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Risk factors and between-hospital variation of caesarean section in Denmark: a cohort study

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Risk factors and between-hospital variation of caesarean section in Denmark: a cohort study

Short running title: Caesarean section: risk and variation

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Abstract

Objectives The aim of this study was to estimate the effects of risk factors on elective and emergency caesarean section (CS) and to examine between-hospital variation of risk-adjusted CS proportions.

Design Historical registry-based cohort study.

Settings and participants The study was based on all singleton deliveries in hospital units in Denmark from January 2009 to December 2012. A total of 226,612 births by 198,590 mothers in 29 maternity units were included.

Primary and secondary outcome measures We estimated 1) odds ratios (OR) of elective and emergency CS adjusted for several risk factors, e.g. body mass index, parity, age, and size of maternity unit and 2) risk-adjusted proportions of elective and emergency CS to evaluate between-hospital variation.

Results The CS proportion was stable at 20-21%, but showed wide variation between units, even in adjusted models. Large units performed significantly more elective CSs than smaller units, but the risk of emergency CS was significantly reduced compared to smaller units. Many of the included risk factors were found to influence the risk of CS. The most important risk factors were breech presentation and previous CS. Four units performed more CSs and one unit fewer CSs than expected.

Conclusion The main risk factors for elective CS were breech presentation and previous CS; for emergency CS they were breech presentation and cephalopelvic disproportion. The proportions of CS were stable during the study period. We found a variation in risk-adjusted CS between hospitals in Denmark. Although exhaustive models were applied, the results indicated the presence of systematic variation between hospital units, which was unexpected in a small, well-regulated country such as Denmark.

Keywords: Obstetrics, Epidemiology, Quality in health care

Abbreviations:

CS = Caesarean section

OR = Odds ratio

CI = Confidence Interval

Strengths and limitations of this study

- Our study was population-based, covering four calendar years and a high number of deliveries and investigating the effects of a wide range of risk factors for elective CS and emergency CS, both maternal-related, foetal-related, labour-related, and unit-related factors.
- The Danish Medical Birth Register includes data on all births at hospital maternity units, where 99% of all Danish births take place.
- This study has all the limitations inherent to a historical registry-based cohort study design, where the coding of events was done after the end of delivery.
- The lack of knowledge about the actual decision for CS is another weakness of this study. Specifically, the term "emergency CS" covers a broad range of situations in a maternity ward, as emergency CS is seen as a homogenous group and distinctions are not made between degrees of urgency.
- Data for this study comes from one country in Northern Europe only, and Denmark is a small, well-regulated country with equal and free access to health services. Even though data homogeneity might be regarded as strength, transferability of the results to other countries is limited.

Introduction

Caesarean section (CS) is one of the essential factors in reducing the risk of intrapartum foetal death. Nevertheless, CS can also cause several complications. For the mother, surgical complications such as bleeding, infection and thrombosis may occur [1], and the risk of uterine rupture and placenta praevia in subsequent pregnancies is increased [2]. Overall, CS has been associated with a higher risk of severe maternal morbidity and mortality as compared with vaginal delivery [3]. For the child, there is a higher risk of neonatal complications such as respiratory distress syndrome, pulmonary hypertension, and iatrogenic prematurity as these conditions occur more often after CS [1,4].

The average proportion of CS has increased dramatically in many countries over the last three decades [5-7]. The World Health Organization states that at population level, caesarean section rates higher than 10% are not associated with reductions in maternal and newborn mortality rates [8], and other studies suggest that proportions above this limit may do more harm than good [9,10]. In Denmark, the CS proportion reached 21% in 2012 [11] as compared with 5% in 1973 [12]. Although this rise has been influenced by many factors such as the increasing age of nulliparous women, the increasing number of pregnant women with previous CS, a greater maternal preference for CS, and changes in women's clinical risk profiles (e.g. higher prevalence of pre-existing diseases/obesity) [13], the reasons for the steep rise remain mysterious.

Besides this general increase in CS, a large variation between countries [10,14,15], regions [6], and hospitals [5,16] has been documented. The variation for emergency CS has been reported to be larger than that for elective CS [5]. Even when proportions were risk-adjusted [5] or restricted to subgroups of women [17,18], the large variation tended to persist, which suggests a strong systematic component. Systematic variation between units could have occurred if key factors were missed in the risk-adjustment and/or guidelines on CS decision were not sufficiently defined or followed to the letter [6].

In Denmark, the CS proportions for 2012 varied between hospital units, ranging from 5% to 27% [11], but the results for risk-adjusted proportions have not been published so far. Based on population-based Danish registry data, we set out to define exhaustive models for the probability of elective or emergency CS, covering a wide range of potential risk factors.

This study aimed to 1) examine the effects of potential risk factors on the risk of delivery by CS, and 2) assess the between-hospital variation of the risk-adjusted CS proportions.

Methods

Data sources

The data source was the Danish Medical Birth Register, which was established in 1973 and includes data on all births at hospital maternity units, where 99% of all Danish births take place. The registry contains information on, for example, parity, birth weight, gestational age, diagnoses regarding pre-pregnancy risk factors, medical diseases, and complications and interventions during pregnancy and delivery. The recorded information is based largely on diagnostic codes such as those found in the International Classification of Diseases, 10th Revision (ICD-10) and procedure codes such as those in the Nordic Medico-Statistical Committee (NOMESCO) classification of surgical procedures. The study period was from 1st January 2009 to 31st December 2012, during which time there were 229,041 singleton births in 32 different maternity units. This number includes both live and stillborn children from gestational week 24 and excludes births after abortion procedure. Births were subsequently excluded if they were registered 1) in very small units with fewer than 100 births per year (in total 28 births from three units), 2) with invalid code for the maternity unit (N=33 births), 3) with missing or incorrect birth diagnosis (N=251), 4) with inconclusive mode of delivery (N=1766), and 5) for mothers younger than 15 or older than 44 years of age, limits inspired by similar limits in a prior study [9] (N=351). Thus, 226,612 singleton births (98.9%) by 198,590 mothers in 29 maternity units were included in the study; 27,651 women had more than one singleton birth during the study period.

Outcome measures

The mode of delivery was classified as elective CS, emergency CS, or vaginal birth (Table S1), where all non-elective CS were classified as emergency CS. Firstly, we analysed the proportion of – and risk for – *elective* CS among all singleton deliveries, and secondly, the proportion of – and risk for – *emergency* CS among all singleton deliveries after excluding those by elective CS. Finally, similar analyses were performed in a low-risk subgroup of nulliparous women giving birth to a child in cephalic presentation at ≥ 37 weeks+0 days in spontaneous labour (definition comparable to Robson's group 1 [19]).

Risk factors

A number of risk factors for CS were included. These were maternal-related factors: age, prenatal smoking, body mass index (BMI), maternal height below 163cm, parity and the complication

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4 factors of diabetes (both gestational and pre-existing), hypertension, pre-eclampsia/eclampsia,
5 placenta praevia (which might have been registered in gestational week 20 at an ultrasound
6 examination and thus may not represent praevia at the time of labour)/placental abruption, and
7 premature rupture of membranes; foetal-related factors: gestational age (in weeks+days), sex and
8 macrosomia (birthweight above 4500g); labour-related factors: stimulation with oxytocin infusion
9 during delivery, induction of labour, foetal presentation, cephalopelvic disproportion and foetal
10 distress; and maternity unit-related factors: size of maternity unit based on numbers of births per
11 year, weekend delivery (Saturday, Sunday and all national holidays), and night delivery (deliveries
12 between 8.00 p.m. to 7.59 a.m.). Missing values of risk factors were treated as no exposure. For
13 detailed definitions of the risk factors and their categorization see Table S2.
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21 *Statistical analysis*

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23 To estimate the effect of the risk factors on the probability of elective or emergency CS, three
24 separate multivariable logistic regression models were fitted, with clusters taken into account. They
25 were used to define risk-adjusted proportions as follows. Summing up the probabilities predicted by
26 the logistic model over deliveries for each maternity unit yielded the predicted proportion per unit.
27 Dividing the observed proportion per unit by the predicted proportion multiplied by the mean
28 national proportion yielded the risk-adjusted proportion per maternity unit. Funnel plots [20] were
29 created for risk-adjusted proportions for both elective and emergency CS; the basis for comparison
30 and confidence was the mean national unadjusted proportion. To incorporate heterogeneity, funnel
31 plot limits were adjusted by an additive over-dispersion term (i.e., an estimate of the between-unit
32 variability, reported as standard deviation in %) based on a random-effects model approach [21].
33 The corresponding test of heterogeneity between maternity units was reported [21]. In addition,
34 variation coefficients between maternity units were calculated. A coefficient of variation is defined
35 as the standard deviation divided by the mean. All analyses were performed using Stata software
36 (StataCorp LP, College Station, TX, USA).
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47 *Ethics approval*

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49 The study was approved by the Danish Data Protection Agency (no. 2013-41-1561).
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51 According to Danish law, review by an ethics board or patient consent is not required for purely
52 register-based studies.
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Results

Analyses were based on 226,612 singleton births. The number of births per maternity unit ranged from 383 to 11,300. There was a 9% decrease of singleton births in Denmark over the study period, from a total of 58,880 in 2009 to 53,574 in 2012 (Table 1). In total, about a fifth (N=45,925, 20.3%) ended in CS, including 19,620 (8.7%) elective CSs (Tables 1+2). Both the overall CS proportion and the proportion of elective CS remained stable at about 20% and 9%, respectively (Tables 1+2). The risk of emergency CS remained stable across the study period for small and medium-sized units, while the risk decreased significantly from 2009 to 2010 for large maternity units and thereafter remained stable (results not shown).

Risk factors for caesarean section

The multivariable odds ratios (ORs) of all risk factors for elective CS included in the logistic model are presented in Table 1. All the included risk factors had an impact on the risk of elective CS except for maternal smoking, maternal height, macrosomia, and sex. The most important risk factors were breech presentation (OR 24.02 [95%CI 22.45-25.7]) and previous CS (OR 16.9 [95%CI 16.08-17.75]). Elective CS was the mode of delivery for 50% of all breech presentations and for 40% with previous CS.

The multivariable ORs of all risk factors for emergency CS are presented in Table 2. Overall, the mean proportion of emergency CS was 12.7%. Over the four-year study period the proportion of emergency CS fell slightly but consistently from 13.1% in 2009 to 12.3% in 2012 (OR 0.93 [95%CI 0.89-0.98], using 2009 as reference). The majority of the included risk factors influenced the risk of emergency CS. The most important risk factors were breech presentation (OR 43.73 [95%CI 40.01-47.79]) and cephalopelvic disproportion (OR 13.96 [95%CI 12.91-15.10]). The risk for emergency CS remained unchanged regardless of the day of the week (OR 1.00 [95%CI 0.97-1.03]), but was slightly less at night compared to daytime (OR 0.93 [95%CI 0.90-0.95]).

Breech presentations with intended vaginal delivery ended with emergency CS in almost 80% of the cases. About two thirds of the women with intended vaginal delivery after previous CS succeeded in having vaginal birth. Nonetheless, the corresponding risk for emergency CS was significantly higher for these women compared with that for nulliparous women (OR 2.97 [95%CI 2.84-3.10]). The risk for emergency CS was lowest for multiparous women without previous CS (OR 0.25 [95%CI 0.24-0.27]).

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4 The (registered) occurrence of maternal complication factors ranged from below 1% for diabetes
5 and placenta praevia/placental abruption to 2-3% for hypertension and pre-eclampsia/eclampsia up
6 to 8% for premature rupture of membranes. In these groups, the proportion of emergency CS was at
7 least about 20% for diabetes, hypertension, and membrane rupture; 36% for pre/eclampsia; 64% for
8 placenta praevia and 68% for placental abruption. The OR for the combined complication factor
9 was 1.98 [95%CI 1.90-2.06]. In this study population there were 1128 women with reported
10 placenta praevia, and of these, 932 (83%) underwent CS. An elective procedure was registered for
11 511 (45%) of these women.

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17 The results for emergency caesarean section in the low-risk nulliparous subgroup are presented in
18 Table 3. The risk factors were largely distributed as in the full dataset. However, women in the
19 subgroup were younger on average (mean age 28.3 compared with 30.1 in the full dataset),
20 relatively more women had labour stimulation (44% versus 29%), and foetal distress was reported
21 more often (30% versus 21%).

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25 The mean proportion of emergency CS was about one percent lower in the low-risk subgroup
26 (11.8%) than in the full dataset. Overall, the emergency CS proportions with respect to risk factors
27 in the subgroup were within +/- 5% of those in the full dataset, except for macrosomia (33.4%
28 emergency CS in the subgroup as compared with 20.8% in the full dataset). Moreover, the ORs
29 resulting from the logistic model in the subgroup were predominantly similar to those of the full
30 dataset. However, the ORs differed for night delivery (a significantly higher risk for emergency CS
31 at night in the subgroup; OR 1.05 [95 % CI 1.0-1.1] versus 0.93 [95 % CI 0.9-0.95] in the full
32 dataset), stimulated labour (1.57 [95%CI 1.49-1.66] versus 1.01 [95%CI 0.98-1.05]), and
33 macrosomia (3.36 [95%CI 2.92-3.87] versus 2.58 [95%CI 2.38-2.79]).

34 35 36 37 38 39 40 41 *Between-hospital variation of risk-adjusted caesarean section proportions*

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43 The median of the observed proportion of elective CS in maternity units was 8.5% with a minimum
44 of 3.6% and a maximum of 10.6%. Risk-adjusted proportions ranged from 5.8% to 9.9% (median
45 8.6%, 25%-75% percentiles: 8.0-9.2), Figure 1, upper part. There was statistically significant
46 heterogeneity among maternity units (p -value < 0.001). Allowing for little over-dispersion (1.1%),
47 no hospital maternity unit was outside the upper 95% funnel limit. However, one medium-sized unit
48 was below the corresponding lower limit, indicating that this unit performed systematically fewer
49 elective CS than expected.
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4 The median of the observed proportion of emergency CS in maternity units was 12.7% with a
5 minimum of 7.0% and a maximum of 17.1%. Risk-adjusted proportions ranged from 9.2% to 19.3%
6 (median 12.2%, 25%-75% percentiles: 11.5-13.5), Figure 1, middle part. There was statistically
7 significant heterogeneity among the 29 maternity units (p -value < 0.001). Taking the estimated
8 over-dispersion (1.5%) into account, there were few maternity units outside the 95% funnel limits:
9 one small unit was below the 95% lower limit and four units (two small, one medium, and one
10 large) were above the 95% upper limit, indicating that the latter units systematically performed
11 more emergency CSs than expected.

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13 In the emergency subgroup the observed emergency CS proportions ranged from 7.8% and 19%
14 (median 11.6%) between maternity units, and risk-adjusted emergency CS proportions ranged from
15 8% to 23.2% (median 11.5%, 25%-75% percentiles: 10.1-14.2), Figure 1, lower part. Risk-adjusted
16 proportions showed statistically significant heterogeneity among maternity units (p -value < 0.001).
17 No hospital maternity unit was below the lower 95% funnel limit (over-dispersion 2.2%). However,
18 two medium-sized units and one large unit were above the corresponding upper limit, indicating
19 systematically more emergency CSs than expected.

20 21 22 23 24 25 26 27 28 29 30 **Discussion**

31 Our study showed that mostly all of the included risk factors had an influence on the risk of CS.
32 Breech presentation and previous CS were found to have the largest impact on elective CS; on
33 emergency CS it was breech presentation and cephalopelvic disproportion. As the proportions of
34 elective and emergency CS were stable throughout the four-year study period, the steep increase of
35 the overall CS proportion in Denmark seems to have stopped. As for organizations, large hospital
36 units performed significantly more elective CSs than smaller units, and the risk and performance of
37 emergency CS was significantly reduced in the larger maternity units compared with small and
38 medium units, which would be expected since there is a centralization of risk births (e.g. congenital
39 anomalies, significant maternal comorbidity) in Denmark. We also found substantial heterogeneity
40 of risk-adjusted CS between Danish maternity units, with higher variation in emergency CS than in
41 elective CS. Even though we applied exhaustive regression models covering a wide range of risk
42 factors, the results still indicated the presence of systematic, i.e. larger than random, variation
43 between hospital units.

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52 Our study had all the limitations inherent to a historical registry-based cohort study design. Coding
53 was done after the end of delivery, implying that the registration of diagnoses for which there are no
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4 precise definitions, for instance, cephalopelvic disproportion [16], might not have been adequate.
5 This has to be taken into consideration when comparing results across studies. For example, based
6 on ICD-10 codes, only 2% of the women in our study had a reported cephalopelvic disproportion,
7 whereas a prior study from the United Kingdom showed that cephalopelvic disproportion was the
8 primary indication for CS in 35% of the women [22].
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11 It is possible that most of the risk factors in our study may not have had an independent, direct
12 causal effect on the CS proportion, even if they were highly significant. For example, the risk factor
13 of labour induction [23] may be linked to a latent unknown status of "problematic delivery", which
14 in turn is linked to CS probability. The lack of knowledge about the decision for CS is another
15 weakness of this study. Specifically, the term "emergency CS" covers a broad range of situations in
16 a maternity ward, as emergency CS is seen as a homogenous group and distinctions are not made
17 between degrees of urgency [24]. Some CSs are performed immediately because of a life-
18 threatening situation, and others are performed for other, non-life-threatening reasons. Former
19 studies have shown that the CS proportions are influenced by a variety of different settings such as
20 the use of foetal monitoring, partograms, or the active management of labour [24-26]. As a first
21 step, the quality of registration in the Medical Birth Register will improve when the degree of
22 urgency is included [27].
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33 To ensure the same quality of care for all women (in Denmark), there should not be any systematic
34 differences in CS decision-making between maternity units, and thus such systematic variation
35 between units should be eliminated. Starting points for such a process could be i) a retrospective
36 inspection of the hospital birth records of the women in our study who were classified as low risk
37 but still underwent CS, which could shed light on the premises for CS decisions, and ii) a
38 comparative prospective study with a specific focus on the precise circumstances influencing the
39 decision to perform a CS (when, why, who) and including units with both fewer and more CSs than
40 expected, which would enable the identification of important key factors that were missed in our
41 study. Besides acquiring more clinical details, the role of women's preferences and the various ways
42 of making clinical decisions in different areas need to be investigated more thoroughly. The World
43 Health Organization recommends that other relevant outcomes such as short- and long-term
44 maternal and paediatric outcomes (including stillbirths and breastfeeding) as well as the
45 psychological or social well-being of both mother and child after birth [8] should be included in
46 future studies. Many obstetricians regard the CS proportion of 20% as too high [22], and with
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4 clearer consensus on when to perform CS, there will be an enhanced possibility of reducing the CS
5 proportion. Recent years have seen the development of a national cardiotocography education
6 program in Denmark with the aim of reducing foetal distress [28]. It has been implemented in all
7 maternity units in the country and includes the education and certification of midwives and
8 obstetricians in cardiotocography.
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13 **Conclusion**

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15 Our study showed that the risk of CS is influenced by several risk factors and also confirmed well-
16 known risk factors. The largest impact on elective CS was found to be breech presentation and
17 previous CS; on emergency CS it was breech presentation and cephalopelvic disproportion. We also
18 found a variation in risk-adjusted CS between Danish hospitals, which was unexpected for such a
19 small, well-regulated country like Denmark. The prior increase of the overall CS proportion in
20 Denmark seems to have stopped, as the proportions of elective and emergency CS were stable
21 throughout the study period. To ensure the same quality of care across the country, CS practices in
22 hospital maternity units should be compared and, if possible, harmonised. Furthermore, the possible
23 lack of consensus about clinical practice as well as the attitudes of parents and healthcare
24 professionals towards mode of delivery should be investigated further.
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33 **Conflict of interest and funding statement**

34 All the authors declare that they had no support from any organisations for the submitted work, that
35 in the last three years they had no financial relationships with any organisations which might have
36 had an interest in the submitted work, and that they did not have any other relationships or
37 undertake any activities that could appear to have influenced the submitted work. The submitted
38 research received no specific grant from any funding agency in the public, commercial or not-for-
39 profit sectors.
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46 **Contributorship statement**

47 SW, RG and BMN devised the concept of the study. SW did the data management and data
48 analysis. RG, SW and BMN drafted the article. All authors revised the manuscript and approved the
49 final version.
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54 **Data sharing statement**

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4 No additional data available.
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7 **Acknowledgement**

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References

1. Grivell RM, Dodd JM. Short- and long-term outcomes after cesarean section. *Expert Rev Obstet Gynecol.* 2011;6(2):205-215.
2. Hemminki E, Meriläinen J. Long-term effects of cesarean sections: Ectopic pregnancies and placental problems. *Am J Obstet Gynecol.* 1996;174(5):1569-1574.
3. Villar J, Carroli G, Zavaleta N, Donner A, Wojdyla D, Faundes A et al. Maternal and neonatal individual risks and benefits associated with caesarean delivery: multicentre prospective study. *BMJ.* 2007;335:1003-1004.
4. Shorten A. Maternal and neonatal effects of caesarean section. *BMJ.* 2007;335:1003.
5. Bragg F, Cromwell DA, Edozien LC, Gurol-Urganci I, Mahmood TA, Templeton A et al. Variation in rates of caesarean section among English NHS trusts after accounting for maternal and clinical risk: cross sectional study. *BMJ.* 2010;341:c5065.
6. Clark SL, Belfort MA, Hankins GD, Meyers JA, Houser FM. Variation in the rates of operative delivery in the United States. *Am J Obstet Gynecol.* 2007;196:526.e1-526.e5.
7. Sydsjö G, Sydsjö A, Brynhildsen J, Josefsson A. Trend in caesarean section and instrumental deliveries in relation to Body Mass Index: a clinical survey during 1978 – 2001. *Reprod Health.* 2010;7:18.
8. World Health Organization. WHO Statement on Caesarean Section Rates. Geneva: World Health Organization; 2015 (WHO/ RHR/15.02).
9. Althabe F, Belizán JM. Caesarean section: the paradox. *Lancet.* 2006;368:1472-1473.
10. Betrán AP, Merialdi M, Lauer JA, Bing-Shun W, Thomas J, Van Look P et al. Rates of caesarean section: analysis of global, regional and national estimates. *Paediatr Perinat Epidemiol.* 2007;21:98-113.
11. Fødsler 1997- [Web-portal for interactive data exploration and retrieval on Births: 1997-]. Available online at: <http://www.esundhed.dk/sundhedsregistre/MFR/Sider/MFR06A.aspx> (Accessed February 26, 2016).
12. Fødsler: 1973- [Web-portal for interactive data exploration and retrieval on Births: 1973-]. Available online at: <http://www.esundhed.dk/sundhedsregistre/MFR/Sider/MFR01.aspx> (Accessed February 26, 2016).
13. Poobalan AS, Aucott LS, Gurung T, Smith WC, Bhattacharya S. Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women – systematic review and meta-analysis of cohort studies. *Obes Rev.* 2009;10(1):28-35.

14. Macfarlane AJ, Blondel B, Mohangoo AD, Cuttini M, Nijhuis J, Novak Z et al. Wide differences in mode of delivery within Europe: risk-stratified analyses of aggregated routine data from the Euro-Peristat study. *Br J Obstet Gynaecol*. 2016;123(4):559-68.
15. García-Armesto S, Angulo-Pueyo E, Martínez-Lizaga N, Mateus C, Joaquim I, Bernal-Delgado E et al. Potential of geographical variation analysis for realigning providers to value-based care. ECHO case study on lower-value indications of C-section in five European countries. *Eur J Public Health*. 2015;25 Suppl 1:44-51.
16. Librero J, Peiró S, Calderón SM. Inter-hospital variations on caesarean sections. A risk adjusted comparison in the Valencia public hospitals. *J Epidemiol Community Health*. 2000;54:631-636.
17. Nippita TA, Lee YY, Patterson JA, Ford JB, Morris JM, Nicholl MC et. Variation in hospital caesarean section rates and obstetric outcomes among nulliparae at term: a population-based cohort study. *Br J Obstet Gynaecol*. 2015;122(5):702-11.
18. Kozhimannil KB, Arcaya MC, Subramanian SV. Maternal Clinical Diagnoses and Hospital Variation in the Risk of Cesarean Delivery: Analyses of a National US Hospital Discharge Database. *PLoS Med*. 2014;11(10):e1001745.
19. Robson MS. Classification of caesarean sections. *Fetal and maternal medicine review*. 2001;12:23-39.
20. Spiegelhalter DJ. Funnel plots for comparing institutional performance. *Stat Med*. 2005;24:1185-1202.
21. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-188.
22. Thomas J, Paranjothy S. Royal College of Obstetricians and Gynaecologists Clinical Effectiveness Support Unit: The National Sentinel Caesarean Section Audit Report. 2001, London: RCOG Press.
23. Yogev Y, Hiersch L, Yariv O, Peled Y, Wiznizer A, Melamed N. Association and risk factors between induction of labor and cesarean section. *J Matern Fetal Neonatal Med*. 2013;26(17):1733-6.
24. National Collaborating Centre for Women's and Children's Health commissioned by The National Institute for Health and Clinical Excellence, Caesarean section. NICE Clinical Guideline. 2011, London: RCOG Press.

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- 4 25. Alfirevic Z, Devane D, Gyte GML. Continuous cardiotocography (CTG) as a form of
- 5 electronic fetal monitoring (EFM) for fetal assessment during labour. Cochrane Database of
- 6 Systematic Reviews. 2006;3:CD006066.
- 7
- 8
- 9 26. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management
- 10 in labour for reducing caesarean section rates in low-risk women. Cochrane Database of
- 11 Systematic Reviews. 2008;4:CD004907.
- 12
- 13 27. Kesmodel US, Jølving LR. Measuring and improving quality in obstetrics - the
- 14 implementation of national indicators in Denmark. Acta Obstet Gynecol Scand.
- 15 2011;90(4):295-304.
- 16
- 17 28. Thellesen L, Hedegaard M, Bergholt T, Colov NP, Hoegh S, Sorensen JL. Curriculum
- 18 development for a national cardiotocography education program: a Delphi survey to obtain
- 19 consensus on learning objectives, Acta Obstet Gynecol Scand. 2015;869-877.
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Table 1. Elective caesarean section. Distribution of singleton deliveries and proportion of elective CS according to risk factors, all included in a multivariable logistic regression model. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	All deliveries		Elective CS	
	N (%)	N (% within category)	OR	95% CI
Singleton deliveries	226 612 (100)	19 620 (8.7)		
Year				
2009	58 880 (27)	5186 (8.8)	1.00	
2010	59 139 (27)	4973 (8.4)	0.94	0.89-0.99
2011	55 099 (24)	4773 (8.7)	0.92	0.87-0.97
2012	53 574 (24)	4688 (8.8)	0.95	0.90-1.00
Size of maternity unit				
Small	13 638 (6)	884 (6.5)	0.74	0.68-0.81
Medium	97 653 (43)	8746 (9.0)	1.00	
Large	115 321 (51)	9990 (8.7)	1.08	1.04-1.12
Weekend delivery (yes)	60 993 (27)	260 (0.4)	0.03	0.03-0.04
Night delivery (yes)	100 718 (44)	361 (0.4)	0.02	0.02-0.02
Maternal age (years)				
15-19	3292 (1)	93 (2.8)	0.62	0.50-0.77
20-34	176 722 (78)	13 179 (7.5)	1.00	
35-44	46 598 (21)	6348 (13.6)	1.58	1.51-1.66
Maternal smoking (yes)	28 150 (12)	2157 (7.7)	0.99	0.93-1.05
Maternal BMI				
14.0-18.4	9321 (4)	642 (6.9)	1.02	0.92-1.13
18.5-24.9	142 597 (63)	10 986 (7.7)	1.00	
25.0-29.9	46 731 (21)	4593 (9.8)	1.17	1.11-1.22
30-34.9	18 291 (8)	2093 (11.4)	1.37	1.29-1.47
35.0+	9672 (4)	1306 (13.5)	1.56	1.43-1.70
Maternal height <=163 cm (yes)	55 288 (24)	5389 (9.7)	1.05	1.00-1.09
Parity				
Nulliparous	104 448 (46)	5299 (5.1)	1.08	1.03-1.14
Multiparous without previous CS	96 166 (42)	3855 (4.0)	1.00	
Multiparous with previous CS	25 998 (11)	10 466 (40.3)	16.9	16.08-17.75
Complication factors				
Diabetes	422 (0.2)	42 (10.0)		
Hypertension	3954 (2)	356 (9.0)		
Pre-eclampsia/Eclampsia	6257 (3)	385 (6.2)		
Placenta praevia	1128 (0.5)	511 (45.3)		
Placental abruption	938 (0.4)	16 (2)		
Premature rupture of membranes	17 548 (8)	98 (0.6)		
Complication (yes)	29 461 (13)	1374 (4.7)	0.46	0.42-0.50
Term				
< 37+0	10 992 (5)	615 (5.6)	0.28	0.25-0.32
37+0 – 41+6	205 338 (91)	18 897 (9.2)	1	
>= 42+0	10 282 (5)	108 (1.1)	0.12	0.10-0.15
Female baby (yes)	110 397 (49)	9812 (8.9)	1.01	0.97-1.05
Breech presentation (yes)	8979 (4)	4382 (48.8)	24.02	22.45-25.70
Macrosomia (yes), >4500g	6220 (3)	578 (9.3)	1.11	0.98-1.25

Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval

Table 2. Emergency caesarean section. Distribution of deliveries (all singleton deliveries without deliveries by elective CS) and proportion of emergency CS according to risk factors. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	Deliveries	Emergency CS		
	N (%)	N (% within category)	OR	95% CI
Singleton deliveries minus elective CS	206 992 (100)	26 305 (12.7)		
Year				
2009	53 614 (27)	7003 (13.1)	1.00	
2010	54 166 (27)	7023 (13.0)	0.96	0.92-1.00
2011	50 326 (24)	6271 (12.5)	0.90	0.86-0.94
2012	48 886 (24)	6008 (12.3)	0.93	0.89-0.98
Size of maternity unit				
Small	12 754 (6)	1464 (11.5)	1.02	0.95-1.09
Medium	88 907 (43)	11 292 (12.7)	1.00	
Large	105 331 (51)	13 549 (12.9)	0.90	0.87-0.93
Weekend delivery (yes)	60 733 (29)	7763 (12.8)	1.00	0.97-1.03
Night delivery (yes)	100 357 (48)	12 046 (12.0)	0.93	0.90-0.95
Maternal age (years)				
15-19	3199 (2)	309 (9.7)	0.60	0.52-0.69
20-34	163 543 (79)	20 034 (12.3)	1.00	
35-44	40 250 (19)	5962 (14.8)	1.48	1.42-1.53
Maternal smoking (yes)	25 993 (13)	3571 (13.7)	1.10	1.05-1.15
Maternal BMI				
14.0-18.4	8679 (4)	774 (8.9)	0.77	0.70-0.84
18.5-24.9	131 611 (64)	14 658 (11.1)	1.00	
25.0-29.9	42 138 (20)	6147 (14.6)	1.34	1.29-1.39
30-34.9	16 198 (8)	2929 (18.1)	1.75	1.66-1.84
35.0+	8366 (4)	1797 (21.5)	2.07	1.94-2.22
Maternal height <=163 cm (yes)	49 899 (24)	8701 (17.4)	1.67	1.62-1.73
Parity				
Nulliparous	99 149 (48)	16 712 (16.9)	1.00	
Multiparous without previous CS	92 311 (45)	3985 (4.3)	0.25	0.24-0.27
Multiparous with previous CS	15 532 (8)	5608 (36.1)	2.97	2.84-3.10
Complication factors				
Diabetes	380 (0.2)	74 (19.5)		
Hypertension	3598 (2)	707 (19.6)		
Pre-eclampsia/Eclampsia	5872 (3)	2110 (35.9)		
Placenta praevia	617 (0.3)	420 (68.1)		
Placental abruption	967 (0.5)	622 (64.3)		
Premature rupture of membranes	17 450 (8)	3536 (20.3)		
Complication (yes)	28 087 (14)	7129 (25.4)	1.98	1.90-2.06
Stimulated labour (yes)	59 228 (29)	9825 (16.6)	1.01	0.98-1.05
Any induced labour (yes)	38 767 (19)	7128 (18.4)	1.40	1.35-1.46
.. induced by medication	27 166 (13)	5303 (19.5)		
.. induced by operation	21 359 (10)	3882 (18.2)		
Term				
< 37+0	10 377 (5)	3823 (36.8)	2.94	2.77-3.12
37+0 – 41+6	186 441 (90)	20 400 (10.9)	1.00	
>= 42+0	10 174 (5)	2082 (20.5)	1.77	1.67-1.89
Female baby (yes)	100 585 (49)	11 923 (11.9)	0.88	0.85-0.91
Breech (yes)	4597 (2)	3607 (78.5)	43.73	40.01-47.79
Foetal distress (yes)	42 963 (21)	9803 (22.8)	2.37	2.28-2.45
Cephalopelvic disproportion (yes)	3911 (2)	2551 (65.2)	13.96	12.91-15.1

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4 **Macrosomia (yes)** 5642 (3) 1173 (20.8) 2.58 (2.38-2.79) 2.38-2.79

5 Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval

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Table 3. Emergency caesarean sections in a low-risk subgroup (nulliparous women who gave birth to a child in cephalic presentation at ≥ 37 weeks + 0 days in spontaneous labour). Distribution of subgroup births and proportion of emergency CS according to risk factors. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	Subgroup, all N (% of all)	Emergency CS N (% within category)	OR	95% CI
Singleton deliveries, subgroup	74 002 (100)	8698 (11.8)		
Year				
2009	19 353 (26)	2357 (12.2)	1.00	
2010	19 186 (26)	2338 (12.2)	0.95	0.89-1.02
2011	17 884 (24)	1994 (11.2)	0.87	0.81-0.93
2012	17 579 (24)	2009 (11.4)	0.94	0.88-1.01
Size of maternity unit				
Small	4343 (6)	543 (12.5)	1.02	0.92-1.13
Medium	27 970 (38)	3416 (12.2)	1.00	
Large	41 689 (56)	4739 (11.4)	0.82	0.77-0.86
Weekend delivery (yes)	22 516 (30)	2672 (11.9)	1.02	0.97-1.08
Night delivery 20.00-07.59 (yes)	35 380 (48)	4239 (12.0)	1.05	1.00-1.10
Maternal age (years)				
15-19	2282 (3)	158 (6.9)	0.65	0.55-0.78
20-34	64 080 (87)	7106 (11.1)	1.00	
35-44	7640 (10)	1434 (18.8)	1.76	1.64-1.89
Maternal smoking (yes)	9708 (13)	1143 (11.8)	1.04	0.97-1.12
Maternal BMI				
14.0-18.4	3644 (5)	275 (7.6)	0.75	0.66-0.86
18.5-24.9	50 370 (68)	5245 (10.4)	1.00	
25.0-29.9	13 432 (18)	1959 (14.6)	1.40	1.32-1.49
30-34.9	4572 (6)	789 (17.3)	1.76	1.61-1.92
35.0+	1984 (3)	430 (21.7)	2.18	1.93-2.46
Maternal height ≤ 163 cm (yes)	17 698 (24)	3008 (17.0)	1.78	1.69-1.88
Complication (yes)	7880 (11)	1572 (19.9)	1.98	1.85-2.11
Stimulated labour (yes)	32 219 (44)	5411 (16.8)	1.57	1.49-1.66
Term				
37+0 – 41+6	71 322 (96)	8089 (11.3)	1.00	
$\geq 42+0$	2680 (4)	609 (22.7)	1.96	1.77-2.18
Female baby (yes)	36 265 (49)	3877 (10.7)	0.87	0.83-0.91
Foetal distress (yes)	22 086 (30)	4311 (19.5)	2.38	2.26-2.51
Cephalopelvic disproportion (yes)	2093 (3)	1293 (61.8)	13.12	11.89-14.48
Macrosomia (yes)	1139 (2)	381 (33.4)	3.36	2.92-3.87

Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval

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4 **Figure 1.** Elective caesarean section (shown in the upper part), emergency caesarean section (the
5 middle part), emergency caesarean section in a low-risk subgroup (the lower part). Risk-adjusted
6 proportions of 29 maternity units, 2009-12. Funnel plot limits: 95% and 99.8%. CV: coefficient of
7 variation.
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14 **Supporting Information**

15 **Table S1.** Definition of mode of delivery based on diagnostic and procedure codes.

16 **Table S2.** Definition of risk factors. Percentages are based on 226,612 included deliveries. Where
17 appropriate, the reference category used in the logistic regression models is indicated.
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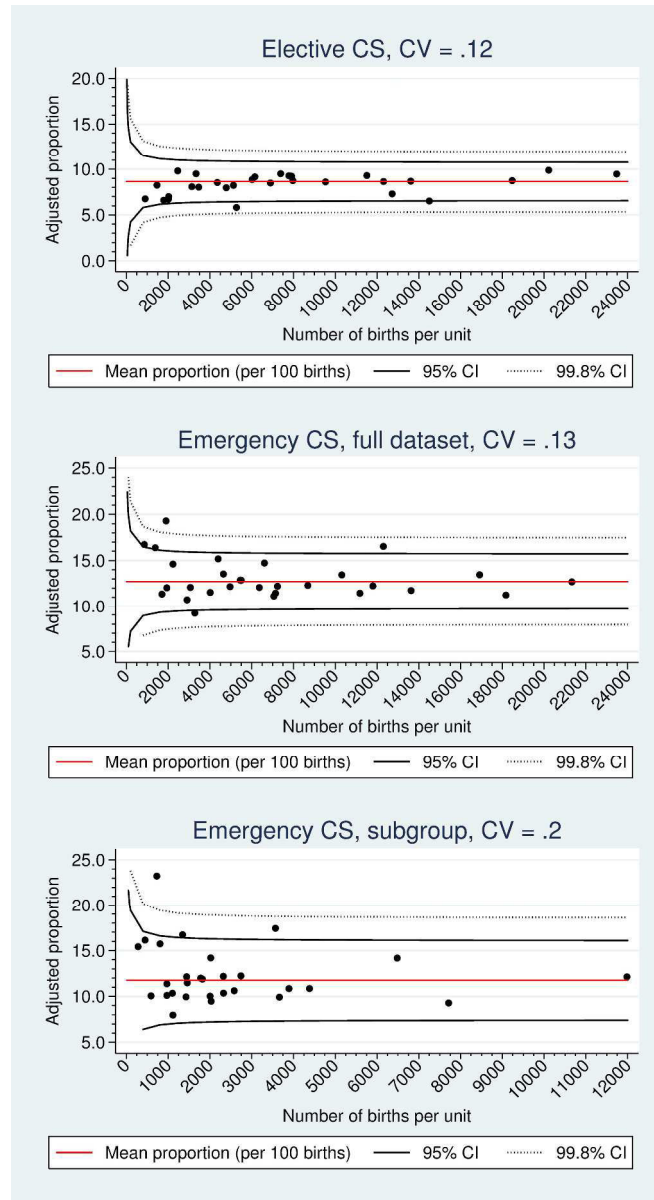


Figure 1. Elective caesarean section (shown in the upper part), emergency caesarean section (the middle part), emergency caesarean section in a low-risk subgroup (the lower part). Risk-adjusted proportions of 29 maternity units, 2009-12. Funnel plot limits: 95% and 99.8%. CV: coefficient of variation.

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Table S1. Definition of mode of delivery based on diagnostic and procedure codes.

	Text	Vaginal birth	Elective CS	Emergency CS
Diagnostic codes				
[D]O80*	Spontaneous singleton birth	X	-	-
[D]O81*	Singleton birth: instrumental extraction (forceps or vacuum extraction)	X	-	-
[D]O82.0	Singleton birth by elective CS	-	X	-
[D]O82* without [D]O82.0	Singleton birth by CS (except elective CS)	-	-	X
[D]O83*	Other forms of singleton birth	X	-	-
Procedure codes				
KMCA10A	CS in isthmus uteri performed as acute procedure before birth	-	-	X
KMCA10B	CS in isthmus uteri performed as planned procedure before birth	-	X	-
KMCA10C	CS before birth in isthmus uteri with exit technique	-	-	X
KMCA10D	CS in isthmus uteri during birth due to pregnancy complication/s	-	-	X
KMCA10E	CS in isthmus uteri during birth due to birth complication/s	-	-	X

CS=caesarean section.

"X"=code is permitted. "-"= code is not permitted.

Diagnostic codes according to the International Classification of Diseases (ICD-10), where * indicates inclusion of all subcodes. Note that codes in the Danish version of ICD-10 have leading letter [D].

Procedure codes according to the NOMESCO classification system of surgical procedures.

Table S2. Definition of risk factors. Percentages are based on 226 612 included deliveries. Where appropriate, the reference category used in logistic regression models is indicated. Note that codes in the Danish version of the ICD-10 have leading letter [D].

Risk factor	Coding
Year	2009 (<i>reference</i>), 2010, 2011, 2012
Size of maternity unit	Small, medium (<i>reference</i>), large: Large units (N=7) had more than 3000 births in all but one active year (some hospital units were closed between 2009 and 2012, i.e. had less than four active years), small units had less than 1100 births in all but one active year (N=6). Remaining units (N=16) are classified as medium size.
Weekend delivery (yes)	Weekend includes Saturday, Sunday and all national holidays
Night delivery (yes)	Deliveries between 8.00 p.m. and 7.59 a.m.. Missing values (N=1110, 0%) are treated as daytime deliveries.
Maternal age (years)	Categories: 15-19, 20-34 (<i>reference</i>), 35-44
Maternal prenatal smoking (yes)	Missing values (N=3990, 2%) are treated as non-smokers.
Maternal BMI	Categories following WHO definition: 14.0-18.4, 18.5-24.9 (<i>reference</i>), 25.0-29.9, 30-34.9, 35+. Missing values (N=6700, 3%) are treated as normal BMI (18.5-24.9).
Maternal height <=163 cm (yes)	Low height is defined as the 25% quantile for all included women. Maternal height outside range of 140-205 cm (N=246, 0%) or missing (N=5335, 2%) is treated as maternal height > 163 cm.
Parity	Categories according to the number and mode of previous deliveries: nulliparous, multiparous without previous CS (<i>reference</i>), and multiparous with previous CS. Missing values (N=2282, 1%) are treated as nulliparous.
Complication factors	
Maternal diabetes (both pre-existing and gestational)	Based on ICD-10 diagnoses [D]E10*, [D]E11*, [D]E12*, [D]E14*, [D]O24*.
Maternal hypertension (both pre-existing and gestational)	Based on ICD-10 diagnoses [D]O10*, [D]O11*, [D]O13*, [D]O16*.
Pre-eclampsia/Eclampsia	Based on ICD-10 diagnoses [D]O14*, [D]O15*.
Placenta praevia	Based on ICD-10 diagnoses [D]O44*.
Placental abruption	Based on ICD-10 diagnoses [D]O45*.
Premature rupture of membranes	Based on ICD-10 diagnoses [D]O42*.
Complication (yes)	At least one of the complication factors is present.
Stimulated labor (yes)	Based on recording of syntocinon infusion during labour (NOMESCO code BKHD3*).
Any induced labor (yes)	Based on recording of either induction by medication (NOMESCO code BKHD2*) or procedure (NOMESCO code KMAC00 or KMAC96a).
Term	Categories based on gestational age at delivery: < 37 weeks + 0 days, 37 weeks + 0 days till 41 weeks + 6 days (<i>reference</i>), >= 42 weeks + 0 days. Missing values are treated as normal term.
Female baby (yes)	Missing values (N=206, 0%) are randomly assigned female gender with probability 0.49 (outcome: 109 assigned females).
Breech presentation (yes)	All presentations beside cephalic presentation. Includes shoulder presentation (N=405, 0%). Inconsistent values (N=426, 0%) are treated as breech presentation and missing values (N=675, 0%) are treated as cephalic presentation.
Fetal distress (yes)	Based on ICD-10 code [D]O68*: Labour and delivery complicated by fetal stress distress.
Cephalopelvic disproportion (yes)	Based on ICD-10 code [D]O65*: Obstructed labour due to maternal pelvic abnormality.
Macrosomia (yes)	Birth weight above 4500 grams. Missing values (N=1572, 1%) are treated as weight below 4500 grams.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page number
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title / page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract / page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Abstract / page 2; Methods / page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Page 5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5, table S1
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	Page 5, table S
Bias	9	Describe any efforts to address potential sources of bias	Discussion of limitations page 3, pages 9-10
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pages 5-6, table S2
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6
		(b) Describe any methods used to examine subgroups and interactions	Page 6
		(c) Explain how missing data were addressed	Page 6, table S2
		(d) If applicable, explain how loss to follow-up was addressed	not applicable
		(e) Describe any sensitivity analyses	Page 6
Results			
Participants	13*	(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	Page 5 and 7
		(b) Give reasons for non-participation at each stage	yes
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic,	Page 7, table 1

		clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Table S2
		(c) Summarise follow-up time (eg, average and total amount)	not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time	Page 7, tables 1-3
Main results	16	(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	Pages 7-9, tables 1-3
		(b) Report category boundaries when continuous variables were categorized	yes
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pages 7-9, tables 1-3
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 11
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	Page 3, page 10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pages 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 3 and 11
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	Page 11

*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 <http://www.strobe-statement.org>.

BMJ Open

Risk factors and between-hospital variation of caesarean section in Denmark: a cohort study

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Risk factors and between-hospital variation of caesarean section in Denmark: a cohort study

Short running title: Caesarean section: risk and variation

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Abstract

Objectives The aim of this study was to estimate the effects of risk factors on elective and emergency caesarean section (CS) and to estimate the between-hospital variation of risk-adjusted CS proportions.

Design Historical registry-based cohort study.

Settings and participants The study was based on all singleton deliveries in hospital units in Denmark from January 2009 to December 2012. A total of 226,612 births by 198,590 mothers in 29 maternity units were included.

Primary and secondary outcome measures We estimated 1) odds ratios (OR) of elective and emergency CS adjusted for several risk factors, e.g. body mass index, parity, age, and size of maternity unit and 2) risk-adjusted proportions of elective and emergency CS to evaluate between-hospital variation.

Results The CS proportion was stable at 20-21%, but showed wide variation between units, even in adjusted models. Large units performed significantly more elective CSs than smaller units, but the risk of emergency CS was significantly reduced compared to smaller units. Many of the included risk factors were found to influence the risk of CS. The most important risk factors were breech presentation and previous CS. Four units performed more CSs and one unit fewer CSs than expected.

Conclusion The main risk factors for elective CS were breech presentation and previous CS; for emergency CS they were breech presentation and cephalopelvic disproportion. The proportions of CS were stable during the study period. We found a variation in risk-adjusted CS between hospitals in Denmark. Although exhaustive models were applied, the results indicated the presence of systematic variation between hospital units, which was unexpected in a small, well-regulated country such as Denmark.

Keywords: Obstetrics, Epidemiology, Quality in health care

Abbreviations:

CS = Caesarean section

OR = Odds ratio

CI = Confidence Interval

Strengths and limitations of this study

- Our study was population-based, covering four calendar years and a high number of deliveries and investigating the effects of a wide range of risk factors for elective CS and emergency CS, both maternal-related, foetal-related, labour-related, and unit-related factors.
- The Danish Medical Birth Register includes data on all births at hospital maternity units, where 99% of all Danish births take place.
- This study has all the limitations inherent to a historical registry-based cohort study design, where not all potential maternal or neonatal risk factors were available and where the coding of events was done after the end of delivery.
- The lack of knowledge about the actual decision for CS is another weakness of this study. Specifically, the term "emergency CS" covers a broad range of situations in a maternity ward, as emergency CS is seen as a homogenous group and distinctions are not made between degrees of urgency.
- Data for this study comes from one country in Northern Europe only, and Denmark is a small, well-regulated country with equal and free access to health services. Even though data homogeneity might be regarded as strength, transferability of the results to other countries is limited.

Introduction

Caesarean section (CS) is one of the essential factors in reducing the risk of intrapartum foetal death. Nevertheless, CS can also cause several complications. For the mother, surgical complications such as bleeding, infection and thrombosis may occur [1], and the risk of uterine rupture and placenta praevia in subsequent pregnancies is increased [2]. Overall, CS has been associated with a higher risk of severe maternal morbidity and mortality as compared with vaginal delivery [3]. For the child, in general there is a higher risk of neonatal complications such as respiratory distress syndrome, pulmonary hypertension, and iatrogenic prematurity as these conditions occur more often after CS [1,4], although CS in some selected situations such as prematurity can reduce neonatal mortality and morbidity [5].

The average proportion of CS has increased dramatically in many countries over the last three decades [6-8]. The World Health Organization states that at population level, caesarean section rates higher than 10% are not associated with reductions in maternal and newborn mortality rates [9], and other studies suggest that proportions above this limit may do more harm than good [10,11]. In Denmark, the CS proportion reached 21% in 2012 [12] as compared with 5% in 1973 [13]. Although this rise has been influenced by many factors such as the increasing age of nulliparous women, the increasing number of pregnant women with previous CS, a greater maternal preference for CS, changes in women's clinical risk profiles (e.g. higher prevalence of pre-existing diseases/obesity) [14], and improved neonatal outcomes, the reasons for the steep rise remain unexplained.

Besides this general increase in CS, a large variation between countries [11,15,16], regions [7], and hospitals [6,17] has been documented. The variation for emergency CS has been reported to be larger than that for elective CS [6]. Even when proportions were risk-adjusted [6] or restricted to subgroups of women [18,19], the large variation tended to persist, which suggests a strong systematic component. Systematic variation between units could have occurred if key factors were missed in the risk-adjustment and/or guidelines on CS decision were not sufficiently defined or followed to the letter [7]. In Denmark, there is no national guideline covering decision making for CS in general. In Denmark, the CS proportions for 2012 varied between hospital units, ranging from 5% to 27% [12], but the results for risk-adjusted proportions have not been published so far. Based on population-based Danish registry data, we set out to define exhaustive models for the probability of elective or emergency CS, covering a wide range of potential risk factors.

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4 This study aimed to 1) estimate associations between risk factors and CS rates, and 2) assess the
5 between-hospital variation of the risk-adjusted CS proportions.
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8 **Methods**

9 *Data sources*

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11 The data source was the Danish Medical Birth Register, which was established in 1973 and includes
12 data on all births at hospital maternity units, where 99% of all Danish births take place. The registry
13 contains information on, for example, parity, birth weight, gestational age, diagnoses regarding pre-
14 pregnancy risk factors, medical diseases, and complications and interventions during pregnancy and
15 delivery. The recorded information is based largely on diagnostic codes such as those found in the
16 International Classification of Diseases, 10th Revision (ICD-10) and procedure codes such as those
17 in the Nordic Medico-Statistical Committee (NOMESCO) classification of surgical procedures.
18 Data from the register are available for researchers on request to the Danish Health Data Authority
19 and specified data required for the study are delivered pseudo anonymized.
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23 The study period was from 1st January 2009 to 31st December 2012, during which time there were
24 229,041 singleton births in 32 different maternity units. This number includes both live and
25 stillborn children from gestational week 24 and excludes births after abortion procedure. Births
26 were subsequently excluded if they were recorded 1) in very small units with fewer than 100 births
27 per year (in total 28 births from three units), 2) with invalid code for the maternity unit (N=33
28 births), 3) with missing or incorrect birth diagnosis (N=251), 4) with inconclusive mode of delivery
29 (N=1766), and 5) for mothers younger than 15 or older than 44 years of age, limits inspired by
30 similar limits in a prior study [10] (N=351). Thus, 226,612 singleton births (98.9%) by 198,590
31 mothers in 29 maternity units were included in the study; 27,651 women had more than one
32 singleton birth during the study period.
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44 *Outcome measures*

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46 The mode of delivery was classified as elective CS, emergency CS, or vaginal birth (Table S1),
47 where all non-elective CS were classified as emergency CS. Firstly, we analysed the proportion of –
48 and risk for – *elective* CS among all singleton deliveries, and secondly, the proportion of – and risk
49 for – *emergency* CS among all singleton deliveries after excluding those by elective CS. Finally,
50 similar analyses were performed in a low-risk subgroup of nulliparous women giving birth to a
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4 child in cephalic presentation at ≥ 37 weeks+0 days in spontaneous labour (definition comparable to
5 Robson's group 1 [20]).
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7 8 *Risk factors* 9

10 A number of risk factors for CS were included. These were maternal-related factors: age, prenatal
11 smoking, body mass index (BMI), maternal height below 163cm, parity and the complication
12 factors of diabetes (both gestational and pre-existing), hypertension, pre-eclampsia/eclampsia,
13 placenta praevia (which might have been recorded in gestational week 20 at an ultrasound
14 examination and thus may not represent praevia at the time of labour)/placental abruption, and
15 premature rupture of membranes; foetal-related factors: gestational age (in weeks+days), sex and
16 macrosomia (birthweight above 4500g); labour-related factors: augmentation of labour with
17 oxytocin infusion during delivery, induction of labour, foetal presentation, cephalopelvic
18 disproportion and foetal distress; and maternity unit-related factors: size of maternity unit based on
19 numbers of births per year, weekend delivery (Saturday, Sunday and all national holidays), and
20 night delivery (deliveries between 8.00 p.m. to 7.59 a.m.). In Denmark, an elective CS is scheduled
21 on week days in the day time (usually between 8.00 a.m. to 3.30 p.m.). Missing values of risk
22 factors were treated as no exposure. For detailed definitions of the risk factors and their
23 categorization see Table S2.
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33 34 *Statistical analysis* 35

36 To estimate the effect of the risk factors on the probability of elective or emergency CS, three
37 separate multivariable logistic regression models were fitted, with clusters taken into account. They
38 were used to define risk-adjusted proportions as follows. Summing up the probabilities predicted by
39 the logistic model over deliveries for each maternity unit yielded the predicted proportion per unit.
40 Dividing the observed proportion per unit by the predicted proportion multiplied by the mean
41 national proportion yielded the risk-adjusted proportion per maternity unit. Funnel plots [21] were
42 created for risk-adjusted proportions for both elective and emergency CS; the basis for comparison
43 and confidence was the mean national unadjusted proportion. To incorporate heterogeneity, funnel
44 plot limits were adjusted by an additive over-dispersion term (i.e., an estimate of the between-unit
45 variability, reported as standard deviation in %) based on a random-effects model approach [22].
46 The corresponding test of heterogeneity between maternity units was reported [22]. In addition,
47 variation coefficients between maternity units were calculated. A coefficient of variation is defined
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4 as the standard deviation divided by the mean. A p-value below .05 was considered statistically
5 significant. All analyses were performed using Stata software (StataCorp LP, College Station, TX,
6 USA).
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10 *Ethics approval*

11 The study was approved by the Danish Data Protection Agency (no. 2013-41-1561).

12 According to Danish law, review by an ethics board or patient consent is not required for purely
13 register-based studies.
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17 **Results**

18 Analyses were based on 226,612 singleton births. The number of births per maternity unit ranged
19 from 383 to 11,300. There was a 9% decrease of singleton births in Denmark over the study period,
20 from a total of 58,880 in 2009 to 53,574 in 2012 (Table 1). In total, about a fifth (N=45,925, 20.3%)
21 ended in CS, including 19,620 (8.7%) elective CSs (Tables 1+2). Both the overall CS proportion
22 and the proportion of elective CS remained stable at about 20% and 9%, respectively (Tables 1+2).
23 The risk of emergency CS remained stable across the study period for small and medium-sized
24 units, while the risk decreased significantly from 2009 to 2010 for large maternity units and
25 thereafter remained stable (results not shown).
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34 *Risk factors for caesarean section*

35 The multivariable odds ratios (ORs) of all risk factors for elective CS included in the logistic model
36 are presented in Table 1. All the included risk factors had an impact on the risk of elective CS
37 except for maternal smoking, maternal height, macrosomia, and sex. The most important risk
38 factors were breech presentation (OR 24.02 [95%CI 22.45-25.7]) and previous CS (OR 16.9
39 [95%CI 16.08-17.75]). Elective CS was the mode of delivery for 50% of all breech presentations
40 and for 40% with previous CS.
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46 The multivariable ORs of all risk factors for emergency CS are presented in Table 2. Overall, the
47 mean proportion of emergency CS was 12.7%. Over the four-year study period the proportion of
48 emergency CS fell slightly but consistently from 13.1% in 2009 to 12.3% in 2012 (OR 0.93 [95%CI
49 0.89-0.98], using 2009 as reference). The majority of the included risk factors influenced the risk of
50 emergency CS. The most important risk factors were breech presentation (OR 43.73 [95%CI 40.01-
51 47.79]) and cephalopelvic disproportion (OR 13.96 [95%CI 12.91-15.10]). The risk for emergency
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4 CS remained unchanged regardless of the day of the week (OR 1.00 [95%CI 0.97-1.03]), but was
5 slightly less at night compared to daytime (OR 0.93 [95%CI 0.90-0.95]).

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7 Breech presentations with intended vaginal delivery ended with emergency CS in almost 80% of the
8 cases. About two thirds of the women with intended vaginal delivery after previous CS succeeded
9 in having vaginal birth. Nonetheless, the corresponding risk for emergency CS was significantly
10 higher for these women compared with that for nulliparous women (OR 2.97 [95%CI 2.84-3.10]).
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12 The risk for emergency CS was lowest for multiparous women without previous CS (OR 0.25
13 [95%CI 0.24-0.27]).

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16 The (recorded) occurrence of maternal complication factors ranged from below 1% for diabetes and
17 placenta praevia/placental abruption to 2-3% for hypertension and pre-eclampsia/eclampsia up to
18 8% for premature rupture of membranes. In these groups, the proportion of emergency CS was at
19 least about 20% for diabetes, hypertension, and membrane rupture; 36% for pre/eclampsia; 64% for
20 placenta praevia and 68% for placental abruption. The OR for the combined complication factor
21 was 1.98 [95%CI 1.90-2.06]. In this study population there were 1128 women with reported
22 placenta praevia, and of these, 932 (83%) underwent CS. An elective procedure was recorded for
23 511 (45%) of these women.

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26 The results for emergency caesarean section in the low-risk nulliparous subgroup are presented in
27 Table 3. The risk factors were largely distributed as in the full dataset. However, women in the
28 subgroup were younger on average (mean age 28.3 compared with 30.1 in the full dataset),
29 relatively more women had augmentation of labour (44% versus 29%), and foetal distress was
30 reported more often (30% versus 21%).

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33 The mean proportion of emergency CS was about one percent lower in the low-risk subgroup
34 (11.8%) than in the full dataset. Overall, the emergency CS proportions with respect to risk factors
35 in the subgroup were within +/- 5% of those in the full dataset, except for macrosomia (33.4%
36 emergency CS in the subgroup as compared with 20.8% in the full dataset). Moreover, the ORs
37 resulting from the logistic model in the subgroup were predominantly similar to those of the full
38 dataset. However, the ORs differed for night delivery (a significantly higher risk for emergency CS
39 at night in the subgroup; OR 1.05 [95 % CI 1.0-1.1] versus 0.93 [95 % CI 0.9-0.95] in the full
40 dataset), augmentation of labour (1.57 [95%CI 1.49-1.66] versus 1.01 [95%CI 0.98-1.05]), and
41 macrosomia (3.36 [95%CI 2.92-3.87] versus 2.58 [95%CI 2.38-2.79]).

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54 *Between-hospital variation of risk-adjusted caesarean section proportions*

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4 The median of the observed proportion of elective CS in maternity units was 8.5% with a minimum
5 of 3.6% and a maximum of 10.6%. Risk-adjusted proportions ranged from 5.8% to 9.9% (median
6 8.6%, 25%-75% percentiles: 8.0-9.2), Figure 1, upper part. There was statistically significant
7 heterogeneity among maternity units (p -value < 0.001). Allowing for little over-dispersion (1.1%),
8 no hospital maternity unit was outside the upper 95% funnel limit. However, one medium-sized unit
9 was below the corresponding lower limit, indicating that this unit performed systematically fewer
10 elective CS than expected.
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15 The median of the observed proportion of emergency CS in maternity units was 12.7% with a
16 minimum of 7.0% and a maximum of 17.1%. Risk-adjusted proportions ranged from 9.2% to 19.3%
17 (median 12.2%, 25%-75% percentiles: 11.5-13.5), Figure 1, middle part. There was statistically
18 significant heterogeneity among the 29 maternity units (p -value < 0.001). Taking the estimated
19 over-dispersion (1.5%) into account, there were few maternity units outside the 95% funnel limits:
20 one small unit was below the 95% lower limit and four units (two small, one medium, and one
21 large) were above the 95% upper limit, indicating that the latter units systematically performed
22 more emergency CSs than expected.
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28 In the emergency subgroup the observed emergency CS proportions ranged from 7.8% and 19%
29 (median 11.6%) between maternity units, and risk-adjusted emergency CS proportions ranged from
30 8% to 23.2% (median 11.5%, 25%-75% percentiles: 10.1–14.2), Figure 1, lower part. Risk-adjusted
31 proportions showed statistically significant heterogeneity among maternity units (p -value < 0.001).
32 No hospital maternity unit was below the lower 95% funnel limit (over-dispersion 2.2%). However,
33 two medium-sized units and one large unit were above the corresponding upper limit, indicating
34 systematically more emergency CSs than expected.
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41 Discussion

42 Our study showed that mostly all of the included risk factors had an influence on the risk of CS.
43 Breech presentation and previous CS were found to have the largest impact on elective CS; on
44 emergency CS it was breech presentation and cephalopelvic disproportion. As the proportions of
45 elective and emergency CS were stable throughout the four-year study period, the steep increase of
46 the overall CS proportion in Denmark seems to have stopped. As for organizations, large hospital
47 units performed significantly more elective CSs than smaller units, and the risk and performance of
48 emergency CS was significantly reduced in the larger maternity units compared with small and
49 medium units, which would be expected since there is a centralization of risk births (e.g. congenital
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4 anomalies, significant maternal comorbidity) in Denmark. For referral to delivery in smaller
5 hospitals in Denmark there are specific criteria such as normal pregnancy at term, uncomplicated
6 pregnancy and delivery at term, whereas more complicated cases (e.g. sick foetus, maternal
7 comorbidities, preterm delivery, and high maternal BMI) are referred to larger hospitals, leading to
8 a higher rate of CS. We also found substantial heterogeneity of risk-adjusted CS between Danish
9 maternity units, with higher variation in emergency CS than in elective CS. Even though we applied
10 exhaustive regression models covering a wide range of risk factors, the results still indicated the
11 presence of systematic, i.e. larger than random, variation between hospital units.

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13 Our study had all the limitations inherent to a historical registry-based cohort study design, where
14 not all potential maternal or neonatal risk factors were available. Coding was done after the end of
15 delivery, implying that the registration of diagnoses for which there are no precise definitions, for
16 instance, cephalopelvic disproportion [17], might not have been adequate. This has to be taken into
17 consideration when comparing results across studies. For example, based on ICD-10 codes, only
18 2% of the women in our study had a reported cephalopelvic disproportion, whereas a prior study
19 from the United Kingdom showed that cephalopelvic disproportion was the primary indication for
20 CS in 35% of the women [23]. A further limitation is the small size of Denmark, with fewer than
21 60,000 births per year and less than thirty maternity units, making it statistically more challenging
22 to detect outliers. Data for this study comes from one country in Northern Europe only, and
23 Denmark is a small, well-regulated country with equal and free access to health services. Even
24 though data homogeneity might be regarded as strength, generalisability of the results to other
25 countries is limited.

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27 It is possible that most of the risk factors in our study may not have had an independent, direct
28 causal effect on the CS proportion, even if they were highly significant. For example, the risk factor
29 of labour induction [24] may be linked to a latent unknown status of "problematic delivery", which
30 in turn is linked to CS probability. The lack of knowledge about the decision for CS is another
31 weakness of this study. Specifically, the term "emergency CS" covers a broad range of situations in
32 a maternity ward, as emergency CS is seen as a homogenous group and distinctions are not made
33 between degrees of urgency [25]. Some CSs are performed immediately because of a life-
34 threatening situation, and others are performed for other, non-life-threatening reasons. Former
35 studies have shown that the CS proportions are influenced by a variety of different settings such as
36 the use of foetal monitoring, partograms, or the active management of labour [25-27]. As a first
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4 step, the quality of registration in the Medical Birth Register will improve when the degree of
5 urgency is included [28].
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9 To ensure the same quality of care for all women (in Denmark), there should not be any systematic
10 differences in CS decision-making between maternity units, and thus such systematic variation
11 between units should be eliminated. Starting points for such a process could be i) a retrospective
12 inspection of the hospital birth records of the women in our study who were classified as low risk
13 but still underwent CS, which could shed light on the premises for CS decisions, and ii) a
14 comparative prospective study with a specific focus on the precise circumstances influencing the
15 decision to perform a CS (when, why, who) and including units with both fewer and more CSs than
16 expected, which would enable the identification of important key factors that were missed in our
17 study. Besides acquiring more clinical details, the role of women's preferences and the various ways
18 of making clinical decisions in different areas need to be investigated more thoroughly. The World
19 Health Organization recommends that other relevant outcomes such as short- and long-term
20 maternal and paediatric outcomes (including stillbirths and breastfeeding) as well as the
21 psychological or social well-being of both mother and child after birth [9] should be included in
22 future studies. Many obstetricians regard the CS proportion of 20% as too high [23], and with
23 clearer consensus on when to perform CS, there will be an enhanced possibility of reducing the CS
24 proportion without compromising the neonatal morbidity or mortality. Recent years have seen the
25 development of a national cardiotocography education program in Denmark with the aim of
26 reducing foetal distress [29]. It has been implemented in all maternity units in the country and
27 includes the education and certification of midwives and obstetricians in cardiotocography.
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41 **Conclusion**

42 Our study showed that the risk of CS is influenced by several risk factors and also confirmed well-
43 known risk factors. The largest impact on elective CS was found to be breech presentation and
44 previous CS; on emergency CS it was breech presentation and cephalopelvic disproportion. We also
45 found a variation in risk-adjusted CS between Danish hospitals, which was unexpected for such a
46 small, well-regulated country like Denmark. The prior increase of the overall CS proportion in
47 Denmark seems to have stopped, as the proportions of elective and emergency CS were stable
48 throughout the study period. To ensure the same quality of care across the country, CS practices in
49 hospital maternity units should be compared and, if possible, harmonised. Furthermore, the possible
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4 lack of consensus about clinical practice as well as the attitudes of parents and healthcare
5 professionals towards mode of delivery should be investigated further.
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8 9 **Conflict of interest and funding statement**

10 All the authors declare that they had no support from any organisations for the submitted work, that
11 in the last three years they had no financial relationships with any organisations which might have
12 had an interest in the submitted work, and that they did not have any other relationships or
13 undertake any activities that could appear to have influenced the submitted work. The submitted
14 research received no specific grant from any funding agency in the public, commercial or not-for-
15 profit sectors. The submitted
16 research received no specific grant from any funding agency in the public, commercial or not-for-
17 profit sectors.
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22 **Contributorship statement**

23 SW, RG and BMN devised the concept of the study. SW did the data management and data
24 analysis. RG, SW and BMN drafted the article. All authors, SW, RGS, KOG, USK, LM, CBA,
25 LRJ, JN and BMN, revised the manuscript and approved the final version.
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30 **Data sharing statement**

31 No additional data available.
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35 **Acknowledgement**

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References

1. Grivell RM, Dodd JM. Short- and long-term outcomes after cesarean section. *Expert Rev Obstet Gynecol.* 2011;6(2):205-215.
2. Colmorn LB, Krebs L, Klyngsøyr K, Jakobsson M, Tapper A-M, Gissler M et al. Mode of first delivery and severe maternal complications in the subsequent pregnancy. *Acta Obstet Gynecol Scand.* 2017;96:1053-1062.
3. Villar J, Carroli G, Zavaleta N, Donner A, Wojdyla D, Faundes A et al. Maternal and neonatal individual risks and benefits associated with caesarean delivery: multicentre prospective study. *BMJ.* 2007;335:1003-1004.
4. Shorten A. Maternal and neonatal effects of caesarean section. *BMJ.* 2007;335:1003.
5. Hamburg A, Härtel C, Paul P, Hanke K, Bossung V, Hartz A et al. Delivery mode and intraventricular hemorrhage risk in very-low-birth-weight infants: Observational data of the German Neonatal Network . *Eur J Obstet Gynecol Reprod Biol.* 2017;212:144-149.
6. Bragg F, Cromwell DA, Edozien LC, Gurol-Urganci I, Mahmood TA, Templeton A et al. Variation in rates of caesarean section among English NHS trusts after accounting for maternal and clinical risk: cross sectional study. *BMJ.* 2010;341:c5065.
7. Clark SL, Belfort MA, Hankins GD, Meyers JA, Houser FM. Variation in the rates of operative delivery in the United States. *Am J Obstet Gynecol.* 2007;196:526.e1-526.e5.
8. Sydsjö G, Sydsjö A, Brynhildsen J, Josefsson A. Trend in caesarean section and instrumental deliveries in relation to Body Mass Index: a clinical survey during 1978 – 2001. *Reprod Health.* 2010;7:18.
9. World Health Organization. WHO Statement on Caesarean Section Rates. Geneva: World Health Organization; 2015 (WHO/ RHR/15.02).
10. Althabe F, Belizán JM. Caesarean section: the paradox. *Lancet.* 2006;368:1472-1473.
11. Betrán AP, Merialdi M, Lauer JA, Bing-Shun W, Thomas J, Van Look P et al. Rates of caesarean section: analysis of global, regional and national estimates. *Paediatr Perinat Epidemiol.* 2007;21:98-113.
12. Fødsler 1997- [Web-portal for interactive data exploration and retrieval on Births: 1997-]. Available online at: <http://www.esundhed.dk/sundhedsregistre/MFR/Sider/MFR06A.aspx> (Accessed February 26, 2016).

13. Fødsler: 1973- [Web-portal for interactive data exploration and retrieval on Births: 1973-]. Available online at: <http://www.esundhed.dk/sundhedsregistre/MFR/Sider/MFR01.aspx> (Accessed February 26, 2016).
14. Poobalan AS, Aucott LS, Gurung T, Smith WC, Bhattacharya S. Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women – systematic review and meta-analysis of cohort studies. *Obes Rev.* 2009;10(1):28-35.
15. Macfarlane AJ, Blondel B, Mohangoo AD, Cuttini M, Nijhuis J, Novak Z et al. Wide differences in mode of delivery within Europe: risk-stratified analyses of aggregated routine data from the Euro-Peristat study. *Br J Obstet Gynaecol.* 2016;123(4):559-68.
16. García-Armesto S, Angulo-Pueyo E, Martínez-Lizaga N, Mateus C, Joaquim I, Bernal-Delgado E et al. Potential of geographical variation analysis for realigning providers to value-based care. ECHO case study on lower-value indications of C-section in five European countries. *Eur J Public Health.* 2015;25 Suppl 1:44-51.
17. Librero J, Peiró S, Calderón SM. Inter-hospital variations on caesarean sections. A risk adjusted comparison in the Valencia public hospitals. *J Epidemiol Community Health.* 2000;54:631-636.
18. Nippita TA, Lee YY, Patterson JA, Ford JB, Morris JM, Nicholl MC et. Variation in hospital caesarean section rates and obstetric outcomes among nulliparae at term: a population-based cohort study. *Br J Obstet Gynaecol.* 2015;122(5):702-11.
19. Kozhimannil KB, Arcaya MC, Subramanian SV. Maternal Clinical Diagnoses and Hospital Variation in the Risk of Cesarean Delivery: Analyses of a National US Hospital Discharge Database. *PLoS Med.* 2014;11(10):e1001745.
20. Robson MS. Classification of caesarean sections. *Fetal and maternal medicine review.* 2001;12:23-39.
21. Spiegelhalter DJ. Funnel plots for comparing institutional performance. *Stat Med.* 2005;24:1185-1202.
22. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7:177-188.
23. Thomas J, Paranjothy S. Royal College of Obstetricians and Gynaecologists Clinical Effectiveness Support Unit: The National Sentinel Caesarean Section Audit Report. 2001, London: RCOG Press.

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3
4 24. Yogeve Y, Hirsch L, Yariv O, Peled Y, Wiznizer A, Melamed N. Association and risk
5 factors between induction of labor and cesarean section. *J Matern Fetal Neonatal Med.*
6 2013;26(17):1733-6.
7
8
9 25. National Collaborating Centre for Women's and Children's Health commissioned by The
10 National Institute for Health and Clinical Excellence, Caesarean section. NICE Clinical
11 Guideline. 2011, London: RCOG Press.
12
13 26. Alfirevic Z, Devane D, Gyte GML. Continuous cardiotocography (CTG) as a form of
14 electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database of*
15 *Systematic Reviews.* 2006;3:CD006066.
16
17 27. Brown HC, Paranjothy S, Dowswell T, Thomas J. Package of care for active management
18 in labour for reducing caesarean section rates in low-risk women. *Cochrane Database of*
19 *Systematic Reviews.* 2008;4:CD004907.
20
21 28. Kesmodel US, Jølvig LR. Measuring and improving quality in obstetrics - the
22 implementation of national indicators in Denmark. *Acta Obstet Gynecol Scand.*
23 2011;90(4):295-304.
24
25 29. Thellesen L, Hedegaard M, Bergholt T, Colov NP, Hoegh S, Sorensen JL. Curriculum
26 development for a national cardiotocography education program: a Delphi survey to obtain
27 consensus on learning objectives, *Acta Obstet Gynecol Scand.* 2015;869-877.
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Table 1. Elective caesarean section. Distribution of singleton deliveries and proportion of elective CS according to risk factors, all included in a multivariable logistic regression model. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	All deliveries		Elective CS	
	N (%)	N (% within category)	OR	95% CI
Singleton deliveries	226 612 (100)	19 620 (8.7)		
Year				
2009	58 880 (27)	5186 (8.8)	Ref	
2010	59 139 (27)	4973 (8.4)	0.94	0.89-0.99
2011	55 099 (24)	4773 (8.7)	0.92	0.87-0.97
2012	53 574 (24)	4688 (8.8)	0.95	0.90-1.00
Size of maternity unit				
Small	13 638 (6)	884 (6.5)	0.74	0.68-0.81
Medium	97 653 (43)	8746 (9.0)	Ref	
Large	115 321 (51)	9990 (8.7)	1.08	1.04-1.12
Weekend delivery (yes)	60 993 (27)	260 (0.4)	0.03	0.03-0.04
Night delivery (yes)	100 718 (44)	361 (0.4)	0.02	0.02-0.02
Maternal age (years)				
15-19	3292 (1)	93 (2.8)	0.62	0.50-0.77
20-34	176 722 (78)	13 179 (7.5)	Ref	
35-44	46 598 (21)	6348 (13.6)	1.58	1.51-1.66
Maternal smoking (yes)	28 150 (12)	2157 (7.7)	0.99	0.93-1.05
Maternal BMI				
14.0-18.4	9321 (4)	642 (6.9)	1.02	0.92-1.13
18.5-24.9	142 597 (63)	10 986 (7.7)	Ref	
25.0-29.9	46 731 (21)	4593 (9.8)	1.17	1.11-1.22
30-34.9	18 291 (8)	2093 (11.4)	1.37	1.29-1.47
35.0+	9672 (4)	1306 (13.5)	1.56	1.43-1.70
Maternal height <=163 cm (yes)	55 288 (24)	5389 (9.7)	1.05	1.00-1.09
Parity				
Nulliparous	104 448 (46)	5299 (5.1)	1.08	1.03-1.14
Multiparous without previous CS	96 166 (42)	3855 (4.0)	Ref	
Multiparous with previous CS	25 998 (11)	10 466 (40.3)	16.9	16.08-17.75
Complication factors				
Diabetes	422 (0.2)	42 (10.0)		
Hypertension	3954 (2)	356 (9.0)		
Pre-eclampsia/Eclampsia	6257 (3)	385 (6.2)		
Placenta praevia	1128 (0.5)	511 (45.3)		
Placental abruption	938 (0.4)	16 (2)		
Premature rupture of membranes	17 548 (8)	98 (0.6)		
Complication (yes)	29 461 (13)	1374 (4.7)	0.46	0.42-0.50
Term				
< 37+0	10 992 (5)	615 (5.6)	0.28	0.25-0.32
37+0 – 41+6	205 338 (91)	18 897 (9.2)	Ref	
>= 42+0	10 282 (5)	108 (1.1)	0.12	0.10-0.15
Female baby (yes)	110 397 (49)	9812 (8.9)	1.01	0.97-1.05
Breech presentation (yes)	8979 (4)	4382 (48.8)	24.02	22.45-25.70
Macrosomia (yes), >4500g	6220 (3)	578 (9.3)	1.11	0.98-1.25

Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval, Ref=reference group

Table 2. Emergency caesarean section. Distribution of deliveries (all singleton deliveries without deliveries by elective CS) and proportion of emergency CS according to risk factors. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	Deliveries N (%)	Emergency CS N (% within category)	OR	95% CI
Singleton deliveries minus elective CS	206 992 (100)	26 305 (12.7)		
Year				
2009	53 614 (27)	7003 (13.1)	Ref	
2010	54 166 (27)	7023 (13.0)	0.96	0.92-1.00
2011	50 326 (24)	6271 (12.5)	0.90	0.86-0.94
2012	48 886 (24)	6008 (12.3)	0.93	0.89-0.98
Size of maternity unit				
Small	12 754 (6)	1464 (11.5)	1.02	0.95-1.09
Medium	88 907 (43)	11 292 (12.7)	Ref	
Large	105 331 (51)	13 549 (12.9)	0.90	0.87-0.93
Weekend delivery (yes)	60 733 (29)	7763 (12.8)	1.00	0.97-1.03
Night delivery (yes)	100 357 (48)	12 046 (12.0)	0.93	0.90-0.95
Maternal age (years)				
15-19	3199 (2)	309 (9.7)	0.60	0.52-0.69
20-34	163 543 (79)	20 034 (12.3)	Ref	
35-44	40 250 (19)	5962 (14.8)	1.48	1.42-1.53
Maternal smoking (yes)	25 993 (13)	3571 (13.7)	1.10	1.05-1.15
Maternal BMI				
14.0-18.4	8679 (4)	774 (8.9)	0.77	0.70-0.84
18.5-24.9	131 611 (64)	14 658 (11.1)	Ref	
25.0-29.9	42 138 (20)	6147 (14.6)	1.34	1.29-1.39
30-34.9	16 198 (8)	2929 (18.1)	1.75	1.66-1.84
35.0+	8366 (4)	1797 (21.5)	2.07	1.94-2.22
Maternal height <=163 cm (yes)	49 899 (24)	8701 (17.4)	1.67	1.62-1.73
Parity				
Nulliparous	99 149 (48)	16 712 (16.9)	Ref	
Multiparous without previous CS	92 311 (45)	3985 (4.3)	0.25	0.24-0.27
Multiparous with previous CS	15 532 (8)	5608 (36.1)	2.97	2.84-3.10
Complication factors				
Diabetes	380 (0.2)	74 (19.5)		
Hypertension	3598 (2)	707 (19.6)		
Pre-eclampsia/Eclampsia	5872 (3)	2110 (35.9)		
Placenta praevia	617 (0.3)	420 (68.1)		
Placental abruption	967 (0.5)	622 (64.3)		
Premature rupture of membranes	17 450 (8)	3536 (20.3)		
Complication (yes)	28 087 (14)	7129 (25.4)	1.98	1.90-2.06
Augmentation of labour (yes)	59 228 (29)	9825 (16.6)	1.01	0.98-1.05
Any induced labour (yes)	38 767 (19)	7128 (18.4)	1.40	1.35-1.46
.. induced by medication	27 166 (13)	5303 (19.5)		
.. induced by operation	21 359 (10)	3882 (18.2)		
Term				
< 37+0	10 377 (5)	3823 (36.8)	2.94	2.77-3.12
37+0 – 41+6	186 441 (90)	20 400 (10.9)	Ref	
>= 42+0	10 174 (5)	2082 (20.5)	1.77	1.67-1.89
Female baby (yes)	100 585 (49)	11 923 (11.9)	0.88	0.85-0.91
Breech (yes)	4597 (2)	3607 (78.5)	43.73	40.01-47.79
Foetal distress (yes)	42 963 (21)	9803 (22.8)	2.37	2.28-2.45
Cephalopelvic disproportion (yes)	3911 (2)	2551 (65.2)	13.96	12.91-15.1

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4 **Macrosomia (yes)** 5642 (3) 1173 (20.8) 2.58 2.38-2.79

5 Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval, Ref=reference group

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Table 3. Emergency caesarean sections in a low-risk subgroup (nulliparous women who gave birth to a child in cephalic presentation at ≥ 37 weeks + 0 days in spontaneous labour). Distribution of subgroup births and proportion of emergency CS according to risk factors. Odds ratios (OR) with 95% confidence intervals (CI) based on a multivariable logistic regression model.

	Subgroup, all N (% of all)	Emergency CS N (% within category)	OR	95% CI
Singleton deliveries, subgroup	74 002 (100)	8698 (11.8)		
Year				
2009	19 353 (26)	2357 (12.2)	Ref	
2010	19 186 (26)	2338 (12.2)	0.95	0.89-1.02
2011	17 884 (24)	1994 (11.2)	0.87	0.81-0.93
2012	17 579 (24)	2009 (11.4)	0.94	0.88-1.01
Size of maternity unit				
Small	4343 (6)	543 (12.5)	1.02	0.92-1.13
Medium	27 970 (38)	3416 (12.2)	Ref	
Large	41 689 (56)	4739 (11.4)	0.82	0.77-0.86
Weekend delivery (yes)	22 516 (30)	2672 (11.9)	1.02	0.97-1.08
Night delivery 20.00-07.59 (yes)	35 380 (48)	4239 (12.0)	1.05	1.00-1.10
Maternal age (years)				
15-19	2282 (3)	158 (6.9)	0.65	0.55-0.78
20-34	64 080 (87)	7106 (11.1)	Ref	
35-44	7640 (10)	1434 (18.8)	1.76	1.64-1.89
Maternal smoking (yes)	9708 (13)	1143 (11.8)	1.04	0.97-1.12
Maternal BMI				
14.0-18.4	3644 (5)	275 (7.6)	0.75	0.66-0.86
18.5-24.9	50 370 (68)	5245 (10.4)	Ref	
25.0-29.9	13 432 (18)	1959 (14.6)	1.40	1.32-1.49
30-34.9	4572 (6)	789 (17.3)	1.76	1.61-1.92
35.0+	1984 (3)	430 (21.7)	2.18	1.93-2.46
Maternal height ≤ 163 cm (yes)	17 698 (24)	3008 (17.0)	1.78	1.69-1.88
Complication (yes)	7880 (11)	1572 (19.9)	1.98	1.85-2.11
Augmentation of labour (yes)	32 219 (44)	5411 (16.8)	1.57	1.49-1.66
Term				
37+0 – 41+6	71 322 (96)	8089 (11.3)	Ref	
$\geq 42+0$	2680 (4)	609 (22.7)	1.96	1.77-2.18
Female baby (yes)	36 265 (49)	3877 (10.7)	0.87	0.83-0.91
Foetal distress (yes)	22 086 (30)	4311 (19.5)	2.38	2.26-2.51
Cephalopelvic disproportion (yes)	2093 (3)	1293 (61.8)	13.12	11.89-14.48
Macrosomia (yes)	1139 (2)	381 (33.4)	3.36	2.92-3.87

Abbreviations: CS=caesarean section, N=Number, OR=Odds ratio, CI=confidence interval, Ref=reference group

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4 **Figure 1.** Elective caesarean section (shown in the upper part), emergency caesarean section (the
5 middle part), emergency caesarean section in a low-risk subgroup (the lower part). Risk-adjusted
6 proportions of 29 maternity units, 2009-12. Funnel plot limits: 95% and 99.8%. CV: coefficient of
7 variation.
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14 **Supporting Information**

15 **Table S1.** Definition of mode of delivery based on diagnostic and procedure codes.

16 **Table S2.** Definition of risk factors. Percentages are based on 226,612 included deliveries. Where
17 appropriate, the reference category used in the logistic regression models is indicated.
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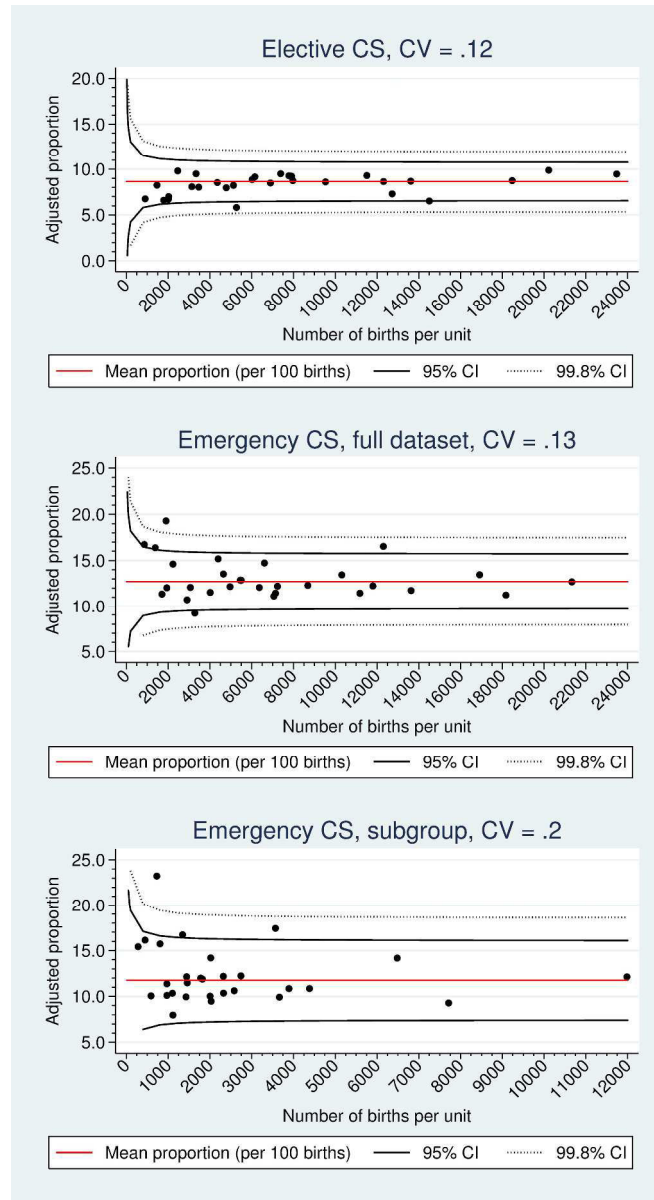


Figure 1. Elective caesarean section (shown in the upper part), emergency caesarean section (the middle part), emergency caesarean section in a low-risk subgroup (the lower part). Risk-adjusted proportions of 29 maternity units, 2009-12. Funnel plot limits: 95% and 99.8%. CV: coefficient of variation.

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Table S1. Definition of mode of delivery based on diagnostic and procedure codes.

	Text	Vaginal birth	Elective CS	Emergency CS
Diagnostic codes				
[D]O80*	Spontaneous singleton birth	X	-	-
[D]O81*	Singleton birth: instrumental extraction (forceps or vacuum extraction)	X	-	-
[D]O82.0	Singleton birth by elective CS	-	X	-
[D]O82* without [D]O82.0	Singleton birth by CS (except elective CS)	-	-	X
[D]O83*	Other forms of singleton birth	X	-	-
Procedure codes				
KMCA10A	CS in isthmus uteri performed as acute procedure before birth	-	-	X
KMCA10B	CS in isthmus uteri performed as planned procedure before birth	-	X	-
KMCA10C	CS before birth in isthmus uteri with exit technique	-	-	X
KMCA10D	CS in isthmus uteri during birth due to pregnancy complication/s	-	-	X
KMCA10E	CS in isthmus uteri during birth due to birth complication/s	-	-	X

CS=caesarean section.

"X"=code is permitted. "-"= code is not permitted.

Diagnostic codes according to the International Classification of Diseases (ICD-10), where * indicates inclusion of all subcodes. Note that codes in the Danish version of ICD-10 have leading letter [D].

Procedure codes according to the NOMESCO classification system of surgical procedures.

Table S2. Definition of risk factors. Percentages are based on 226 612 included deliveries. Where appropriate, the reference category used in logistic regression models is indicated. Note that codes in the Danish version of the ICD-10 have leading letter [D].

Risk factor	Coding
Year	2009 (<i>reference</i>), 2010, 2011, 2012
Size of maternity unit	Small, medium (<i>reference</i>), large: Large units (N=7) had more than 3000 births in all but one active year (some hospital units were closed between 2009 and 2012, i.e. had less than four active years), small units had less than 1100 births in all but one active year (N=6). Remaining units (N=16) are classified as medium size.
Weekend delivery (yes)	Weekend includes Saturday, Sunday and all national holidays
Night delivery (yes)	Deliveries between 8.00 p.m. and 7.59 a.m.. Missing values (N=1110, 0%) are treated as daytime deliveries.
Maternal age (years)	Categories: 15-19, 20-34 (<i>reference</i>), 35-44
Maternal prenatal smoking (yes)	Missing values (N=3990, 2%) are treated as non-smokers.
Maternal BMI	Categories following WHO definition: 14.0-18.4, 18.5-24.9 (<i>reference</i>), 25.0-29.9, 30-34.9, 35+. Missing values (N=6700, 3%) are treated as normal BMI (18.5-24.9).
Maternal height <=163 cm (yes)	Low height is defined as the 25% quantile for all included women. Maternal height outside range of 140-205 cm (N=246, 0%) or missing (N=5335, 2%) is treated as maternal height > 163 cm.
Parity	Categories according to the number and mode of previous deliveries: nulliparous, multiparous without previous CS (<i>reference</i>), and multiparous with previous CS. Missing values (N=2282, 1%) are treated as nulliparous.
Complication factors	
Maternal diabetes (both pre-existing and gestational)	Based on ICD-10 diagnoses [D]E10*, [D]E11*, [D]E12*, [D]E14*, [D]O24*.
Maternal hypertension (both pre-existing and gestational)	Based on ICD-10 diagnoses [D]O10*, [D]O11*, [D]O13*, [D]O16*.
Pre-eclampsia/Eclampsia	Based on ICD-10 diagnoses [D]O14*, [D]O15*.
Placenta praevia	Based on ICD-10 diagnoses [D]O44*.
Placental abruption	Based on ICD-10 diagnoses [D]O45*.
Premature rupture of membranes	Based on ICD-10 diagnoses [D]O42*.
Complication (yes)	At least one of the complication factors is present.
Stimulated labor (yes)	Based on recording of syntocinon infusion during labour (NOMESCO code BKHD3*).
Any induced labor (yes)	Based on recording of either induction by medication (NOMESCO code BKHD2*) or procedure (NOMESCO code KMAC00 or KMAC96a).
Term	Categories based on gestational age at delivery: < 37 weeks + 0 days, 37 weeks + 0 days till 41 weeks + 6 days (<i>reference</i>), >= 42 weeks + 0 days. Missing values are treated as normal term.
Female baby (yes)	Missing values (N=206, 0%) are randomly assigned female gender with probability 0.49 (outcome: 109 assigned females).
Breech presentation (yes)	All presentations beside cephalic presentation. Includes shoulder presentation (N=405, 0%). Inconsistent values (N=426, 0%) are treated as breech presentation and missing values (N=675, 0%) are treated as cephalic presentation.
Fetal distress (yes)	Based on ICD-10 code [D]O68*: Labour and delivery complicated by fetal stress distress.
Cephalopelvic disproportion (yes)	Based on ICD-10 code [D]O65*: Obstructed labour due to maternal pelvic abnormality.
Macrosomia (yes)	Birth weight above 4500 grams. Missing values (N=1572, 1%) are treated as weight below 4500 grams.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page number
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title / page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract / page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Abstract / page 2; Methods / page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Page 5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5, table S1
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	Page 5, table S
Bias	9	Describe any efforts to address potential sources of bias	Discussion of limitations page 3, pages 9-10
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pages 5-6, table S2
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6
		(b) Describe any methods used to examine subgroups and interactions	Page 6
		(c) Explain how missing data were addressed	Page 6, table S2
		(d) If applicable, explain how loss to follow-up was addressed	not applicable
		(e) Describe any sensitivity analyses	Page 6
Results			
Participants	13*	(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	Page 5 and 7
		(b) Give reasons for non-participation at each stage	yes
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic,	Page 7, table 1

		clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Table S2
		(c) Summarise follow-up time (eg, average and total amount)	not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time	Page 7, tables 1-3
Main results	16	(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	Pages 7-9, tables 1-3
		(b) Report category boundaries when continuous variables were categorized	yes
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pages 7-9, tables 1-3
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 11
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	Page 3, page 10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pages 9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 3 and 11
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	Page 11

*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 <http://www.strobe-statement.org>.