol* 2008;**111**:1053-7.
25. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;**71**:520-4.
26. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol* 1988;**27**:27-32.

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27. Legino LJ, Woods MP, Rayburn WF, McGoogan LS. Third- and fourth-degree perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;**33**:423-6.
28. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol* 1997;**104**:563-6.
29. Hartmann K, Viswanathan M, Palmieri R, Gartlehner G, Thorp J, Jr., Lohr KN. Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;**293**:2141-8.
30. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;**115**:104-8.
31. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;**7**:CD005461.
32. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;**43**:3-10.

Comment [ar27]: New ref. (32), Steer 8

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(R) In abstract; a cross sectional study, analyzed as case-control study.</p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>(R) Fulfilled</p>
Introduction		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>(R) Recent studies have shown the importance of the perineal protection technique in preventing perineal tears. Oxytocin augmentation could impair the control of the perineum during the delivery by causing too fast progress in the last minutes of labour. Oxytocin augmentation is widely used (50% of births). Guidelines for its use are often deficient and the evidence for its positive effect is challenged. Therefore, oxytocin augmentation as a risk factor for obstetric anal sphincter injuries, and should be explored in a study taking other relevant risk factors into account.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>(R) To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.</p>
Methods		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>(R) Present in Abstract and Methods.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>(R) Setting: Tertiary teaching hospital.</p> <p>Location: Delivery department of Stavanger University Hospital, serving the total obstetric population of the region of South Rogaland.</p> <p>Dates 15 May 1999 – 15 May 2012.</p> <p>Data were collected consecutively.</p>
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants.</p> <p>(R) Nulliparous women with spontaneous start of labour, single, cephalic pregnancy and ≥ 37 weeks gestation who delivered vaginally, where we had access to complete information on the main exposure and the explanatory variables. The source population was the entire obstetric population of the region.</p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect</p>

1		modifiers. Give diagnostic criteria, if applicable
2		(R) Outcome: Obstetric anal sphincter injury; that is grade 3 and 4 perineal tears as
3		defined by International Society of Incontinence.
4		Exposure: Oxytocin augmentation in active labour, that is oxytocin intravenous
5		infusion (5 international units (0.01mg) oxytocin in 500 ml saline) used in incremental
6		doses during active labour.
7		Predictors: NA
8		Effect modifiers: Episiotomy, operative vaginal delivery, birth weight <4000 g vs
9		≥4000 g.
10		Potential confounders: maternal age, ethnicity, occiput posterior position, duration of
11		second stage of labour and epidural analgesia.
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17	Data sources/ measurement	8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. (R) All variables are precisely defined in the obstetric databases of Stavanger University Hospital. The grade of perineal injury was assessed during operative repair and plotted directly into the database.
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26	Bias	9 Describe any efforts to address potential sources of bias. (R) In this cross-sectional study all women giving births and who fulfil the inclusion criteria are included. There were very few cases with missing data. We may have missed some cases of perineal injury due to underreporting. The variables are hard variables with clear definitions: Use of oxotocin (yes/no), episiotomy (yes/no), mode of delivery (spontaneous/operative vaginal), birth weight categorized <4000/ ≥4000 g.
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34	Study size	10 Explain how the study size was arrived at (R) The study size is given by the number of women fulfilling the eligibility criteria and who delivered at Stavanger University Hospital from 15 May 1999 to 15 May 2012.
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40	Quantitative variables	11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. (R) Birth weight was categorized into < 4000/ ≥4000 g.
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44	Statistical methods	12 (a) Describe all statistical methods, including those used to control for confounding (R) Chi-square test and stepwise forward logistic regression using IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp. (b) Describe any methods used to examine subgroups and interactions (R) We applied a stratified approach to control for interaction between the main variables (oxytocin augmentation, episiotomy, instrumental delivery and birth weight). Then we tested for confounding and interaction to a modified model by entering one variable at time. (c) Explain how missing data were addressed (R) Cases with missing data for estimated date of delivery were excluded. Cases with
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other missing data were recoded to the reference value in the logistic regression analyses. Very few cases with missing data (n=52).

(d) If applicable, describe analytical methods taking account of sampling strategy

(R) NA

(e) Describe any sensitivity analyses

(R) NA

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(R) Potentially eligible: 15 545 Confirmed eligible: 15 493 Included/analyzed: 15 493</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(R) Cases with missing data for estimated date of delivery were excluded (n=52)</p> <p>(c) Consider use of a flow diagram</p> <p>(R) Not useful in this study.</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(R) Given in Table 1.</p> <p>The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(R) Cases with missing data for estimated date of delivery were excluded from the study population (n=52)</p> <p>Recoded to the reference category of the variable and included in the analyses:</p> <p>Birth weight 3 cases. Maternal age 2 cases. Lie at delivery 8 cases. Duration of second stage of labour 92 cases.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>(R) Table 1.</p> <p>Outcome event, the dependant variable, anal sphincter injury: 1014 cases.</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(R) Table 2 and 3. Confounders: paragraph 4 in Material and Methods.</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(R) Table 1</p>

1		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
2		meaningful time period
3		(R) NA
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6	Other analyses	17 Report other analyses done—eg analyses of subgroups and interactions, and
7		sensitivity analyses
8		(R) NA
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10	Discussion	
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12	Key results	18 Summarise key results with reference to study objectives
13		(R) Fulfilled.
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15	Limitations	19 Discuss limitations of the study, taking into account sources of potential bias or
16		imprecision. Discuss both direction and magnitude of any potential bias
17		(R) Bias regarding main outcome: We do not know the magnitude of underreporting
18		of anal sphincter tear grade 3 and 4, however believe this to be low.
19		Bias regarding main exposure: The quality system of the department relies on honest
20		reporting by midwives and obstetricians, and has been a cornerstone in the systematic
21		interdisciplinary work towards better clinical outcomes since 1996. We have reason to
22		believe that ownership to the concept has resulted in good adherence to the reporting
23		routines, and we believe the reporting of oxytocin augmentation to be a robust
24		measure of what was actually practised. The midwives plotting the information were
25		not aware of any research issue related to oxytocin augmentation.
26		We consider the other main exposure variables to be robust: It is unlikely that reports
27		of episiotomy, instrumental delivery and birth weight are skewed in any direction. The
28		same applies to the possible confounders age, ethnicity, occiput posterior position and
29		epidural analgesia.
30		We believe that the reporting of these variables reflects the actual practice. Therefore
31		we consider the estimates for risks related to anal sphincter tear grade 3 and 4 to be
32		precise with little bias. Our stratified approach, modified model, takes care of the
33		interaction problems between episiotomy, operative vaginal delivery, birth weight and
34		oxytocin augmentation.
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43	Interpretation	20 Give a cautious overall interpretation of results considering objectives, limitations,
44		multiplicity of analyses, results from similar studies, and other relevant evidence
45		(R) Fulfilled.
46		
47	Generalisability	21 Discuss the generalisability (external validity) of the study results.
48		(R) The study participants represent the total population of women fulfilling the
49		inclusion criteria in a Norwegian region of 320 000 people. The study population is
50		heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%),
51		social status and ethnicity. This adds value to the external validity of the study results.
52		We encourage other study groups to make research on the effect of oxytocin
53		augmentation on anal sphincter injury in other populations.
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57	Other information	
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59	Funding	22 Give the source of funding and the role of the funders for the present study and, if
60		

applicable, for the original study on which the present article is based

(R) No specific funding.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women – a population-based, case-control study

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3 **ASSESSING THE ASSOCIATION OF OXYTOCIN AUGMENTATION WITH**
4 **OBSTETRIC ANAL SPHINCTER INJURY IN NULLIPAROUS WOMEN – A**
5 **POPULATION-BASED, CASE CONTROL-STUDY**
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29 Oxytocin augmentation and anal sphincter injury
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32 *Key words:* anal sphincter injury, oxytocin, episiotomy, operative vaginal delivery, birth
33 weight,
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35 Word Count: 2619
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ABSTRACT

Objective: To assess the association of oxytocin augmentation with obstetric anal sphincter injury among nulliparous women.

Design: A population-based, case-control study.

Setting: Primary and secondary teaching hospital serving a Norwegian region.

Population: 15 476 nulliparous women with spontaneous start of labour, single cephalic presentation, and gestation ≥ 37 weeks delivering vaginally between 1999 and 2012.

Methods: Based on the presence or absence of oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (< 4000 g vs. ≥ 4000 g), we did stratified analysis of all 16 combinations to assess the odds ratios (OR) of anal sphincter injury. Within a modified model, we tested for possible confounding, and interactions between maternal age, ethnicity, occiput posterior position, and epidural analgesia.

Main outcome measure: Obstetric anal sphincter injury.

Results: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries in women giving spontaneous birth to infants weighing < 4000 g (OR 1.8; 95% CI: 1.5–2.2). Episiotomy was not associated with sphincter injuries in spontaneous births, but with a lower OR in operative vaginal deliveries. Spontaneous delivery of infants weighing ≥ 4000 g was associated with a 3-fold higher OR, and epidural analgesia was associated with a 30% lower OR in comparison to no epidural analgesia.

Conclusions: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants. We observed a

1
2
3 considerable effect modification between the most important factors involved in the active
4
5 second stage of labour when anal sphincter injuries occur.
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13 **ARTICLE SUMMARY**

14 **Strengths and limitations of this study**

- 15 • Stratifying by the main risk factors that are active during the expulsive phase of labour
16 and testing for confounders are strengths of the study.
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- 18 • We reveal how oxytocin augmentation interacts with the major factors active in the
19 expulsive phase of labour.
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- 21 • The study is based on prospectively collected data from a large, unselected population,
22 which makes bias unlikely.
23
- 24 • The study design is a limitation, as we cannot prove causality between oxytocin
25 augmentation and obstetric anal sphincter injuries in an observational study.
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INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} Asian or African ethnicity,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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3 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
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5 According to our routines and national guidelines, operative vaginal delivery was indicated if
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7 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
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9 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
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11 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
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13 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
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15 originating from Europe or North America, or non-Western.
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19 We analysed our dataset using the Chi-squared test and forward stepwise logistic
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21 regression analyses with $p < 0.05$ as significance level. We applied a stratified approach to
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23 investigate the association of oxytocin augmentation and the outcome across the presence (+)
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25 or absence (-) during labour of episiotomy, operative vaginal delivery, and birth weight
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27 (<4000 g or ≥ 4000 g). We displayed all 16 possible combinations of the four variables, with
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29 absence of oxytocin augmentation, episiotomy, and operative vaginal delivery, and birth
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31 weight <4000 g set as the reference value. From these stratified analyses, we collapsed strata
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33 that were non-significant, taking the order of occurrence and the clinical impact of the
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35 variable into consideration. In this modified model, we tested for possible confounding effects
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37 and interactions from maternal age, ethnicity, occiput posterior position, and epidural
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39 analgesia in forward stepwise logistic regression analyses. Confounders were tested one by
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41 one and set to at least 10% change in any estimate of combinations of the modified target
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43 variables on obstetric anal sphincter injuries. Interaction terms were significant at $p < 0.05$.
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45 Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk,
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47 NY: IBM Corp.
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52 The Regional Committee for Medical and Health Research Ethics, Western Norway,
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54 approved the protocol as a quality assurance study in obstetric care, and fulfilling the
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56 requirements for data protection procedures (REK 2011-1247).
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RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					
Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	

30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥ 4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The results of the stratified analysis are presented in Table 2.

Table 2 Stratified analyses of the prevalence of obstetric anal sphincter injury by the presence (+) or absence (-) of: oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (strata 1–16; group 1 as reference). Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	+	-	-	-	2621	148 (5.6)	1.5	1.3-1.9
4	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
5	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
6	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
7	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
8	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
9	-	-	-	+	539	59 (10.9)	3.2	2.4-4.3
10	+	-	-	+	438	45 (10.3)	3.0	2.1-4.2

11	-	+	-	+	203	20 (9.9)	2.8	1.7-4.6
12	+	+	-	+	215	20 (9.3)	2.7	1.6-4.3
13	-	+	+	+	101	11 (10.9)	3.2	1.7-6.0
14	+	+	+	+	292	44 (15.1)	4.6	3.2-6.5
15	-	-	+	+	42	15 (35.7)	14.4	7.5-27.5
16	+	-	+	+	192	47 (24.5)	8.4	5.9-12.0

We found a strong effect modification between episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight on obstetric anal sphincter injuries. Oxytocin augmentation was associated with an increased odds ratio of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants, and was independent of episiotomy (groups 3 and 4). Episiotomy was not associated with anal sphincter injuries when the other factors were absent (groups 1 and 2). Oxytocin augmentation was not associated with anal sphincter injury during instrumental deliveries of normal-sized infants without episiotomy (groups 7 and 8), nor in spontaneous deliveries of infants weighing ≥ 4000 g without episiotomy (groups 9 and 10). Furthermore, oxytocin use was not associated with anal sphincter injuries in spontaneous (groups 11 and 12) or operative vaginal deliveries (groups 13 and 14) of infants weighing ≥ 4000 g when episiotomy was applied. Operative vaginal delivery of an infant weighing ≥ 4000 g without episiotomy represented the group with the highest prevalence of injury (groups 15 and 16) and was not associated with oxytocin use. Episiotomy appeared to be negatively associated with sphincter rupture in operative vaginal deliveries regardless of the birth weight and the use of oxytocin (groups 5-8 and 13-16).

In the modified model (Table 3), we collapsed the groups from Table 2 that had odds ratios of similar magnitude for obstetric anal sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–16) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (3,4)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (5,6)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (7,8)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-12)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.4-3.9)
F (13,14)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (15,16)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

Age, origin of the mother, and occiput posterior position had no confounding effect on odds ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3). The use of oxytocin augmentation was restricted in the department from 2010 onwards, however, we observed a significant association between oxytocin augmentation and anal sphincter injuries through all time periods (1999-2003, 2004-2006, 2007-2009, 2010-2012). The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural analgesia was associated with a 30% lower odds ratio of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30–59 minutes group, and 65% (range 49–76%) in the ≥60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45–49% when the active part of the second stage of labour lasted ≥60

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3 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
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5 strong associations between oxytocin augmentation and the duration of second stage, and
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7 between operative delivery and the duration of second stage (collinearity), which means that
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9 the duration of second stage is measured through operative delivery and oxytocin
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11 augmentation.
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13 14 15 16 **DISCUSSION**

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18 We found that oxytocin augmentation during active labour was associated with a 70%
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20 increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving
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22 spontaneous birth to an infant weighing <4000 g. We did not find an association between
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24 episiotomy and tears during spontaneous deliveries, but a significantly reduced association in
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26 all operative vaginal deliveries.
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30 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
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32 However, a Cochrane review concluded that a reduction of labour by two hours was the only
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34 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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36 the entire concept of active management of labour to be associated with a slightly reduced
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38 risk of caesarean delivery.²¹ As in other studies, we found that approximately 50% of
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40 nulliparous women received oxytocin augmentation.^{16, 17, 22} There is reason to believe that
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42 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
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44 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
45
46 progress of the expulsive phase of labour, leading to rushed situations, impaired
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48 communication with the mother, and less focus on protection of the perineum and a controlled
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50 delivery of the head. Recent studies from Norway indicate that focus on these elements is
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52 important in preventing perineal injuries.^{23, 24}
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3 Many authors have used logistic regression analysis to identify risk factors for
4 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
5 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
6 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
7 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
8 which is a methodological weakness since the true effect of other factors is concealed by the
9 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
10 women, entering oxytocin augmentation, duration of active second stage of labour, and
11 instrumental delivery into the same model.¹⁵

12
13 Our study shows strong collinearity between a prolonged active second stage of labour
14 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
15 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
16 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
17 second stage is a time related event before the expulsion of the head. During this latency the
18 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
19 during the expulsive phase. Consequently, we do not consider the duration of the active
20 second stage as a risk factor for anal sphincter injuries.

21
22 Jander et al. conducted a single institution, retrospective, case-control study of 214
23 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
24 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
25 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
26 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
27 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
28 for induction or augmentation purposes.²⁵⁻²⁷ Three large population-based studies on the risk
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3 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.^{1, 7,}
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7 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
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9 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhed found epidural
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11 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
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13 by parity and found a significantly increased odds ratio associated with epidural analgesia in
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15 nulliparous women.²⁸ In our study, epidural analgesia was associated with a significantly
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17 reduced odds ratio for sphincter tears.
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21 Our study takes into account four factors that exert their effect on the anal sphincter
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23 during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both operative
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25 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
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27 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
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29 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
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31 national registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 29, 30} In our study,
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33 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
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35 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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39 Our methodological approach, stratifying by the factors that are active during the
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41 expulsive phase of labour and testing for confounders, is considered a strength of the study.
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43 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
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45 with these major risk factors. Stepwise, forward multivariable regression analyses, without
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47 testing for possible interactions, would fail to reveal this information. This case-control study
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49 is based on prospectively collected data from a large unselected population, and represents all
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51 deliveries meeting the inclusion criteria that occurred during the study period, which make
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53 bias unlikely. Our department has a high proportion of vaginal deliveries. The overall
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55 caesarean delivery rate in our institution was 12.5% over the study period. For women in
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3 TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012.
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5 Accordingly, the study population includes both high- and low-risk pregnancies, which adds
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7 to the external validity of our results.
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10 However, some limitations apply. We cannot prove causality between oxytocin
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12 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
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14 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
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16 support technique, and the birth attendant's experience level may be possible risk modifiers
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18 not included in our database. Finally, single institution studies, also when based on unselected
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20 populations, should be interpreted with caution.
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23 Our findings have some important implications. Birth attendants should be aware of
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25 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
26
27 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
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29 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
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31 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
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33 World Health Organization recommends the use of a partogram with an action line defining
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35 failure to progress. However, a recent Cochrane review could not confirm that such a
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37 partogram was beneficial in high resource settings.³¹ Given the doubtful benefits from
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39 augmentation of labour, randomized controlled trials are strongly needed, and we propose
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41 anal sphincter injury as one of the most important endpoints.
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46 Moreover, our study supports restricted use of episiotomy during normal births and as
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48 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
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50 unpredictable risk factor as weight estimation of a large fetus is unreliable.³²
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Contributorship Statement

All four authors have contributed to the idea and design of the research project. ABR, TME managed the dataset and the statistical analyses were performed by FES. All four authors have contributed to the interpretation of the results and the writing of the manuscript.

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Competing interests

None

Data Sharing Statement

There is no additional data material to be shared.

References

1. Baghestan E, Irgens LM, Bordahl PE, et al. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;**116**:25-34.
2. Laine K, Skjeldestad FE, Sanda B, et al. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;**90**:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;**247**:224-37.
4. Sultan AH, Thakar R, Fenner DE. *Perineal and anal sphincter trauma : diagnosis and clinical management*. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;**80**:229-34.
6. Hornemann A, Kamischke A, Luedders DW, et al. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;**281**:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;**98**:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, et al. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;**108**:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;**29**:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;**85**:1252-8.

- 1
2
3 11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, et al. Hospital-based lateral
4
5 episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register
6
7 study. *Am J Obstet Gynecol* 2012;**206**:347 e1-6.
8
- 9
10 12. Murphy DJ, Macleod M, Bahl R, et al. A randomised controlled trial of routine versus
11
12 restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG*
13
14 2008;**115**:1695-702; discussion 702-3.
15
- 16
17 13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev*
18
19 2009:CD000081.
20
- 21
22 14. Samuelsson E, Ladfors L, Wennerholm UB, et al. Anal sphincter tears: prospective
23
24 study of obstetric risk factors. *BJOG* 2000;**107**:926-31.
25
- 26
27 15. Prager M, Andersson KL, Stephansson O, et al. The incidence of obstetric anal
28
29 sphincter rupture in primiparous women: a comparison between two European delivery
30
31 settings. *Acta Obstet Gynecol Scand* 2008;**87**:209-15.
32
- 33
34 16. Blix E, Pettersen SH, Eriksen H, et al. [Use of oxytocin augmentation after
35
36 spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;**122**:1359-62.
37
- 38
39 17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, et al. Outcome in obstetric care related
40
41 to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;**85**:1094-8.
42
- 43
44 18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment
45
46 for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*
47
48 2011:CD007123.
49
- 50
51 19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet*
52
53 *Gynaecol* 2001;**15**:179-94.
54
- 55
56 20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors.
57
58 *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
59
60

- 1
2
3 21. Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management
4 in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst*
5 *Rev* 2013;**9**:CD004907.
6
7
- 8
9 22. Selin L, Almstrom E, Wallin G, et al. Use and abuse of oxytocin for augmentation of
10 labor. *Acta Obstet Gynecol Scand* 2009;**88**:1352-7.
11
12
- 13 23. Hals E, Oian P, Pirhonen T, et al. A multicenter interventional program to reduce the
14 incidence of anal sphincter tears. *Obstet Gynecol* 2010;**116**:901-8.
15
16
- 17 24. Laine K, Pirhonen T, Rolland R, et al. Decreasing the incidence of anal sphincter tears
18 during delivery. *Obstet Gynecol* 2008;**111**:1053-7.
19
20
- 21 25. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with
22 complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;**71**:520-4.
23
24
- 25 26. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter
26 rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol*
27 1988;**27**:27-32.
28
29
- 30 27. Legino LJ, Woods MP, Rayburn WF, et al. Third- and fourth-degree perineal tears. 50
31 year's experience at a university hospital. *J Reprod Med* 1988;**33**:423-6.
32
33
- 34 28. Poen AC, Felt-Bersma RJ, Dekker GA, et al. Third degree obstetric perineal tears: risk
35 factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol*
36 1997;**104**:563-6.
37
38
- 39 29. Hartmann K, Viswanathan M, Palmieri R, et al. Outcomes of routine episiotomy: a
40 systematic review. *JAMA* 2005;**293**:2141-8.
41
42
- 43 30. de Leeuw JW, de Wit C, Kuijken JP, et al. Mediolateral episiotomy reduces the risk
44 for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;**115**:104-8.
45
46
- 47 31. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in
48 spontaneous labour at term. *Cochrane Database Syst Rev* 2013;**7**:CD005461.
49
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32. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;**43**:3-10.

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7 | **Assessing the association of oxytocin augmentation with obstetric anal sphincter injury**
8 **in nulliparous women – a population-based, case-control study**
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12 **ARTICLE SUMMARY**
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14 **Strengths and limitations of this study**
15

- 16 • Stratifying by the main risk factors that are active during the expulsive phase of labour
17 and testing for confounders are strengths of the study.
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- 19 • We reveal how oxytocin augmentation interacts with the major factors active in the
20 expulsive phase of labour.
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- 22 • The study is based on prospectively collected data from a large, unselected population,
23 which makes bias unlikely.
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- 25 • The study design is a limitation, as we cannot prove causality between oxytocin
26 augmentation and obstetric anal sphincter injuries in an observational study.
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INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1, 3, 5} high birth weight,^{1, 3, 5, 6} operative vaginal delivery,^{1, 3, 5} advanced maternal age,^{1, 5, 6} Asian or African ethnicity,^{1, 7} and prolonged second stage of labour^{3, 7, 8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9, 10} and episiotomy^{1, 11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5, 14, 15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16, 17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded.

The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of >300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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Throughout the study period, episiotomy was performed either medio-laterally or laterally. According to our routines and national guidelines, operative vaginal delivery was indicated if delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction with a Malmström metal cup as the preferred procedure for operative vaginal delivery. Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e. originating from Europe or North America, or non-Western.

We analysed our dataset using the Chi-squared test and forward stepwise logistic regression analyses with $p < 0.05$ as significance level. We applied a stratified approach to investigate the association of oxytocin augmentation and the outcome across the presence (+) or absence (-) during labour of episiotomy, operative vaginal delivery, and birth weight (< 4000 g or ≥ 4000 g). We displayed all 16 possible combinations of the four variables, with absence of oxytocin augmentation, episiotomy, and operative vaginal delivery, and birth weight < 4000 g set as the reference value. From these stratified analyses, we collapsed strata that were non-significant, taking the order of occurrence and the clinical impact of the variable into consideration. In this modified model, we tested for possible confounding effects and interactions from maternal age, ethnicity, occiput posterior position, and epidural analgesia in forward stepwise logistic regression analyses. Confounders were tested one by one and set to at least 10% change in any estimate of combinations of the modified target variables on obstetric anal sphincter injuries. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					
Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	

Comment [ar1]: Remark by Watson

Comment [ar2]: Changed to non-Western (Gissler)

30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥ 4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The results of the stratified analysis are presented in Table 2.

Table 2 Stratified analyses of the prevalence of obstetric anal sphincter injury by the presence (+) or absence (-) of: oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (strata 1–16; group 1 as reference). Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	+	-	-	-	2621	148 (5.6)	1.5	1.3-1.9
4	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
5	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
6	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
7	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
8	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
9	-	-	-	+	539	59 (10.9)	3.2	2.4-4.3
10	+	-	-	+	438	45 (10.3)	3.0	2.1-4.2

11	-	+	-	+	203	20 (9.9)	2.8	1.7-4.6
12	+	+	-	+	215	20 (9.3)	2.7	1.6-4.3
13	-	+	+	+	101	11 (10.9)	3.2	1.7-6.0
14	+	+	+	+	292	44 (15.1)	4.6	3.2-6.5
15	-	-	+	+	42	15 (35.7)	14.4	7.5-27.5
16	+	-	+	+	192	47 (24.5)	8.4	5.9-12.0

We found a strong effect modification between episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight on obstetric anal sphincter injuries. Oxytocin augmentation was associated with an increased odds ratio of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants, and was independent of episiotomy (groups 3 and 4). Episiotomy was not associated with anal sphincter injuries when the other factors were absent (groups 1 and 2). Oxytocin augmentation was not associated with anal sphincter injury during instrumental deliveries of normal-sized infants without episiotomy (groups 7 and 8), nor in spontaneous deliveries of infants weighing ≥ 4000 g without episiotomy (groups 9 and 10). Furthermore, oxytocin use was not associated with anal sphincter injuries in spontaneous (groups 11 and 12) or operative vaginal deliveries (groups 13 and 14) of infants weighing ≥ 4000 g when episiotomy was applied. Operative vaginal delivery of an infant weighing ≥ 4000 g without episiotomy represented the group with the highest prevalence of injury (groups 15 and 16) and was not associated with oxytocin use. Episiotomy appeared to be negatively associated with sphincter rupture in operative vaginal deliveries regardless of the birth weight and the use of oxytocin (groups 5-8 and 13-16).

In the modified model (Table 3), we collapsed the groups from Table 2 that had odds ratios of similar magnitude for obstetric anal sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–16) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (3,4)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (5,6)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (7,8)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-12)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.4-3.9)
F (13,14)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (15,16)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

Age, origin of the mother, and occiput posterior position had no confounding effect on odds ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3). The use of oxytocin augmentation was restricted in the department from 2010 onwards, however, we observed a significant association between oxytocin augmentation and anal sphincter injuries through all time periods (1999-2003, 2004-2006, 2007-2009, 2010-2012). The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural analgesia was associated with a 30% lower odds ratio of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30-59 minutes group, and 65% (range 49-76%) in the ≥ 60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45-49% when the active part of the second stage of labour lasted ≥ 60

Comment [ar3]: Gissler

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6 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
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8 strong associations between oxytocin augmentation and the duration of second stage, and
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10 between operative delivery and the duration of second stage (collinearity), which means that
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12 the duration of second stage is measured through operative delivery and oxytocin
13
14 augmentation.
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Comment [ar4]: Gissler

16 17 18 **DISCUSSION**

19
20 We found that oxytocin augmentation during active labour was associated with a 70%
21
22 increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving
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24 spontaneous birth to an infant weighing <4000 g. We did not find an association between
25
26 episiotomy and tears during spontaneous deliveries, but a significantly reduced association in
27
28 all operative vaginal deliveries.

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30 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
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32 However, a Cochrane review concluded that a reduction of labour by two hours was the only
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34 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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36 the entire concept of active management of labour to be associated with a slightly reduced
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38 risk of caesarean delivery.²¹ As in other studies, we found that approximately 50% of
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40 nulliparous women received oxytocin augmentation.^{16, 17, 22} There is reason to believe that
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42 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
43
44 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
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46 progress of the expulsive phase of labour, leading to rushed situations, impaired
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48 communication with the mother, and less focus on protection of the perineum and a controlled
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50 delivery of the head. Recent studies from Norway indicate that focus on these elements is
51
52 important in preventing perineal injuries.^{23, 24}
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7 Many authors have used logistic regression analysis to identify risk factors for
8 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
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10 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
11
12 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
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14 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
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16 which is a methodological weakness since the true effect of other factors is concealed by the
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18 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
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20 women, entering oxytocin augmentation, duration of active second stage of labour, and
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22 instrumental delivery into the same model.¹⁵
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24 Our study shows strong collinearity between a prolonged active second stage of labour
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26 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
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28 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
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30 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
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32 second stage is a time related event before the expulsion of the head. During this latency the
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34 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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36 during the expulsive phase. Consequently, we do not consider the duration of the active
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38 second stage as a risk factor for anal sphincter injuries.

39 Jander et al. conducted a single institution, retrospective, case-control study of 214
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41 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
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43 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
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45 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
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47 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
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49 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
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51 for induction or augmentation purposes.²⁵⁻²⁷ Three large population-based studies on the risk
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Comment [ar5]: Gissler

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6 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.^{1,7,}
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10 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
11 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhede found epidural
12 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
13 by parity and found a significantly increased odds ratio associated with epidural analgesia in
14 nulliparous women.²⁸ In our study, epidural analgesia was associated with a significantly
15 reduced odds ratio for sphincter tears.
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22 Our study takes into account four factors that exert their effect on the anal sphincter
23 during the final minutes of delivery. As in previous studies,^{1,3,5} we found both operative
24 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
25 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
26 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
27 national registry study from Norway,¹ but differs from other studies.^{8,11,13,29,30} In our study,
28 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
29 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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37 Our methodological approach, stratifying by the factors that are active during the
38 expulsive phase of labour and testing for confounders, is considered a strength of the study.
39 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
40 with these major risk factors. Stepwise, forward multivariable regression analyses, without
41 testing for possible interactions, would fail to reveal this information. This case-control study
42 is based on prospectively collected data from a large unselected population, and represents all
43 deliveries meeting the inclusion criteria that occurred during the study period, which make
44 bias unlikely. Our department has a high proportion of vaginal deliveries. The overall
45 caesarean delivery rate in our institution was 12.5% over the study period. For women in
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7 TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012.
8 Accordingly, the study population includes both high- and low-risk pregnancies, which adds
9 to the external validity of our results.
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12 However, some limitations apply. We cannot prove causality between oxytocin
13 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
14 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
15 support technique, and the birth attendant's experience level may be possible risk modifiers
16 not included in our database. Finally, single institution studies, also when based on unselected
17 populations, should be interpreted with caution.
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21 Our findings have some important implications. Birth attendants should be aware of
22 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
23 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
24 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
25 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
26 World Health Organization recommends the use of a partogram with an action line defining
27 failure to progress. However, a recent Cochrane review could not confirm that such a
28 partogram was beneficial in high resource settings.³¹ Given the doubtful benefits from
29 augmentation of labour, randomized controlled trials are strongly needed, and we propose
30 anal sphincter injury as one of the most important endpoints.
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34 Moreover, our study supports restricted use of episiotomy during normal births and as
35 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
36 unpredictable risk factor as weight estimation of a large fetus is unreliable.³²
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Comment [ar6]: Gissler

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Competing interests

None

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No specific

References

1. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;**116**:25-34.
2. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;**90**:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;**247**:224-37.
4. Sultan AH, Thakar R, Fenner DE. *Perineal and anal sphincter trauma : diagnosis and clinical management*. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;**80**:229-34.
6. Hornemann A, Kamischke A, Luedders DW, Beyer DA, Diedrich K, Bohlmann MK. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;**281**:59-64.

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7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;**98**:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, Wallenburg HC. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;**108**:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;**29**:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;**85**:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;**206**:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;**115**:1695-702; discussion 702-3.
13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009:CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, Gareberg B, Nyberg K, Hagberg H. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;**107**:926-31.
15. Prager M, Andersson KL, Stephansson O, Marchionni M, Marions L. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;**87**:209-15.
16. Blix E, Pettersen SH, Eriksen H, Royset B, Pedersen EH, Oian P. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;**122**:1359-62.

17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;**85**:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011:CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;**15**:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev* 2013;**9**:CD004907.
22. Selin L, Almstrom E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation of labor. *Acta Obstet Gynecol Scand* 2009;**88**:1352-7.
23. Hals E, Oian P, Pirhonen T, Gissler M, Hjelle S, Nilsen EB, et al. A multicenter interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;**116**:901-8.
24. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal sphincter tears during delivery. *Obstet Gynecol* 2008;**111**:1053-7.
25. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;**71**:520-4.
26. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol* 1988;**27**:27-32.

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27. Legino LJ, Woods MP, Rayburn WF, McGoogan LS. Third- and fourth-degree perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;**33**:423-6.
28. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol* 1997;**104**:563-6.
29. Hartmann K, Viswanathan M, Palmieri R, Gartlehner G, Thorp J, Jr., Lohr KN. Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;**293**:2141-8.
30. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;**115**:104-8.
31. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;**7**:CD005461.
32. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;**43**:3-10.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(R) In abstract; a cross sectional study, analyzed as case-control study.</p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>(R) Fulfilled</p>
Introduction		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>(R) Recent studies have shown the importance of the perineal protection technique in preventing perineal tears. Oxytocin augmentation could impair the control of the perineum during the delivery by causing too fast progress in the last minutes of labour. Oxytocin augmentation is widely used (50% of births). Guidelines for its use are often deficient and the evidence for its positive effect is challenged. Therefore, oxytocin augmentation as a risk factor for obstetric anal sphincter injuries, and should be explored in a study taking other relevant risk factors into account.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>(R) To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.</p>
Methods		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>(R) Present in Abstract and Methods.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>(R) Setting: Tertiary teaching hospital.</p> <p>Location: Delivery department of Stavanger University Hospital, serving the total obstetric population of the region of South Rogaland.</p> <p>Dates 15 May 1999 – 15 May 2012.</p> <p>Data were collected consecutively.</p>
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants.</p> <p>(R) Nulliparous women with spontaneous start of labour, single, cephalic pregnancy and ≥ 37 weeks gestation who delivered vaginally, where we had access to complete information on the main exposure and the explanatory variables. The source population was the entire obstetric population of the region.</p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect</p>

1		modifiers. Give diagnostic criteria, if applicable
2		(R) Outcome: Obstetric anal sphincter injury; that is grade 3 and 4 perineal tears as
3		defined by International Society of Incontinence.
4		Exposure: Oxytocin augmentation in active labour, that is oxytocin intravenous
5		infusion (5 international units (0.01mg) oxytocin in 500 ml saline) used in incremental
6		doses during active labour.
7		Predictors: NA
8		Effect modifiers: Episiotomy, operative vaginal delivery, birth weight <4000 g vs
9		≥4000 g.
10		Potential confounders: maternal age, ethnicity, occiput posterior position, duration of
11		second stage of labour and epidural analgesia.
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17	Data sources/ measurement	8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. (R) All variables are precisely defined in the obstetric databases of Stavanger University Hospital. The grade of perineal injury was assessed during operative repair and plotted directly into the database.
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26	Bias	9 Describe any efforts to address potential sources of bias. (R) In this cross-sectional study all women giving births and who fulfil the inclusion criteria are included. There were very few cases with missing data. We may have missed some cases of perineal injury due to underreporting. The variables are hard variables with clear definitions: Use of oxotocin (yes/no), episiotomy (yes/no), mode of delivery (spontaneous/operative vaginal), birth weight categorized <4000/ ≥4000 g.
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34	Study size	10 Explain how the study size was arrived at (R) The study size is given by the number of women fulfilling the eligibility criteria and who delivered at Stavanger University Hospital from 15 May 1999 to 15 May 2012.
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40	Quantitative variables	11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. (R) Birth weight was categorized into < 4000/ ≥4000 g.
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44	Statistical methods	12 (a) Describe all statistical methods, including those used to control for confounding (R) Chi-square test and stepwise forward logistic regression using IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp. (b) Describe any methods used to examine subgroups and interactions (R) We applied a stratified approach to control for interaction between the main variables (oxytocin augmentation, episiotomy, instrumental delivery and birth weight). Then we tested for confounding and interaction to a modified model by entering one variable at time. (c) Explain how missing data were addressed (R) Cases with missing data for estimated date of delivery were excluded. Cases with
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other missing data were recoded to the reference value in the logistic regression analyses. Very few cases with missing data (n=52).

(d) If applicable, describe analytical methods taking account of sampling strategy

(R) NA

(e) Describe any sensitivity analyses

(R) NA

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(R) Potentially eligible: 15 545 Confirmed eligible: 15 493 Included/analyzed: 15 493</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(R) Cases with missing data for estimated date of delivery were excluded (n=52)</p> <p>(c) Consider use of a flow diagram</p> <p>(R) Not useful in this study.</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(R) Given in Table 1.</p> <p>The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(R) Cases with missing data for estimated date of delivery were excluded from the study population (n=52)</p> <p>Recoded to the reference category of the variable and included in the analyses:</p> <p>Birth weight 3 cases. Maternal age 2 cases. Lie at delivery 8 cases. Duration of second stage of labour 92 cases.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>(R) Table 1.</p> <p>Outcome event, the dependant variable, anal sphincter injury: 1014 cases.</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(R) Table 2 and 3. Confounders: paragraph 4 in Material and Methods.</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(R) Table 1</p>

1		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
2		meaningful time period
3		(R) NA
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6	Other analyses	17 Report other analyses done—eg analyses of subgroups and interactions, and
7		sensitivity analyses
8		(R) NA
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10	Discussion	
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12	Key results	18 Summarise key results with reference to study objectives
13		(R) Fulfilled.
14		
15	Limitations	19 Discuss limitations of the study, taking into account sources of potential bias or
16		imprecision. Discuss both direction and magnitude of any potential bias
17		(R) Bias regarding main outcome: We do not know the magnitude of underreporting
18		of anal sphincter tear grade 3 and 4, however believe this to be low.
19		Bias regarding main exposure: The quality system of the department relies on honest
20		reporting by midwives and obstetricians, and has been a cornerstone in the systematic
21		interdisciplinary work towards better clinical outcomes since 1996. We have reason to
22		believe that ownership to the concept has resulted in good adherence to the reporting
23		routines, and we believe the reporting of oxytocin augmentation to be a robust
24		measure of what was actually practised. The midwives plotting the information were
25		not aware of any research issue related to oxytocin augmentation.
26		We consider the other main exposure variables to be robust: It is unlikely that reports
27		of episiotomy, instrumental delivery and birth weight are skewed in any direction. The
28		same applies to the possible confounders age, ethnicity, occiput posterior position and
29		epidural analgesia.
30		We believe that the reporting of these variables reflects the actual practice. Therefore
31		we consider the estimates for risks related to anal sphincter tear grade 3 and 4 to be
32		precise with little bias. Our stratified approach, modified model, takes care of the
33		interaction problems between episiotomy, operative vaginal delivery, birth weight and
34		oxytocin augmentation.
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43	Interpretation	20 Give a cautious overall interpretation of results considering objectives, limitations,
44		multiplicity of analyses, results from similar studies, and other relevant evidence
45		(R) Fulfilled.
46		
47	Generalisability	21 Discuss the generalisability (external validity) of the study results.
48		(R) The study participants represent the total population of women fulfilling the
49		inclusion criteria in a Norwegian region of 320 000 people. The study population is
50		heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%),
51		social status and ethnicity. This adds value to the external validity of the study results.
52		We encourage other study groups to make research on the effect of oxytocin
53		augmentation on anal sphincter injury in other populations.
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57	Other information	
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59	Funding	22 Give the source of funding and the role of the funders for the present study and, if
60		

applicable, for the original study on which the present article is based
(R) No specific funding.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women – a population-based, case-control study

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ASSESSING THE ASSOCIATION OF OXYTOCIN AUGMENTATION WITH
OBSTETRIC ANAL SPHINCTER INJURY IN NULLIPAROUS WOMEN – A
POPULATION-BASED, CASE CONTROL-STUDY

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Oxytocin augmentation and anal sphincter injury

Key words: anal sphincter injury, oxytocin, episiotomy, operative vaginal delivery, birth
weight.

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FOR PEER REVIEW

ABSTRACT

Objective: To assess the association of oxytocin augmentation with obstetric anal sphincter injury among nulliparous women.

Design: A population-based, case-control study.

Setting: Primary and secondary teaching hospital serving a Norwegian region.

Population: 15 476 nulliparous women with spontaneous start of labour, single cephalic presentation, and gestation ≥ 37 weeks delivering vaginally between 1999 and 2012.

Methods: Based on the presence or absence of oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (<4000 g vs. ≥ 4000 g), we modelled in logistic regression the best fit for prediction of anal sphincter injury. Within the modified model of main exposures, we tested for possible confounding, and interactions between maternal age, ethnicity, occiput posterior position, and epidural analgesia.

Comment [ar1]: New modeling

Main outcome measure: Obstetric anal sphincter injury.

Results: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries in women giving spontaneous birth to infants weighing <4000 g (OR 1.8; 95% CI: 1.5–2.2). Episiotomy was not associated with sphincter injuries in spontaneous births, but with a lower OR in operative vaginal deliveries. Spontaneous delivery of infants weighing ≥ 4000 g was associated with a 3-fold higher OR, and epidural analgesia was associated with a 30% lower OR in comparison to no epidural analgesia.

Conclusions: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants. We observed a considerable effect modification between the most important factors predicting anal sphincter injuries in the active second stage of labour.

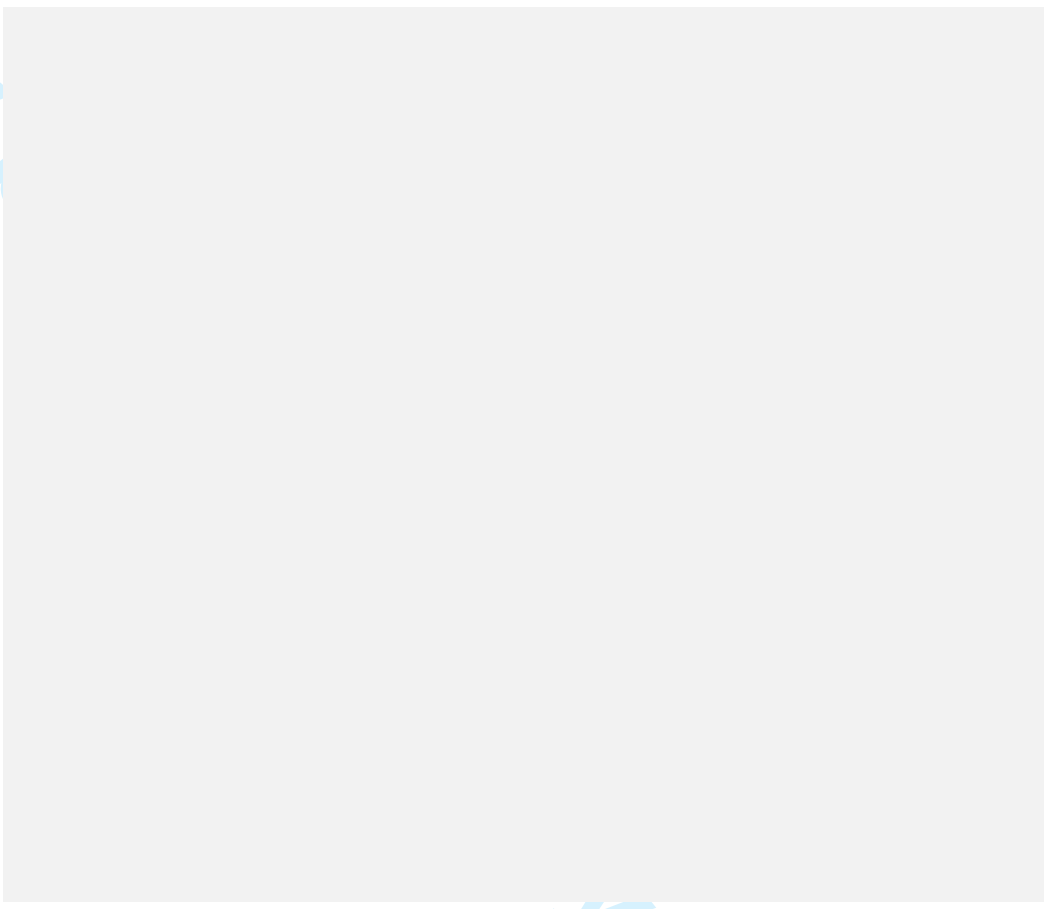
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ARTICLE SUMMARY

Strengths and limitations of this study

- Stratifying by the main risk factors that are active during the expulsive phase of labour and testing for confounders are strengths of the study.
- We reveal how oxytocin augmentation interacts with the major factors active in the expulsive phase of labour.
- The study is based on prospectively collected data from a large, unselected population, which makes bias unlikely.
- The study design is a limitation, as we cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study.

For



INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.^{2,4} Nulliparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} Asian or African ethnicity,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11–13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department. Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound examination was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01 mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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19 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
20 According to our routines and national guidelines, operative vaginal delivery was indicated if
21 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
22 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
23 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
24 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
25 originating from Europe or North America, or non-Western.

26 The intention of this study was to explore the effect of three obstetric practices
27 (oxytocin augmentation (O), episiotomy (E) and vacuum/forceps (VF)) and birth weight
28 (BW) on obstetric anal sphincter injuries before other risk factors were considered. These
29 main risk factors correlate as episiotomy is often used for instrumental deliveries and when
30 large babies are expected. Furthermore, oxytocin augmentation is provided for failure to
31 progress because of dystocia. Women with dystocia are more often delivered instrumentally
32 than women without dystocia. This basic understanding of the birth dynamics of the first and
33 second stage of labour indicates that the main risk factors may have a direct or indirect effect
34 on obstetric anal sphincter injuries, and that the effects of categories across different
35 explanatory variables are not constant on the outcome.

36 We analysed our dataset using the Chi-squared test and backward manual
37 stepwise logistic regression analyses with $p < 0.05$ as significance level. We built and checked
38 the fit of our regression model as proposed by Agresti²¹. At step one we compared a model of
39 the highest order interaction term (four-way product term; $E*O*VF*BW$) and the main risk
40 factors ($E+O+VF+BW$) with a model comprising only the main risk factors. If the highest
41 order product term is not significant, Agresti propose to continue with second highest order
42 terms by removing the term with the highest p-value until the model of best fit is reached.
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Confounders, possible risk factors in addition to the main factors of interest, were tested one by one and set to at least 10% change in any estimate in the model of best fit. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					<0.001
Age (years)					
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	

30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	
30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

*Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The log likelihood-ratio score from the highest order model (O*E*VF*FW+O+E+VF+BW; -2 LR: 7213.8) did not differ from the model comprising the main effects (O+E+VF+BW, -2 LR: 7215.9). After removing insignificant three-way interaction product terms, and playing with the remaining two-ways interaction terms, the model that gave the best fit comprised the interaction of oxytocin augmentation, episiotomy and instrumental delivery (O*E*VF), in addition to episiotomy/birth weight (E*BW) and instrumental delivery/birth weight (VF*BW) (-2 LR: 7371.2) (Model A). We could resolve

interaction terms into stratified analysis of 8 strata of combinations of oxytocin augmentation, episiotomy and instrumental delivery for birth weights <4000 g, and 4 strata of combinations of episiotomy, instrumental delivery and birth weight ≥4000 g, independent of oxytocin augmentation. The results are displayed in Table 2.

Table 2 Model A. Stratified analyses of 8 strata of combinations of oxytocin augmentation, episiotomy, instrumental delivery and birth weights <4000 g, and 4 strata of episiotomy, instrumental delivery and birth weights ≥4000 g, independent of oxytocin augmentation. Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
4	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
5	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
6	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
7	+	-	-	-	2621	148 (5.6)	1.6	1.3-1.9
8	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
9	+/-	+	-	+	418	40 (9.6)	2.7	1.9-3.9
10	+/-	-	-	+	977	104 (10.6)	3.1	2.4-4.0
11	+/-	+	+	+	393	55 (14.0)	4.2	3.1-5.8
12	+/-	-	+	+	234	62 (26.5)	9.3	6.8-12.9

From a clinical perspective we can simplify model A into model B by collapsing groups that comprise similar risks for sphincter injury by obstetric interventions despite overlapping confidence intervals. Spontaneous delivery of an infant weighing <4000 g without oxytocin augmentation and episiotomy was chosen as the reference group (group 1). We collapsed group 1 and 2 as the odds for sphincter injury was similar with and without episiotomy in unstimulated, spontaneous births of normal-sized infants. Group 3 to 6 display the odds for sphincter injury in instrumental deliveries of normal-sized infants with and without oxytocin

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augmentation and episiotomy. A marked difference in the odds for sphincter injury was observed between women delivered instrumentally with (group 3 and 5) and without (group 4 and 6) episiotomy, despite the fact that those stimulated with oxytocin had a non-significant lower odds for sphincter injury. It was therefore reasonable to collapse group 3 and 5, and group 4 and 6. Furthermore, we collapsed group 7 and 8 as the odds for sphincter injury was similar with and without episiotomy during spontaneous deliveries of infants <4000 g, regardless of oxytocin augmentation. Finally, the use of episiotomy appeared to be strongly associated with lower odds for sphincter injury in instrumental deliveries of infants ≥4000 g (group 11 and 12). The modified model B (Table 3) comprises a clinically relevant risk estimation of anal sphincter injury among the main modified risk factors for sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–12) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (7,8)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (3,5)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (4,6)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-10)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.5-3.9)
F (11)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (12)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

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Age, origin of the mother, and occiput posterior position had no confounding effect on odds ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3).

The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural analgesia was associated with a 30% lower odds ratio of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30-59 minutes group, and 65% (range 49-76%) in the ≥60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45-49% when the active part of the second stage of labour lasted ≥60 minutes vs. 12-21% for durations of the second stage of labour of <60 minutes. We found strong associations between oxytocin augmentation and the duration of second stage, and between operative delivery and the duration of second stage (collinearity), which means that the duration of second stage is measured through operative delivery and oxytocin augmentation.

DISCUSSION

We found that oxytocin augmentation during active labour was associated with a 80% increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving spontaneous birth to an infant weighing <4000 g. We did not find an association between episiotomy and tears during spontaneous deliveries, but a significantly reduced association in all operative vaginal deliveries.

Oxytocin augmentation is widely used in delayed labour to prevent operative delivery. However, a Cochrane review concluded that a reduction of labour by two hours was the only

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19 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
20 the entire concept of active management of labour to be associated with a slightly reduced
21 risk of caesarean delivery.²² As in other studies, we found that approximately 50% of
22 nulliparous women received oxytocin augmentation.^{16, 17, 23} There is reason to believe that
23 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
24 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
25 progress of the expulsive phase of labour, leading to rushed situations, impaired
26 communication with the mother, and less focus on protection of the perineum and a controlled
27 delivery of the head. Recent studies from Norway indicate that focus on these elements is
28 important in preventing perineal injuries.^{24, 25}

29 Many authors have used logistic regression analysis to identify risk factors for
30 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
31 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
32 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
33 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
34 which is a methodological weakness since the true effect of other factors is concealed by the
35 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
36 women, entering oxytocin augmentation, duration of active second stage of labour, and
37 instrumental delivery into the same model.¹⁵

38 Our study shows strong collinearity between a prolonged active second stage of labour
39 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
40 active second stage of labour to be a "proxy" for oxytocin augmentation and instrumental
41 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
42 second stage is a time related event before the expulsion of the head. During this latency the
43 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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19 during the expulsive phase. Consequently, we do not consider the duration of the active
20 second stage as a risk factor for anal sphincter injuries.

21 Jander et al. conducted a single institution, retrospective, case-control study of 214
22 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
23 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
24 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
25 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
26 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
27 for induction or augmentation purposes.^{26–28} Three large population-based studies on the risk
28 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.<sup>1,7,
29 s</sup>

30 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
31 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjolhede found epidural
32 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
33 by parity and found a significantly increased odds ratio associated with epidural analgesia in
34 nulliparous women.²⁹ In our study, epidural analgesia was associated with a significantly
35 reduced odds ratio for sphincter tears.

36 Our study takes into account four factors that exert their effect on the anal sphincter
37 during the final minutes of delivery. As in previous studies,^{1,3,5} we found both operative
38 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
39 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
40 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
41 national registry study from Norway,¹ but differs from other studies.^{5, 11, 13, 30, 31} In our study,
42 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
43 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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Our methodological approach, stratifying by the factors that are active during the expulsive phase of labour and testing for confounders, is considered a strength of the study. This approach leads to a more detailed understanding of how oxytocin augmentation interacts with these major risk factors. Logistic regression analyses, without testing for possible interactions, would fail to reveal this information. This case-control study is based on prospectively collected data from a large unselected population, and represents all deliveries meeting the inclusion criteria that occurred during the study period, which make bias unlikely. Our department has a high proportion of vaginal deliveries. The overall caesarean delivery rate in our institution was 12.5% over the study period. For women in TGCS group 1 the acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012. Accordingly, the study population includes both high- and low-risk pregnancies, which adds to the external validity of our results.

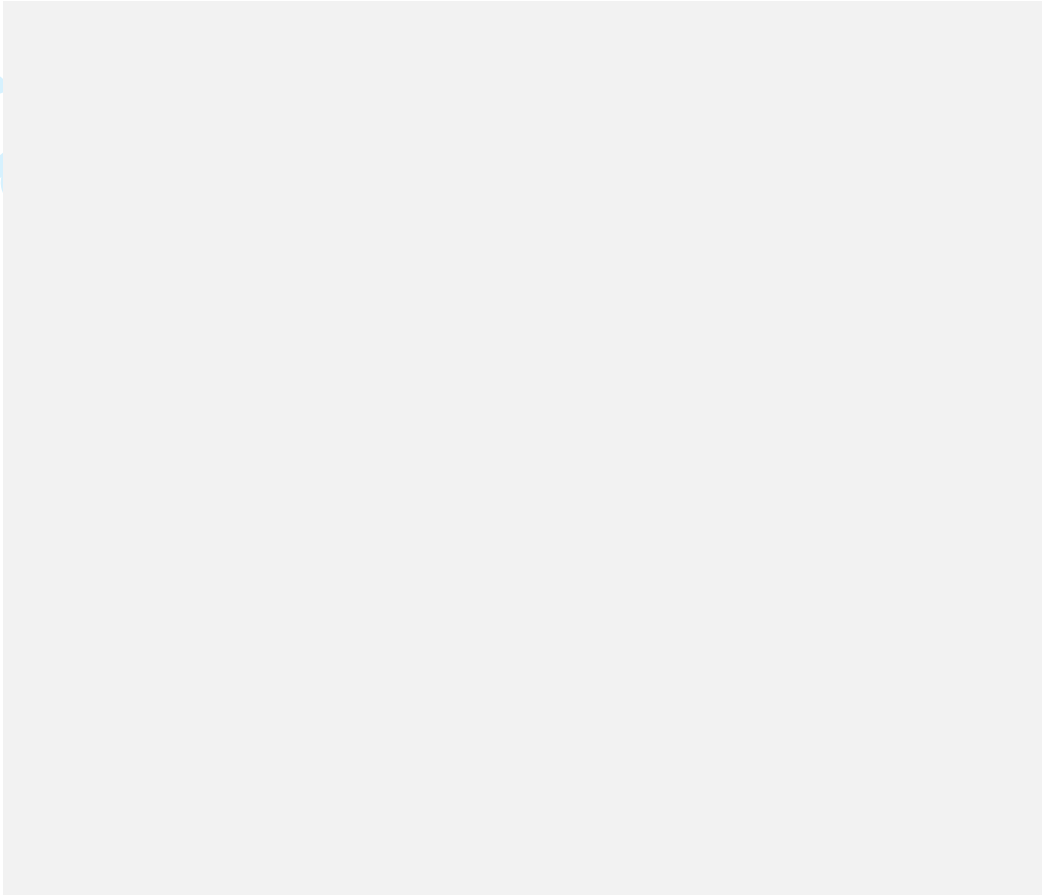
However, some limitations apply. We cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study. Furthermore, socioeconomic status, smoking, body mass index, maternal delivery positions, perineal support technique, and the birth attendant's experience level may be possible risk modifiers not included in our database. Finally, single institution studies, also when based on unselected populations, should be interpreted with caution.

Our findings have some important implications. Birth attendants should be aware of the association between oxytocin augmentation and obstetric anal sphincter injuries in the large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation of evidence-based guidelines for using oxytocin augmentation should be encouraged. The World Health Organization recommends the use of a partogram with an action line defining failure to progress. However, a recent Cochrane review could not confirm that such a

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partogram was beneficial in high resource settings.³² Given the doubtful benefits from augmentation of labour, randomized controlled trials are strongly needed, and we propose anal sphincter injury as one of the most important endpoints.

Moreover, our study supports restricted use of episiotomy during normal births and as a recommendation for operative vaginal deliveries. Birth weight is an important, albeit unpredictable risk factor as weight estimation of a large fetus is unreliable.³³



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Competing interests

None

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Contributorship Statement

All four authors have contributed to the idea and design of the research project. ABR, TME managed the dataset and the statistical analyses were performed by FES. All four authors have contributed to the interpretation of the results and the writing of the manuscript.

Data Sharing Statement

No additional data available

References

1. Baghestan E, Irgens LM, Bordahl PE, et al. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol*. 2010;116:25-34.
2. Laine K, Skjeldestad FE, Sanda B, et al. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand*. 2011;90:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg*. 2008;247:224-37.
4. Sultan AH, Thakar R, Fenner DE. Perineal and anal sphincter trauma: diagnosis and clinical management. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand*. 2001;80:229-34.
6. Hornemann A, Kamischke A, Luedders DW, et al. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet*. 2010;281:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol*. 2001;98:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, et al. Risk factors for third degree perineal ruptures during delivery. *BJOG*. 2001;108:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol*. 2009;29:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand*. 2006;85:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, et al. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol*. 2012;206:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, et al. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG*. 2008;115:1695-702; discussion 702-3.
13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev*. 2009;CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, et al. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG*. 2000;107:926-31.
15. Prager M, Andersson KL, Stephansson O, et al. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand*. 2008;87:209-15.
16. Blix E, Petersen SH, Eriksen H, et al. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Lægeforen*. 2002;122:1359-62.
17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, et al. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand*. 2006;85:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*. 2011;CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol*. 2001;15:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Agresti A. *An introduction to categorical data analysis*. 2nd ed. ed. Hoboken, NJ ; Chichester: Wiley-Interscience; 2007.

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22. Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev* 2013;9:CD004907.
23. Selin L, Almstrom E, Wallin G, et al. Use and abuse of oxytocin for augmentation of labor. *Acta Obstet Gynecol Scand* 2009;88:1352-7.
24. Hals E, Oian P, Pirhonen T, Gissler M, et al. A multicenter interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;116:901-8.
25. Laine K, Pirhonen T, Rolland R, et al. Decreasing the incidence of anal sphincter tears during delivery. *Obstet Gynecol* 2008;111:1053-7.
26. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;71:520-4.
27. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter rupture caused by delivery—a hidden problem. *Eur J Obstet Gynecol Reprod Biol* 1988;27:27-32.
28. Legino LJ, Woods MP, Rayburn WF, et al. Third- and fourth-degree perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;33:423-6.
29. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol* 1997;104:563-6.
30. Hartmann K, Viswanathan M, Palmieri R, et al. Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;293:2141-8.
31. de Leeuw JW, de Wit C, Kuijken JP, et al. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;115:104-8.
32. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;7:CD005461.
33. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;43:3-10.

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Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women – a population-based, case-control study

ARTICLE SUMMARY

Strengths and limitations of this study

- Stratifying by the main risk factors that are active during the expulsive phase of labour and testing for confounders are strengths of the study.
- We reveal how oxytocin augmentation interacts with the major factors active in the expulsive phase of labour.
- The study is based on prospectively collected data from a large, unselected population, which makes bias unlikely.
- The study design is a limitation, as we cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study.

INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1, 3, 5} high birth weight,^{1, 3, 5, 6} operative vaginal delivery,^{1, 3, 5} advanced maternal age,^{1, 5, 6} Asian or African ethnicity,^{1, 7} and prolonged second stage of labour^{3, 7, 8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9, 10} and episiotomy^{1, 11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5, 14, 15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16, 17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded.

The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound examination was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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7 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
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9 According to our routines and national guidelines, operative vaginal delivery was indicated if
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11 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
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13 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
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15 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
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17 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
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19 originating from Europe or North America, or non-Western.

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21 The intention of this study was to explore the effect of three obstetric practices
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23 (oxytocin augmentation (O), episiotomy (E) and vacuum/forceps (VF)) and birth weight
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25 (BW) on obstetric anal sphincter injuries before other risk factors were considered. These
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27 main risk factors correlate as episiotomy is often used for instrumental deliveries and when
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29 large babies are expected. Furthermore, oxytocin augmentation is provided for failure to
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31 progress because of dystocia. Women with dystocia are more often delivered instrumentally
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33 than women without dystocia. This basic understanding of the birth dynamics of the first and
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35 second stage of labour indicates that the main risk factors may have a direct or indirect effect
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37 on obstetric anal sphincter injuries, and that the effects of categories across different
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39 explanatory variables are not constant on the outcome.

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41 We analysed our dataset using the Chi-squared test and backward manual
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43 stepwise logistic regression analyses with $p < 0.05$ as significance level. We built and checked
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45 the fit of our regression model as proposed by Agresti²¹. At step one we compared a model of
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47 the highest order interaction term (four-way product term; E*O*VF*BW) and the main risk
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49 factors (E+O+VF+BW) with a model comprising only the main risk factors. If the highest
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51 order product term is not significant, Agresti propose to continue with second highest order
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53 terms by removing the term with the highest p-value until the model of best fit is reached.
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Confounders, possible risk factors in addition to the main factors of interest, were tested one by one and set to at least 10% change in any estimate in the model of best fit. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					
Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	

30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	
30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥ 4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

The log likelihood-ratio score from the highest order model ($O*E*VF*FW+O+E+VF+BW$; -2 LR: 7213.8) did not differ from the model comprising the main effects ($O+E+VF+BW$, -2 LR: 7215.9). After removing insignificant three-way interaction product terms, and playing with the remaining two-ways interaction terms, the model that gave the best fit comprised the interaction of oxytocin augmentation, episiotomy and instrumental delivery ($O*E*VF$), in addition to episiotomy/birth weight ($E*BW$) and instrumental delivery/birth weight ($VF*BW$) (-2 LR: 7371.2) (Model A). We could resolve

interaction terms into stratified analysis of 8 strata of combinations of oxytocin augmentation, episiotomy and instrumental delivery for birth weights <4000 g, and 4 strata of combinations of episiotomy, instrumental delivery and birth weight \geq 4000 g, independent of oxytocin augmentation. The results are displayed in Table 2.

Table 2 Model A. Stratified analyses of 8 strata of combinations of oxytocin augmentation, episiotomy, instrumental delivery and birth weights <4000 g, and 4 strata of episiotomy, instrumental delivery and birth weights \geq 4000 g, independent of oxytocin augmentation.

Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight \geq 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
4	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
5	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
6	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
7	+	-	-	-	2621	148 (5.6)	1.6	1.3-1.9
8	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
9	+/-	+	-	+	418	40 (9.6)	2.7	1.9-3.9
10	+/-	-	-	+	977	104 (10.6)	3.1	2.4-4.0
11	+/-	+	+	+	393	55 (14.0)	4.2	3.1-5.8
12	+/-	-	+	+	234	62 (26.5)	9.3	6.8-12.9

From a clinical perspective we can simplify model A into model B by collapsing groups that comprise similar risks for sphincter injury by obstetric interventions despite overlapping confidence intervals. Spontaneous delivery of an infant weighing <4000 g without oxytocin augmentation and episiotomy was chosen as the reference group (group 1). We collapsed group 1 and 2 as the odds for sphincter injury was similar with and without episiotomy in unstimulated, spontaneous births of normal-sized infants. Group 3 to 6 display the odds for sphincter injury in instrumental deliveries of normal-sized infants with and without oxytocin

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7 augmentation and episiotomy. A marked difference in the odds for sphincter injury was
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9 observed between women delivered instrumentally with (group 3 and 5) and without (group 4
10 and 6) episiotomy, despite the fact that those stimulated with oxytocin had a non-significant
11 lower odds for sphincter injury. It was therefore reasonable to collapse group 3 and 5, and
12 group 4 and 6. Furthermore, we collapsed group 7 and 8 as the odds for sphincter injury was
13 similar with and without episiotomy during spontaneous deliveries of infants <4000 g,
14 regardless of oxytocin augmentation. Finally, the use of episiotomy appeared to be strongly
15 associated with lower odds for sphincter injury in instrumental deliveries of infants ≥ 4000 g
16 (group 11 and 12). The modified model B (Table 3) comprises a clinically relevant risk
17 estimation of anal sphincter injury among the main modified risk factors for sphincter injury.

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28 **Table 3** Modified model displaying the collapsed non-significant strata (1–12) from Table 2
29 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence
30 intervals (95% CI) after adjusting for epidural analgesia
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Group (Group in Table 2)	Oxytocin augmentation	Episiotomy	Operative vaginal delivery	Birth weight ≥ 4000 g	Women N	Obstetric anal sphincter injury N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (7,8)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (3,5)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (4,6)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-10)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.5-3.9)
F (11)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (12)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

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Age, origin of the mother, and occiput posterior position had no confounding effect on odds ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3).

The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02; however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural analgesia was associated with a 30% lower odds ratio of anal sphincter injury.

The use of oxytocin augmentation increased with the duration of the second stage of labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the 30–59 minutes group, and 65% (range 49–76%) in the ≥ 60 minutes group during the active second stage of labour. The prevalence of operative deliveries across all study periods was consistently between 45–49% when the active part of the second stage of labour lasted ≥ 60 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found strong associations between oxytocin augmentation and the duration of second stage, and between operative delivery and the duration of second stage (collinearity), which means that the duration of second stage is measured through operative delivery and oxytocin augmentation.

DISCUSSION

We found that oxytocin augmentation during active labour was associated with a 80% increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving spontaneous birth to an infant weighing <4000 g. We did not find an association between episiotomy and tears during spontaneous deliveries, but a significantly reduced association in all operative vaginal deliveries.

Oxytocin augmentation is widely used in delayed labour to prevent operative delivery. However, a Cochrane review concluded that a reduction of labour by two hours was the only

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7 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
8 the entire concept of active management of labour to be associated with a slightly reduced
9 risk of caesarean delivery.²² As in other studies, we found that approximately 50% of
10 nulliparous women received oxytocin augmentation.^{16, 17, 23} There is reason to believe that
11 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
12 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
13 progress of the expulsive phase of labour, leading to rushed situations, impaired
14 communication with the mother, and less focus on protection of the perineum and a controlled
15 delivery of the head. Recent studies from Norway indicate that focus on these elements is
16 important in preventing perineal injuries.^{24, 25}

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26 Many authors have used logistic regression analysis to identify risk factors for
27 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
28 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
29 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
30 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
31 which is a methodological weakness since the true effect of other factors is concealed by the
32 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
33 women, entering oxytocin augmentation, duration of active second stage of labour, and
34 instrumental delivery into the same model.¹⁵

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43 Our study shows strong collinearity between a prolonged active second stage of labour
44 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
45 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
46 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
47 second stage is a time related event before the expulsion of the head. During this latency the
48 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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6 during the expulsive phase. Consequently, we do not consider the duration of the active
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8 second stage as a risk factor for anal sphincter injuries.
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10 Jander et al. conducted a single institution, retrospective, case-control study of 214
11 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
12 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
13 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
14 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
15 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
16 for induction or augmentation purposes.²⁶⁻²⁸ Three large population-based studies on the risk
17 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.<sup>1, 7,
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The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhedde found epidural
analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
by parity and found a significantly increased odds ratio associated with epidural analgesia in
nulliparous women.²⁹ In our study, epidural analgesia was associated with a significantly
reduced odds ratio for sphincter tears.

Our study takes into account four factors that exert their effect on the anal sphincter
during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both operative
vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
national registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 30, 31} In our study,
neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
injury during spontaneous delivery of an infant weighing ≥ 4000 g.

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7 Our methodological approach, stratifying by the factors that are active during the
8 expulsive phase of labour and testing for confounders, is considered a strength of the study.
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10 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
11 with these major risk factors. Logistic regression analyses, without testing for possible
12 interactions, would fail to reveal this information. This case-control study is based on
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14 prospectively collected data from a large unselected population, and represents all deliveries
15 meeting the inclusion criteria that occurred during the study period, which make bias unlikely.
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17 Our department has a high proportion of vaginal deliveries. The overall caesarean delivery
18 rate in our institution was 12.5% over the study period. For women in TGCS group 1 the
19 acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012. Accordingly, the
20 study population includes both high- and low-risk pregnancies, which adds to the external
21 validity of our results.
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30 However, some limitations apply. We cannot prove causality between oxytocin
31 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
32 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
33 support technique, and the birth attendant's experience level may be possible risk modifiers
34 not included in our database. Finally, single institution studies, also when based on unselected
35 populations, should be interpreted with caution.
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41 Our findings have some important implications. Birth attendants should be aware of
42 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
43 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
44 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
45 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
46 World Health Organization recommends the use of a partogram with an action line defining
47 failure to progress. However, a recent Cochrane review could not confirm that such a
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7 partogram was beneficial in high resource settings.³² Given the doubtful benefits from
8 augmentation of labour, randomized controlled trials are strongly needed, and we propose
9 anal sphincter injury as one of the most important endpoints.
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13 Moreover, our study supports restricted use of episiotomy during normal births and as
14 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
15 unpredictable risk factor as weight estimation of a large fetus is unreliable.³³
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Competing interests

None

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No specific

References

1. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;116:25-34.
2. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;90:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;247:224-37.
4. Sultan AH, Thakar R, Fenner DE. Perineal and anal sphincter trauma : diagnosis and clinical management. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;80:229-34.
6. Hornemann A, Kamischke A, Luedders DW, Beyer DA, Diedrich K, Bohlmann MK. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;281:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;98:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, Wallenburg HC. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;108:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;29:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;85:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;206:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;115:1695-702; discussion 702-3.

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13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009;CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, Gareberg B, Nyberg K, Hagberg H. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;107:926-31.
15. Prager M, Andersson KL, Stephansson O, Marchionni M, Marions L. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;87:209-15.
16. Blix E, Pettersen SH, Eriksen H, Royset B, Pedersen EH, Oian P. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;122:1359-62.
17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;85:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011;CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;15:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Agresti A. *An introduction to categorical data analysis*. 2nd ed. ed. Hoboken, N.J. ; Chichester: Wiley-Interscience; 2007.
22. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev* 2013;9:CD004907.
23. Selin L, Almstrom E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation of labor. *Acta Obstet Gynecol Scand* 2009;88:1352-7.
24. Hals E, Oian P, Pirhonen T, Gissler M, Hjelle S, Nilsen EB, et al. A multicenter interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;116:901-8.
25. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal sphincter tears during delivery. *Obstet Gynecol* 2008;111:1053-7.
26. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;71:520-4.
27. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol* 1988;27:27-32.
28. Legino LJ, Woods MP, Rayburn WF, McGoogan LS. Third- and fourth-degree perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;33:423-6.
29. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol* 1997;104:563-6.
30. Hartmann K, Viswanathan M, Palmieri R, Gartlehner G, Thorp J, Jr., Lohr KN. Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;293:2141-8.
31. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;115:104-8.
32. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;7:CD005461.
33. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;43:3-10.

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Comment [ar1]: 21. Agresti new ref, statistical modeling

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(R) In abstract; a cross sectional study, analyzed as case-control study.</p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>(R) Fulfilled</p>
Introduction		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>(R) Recent studies have shown the importance of the perineal protection technique in preventing perineal tears. Oxytocin augmentation could impair the control of the perineum during the delivery by causing too fast progress in the last minutes of labour. Oxytocin augmentation is widely used (50% of births). Guidelines for its use are often deficient and the evidence for its positive effect is challenged. Therefore, oxytocin augmentation as a risk factor for obstetric anal sphincter injuries, and should be explored in a study taking other relevant risk factors into account.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>(R) To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.</p>
Methods		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>(R) Present in Abstract and Methods.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>(R) Setting: Tertiary teaching hospital.</p> <p>Location: Delivery department of Stavanger University Hospital, serving the total obstetric population of the region of South Rogaland.</p> <p>Dates 15 May 1999 – 15 May 2012.</p> <p>Data were collected consecutively.</p>
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants.</p> <p>(R) Nulliparous women with spontaneous start of labour, single, cephalic pregnancy and ≥ 37 weeks gestation who delivered vaginally, where we had access to complete information on the main exposure and the explanatory variables. The source population was the entire obstetric population of the region.</p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect</p>

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modifiers. Give diagnostic criteria, if applicable

(R) Outcome: Obstetric anal sphincter injury; that is grade 3 and 4 perineal tears as defined by International Society of Incontinence.

Exposure: Oxytocin augmentation in active labour, that is oxytocin intravenous infusion (5 international units (0.01mg) oxytocin in 500 ml saline) used in incremental doses during active labour.

Predictors: NA

Effect modifiers: Episiotomy, operative vaginal delivery, birth weight <4000 g vs \geq 4000 g.

Potential confounders: maternal age, ethnicity, occiput posterior position, duration of second stage of labour and epidural analgesia.

Data sources/ measurement	8*	<p>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.</p> <p>(R) All variables are precisely defined in the obstetric databases of Stavanger University Hospital. The grade of perineal injury was assessed during operative repair and plotted directly into the database.</p>
Bias	9	<p>Describe any efforts to address potential sources of bias.</p> <p>(R) In this cross-sectional study all women giving births and who fulfil the inclusion criteria are included. There were very few cases with missing data. We may have missed some cases of perineal injury due to underreporting. The variables are hard variables with clear definitions: Use of oxotocin (yes/no), episiotomy (yes/no), mode of delivery (spontaneous/operative vaginal), birth weight categorized <4000/ \geq4000 g.</p>
Study size	10	<p>Explain how the study size was arrived at</p> <p>(R) The study size is given by the number of women fulfilling the eligibility criteria and who delivered at Stavanger University Hospital from 15 May 1999 to 15 May 2012.</p>
Quantitative variables	11	<p>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.</p> <p>(R) Birth weight was categorized into < 4000/ \geq4000 g.</p>
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(R) Chi-square test and stepwise forward logistic regression using IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.</p> <hr/> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(R) We applied a stratified approach to control for interaction between the main variables (oxytocin augmentation, episiotomy, instrumental delivery and birth weight). Then we tested for confounding and interaction to a modified model by entering one variable at time.</p> <hr/> <p>(c) Explain how missing data were addressed</p> <p>(R) Cases with missing data for estimated date of delivery were excluded. Cases with</p>

other missing data were recoded to the reference value in the logistic regression analyses. Very few cases with missing data (n=52).

(d) If applicable, describe analytical methods taking account of sampling strategy

(R) NA

(e) Describe any sensitivity analyses

(R) NA

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(R) Potentially eligible: 15 545 Confirmed eligible: 15 493 Included/analyzed: 15 493</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(R) Cases with missing data for estimated date of delivery were excluded (n=52)</p> <p>(c) Consider use of a flow diagram</p> <p>(R) Not useful in this study.</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(R) Given in Table 1.</p> <p>The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(R) Cases with missing data for estimated date of delivery were excluded from the study population (n=52)</p> <p>Recoded to the reference category of the variable and included in the analyses:</p> <p>Birth weight 3 cases. Maternal age 2 cases. Lie at delivery 8 cases. Duration of second stage of labour 92 cases.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>(R) Table 1.</p> <p>Outcome event, the dependant variable, anal sphincter injury: 1014 cases.</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(R) Table 2 and 3. Confounders: paragraph 4 in Material and Methods.</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(R) Table 1</p>

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		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period (R) NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (R) NA
Discussion		
Key results	18	Summarise key results with reference to study objectives (R) Fulfilled.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (R) Bias regarding main outcome: We do not know the magnitude of underreporting of anal sphincter tear grade 3 and 4, however believe this to be low. Bias regarding main exposure: The quality system of the department relies on honest reporting by midwives and obstetricians, and has been a cornerstone in the systematic interdisciplinary work towards better clinical outcomes since 1996. We have reason to believe that ownership to the concept has resulted in good adherence to the reporting routines, and we believe the reporting of oxytocin augmentation to be a robust measure of what was actually practised. The midwives plotting the information were not aware of any research issue related to oxytocin augmentation. We consider the other main exposure variables to be robust: It is unlikely that reports of episiotomy, instrumental delivery and birth weight are skewed in any direction. The same applies to the possible confounders age, ethnicity, occiput posterior position and epidural analgesia. We believe that the reporting of these variables reflects the actual practice. Therefore we consider the estimates for risks related to anal sphincter tear grade 3 and 4 to be precise with little bias. Our stratified approach, modified model, takes care of the interaction problems between episiotomy, operative vaginal delivery, birth weight and oxytocin augmentation.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (R) Fulfilled.
Generalisability	21	Discuss the generalisability (external validity) of the study results. (R) The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity. This adds value to the external validity of the study results. We encourage other study groups to make research on the effect of oxytocin augmentation on anal sphincter injury in other populations.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if

applicable, for the original study on which the present article is based
(R) No specific funding.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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BMJ Open

Assessing the association of oxytocin augmentation with obstetric anal sphincter injury in nulliparous women – a population-based, case-control study

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Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Epidemiology
Keywords:	Maternal medicine < OBSTETRICS, EPIDEMIOLOGY, Colorectal surgery < SURGERY

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4 **in nulliparous women – a population-based, case-control study**
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27 Oxytocin augmentation and anal sphincter injury
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30 *Key words:* anal sphincter injury, oxytocin, episiotomy, operative vaginal delivery, birth
31 weight,
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33 Word Count: 2804
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ABSTRACT

Objective: To assess the association of oxytocin augmentation with obstetric anal sphincter injury among nulliparous women.

Design: Population-based, case-control study.

Setting: Primary and secondary teaching hospital serving a Norwegian region.

Population: 15 476 nulliparous women with spontaneous start of labour, single cephalic presentation, and gestation ≥ 37 weeks delivering vaginally between 1999 and 2012.

Methods: Based on the presence or absence of oxytocin augmentation, episiotomy, operative vaginal delivery, and birth weight (<4000 g vs. ≥ 4000 g), we modelled in logistic regression the best fit for prediction of anal sphincter injury. Within the modified model of main exposures, we tested for possible confounding, and interactions between maternal age, ethnicity, occiput posterior position, and epidural analgesia.

Main outcome measure: Obstetric anal sphincter injury.

Results: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries in women giving spontaneous birth to infants weighing <4000 g (OR 1.8; 95% CI: 1.5–2.2). Episiotomy was not associated with sphincter injuries in spontaneous births, but with a lower OR in operative vaginal deliveries. Spontaneous delivery of infants weighing ≥ 4000 g was associated with a 3-fold higher OR, and epidural analgesia was associated with a 30% lower OR in comparison to no epidural analgesia.

Conclusions: Oxytocin augmentation was associated with a higher OR of obstetric anal sphincter injuries during spontaneous deliveries of normal-sized infants. We observed a considerable effect modification between the most important factors predicting anal sphincter injuries in the active second stage of labour.

ARTICLE SUMMARY

Strengths and limitations of this study

- Stratifying by the main risk factors that are active during the expulsive phase of labour and testing for confounders are strengths of the study.
- We reveal how oxytocin augmentation interacts with the major factors active in the expulsive phase of labour.
- The study is based on prospectively collected data from a large, unselected population, which makes bias unlikely.
- The study design is a limitation, as we cannot prove causality between oxytocin augmentation and obstetric anal sphincter injuries in an observational study.

INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} Asian or African ethnicity,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound examination was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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3 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
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5 According to our routines and national guidelines, operative vaginal delivery was indicated if
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7 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
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9 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
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11 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
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13 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
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15 originating from Europe or North America, or non-Western.
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18 The intention of this study was to explore the effect of three obstetric practices
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20 (oxytocin augmentation (O), episiotomy (E) and vacuum/forceps (VF)) and birth weight
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22 (BW) on obstetric anal sphincter injuries before other risk factors were considered. These
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24 main risk factors correlate as episiotomy is often used for instrumental deliveries and when
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26 large babies are expected. Furthermore, oxytocin augmentation is provided for failure to
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28 progress because of dystocia. Women with dystocia are more often delivered instrumentally
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30 than women without dystocia. This basic understanding of the birth dynamics of the first and
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32 second stage of labour indicates that the main risk factors may have a direct or indirect effect
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34 on obstetric anal sphincter injuries, and that the effects of categories across different
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36 explanatory variables are not constant on the outcome.
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40 We analysed our dataset using the Chi-squared test and backward manual
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42 stepwise logistic regression analyses with $p < 0.05$ as significance level. We built and checked
43
44 the fit of our regression model as proposed by Agresti²¹. Step one compares the model
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46 including the highest order four-way interaction with a model without the four-way
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48 interaction. If the highest order product is not significant, Agresti proposes continuing
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50 removing the highest order term with the highest non-significant p-value until all remaining
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52 terms have statistically significant p-values. Four main predictors (O=oxytocin augmentation,
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54 E=episiotomy, VF=Vacuum/forceps and BW=birth weight) are used to predict the
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proportions of women with sphincter injuries. Confounders, possible risk factors in addition to the main factors of interest, were tested one by one and set to at least 10% change in any estimate in the model of best fit. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					

Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	
30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

After adopting the strategy of Agresti by deleting the highest statistically non-significant terms in the model until all remaining terms are statistically significant, we ended up with a best fitting model involving the three-way interaction of oxytocin augmentation, episiotomy and vacuum/forceps (O x E x VF) and the two two-way interactions episiotomy/birth weight (E x BW) and vacuum/forceps (VF x BW). (Model A). We could resolve interaction terms into stratified analysis of 8 strata of combinations of oxytocin augmentation,

episiotomy and instrumental delivery for birth weights <4000 g, and 4 strata of combinations of episiotomy, instrumental delivery and birth weight \geq 4000 g, independent of oxytocin augmentation. The results are displayed in Table 2.

Table 2 Model A. Stratified analyses of 8 strata of combinations of oxytocin augmentation, episiotomy, instrumental delivery and birth weights <4000 g, and 4 strata of episiotomy, instrumental delivery and birth weights \geq 4000 g, independent of oxytocin augmentation. Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation ^a	Episiotomy ^a	Operative vaginal delivery ^a	Birth Weight ^b	Women N	OASI ^c N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
4	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
5	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
6	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
7	+	-	-	-	2621	148 (5.6)	1.6	1.3-1.9
8	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
9	+/-	+	-	+	418	40 (9.6)	2.7	1.9-3.9
10	+/-	-	-	+	977	104 (10.6)	3.1	2.4-4.0
11	+/-	+	+	+	393	55 (14.0)	4.2	3.1-5.8
12	+/-	-	+	+	234	62 (26.5)	9.3	6.8-12.9

^aUsed (+) / unused (-), ^b \geq 4000 g (+) / <4000 g (-), ^cObstetric anal sphincter injury

From a clinical perspective we can simplify model A into model B by collapsing groups that comprise similar risks for sphincter injury by obstetric interventions despite overlapping confidence intervals. Spontaneous delivery of an infant weighing <4000 g without oxytocin augmentation and episiotomy was chosen as the reference group (group 1). We collapsed group 1 and 2 as the odds for sphincter injury was similar with and without episiotomy in unstimulated, spontaneous births of normal-sized infants. Group 3 to 6 display the odds for sphincter injury in instrumental deliveries of normal-sized infants with and without oxytocin

augmentation and episiotomy. A marked difference in the odds for sphincter injury was observed between women delivered instrumentally with (group 3 and 5) and without (group 4 and 6) episiotomy, despite the fact that those stimulated with oxytocin had a non-significant lower odds for sphincter injury. It was therefore reasonable to collapse group 3 and 5, and group 4 and 6. Furthermore, we collapsed group 7 and 8 as the odds for sphincter injury was similar with and without episiotomy during spontaneous deliveries of infants <4000 g, regardless of oxytocin augmentation. Finally, the use of episiotomy appeared to be strongly associated with lower odds for sphincter injury in instrumental deliveries of infants \geq 4000 g (group 11 and 12). The modified model B (Table 3) comprises a clinically relevant risk estimation of anal sphincter injury among the main modified risk factors for sphincter injury.

Table 3 Modified model displaying the collapsed non-significant strata (1–12) from Table 2 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence intervals (95% CI) after adjusting for epidural analgesia

Group (Group in Table 2)	Oxytocin augmentation ^a	Episiotomy ^a	Operative vaginal delivery ^a	Birth weight ^b	Women N	OASI ^c N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (7,8)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (3,5)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (4,6)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-10)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.5-3.9)
F (11)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (12)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

^aUsed (+) / unused (-), ^b \geq 4000 g (+) / <4000 g (-), ^cObstetric anal sphincter injury

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3 Age, origin of the mother, and occiput posterior position had no confounding effect on odds
4 ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin
5 augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3).
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9 The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02;
10 however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural
11 analgesia was associated with a 30% lower odds ratio of anal sphincter injury.
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16 The use of oxytocin augmentation increased with the duration of the second stage of
17 labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the
18 30–59 minutes group, and 65% (range 49–76%) in the ≥ 60 minutes group during the active
19 second stage of labour. The prevalence of operative deliveries across all study periods was
20 consistently between 45–49% when the active part of the second stage of labour lasted ≥ 60
21 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
22 strong associations between oxytocin augmentation and the duration of second stage, and
23 between operative delivery and the duration of second stage (collinearity), which means that
24 the duration of second stage is measured through operative delivery and oxytocin
25 augmentation.
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40 **DISCUSSION**

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42 We found that oxytocin augmentation during active labour was associated with a 80%
43 increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving
44 spontaneous birth to an infant weighing <4000 g. We did not find an association between
45 episiotomy and tears during spontaneous deliveries, but a significantly reduced association in
46 all operative vaginal deliveries.
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54 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
55 However, a Cochrane review concluded that a reduction of labour by two hours was the only
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3 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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5 the entire concept of active management of labour to be associated with a slightly reduced
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7 risk of caesarean delivery.²² As in other studies, we found that approximately 50% of
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9 nulliparous women received oxytocin augmentation.^{16, 17, 23} There is reason to believe that
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11 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
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13 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
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15 progress of the expulsive phase of labour, leading to rushed situations, impaired
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17 communication with the mother, and less focus on protection of the perineum and a controlled
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19 delivery of the head. Recent studies from Norway indicate that focus on these elements is
20
21 important in preventing perineal injuries.^{24, 25}

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25 Many authors have used logistic regression analysis to identify risk factors for
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27 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
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29 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
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31 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
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33 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
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35 which is a methodological weakness since the true effect of other factors is concealed by the
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37 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
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39 women, entering oxytocin augmentation, duration of active second stage of labour, and
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41 instrumental delivery into the same model.¹⁵

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45 Our study shows strong collinearity between a prolonged active second stage of labour
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47 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
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49 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
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51 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
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53 second stage is a time related event before the expulsion of the head. During this latency the
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55 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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3 during the expulsive phase. Consequently, we do not consider the duration of the active
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5 second stage as a risk factor for anal sphincter injuries.
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7 Jander et al. conducted a single institution, retrospective, case-control study of 214
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9 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
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11 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
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13 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
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15 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
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17 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
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19 for induction or augmentation purposes.²⁶⁻²⁸ Three large population-based studies on the risk
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21 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.<sup>1, 7,
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27 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
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29 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhed found epidural
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31 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
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33 by parity and found a significantly increased odds ratio associated with epidural analgesia in
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35 nulliparous women.²⁹ In our study, epidural analgesia was associated with a significantly
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37 reduced odds ratio for sphincter tears.
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40 Our study takes into account four factors that exert their effect on the anal sphincter
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42 during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both operative
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44 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
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46 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
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48 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
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50 national registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 30, 31} In our study,
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52 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
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54 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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3 Our methodological approach, stratifying by the factors that are active during the
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5 expulsive phase of labour and testing for confounders, is considered a strength of the study.
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7 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
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9 with these major risk factors. Logistic regression analyses, without testing for possible
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11 interactions, would fail to reveal this information. This case-control study is based on
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13 prospectively collected data from a large unselected population, and represents all deliveries
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15 meeting the inclusion criteria that occurred during the study period, which make bias unlikely.
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17 Our department has a high proportion of vaginal deliveries. The overall caesarean delivery
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19 rate in our institution was 12.5% over the study period. For women in TGCS group 1 the
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21 acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012. Accordingly, the
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23 study population includes both high- and low-risk pregnancies, which adds to the external
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25 validity of our results.
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30 However, some limitations apply. We cannot prove causality between oxytocin
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32 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
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34 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
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36 support technique, and the birth attendant's experience level may be possible risk modifiers
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38 not included in our database. Finally, single institution studies, also when based on unselected
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40 populations, should be interpreted with caution.
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44 Our findings have some important implications. Birth attendants should be aware of
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46 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
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48 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
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50 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
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52 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
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54 World Health Organization recommends the use of a partogram with an action line defining
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56 failure to progress. However, a recent Cochrane review could not confirm that such a
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3 partogram was beneficial in high resource settings.³² Given the doubtful benefits from
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5 augmentation of labour, randomized controlled trials are strongly needed, and we propose
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7 anal sphincter injury as one of the most important endpoints.
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11 Moreover, our study supports restricted use of episiotomy during normal births and as
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13 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
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15 unpredictable risk factor as weight estimation of a large fetus is unreliable.³³
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Contributorship Statement

All four authors have contributed to the idea and design of the research project. ABR, TME managed the dataset and the statistical analyses were performed by FES. All four authors have contributed to the interpretation of the results and the writing of the manuscript.

Competing interests

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Data Sharing Statement

No additional data available

References

1. Baghestan E, Irgens LM, Bordahl PE, et al. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;116:25-34.
2. Laine K, Skjeldestad FE, Sanda B, et al. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;90:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;247:224-37.
4. Sultan AH, Thakar R, Fenner DE. Perineal and anal sphincter trauma : diagnosis and clinical management. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;80:229-34.
6. Hornemann A, Kamischke A, Luedders DW, et al. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;281:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;98:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, et al. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;108:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;29:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;85:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, et al. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;206:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, et al. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;115:1695-702; discussion 702-3.
13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009:CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, et al. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;107:926-31.
15. Prager M, Andersson KL, Stephansson O, et al. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;87:209-15.
16. Blix E, Pettersen SH, Eriksen H, et al. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;122:1359-62.
17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, et al. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;85:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011:CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;15:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Agresti A. An introduction to categorical data analysis. 2nd ed. ed. Hoboken, N.J. ; Chichester: Wiley-Interscience; 2007.

- 1
2
3 22. Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management
4 in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst*
5 *Rev* 2013;9:CD004907.
- 6 23. Selin L, Almstrom E, Wallin G, et al. Use and abuse of oxytocin for augmentation of
7 labor. *Acta Obstet Gynecol Scand* 2009;88:1352-7.
- 8 24. Hals E, Oian P, Pirhonen T, Gissler M, et al. A multicenter interventional program to
9 reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;116:901-8.
- 10 25. Laine K, Pirhonen T, Rolland R, et al. Decreasing the incidence of anal sphincter tears
11 during delivery. *Obstet Gynecol* 2008;111:1053-7.
- 12 26. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with
13 complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;71:520-4.
- 14 27. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter
15 rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol*
16 1988;27:27-32.
- 17 28. Legino LJ, Woods MP, Rayburn WF, et al. Third- and fourth-degree perineal tears. 50
18 year's experience at a university hospital. *J Reprod Med* 1988;33:423-6.
- 19 29. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third
20 degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy.
21 *Br J Obstet Gynaecol* 1997;104:563-6.
- 22 30. Hartmann K, Viswanathan M, Palmieri R, et al. Outcomes of routine episiotomy: a
23 systematic review. *JAMA* 2005;293:2141-8.
- 24 31. de Leeuw JW, de Wit C, Kuijken JP, et al. Medi lateral episiotomy reduces the risk
25 for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;115:104-8.
- 26 32. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in
27 spontaneous labour at term. *Cochrane Database Syst Rev* 2013;7:CD005461.
- 28 33. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet*
29 *Gynecol* 2014;43:3-10.
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3 **Assessing the association of oxytocin augmentation with obstetric anal sphincter injury**
4 **in nulliparous women – a population-based, case-control study**
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10 **ARTICLE SUMMARY**

11 **Strengths and limitations of this study**

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 - 14 • Stratifying by the main risk factors that are active during the expulsive phase of labour
15 and testing for confounders are strengths of the study.
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 - 18 • We reveal how oxytocin augmentation interacts with the major factors active in the
19 expulsive phase of labour.
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 - 23 • The study is based on prospectively collected data from a large, unselected population,
24 which makes bias unlikely.
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 - 28 • The study design is a limitation, as we cannot prove causality between oxytocin
29 augmentation and obstetric anal sphincter injuries in an observational study.
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INTRODUCTION

Obstetric anal sphincter injuries occur in 0.5–5.0% of vaginal deliveries,¹ with a subsequently increased risk of fecal incontinence.²⁻⁴ Nulliparity,^{1,3,5} high birth weight,^{1,3,5,6} operative vaginal delivery,^{1,3,5} advanced maternal age,^{1,5,6} Asian or African ethnicity,^{1,7} and prolonged second stage of labour^{3,7,8} are consistently reported as risk factors for obstetric anal sphincter injuries, whereas the effect of epidural analgesia^{9,10} and episiotomy^{1,11-13} is debated.

However, only a few authors have evaluated oxytocin augmentation as a possible risk factor for obstetric anal sphincter injuries.^{5,14,15} Further, the current literature dealing with risk factors for obstetric anal sphincter injuries has not sufficiently addressed their possible interactions. Studies usually present a summary of associations between risk factors and obstetric anal sphincter injuries adjusted for confounders without investigating effect modification, i.e. exploring whether the effects are uniform across various levels of the studied risk factors.

In many delivery units, oxytocin augmentation is used during more than half of births.^{16,17} Oxytocin augmentation has been shown to shorten the duration of labour, but not to decrease the need for operative deliveries.¹⁸ We hypothesize that oxytocin augmentation may reduce control over contractions and impair perineal support by causing the delivery to progress too quickly, and thereby increase the risk of perineal injury. Thus, the widespread use of oxytocin in daily obstetric practice calls for an exploration of its possible harmful effects. The aim of our study was to assess the association between oxytocin augmentation and obstetric anal sphincter injuries in a dynamic model related to the active second stage of labour.

MATERIALS AND METHODS

The Department of Obstetrics and Gynaecology of Stavanger University Hospital serves as the only delivery unit for a population of 320 000 people, and approximately 4500 deliveries occur there annually. From 1996 onward, all obstetric data have been consecutively recorded. The electronic database consists of clearly defined variables, and is continuously maintained using standardized procedures for data entry and quality control. During the study period 15 May 1999 to 15 May 2012, 56 517 women with a pregnancy duration of ≥ 23 weeks of gestation and infants with a birth weight of > 300 grams delivered in the department.

Estimated day of delivery was determined by second trimester ultrasound scan or from menstrual data when no ultrasound examination was performed. We restricted the study population to nulliparous women whose labour started spontaneously, with single cephalic presentation, pregnancies of ≥ 37 weeks of gestation (Group 1 in Robson's Ten Group Classification System; TGCS¹⁹), and who delivered vaginally. After excluding 69 women with missing data, (52 without an estimated day of delivery, 17 with missing information of fetal presentation at delivery), this case-control study comprised 15 476 women.

The main outcome measure was obstetric anal sphincter injuries as defined by the International Continence Society, i.e. partial or complete tears of the anal sphincter muscles, with or without disruption of the anal mucosa (grade 3–4 perineal tears).²⁰ When an obstetric anal sphincter injury was suspected, the obstetrician on call diagnosed the grade of the tear during surgical repair.

Oxytocin augmentation was defined as oxytocin used to stimulate contractions during established labour. An intravenous infusion of 5 international units (0.01mg) oxytocin in 500 ml saline was administered, starting with 30 ml per hour, and a dose increment of 15 ml per hour every 15 minutes to a maximum of 180 ml per hour, guided by the response. Normal births were taken care of by midwives, while doctors performed the operative deliveries.

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3 Throughout the study period, episiotomy was performed either medio-laterally or laterally.
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5 According to our routines and national guidelines, operative vaginal delivery was indicated if
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7 delivery had not taken place after 60 minutes of bearing down. We used vacuum extraction
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9 with a Malmström metal cup as the preferred procedure for operative vaginal delivery.
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11 Vacuum extraction was applied for mid-cavity and outlet release. A combination of low-dose
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13 ropivacaine/fentanyl was used for epidural analgesia. Ethnicity was classified as Western i.e.
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15 originating from Europe or North America, or non-Western.
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18 The intention of this study was to explore the effect of three obstetric practices
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20 (oxytocin augmentation (O), episiotomy (E) and vacuum/forceps (VF)) and birth weight
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22 (BW) on obstetric anal sphincter injuries before other risk factors were considered. These
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24 main risk factors correlate as episiotomy is often used for instrumental deliveries and when
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26 large babies are expected. Furthermore, oxytocin augmentation is provided for failure to
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28 progress because of dystocia. Women with dystocia are more often delivered instrumentally
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30 than women without dystocia. This basic understanding of the birth dynamics of the first and
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32 second stage of labour indicates that the main risk factors may have a direct or indirect effect
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34 on obstetric anal sphincter injuries, and that the effects of categories across different
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36 explanatory variables are not constant on the outcome.
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40 We analysed our dataset using the Chi-squared test and backward manual
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42 stepwise logistic regression analyses with $p < 0.05$ as significance level. We built and checked
43
44 the fit of our regression model as proposed by Agresti²¹. Step one compares the model
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46 including the highest order four-way interaction with a model without the four-way
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48 interaction. If the highest order product is not significant, Agresti proposes continuing
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50 removing the highest order term with the highest non-significant p-value until all remaining
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52 terms have statistically significant p-values. Four main predictors (O=oxytocin augmentation,
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54 E=episiotomy, VF=Vacuum/forceps and BW=birth weight) are used to predict the
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proportions of women with sphincter injuries. Confounders, possible risk factors in addition to the main factors of interest, were tested one by one and set to at least 10% change in any estimate in the model of best fit. Interaction terms were significant at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp.

The Regional Committee for Medical and Health Research Ethics, Western Norway, approved the protocol as a quality assurance study in obstetric care, and fulfilling the requirements for data protection procedures (REK 2011-1247).

RESULTS

The study population comprised 15 476 (27%) of the 56 517 women giving birth during the study period, including 1013 (53%) of a total of 1894 women diagnosed with obstetric anal sphincter injuries.

The overall prevalence of obstetric anal sphincter injuries was 6.5%. The rate declined from 9.6% in 1999–2000 to 2.8% in 2010–2012. The characteristics of the study population and the prevalence of obstetric anal sphincter injuries are displayed in Table 1.

Table 1 Characteristics of the study population and the prevalence of obstetric anal sphincter injury. P-values from Chi-square tests.

Factor	Obstetric anal sphincter injury		In total N=15 476	Prevalence %	P
	No N=14 463 %	Yes N=1013 %			
Time period					<0.001
1999-2000	11.1	16.9	1781	9.6	
2001-2003	19.8	30.7	3169	9.8	
2004-2006	22.9	29.6	3611	8.3	
2007-2009	25.5	14.3	3826	3.8	
2010-2012	20.8	8.6	3089	2.8	
Maternal factors					

Age (years)					<0.001
<25	26.6	19.3	4040	4.9	
25-29	33.5	37.6	5233	7.3	
30-34	17.8	20.8	2785	7.6	
≥35	22.1	22.2	3418	6.6	
Origin					NS*
Western	90.5	92.0	14 025	6.6	
Non-Western	9.5	8.0	1451	5.6	
Obstetric factors					
Epidural analgesia					NS
No	58.1	57.7	8992	6.5	
Yes	41.9	42.3	6484	6.6	
Oxytocin augmentation					<0.001
No	55.6	44.7	8500	5.3	
Yes	44.4	55.3	6976	8.0	
Active 2 nd stage of labour (min)					<0.001
Missing information	0.6	0.3	92	3.3	
0-14	10.8	6.8	1627	4.2	
15-29	26.8	18.5	4063	4.6	
30-59	40.1	37.8	6181	6.2	
≥60	21.7	36.6	3513	10.6	
Episiotomy					NS
No	67.1	65.4	10 372	6.4	
Yes	32.9	34.6	5104	6.9	
Operative vaginal delivery					<0.001
No	77.5	60.3	11 817	5.2	
Yes	22.5	39.7	3659	11.0	
Fetal factors					
Birth weight (g)					<0.001
<4000	87.8	74.2	13 454	5.6	
≥4000	12.2	25.8	2022	12.9	
Occiput posterior position					NS
No	95.4	94.8	14 771	6.5	
Yes	4.5	5.2	705	7.4	

* Non significant

The prevalence was higher in women who received oxytocin augmentation (8.0% vs. 5.3%), those who were delivered instrumentally (11.0% vs. 5.2%), and in those who gave birth to an infant weighing ≥4000 g (12.9% vs. 5.6%). Furthermore, the prevalence increased with longer durations of the active part of the second stage of labour.

After adopting the strategy of Agresti by deleting the highest statistically non-significant terms in the model until all remaining terms are statistically significant, we ended up with a best fitting model involving the three-way interaction of oxytocin augmentation, episiotomy and vacuum/forceps (O x E x VF) and the two two-way interactions episiotomy/birth weight (E x BW) and vacuum/forceps (VF x BW). (Model A). We could resolve interaction terms into stratified analysis of 8 strata of combinations of oxytocin augmentation,

episiotomy and instrumental delivery for birth weights <4000 g, and 4 strata of combinations of episiotomy, instrumental delivery and birth weight \geq 4000 g, independent of oxytocin augmentation. The results are displayed in Table 2.

Table 2 Model A. Stratified analyses of 8 strata of combinations of oxytocin augmentation, episiotomy, instrumental delivery and birth weights <4000 g, and 4 strata of episiotomy, instrumental delivery and birth weights \geq 4000 g, independent of oxytocin augmentation.

Crude odds ratio (OR) and 95% confidence intervals (95% CI)

Group	Oxytocin augmentation ^a	Episiotomy ^a	Operative vaginal delivery ^a	Birth Weight ^b	Women N	OASI ^c N (%)	OR	95% CI
1	-	-	-	-	5328	198 (3.7)	1.0	
2	-	+	-	-	1434	60 (4.2)	1.1	0.8-1.5
3	-	+	+	-	537	43 (8.0)	2.3	1.6-3.2
4	-	-	+	-	316	47 (14.9)	4.5	3.2-6.4
5	+	+	+	-	1283	92 (7.2)	2.0	1.6-2.6
6	+	-	+	-	896	103 (11.5)	3.4	2.6-4.3
7	+	-	-	-	2621	148 (5.6)	1.6	1.3-1.9
8	+	+	-	-	1039	61 (5.9)	1.6	1.2-2.2
9	+/-	+	-	+	418	40 (9.6)	2.7	1.9-3.9
10	+/-	-	-	+	977	104 (10.6)	3.1	2.4-4.0
11	+/-	+	+	+	393	55 (14.0)	4.2	3.1-5.8
12	+/-	-	+	+	234	62 (26.5)	9.3	6.8-12.9

^aUsed (+) / unused (-), ^b \geq 4000 g (+) / <4000 g (-), ^cObstetric anal sphincter injury

From a clinical perspective we can simplify model A into model B by collapsing groups that comprise similar risks for sphincter injury by obstetric interventions despite overlapping confidence intervals. Spontaneous delivery of an infant weighing <4000 g without oxytocin augmentation and episiotomy was chosen as the reference group (group 1). We collapsed group 1 and 2 as the odds for sphincter injury was similar with and without episiotomy in unstimulated, spontaneous births of normal-sized infants. Group 3 to 6 display the odds for sphincter injury in instrumental deliveries of normal-sized infants with and without oxytocin

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3 augmentation and episiotomy. A marked difference in the odds for sphincter injury was
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5 observed between women delivered instrumentally with (group 3 and 5) and without (group 4
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7 and 6) episiotomy, despite the fact that those stimulated with oxytocin had a non-significant
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9 lower odds for sphincter injury. It was therefore reasonable to collapse group 3 and 5, and
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11 group 4 and 6. Furthermore, we collapsed group 7 and 8 as the odds for sphincter injury was
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13 similar with and without episiotomy during spontaneous deliveries of infants <4000 g,
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15 regardless of oxytocin augmentation. Finally, the use of episiotomy appeared to be strongly
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17 associated with lower odds for sphincter injury in instrumental deliveries of infants ≥ 4000 g
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19 (group 11 and 12). The modified model B (Table 3) comprises a clinically relevant risk
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21 estimation of anal sphincter injury among the main modified risk factors for sphincter injury.
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27 **Table 3** Modified model displaying the collapsed non-significant strata (1–12) from Table 2
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29 into new strata (A–G). Unadjusted odds ratios (OR), adjusted (aOR), and 95% confidence
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31 intervals (95% CI) after adjusting for epidural analgesia
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Group (Group in Table 2)	Oxytocin augmentation ^a	Episiotomy ^a	Operative vaginal delivery ^a	Birth weight ^b	Women N	OASI ^c N (%)	OR	aOR (95% CI)
A (1,2)	-	+/-	-	-	6762	258 (3.8)	1.0	1.0
B (7,8)	+	+/-	-	-	3660	209 (5.7)	1.5	1.8 (1.5-2.2)
C (3,5)	+/-	+	+	-	1820	135 (7.4)	2.0	2.3 (1.8-2.8)
D (4,6)	+/-	-	+	-	1212	150 (12.4)	3.6	4.1 (3.3-5.1)
E (9-10)	+/-	+/-	-	+	1395	144 (10.3)	2.9	3.1 (2.5-3.9)
F (11)	+/-	+	+	+	393	55 (14.0)	4.1	4.7 (3.4-6.5)
G (12)	+/-	-	+	+	234	62 (26.5)	9.1	10.5 (7.6-14.4)

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56 ^aUsed (+) / unused (-), ^b ≥ 4000 g (+) / <4000 g (-), ^cObstetric anal sphincter injury
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3 Age, origin of the mother, and occiput posterior position had no confounding effect on odds
4 ratios for obstetric anal sphincter injury across combinations of episiotomy, oxytocin
5 augmentation, operative vaginal delivery, and birth weight (groups A to G in Table 3).
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9 The unadjusted odds ratio (OR) for the presence or absence of epidural analgesia was 1.02;
10 however, the adjusted OR for epidural analgesia was 0.73, (95% CI 0.63-0.84) i.e. epidural
11 analgesia was associated with a 30% lower odds ratio of anal sphincter injury.
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16 The use of oxytocin augmentation increased with the duration of the second stage of
17 labour over all the time periods from an average of 32% in the <30 minutes group, 46% in the
18 30–59 minutes group, and 65% (range 49–76%) in the ≥ 60 minutes group during the active
19 second stage of labour. The prevalence of operative deliveries across all study periods was
20 consistently between 45–49% when the active part of the second stage of labour lasted ≥ 60
21 minutes vs. 12–21% for durations of the second stage of labour of <60 minutes. We found
22 strong associations between oxytocin augmentation and the duration of second stage, and
23 between operative delivery and the duration of second stage (collinearity), which means that
24 the duration of second stage is measured through operative delivery and oxytocin
25 augmentation.
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40 **DISCUSSION**

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42 We found that oxytocin augmentation during active labour was associated with a 80%
43 increased odds ratio of obstetric anal sphincter injury in women in TGCS group 1 giving
44 spontaneous birth to an infant weighing <4000 g. We did not find an association between
45 episiotomy and tears during spontaneous deliveries, but a significantly reduced association in
46 all operative vaginal deliveries.
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54 Oxytocin augmentation is widely used in delayed labour to prevent operative delivery.
55 However, a Cochrane review concluded that a reduction of labour by two hours was the only
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3 proven effect, and there was no effect on operative deliveries.¹⁸ Another recent review found
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5 the entire concept of active management of labour to be associated with a slightly reduced
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7 risk of caesarean delivery.²² As in other studies, we found that approximately 50% of
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9 nulliparous women received oxytocin augmentation.^{16, 17, 23} There is reason to believe that
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11 guidelines for the diagnosis and treatment of protracted labour are unclear or inconsistently
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13 applied in daily practice.¹⁷ We hypothesize that stimulation with oxytocin may speed up the
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15 progress of the expulsive phase of labour, leading to rushed situations, impaired
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17 communication with the mother, and less focus on protection of the perineum and a controlled
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19 delivery of the head. Recent studies from Norway indicate that focus on these elements is
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21 important in preventing perineal injuries.^{24, 25}

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25 Many authors have used logistic regression analysis to identify risk factors for
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27 obstetric anal sphincter injuries, but only a few have included oxytocin augmentation.
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29 Samuelsson et al.,¹⁴ Prager et al.,¹⁵ and Jander et al.⁵ found oxytocin augmentation to be
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31 predictive of obstetric anal sphincter injuries in univariate analysis, but only Jander et al.
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33 confirmed this finding in multivariable analyses. Samuelsson et al. did not stratify by parity,
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35 which is a methodological weakness since the true effect of other factors is concealed by the
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37 strong impact of parity.¹⁴ Prager et al. studied obstetric anal sphincter injuries in nulliparous
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39 women, entering oxytocin augmentation, duration of active second stage of labour, and
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41 instrumental delivery into the same model.¹⁵

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45 Our study shows strong collinearity between a prolonged active second stage of labour
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47 and both oxytocin augmentation and instrumental delivery. We consider the duration of the
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49 active second stage of labour to be a “proxy” for oxytocin augmentation and instrumental
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51 delivery, and not a risk factor for obstetric anal sphincter injury in itself. Long duration of the
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53 second stage is a time related event before the expulsion of the head. During this latency the
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55 active forces do not inflict injury on the sphincter apparatus, the sphincter injury occurs
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3 during the expulsive phase. Consequently, we do not consider the duration of the active
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5 second stage as a risk factor for anal sphincter injuries.
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7 Jander et al. conducted a single institution, retrospective, case-control study of 214
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9 cases to explore 44 possible risk factors, and found that oxytocin augmentation was a
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11 significant risk factor for obstetric anal sphincter injuries in multivariable analyses (OR 2.00;
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13 95% CI 1.13–3.53).⁵ However, these researchers did not stratify by parity or state whether or
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15 not interactions were tested for. Furthermore, three older studies on the risk of obstetric anal
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17 sphincter injury included oxytocin use without differentiating whether oxytocin was provided
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19 for induction or augmentation purposes.²⁶⁻²⁸ Three large population-based studies on the risk
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21 of obstetric anal sphincter injuries did not include oxytocin augmentation in their analyses.<sup>1, 7,
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27 The influence of epidural analgesia on anal sphincter injuries is unclear. Eskandar and
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29 Shet found a reduced risk, but did not stratify by parity.⁹ Dahl and Kjølhed found epidural
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31 analgesia to be an independent protective factor in nulliparous women.¹⁰ Poen et al. stratified
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33 by parity and found a significantly increased odds ratio associated with epidural analgesia in
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35 nulliparous women.²⁹ In our study, epidural analgesia was associated with a significantly
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37 reduced odds ratio for sphincter tears.
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40 Our study takes into account four factors that exert their effect on the anal sphincter
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42 during the final minutes of delivery. As in previous studies,^{1, 3, 5} we found both operative
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44 vaginal delivery and high birth weight to be strongly associated with obstetric anal sphincter
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46 injuries. We found episiotomy to be associated with a lower prevalence of sphincter tears in
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48 operative vaginal deliveries, but not in spontaneous births. This is consistent with a large
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50 national registry study from Norway,¹ but differs from other studies.^{8, 11, 13, 30, 31} In our study,
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52 neither oxytocin augmentation nor episiotomy were associated with obstetric anal sphincter
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54 injury during spontaneous delivery of an infant weighing ≥ 4000 g.
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3 Our methodological approach, stratifying by the factors that are active during the
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5 expulsive phase of labour and testing for confounders, is considered a strength of the study.
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7 This approach leads to a more detailed understanding of how oxytocin augmentation interacts
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9 with these major risk factors. Logistic regression analyses, without testing for possible
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11 interactions, would fail to reveal this information. This case-control study is based on
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13 prospectively collected data from a large unselected population, and represents all deliveries
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15 meeting the inclusion criteria that occurred during the study period, which make bias unlikely.
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17 Our department has a high proportion of vaginal deliveries. The overall caesarean delivery
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19 rate in our institution was 12.5% over the study period. For women in TGCS group 1 the
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21 acute caesarean section rate increased from 5.0% in 1999 to 7.5% in 2012. Accordingly, the
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23 study population includes both high- and low-risk pregnancies, which adds to the external
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25 validity of our results.
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30 However, some limitations apply. We cannot prove causality between oxytocin
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32 augmentation and obstetric anal sphincter injuries in an observational study. Furthermore,
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34 socioeconomic status, smoking, body mass index, maternal delivery positions, perineal
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36 support technique, and the birth attendant's experience level may be possible risk modifiers
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38 not included in our database. Finally, single institution studies, also when based on unselected
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40 populations, should be interpreted with caution.
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44 Our findings have some important implications. Birth attendants should be aware of
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46 the association between oxytocin augmentation and obstetric anal sphincter injuries in the
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48 large subgroup of nulliparous women giving spontaneous birth to a normal-sized infant. More
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50 restrictive use of oxytocin may help prevent obstetric anal sphincter injuries. Implementation
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52 of evidence-based guidelines for using oxytocin augmentation should be encouraged. The
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54 World Health Organization recommends the use of a partogram with an action line defining
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56 failure to progress. However, a recent Cochrane review could not confirm that such a
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3 partogram was beneficial in high resource settings.³² Given the doubtful benefits from
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5 augmentation of labour, randomized controlled trials are strongly needed, and we propose
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7 anal sphincter injury as one of the most important endpoints.
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11 Moreover, our study supports restricted use of episiotomy during normal births and as
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13 a recommendation for operative vaginal deliveries. Birth weight is an important, albeit
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15 unpredictable risk factor as weight estimation of a large fetus is unreliable.³³
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Competing interests

None

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No specific

References

1. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. Trends in risk factors for obstetric anal sphincter injuries in Norway. *Obstet Gynecol* 2010;116:25-34.
2. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. *Acta Obstet Gynecol Scand* 2011;90:319-24.
3. Dudding TC, Vaizey CJ, Kamm MA. Obstetric anal sphincter injury: incidence, risk factors, and management. *Ann Surg* 2008;247:224-37.
4. Sultan AH, Thakar R, Fenner DE. Perineal and anal sphincter trauma : diagnosis and clinical management. New York ; London: Springer; 2009.
5. Jander C, Lyrenas S. Third and fourth degree perineal tears. Predictor factors in a referral hospital. *Acta Obstet Gynecol Scand* 2001;80:229-34.
6. Hornemann A, Kamischke A, Luedders DW, Beyer DA, Diedrich K, Bohlmann MK. Advanced age is a risk factor for higher grade perineal lacerations during delivery in nulliparous women. *Arch Gynecol Obstet* 2010;281:59-64.
7. Handa VL, Danielsen BH, Gilbert WM. Obstetric anal sphincter lacerations. *Obstet Gynecol* 2001;98:225-30.
8. de Leeuw JW, Struijk PC, Vierhout ME, Wallenburg HC. Risk factors for third degree perineal ruptures during delivery. *BJOG* 2001;108:383-7.
9. Eskandar O, Shet D. Risk factors for 3rd and 4th degree perineal tear. *J Obstet Gynaecol* 2009;29:119-22.
10. Dahl C, Kjolhede P. Obstetric anal sphincter rupture in older primiparous women: a case-control study. *Acta Obstet Gynecol Scand* 2006;85:1252-8.
11. Raisanen S, Vehvilainen-Julkunen K, Gissler M, Heinonen S. Hospital-based lateral episiotomy and obstetric anal sphincter injury rates: a retrospective population-based register study. *Am J Obstet Gynecol* 2012;206:347 e1-6.
12. Murphy DJ, Macleod M, Bahl R, Goyder K, Howarth L, Strachan B. A randomised controlled trial of routine versus restrictive use of episiotomy at operative vaginal delivery: a multicentre pilot study. *BJOG* 2008;115:1695-702; discussion 702-3.

13. Carroli G, Mignini L. Episiotomy for vaginal birth. *Cochrane Database Syst Rev* 2009;CD000081.
14. Samuelsson E, Ladfors L, Wennerholm UB, Gareberg B, Nyberg K, Hagberg H. Anal sphincter tears: prospective study of obstetric risk factors. *BJOG* 2000;107:926-31.
15. Prager M, Andersson KL, Stephansson O, Marchionni M, Marions L. The incidence of obstetric anal sphincter rupture in primiparous women: a comparison between two European delivery settings. *Acta Obstet Gynecol Scand* 2008;87:209-15.
16. Blix E, Pettersen SH, Eriksen H, Royset B, Pedersen EH, Oian P. [Use of oxytocin augmentation after spontaneous onset of labor]. *Tidsskr Nor Laegeforen* 2002;122:1359-62.
17. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. *Acta Obstet Gynecol Scand* 2006;85:1094-8.
18. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev* 2011:CD007123.
19. Robson MS. Can we reduce the caesarean section rate? *Best Pract Res Clin Obstet Gynaecol* 2001;15:179-94.
20. Norton C. Anal incontinence. In: Abrams P, Cardozo L, Khoury, Wein A, editors. *Incontinence*. Plymouth: Health Publication Ltd; 2002. p. 985-1044.
21. Agresti A. An introduction to categorical data analysis. 2nd ed. ed. Hoboken, N.J. ; Chichester: Wiley-Interscience; 2007.
22. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev* 2013;9:CD004907.
23. Selin L, Almstrom E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation of labor. *Acta Obstet Gynecol Scand* 2009;88:1352-7.
24. Hals E, Oian P, Pirhonen T, Gissler M, Hjelle S, Nilsen EB, et al. A multicenter interventional program to reduce the incidence of anal sphincter tears. *Obstet Gynecol* 2010;116:901-8.
25. Laine K, Pirhonen T, Rolland R, Pirhonen J. Decreasing the incidence of anal sphincter tears during delivery. *Obstet Gynecol* 2008;111:1053-7.
26. Moller Bek K, Laurberg S. Intervention during labor: risk factors associated with complete tear of the anal sphincter. *Acta Obstet Gynecol Scand* 1992;71:520-4.
27. Haadem K, Ohrlander S, Lingman G. Long-term ailments due to anal sphincter rupture caused by delivery--a hidden problem. *Eur J Obstet Gynecol Reprod Biol* 1988;27:27-32.
28. Legino LJ, Woods MP, Rayburn WF, McGoogan LS. Third- and fourth-degree perineal tears. 50 year's experience at a university hospital. *J Reprod Med* 1988;33:423-6.
29. Poen AC, Felt-Bersma RJ, Dekker GA, Deville W, Cuesta MA, Meuwissen SG. Third degree obstetric perineal tears: risk factors and the preventive role of mediolateral episiotomy. *Br J Obstet Gynaecol* 1997;104:563-6.
30. Hartmann K, Viswanathan M, Palmieri R, Gartlehner G, Thorp J, Jr., Lohr KN. Outcomes of routine episiotomy: a systematic review. *JAMA* 2005;293:2141-8.
31. de Leeuw JW, de Wit C, Kuijken JP, Bruinse HW. Mediolateral episiotomy reduces the risk for anal sphincter injury during operative vaginal delivery. *BJOG* 2008;115:104-8.
32. Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev* 2013;7:CD005461.
33. Campbell S. Fetal macrosomia: a problem in need of a policy. *Ultrasound Obstet Gynecol* 2014;43:3-10.

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(R) In abstract; a cross sectional study, analyzed as case-control study.</p> <hr/> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p> <p>(R) Fulfilled</p>
Introduction		
Background/rationale	2	<p>Explain the scientific background and rationale for the investigation being reported</p> <p>(R) Recent studies have shown the importance of the perineal protection technique in preventing perineal tears. Oxytocin augmentation could impair the control of the perineum during the delivery by causing too fast progress in the last minutes of labour. Oxytocin augmentation is widely used (50% of births). Guidelines for its use are often deficient and the evidence for its positive effect is challenged. Therefore, oxytocin augmentation as a risk factor for obstetric anal sphincter injuries, and should be explored in a study taking other relevant risk factors into account.</p>
Objectives	3	<p>State specific objectives, including any prespecified hypotheses</p> <p>(R) To assess the effect of oxytocin augmentation on obstetric anal sphincter injury among nulliparous women.</p>
Methods		
Study design	4	<p>Present key elements of study design early in the paper</p> <p>(R) Present in Abstract and Methods.</p>
Setting	5	<p>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</p> <p>(R) Setting: Tertiary teaching hospital.</p> <p>Location: Delivery department of Stavanger University Hospital, serving the total obstetric population of the region of South Rogaland.</p> <p>Dates 15 May 1999 – 15 May 2012.</p> <p>Data were collected consecutively.</p>
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants.</p> <p>(R) Nulliparous women with spontaneous start of labour, single, cephalic pregnancy and ≥ 37 weeks gestation who delivered vaginally, where we had access to complete information on the main exposure and the explanatory variables. The source population was the entire obstetric population of the region.</p>
Variables	7	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect</p>

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modifiers. Give diagnostic criteria, if applicable

(R) Outcome: Obstetric anal sphincter injury; that is grade 3 and 4 perineal tears as defined by International Society of Incontinence.

Exposure: Oxytocin augmentation in active labour, that is oxytocin intravenous infusion (5 international units (0.01mg) oxytocin in 500 ml saline) used in incremental doses during active labour.

Predictors: NA

Effect modifiers: Episiotomy, operative vaginal delivery, birth weight <4000 g vs \geq 4000 g.

Potential confounders: maternal age, ethnicity, occiput posterior position, duration of second stage of labour and epidural analgesia.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. (R) All variables are precisely defined in the obstetric databases of Stavanger University Hospital. The grade of perineal injury was assessed during operative repair and plotted directly into the database.
Bias	9	Describe any efforts to address potential sources of bias. (R) In this cross-sectional study all women giving births and who fulfil the inclusion criteria are included. There were very few cases with missing data. We may have missed some cases of perineal injury due to underreporting. The variables are hard variables with clear definitions: Use of oxotocin (yes/no), episiotomy (yes/no), mode of delivery (spontaneous/operative vaginal), birth weight categorized <4000/ \geq 4000 g.
Study size	10	Explain how the study size was arrived at (R) The study size is given by the number of women fulfilling the eligibility criteria and who delivered at Stavanger University Hospital from 15 May 1999 to 15 May 2012.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. (R) Birth weight was categorized into < 4000/ \geq 4000 g.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (R) Chi-square test and stepwise forward logistic regression using IBM SPSS Statistics for Windows, v. 19.0 Armonk, NY: IBM Corp. <hr/> (b) Describe any methods used to examine subgroups and interactions (R) We applied a stratified approach to control for interaction between the main variables (oxytocin augmentation, episiotomy, instrumental delivery and birth weight). Then we tested for confounding and interaction to a modified model by entering one variable at time. <hr/> (c) Explain how missing data were addressed (R) Cases with missing data for estimated date of delivery were excluded. Cases with

other missing data were recoded to the reference value in the logistic regression analyses. Very few cases with missing data (n=52).

(d) If applicable, describe analytical methods taking account of sampling strategy

(R) NA

(e) Describe any sensitivity analyses

(R) NA

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(R) Potentially eligible: 15 545 Confirmed eligible: 15 493 Included/analyzed: 15 493</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(R) Cases with missing data for estimated date of delivery were excluded (n=52)</p> <p>(c) Consider use of a flow diagram</p> <p>(R) Not useful in this study.</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(R) Given in Table 1.</p> <p>The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity.</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(R) Cases with missing data for estimated date of delivery were excluded from the study population (n=52)</p> <p>Recoded to the reference category of the variable and included in the analyses:</p> <p>Birth weight 3 cases. Maternal age 2 cases. Lie at delivery 8 cases. Duration of second stage of labour 92 cases.</p>
Outcome data	15*	<p>Report numbers of outcome events or summary measures</p> <p>(R) Table 1.</p> <p>Outcome event, the dependant variable, anal sphincter injury: 1014 cases.</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(R) Table 2 and 3. Confounders: paragraph 4 in Material and Methods.</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(R) Table 1</p>

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(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

(R) NA

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses R) NA
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Discussion

Key results	18	Summarise key results with reference to study objectives (R) Fulfilled.
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Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (R) Bias regarding main outcome: We do not know the magnitude of underreporting of anal sphincter tear grade 3 and 4, however believe this to be low. Bias regarding main exposure: The quality system of the department relies on honest reporting by midwives and obstetricians, and has been a cornerstone in the systematic interdisciplinary work towards better clinical outcomes since 1996. We have reason to believe that ownership to the concept has resulted in good adherence to the reporting routines, and we believe the reporting of oxytocin augmentation to be a robust measure of what was actually practised. The midwives plotting the information were not aware of any research issue related to oxytocin augmentation. We consider the other main exposure variables to be robust: It is unlikely that reports of episiotomy, instrumental delivery and birth weight are skewed in any direction. The same applies to the possible confounders age, ethnicity, occiput posterior position and epidural analgesia. We believe that the reporting of these variables reflects the actual practice. Therefore we consider the estimates for risks related to anal sphincter tear grade 3 and 4 to be precise with little bias. Our stratified approach, modified model, takes care of the interaction problems between episiotomy, operative vaginal delivery, birth weight and oxytocin augmentation.
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Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (R) Fulfilled.
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Generalisability	21	Discuss the generalisability (external validity) of the study results. (R) The study participants represent the total population of women fulfilling the inclusion criteria in a Norwegian region of 320 000 people. The study population is heterogeneous with regard to obstetric risk (overall caesarean section rate 12,5%), social status and ethnicity. This adds value to the external validity of the study results. We encourage other study groups to make research on the effect of oxytocin augmentation on anal sphincter injury in other populations.
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Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if
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applicable, for the original study on which the present article is based
(R) No specific funding.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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