

BMJ Open Does caesarean delivery in the first pregnancy increase the risk for adverse outcome in the second? A registry-based cohort study on first and second singleton births in Norway

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ABSTRACT

Objective To explore if newborns in the second pregnancy following a previous caesarean delivery (CD) have higher risk of perinatal mortality or cerebral palsy than newborns in pregnancies following a previous vaginal delivery (VD).

Design Cohort study with information from the Medical Birth Registry of Norway and the Cerebral Palsy Registry of Norway.

Setting Births in Norway.

Participants 294 598 women with their first and second singleton delivery during 1996–2015.

Main outcome measures Stillbirth, perinatal mortality, neonatal mortality and cerebral palsy.

Results Among 294 598 included women, 42 962 (15%) had a CD in their first pregnancy while 251 636 (85%) had a VD. Compared with the second delivery of mothers with a previous VD, the adjusted OR (adjOR), for stillbirth in the second pregnancy following a previous CD was 1.45, 95% CI 1.22 to 1.73; for perinatal death the adjOR was 1.42 (1.22 to 1.73) and for neonatal death 1.13 (0.86 to 1.49). Among children who survived the neonatal period, the adjOR for cerebral palsy was 1.27 (0.99 to 1.64). Secondary outcomes, including small for gestational age, preterm and very preterm birth, uterine rupture and placental complications (eg, postpartum haemorrhage and pre-eclampsia) were more frequent in the subsequent pregnancy following a previous CD compared with a previous VD, in particular for uterine rupture adjOR 86.7 (48.2 to 156.1). Adjustment for potential confounders attenuated the ORs somewhat, but the excess risk in the second pregnancy persisted for all outcomes.

Conclusion A previous CD was in this study associated with increased risk for stillbirth and perinatal death compared with a previous VD. Although less robust, we also found that a previous CD was associated with a slightly increased risk of cerebral palsy among children surviving the neonatal period. The aetiology behind these associations needs further investigation.

INTRODUCTION

Between year 2000 and 2015, the number of caesarean deliveries (CD) increased from 16 to 29.7 million deliveries worldwide.¹ Moreover,

Strengths and limitations of this study

- Prospectively recording of high-quality data in the two national registers.
- Large number of births.
- Misclassification may occur for some of the clinical outcomes.
- Limited ability to address explanatory factors.

in 2008, WHO estimated that 6.2 million not medically indicated CDs were performed each year.² The ‘ideal’ CD rate has been debated for many years, and different studies have argued that a higher rate than 15% would not improve maternal and neonatal outcomes,^{3–5} while others have suggested national CD rate up to 19%.⁶ However, many middle-income and high-income countries have CD rates of 30%–50%.⁷ Although the risk for severe acute complications of CD is low in these countries,⁸ concerns regarding long-term complications, both for the mother and her child have been raised, also in subsequent pregnancy.^{9 10}

In Norway, a country with a CD rate of 16%, approximately 65% of the total number are emergency CDs.¹¹ However, in deliveries when planned CD is recommended to prevent potentially adverse outcomes of vaginal delivery (VD), these advantages should be weighed against potential long-term complications, including those in later pregnancies. This is particularly important when the absolute risk for acute complications during VD is low, such as in breech VD.¹² Studies have also reported higher risk for placental complications and uterine rupture in pregnancies following a previous CD.^{10 13 14} These complications are also associated with higher risk for delayed neurodevelopment and cerebral

palsy in the offspring.^{15 16} A balanced information on potential long-term consequences of CD is even more important when the mother requests her baby to be delivered by CD, but where medical evidence to support this choice is limited.¹⁷

On this background, the main aim of the present study was to explore if offspring in deliveries following a previous CD, have higher risk for perinatal death or cerebral palsy than offspring where the mother had a previous VD. As secondary outcomes, we also assessed the risks for placental complications, uterine rupture, preterm birth, fetal growth restriction and neonatal morbidity in the offspring following an earlier CD compared with those following a previous VD.

METHODS

In this population-based cohort study, including all births in Norway between 1996 and 2015 and information regarding pregnancy, delivery and the neonatal period was retrieved from the Medical Birth Registry of Norway (MBRN). This information was combined with information on a diagnosis of cerebral palsy recorded in the Cerebral palsy Registry of Norway (CPRN). The unique 11-digit personal identification number for every Norwegian citizen was used to link information from the two registers and made it possible to follow the women throughout all her pregnancies. Registration in the MBRN has been compulsory since 1967 with prospectively recorded information during pregnancy and at birth, including demographic variables, information on maternal health before and during pregnancy, interventions and complications during pregnancies, delivery and neonatal outcomes (including stillbirth). The CPRN is an informed consent-based national quality register established in 2006 and aims to record detailed information on all children with cerebral palsy born in Norway since 1996. Paediatricians at the neurohabilitation centres in Norway complete the information of each child using a standardised form. A validation study indicated that ~80% of the children with cerebral palsy born in Norway in 1996–2007 had detailed information in the CPRN.¹⁸ Later validations have suggested that the completeness is around 90% in recent years (annual reports of the CPRN).

Eligible for inclusion in this population-based study was women who delivered their first and second singleton child in Norway during 1996–2015. We excluded offspring who were born before 22 completed weeks of gestation and had a birth weight below 500 g. The offsprings were linked to their mothers by means of the national identification numbers, yielding maternal sibship files with the mother as the observation unit.

Study variables

The exposure variable was CD in the first pregnancy, regardless of whether this was emergency or planned. The reference group comprised mothers who delivered their first child vaginally (VD).

The predefined main outcome measures were stillbirth (antepartum and intrapartum and those with unspecified timing of death), perinatal mortality (stillbirth and deaths during first week of life), early neonatal mortality (deaths during first week of life), neonatal mortality (deaths during first 28 days of life) and cerebral palsy. In the CPRN, the diagnosis cerebral palsy is confirmed at 5 years of age according to the definition and classification proposed by the Surveillance of Cerebral Palsy in Europe.¹⁹

Secondary outcomes were preterm birth, evidence of fetal growth restriction, uterine rupture and placental complications such as placenta previa, placental abruption, abnormal invasive placenta, pre-eclampsia and postpartum haemorrhage. Preterm birth was defined as a birth before 37 weeks, and very preterm birth as a birth before 32 completed weeks of gestation. Evidence of fetal growth restriction was assessed by the proxy small for gestational age (SGA) defined by a birth weight below—2 SD of the population mean weight for GA, adjusted for sex.²⁰

Other variables extracted from the MBRN were maternal and pregnancy-related disorders such as pregestational diabetes, gestational diabetes and pre-eclampsia. For the purpose of the present study, we included gestational diabetes, and diabetes mellitus type 1 and 2 in the composite variable ‘diabetes’, while pre-eclampsia included mild, severe and unspecified pre-eclampsia, in addition to eclampsia and haemolysis, elevated liver enzymes, low platelets. Maternal age, birth year, smoking and congenital anomalies were also extracted. Information on smoking, recorded in the MBRN since December 1998, is based on information from ‘the antenatal chart’, a standardised form intended for clinical use, carried by the mother to each antenatal visit and completed by midwives and doctors responsible for the antenatal care. The mother is asked about smoking habits (daily smoking, occasionally or not at all) at first antenatal visit and at the end of the pregnancy. However, in contrast to all other variables registered in the MBRN, the mother may decline that her information on smoking is reported to the MBRN. Thus, information on smoking is missing for a subsample of mothers (around 12% in 1999–2000, nearly 20% in 2004–2007 and decreasing to less than 10% since 2015). For those with smoking information registered, we defined smokers as mothers who indicated that they smoked daily or occasionally either at the beginning or at the end of the pregnancy or both. Non-smokers were mothers who responded that they did not smoke during the pregnancy.

Gestational age was based on ultrasound examination before 20 weeks of gestation in 84% of the pregnant women, while in the remaining it was calculated from the last menstrual period.

Statistical analyses

Differences in proportions between groups were analysed using the X^2 test, and differences in means for continuous

variables were analysed using the Student's t-test not assuming equal variances.

Logistic regression analyses were used to calculate crude and adjusted ORs (OR) with 95% CIs for adverse outcomes of the second delivery following a CD in the first, compared with the outcomes of second deliveries following a first VD.

Potential confounders included in the multivariable analyses were selected based on availability, a priori knowledge and directed acyclic graphs methodology.²¹ These variables included pregnancy-related disorders (such as diabetes and pre-eclampsia), maternal age, birth year, SGA and congenital anomalies all recorded at the first delivery.

Since there is a risk of recurrence of adverse outcomes, such as stillbirth, perinatal death, preterm birth, fetal growth restriction and pre-eclampsia from one delivery to the next,^{22–24} we included complications in the first pregnancy that were defined as an adverse outcome in the second, as potential confounders. These complications may also affect the choice of mode of delivery in the first pregnancy, leading to potential confounding by indication, partly adjusted for in the logistic regression analyses described above. In addition, we also assessed confounding by indication in stratified analyses within subgroups of pregnancies with high and low risk for adverse outcomes.²⁵ The high-risk group comprised women with any complication in the first pregnancy that in the second pregnancy were considered as primary or secondary outcomes (stillbirth, perinatal mortality, neonatal mortality, SGA, placenta previa, postpartum haemorrhage, uterine rupture, placental abruption, preterm delivery and pre-eclampsia). The low-risk group included mothers without any of the specified primary or secondary outcomes in the first delivery, and where the first infant was born at term.

In separate analyses, maternal smoking was explored as a potential additional confounder in the population of mothers who had available information on smoking, with first deliveries from 1999.

Moreover, the birth intervals between pregnancies are likely to be shorter in mothers with a perinatal loss than in mothers whose first baby survived.²⁶ Mothers with a first delivery towards the end of the study period will have shorter interpregnancy intervals, and therefore, be more likely to have a first perinatal loss, and thus at increased risk for a recurrent second loss. In order to assess this possible bias, we performed a sensitivity analysis where we excluded women who had their first birth in 2012 or later, since these women had interpregnancy interval less than 4 years. Analyses from the MBRN show that 95% of women with two or more births, have their second child within 7 years following the first.²⁷ IBM SPSS Statistics V.25 was used for data analyses.

Patient involvement

Patients were not involved in setting the research question or the outcome measures nor were they involved in the design and implementation of the study. There are currently no plans to involve patients in dissemination.

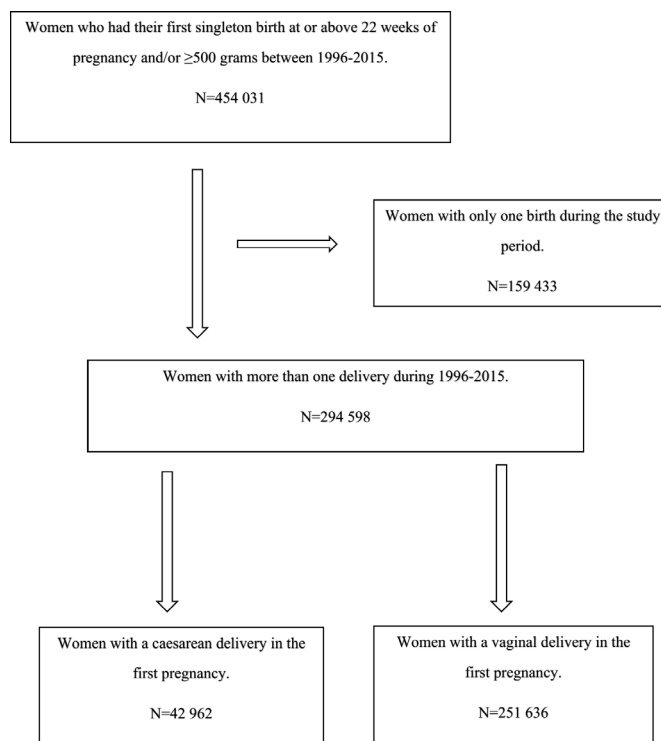


Figure 1 Flow chart of the study population. Only the first (exposure) and second (outcome) delivery of these women were included in the study.

RESULTS

During the study period, 454 031 mothers gave birth to a singleton as their first birth, but 159 433 had only one delivery. Among the remaining 294 598 mothers, 42 962 (15%) had a CD in their first pregnancy while 251 636 (85%) had a VD (figure 1).

Characteristics of the mothers and their babies, as well as adverse outcomes in the first pregnancy when mothers had a caesarean or VD are shown in table 1. The table shows that intrapartum stillbirth and neonatal loss occurred more frequently, whereas antepartum and total stillbirth occurred less frequently in the group of mothers with CD than mothers with a VD. Perinatal mortality did not differ between the two groups. A higher proportion of mothers in the CD group than in the VD group had pre-eclampsia and diabetes and more children were SGA, had congenital anomalies and were later diagnosed with cerebral palsy (table 1).

In their second delivery, approximately half of the women with a previous CD also had CD in their subsequent pregnancy, compared with 6% among those with a previous VD (table 2). Gestational age and mean birth weight were slightly lower and congenital anomalies, Apgar scores below 7 after 5 min and being transferred to the NICU were more common in the group with a previous CD (table 2).

When adjusting for potential confounders, the second infant of mothers with a previous CD had higher odds for antepartum and intrapartum stillbirth, total stillbirth and perinatal death compared with the second infant of a mother with a previous VD (table 3). The adjusted OR for early neonatal mortality was 1.27 (95% CI 0.92 to 1.73), for

Table 1 Maternal and infant characteristics and adverse outcomes in the first pregnancy of 42 962 women who had a caesarean and 251 636 women who had a vaginal delivery (VD) during 1996–2015

	CD	VD
Age, mean (SD)	27.8 (4.7)	26.5 (4.5)
Smoking, N (%)		
Information about smoking in the MBRN	29 229 (68.0)	170 040 (67.6)
Smoked during pregnancy	4571 (15.6)*	27 273 (16.0)*
Pre-eclampsia N (%)	5348 (12.4)	9346 (3.7)
Diabetes, N (%)	1366 (3.2)	2977 (1.2)
Placenta previa N (%)	474 (1.1)	52 (0.02)
Placenta abruption N (%)	865 (2.0)	258 (0.1)
Uterine rupture N (%)	5 (0.01)	5 (0.002)
Start of delivery, N (%)		
Spontaneous	18 568 (43.2)	215 243 (85.5)
Induced	10 626 (24.7)	36 393 (14.5)
Caesarean delivery (CD)	13 768 (33.0)	0
Gestational age at birth in weeks, mean (SD)	39.0 (2.9)	39.6 (1.9)
Birth weight in grams, mean (SD)	3401 (810)	3477 (524)
Sex, N (%)		
Female	19 597 (46.0)	123 230 (49.0)
SGA†, N (%)	1995 (5.0)	4823 (2.0)
Congenital anomalies, N (%)	3004 (7.0)	10 386 (4.1)
Total stillbirth, N (%)	110 (0.3)	1408 (0.6)
Antepartum stillbirth, N (%)	55 (0.1)	1039 (0.4)
Intrapartum stillbirth, N (%)	28 (0.1)	102 (0.04)
Perinatal mortality, N (%)	301 (0.7)	1714 (0.7)
Early neonatal mortality, N (%)	191 (0.4)	306 (0.1)
Neonatal mortality, N (%)	262 (0.6)	399 (0.2)
Cerebral palsy, N (%)	189 (0.4)	350 (0.1)
Apgar score after five min‡, N (%)		
0–3	406 (0.9)	1662 (0.7)
4–6	2314 (5.4)	5972 (2.3)
7–10	40 142 (93.7)	243 221 (97.0)
Transferred NICU, N (%)		
Yes	8965 (26.0)	18 971 (10.0)

Continued

Table 1 Continued

	CD	VD
*Percentage of mothers with information on smoking (available in the MBRN since 1999).		
†971 (2.3%) deliveries with missing information about SGA in the CD group and 5280 (2.1%) in the VD group.		
‡100 (0.2%) deliveries with missing information about Apgar score in the CD group and 781 (0.3%) in the VD group.		
MBRN, Medical Birth Registry of Norway; NICU, neonatal intensive care unit; SGA, small for gestational age.		

Table 2 Maternal and infant characteristics, including mode of delivery and adverse outcomes in the second pregnancy of 42 962 who had a caesarean and 251 636 who had a vaginal delivery in their first pregnancy (CD vs VD) during 1996–2015

	Previous CD	Previous VD	P value
Mothers age in years, mean (SD)	31.1 (4.6)	29.9 (4.4)	<0.001
Diabetes, N (%)	2095 (4.9)	4834 (1.9)	<0.001
Start of delivery, N (%)			
Spontaneous	22 707 (53.0)	211 165 (84.0)	
Induced	7179 (17.0)	30 895 (12.0)	<0.001
CD	13 074 (30.0)	9570 (4.0)	
Mode of delivery*, N (%)			
Vaginal delivery	20 826 (48.0)	235 372 (94.0)	<0.001
CD	22 136 (52.0)	16 264 (6.0)	
Gestational age at birth in weeks mean (SD)	39.1 (2.0)	39.5 (1.7)	<0.001
Birth weight in grams mean (SD)	3577 (613)	3630 (541)	<0.001
Congenital anomalies, N (%)	2007 (4.7)	9537 (3.8)	<0.001
Sex†, N (%)			
Female	20 958 (49.0)	122 307 (49.0)	0.50
Apgar score after 5 min‡, N (%)			
0–3	292 (1.0)	1048 (0.4)	
4–6	1196 (3.0)	2955 (1.2)	<0.001
7–10	41 407 (96.0)	247 028 (98.4)	
Transferred NICU, N (%)			
Yes	5424 (13.0)	16 502 (7.0)	<0.001

*2 (0.005%) deliveries with missing information about start of delivery in the previous CD group and 6 (0.002%) in the previous VD group.

†12 (0.005%) deliveries with missing information about sex in the previous VD group.

‡67 (0.16%) deliveries with missing information about Apgar score in the previous CD group and 605 (0.24%) in the previous VD group.

CD, caesarean delivery; NICU, neonatal intensive care unit; VD, vaginal delivery.

Table 3 OR with 95% CIs for adverse outcomes in the second pregnancy of 42 962 mothers who had a caesarean delivery (CD) in the first pregnancy compared with 251 636 mothers who had a previous vaginal delivery (VD)

	1st birth	2nd birth		
		Antepartum stillbirth	Crude OR (95% CI)	Adjusted OR (95% CI)*
CD 1st	N (%)	128 (0.3)	1.44 (1.19 to 1.75)	1.33 (1.08 to 1.63)
VD 1st	N (%)	520 (0.2)	1.0 (ref)	1.0 (ref)
		Intrapartum stillbirth		
CD 1st	N (%)	14 (0.03)	1.58 (0.87 to 2.85)	1.84 (1.00 to 3.38)
VD 1st	N (%)	52 (0.02)	1.0 (ref)	1.0 (ref)
		Stillbirth (total)†		
CD 1st	N (%)	179 (0.4)	1.52 (1.29 to 1.79)	1.45 (1.22 to 1.73)
VD 1st	N (%)	693 (0.3)	1.0 (ref)	1.0 (ref)
		Perinatal mortality		
CD 1st	N (%)	231 (0.5)	1.47 (1.27 to 1.70)	1.42 (1.22 to 1.65)
VD 1st	N (%)	921 (0.4)	1.0 (ref)	1.0 (ref)
		Early neonatal mortality		
CD 1st	N (%)	52 (0.1)	1.34 (0.99 to 1.81)	1.27 (0.92 to 1.73)
VD 1st	N (%)	228 (0.1)	1.0 (ref)	1.0 (ref)
		Neonatal mortality		
CD 1st	N (%)	68 (0.2)	1.24 (0.95 to 1.61)	1.13 (0.86 to 1.49)
VD 1st	N (%)	321 (0.1)	1.0 (ref)	1.0 (ref)
		Cerebral palsy		
CD 1st	N (%)	83 (0.2)	1.44 (1.13 to 1.83)	1.27 (0.99 to 1.64)
VD 1st	N (%)	338 (0.1)	1.0 (ref)	1.0 (ref)

Singleton deliveries during 1996–2015.

*Adjusted for maternal age, birth year, pregnancy-related disorders (pre-eclampsia and diabetes), SGA, congenital anomalies, uterine rupture, placenta previa, placental abruption in first pregnancy and the studied outcome in the first pregnancy.

†including stillbirths with unknown timing of death.

SGA, small for gestational age.

neonatal mortality the OR was 1.13 (95% CI 0.86 to 1.49) and for cerebral palsy OR was 1.27 (95% CI 0.99 to 1.64) (table 3).

When these associations were studied among women with high (n=78 056) and low (n=211 313) risk for adverse outcomes, the results were essentially the same as in the total study population (data are not shown).

All secondary outcomes, except abnormal invasive placenta, were more frequent in the subsequent pregnancy of women with a previous CD than among those with a previous VD (table 4). Most of these associations

were attenuated in multivariable analyses, but the main findings persisted.

In the subsample of 199 269 women where information about smoking was available (68% of the total study population), the results regarding antepartum and intrapartum stillbirth, overall stillbirth, perinatal early and neonatal mortality persisted, but were slightly attenuated in the multivariable analyses (see online supplementary table 1). The crude OR for cerebral palsy was also unchanged but was reduced in the multivariable analyses to 1.23 (95% CI 0.90 to 1.67). However, adding smoking as a potential confounder to the other confounders did not change the adjusted OR neither for primary nor for the secondary outcomes (see online supplementary tables 1 and 2).

In the sensitivity analyses excluding women who had their first birth in 2012 or later (leaving 274 041 women for analysis), the results were nearly identical to the results in the total population. In this subsample, 39 812 (15%) had a CD in their first pregnancy and 234 229 (85%) had a VD (see online supplementary tables 3 and 4).

DISCUSSION

In this population-based cohort study in Norway, we found increased risk for stillbirth, perinatal death and cerebral palsy in the second pregnancy of mothers who had a CD in their first pregnancy, compared with mothers who had a VD in their first pregnancy. In contrast we did not find a higher risk for neonatal mortality, although there was a trend towards increased risk for early neonatal mortality. Also, growth restriction, preterm delivery, pre-eclampsia, placental complications, postpartum haemorrhage and especially uterine rupture were increased in pregnancies following a CD.

Strength and limitations

The strength of this study is the large number of births based on mandatory registration and thus minimal risk of selection bias. The prospectively collected data from the MBRN and the CPRN, and the ability to link births to their mothers by the identification numbers enabled complete analyses of the first and second births to all mothers giving birth in 1996–2015. We restricted the analyses to singletons, since both CD and the studied outcomes are more frequent in multiple pregnancies. Moreover, the main findings persisted when adjusted for potential confounders in multivariable analyses, and when we assessed confounding by indication in analyses restricted to mothers with high and low risk of adverse outcomes. In these latter analyses, the main findings persisted in both groups, suggesting that confounding by indication was less likely. Finally, in the subpopulation with information on smoking, the main results also persisted.

A potential selection bias of the study population may arise from the fact that women with a perinatal loss in their first pregnancy tend to proceed to their second pregnancy earlier than women without such an event,

**Table 4** OR with 95% CIs for adverse secondary outcomes in the second pregnancy of 42 962 mothers who had a caesarean delivery (CD) in the first pregnancy compared with 251 636 mothers who had a previous vaginal delivery (VD)

1st birth	2nd birth		Crude OR (95% CI)	Adj OR (95% CI)†
	Small for gestational age*			
CD 1st	N (%)	636 (1.5)	1.63 (1.49 to 1.78)	1.32 (1.20 to 1.45)
VD 1st	N (%)	2295 (0.9)	1.0 (ref)	1.0 (ref)
Preterm birth‡				
CD 1st	N (%)	2647 (6.2)	1.72 (1.64 to 1.80)	1.18 (1.12 to 1.24)
VD 1st	N (%)	9254 (3.7)	1.0 (ref)	1.0 (ref)
Very preterm birth‡				
CD 1st	N (%)	570 (1.3)	1.97 (1.79 to 2.17)	1.29 (1.16 to 1.44)
VD 1st	N (%)	1703 (0.7)	1.0 (ref)	1.0 (ref)
Postpartum haemorrhage				
CD 1st	N (%)	12 232 (28)	2.76 (2.70 to 2.83)	2.32 (2.26 to 2.38)
VD 1st	N (%)	31 705 (12)	1.0 (ref)	1.0 (ref)
Placenta previa				
CD 1st	N (%)	292 (0.7)	2.60 (2.27 to 2.99)	2.33 (2.01 to 2.70)
VD 1st	N (%)	660 (0.3)	1.0 (ref)	1.0 (ref)
Placental abruption				
CD 1st	N (%)	282 (0.7)	2.48 (2.16 to 2.86)	2.14 (1.84 to 2.49)
VD 1st	N (%)	668 (0.3)	1.0 (ref)	1.0 (ref)
Abnormal invasive placenta				
CD 1st	N (%)	131 (0.3)	1.14 (0.95 to 1.38)	1.00 (0.82 to 1.21)
VD 1st	N (%)	672 (0.3)	1.0 (ref)	1.0 (ref)
Uterine rupture				
CD 1st	N (%)	190 (0.4)	93.4 (51.9 to 166.9)	86.7 (48.2 to 156.1)
VD 1st	N (%)	12 (0.005)	1.0 (ref)	1.0 (ref)
Pre-eclampsia				
CD 1st	N (%)	1970 (4.6)	2.58 (2.44 to 2.72)	1.60 (1.51 to 1.70)
VD 1st	N (%)	4609 (1.8)	1.0 (ref)	1.0 (ref)

Singleton deliveries during 1996–2015.

*308 (0.7%) deliveries with missing information on SGA in the caesarean group and 2000 (0.8%) in the vaginal group.

†Adjusted maternal age, birth year, pregnancy-related disorders (pre-eclampsia and diabetes), SGA and congenital anomalies, uterine rupture, placenta previa, placental abruption in first pregnancy and the studied outcome in the first pregnancy.

‡306 (0.7%) deliveries with missing information on GA in the caesarean group and 1958 (0.8%) in the vaginal group.

GA, gestational age; SGA, small for gestational age.

thereby artificially increasing the proportion of women with losses in their second pregnancy (due to the known recurrence risk of perinatal losses). Since the implications of this selection bias is unclear, we performed sensitivity analyses where we excluded women who had their first birth in 2012 or later, and hence had an interpregnancy interval shorter than 4 years. Moreover, in the population born after 2012 there may be some underreporting of cases with cerebral palsy, since this diagnosis is reported to the CPRN at age 5 years, and since there may be some delay in the registration. Nonetheless, all results were essentially unchanged.

Other limitations of this study are related to potential misclassification of both exposure and outcome. The data on mortality and delivery mode are variables with

high quality and are unlikely to be misclassified.²⁸ For the secondary outcomes, both pre-eclampsia, SGA and preterm delivery are variables with high quality,²⁹ while the validity for placenta previa and placental abruption has not been studied. In addition, inconsistent definitions may have led to some misclassification of uterine rupture and abnormal invasive placenta.³⁰

Further limitations are related to unmeasured confounders, as well as to potential confounders with limited available data, such as body mass index and weight change during the pregnancy.

Comparison with other studies

Our findings regarding excess risk for stillbirth in subsequent pregnancies after a previous CD is consistent with

several other studies.^{31–34} In a retrospective cohort study and meta-analysis published in 2015, the authors found an association between previous CD and the risk for antepartum stillbirth in the second pregnancy with a pooled HR 1.40 (95% CI 1.10 to 1.77),³⁵ similar to our results.

Another systematic review and a meta-analysis published in 2018 reported no clear association of mode of delivery with perinatal death comparing previous CD with previous VD,⁹ as opposed to the results of the present study. However, this meta-analysis included only two studies with considerably smaller populations than the present study and in one of them, the estimated OR for perinatal death was 1.29 (95% CI 0.94 to 1.79),³² more in line with our study. Moreover, an older study not included in the meta-analysis but with a population of the same size as our study, found increased risk for perinatal death among children born by a mother with a previous CD compared with previous VD (RR 1.33, 95% CI 1.10 to 1.62).³⁶

We have not found other studies addressing the risk of cerebral palsy in deliveries following a previous CD.

Regarding the secondary outcomes, the increased risks of SGA, preterm birth, uterine rupture and several placental complications in the second delivery following a previous CD compared with a previous VD, are in line with other studies.^{10 13 32 37–42} Somewhat unexpected the proportion with abnormal invasive placenta did not differ between the two groups, which may partly be explained by the quality of this variable in the MBRN. Another explanation may be that our study was limited to adverse outcomes only in the second pregnancy, and studies have reported that abnormal invasive placenta is strongly associated with increasing numbers of CD performed.^{43 44}

Interpretation

The findings regarding antepartum and total stillbirth, and perinatal death were all in the same direction, relatively precise and in line with previous literature, indicating that these findings are robust. The increased odds for cerebral palsy and the trend towards increased risk for early neonatal death were less robust. However, the number of infants with cerebral palsy was low, and the number of infants who died during delivery and in the neonatal period were even lower, and these findings should therefore be interpreted with caution.

The increased risk for any of the primary adverse outcomes in the second pregnancy may be due to placental complications, as indicated by the higher occurrence of infants born SGA, as well as a higher occurrence of placenta previa, placental abruption and pre-eclampsia compared with pregnancies without a previous CD. We speculate that the scar in the uterus after previous surgery may play a role in the development of such placental complications, for example, through suboptimal placental implantation in the following pregnancy. In addition, a scar in the uterus is a locus minoris resistentiae, increasing the risk for rupture of the uterus in the following pregnancies, as supported by the very high increased risk of uterine rupture associated with previous CD found in our study.

Moreover, it is well documented that placental pathology, placental abruption, pre-eclampsia, uterine rupture, preterm birth and being born SGA are all risk factors for cerebral palsy.^{45–47} These risk factors may be involved both in antenatal as well as in perinatal events, leading to an insult of the brain. The increased risk for cerebral palsy is also consistent with the lower Apgar score among infants born by mothers with a previous CD, compared with those whose mothers had a previous VD, found in our study.

The trend towards increased risk for early neonatal mortality may be consistent with increased risk for intra-partum death. However, the risk for neonatal death was only slightly different between the groups, which may be reasonable due to other causes of death later in the neonatal period rather than complications during the delivery. More studies are required to investigate if and how mode of delivery in the second pregnancy may have affected this outcome.

Implication

In this population-based study from Norway, the absolute risk for stillbirth, neonatal death and cerebral palsy in the second pregnancy was low, as were the absolute risk for the secondary outcomes. Nonetheless, the increased relative risk for these complications should be included in the discussion with parents regarding mode of delivery, both when the mother requests a CD in the absence of a clear medical indication as well as in cases when a VD is associated with increased relative, but low absolute risk for adverse outcome. If the increased risk was entirely related to the actual mode of delivery in the second pregnancy, it might be reasonable to recommend a planned CD to all women with a previous CD in their subsequent pregnancy. However, this would not abolish the risk for antepartum stillbirth, SGA and preterm birth. Therefore, the main prevention of these severe complications in subsequent pregnancy may be to take individual plans for further pregnancies into account when considering CD without a clear medical indication. On the other hand, it should be underscored that overall, the absolute risks for stillbirth, perinatal mortality and cerebral palsy after a previous CD are indeed low in the following pregnancy.

CONCLUSION

A previous CD was in this study associated with increased risk for stillbirth and perinatal death compared with a previous VD. Although less robust, we also found that a previous CD was associated with a slightly increased risk of cerebral palsy among children surviving the neonatal period. The aetiology behind these associations needs further investigation.

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Patient consent for publication Not required.

Ethics approval The study was approved by the Regional Ethical Committee for Medical Research in Mid-Norway (ref 2018/2145). We intend to present results directly to the Association for persons with cerebral palsy. In addition, dissemination to the Norwegian population (which constitutes the study population) and the broader public will be achieved through media outreach or other public presentations.

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Data availability statement Data may be obtained from a third party and are not publicly available. No data are available. For question regarding the analyses of the data, please contact the corresponding author at: solveigbjellmo@gmail.com. The protocol is also available on request.

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REFERENCES

- Boerma T, Ronsmans C, Melesse DY, *et al*. Global epidemiology of use of and disparities in caesarean sections. *Lancet* 2018;392:1341–8.
- Gibbons L, Belizán JM, Lauer JA, *et al*. The global numbers and costs of additionally needed and unnecessary caesarean sections performed per year: overuse as a barrier to universal coverage. *World Health Report* 2010;30:1–31.
- Appropriate technology for birth. *Lancet* 1985;2:436–7.
- Kupari M, Talola N, Luukkaala T, *et al*. Does an increased caesarean section rate improve neonatal outcome in term pregnancies? *Arch Gynecol Obstet* 2016;294:41–6.
- Ye J, Zhang J, Mikolajczyk R, *et al*. Association between rates of caesarean section and maternal and neonatal mortality in the 21st century: a worldwide population-based ecological study with longitudinal data. *BJOG* 2016;123:745–53.
- Molina G, Weiser TG, Lipsitz SR, *et al*. Relationship between cesarean delivery rate and maternal and neonatal mortality. *JAMA* 2015;314:2263–70.
- Betrán AP, Ye J, Moller A-B, *et al*. The increasing trend in caesarean section rates: global, regional and national estimates: 1990–2014. *PLoS One* 2016;11:e0148343.
- National Institute for Health and Clinical Excellence. Caesarean section (NICE clinical guideline 132), 2011. Available: <https://www.nice.org.uk/guidance/CG132>
- Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. *PLoS Med* 2018;15:e1002494.
- Daltveit AK, Tollånes MC, Pihlstrøm H, *et al*. Caesarean delivery and subsequent pregnancies. *Obstet Gynecol* 2008;111:1327–34.
- MBRN. Norwegian Institute of public health. Medical birth registry of Norway, 2018. Available: <http://statistikkbank.fhi.no/mfr/>
- Hannah ME, Hannah WJ, Hewson SA, *et al*. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. Term breech trial collaborative group. *Lancet* 2000;356:1375–83.
- Jackson S, Fleege L, Fridman M, *et al*. Morbidity following primary cesarean delivery in the Danish national birth cohort. *Am J Obstet Gynecol* 2012;206:139.e1–5.
- Rageth JC, Juzi C, Grossenbacher H. Delivery after previous cesarean: a risk evaluation. *Obstet Gynecol* 1999;93:332–7.
- Stoknes M, Andersen GL, Elkamil AI, *et al*. The effects of multiple pre- and perinatal risk factors on the occurrence of cerebral palsy. A Norwegian register based study. *Eur J Paediatr Neurol* 2012;16:56–63.
- Thorngren-Jerneck K, Herbst A. Perinatal factors associated with cerebral palsy in children born in Sweden. *Obstet Gynecol* 2006;108:1499–505.
- O'Donovan C, O'Donovan J. Why do women Request an elective cesarean delivery for non-medical reasons? A systematic review of the qualitative literature. *Birth* 2018;45:109–19.
- Hollung SJ, Vik T, Wiik R, *et al*. Completeness and correctness of cerebral palsy diagnoses in two health registers: implications for estimating prevalence. *Dev Med Child Neurol* 2017;59:402–6.
- Cans C. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. *Dev Med Child Neurol* 2000;42:816–24.
- Skjaerven R, Gjessing HK, Bakketeig LS. Birthweight by gestational age in Norway. *Acta Obstet Gynecol Scand* 2000;79:440–9.
- Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10:37–48.
- Lamont K, Scott NW, Jones GT, *et al*. Risk of recurrent stillbirth: systematic review and meta-analysis. *BMJ* 2015;350:h3080.
- Melve KK, Skjaerven R. Birthweight and perinatal mortality: paradoxes, social class, and sibling dependencies. *Int J Epidemiol* 2003;32:625–32.
- Klungsoyr K, Morken NH, Irgens L, *et al*. Secular trends in the epidemiology of pre-eclampsia throughout 40 years in Norway: prevalence, risk factors and perinatal survival. *Paediatr Perinat Epidemiol* 2012;26:190–8.
- Aronson JK BC, Mahtani KR, Nunan D. Confounding by indication. In catalogue of biases, 2018. Available: <https://catalogofbias.org/biases/confounding-by-indication>
- Regan AK, Gissler M, Magnus MC, *et al*. Association between interpregnancy interval and adverse birth outcomes in women with a previous stillbirth: an international cohort study. *Lancet* 2019;393:1527–35.
- Skjaerven R, Wilcox AJ, Klungsoyr K, *et al*. Cardiovascular mortality after pre-eclampsia in one child mothers: prospective, population based cohort study. *BMJ* 2012;345:e7677.
- Lehmann S, Baghestan E, Børdaahl P, *et al*. Validation of data in the medical birth registry of Norway on delivery after a previous cesarean section. *Acta Obstet Gynecol Scand* 2017;96:892–7.
- Thomsen LCV, Klungsoyr K, Roten LT, *et al*. Validity of the diagnosis of pre-eclampsia in the medical birth registry of Norway. *Acta Obstet Gynecol Scand* 2013;92:943–50.
- Al-Zirqi I, Stray-Pedersen B, Forsén L, *et al*. Validation study of uterine rupture registration in the medical birth registry of Norway. *Acta Obstet Gynecol Scand* 2013;92:1086–93.
- Osborne C, Ecker JL, Gauvreau K, *et al*. First birth cesarean and risk of antepartum fetal death in a subsequent pregnancy. *J Midwifery Womens Health* 2012;57:12–17.
- Kennare R, Tucker G, Heard A, *et al*. Risks of adverse outcomes in the next birth after a first cesarean delivery. *Obstet Gynecol* 2007;109:270–6.

- 33 Gray R, Quigley MA, Hockley C, *et al.* Caesarean delivery and risk of stillbirth in subsequent pregnancy: a retrospective cohort study in an English population. *BJOG: Int J Obstet Gy* 2007;114:264–70.
- 34 Smith GCS, Pell JP, Dobbie R. Caesarean section and risk of unexplained stillbirth in subsequent pregnancy. *Lancet* 2003;362:1779–84.
- 35 Moraitis AA, Oliver-Williams C, Wood AM, *et al.* Previous caesarean delivery and the risk of unexplained stillbirth: retrospective cohort study and meta-analysis. *BJOG: Int J Obstet Gy* 2015;122:1467–74.
- 36 Rageth JC, Juzi C, Grossenbacher H. Delivery after previous cesarean: a risk evaluation. Swiss working group of obstetric and gynecologic institutions. *Obstet Gynecol* 1999;93:332–7.
- 37 Taylor LK, Simpson JM, Roberts CL, *et al.* Risk of complications in a second pregnancy following caesarean section in the first pregnancy: a population-based study. *Med J Aust* 2005;183:515–9.
- 38 Hemminki E, Shelley J, Gissler M. Mode of delivery and problems in subsequent births: a register-based study from Finland. *Am J Obstet Gynecol* 2005;193:169–77.
- 39 Getahun D, Oyelese Y, Salihu HM, *et al.* Previous cesarean delivery and risks of placenta previa and placental abruption. *Obstet Gynecol* 2006;107:771–8.
- 40 Downes KL, Hinkle SN, Sjaarda LA, *et al.* Previous prelabor or intrapartum cesarean delivery and risk of placenta previa. *Am J Obstet Gynecol* 2015;212:669.e1–6.
- 41 Salihu HM, Bekan B, Aliyu MH, *et al.* Perinatal mortality associated with abruptio placenta in singletons and multiples. *Am J Obstet Gynecol* 2005;193:198–203.
- 42 Gurol-Urganci I, Cromwell DA, Edozien LC, *et al.* Risk of placenta previa in second birth after first birth cesarean section: a population-based study and meta-analysis. *BMC Pregnancy Childbirth* 2011;11:95.
- 43 Silver RM, Landon MB, Rouse DJ, *et al.* Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol* 2006;107:1226–32.
- 44 Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year analysis. *Am J Obstet Gynecol* 2005;192:1458–61.
- 45 Nelson KB, Blair E. Prenatal factors in singletons with cerebral palsy born at or near term. *N Engl J Med* 2015;373:946–53.
- 46 Vik T, Redline R, Nelson KB, *et al.* The placenta in neonatal encephalopathy: a case-control study. *J Pediatr* 2018;202:77–85.
- 47 McIntyre S, Taitz D, Keogh J, *et al.* A systematic review of risk factors for cerebral palsy in children born at term in developed countries. *Dev Med Child Neurol* 2013;55:499–508.