Birth after Caesarean Section

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Abstract: Birth after caesarean section (CS) is an issue of growing importance. As a consequence of increasing CS rates, more women having experienced a prior CS will need counselling about preferred second delivery mode. There are two choices: elective repeat caesarean section (ERCS) or trial of labour (TOL). It is well known, that a TOL ending in an emergency CS carries the largest risks for mother and child. We wanted to investigate for which women and infants it would be safest to recommend an ERCS or a TOL. We assumed, that underlying conditions/indications for the first CS performed would often recur in the second pregnancy and be important for the second delivery outcome. Therefore, a hierarchical system was developed, in which efforts were made to classify according to underlying conditions instead of focusing on conditions appearing during labour, in an attempt to diminish the subjective impact of diagnoses recorded after delivery. The hierarchical system was used through the four papers.

We investigated women in the Swedish medical birth register with their first two deliveries 1987-2007 (Paper I-III), or giving birth at least twice, including one CS and at least one delivery after the CS 1992-2011 (Paper IV). In Papers I-III, we have shown that all first CS indications had a statistically significant risk to recur in the second pregnancy/delivery. Women with a first CS were older, shorter, and had a higher body mass index than women with a first vaginal delivery. The risk for unplanned CS in TOL increased by the women's age, body mass index, and smoking, while increasing height lowered the risk. Women with a prior CS had an all-over increased risk for unplanned CS in TOL, compared with primiparous women. Infants born to mothers with one prior CS had an almost doubled risk for low Apgar score and perinatal death compared with infants of women with one prior vaginal birth. The risk was lower but still statistically significant after adjustment for possible maternal and fetal/infant confounders. For infants of women with one previous CS, the risk for low Apgar score was higher after a TOL than after an ERCS. In all studies, the risk for adverse outcomes differed substantially between hierarchical indications for the first CS performed. When the first CS was performed without medical indication, no inreased risk for low Apgar score or perinatal death could be detected. The results suggest that underlying conditions, not the previous CS *per se*, contributed to the risk increase. In Paper IV, we validated a widely used prediction model for chance of successful TOL after CS, developed by Grobman et al. (2007) for US conditions. As the original model was not directly applicable for Swedish settings, we modified it stepwise. The final, new model included maternal age, body mass index, prior vaginal birth, prior vaginal birth after CS, maternal height, first CS hierarchical indication, and the rates of ERCS and unplanned CS in the respective delivery wards. We reached an excellent predictability for vaginal birth in TOL after CS.

Counselling about the safest delivery mode after one CS is a challenge. Our study results, combined with previous findings, add important scientific knowledge. However, non-medical factors are vital in the decision-making after one CS, and a trust between the woman, her partner, the obstetrician and the midwife is fundamental. Considering the new information would possibly make counselling easier and, hopefully, lower the rate of unplanned CS in TOL after CS and decrease the rate of low Apgar score and perinatal death in the birth after a caesarean delivery.

Key words: caesarean section, prediction model, trial of labour, vaginal birth after caesarean

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For Alva, Hilda & Olle

All things are so very uncertain,
and that's exactly what makes me feel reassured.

Too-Ticky in Moominland Midwinter by Tove Jansson

Contents

Abstract

Birth after caesarean section (CS) is an issue of growing importance. As a consequence of increasing CS rates, more women having experienced a prior CS will need counselling about preferred second delivery mode. There are two choices: elective repeat CS (ERCS) or trial of labour (TOL). It is well known, that a TOL ending in an unplanned CS carries the largest risks for mother and child.

We wanted to investigate for which women it would be safest to recommend an ERCS or a TOL, by studying the rate of unplanned CS in TOL and the infant outcome (low Apgar score, <7 at 5 minutes, or perinatal death) of TOL. We assumed, that underlying conditions/indications for the first CS performed would often recur in the second pregnancy and be important for the second delivery outcome. Therefore, a hierarchical system was developed, in which efforts were made to classify according to underlying conditions instead of focusing on conditions appearing during labour (e.g., fetal distress), in an attempt to diminish the subjective impact of diagnoses recorded after delivery. The hierarchical system was used through the four papers. We investigated women in the Swedish medical birth register with their first two deliveries 1987-2007 (**Paper I-III**), or giving birth at least twice, including one CS and at least one delivery after the CS 1992-2011 (**Paper IV**).

In **Papers I-III**, we have shown that all first CS indications had a statistically significant risk to recur in the second pregnancy/delivery. Women with a first CS were older, shorter, and had a higher body mass index than women with a first vaginal delivery. The risk for unplanned CS in TOL increased by the women's age, BMI, and smoking, while increasing height lowered the risk.

Women with a prior CS had an all-over increased risk for unplanned CS in TOL, compared with primiparous women. Infants born to mothers with one prior CS had an almost doubled risk for low Apgar score and perinatal death compared with infants of women with one prior vaginal birth. The risk was lower but still statistically significant after adjustment for possible maternal and fetal/infant confounders. For infants of women with one previous CS, the risk for low Apgar score was higher after a TOL than after an ERCS.

In all studies, the risk for adverse outcomes differed substantially between hierarchical indications for the first CS performed. When the first CS was performed without medical indication, no increased risk for low Apgar score or perinatal death was

detected. The results suggest that underlying conditions, not the previous CS *per se*, contributed to the risk increase.

In **Paper IV**, we validated a widely used prediction model for chance of successful TOL after CS, developed by Grobman et al. (2007) for US conditions. As the original model was not directly applicable for Swedish settings, we modified it stepwise. The final, new model included maternal age, body mass index, prior vaginal birth, prior vaginal birth after CS, maternal height, first CS hierarchical indication, and the rates of ERCS and of unplanned CS in the respective delivery wards. We reached an excellent predictability for vaginal birth in TOL after CS.

Counselling about the safest delivery mode after one CS is a challenge. Our study results, combined with previous findings, add important scientific knowledge. However, non-medical factors are vital in the decision-making after one CS, and a trust between the woman, her partner, the obstetrician and the midwife is fundamental. Considering the new information would possibly make counselling easier and, hopefully, lower the rate of unplanned CS in TOL after CS and decrease the rate of low Apgar score and perinatal death in the birth after a caesarean delivery.

Abbreviations

AUC	Area under curve
BW	Birthweight
BMI	Body mass index
CI	Confidence interval
CS	Caesarean section
ERCS	Elective repeat caesarean section
FV	Förlossningsvård (Delivery care)
GA	Gestational age
ICD	International classification of diseases
LGA	Large for gestational age
MHV	Mödrahälsovård (Maternal health care)
MBR	Medical birth register
NBH	National board of health
NNH	Number needed to harm
NNT	Number needed to treat
OR	Odds ratio
PRS	Perinatal revision south register
ROC	Receiver operating curve
RR	Risk ratio
SD	Standard deviation
SGA	Small for gestational age
TOL	Trial of labour
VBAC	Vaginal birth after caesarean
Vs.	versus

Original Publications

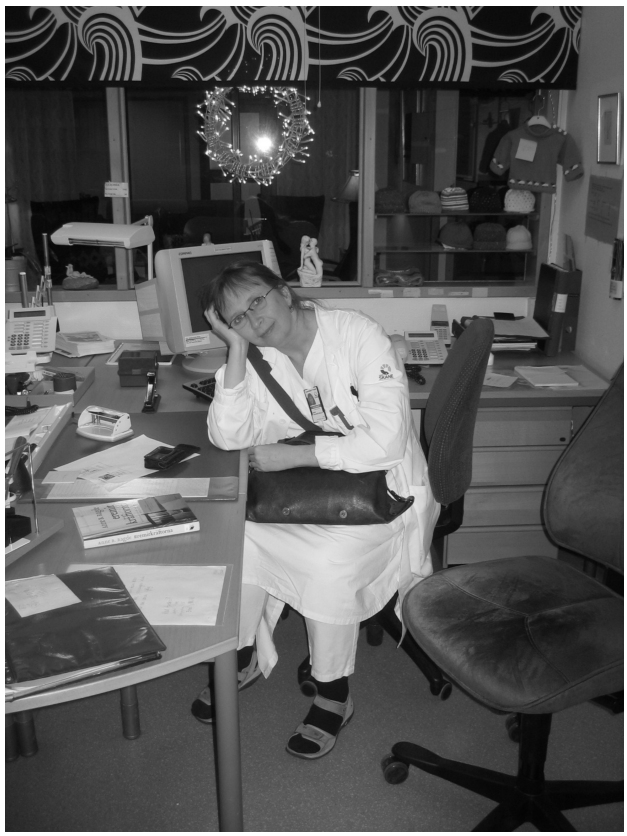
This thesis is based on the following papers, referred to in the text by their roman numerals. The publications are appended at the end of the thesis.

I. Carlsson Wallin M, Ekstrom P, Marsal K, Kallen K. Apgar score and perinatal death after one previous caesarean delivery. BJOG 2010;117:1088-97.

II. Fagerberg MC, Marsal K, Ekstrom P, Kallen K. Indications for first caesarean and delivery mode in subsequent trial of labour. Paediatr Perinat Epidemiol 2013;27:72-80.

III. Fagerberg MC, Marsal K, Kallen K. Neonatal outcome after trial of labor or elective cesarean section in relation to the indication for the previous cesarean delivery. Acta Obstet Gynecol Scand 2013;92:1151-8.

IV. Marie Carlsson Fagerberg, Karel Maršál, Karin Källén. Predicting the chance of vaginal delivery after one caesarean section. Validation and elaboration of a published prediction model. Submitted 2014.



Preface

To give birth is an overwhelming experience. Ask 1000 women about their deliveries and you will be told 1000 completely different stories, all filled with emotions.

Being a part of the team guiding a woman and her partner through delivery is something special. To help a new family-to-be to a positive experience, an event to look back at with satisfaction, whether the delivery be vaginal or by caesarean and whether the baby be in full health or not, is a major professional challenge.

For more than twenty years, I have been a specialist in gynaecology and obstetrics, successively profiling in the field of obstetrics. And still, every delivery I am involved in – just attending, as a part of the team, or helping the child out with a vacuum extractor or by a caesarean section – is a very special event. I can surely get very tired of working too much, but I never get tired of these moments. To have a profession where you deal with so much life, sometimes with death, and with everything in between, has made me humble towards life itself. That is a gift!

Regardless the wonders and miracles of my everyday work, it can also be hard and fatiguing. One dark night in the beginning of 2007, I was on call at Ystad BB. One of the women in labour had undergone a first delivery by caesarean, and my thoughts wandered to the small epidemic of almost-ruptures of the uterus we had encountered in the previous weeks. An unusual number of caesareans because of non-reassuring fetal heart rates and maternal abdominal pain between contractions had been performed. We had seen the babies through the membranes of half-ruptured uterine walls, looking like fishes in an aquarium. So, I sat there, thinking about what the future would look like, with an increasing part of women attending delivery with a former experience of a caesarean – about 9% of women at that time. We did not have any special policy for treating these women. Would we need to learn more, and to develop guidelines for delivery mode planning?

Some weeks later, I went to Lund to see Karin Källén, reproduction epidemiologist and supervisor of the Perinatal Revision South Register (PRS), for advice. Could she please help me to search for facts about deliveries after caesarean sections? When we had talked for a couple of hours, Karin said: The PRS will not be enough for answering your questions. But you have enough questions for writing a whole dissertation! Wouldn't you like to? I can be your tutor.

That was the start of this project, going on far longer than a normal pregnancy, but certainly including all its ups and downs. This is the offspring.

I dreamed of having a book of my own,
of writing one that I could put on a shelf

Patti Smith

Introduction

Caesarean section (CS) is the most common surgical procedure performed in modern obstetrics. Its availability has been, and is still, of utmost importance for the safety and health of billions of women and their children worldwide. A CS is a perfect solution when vaginal birth is not suitable for the mother or her infant, or when complications occur during delivery. Simultaneously, in most developed countries, the CS rates have been increasing for the last fifty years without any major effect on adverse delivery outcomes.

In everyday obstetrics, the CS rate is one of the most discussed and debated subjects. The optimal rate of births by CS remains controversial in both developing and developed countries (Betrán et al., 2007). In Sweden, we use the "Ten groups" (Robson, 2004) to compare CS rates over time in specific delivery wards and between hospitals. There are many undebatable medical reasons for performing a CS. Nevertheless, in developed countries, the characteristics of the population belonging to the delivery ward in question, the staff's traditions regarding choice of delivery mode, and trends in society at large, are other factors of greatest importance when discussing the CS rates. In developing countries, the issue is often more about availability of maternal health care, and a corresponding underuse of CS is part of a web of factors predisposing to high maternal and perinatal mortality (Betrán et al., 2007).

Following every CS performed, there is a possible delivery-to-come. In Sweden, between 1992 and 2007, almost two thirds of women having experienced one CS would give birth again. In the group of women with one previous vaginal delivery, the corresponding part was almost four out of five.

The knowledge about the outcomes of deliveries after CS is growing, but is still not as extensive as about CS *per se*. Several studies considering infant and, particularly, maternal adverse outcomes in a delivery following a CS have been published (Hemminki et al., 2004; Taylor et al., 2005; Kaczmarczyk et al., 2007; Kennare et al., 2007; Daltveit et al., 2008).

In our studies, resulting in Publication I-IV, we aimed to make a thorough exploration of underlying factors possibly playing a role in the delivery after a first CS.

We would start by investigating the population characteristics.

Second, to find the most probable, robust indication for the first CS performed, we would develop a hierarchical system of indications/diagnoses/conditions present at the first delivery CS. We would use this hierarchical system to study the impact of a first delivery CS on the infant outcome of the following delivery, in terms of low Apgar score (less than seven at five minutes of age) and perinatal death (fetal/infant death from 28 full gestational weeks to six days of age), compared with the infant outcome of the delivery following a vaginal birth.

Third, we would use the hierarchical system of first CS indications to explore the delivery mode in the delivery subsequent to a CS, compared with the delivery mode for primiparous women.

Fourth, focusing only on women having experienced one CS, we would compare the success rate and infant outcome of a trial of labour (TOL) with the corresponding outcomes of an elective repeat caesarean section (ERCS).

Finally, we would combine our new scientific knowledge with findings from other authors, to develop a prediction model for vaginal birth after caesarean (VBAC), suitable for Swedish conditions.

Background

The First Caesarean Section

Caesarean Section Rate

The CS rate in Sweden increased steadily until 2006. Thereafter, it has remained quite constant, at about 17% (The Swedish Medical Birth Register (MBR)).

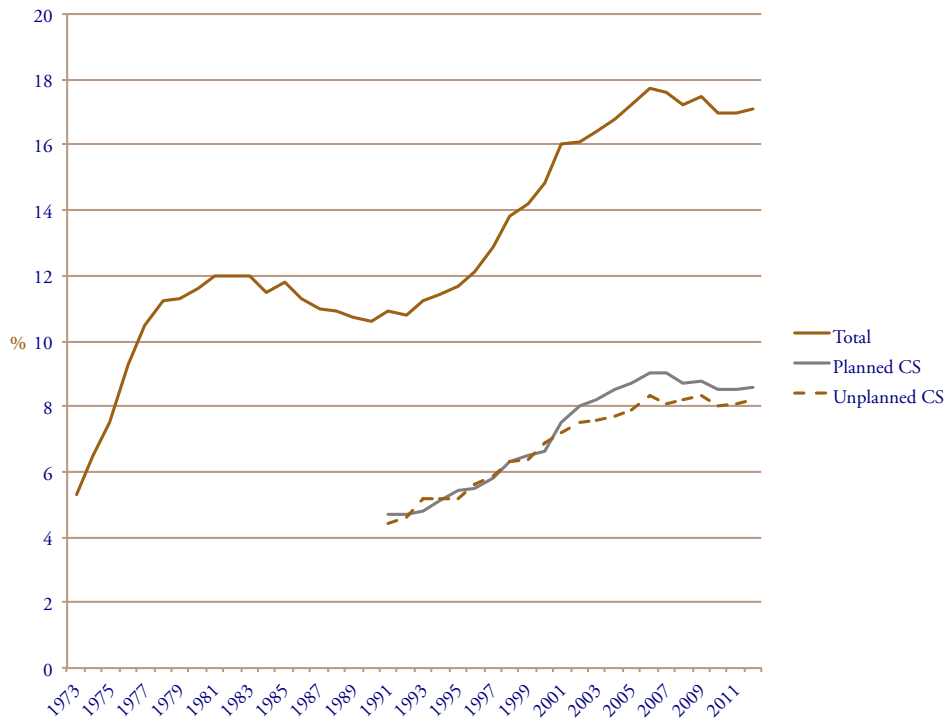


Figure 1. Caesarean deliveries, total and performed before or after start of contractions, respectively. Sweden 1975-2012 (The Swedish MBR).

From 1991 to 2000, the CS rate increase was nearly parallel for CS performed before and CS performed after the start of contractions. From 2000 to 2006, the increase was almost totally due to CS performed before contractions.

To deepen the understanding of the rising CS rates in Sweden until 2006, it might be of benefit to study subgroups of women giving birth.

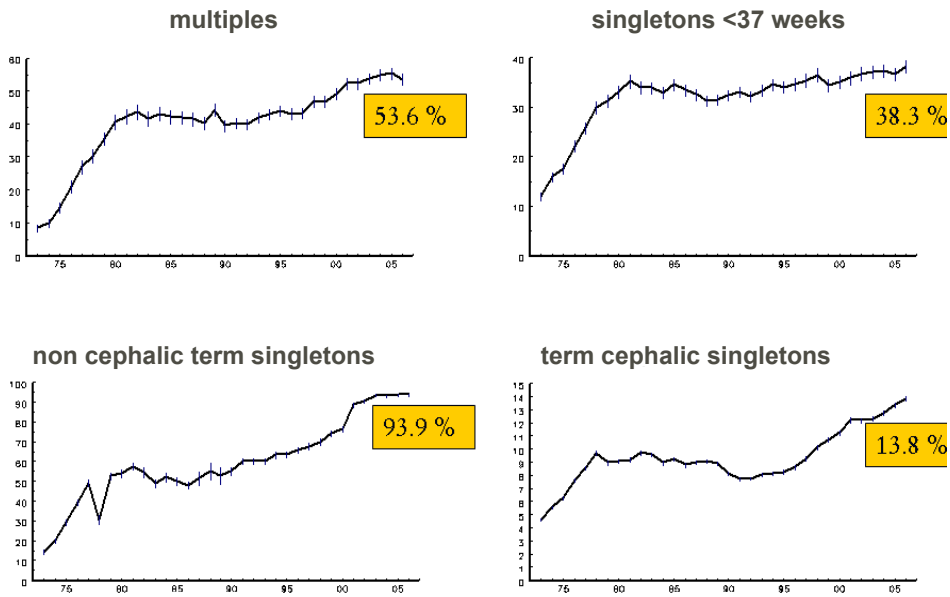


Figure 2. Percentages of caesarean section by year of delivery in four groups of women, Sweden 1973-2006 (Swedish Report on Caesarean Delivery, 2010).

The group showing the largest relative increase in CS rate was also the largest group: women with singleton term (gestational age [GA] ≥37+0 weeks) pregnancies and the fetus in a cephalic position. In this group, the CS rate was 8.2% in 1995 and 12.2% in 2001 – an increase of almost 50%. In 2006, the corresponding CS rate was even higher, 13.8% (Swedish Report on Caesarean Delivery, 2010). In the same report, it was shown that about one third of the increase in CS rates was due to population alterations. It is of interest, that the rate of CS frequency increase in the large group of women with singleton term pregnancies in cephalic position was about the same regardless of maternal age, body mass index (BMI), parity, educational level or smoking. That is, there must be other factors playing important roles in the decision of delivery mode.

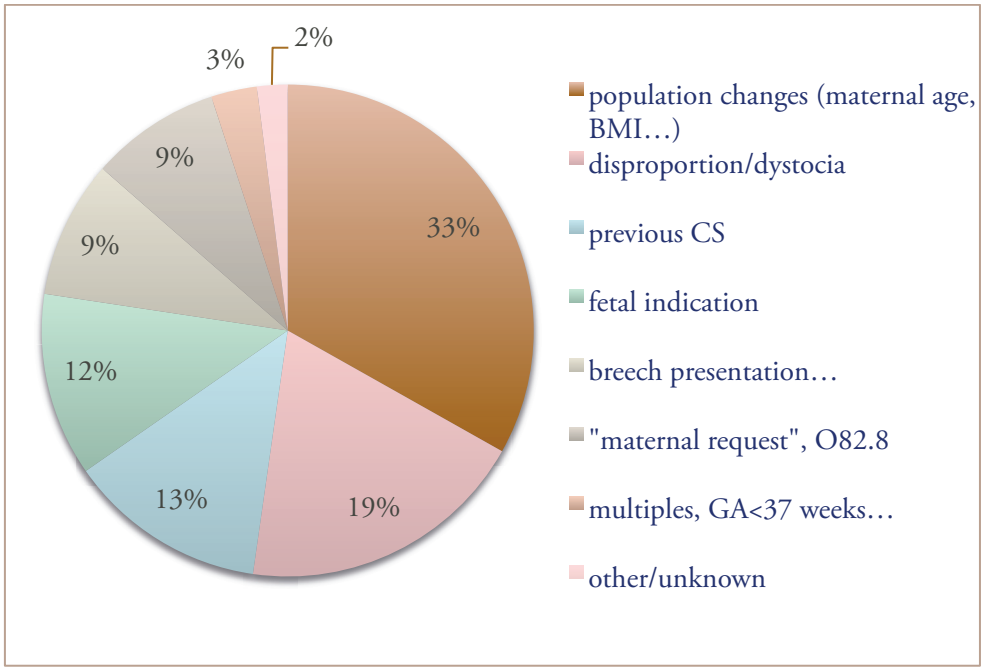


Figure 3. CS indication groups' share of the total CS rate increase. Sweden 1995-2006 (Swedish Report on Caesarean Delivery, 2010).

In the investigation of indications for the CS performed, it was found that the groups of women with singleton term pregnancies in cephalic position and with indications for CS of disproportion/dystocia or of imminent fetal asphyxia, yielded a large contribution to the increasing CS rate: 19% and 12%, respectively. The increasing tendency to choose CS for delivery of multiple pregnancies, premature infants, or infants in breech presentation, would together explain about 12% of the increase in CS rate.

In media, much interest has been focused on the group "CS on maternal request", or psychosocial indication for CS, O82.8 in the International Classification of Diseases (ICD) 10. Due to different traditions in diagnose setting; this group can be hard to define. In Sweden, this was the single most increasing group during the studied period, but as the group was small from the beginning, it contributed to no more than 9% of the total CS rate increase.

To reach further in the exploring of CS rates, it is also necessary to adjust for possible confounding factors. In a report including deliveries by CS between 1990 and 2001 in Sweden (Källén et al., 2005) it was stated, that even after adjustment for year of birth, parity, maternal smoking, maternal education level and maternal country of birth, the risk, or possibility, of giving birth by caesarean delivery was increased

- by maternal age
- by BMI
- for nulliparous women
- for women with a low educational level
- for smokers, and
- for women being born outside Sweden.

During the same period, the rate of children with birthweight (BW) >4500 g increased substantially, but all this increase could be explained by the increasing maternal BMI (Källén et al., 2005).

Furthermore, in Sweden between 1990 and 2001, with a rise in CS rates of about 50%, no statistically significant reduction in perinatal mortality could be shown (Källén et al., 2005).

Planned or Unplanned Caesarean Delivery

A CS can be performed as a more or less planned procedure. For Swedish purposes, and in our studies, we defined and classified each CS referring to the Swedish MBR, where one can find information on whether a CS was performed before or after the start of contractions. Other definitions, based on for example a special time limit between the decision for and the performance of a CS, have not been considered.

Maternal Risks and Benefits of a Caesarean Delivery

According to Villar et al. (2007), increased risks of CS, compared with vaginal delivery, were severe maternal morbidity (hysterectomy, blood transfusion, admission to intensive care unit, or hospital stay more than seven days), and maternal death. The odds ratio (OR) for maternal morbidity, intrapartum CS versus (vs.) vaginal birth, was 2.0 with a 95% confidence interval (CI) of 1.6-2.5. For elective CS, the corresponding OR for maternal morbidity was 2.3; 95% CI: 1.7-3.1. The over-all risk for antibiotic treatment after the delivery was increased about five times. Infection risk was increased for all CS vs. vaginal deliveries, and the risk for venous thromboembolism was increased at least three-fold (Silver, 2012).

Andolf et al. (2013) found an association between CS and a later in-hospital diagnosis of general pelvic endometriosis. Women with a pre-delivery diagnosis of endometriosis were excluded. Further studies were considered necessary to confirm the findings.

The impact of CS on subsequent fertility has recently been investigated in a meta-analysis (Gurol-Urganci et al., 2013). Women who had delivered by CS had a 9% lower subsequent pregnancy rate and an 11% lower birth rate compared with women who had delivered vaginally. The authors concluded that further research was needed to reduce the impact of selection bias by indication for the CS performed.

A benefit of CS was, that women having undergone only caesarean deliveries had a significantly decreased risk of stress urinary incontinence and pelvic organ prolapse surgery later in life compared with women only having had vaginal deliveries (Leijonhufvud et al., 2011). Larsson et al. (2009) had earlier shown a lower risk of pelvic organ prolapse after caesarean than after vaginal delivery.

Another, more obvious benefit was a low OR for maternal 3rd or 4th degree perineal lacerations and/or postpartum fistulas for CS vs. vaginal delivery (Villar et al., 2007).

Infant Risks and Benefits of a Caesarean Delivery

For infants in cephalic presentation, the OR for a more than seven days stay in a neonatal intensive care unit was significantly higher after a CS than after a vaginal delivery (Villar et al., 2007).

A significantly increased risk for children older than one year to develop asthma and/or gastroenteritis that motivated admission for hospital care, CS vs. vaginal delivery, was shown by Hakansson & Kallen (2003).

To study CS benefits on risk for fetal death is almost impossible. No CS would be performed in cases of intrauterine death, except in cases of immediate risk for maternal death. That is, no "intrauterine fetal death" indication for CS would be set. Furthermore, as the number of fetuses dying during surgery would be negligible, no case of intrapartum death would be reported in caesarean deliveries. In summary, hardly any cases of stillbirth would be reported in connection with CS. Despite the obvious methodological difficulties, there are investigators who have tried to compare the risk for fetal death between caesarean delivery and vaginal birth (MacDorman et al., 2006; Villar et al., 2007).

The Delivery Following a First Caesarean Section

An increasing rate of deliveries after one CS, and among them, a rising rate of repeat CS, are obvious consequences and parts of the over-all increasing caesarean delivery rates. In 2012, about 10% of all the deliveries in the southern part of Sweden were deliveries subsequent to one or several CS. Between 1990 and 2001, the rate of repeated CS contributed to about 13% of the increase in total CS (Källén et al., 2005).

Risks Encountered in Deliveries Following Caesarean Sections

Abnormal Placentation

The risk of abnormal placentation, including placenta praevia and placenta accreta, is increased after caesarean delivery. Increasing numbers of CS magnify the risk (Silver et al., 2006; Kamara et al., 2013). Among caesarean deliveries, women who undergo a CS before contractions are three times more likely to develop a placenta accreta in a subsequent pregnancy complicated by placenta praevia, than are women whose primary CS was performed after the start of contractions (Kamara et al., 2013).

Uterine Rupture

The probably most feared complication in a birth after caesarean delivery is rupture of the uterus. Fortunately, the absolute risk is low. Definitions and diagnose setting in cases of uterine rupture might be ambiguous. The rupture can be of different degrees, from 1) a dehiscence, when a previous uterine scar separates, with a somewhat vague transition over to 2) an incomplete uterine rupture, where the overlying visceral peritoneum remains intact, and to 3) a complete uterine rupture: a uterine scar separation with the overlying visceral peritoneum (uterine serosa) opened (Bujold & Gauthier, 2002). A Danish material showed total uterine ruptures in 0,2% of the deliveries after one CS, but after a thorough review of maternal and neonatal medical records, 0.8% ruptures were estimated (Danish Report on Delivery after Caesarean Section, 2013). A revision of Danish medical records between 1997 and 2007 showed both under- and over-reporting of ruptures to the Danish MBR (Thisted et al., 2014).

In an investigation of Swedish MBR data regarding women with their first two deliveries 1992-2007, the uterine rupture rate varied from 0% (women giving birth for the first time or women with one previous vaginal delivery) to 1.1% for women attempting a TOL after CS (Table 1). The results were similar to the results of other authors.

The over-all risk of 0.8% was similar to the risk in the thorough review from Denmark, mentioned above. In data from Norway 1999-2005, 94 women (0.5%) with one previous CS had a second delivery uterine rupture. The odds for rupture was increased in groups with emergency prelabour CS, spontaneous labour, or induced labour, compared with the odds for rupture in ERCS (Al-Zirqi et al., 2010).

Table 1. Uterine rupture by planned delivery mode. Women with their first two deliveries 1992-2007, Sweden.

	Planned vaginal delivery		Planned caesarean delivery		Total	
	n / N	(%)	n / N	(%)	n / N	(%)
First delivery	102 / 339 514	(0.0)	1 / 14 539	(0.0)	103 / 354 053	(0.0)
One previous vaginal delivery	74 / 394 565	(0.0)	3 / 12 594	(0.0)	77 / 407 159	(0.0)
One previous caesarean delivery	447 / 41 450	(1.1)	27 / 18 193	(0.1)	474 / 59 643	(0.8)

In Table 2, all two-parous women were classified by first delivery mode and second planned delivery mode (TOL or ERCS). Here, the rate of uterine rupture varied from 0% for women with a first vaginal delivery to 1.2% for women with TOL after a first unplanned CS. Maybe unexpected, no statistically significant difference was seen between TOL after planned CS and TOL after unplanned CS.

Table 2. Uterine rupture by first delivery mode and planned secod delivery mode. Women with their first two deliveries 1992-2007, Sweden.

	Total deliveries, N	Uterine rupture second delivery	
		n	(%)
First delivery vaginal	407 159	83	(0.0)
First delivery unplanned CS, second delivery TOL	29 852	345	(1.2)
First delivery planned CS, second delivery TOL	11 598	125	(1.1)
First delivery unplanned CS, second delivery ERCS	12 631	18	(0.1)
First delivery planned CS, second delivery ERCS	5562	17	(0.3)
Total	466 802	588	(0.1)

Rupture of the uterus is indisputably a serious late complication of a previous CS. But, as already pointed out, the absolute numbers are small. Table 2 shows that during a period of 16 years in Sweden, there were approximately 500 reported cases of uterine rupture.

In order to explore if the observed association between poor infant outcome and previous CS could be explained by the increased risk for uterine rupture in births following caesarean deliveries, a sub-study was performed. After exclusion of deliveries for which a uterine rupture was reported, the OR for perinatal death, previous CS vs. previous vaginal delivery, was 1.5 (95% CI: 1.3-1.7). The corresponding OR for low Apgar score was 1.8 (95% CI: 1.7-2.0).

Thus, the association between previous CS and poor infant outcome could not be explained solely by the increased risk for uterine rupture. The question remained, whether the increased risk for poor outcome was due to the caesarean delivery *per se*, or if it was due to maternal characteristics and/or recurrent, underlying conditions.

Infant morbidity

In comparison with infants born in VBAC, infants born by ERCS had significantly higher rates of respiratory morbidity and admission to neonatal intensive care units. They also had longer hospital stays (Kamath et al., 2009).

Planning the Delivery Mode after a First Caesarean Section

In a global perspective, Sweden is a country with a relatively low CS rate. Furthermore, we have a high rate of TOL after CS, and a correspondingly low rate of ERCS. Between 1992 and 2007, the success rate in TOL varied substantially by the indication for the first CS performed. The over-all VBAC rate showed some decrease during the same period (The Swedish MBR).

The policy of delivery mode planning after one CS is widely discussed. The policy, and yet more the compliance to the policy, differ tremendously between countries (SOGC Clinical practice guidelines, No. 155, 2005; RCOG Green-top guideline, No. 45, 2007; ACOG Practice bulletin No. 115, 2010; Bujold, 2010; National Institutes of Health consensus development conference statement, 2010; Zhang et al., 2010; Grobman et al., 2011; Boyle & Reddy, 2012; Sentilhes et al., 2013; Knight et al., 2014). In fact, the policy of second delivery planning might even differ a lot between neighbouring delivery wards.

All-over, VBAC is associated with fewer complications, and a failed TOL is associated with more complications, than an ERCS (ACOG Practice bulletin No. 115, 2010). In the process of second delivery mode planning, an estimation of probable outcomes is crucial. When would it be safe, for the mother and her infant, to recommend a TOL? When would an ERCS be the best choice? How would it be possible to get a fair prediction of the chance for VBAC in TOL?

Methodological Considerations

When estimating the result of a certain intervention, a major challenge is to take underlying conditions into account. For example, when investigating infant outcome of the delivery following one CS, it could certainly be tempting just to "control for" diagnoses or indications of interest. Then, one must realise that any intervention performed - a CS, a vacuum extraction, or a resuscitation of an infant - would usually result in a list of reported diagnoses, whilst in a normal vaginal birth without interventions, possible underlying conditions would stay heavily underreported, yielding few diagnoses to "control for".

For the purpose of our studies, we aimed to use robust data for underlying conditions of possible interest when exploring outcomes of the delivery subsequent to a CS. We also wanted that indication data be as independent of the post surgery diagnose setting as possible. The need for a rectifying hierarchy seemed obvious.

As we presumed that conditions present at a first CS would often recur in the following delivery, we decided to use the indication for this first CS as a proxy for "recurrent condition". To estimate the one most important factor underlying each first CS performed, we chose to develop a hierarchical system of the underlying conditions present, diagnoses set, or indications reported for each CS performed. Within the hierarchical system, we aimed to combine "hard facts" from the record forms sent to the National Board of Health (NBH) and saved in the MBR, with ICD-codes.

The Swedish Medical Birth Register

Fortunately, outcomes like low Apgar score and perinatal death are rare events in countries like Sweden with well-developed health care systems. Therefore, when these rare outcomes are studied, giant data sets are required to detect differences between groups. We chose to use the Swedish MBR, comprising about 99% of all Swedish births since 1973 (Cnattingius et al., 1990) to perform our studies. The size of the MBR made it possible to get enough power in most calculations even when we needed to sub-group the population of women with one previous CS.

Every woman in Sweden is offered free maternity care. One ultrasound examination before 20 completed weeks of pregnancy is included, in order to estimate the expected date of delivery and to check for multiple pregnancy and fetal malformations. Midwives or physicians fill in record forms at every visit to the maternity care unit, every delivery, and every examination of infants after birth. Selected parts of the data records are sent to the NBH, were they are computerised and entered into the MBR. Over time, some of the data recorded in the MBR has changed. Smoking habits and maternal weight have been recorded since 1983. From 1992 onwards, it is possible to find "start of labour" in the records: "spontaneous", "by induction", or "by CS before the start of contractions". From 1998 onwards, CS can also be reported as "elective" or "emergent".

Table 3. Data exported to the National Board of Health from maternity care record forms.

"MHV 1" form	"MHV 2" form
The unique Swedish personal number	Summary of the pregnancy in gestational week 37+
Date of enrolment	Number of maternity care visits
Office number	Medications during pregnancy
First date of last menstrual period	Tobacco use gestational week 30-32: no / 1-9 cigarettes/day / ≥10 cigarettes/day / snuff
Predicted delivery date/last menstrual period	Fetal diagnostics
Predicted delivery date/ultrasound examination	
Maternal weight and height at enrolment	
Tobacco use three months before pregnancy and at enrolment, respectively: no / 1-9 cigarettes/day / ≥10 cigarettes/day / snuff	
Family situation	
Working at enrolment: full time/part/no. Occupation	
Infertility problems, years, care taken	
Previous pregnancies: number of spontaneous abortions, extrauterine pregnancies, stillborn infants, live born infants, children dead within 7 days, children dead later	
Certain previous diseases	
Medications before enrolment	

Table 4. Data exported to the National Board of Health from delivery ward and postnatal ward record forms.

"FV 1" form	"FV 2" form
Enrolment date	Date and time of birth
Maternal weight at enrolment	Birth single/multiple (one record form/child)
Previous CS, yes/no, year	Live birth/dead before delivery/dead during delivery

Delivery start spont./induction/CS, elective/emergent	Boy/girl
Delivery mode vaginal, non instrumental / vacuum/forceps / CS	GA, full weeks+days
Pain relief, choice of 15 different/none	BW and height at birth
Lacerations	Head circumference
Episiotomy	Apgar score at 1, 5 and 10 minutes
Birth single/multiple (one record form/child)	Resuscitation needed
BW and height at birth	Healthy infant examined in the postnatal ward / ICD-codes
Birth presentation occiput anterior /occiput posterior / breech or foot / other	Malformations (specified if present)
Maternal ICD-codes	Child staying in hospital for ≥28 days and/or date of leave
Maternal date of leave (home/transferred)	Dead, date and time (data linked from Statistics Sweden)
Hospital and delivery ward numbers	Autopsy

The International Classification of Diseases

The international classification used for diagnose coding was changed from ICD9 to ICD10 in 1997 for all regions of Sweden except the southern region, which changed in 1998. This is one of the reasons why it is necessary to choose large, robust groups to follow through the years when studying a population.

When aiming to study the indication for a first CS performed, to compare it with diagnoses set in a first vaginal delivery and, finally, investigate the following delivery mode and infant outcome, it would be tempting to just go through the specific ICD-codes for each delivery. Unfortunately, this method would have several disadvantages.

- As already pointed out, diagnoses/indications, except for "normal delivery", are rarely given in vaginal deliveries in Sweden. In most cases, vaginal deliveries are supervised by midwives, and few diagnose codes are set.
- Coding traditions might differ a lot between delivery wards. For example, in one delivery ward in southern Sweden, a woman undergoing a CS because of breech presentation would get an ICD10 code for "breech presentation" in the majority of cases, and for "maternal request" (O82.8) in 1.7%. In the neighbouring clinic, the O82.8 code was set in 46.8% of the CS with breech presentation. (Källén et al., 2005).
- Usually, each CS performed yields several indication codes. According to the Swedish Report on Caesarean Delivery (2010), almost one third of the CS with a diagnosis of disproportion or dystocia had also got a diagnosis implying a fetal indication for the CS.

- It might be difficult to set an unprejudiced diagnose code after having performed a CS, being aware of the maternal and infant outcomes. The coding might well be influenced/biased by findings during and after surgery.

The Hierarchical System of Indications

In the hierarchical system developed, efforts were made to classify according to underlying conditions instead of focusing on conditions appearing during labour, in an attempt to diminish the subjective impact of diagnoses recorded after delivery.

Table 5. Hierarchical classification of indications for the first delivery caesarean. Women with their first delivery by caesarean between 1987 and 2007 and their second delivery between 1992 and 2007 in Sweden.

Classification group; condition present/diagnosis set/indication for the first delivery CS	**Explanation and specification**	**Hierarchical system %**	**Non-hierarchical system %**
1. Multiple gestation	Information on type of gestation available in the Swedish MBR. (no ICD-codes)	2.5	2.5
2. Preterm birth, <37 weeks	Information on gestational length available in the Swedish MBR	13.5	14.9
3. Breech or other malpresentation	Information on fetal presentation available in the Swedish MBR	18.2	22.3
4. Congenital malformations	Malformation diagnoses, except congenital dislocation/unstable hip, undescended testicle, persistent ductus arteriosus in preterm infants, single umbilical artery, and preauricular tags	2.0	3.7
5. Rupture of uterus	Small group placed high in the hierarchy, to make tracing of diagnoses possible in subsequent pregnancies. ICD9: 665.0-1; ICD10: O71.0-1	0.0	0.0
6. Placenta praevia	Small group placed high in the hierarchy, to make tracing possible in subsequent pregnancies. ICD9: 641.0-1; ICD10: O44.0-1	0.5	1.1
7. Diabetes mellitus/ gestational diabetes	Placed high in the hierarchy to refine from large for gestational age (LGA) and GA ≥42 weeks. ICD9: 648.0, 648.8; ICD10: O24.0-4, O24.9	1.4	2.1
8. Small for gestational age (SGA)/poor fetal growth	<-2 BW standard deviation (SD) scores according to a Swedish ultrasound-based weight curve (Marsal et al., 1996), or ICD9: 656.5; ICD10: O36.5	3.9	9.8
9. LGA/suspect LGA/ excessive fetal growth	>+2 BW SD scores according to the Swedish weight curve, (Marsal et al., 1996) or BW >4500 g, or ICD9: 656.6; ICD10: O36.6	5.2	6.9
10. Prolonged pregnancy ≥42 weeks	Group refined from diabetes and LGA indications. Information on gestational length available in the Swedish MBR	9.8	13.2

11. Severe conditions complicating pregnancy/ severe maternal disease	Premature separation of placenta. ICD9: 641.2; ICD10: O45 Antepartum haemorrhage. ICD9: 641.3, 641.8-9; ICD10: O46 Pre-existing hypertension, severe pre-eclampsia, eclampsia. ICD9: 642.0-2, 642.5-7; ICD10: O10,O11, O14.0-1,O15.0-1, O15.9 Maternal renal, cardiovascular or thyroid disease. ICD9: 646.2, 648.1, 648.5-6; ICD10: E00-E07, I00-I99 Maternal care for known or suspected fetal abnormality/damage, including fetal-maternal haemorrhage, iso-immunisation and fetal hydrops. ICD9: 655, 656.0-2; ICD10: O35, O36.0-2 Polyhydramniosis or oligohydramniosis. ICD9: 657, 658.0; ICD10: O40, O41.0	2.5	9.0
12. Complications during labour and delivery	Dystocia, prolonged labour, or suspected cephalopelvic disproportion. ICD9: 653, 660, 661, 662; ICD10: O33, O62, O63.0-1, O63.9, O64.0, O66, O75.0, O75.8-9 Abnormalities of pelvic organs. ICD9: 654.0-1, 654.3-9; ICD10: O34.0-1, O34.4-9, O65 Problems associated with amniotic cavity and membranes. ICD9: 658.1-2, 658.4-9, 659.2, 663.5; ICD10: O41.1-9, O69.4, O75.2, O75.6 Problems associated with induction of labour. ICD9: 658.3, 659.0-1; ICD10: O61.0-1, O75.5 Prolapse of cord, or cord entanglement with compression. ICD9: 663.0-2; ICD10: O69.0-2 Other complications of obstetric surgery and procedures. ICD10: O75.4	24.6	56.8
13. Fetal distress or fetal death	Fetal distress, fetal hypoxia, or birth asphyxia. ICD9: 656.3, 768; ICD10: O36.3, O68, P21.0 Intrauterine death. ICD9: 656.4, ICD10: O36.4	8.2	27.7
14. Caesarean delivery on maternal request, or mild conditions not likely to legitimise a decision of CS	Other or not specified indication for CS. ICD9: 659.8-9, 669.7; ICD10: O82.8 Mild hypertension or mild pre-eclampsia. ICD9: 642.3-4, 642.9; ICD10: O13, O14.9 Oedema or excessive weight gain in pregnancy, without mention of hypertension. ICD9: 646.1; ICD10: O12 Peripheral neuritis, liver disorders, anaemia, bone and joint disorders. ICD9: 646.4, 646.7, 648.2, 648.7; ICD10: O99.0 Mild infections in pregnancy or labour. ICD9: 646.5-6; ICD10: O23, O75.3 Other conditions predominantly related to pregnancy. ICD9: 646.8-9, 656.7-9, 663.3-4, 663.6, 663.8-9; ICD10: O26, O36.8-9, O69.3, O69.5, O69.8-9	5.3	22.4
15. No diagnosis available	Neither abnormal conditions, nor indications for CS could be detected using data from the Swedish MBR.	2.3	2.3
Total		100	194.7[1]

[1]More than 100%: Several diagnoses/indications possible for each CS in a non-hierarchical system.

For example, hierarchical groups 7-10 ("Diabetes mellitus/gestational diabetes", "SGA/poor fetal growth", "LGA/suspect LGA/BW >4500 g", and "GA ≥42 weeks") were designed to show the impact of fetal growth independent of maternal diabetes and the impact of prolonged pregnancy independent of fetal size, respectively. Group 13, "Fetal distress/death", was placed low in the hierarchy, to refine it from indications probably preceding the development of fetal asphyxia.

As seen in Figure 4, the largest group in the hierarchical system was "Complications during labour and delivery", followed by "Breech or other malpresentation", "GA <37 weeks", "GA ≥42 weeks", and "Fetal distress/death". Likewise, when exploring the non-hierarchical indications, "Complications during labour and delivery" dominated. Here, "Fetal distress/death", was the second largest group. This might be expected: for many of the CS with several diagnoses coded, one of them was "Fetal distress". Hereafter, "CS without medical indication" and "Breech or other malpresentation" followed.

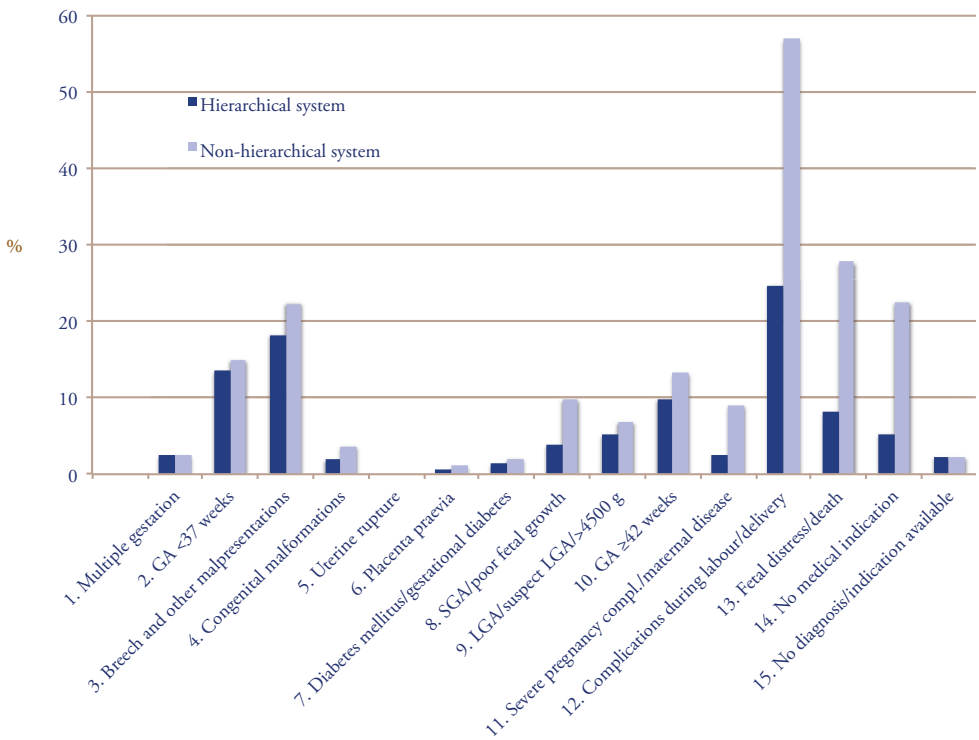


Figure 4. Size of the first caesarean indication groups in the hierarchical and in the non-hierarchical system, respectively. Non-hierarchical system diagnoses yielded a sum of 194.7%, due to multiple diagnoses set for many of the CS performed. Sweden 1987-2007.

One might argue, that the 15 categories in the hierarchical system are too many, and that clinicians rarely would use such a complicated system. We do not agree that the proposed system is that complicated. There are several other classification systems in use, e.g., the Bishop scoring system (Bishop, 1964) and the "Ten groups" classification (Robson, 2001). The last-mentioned can reach about 20 groups when sub-groups are included, but the classification is frequently used in clinical practice.

Study Populations

In order to keep our studies streamlined, we chose to include women with no more than one previous CS. Women not being born in Sweden were included only if their first two children were born in Sweden. In **Papers II-IV**, only singleton index pregnancies were included.

To compare the outcomes of deliveries following one CS, we aimed to use only one comparison group – two-parous women with one previous vaginal delivery – in all studies, to keep the publications uniform. In **Paper II**, trying to compare the delivery mode of women with one prior CS with the delivery mode of women with one prior vaginal delivery, we found huge differences in outcome. We chose to make the comparisons between women with one prior CS and primiparous women (giving birth at least once more during the study period) instead.

To divide between deliveries by planned and unplanned CS, we chose to define a planned caesarean delivery as a CS performed before the start of contractions, and an unplanned caesarean delivery as a CS performed after the start of contractions. As do other definitions used for retrospective data, our definition would have its advantages and disadvantages. No really perfect method for distinguishing the sometimes very different procedures of CS from each other was found.

The most widely used clinical definition of "emergent" CS in Sweden, is "CS performed within eight hours after decision", which might be valid for many different kinds of deliveries by caesarean. The "emergent" CS could be anything from a caesarean delivery very similar to an elective procedure, with surgery performed under calm conditions on a fasting, well informed woman with a regional anaesthesia, to an emergency CS in anything but calm circumstances, performed under general anaesthesia. Similarly, a CS performed before contractions would usually be elective but might also be emergent, for example in cases of placental abruption.

In a clinical situation, when aiming to use the new study results, no problem would be at hand. The actual kind of previous CS would be well known.

Infant Outcomes

When starting up our studies, we were interested in investigating whether there would be any difference in health outcome between infants born after one previous vaginal delivery and infants born after one previous CS. As mentioned earlier, serious adverse outcomes are seldom encountered in a Swedish setting.

We considered several possible outcome measures, including umbilical artery pH, Apgar score, hypoxic ischemic encephalopathy, neonatal seizures, transferral to neonatal intensive care, perinatal death, and ICD-codes for illness in childhood. Umbilical artery pH is not routinely examined in all Swedish delivery wards, and furthermore is not entered into the records of the Swedish MBR. Apgar score is a relatively subjective assessment, but recorded for almost every delivery and sent to the Swedish MBR. Severe forms of hypoxic ischemic encephalopathy and neonatal seizures are rare events, and yield less robust data than does perinatal death. The rate of transferral to neonatal intensive care is often used as a proxy for infant illness, but the transferral traditions are dependent on the available number of neonatal beds, and varying too much to yield credible data. Perinatal death is robust data, but yields power problems due to its rareness.

We ended by choosing the outcomes Apgar score and perinatal death. In further studies on child outcomes of the delivery after a previous CS, it could be interesting to look at for example ICD-diagnoses for neurodevelopmental delay or cerebral palsy in later childhood.

Apgar Score

Table 6. The Apgar scoring system.

	0 Points	1 Point	2 Points	1 min	5 min	10 min
Activity (muscle tone)	Absent	Arms and legs flexed	Actve movement			
Pulse	Absent	Below 100 beats/minute	Over 100 beats/minute			
Grimace (reflex irritability)	Flaccid	Some flexion of extremities	Active motion (sneeze, cough, pull away)			
Appearance (skin colour)	Blue, pale	Body pink, extremities blue	Completely pink			
Respiration	Absent	Slow, irregular	Vigorous cry			
				Sum	Sum	Sum

The Apgar scoring system was developed in the fifties (Apgar, 1953). It was designed to quickly evaluate the status of newborns and is still in use in delivery wards all over the world.

The score is computed after one, five and ten minutes of age. The typical, healthy baby gets a score of 9-10-10, with one point reduction for skin colour at one minute of age. At five minutes, a term infant is judged to be in excellent condition with a total of 7-10 points, moderately depressed with 4-6 points, or severely depressed with 0-3 points.

We chose a widely used cut-off for our study results: Apgar score less than seven at five minutes of age.

It has often been argued that Apgar score is a surrogate outcome, which is true. However, clear relationships between low Apgar score and adverse infant outcomes have been shown. Apgar score <7 in 5 minutes was associated with a substantially increased risk of severe neurologic morbidity (cerebral palsy, epilepsy, or mental retardation) in term infants (Thorngren-Jerneck & Herbst, 2001). Low Apgar score has also been shown to have a significant association with cognitive impairment in later childhood, as measured by academic achievement at 16 years of age (Stuart et al., 2011).

Perinatal Death

A live birth that results in death within the first year (<365 days) is defined as an infant death. Infant deaths are further subdivided as early neonatal (<7 days), late neonatal (7–27 days), neonatal (<28 days), or post neonatal (28–364 days) (Barfield, 2011).

The term "perinatal death" is used for statistical purposes. Perinatal deaths refer to fetal deaths and live births with only brief survival and are grouped on the assumption that similar factors are associated with these losses. Perinatal death can be defined in three different ways (Barfield, 2011). For the purpose of our studies, we chose the definition in which fetal deaths from 28 completed weeks of pregnancy and early neonatal deaths at 0-6 days of age are included.

Data regarding perinatal death is very robust, but as perinatal death is rare, choosing it as an outcome measure yields power problems even using a database as large as the Swedish MBR. Huge amounts of data are needed to detect differences between groups.

Supplementary Considerations

The field of scientific issues regarding deliveries following CS is growing. Examples of some interesting aspects being beyond the scope of our studies are given here:

- Impact of the type of prior uterine incision. No such information is available in the Swedish MBR. A low-transverse caesarean incision confers the lowest risk of uterine rupture in the subsequent labour, whereas incisions made in the uterine corpus, such as classic caesarean incisions or extensions into the uterine body, confer a markedly increased risk for rupture of the uterus (ACOG Practice bulletin No. 115, 2010).
- Ultrasonic measurement of the uterine scar during the pregnancy following a CS, aiming to predict subsequent delivery outcomes and support planning of second delivery mode. Ultrasonic methods have been analysed by several authors. Vikhareva Osser & Valentin (2010) found an association between CS in advanced labour and incomplete healing of the uterine incision, as measured with vaginal ultrasound. Naji et al. (2013) found, that addition of ultrasonic measurement of the difference in residual myometrial thickness between the first and second trimester yielded a better predictability of successful TOL after CS than did maternal characteristics and obstetrical history alone. An overview of the current knowledge has recently been published (Valentin, 2013).
- Other measurements that could improve the prediction of unplanned CS or VBAC in TOL. Recently, Macones et al. (2013) have used the fetal-pelvic index, based on ultrasound measures of the fetal head and abdomen within two weeks of delivery and x-ray pelvimetry within 48 hours of delivery. Combined with clinical risk factors, the fetal-pelvic index could accurately identify primiparous women, as well as women with a previous CS, with a high risk for CS in TOL.
- Influence of the interpregnancy interval and the interval between deliveries on the outcome of the delivery subsequent to a CS. In **Paper I**, no differences were detected between the groups of women with one previous vaginal delivery and one previous CS regarding time interval between deliveries. We did not study outcome by delivery interval. Other authors having explored the outcome of deliveries with short delivery intervals have used different time limits and come to somewhat different conclusions. A thorough review of the professional society guidelines has been published (Bujold, 2010).

- Attempt of TOL after caesarean in a following twin pregnancy. Studies regarding this issue have consistently demonstrated that, for the few women attempting a TOL; the outcomes are similar to those of women with single gestations (Cahill et al., 2005; ACOG Practice Bulletin No. 115, 2010).
- External cephalic version for breech presentation in women with a first CS. Limited data suggest external version after CS not to be contraindicated. The chances of success in version have been reported to be similar to the chances for women without a prior CS (ACOG Practice Bulletin No. 115, 2010).
- Impact of labour induction on the delivery after one CS. Here, it would be interesting to complement our current findings with results regarding induction all-over as well as inductions by different methods using data from the Swedish MBR together with results from earlier studies (Landon et al., 2004; Macones et al., 2005; Bujold, 2010).
- Intrapartum management of women undergoing a TOL after caesarean. For example, the setting and the staff in the delivery ward must be dimensioned for emergency CS. The woman should be monitored continuously rather than intermittently (Cahill & Macones, 2007). TOL after caesarean is not a contraindication to epidural anaesthesia (ACOG Practice bulletin No. 115, 2010), but staff must be aware that the pain associated with a uterine rupture might be blunted or atypical in presentation (Cahill & Macones, 2007). A review article has recently been published (Scott, 2014).
- Outcome of deliveries after two or multiple caesarean deliveries. Silver et al. (2006) showed successively increased risk for maternal adverse outcomes by number of CS performed. A systematic review with meta-analyses of success rates and maternal/infant adverse outcomes of TOL after two or more CS showed somewhat divergent results (Tahseen & Griffiths, 2009). Cahill et al. (2010) showed, that women with three or more prior caesareans who attempted TOL had similar risks for maternal morbidity and rate of success as women who delivered by ERCS.
- Interventions for supporting pregnant women's decision-making regarding delivery mode after caesarean delivery. A Cochrane collaboration review regarding this issue has been published (Horey et al., 2013).

Epidemiology and Statistics

Statistical analyses in **Papers I-IV** were performed using Gauss (Gauss™; Aptec Systems Inc., Maple Valley, WA, USA; http://www.aptech.com).

Odds Ratio and Risk Ratio

In an investigation yielding binary outcomes, it is convenient to display the result as an OR or, alternatively, as a risk ratio (RR).

Referring to the four-field table in Table 7, the OR and the RR are calculated as follows:

OR = a/c/b/d = a x d/b x c = a/b/c/d i.e. OR is symmetrical (the OR for exposure yields the same results as does the OR for cases).

RR = a/(a+c)/b/(b+d) i.e. RR is not symmetrical.

Table 7. The four-field table.

	Exposed	Unexposed	
Cases	a	b	a+b
Controls (non-cases)	c	d	c+d
	a+c	b+d	

In investigations of rare events in large populations, the number of cases in a and b will be low, and the denominators (a+c) ≈ c and (b+d) ≈ d. In such cases, obviously, RR ≈ OR.

In a comparison between OR and RR, OR has some advantages.

- It is easier to compute. Several methods, i. e. logistic regression, yields results in the form of OR.
- It makes it possible to compare results between case-control and cohort studies – it can be computed "in both directions" in the four-field table.
- It is less influenced by population differences than is a RR.

A disadvantage for OR is that the interpretation of an odds, or a ratio between odds, is more difficult than the interpretation of a risk, or a ratio between risks.

Confounding

Confounding is a systematic error. Exposed and unexposed individuals might differ with respect to other factors than the exposure, which *per se* could influence the risk of becoming a case.

- A confounder must be associated with the exposure.
- A confounder must be associated with, or be a risk factor for, the outcome in question – either as a cause or as a proxy for a cause.
- A confounder must not be an effect of the exposure or a link in the chain from exposure to outcome.

Confounding can be dealt with by adjustment for the possible confounders. The two most commonly used methods to compute the OR, when wanting to adjust for possible confounders, are the Mantel Haenzsel technique (stratified analysis) and the multiple logistic regression analysis.

Mantel Haenzsel

Stratified analysis by the Mantel Haenzsel method requires large numbers. The material is grouped in many different cells (four-field tables), and then the groups are compared, one after the other, to yield a calculated weighted estimate from many cells.

Advantages of the Mantel-Haenzsel model are, that no assumption of, for example, linearity of the confounder in question, and no control of the fit of the model need to be performed. Drawbacks of the model are, that if adjusting for too many possible confounders, information gets lost because of lack of controls in some cells (0 in the denominator). Also, as the cells are unrelated to each other, the difference between for example a woman 20 years of age and a woman 40 years of age will be similar to the difference between a 30 and a 40 years old woman.

Multiple Logistic Regression

In multiple logistic regression models, compared with Mantel Haenzsel, data sets can be smaller as it is possible to interpolate between results.

A disadvantage of the method is, that correct assumptions of the model have to be made. For example, making assumption of a linear model when the model is in fact U-shaped will yield misleading results. Therefore, it is important to always control the model, by looking at data and control the "goodness of fit" (Hosmer & Lemeshow, 1989) and the R squared (R^2). Controlling for too many confounders, it is possible to get over-fitted models, with sudden changes of the results. As a rule, the number of confounders should always be less than 1/10 of the number of cases/outcomes (Peduzzi et al., 1996). If the number of confounders is between 10 and 19, it is only advisable to compute crude results (investigate only the exposure of interest). If the

number of cases is very small (n <10), an exact test, the Fisher's exact test, is preferable to use.

When comparing many OR, a heterogeneity test is of value: would all the OR possibly be random variations of the same OR? In our studies, the tests of homogeneity of the OR across indication groups were based on weighted sums of the squared deviations of the stratum specific log-OR from their weighted means (Hosmer & Lemeshow, 1989). The tests yielded P-values for homogeneity between groups.

Multiple Logistic Regression Models Used for Papers I-IV

As the main analyses yielded binary outcomes, we first controlled our models. We decided to choose logistic regression to compare the different groups and obtain ORs and adjusted ORs with 95% CI.

In all linear multiple regression models, we considered the following variables, and chose to show the results as:

1) crude (unadjusted) OR.

2) OR adjusted for year of birth (continuous, linear variable) and maternal characteristics: maternal age (years, continuous, linear variable), maternal height (cm, continuous, linear variable), maternal BMI (kg/m^2, continuous, linear variable), and maternal smoking (no / 1-9 cigarettes/day / ≥10 cigarettes/day, semi-continuous variable).

3) OR adjusted for year of birth, maternal characteristics, and fetal/infant parameters: multiple birth (**Paper I** only, yes/no), GA <37 weeks (yes/no), breech or other malpresentation (yes/no), and BW SD scores (continuous, second grade model) (Marsal et al., 1996).

Adjustment was performed for all possible confounders – maternal or fetal/infant – valid for the index delivery: the first delivery of the primiparous women (**Paper II**), or the second delivery of the two-parous women.

Confidence Interval

We used confidence intervals at the 95% level for our studies. A 95% CI covers, with 95% probability, the true value. CI is influenced by the SD and the sample size and gets more precise as samples become larger. One can argue, that CI should not be used when studying a whole population, but this population can often be regarded as a subset of future populations.

P-value

The p-value is the probability of obtaining a test statistic at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. For our studies, we have chosen a p-value at the 0.05 level, (the risk of falsely rejecting the null

hypothesis=5%), although most p-values calculated were much lower. A disadvantage when using p-values is that in large materials, such as ours, one can get statistically significant results even if the association is so small that it is not clinically relevant.

One- or Two-tailed Statistics

In our studies, we always used two-tailed statistics. We did not presume the differences in outcome to be one-sided.

Power

Power is the probability of finding a difference or effect that really exists - the sensitivity of a test.

Studying rare events, it is necessary to have large materials to be able to detect differences between outcomes. Even our large Swedish MBR did not yield enough power to study differences in perinatal death in sub-groups of the population, and we had to refrain from some of the studies planned.

Descriptive Statistics Used for Papers I-III: Chi-squared Test and Mann-Whitney U-Test

For descriptive statistics, we have used two non-parametric tests: Chi-squared test and Mann-Whitney U-test.

The Chi-squared test just tells if there is a difference between groups. The observed frequency in each cell is compared with the predicted frequency. The test result yields a Chi2 sum that, given the number of degrees of freedom (the number of groups minus one), yields a p-value. The Chi-squared test was used in **Papers I-III** to compare background characteristics yielding categorical data: infant gender, or maternal country of birth (Sweden/other).

The Mann-Whitney U-test was used in **Papers I-III** to compare background characteristics with continuous or semi-continuous data between the study groups: maternal age, BMI, height, smoking, year of delivery, GA at delivery, and BW SD scores. P-values for the differences in characteristics between groups were yielded.

When background characteristics data was missing, for example when BMI was unknown, we imputed with the mean.

Table 8. Background to the area under the receiver operating characteristics curve.

	Identified (e. g. above a certain cut-off point)	Not identified (e. g. below a certain cut-off point)	Total
Cases	a	b	m1
Non-cases	c	d	m2
Total	n1	n2	N

An explanation of some expressions describing diagnostic accuracy, based on Table 8, is given here:

Sensitivity

The chance of identifying cases using the test (or the specific cut-off point): a/m1

Specificity

The chance of correctly identifying the non-cases as non-cases: d/m2

False positive rate

1- specificity (1-d/m2)

Positive predictive value

The proportion of cases among the persons identified as cases: a/n1

Negative predictive value

The chance of being a non-case if not identified as a case: d/n2

A **receiver operating characteristics (ROC) curve** (Figure 5) is derived from two of the above-mentioned entities: The sensitivity (on the y-axis), and the false positive rate (on the x-axis). For each cut-off-point, the sensitivity and the false positive rate are plotted, and then connected with a line, resulting in the ROC-curve. The evaluated factor's overall ability to detect cases could be measured using the area under the ROC curve entity (ROC AUC). If the factor tested has no prediction ability at all, the ROC-curve would simply be a straight line, the y=x line, and the ROC AUC would be 0.5.

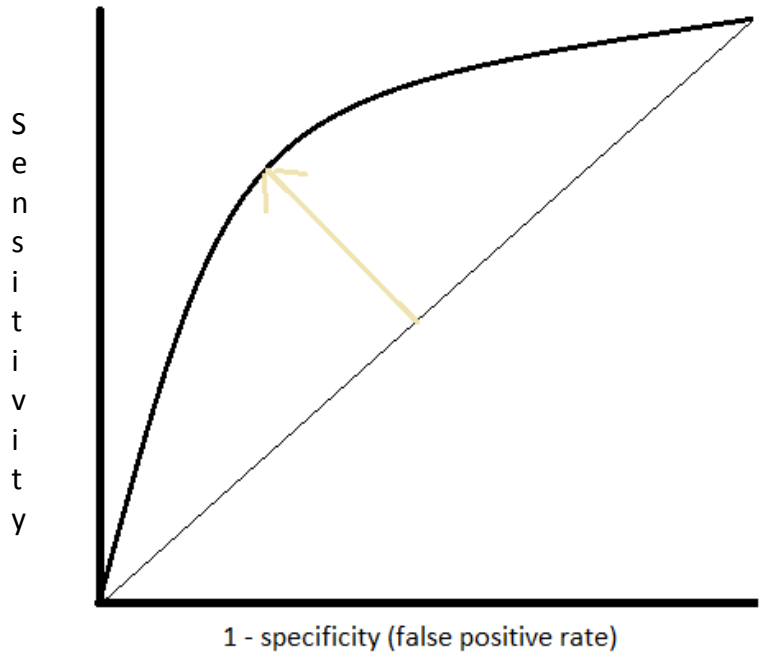


Figure 5. Receiver operating characteristics curve.

Often, investigators aim to identify the "optimal cut-off-point". That is the point that maximises the sensitivity while keeping the false-positive rate at an adequate level. This point could sometimes be identified as the point on the ROC-curve with the largest height over the y=x line (Se the arrow in Figure 5).

The performance of our prediction models applied on the validation data set in **Paper IV** was evaluated studying the AUC ROC, the Pearson's correlation coefficient (r), and the R squared (R^2), respectively.

The Pearson's r is a measure of the linear correlation/dependence between two variables x and y. Pearson's r can have a value from -1 to +1, where 1 is total positive correlation, 0 is no correlation, and –1 is total negative correlation. Pearson's r was calculated to show the agreement between the predicted and the observed probabilities for success in TOL.

The R^2 is the proportion of the total variance that is explained by the model.

The variance of each ROC AUC, or the variance of the difference between two dependent ROC AUC, respectively, was computed using the method proposed by DeLong et al. (1988).

When evaluating the performance of the previously published prediction model (Grobman et al., 2007) applied on the Swedish population, we let the published OR estimates enter the logistic regression model as offset variables (variables that should not be calculated) and the overall performance was measured by studying the ROC AUC and the R^2.

The development of our new prediction model was made in two steps, after an initial division of the total data set into two sub sets (one development and one validation data set). First, we used the development data set to evaluate potentially important factors, using multiple logistic regression analyses to calculate independent ORs. Secondly, the performance of the final model was tested on the validation data set by letting the OR estimates enter a logistic regression model as offset variables, as described above.

Numbers Needed to Treat or Numbers Needed to Harm

A result obtained as an OR says that an association exists, but the impact of this association on the individual woman is not relieved. To make a clinically more understandable calculation of how common, or unusual, a specific event would be, one can use the number needed to treat (NNT), or number needed to harm (NNH).

NNT or NNH = 1/(a/(a+c))-(b/(b+d)) = 1/the absolute risk difference

Aims

Paper I

To assess the impact of the indication for a previous CS on the infant outcome, in terms of low Apgar score or perinatal death, of the subsequent delivery.

Paper II

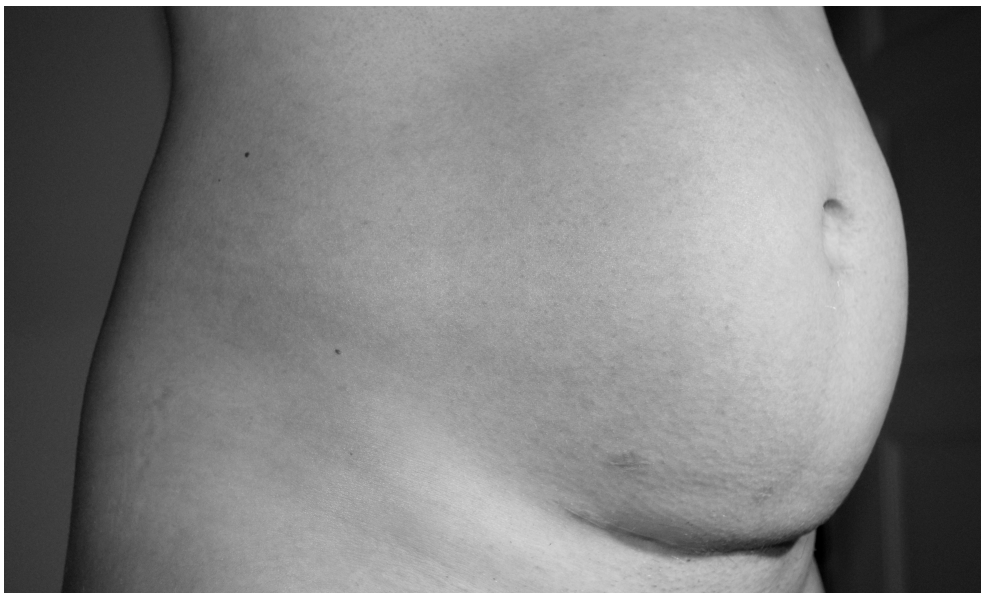
To identify women being good candidates for TOL after caesarean delivery, by exploring the association between the indication for the first CS and the risk for unplanned caesarean second delivery.

Paper III

To compare the outcome, in terms of low Apgar score, between infants of women with one previous CS and a second delivery TOL or ERCS, respectively, considering the indication for the first caesarean performed.

Paper IV

To validate a prediction model for success in TOL after caesarean delivery, developed for a US population (Grobman et al, 2007), and to elaborate and modify the model to fit Swedish conditions.



Methods, Results and Comments, Papers I – IV

The Four Study Populations

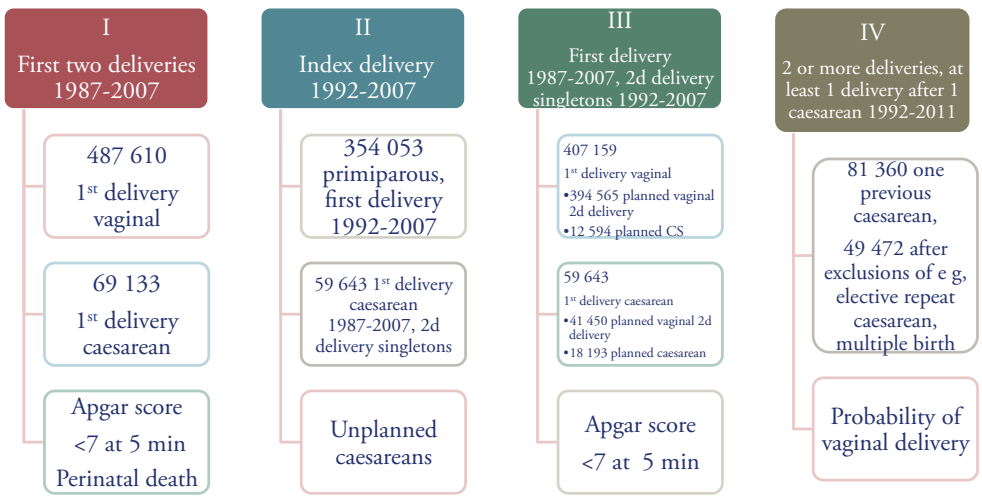


Figure 6. An overview of the populations chosen for the four papers.

Paper I

Methods

We aimed to compare infant outcomes, in terms of low Apgar score or perinatal death, between deliveries subsequent to one CS and deliveries following one vaginal delivery. We did not consider outcome by second delivery mode.

556 743 women with their first two deliveries between 1987 and 2007 were identified in the Swedish MBR. 487 610 women had experienced a first vaginal delivery and 69 133 a first caesarean delivery.

We studied the following demographic characteristics, all valid for the second pregnancy: year of delivery (continuous, linear variable), maternal age (years, continuous, linear variable), interval between deliveries (years, continuous, linear variable), maternal country of birth (Sweden/other), maternal height (cm, continuous, linear variable), maternal BMI (kg/m^2, continuous, linear variable), maternal smoking (no / <10 cigarettes/day / ≥10 cigarettes/day, semi-continuous variable), infant gender, gestational length (completed weeks, continuous variable), and BW SD scores (deviation in SD from the expected BW according to Swedish growth standard curves) (Marsal et al, 1996).

Chi-squared tests and Mann-Whitney U-tests were performed to compare the background characteristics of the two study groups.

The new hierarchical system, described in Methodological Considerations, was developed for this paper in order to explore the conditions/indications/diagnoses for the first deliveries by CS.

OR with 95% CI for low Apgar score or perinatal death were obtained using multiple logistic regression analyses. For each first CS indication, the OR for low Apgar score or perinatal death second delivery was computed in three steps, as shown in the Methodological Considerations and Statistics sections.

All possible confounders were valid for the second delivery.

Results

Compared with women with one previous vaginal delivery, women with one previous CS were more likely to give birth towards the end of the study period, to be older, to be shorter, to have a higher BMI, and to give birth before term. No differences were detected regarding interval between deliveries, country of birth, or smoking.

The infants of women with a prior CS were more likely to weigh less than 2 SD below, or more than 2 SD above, the expected BW for GA according to the Swedish ultrasound-based weight curves (Marsal et al, 1996) than infants of women with a prior vaginal delivery. The gender distribution did not differ between the infant groups.

The over-all first delivery CS rate was 12%, ranging from 9% in term singleton cephalic presentation deliveries to 69% in term singleton breech deliveries. The corresponding over-all second delivery CS rate was 11%, with a similar range. For women with a first vaginal delivery, the over-all second delivery CS rate was 6%, compared with 50% for women with a first CS.

As we had a presumption that underlying conditions would explain a great deal of the CS performed, an investigation of recurring CS indications was fundamental for our studies and for the development of the hierarchical system. That is, we assumed that the underlying condition for the first CS would recur at a considerable rate in the second delivery.

We found statistically significant ORs for recurrence for all first CS indications; women with the same diagnosis in both deliveries vs. women with a different diagnosis in the second delivery than the first delivery CS indication. These results were valid for the hierarchical classification as well as for a non-hierarchical setting. The strongest correlations between first and second delivery diagnoses were seen for the groups “Diabetes mellitus/gestational diabetes”, “LGA/suspect LGA/BW >4500 g”, “SGA/poor fetal growth”, and “Placenta praevia”.

Comparing the rate of low Apgar score between infants of women with one previous CS and infants of women with one previous vaginal delivery, absolute risks were low: 1.6% and 0.8%, respectively. Nevertheless, the risk was doubled for an infant of a mother with a previous CS (OR 2.0; 95% CI: 1.9-2.1). After adjustment for probable maternal and fetal confounders, the OR was still increased, 1.6 (95% CI: 1.5-1.8).

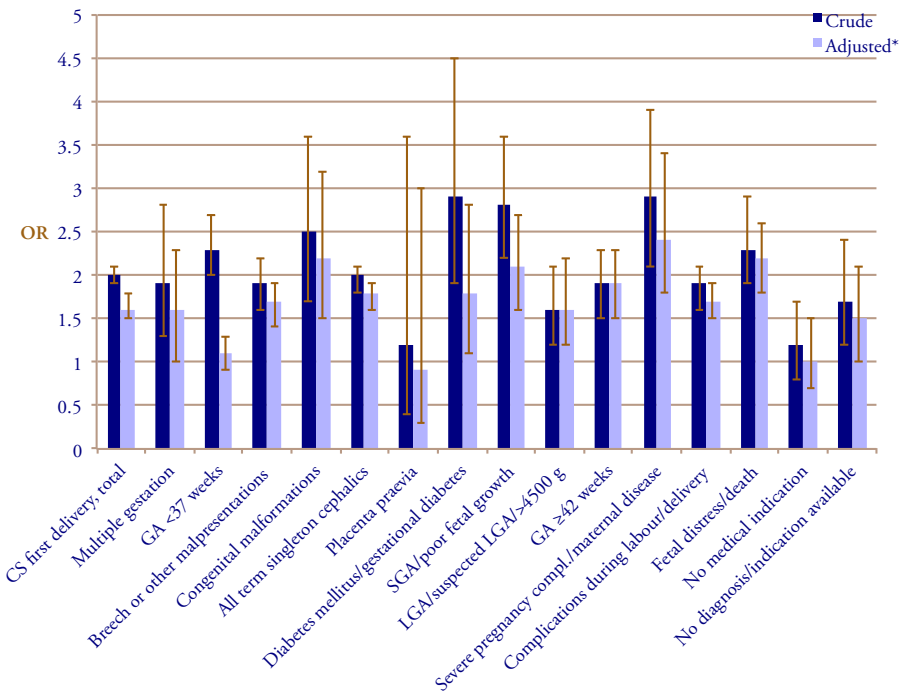


Figure 7. OR with 95% CI for low Apgar score; infants of women with one previous CS (hierarchical indication system) vs. infants of women with one previous vaginal delivery. Crude OR and OR adjusted for year of birth, maternal age, smoking, height, BMI, multiple birth, preterm birth, breech presentation and BW SD score, second delivery. Women with their first two deliveries 1987-2007 in Sweden.

The OR for low Apgar score second delivery varied substantially between hierarchical indications for the first CS performed (Figure 7). After adjustments, the OR was still significantly increased for most first CS indication groups. A more than doubled risk (adjusted OR) was shown for the first CS indications "Congenital malformations", "SGA/poor fetal growth", "Severe pregnancy complications/severe maternal disease", "Complications during labour/delivery", and "Fetal distress/death". When the first CS was performed without any obvious medical indication, no increased risk for low Apgar score second delivery could be demonstrated, indicating that the CS *per se* did not yield an increased risk of poor infant outcome second delivery.

Performing corresponding calculations for "perinatal death" (Figure 8), the results were similar to the Apgar score comparison results. As perinatal death was a rare outcome, the groups showing statistically significant results were few. In the hierarchical system of first CS indications, the adjusted OR for second delivery perinatal death was significantly increased in the following groups: "Multiple gestation", groups 6-15: term single cephalic pregnancies without major malformations all-over, and "GA ≥42 weeks". As for the case of low Apgar score risk, infants of women with a first CS without medical indication had no detected increased OR for perinatal death.

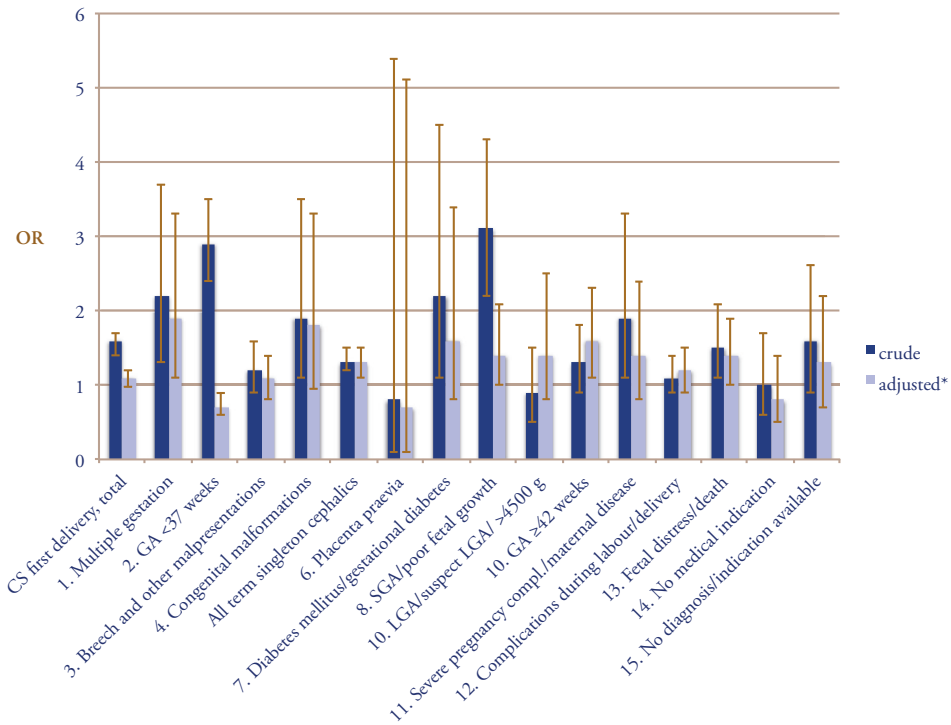


Figure 8. OR with 95% CI for perinatal death (28+0 weeks – 6 days); infants of women with one previous CS (hierarchical indication system) vs. infants of women with one previous vaginal delivery. Crude OR and OR adjusted for year of birth, maternal age, smoking, height, BMI, multiple birth, preterm birth, breech presentation and BW SD score, second delivery.

When we planned our studies, we decided, aside from the essential discussion about recurrence of conditions/indications/diagnoses, not to focus on diagnoses set for the second delivery. Our hypothesis was that maternal characteristics and conditions present at the first delivery be fundamental when studying outcomes of the delivery following one CS. Therefore, our main efforts have laid on first delivery diagnoses.

Nevertheless, to get a deeper understanding of which infants got a low second delivery Apgar score, it might also be of interest to study the delivery mode and the indications in the delivery following one CS. Table 9 shows the number of infants with low Apgar score for each second delivery mode, by indication for the *second* delivery.

Table 9. Infants with Apgar score <7 at 5 minutes at the second delivery of two-parous women with one previous CS, by diagnosis or indication for the second delivery (hierarchical system) and by second delivery mode. Sweden 1987-2007.

Second delivery indication, hierarchical system	**Vaginal, non-instrumental delivery.** n (%)	**Planned caesarean delivery** n (%)	**Unplanned caesarean delivery** n (%)	**Vacuum or forceps delivery** n (%)	**Total** N (%)
1. Multiple gestation	9 (3.4)	15 (6.5)	20 (4.6)	5 (2.8)	49 (4.4)
2. GA <37 weeks	63 (23.9)	95 (40.9)	75 (17.2)	6 (3.4)	239 (21.6)
3. Breech or other malpresentation	4 (1.5)	13 (15.6)	7 (1.6)	1 (0.6)	25 (2.3)
4. Congenital malformations	11 (4.2)	9 (3.9)	11 (2.5)	8 (4.5)	39 (3.5)
5. Rupture of uterus	1 (0.4)	1 (0.4)	83 (19.0)	13 (7.4)	98 (8.8)
6. Placenta praevia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
7. Diabetes mellitus/gestational diabetes	3 (1.1)	3 (1.3)	4 (0.9)	3 (1.7)	13 (1.2)
8. SGA/poor fetal growth	14 (5.3)	8 (3.4)	14 (3.2)	1 (0.6)	37 (3.3)
9. LGA/suspect LGA/ >4500 g	13 (4.9)	14 (6.0)	19 (4.4)	4 (2.3)	50 (4.5)
10. GA ≥42 weeks	13 (4.9)	1 (0.4)	24 (5.5)	22 (12.5)	60 (5.4)
11. Severe pregnancy complications/ severe maternal disease	3 (1.1)	4 (1.7)	9 (2.1)	3 (1.7)	19 (1.7)
12. Complications during labour/ delivery	32 (12.1)	16 (6.9)	79 (18.1)	68 (38.6)	195 (17.6)
13. Fetal distress/death	18 (6.8)	4 (1.7)	73 (16.7)	37 (21.0)	132 (11.9)
14. Previous CS/no medical indication	80 (30.3)	49 (21.1)	18 (4.1)	5 (2.8)	152 (13.7)
15. No diagnosis available (Not applicable as the table only shows women with one previous CS)					
Total	264 (100)	232 (100)	436 (100)	176 (100)	1108 (100)

Amongst the 1108 infants with low Apgar score in the delivery following one CS, the following second delivery indications in the hierarchical system were the most common: "GA <37 weeks", "Complications during labour/delivery", "Previous CS/no medical indication", and "Fetal distress/death", respectively.

Comments

- Women with a first CS were more likely than women with a first vaginal delivery to give birth a second time late during the study period, to be older, to be shorter, and to have a higher BMI.
- The OR for recurrence was statistically significant for all the encountered first CS indications/conditions/diagnoses.
- Infants of women with one previous CS were at increased risk of low Apgar score compared with infants of women with one previous vaginal delivery (OR: 2.0; 95% CI: 1.9-2.1). The risk estimate was reduced but still significant when adjustment for maternal and fetal/infant characteristics was made (OR: 1.6; 95% CI: 1.5-1.8).
- The corresponding crude and adjusted ORs for perinatal death were 1.6 (95% CI: 1.4-1.7) and 1.1 (95% CI: 1.0-1.2), respectively.
- The infant outcome of the delivery after one CS was mainly dependent on the indication for the first delivery CS.
- The association between the first delivery CS and the second delivery infant outcomes could, to some extent, be explained by underlying maternal and fetal characteristics, as adjustments for these parameters considerably lowered the overall risk estimates.
- When no medical indication was present, no risk increase was detected.

The results suggest that underlying conditions, not the previous CS *per se*, contributed to the risk increase.

Paper II

Methods

We aimed to investigate second delivery mode after one CS, identifying women being candidates for a TOL after caesarean.

Women having experienced their first two deliveries in Sweden were identified in the Swedish MBR. The two-parous women would have given birth for the first time between 1987 and 2007. The index delivery – the first delivery of the primiparous women and the second delivery of the two-parous women – would have taken place between 1992 and 2007. The primiparous women (giving birth for the first time) would also give birth at least once more during the study period.

Initially, we selected three groups of women for the study. An overview of the delivery modes in the three groups is shown in Table 10. Multiple gestations were excluded.

Table 10. Delivery mode of women with singleton pregnancies, Sweden 1992-2007.

	Vaginal, non-instrumental delivery, %	Planned caesarean delivery, %	Unplanned caesarean delivery, %	Vacuum or forceps delivery, %	Total, N (%)
First delivery	75	4	9	12	354 053 (100)
One previous vaginal delivery	92	3	2	2	407 159 (100)
One previous caesarean delivery	41	30	20	9	59 643 (100)

When we explored the results of the three groups of women (Table 10), we found that the differences in second delivery mode between women with a prior vaginal delivery and women with a prior CS would be too large to handle, especially when aiming to display the results in comprehensible graphs or tables. We decided to change our setting and compare the delivery mode after one CS with the delivery mode of women attempting their first delivery.

The choice of any of the comparison methods could have its advantages and disadvantages. If the previous CS were performed before contractions or in early labour, a nulliparous woman would probably be the most relevant comparison object.

Contrariwise, when a prior CS was performed in late labour, a woman with a previous vaginal delivery would be more appropriate for comparison. Anyhow, the registry data did not include any information on the stage of progress in labour at the time the first CS was performed.

The main analyses focused on women for whom a TOL after caesarean was planned. For every first CS indication in the hierarchical system described in Methodological Considerations, the OR for failed TOL (unplanned CS second delivery); women with one previous CS vs. primiparous women, was computed using the three different models also described in Methodological Considerations. Adjustments were performed for all possible confounders for the index delivery.

Results

Analyses of the descriptive characteristics showed, that women having experienced one former CS were likely to be older, shorter, and have a higher BMI than the nulliparous women.

When investigating the association between maternal characteristics and delivery mode in TOL, without considering the obstetrical history, a positive and linear association between unplanned CS (failed TOL) and year of delivery, maternal smoking, increasing maternal age and increasing BMI was shown. For maternal height, there was a negative association with unplanned CS in TOL.

Amongst all women having experienced one previous CS, the rate of ERCS was 30% with a corresponding TOL rate of 70%.

The success rate in TOL after caesarean was 71%, yielding an all-over VBAC rate of 50%.

During the study period, the all-over VBAC rate decreased, from 55% in 1992-95 to 45% in 2004-2007.

As seen in Figure 9, the rates of planned and unplanned CS in the delivery after one CS varied substantially by the hierarchical indication for the first CS performed. Two groups, "Rupture of the uterus" and "No medical indication", had planned second delivery CS rates of over 50%.

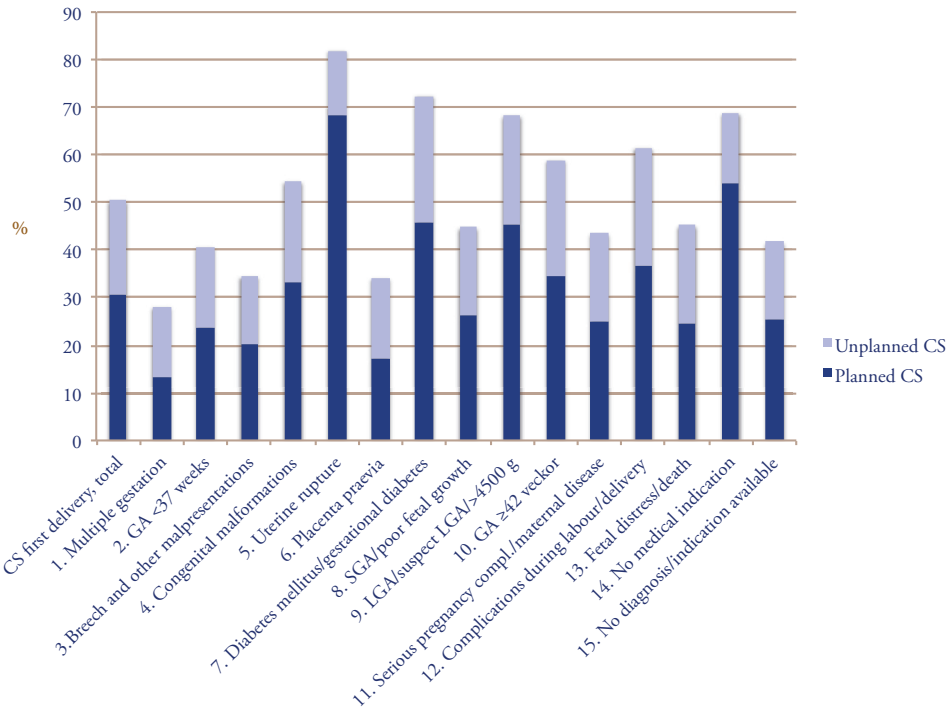


Figure 9. Planned and unplanned caesarean deliveries in the delivery following one CS, by hierarchical indication for the first CS. Sweden 1992-2007.

In some groups with high rates of ERCS, the rates of unplanned CS were also considerably high, pointing at the difficulty of choosing the right women for TOL after caesarean.

In Figure 10, the rate of unplanned CS was compared between the group of primiparous women with a planned vaginal delivery and the group of women with a TOL after one previous CS.

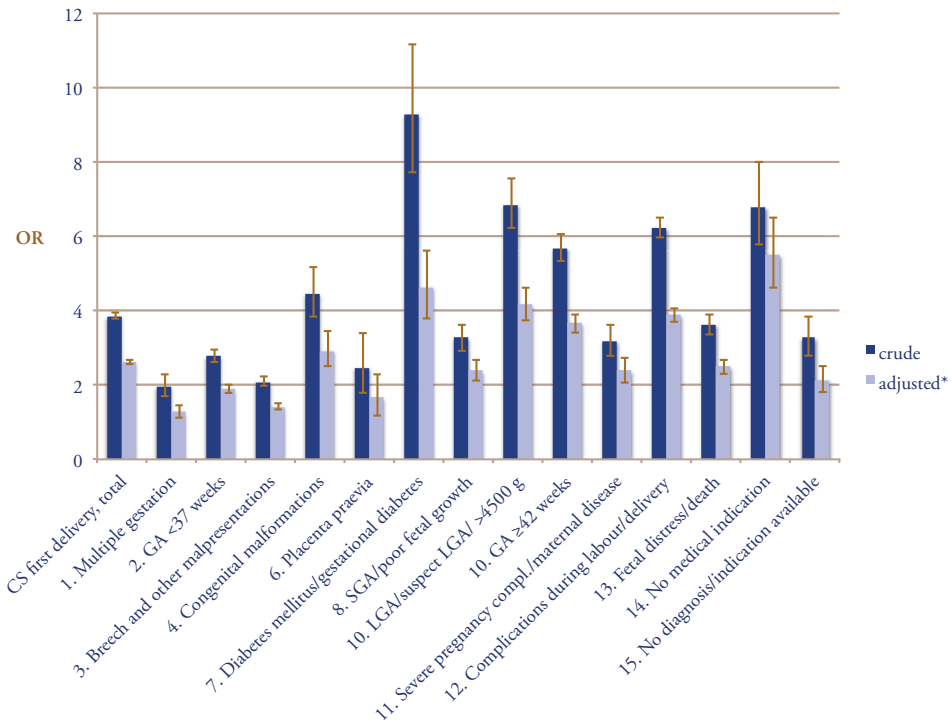


Figure 10. OR with 95% CI for unplanned CS; women with one previous CS (by hierarchical indication for the first delivery CS), vs. primiparous women with a planned vaginal first delivery. Crude OR and OR adjusted for year of birth, maternal age, smoking, height, BMI, GA <37 weeks, breech presentation, and BW SD score, second delivery. Sweden 1992-2007.

Women with one prior CS had increased crude and adjusted OR for unplanned CS (failed TOL) all-over, the unadjusted OR being 3.9 (95% CI: 3.8-4.0). The OR decreased significantly when adjustments were made for maternal factors, but adjustments for fetal/infant parameters did not further lower the estimate. For some previous CS indication groups, there were strong associations between previous CS and failed TOL: "Diabetes mellitus/gestational diabetes", "LGA/suspect LGA/BW >4500 g", "GA ≥42 weeks", "Complications during labour/delivery", and "No medical indication".

Comments

- Women with a first CS delivery were more likely to be older, to be shorter, to have a higher BMI, and to be smokers, than nulliparous women.
- Among all women in the two study groups, the adjusted OR for unplanned caesarean delivery increased by year of delivery, maternal age, BMI, and maternal smoking. In contrast, the OR decreased by maternal height.
- A first delivery by CS yielded an all-over increased risk of unplanned CS second delivery, compared with the risk of unplanned CS for a nulliparous woman attempting a vaginal delivery, with an adjusted OR of 2.6 (95% CI: 2.6-2.7).
- The magnitude of the risk increase varied substantially by the indication for the first CS performed. The adjusted OR for unplanned CS varied from 1.3 (95% CI: 1.1-1.5) for "Multiple gestation" and 1.4 (95% CI: 1.3-1.5) for "Breech and other malpresentation" up to 4.6 (95% CI: 3.8-5.6) for "Diabetes mellitus/gestational diabetes" and 5.5 (95% CI: 4.6-6.5) for "No medical indication" (presumably mainly "CS on maternal request").
- Women in the largest indication group in the hierarchical system, "Complications during labour/delivery", had a rate of unplanned CS in TOL of 39%. The adjusted OR for failed TOL in this group, compared with nulliparous women, was 3.9 (95% CI: 3.7-4.1).
- Some indication groups with a high frequency of planned second delivery CS also showed high rates of unplanned CS in TOL, suggesting that there was a non-optimal choice of women for TOL.

A planned caesarean second delivery was considered for 4% of nulliparous women and for 30% of women with a previous CS (Table 10). For some women with a "non-recurring" indication for the first CS, for example "Multiple gestation" or "Breech presentation" in the hierarchical system of indications, the rate of ERCS might seem unnecessary high. We presume that there is still a "Once a caesarean, always a caesarean" (Cragin, 1916) thinking among women, obstetricians and midwives. There must also be several, less well known medical and non-medical variables playing roles when requesting an ERCS, and when counselling and making decisions about second delivery mode.

An unplanned CS has repeatedly been shown to yield the highest risks of adverse outcomes for mother and child (Kallen & Olausson, 2007; El-Sayed et al., 2007; Oboro et al., 2010; Sentilhes et al., 2013) and making efforts to avoid failed TOL is of fundamental importance in the planning of delivery mode after CS. Undoubtedly, the fear of unplanned/emergency CS delivery is one of the main reasons for the high ERCS rate in many countries. Nevertheless, if individual risk factors are taken into account, TOL after caesarean is a reasonable option for pregnant women, despite an

increased risk for adverse neonatal outcomes compared with an ERCS on maternal request (Studsgaard et al., 2013).

In this second paper, we aimed to identify women suitable for a TOL after caesarean, i. e. women having a good chance for a VBAC. This was achieved by investigating the association between the hierarchical indication for the first caesarean and the risk of unplanned CS in TOL in the following pregnancy, compared with the risk for unplanned CS for nulliparous women attempting a planned vaginal delivery. (Thus, actually, we primarily identified women being the worst candidates for TOL after CS.)

If we had chosen to compare the group of women with a previous CS with the women with a previous vaginal delivery instead, it would have been very satisfactory to be able to divide the women with one previous vaginal delivery by first delivery indication, in the same manner as the women with one previous CS. However, as the hierarchical system of indications mostly depends on ICD-codes, such a comparison would suffer from severe bias. A CS would be much more likely than a vaginal delivery to yield diagnoses. In Sweden, as already mentioned, midwives supervise most of the vaginal deliveries, and diagnoses other than "Partus normalis" are quite rare.

In a US paper, Shipp et al. (2000) stated that over-all rates of caesareans were higher for women with one prior caesarean than for nulliparous women. Rates of caesarean after TOL were related to the prior caesarean indication; the lowest rates seen for women whose prior CS were for breech presentation, and the highest rates for women whose prior CS were performed for failure to progress. Additionally, the duration of labour in TOL for women who had a repeat CS for failure to progress was related to the indication for the prior caesarean, and was shortest for women whose prior CS also was for failure to progress, suggesting that obstetricians might have intervened earlier.

Our study results confirmed the main results of the publication by Shipp et al. (2000). Unfortunately, we had no accessible data for delivery duration. The finding that obstetricians might have intervened earlier, being aware of the course of the first delivery, could well be another brick in the wall of probable explanations for the final delivery mode after CS.

When investigating the delivery mode after one CS, it would certainly be of much help to have information on the first CS procedure, for example in what stage of labour it was performed, surgical techniques used, difficulties encountered, and postoperative infections. Unfortunately, the Swedish MBR does not include any such data. In a clinical situation, planning the delivery to follow, these data would almost always be known from medical records. Together with the story told by the woman and her partner and the scientific knowledge from the current and other studies, these data would support the final decision of subsequent delivery mode.

Paper III

Methods

We aimed to study infants in the second delivery of women having experienced one CS. We compared the rate of low Apgar score of infants born after TOL or after ERCS, considering the indication for the first caesarean performed.

In the Swedish MBR, we found 466 802 women with their two first deliveries between 1987 and 2007, the second delivery singleton (index) born between 1992 and 2007. First, 407 159 women with a first vaginal delivery and 59 643 women with a first CS were chosen, to compare the maternal and fetal characteristics by obstetric history and planned second delivery mode. Second, only the group of women with a previous CS was investigated. The infant outcome, in terms of low Apgar score, was compared between infants of the 18 193 women in the ERCS group and infants of the 41 450 women in the TOL after caesarean group. Mann-Whitney U-test for continuous data and Chi-squared test for categorical data were performed to compare the background characteristics of the study groups.

Information on the first CS indication was based on registry data and reported ICD-codes and estimated by applying the previously developed hierarchical system of indications, described in Methodological Considerations. OR with 95% CI for low Apgar score; infants of women with TOL after caesarean vs. infants of women with an ERCS, were obtained using logistic regression analyses. When making adjustments, we had to take into account that the number of cases with low Apgar score was low in some indication groups. When the number was sufficient (when the number of independent variables did not exceed 1/10 of the number of cases), the OR for low Apgar score was computed in three steps, as described in Methodological Considerations. All maternal and infant characteristics were valid for the index, second delivery.

In the total material all variables were associated, at the 20% significance level, with a low Apgar score. When the numbers of cases with low Apgar score were sufficient, we included all the possible confounders regardless of the level of significance (but again, all factors had a p-value <0.2). Seven of the 15 indication groups had too few numbers of cases to make the adjustment of the OR estimates by the method described above. Instead, we performed forward and backward selection procedures, to choose the best restricted adjustment models (crude OR, OR adjusted for the best maternal characteristic, and OR adjusted for the best maternal or fetal/infant parameter). The final models only included variables with p-values <0.2.

Tests of homogeneity of the OR across indication groups were based on weighted sums of the squared deviations of the stratum specific log-OR from their weighted means (Hosmer & Lemeshow, 1989).

Results

In the comparison of second delivery characteristics between women with one previous vaginal birth and women with one prior CS, women with one prior vaginal delivery gave birth earlier in the study period, they were younger, taller, and had a lower BMI. Their infants were more likely to be born between gestational weeks 37+0 and 41+6, and to have a normal BW for GA ($p < 0.05$ for all results).

In the group of women having experienced one CS, the sub-group of women with planned TOL was compared with the sub-group with ERCS. Women in the TOL group gave birth earlier during the study period, they were younger, taller, and had a lower BMI. Their infants were less likely to be born preterm. They were more likely to have a normal BW, and to be male ($p < 0.05$ for all results).

Infants of women with a first vaginal delivery followed by a planned CS had a 2.6% risk of low Apgar score, compared with a 1.1% risk for infants of women with a first CS and an ERCS. This might seem unexpected, but in the rare events when women with a first vaginal delivery get a planned second delivery CS, some kind of adverse event is often expected.

The over-all OR, crude as well as adjusted, for low Apgar score was increased for infants of women in the TOL after CS group compared with infants of women in the ERCS group: crude OR 1.6; 95% CI: 1.4-1.9, OR adjusted for year of birth and maternal characteristics 1.7; 95% CI: 1.5-2.0, OR adjusted for year of birth, maternal characteristics and fetal/infant characteristics 1.8; 95% CI: 1.5-2.1.

Using the hierarchical system of first CS indications described in Methodological Considerations, we found that the OR for low Apgar score, TOL after CS vs. ERCS, varied substantially between first CS indications.

As seen in Figure 11, a more than doubled risk for low Apgar score; infants of woman after TOL after caesarean vs. infants of women after ERCS, were seen for the first CS hierarchical indications "LGA/suspected LGA/BW >4500 g", "GA ≥42 weeks", "Complications during labour/delivery", and "Fetal distress/death". The first CS hierarchical indication group "Congenital malformations" had a more than five-fold risk for low Apgar score. We believe that this particular result was likely to be a random finding, which has to be confirmed in an independent study before further actions should be taken. In the first CS hierarchical indication group "No medical indication", no association between low Apgar score and planned mode of delivery was detected.

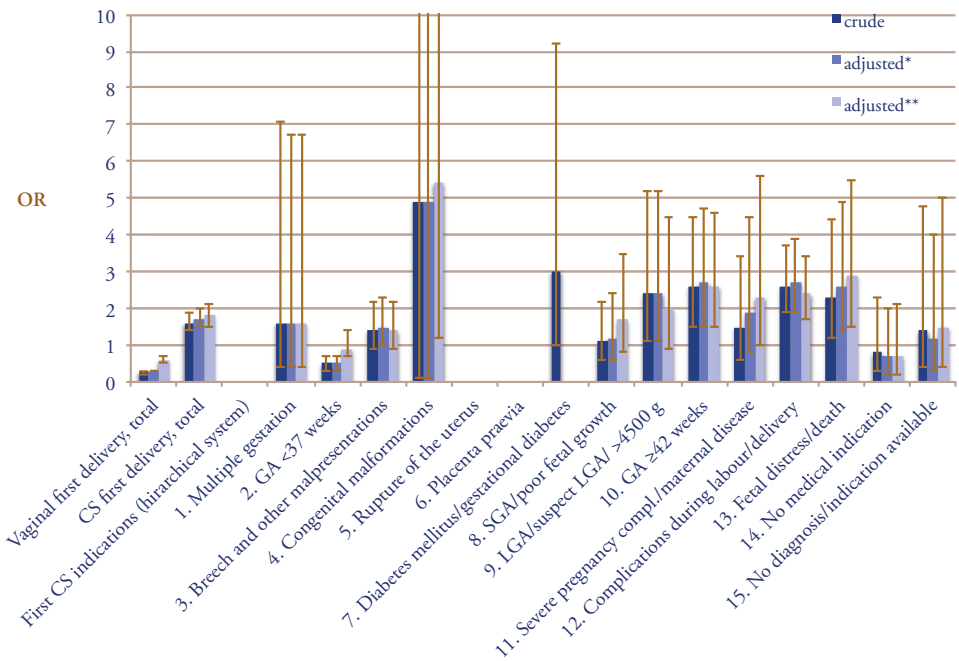


Figure 11. OR with 95% CI for low Apgar score for infants of two-parous women with a singleton pregnancy; planned vaginal delivery vs. planned caesarean. For infants of women with a first CS, low Apgar score by hierarchical indication for the first CS performed. Crude OR and, when appropriate, OR adjusted for 1) year of birth and maternal characteristics, and 2) year of birth, maternal characteristics and fetal/infant characteristics second delivery, as described in Methodological Considerations. Sweden 1992-2007.

We also investigated recurrence of the first CS indication, using another method than the one used for **Paper I**. We based the investigation on the hierarchical indication for the first CS, but thereafter explored the second delivery indications irrespective of the hierarchical system. We found that in all second delivery groups (the group "irrespective of planned second delivery mode", and the TOL or the ERCS groups), the first CS indication group "Diabetes mellitus/gestational diabetes" had the highest recurrence rate (>60%) followed by "Complications during labour/delivery" (45%), and "LGA/suspected LGA/>4500 g" (>30%). As already mentioned, indications set for TOL ending in a vaginal delivery would be sparse, which makes it difficult to interpret and compare the results between the TOL and the ERCS groups. Second delivery multiple gestations were excluded.

Comments

When planning this third study, we aimed to yield new evidence to be useful in the decision-making after one previous caesarean delivery. Our primary endeavour was not to decrease the second delivery CS rate *per se*, but to investigate for which second deliveries it would be best to recommend a TOL, and for which an ERCS would be the safest choice. That is, by considering the hierarchical indication for the first CS performed, we wanted to choose the right women for TOL after caesarean, aiming to achieve VBACs with infants getting Apgar scores ≥7 at 5 minutes.

Some authors have studied infant outcomes of TOL after caesarean compared with outcomes after ERCS. Landon et al. (2004) found no significant increase in term neonatal mortality in infants of women who undertook a TOL, but did find an increased rate of hypoxic ischemic encephalopathy. The absolute risk of hypoxic ischemic encephalopathy in TOL after caesarean was very low (Cahill & Macones, 2007).

- For infants of women with a first vaginal delivery, the OR for low Apgar score was lower after a planned vaginal birth than after a planned caesarean second delivery, suggesting that a planned caesarean after vaginal birth was chosen in cases for which an adverse event was predicted.
- For infants of women with a first delivery by caesarean, the OR for low Apgar score was higher after a planned vaginal birth than after a planned caesarean second delivery. The risk varied substantially by the indication for the first caesarean.
- By considering the hierarchical indication for the first CS performed when planning the second delivery mode, it might be possible to choose the right

women for the respective delivery mode – TOL or ERCS - and to lower the rate of infants with low Apgar score in the subsequent delivery.

To get a somewhat less abstract look at the number of extra ERCS needed in order to decrease the risk of second delivery low Apgar, it is possible to calculate the "number needed to treat" (NNT).

In the all-over material of women with one previous CS, ERCS would have to be chosen in the place of TOL for 101 women (crude), or for 151 women (adjusted for year of birth, maternal and fetal/infant characteristics), to avoid low Apgar score for one infant. After a first CS due to "Complications during labour/delivery" in the hierarchical system, the corresponding adjusted NNT would be 74, and for "Fetal distress/death", the adjusted NNT would be 44. That is, with a first CS performed with the hierarchical indication "Fetal distress/death", ERCS would have to be chosen instead of TOL for 44 women to avoid one infant with a low Apgar score.

For comparison, to avoid a low Apgar score for one infant in breech presentation, one has to perform 80 planned CS instead of planned vaginal deliveries.

Needless to say, there is no cut-off for NNT. Decision-making is complex.

Paper IV

Methods

We aimed to investigate if the probably most commonly used prediction model for successful TOL after CS, developed for a US population by Grobman et al. (2007) and recommended in the ACOG Practice Bulletin No. 115 (2010), would be applicable on a Swedish population. If not so, we wanted to explore how to modify it for Swedish conditions. For this purpose, women with one CS and at least one subsequent delivery between 1992 and 2011 (n=81 360) were identified in the Swedish MBR. Only the last delivery of each woman was counted.

Besides the prediction model mentioned above, several other models aiming to predict VBAC have been developed in later years: Hashima & Guise (2007), Srinivas et al. (2007), and Metz et al. (2013). Just recently, a study from the Netherlands (Schoorel et al., 2014), aiming to develop and internally validate a model for VBAC prediction for term deliveries in a Western European population, has been published. Compared with our study, this last-mentioned study was considerably smaller, including 515 women with a prior CS. Variables apparent first at labour were included, and only two of the variables considered gave statistically significant ORs, which would result in low precision of the other estimates. The ROC AUC yielded by the model was 70.8%.

Validations of prediction models (Costantine et al., 2009; Grobman et al., 2009; Costantine et al., 2011; Yokoi et al., 2012; Tessmer-Tuck et al., 2014) have also been published. The majority of the studies and the validation studies have been designed for US populations. A thorough evaluation and meta-analysis of prediction models/screening tools published until 2007 has been performed (Eden et al., 2010).

To perform our study, we used the same exclusion criteria as Grobman et al. (2007): antenatal death (n=128), multiple gestation (n=1365), GA <37 weeks (n=4330), breech or other malpresentation (n=2818), ERCS (n=21 888), and no indication reported for the previous CS (n=1359). After exclusion, the 49 472 women available for the study (61% of all women with one previous CS) were equally divided into one development and one validation data set, every second woman belonging to either of the sets. The new models, with variables considered as conceivable VBAC predictors, were developed on the development data set using multiple logistic regression analyses, and then tested on the validation data set.

The validation of the prediction model by Grobman et al. (2007) started by letting the original OR estimates enter the logistic regression analyses as offset variables, to test the application of the original model on our validation data set. All variables were valid for each woman's last, index, pregnancy:

1. "Maternal age" (entered as a continuous, linear variable),
2. "BMI" (continuous, linear variable),
3. "Maternal race", changed to "Maternal country of birth" for Swedish conditions, where the variables were substituted as follows: "Latina" by "Spain, Portugal, or South America", "African American" by "Sub-Sahara" and "White and others" by "Sweden or remaining countries",
4. "Recurring indication for caesarean delivery", defined as "Arrest of dilation or descent as the indication for the previous caesarean" (Grobman et al., 2007) was substituted by ICD-codes for cephalopelvic disproportion, abnormalities of pelvic organs, dystocia or prolonged labour (ICD9: 653, 654.0, 1, 3, 4, 6-9, 660.1-3, 6, 8-9, 661, 662.0-2. ICD10: O33, O34.0-1, 4-9, O62, O63.0-1, 9, O64.0, O65, O66.2-4, 8-9, O75.0. 8-9),
5. "Any prior vaginal delivery" (yes/no), and
6. "Vaginal delivery after prior caesarean" (yes/no).

In the second step, the values of the original variables were re-calculated using the development data set, and the performance of the new OR estimates was tested on the validation data set. Third, we wanted to replace "Recurring indication for caesarean delivery" with our hierarchical system of first CS indications, described in Methodological Considerations. Thus, "Recurring indication for caesarean delivery" was not considered, as it would double the hierarchical indication system. Hierarchical indication group three, "Breech or other malpresentation", was regarded as reference. The performance of this expanded model was evaluated on the validation data set.

Fourth, after univariate and multivariate analyses based on the development data set, three new, presumably important variables were selected to supplement or substitute the original variables (Grobman et al., 2007): maternal height and delivery ward specific CS rates: percentages of ERCS and unplanned CS after one caesarean delivery, respectively.

The performance of each of the models applied on the validation data set was tested creating ROC curves, to illustrate the respective sensitivity and specificity for VBAC predictability. The variance of the ROC AUC, and the variance of the difference between two dependent AUCs, respectively, was computed using a method proposed by DeLong et al. (1988). The agreement between the individual predicted probability of VBAC and the observed VBAC rate for each predicted probability decentile was evaluated by calculating the Pearson's r.

Results

When we compared the maternal characteristics of the original study population (Grobman et al., 2007) with the current study population, we found that the mean maternal age in the current study population was higher (32 vs. 29 years), the current proportion of women older than 35 years was higher (29 vs. 18%), and the percentage of women born in "Sweden or remaining countries", as compared to "White and others" was much higher (98 vs. 44%).

The background descriptive characteristics of the current study development and validation data sets were found to be similar, suggesting a successful randomisation process.

The OR estimates for VBAC for the following variables: maternal age, BMI, recurring indication for caesarean delivery, and any prior vaginal delivery, were similar to those published by Grobman et al. (2007). For the groups corresponding to the "Maternal race" groups, the OR estimates differed substantially from the original OR, indicating that data regarding maternal country of birth was of minor importance for Swedish conditions.

In the original publication, a VBAC prediction ROC AUC of 0.75 was yielded (Grobman et al., 2007). Using the original OR estimates on the current Swedish development data set, the ROC AUC yielded was lower, 0.69; 95% CI: 0.68-0.70. The percentage of variation of success in TOL explained (R^2) was only 12.3%. Using exactly the same variables, but with OR estimates from the current development population, the ROC AUC yielded was the same, but the R^2 marginally higher, 12.4%.

The VBAC prediction ability increased significantly ($p < 0.001$) when, in the third step, detailed information on previous CS hierarchical indication was added to the model (ROC AUC=0.71; 95% CI: 0.71-0.72, R^2 15.6%). Compared with the reference "Breech or other malpresentation", all first CS hierarchical indications yielded lower ORs for VBAC. The lowest ORs were seen for "Rupture of uterus", "No medical indication", "Diabetes mellitus/gestational diabetes", "Complications during labour/delivery", "LGA/suspected LGA/BW >4500 g", and "GA >42 weeks", respectively.

The predictability of VBAC increased even more when, in the fourth and final step, maternal height and delivery ward specific CS rates were included. Maternal height was shown to be a strong predictor for successful TOL: OR for vaginal birth increased with 1.05 for each cm of height. The delivery unit specific rate of unplanned CS after one CS was also found to be a strong (negative) predictor for a successful TOL. Compared with the reference "Breech or other malpresentation", the same first CS indications as mentioned for the third model gave the lowest ORs for VBAC.

The final model ROC AUC was 0.74; 95% CI: 0.73-0.74. The model explained 18.7% of the total variation of success in TOL, i. e. VBAC.

When we applied the final prediction model on the validation data set, the agreement between the predicted and the observed VBAC rates was excellent in all VBAC probability decentiles. The over-all correlation obtained (Pearson's r) was 0.98; 95% CI: 0.98-0.98.

Comments

In accordance with our hypothesis, the US model for predicting success in TOL after caesarean (Grobman et al., 2007) was not immediately applicable to Swedish conditions. After modification of the original model and addition of information regarding first caesarean hierarchical indications, maternal height, and delivery unit specific CS rates, we managed to develop a prediction model with excellent prediction ability to be used in a Swedish setting.

Grobman (2010) have stated important factors to consider when developing a predictive model for potential clinical usefulness:

1. Multivariable model
2. Validation with independent test set
3. Non-unity scoring (not just presence or absence)
4. Generation of continuous probabilities possible
5. Model includes only factors known early in prenatal care
6. Model includes factors unknown until admission for delivery/intrapartum/ postpartum
7. Discrimination assessed by ROC, or by other than by ROC
8. Assessment in population other than original population

In our new prediction model, we have considered all the above-mentioned factors, and implemented factors 1-5 and 7 (by ROC).

For Swedish clinical settings, we found it preferable to use only variables known well before labour and delivery. As maternal health care, as well as delivery care, in Sweden is primarily midwife-based, a woman with one previous CS would probably see an obstetrician only once during her following pregnancy if no complications were present. Hence, it would be easiest to base a prediction aid on factors already known at this visit. Evidently, the decision of second delivery mode could always be modified later, by new facts revealed in late pregnancy, at admittance to the delivery ward, or in labour.

In our three first papers, no women with more than one previous delivery were included. In this fourth paper, we wanted to include also women with earlier vaginal births, before and/or after the first CS.

It is well known, that a history of a prior vaginal delivery is the strongest predictor of a successful VBAC in TOL (Landon et al., 2005). According to Cahill et al. (2006), the sub-group of VBAC candidates who had experienced a prior vaginal delivery also had a decreased risk for over-all maternal morbidities (uterine rupture, bladder injury, fever, or need for blood transfusions) compared with women who underwent an ERCS, and that those women should not only be advised, but encouraged to attempt TOL after caesarean.

The results of our study emphasise the importance of considering local/national demographic characteristics and obstetrical traditions before adopting a VBAC prediction model. By choosing relevant indicators for a Swedish setting, we were able to reach an excellent accuracy in predicting a successful TOL after caesarean.

That said, I would like to stress the presence of other, primarily non-medical, factors to take into consideration in the complex process of decision-making after one CS. The personal wishes of the pregnant woman and her partner would influence the decision to a great extent, as would the preferences of the counselling obstetrician, the experiences of the midwife, and the traditions of the delivery ward in question.

According to Bernstein et al. (2012), candidates for TOL after caesarean appeared to know little about risks and benefits associated with their mode of delivery, and provider bias affected the choice of delivery mode. Metz et al. (2013) found, that less than one-third of women considered good candidates for a TOL after caesarean delivery (VBAC chance of ≥70% using the original model by Grobman et al. (2007)) finally chose TOL.

Although there is no universally agreed on discriminatory point, evidence suggests that women with at least a 60-70% chance of VBAC have equal or less maternal morbidity when they undergo a TOL after caesarean than have women undergoing an ERCS. Conversely, women who have a lower than 60% probability of VBAC have a greater risk of morbidity than have women undergoing an ERCS (Cahill et al., 2006; Grobman et al., 2009; ACOG Practice bulletin No. 115, 2010).

In Table 11, it is possible to get an estimate of the chance of VBAC in TOL when deciding on a specific cut-off for a specific delivery ward or other setting.

Table 11. Estimated chance of having a successful TOL after caesarean section, i. e. VBAC, for different ROC curve cutoffs, according to our new prediction model. Women in Sweden with one delivery by CS 1992- 2009 and at least one following delivery 1994-2011.

Estimated chance of successful TOL	At cutoff or above		Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %	Height over line, x=y
Cutoff	Successful TOL , n	Unplanned CS, n	ref				
100	0	0	0	100	0	25	0
95	1971	75	11	99	96	27	0.094
90	4544	304	25	95	94	30	0.197
85	7532	710	41	89	91	34	0.293
80	9998	1210	54	81	89	37	0.346
75	11 789	1780	64	71	87	40	0.351
70	13 334	2344	72	62	85	43	0.344
65	14 696	3063	79	51	83	45	0.303
60	15 952	3814	86	39	81	49	0.25
55	16 980	4530	92	27	79	53	0.191
50	17 663	5175	96	17	77	56	0.124
45	18 104	5636	98	10	76	60	0.074
40	18 332	5932	99	4.8	76	64	0.039
35	18 435	6094	100	2.2	75	67	0.018
30	18 484	6178	100	0.9	75	73	0.008
25	18 496	6220	100	0.2	75	60	0.001
20	18 503	6228	100	0.1	75	80	0.001

The highest value for “height over line” in the ROC-curve corresponding to Table 11 was 0.351, corresponding to a cut-off of 75%.

If we chose to use the 75% cut-off, we would thereby decide that women with a VBAC chance of 75% or more according to our new prediction model would be eligible for TOL in our delivery ward. Then, according to Table 11,

- we would correctly identify 64% of the women who would succeed in TOL, i. e. reach a VBAC (sensitivity).
- we would correctly identify 71% of the women who would fail in TOL, i. e. have an unplanned CS performed (specificity).
- a woman attempting a TOL would have 87% chance to reach a VBAC (positive predictive value).
- among women being told they would not reach a VBAC, that would be a true statement for 40% (negative predictive value). But, as we would have planned for an ERCS, we would never realise that.

"Ultimately, the clinical usefulness of any predictive model can only be judged according to whether it actually results in improvements in clinical care and outcomes; a demonstration of its accuracy is a necessary first step, but not sufficient to establish this usefulness." (Grobman, 2010)

Our model, customised for the Swedish population, made it possible to reach an excellent prediction of VBAC rate in all prediction groups. Better awareness of the chances for a successful TOL after caesarean delivery could possibly contribute to the accuracy of Swedish maternity care counselling on delivery mode after one CS, and result in fewer deliveries by emergency CS in TOL.

Summary

Clinical Implications

General Considerations

Finally, would our findings be of any use? First, do women having undergone a caesarean delivery want to give birth again? Yes, they do. A conclusion drawn from Table 12 is, that a large proportion of women attending Swedish maternity care and labour wards is, and will continue to be, women having experienced one or multiple caesarean deliveries. Thus, we have to ensure medical care of these women and their deliveries by scientific knowledge and proven experience.

Table 12. Primiparous and two-parous women giving birth between 1992 and 2005 (first delivery) and between 1994 and 2007 (second delivery). Data from the Swedish MBR.

	First delivery caesarean, n	(%)	First delivery vaginal, n	(%)
Two-parous women	52 615	(62.0)	346 067	(77.1)
Primiparous women	84 907	(100)	448 606	(100)

Sometimes it is argued, that the only concern about giving birth vaginally after a CS is about the risks associated with a possible rupture of the scarred uterus. In an editorial, it was stated: "In my view, VBAC is essentially a uterine-rupture issue" (Scott, 2010).

Our study results do not confirm this opinion. For infants of women with one previous CS, only 9% of the second delivery low Apgar scores all-over were recorded in deliveries complicated by a uterine rupture. In second deliveries with failed TOL, the corresponding share was 19%. Evidently, being aware of the uterine rupture risk, and making efforts to avoid ruptures, is of importance in every delivery following a CS. However, various other underlying factors played the major role for the second delivery infant outcomes.

To reduce the primary CS rate by performing CS only when it is absolutely needed, would naturally solve a great deal of the problems regarding deliveries after CS. Though maybe utopian, it is certainly a goal worth striving for. But, once the first CS is performed, the old "Once a caesarean, always a caesarean" (Cragin, 1916) should be handled with care and suspicion. Leaning on our study results, the safest option for many women would certainly be an ERCS in the subsequent delivery. Still, a majority of women would be given advice about a preferable TOL with a possible VBAC. This is already true for Sweden – but we have to do much better in the selection process, choosing the right women for TOL and for ERCS. Here, our new results could be of great benefit, in combination with earlier findings.

Hierarchical Indication Groups followed through the Papers

How did the women in the 15 groups of the hierarchical system of indications do through the four papers? In Table 13, I have tried to follow each group, giving the results yielded in each paper. Although a rather non-scientific summary, it might be interesting to explore. For example, the first CS hierarchical indication group "Diabetes mellitus/gestational diabetes" showed high risk for adverse events in most of the investigations, whereas "Breech or other malpresentation" showed low risks all-over.

Please be well aware that the populations in the four papers were different!

Table 13. Results for the indication groups in the hierarchical system through the four papers.

	Women with one previous CS (I)	Re-curr. of indic. (I)	Infant outcome after one CS vs. after one vaginal birth (Paper I)		Uterine rupture		CS second delivery (Paper II)		Failed TOL after CS vs. TOL for nullips (II)	Low Apgar score in TOL after CS vs. ERCS (III)	VBAC in TOL after CS vs. ref. group 3 (IV)
			Low Apgar score	Peri-natal death	TOL	ERCS	Planned	TOL			
First CS indications, hierarchical system	n (%)	OR	Adj. OR	Adj. OR	%	%	%	%	Adj. OR	Adj. OR	OR
First CS, total	69 133 (100)		1.6	1.1 NS	1.1	0.1	30	20	2.6	1.8	
1. Multiple gestation	1674 (2)	2.0	1.6	1.9	0.7	0	12	17	1.2	NS	0.90 NS
2. GA <37 weeks	9584 (14)	5.5	NS	NS	0.7	0.3	22	19	1.8	NS	0.68

3. Breech or other malpresent.	11 408 (17)	2.6	1.7	NS	1.2	0.3	20	15	1.4	NS	Ref
4. Congen. malform.	1412 (2)	1.8	2.2	NS	2.0	0	32	20	2.9	5.4	0.35
5. Uterine rupture	24 (0)				0	0	68	13			0.15 NS
6. Placenta praevia	325 (0)	6.8	NS	NS	1.3	2.1	18	16	1.6		0.75 NS
7. Diabetes mellitus/ gestational diabetes	896 (1)	78.8	1.8	NS	1.4	0.5	46	26	4.6	NS	0.27
8. SGA/poor fetal growth	2871 (4)	6.1	2.1	1.4	0.9	0	26	18	2.3	NS	0.47
9. LGA/ suspect LGA/ >4500 g	3474 (5)	8.4	1.6	NS	1.1	0	45	22	4.2	NS	0.26
10. GA ≥42 weeks	6658 (10)	2.9	1.8	1.6	1.5	0	34	26	3.7	2.6	0.29
11. Severe pregnancy compl./severe maternal disease	1726 (2)	4.4	2.4	NS	0.8	0	24	18	2.3	NS	0.59
12. Compl. during labour/ delivery	17 560 (25)	2.2	1.7	NS	1.4	0.2	37	24	3.8	2.3	0.30
13. Fetal distress/death	5717 (8)	2.2	2.2	NS	1.1	0.2	24	20	2.5	2.9	0.50
14. No medical indication	3572 (5)		NS	NS	0.6	0.1	53	16	5.4	NS	0.17
15. No diagnosis available	2232 (3)		1.5	NS	0.8	0	25	16	2.2	NS	

The New Prediction Model

In order to demonstrate the application of the prediction model developed in **Paper IV**, we wanted to estimate the chance of VBAC in TOL for four fictitious women. The four women would give birth at least twice between 1992 and 2007, and have had one CS performed between 1992 and 2005. In 2005, each of the four women would attempt a TOL after caesarean in one of four specified Swedish delivery wards. The delivery ward CS rates for 2005 were investigated using the Swedish MBR.

Table 15. Probability of success in TOL after one caesarean. Four fictitious examples of women giving birth, based on the new predictive model for VBAC in TOL. Sweden, 2005.

	 **Flora in Falun**	 **Line in Lund**	 **Maria in Malmö**	 **Ylva in Ystad**
Age, years	35	42	21	27
BMI, kg/m^2	24	21	27	34
Previous vaginal delivery	yes	no	no	no
Previous VBAC	no	no	no	no
Height, m	1.69	1.75	1.55	1.60
Delivery ward ERCS, %	29.7	33.6	22.3	32.2
Delivery ward un-planned second CS, %	19.5	16.0	15.8	22.6
Hierarchical indication for the previous CS	Placenta praevia	Maternal request	Multiple birth	Labour complications
Probability of vaginal birth in TOL after caesarean, %	89.8	55.7	84.1	37.2

Numbers Needed to Treat

If we wanted to yield a certain, desired result, how large a change of medical practice would have to be implemented? Regarding our studies, "How many more deliveries after one CS would have to be planned as an ERCS instead of a TOL, to avoid a certain outcome?"

As already described in the Statistics section, calculating the "number needed to treat", or "number needed to harm" (NNH), might give a less abstract image, and yield an easier way to understand rates, when dealing with big populations and rare events. Some of the NNT in Table 14 have already been shown in the Conclusions section of **Paper III**.

Table 14. Numbers needed to treat or numbers needed to harm to reach or avoid specified events.

Event	NNT or NNH	Data source
One extra serious maternal venous complication	820 CS	Swedish Report on Caesarean Delivery, 2010
One extra infant to neonatal ward due to neonatal respiratory distress	30 planned CS on non-fetal indication	Swedish Report on Caesarean Delivery, 2010"
One extra child with serious asthmatic disease due to the CS	170 CS	Hakansson & Kallen, 2003
One extra uterine rupture in the following pregnancy	185 CS	Swedish report on Caesarean Delivery, 2010
Avoidance of one perinatal or neonatal death of an infant in breech presentation	400 planned CS in gestational week 38+	Swedish Collaborative Breech Study Group, 2005
Avoidance of one infant with low Apgar score in breech presentation	80 planned CS in gestational week 38+	Swedish Collaborative Breech Study Group, 2005
Avoidance of one surgical procedure for maternal stress incontinence	280 CS	Based on results by Persson et al., 2000
Avoidance of one uterine rupture after one previous CS	106 ERCS	The Swedish MBR
Avoidance of one infant with Apgar score <7 at 5 minutes in the delivery after one CS, all-over	101 ERCS (crude), or 151 ERCS (adjusted)	The Swedish MBR
Avoidance of one infant with low Apgar score second delivery in the first CS hierarchical group "Complications during labour/delivery"	74 ERCS (adjusted)	The Swedish MBR
Avoidance of one infant with low Apgar score second delivery in the herarchical group of first delivery CS "Fetal distress/death"	44 ERCS (adjusted)	The Swedish MBR

Conclusions

The increasing rate of women having undergone a caesarean delivery has stressed the importance of adequate counselling on preferable delivery mode in pregnancies following CS. An important issue would be to avoid that a planned TOL end in an emergency CS. Therefore, we wanted to investigate for which women a TOL after CS or an ERCS, respectively, be the safest choice.

First, starting by not considering the condition present at/the indication set for the first delivery CS, the main findings from our three first papers were:

1. The risk for low Apgar score was higher for an infant in a delivery after one CS than in a delivery after one vaginal birth.
2. The risk for perinatal death was higher for an infant in a delivery after one CS than in a delivery after one vaginal birth.
3. The risk of having an unplanned CS in TOL was higher in a delivery after one CS than for primiparous women.
4. The risk for low Apgar score was higher for an infant of a woman in a TOL after CS than in an ERCS.
5. The risk for almost all adverse outcomes encountered differed substantially by maternal characteristics.

Second, when we considered the results yielded using our new hierarchical system of conditions present at, or indications set for the first delivery CS, it became evident that:

6. The above-mentioned risks/adverse outcomes differed substantially between first CS indications, indicating that underlying factors, not the CS *per se*, contributed to the increased risks in deliveries following CS.

Third, aiming to construct a custom-built model for prediction of a successful TOL after caesarean, we modified a US prediction model (Grobman et al., 2007) to be applicable for Swedish conditions. By substituting the original variables "Maternal race" and "Recurring indication for caesarean delivery" with maternal height and our hierarchical system of first CS indications, respectively, and thereafter adding information on the specific delivery ward CS rates in deliveries after CS, we reached an excellent predictability of VBAC.

We have shown, that knowledge of underlying factors (maternal characteristics, "recurrence" of the indication for the first CS performed, and characteristics of the delivery ward in question) is fundamental for a safe delivery mode planning in the pregnancy following one CS. As scientifically clear this decision-making might seem, we have also shown that medical data and results only make a modest contribution to the final decision of delivery mode.

The wishes and desires of the pregnant woman and her partner, the experience and preferences of the midwives and obstetricians involved in counselling, and the prevailing trends in society, also play major roles in the decision of delivery mode.

"This decision (of VBAC) is still best made through a pact between the physician and patient based on mutual trust" (Scott, 2011). I certainly agree, but I would like to add the woman's partner and the midwife to the alliance. I would prefer to use our new findings and our new prediction model pragmatically, as an important utensil among others in the every day life as obstetrician.


Förlossning

Svensk sammanfattning

Förlossning efter kejsarsnitt

Kejsarsnitt utgör för närvarande cirka 17% av alla förlossningar i Sverige. En konsekvens av detta är att allt fler kvinnor kommer till specialistmödravården för rådgivning om vilket förlossningssätt som är säkrast vid förlossningen efter ett kejsarsnitt. Två möjligheter finns: planerad vaginal förlossning eller planerat kejsarsnitt. När man beslutar om förlossningssätt andra förlossningen vill man först och främst undvika en planerad vaginal förlossning som avslutas med ett akut kejsarsnitt, eftersom det medför de största riskerna för mor och barn. Samtidigt önskar man en rimlig andel planerade kejsarsnitt, eftersom upprepade kejsarsnitt inte heller är riskfria. Många faktorer måste vägas samman, och det är viktigt att välja rätt.

Med våra studier ville vi öka kunskapen om förlossning efter ett tidigare kejsarsnitt. I alla fyra studierna har vi utgått från det svenska medicinska födelseregistret, med data från nästan alla förlossningar i Sverige sedan 1973. I **studierna I-III** undersökte vi data från över 400 000 kvinnor med sina två första förlossningar 1987-2007 och i **studie IV** data från cirka 80 000 kvinnor med minst två förlossningar 1992-2011, varav ett kejsarsnitt och minst en förlossning efter detta kejsarsnitt.

Gemensamt för **studierna I-III** var, att alla indikationer för det första kejsarsnittet hade statistiskt signifikant risk att upprepas andra graviditeten eller andra förlossningen. Vi visade också att kvinnor med ett första kejsarsnitt var äldre, kortare till växten och hade högre body mass index (BMI) vid andra graviditeten än kvinnor som haft en första vaginal förlossning, eller jämfört med förstföderskor.

I **studie I** ville vi ta reda på om ett tidigare kejsarsnitt var en riskfaktor för att barnen skulle vara medtagna efter andra förlossningen (mätt som låg Apgarpoäng, mindre än sju poäng vid fem minuters ålder) eller för att barnen skulle dö i livmodern eller under första levnadsveckan (perinatal död). Vi jämförde med barn till mödrar som haft en första vaginal förlossning. Vi fann en fördubblad risk för låg Apgarpoäng (1,6% jämfört med 0,8%) och en cirka 60-procentig riskökning för perinatal död (0,6% av alla barn efter ett tidigare kejsarsnitt jämfört med 0,4% av alla barn efter en tidigare vaginal förlossning). En stor del av överriskerna kunde dock förklaras av att de riskfaktorer som ledde fram till att den första förlossningen avslutades med kejsarsnitt förelåg även vid den andra förlossningen. Vi utvecklade därför ett hierarkiskt system för att klassificera indikationerna för det första kejsarsnittet.

Därefter analyserade vi Apgarpoäng och perinatal död vid den andra förlossningen utifrån detta indikationssystem. Vi såg då att riskerna varierade stort mellan olika indikationer för det första kejsarsnittet. När det första kejsarsnittet utförts utan någon klar medicinsk indikation såg man ingen signifikant risk för låg Apgarpoäng eller perinatal död för barnen andra förlossningen, jämfört med barn till kvinnor med en tidigare vaginal förlossning. Av resultaten drog vi slutsatsen att det snarast var de underliggande faktorerna, inte det förra kejsarsnittet i sig, som bidrog till de beskrivna överriskerna för ohälsa hos nyfödda barn till kvinnor som tidigare varit med om ett kejsarsnitt. I analyserna tog vi även hänsyn till kvinnornas karakteristika såsom längd, BMI, och rökvanor, samt till barnens bjudning och födelsevikt.

I **studie II** ville vi undersöka vilka kvinnor som hade god chans att kunna föda vaginalt efter ett tidigare kejsarsnitt, och vilka som hade stor risk att förlösas med ett akut kejsarsnitt. Risken för akut kejsarsnitt vid planerad vaginal förlossning ökade med kvinnans ålder, BMI och om hon var rökare. Risken minskade däremot med kvinnans längd. Kvinnor med ett tidigare kejsarsnitt hade ökad risk för akut kejsarsnitt vid planerad vaginal förlossning jämfört med förstföderskor med planerad vaginal förlossning. Riskökningen varierade dock kraftigt beroende på indikationen för det första kejsarsnittet. Det var främst kvinnor som genomgick ett första kejsarsnitt utan någon medicinsk indikation (vanligen kejsarsnitt på kvinnans önskan), kvinnor med diabetes och kvinnor som genomgick ett första kejsarsnitt på grund av förlossningskomplikationer eller stort barn som löpte hög risk för att deras andra förlossning skulle avslutas med ett akut kejsarsnitt.

I **studie III** ville vi utreda hur valet av förlossningssätt efter ett tidigare kejsarsnitt kunde påverka barnens hälsa (låg Apgarpoäng). Vi ville framförallt undersöka om man kunde ringa in vilka kvinnor som borde få ett planerat kejsarsnitt andra förlossningen. Bland barn till kvinnor som haft ett första kejsarsnitt på grund av misstänkt stort barn, överburenhet eller någon tillstötande förlossningskomplikation fanns en mer än fördubblad risk för låg Apgarpoäng vid en planerad vaginal förlossning än vid ett planerat kejsarsnitt. Resultaten visade alltså att det, med barnens hälsa i åtanke, finns anledning att ta hänsyn till de förhållanden som rådde vid det första kejsarsnittet i planeringen av förlossningssättet för nästa förlossning. Samtidigt får man beakta att den absoluta risken för låg Apgarpoäng fortfarande är låg, och väga samman riskerna i en samlad klinisk bedömning.

I **studie IV** utvärderade vi en välkänd metod för att förutsäga lyckandefrekvens vid planerad vaginal förlossning efter kejsarsnitt, utvecklad av Grobman och medarbetare i USA (2007). Eftersom originalmodellen inte visade sig direkt tillämplig för svenska förhållanden modifierade vi den stegvis. Den slutliga, nya modellen inkluderade originalvariablerna mors ålder, BMI, tidigare vaginal förlossning och tidigare vaginal förlossning efter kejsarsnitt. Vi lade till variablerna mors längd, indikation för det första kejsarsnittet enligt vår hierarki samt andel planerade respektive akuta kejsarsnitt efter tidigare kejsarsnitt vid den aktuella förlossningskliniken. Vi fick på så sätt fram en svensk modell med mycket god förmåga att förutsäga lyckad planerad vaginal förlossning efter kejsarsnitt – dvs. en planerad vaginal förlossning som också avslutas vaginalt.

Om man utgår från våra studieresultat skulle ett upprepat kejsarsnitt andra förlossningen vara det säkraste för en hel del kvinnor. Fortfarande skulle dock, precis som rutinen är i Sverige idag, majoriteten av kvinnorna kunna rekommenderas en planerad vaginal förlossning.

Under tiden för **studierna I-III**, 1987-2007, planerades ett upprepat kejsarsnitt för cirka 30% av kvinnorna efter ett kejsarsnitt. För 70% av kvinnorna planerades följaktligen en vaginal förlossning. För cirka 70% av dessa kvinnor avslutades också förlossningen vaginalt. Totalt avslutades alltså hälften av förlossningarna efter ett kejsarsnitt vaginalt och hälften med kejsarsnitt. Vi skulle behöva bli bättre på att välja ut rätt kvinnor till rätt förlossningssätt efter kejsarsnitt. Här skulle resultaten från **studierna I-IV**, kombinerade med resultat från tidigare studier, kunna komma till stor nytta.

Även om man tar hänsyn till vad som framkommit i vetenskapliga studier, kommer man bara en bit på vägen i frågor som rör förlossningssätt efter tidigare kejsarsnitt. Icke-medicinska faktorer väger tungt. Den blivande mammans och hennes partners önskemål, vilka råd barnmorskan och förlossningsläkaren ger under graviditeten och inte minst rådande samhällstrender spelar stor roll.

Jag önskar att resultaten av våra fyra studier skall kunna användas pragmatiskt, som ett av flera hjälpmedel i de viktiga samtal som förs med kvinnan och hennes partner efter en kejsarsnittsförlossning. Min förhoppning är att man, genom att ta hänsyn till studieresultaten, skall planera rätt förlossningssätt för rätt kvinna. Därmed skulle man kunna minska andelen akuta kejsarsnitt och andelen barn med låg Apgarpoäng eller perinatal död vid förlossningen efter ett kejsarsnitt.

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Paper I

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Apgar score and perinatal death after one previous caesarean delivery

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Objective To assess the impact of the indication for a previous caesarean section on the outcome of a subsequent delivery.

Design Population-based cohort study.

Setting Sweden.

Population Women with two deliveries between 1987 and 2007 identified using the Swedish Medical Birth Registry.

Methods The outcome of 69 133 pregnancies after one caesarean section was compared with the outcome of 487 610 pregnancies following one vaginal delivery. The indication for the first caesarean section was estimated using a new hierarchical system based on information from birth records.

Main outcome measures Perinatal death, low Apgar score (less than seven at 5 minutes).

Results Infants of women with one previous caesarean section were at increased risk of low Apgar score compared with infants of women with one previous vaginal delivery (OR, 2.0; 95% CI, 1.9–2.1). The risk estimate was reduced when adjustment for maternal and fetal/infant characteristics was made (OR, 1.6; 95% CI, 1.5–1.8). The corresponding crude and adjusted odds ratios for perinatal death were 1.6 (95% CI, 1.4–1.7) and 1.1 (95% CI, 1.0–1.2), respectively. The infant outcome of the delivery after one caesarean section was mainly dependent on the indication for the first-delivery caesarean section and, when no medical indication was present, no increase in risk was detected.

Conclusions Infants of women with one previous caesarean section were at increased risk of low Apgar score and/or perinatal death compared with infants of women with one previous vaginal delivery. The results suggest that medical conditions, not the previous caesarean section *per se*, contributed to the increase in risk.

Keywords Apgar score, caesarean section, perinatal death, Sweden.

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Introduction

The increasing frequency of deliveries by caesarean section (CS) has generated animated discussions regarding the benefits and harm of caesarean versus vaginal delivery. Studies have focused on the possible complications, immediate and delayed, that could threaten the mother and her infant in association with a CS.[1,2] More recently, these investigations have been followed by several studies on delivery following one CS.[3–9] It is obvious that every surgical intervention yields tissue damage. When a CS is performed in the first delivery, risks will be increased in the second pregnancy and delivery for, for example, rupture of the uterus, placenta praevia or placenta accreta. Furthermore, it has been suggested by Smith *et al.*[3] that the risk of unexplained stillbirth in the pregnancy following a first CS is augmented. However, evidence remains to be explored regarding the infant outcome of delivery after one CS.

Sweden has, in concordance with many other countries, experienced an increase in the caesarean delivery rate over the years, from just below 11% in 1990 to 18% in 2007.[6,10] Factors contributing to the increase in frequency include increased maternal age at the first delivery, increasing body mass index (BMI) among pregnant women, increasing proportion of elective CS for breech presentation, CS being performed on maternal request, and a trend among obstetricians to intervene more liberally.[11] Furthermore, every CS performed increases the likelihood for a CS to be performed without any strict medical indication in the subsequent pregnancy.[6,10] Thus, the perinatal outcome of

the delivery following a CS is bound to be a matter of great importance in countries with increasing caesarean delivery rates.

Many complications appearing in the first pregnancy or birth are likely to recur in subsequent pregnancies.[7] Therefore, it is essential that the underlying medical conditions be controlled for in an analysis of the perinatal outcome of the second delivery. By using retrospective data from the Swedish Medical Birth Registry, the present study focused on the outcome of deliveries preceded by a CS, compared with the outcome of deliveries preceded by a vaginal delivery, in terms of low Apgar score and perinatal death. To our knowledge, the influence of the indication for a CS to be performed at the first delivery on the perinatal outcome of the second delivery has not been investigated thoroughly.[6,8] In the present study, a new hierarchical system using objective medical information was developed, and the main condition/indication for the first-delivery CS was assessed. For each indication group, the infant outcome of the subsequent pregnancy was compared with the infant outcome of the pregnancy following one vaginal delivery.

Methods

Women having experienced their first two deliveries between 1987 and 2007 were identified using the Swedish Medical Birth Registry,[10] containing medical information on nearly all deliveries in Sweden (coverage about 99%).[12] The obstetric history of each woman could be tracked using the unique Swedish personal identification number. Medical diagnoses were reported by the International Classification of Diseases (ICD) codes (1987–1997, ICD-9; 1997 onwards, ICD-10). In Sweden, standardised record forms are used at all antenatal clinics, all delivery units and all paediatric examinations of newborn infants. Copies of these forms are sent to the National Board of Health where they are computerised and linked with Statistics Sweden to obtain, among other things, information on the date of death.

Nearly all pregnant women receive free antenatal care. At the first visit to the antenatal clinic, each woman is interviewed by her midwife, and maternal height, weight and smoking habits are recorded. Thus, information regarding maternal BMI and smoking used in the present study refers to the first trimester of pregnancy. All women are offered a free routine ultrasound examination before 20 weeks of pregnancy, in order to estimate the expected date of delivery, and to check for multiple pregnancy and fetal anomalies.

Infants weighing less than two standard deviations (SDs) below the expected birth weight according to gestational age[13] were defined as small for gestational age (SGA), whereas infants weighing more than two SDs above the expected birth weight were regarded as large for gestational age (LGA).

In the Swedish Medical Birth Registry, several diagnoses were recorded for the majority of the CSs registered. To avoid each CS appearing in more than one group, a hierarchical system was created. In this system, efforts were made to classify according to the underlying conditions, instead of focusing on conditions appearing during labour (e.g. fetal distress), in an attempt to diminish the subjective impact of diagnoses being recorded after delivery. Information on the medical indication for caesarean delivery was based on the reported ICD codes and well-defined medical information obtainable from registry data (see Table 1).

The first three groups consisted of mutually exclusive, well-defined conditions (multiple gestation, preterm singleton birth and term singleton breech birth). The fourth group consisted of major congenital malformations. The following main group comprised all term singleton cephalic births without major malformations. This group was further divided using medical diagnoses combined with information on birth weight and gestational length. Groups 5 and 6 (rupture of the uterus and placenta praevia, respectively) consisted of severe conditions/diagnoses that were imperative indications for CS. Furthermore, the diagnosis 'rupture of the uterus' was of special interest for further planned studies, and was highlighted in the hierarchy instead of being combined with other severe labour complications. Groups 7–10 (diabetes or gestational diabetes, SGA, LGA or macrosomia, and pregnancy ≥42 weeks, respectively) were designed to show the impact of fetal growth independent of maternal diabetes, and the impact of prolonged pregnancy independent of fetal size, respectively. Group 11 (severe conditions complicating pregnancy/severe maternal disease) consisted of conditions for which CS is likely to be considered. Group 12 consisted of conditions arising during labour and delivery. Group 13 consisted of cases of fetal distress or fetal death, not explained by any of the conditions mentioned above. Group 14 comprised CSs for which medical information was available, but reflected mild conditions which were seldom judged to be true indications for CS. It also included ICD codes for 'other or not specified indication for caesarean section'. Group 15 consisted of CSs for which the underlying indication could not be assessed – the records lacked ICD codes, and did not provide any other medical information implying an increased risk for CS.

The perinatal outcome of women who had experienced one previous CS was compared with that of women with one previous vaginal delivery. The outcomes studied were an Apgar score below seven at 5 minutes and perinatal death (stillbirth from 28 completed weeks of pregnancy or early neonatal death at 0–6 days).

Table 1. Hierarchical classification of indications/conditions

Classification group	Specification
1. Multiple gestation	Information on type of gestation available in Swedish Medical Birth Registry
2. Preterm birth, <37 weeks	Information on gestational length available in Swedish Medical Birth Registry
3. Breech or other malpresentation	Information on fetal presentation available in Swedish Medical Birth Registry
4. Congenital malformations	Significant congenital malformations*
5. Rupture of uterus	ICD9: 665.0–1; ICD10: O71.0–1
6. Placenta praevia	ICD9: 641.0–1; ICD10: O44.0–1
7. Diabetes mellitus or gestational diabetes	ICD9: 648.0, 648.8; ICD10: O24.0–4, O24.9
8. Small for gestational age/poor fetal growth	<−2 birth weight SD scores according to a Swedish ultrasound-based weight curve[13] or ICD9: 656.5; ICD10: O36.5
9. Large for gestational age/excessive fetal growth	>+2 birth weight SD scores according to a Swedish ultrasound-based weight curve[13] or birth weight > 4500 g or ICD9: 656.6; ICD10: O36.6
10. Prolonged pregnancy ≥42 weeks	Information on gestational length available in Swedish Medical Birth Registry
11. Severe conditions complicating pregnancy/severe maternal disease	Premature separation of placenta (ICD9: 641.2; ICD10: O45) Antepartum haemorrhage (ICD9: 641.3, 641.8–9; ICD10: O46) Pre-existing hypertension, severe pre-eclampsia, eclampsia (ICD9: 642.0–2, 642.5–7; ICD10: O10, O11, O14.0–1, O15.0–1, O15.9) Maternal renal, cardiovascular or thyroid disease (ICD9: 646.2, 648.1, 648.5–6; ICD10: E00–E07, I00–I99) Maternal care for known or suspected fetal abnormality/damage, including fetal–maternal haemorrhage, iso-immunisation and fetal hydrops (ICD9: 655, 656.0–2; ICD10: O35, O36.0–2) Polyhydramniosis or oligohydramniosis (ICD9: 657, 658.0; ICD10: O40, O41.0)
12. Complications during labour and delivery	Dystocia, prolonged labour or suspected cephalopelvic disproportion (ICD9: 653, 660, 661, 662; ICD10: O33, O62, O63.0–1, O63.9, O66, O75.0, O75.8–9) Abnormalities of pelvic organs (ICD: 654.0–1, 654.3–9; ICD10: O34.0–1, O34.4–9, O65) Problems associated with amniotic cavity and membranes (ICD9: 658.1–2, 658.4–9, 659.2, 663.5; ICD10: O41.1–9, O69.4, O75.2, O75.6) Problems associated with induction of labour (ICD9: 658.3, 659.0–1; ICD10: O61.0–1, O75.5) Prolapse of cord, or cord entanglement with compression (ICD9: 663.0–2; ICD10: O69.0–2) Other complications of obstetric surgery and procedures (ICD10: O75.4)
13. Fetal distress or fetal death unexplained by conditions mentioned above	Fetal distress, fetal hypoxia, or birth asphyxia (ICD9: 656.3, 768; ICD10: O36.3, O68, P21.0) Intrauterine death (ICD9: 656.4, ICD10: O36.4)
14. Caesarean section (CS) without medical indication mentioned above, or mild conditions not classified elsewhere	Other or not specified indication for CS (ICD9: 659.8–9, 669.7; ICD10: O82.8) Mild hypertension or mild pre-eclampsia (ICD9: 642.3–4, 642.9; ICD10: O13, O14.9) Oedema or excessive weight gain in pregnancy, without mention of hypertension (ICD9: 646.1; ICD10: O12) Peripheral neuritis, liver disorders, anaemia, bone and joint disorders of pregnancy (ICD9: 646.4, 646.7, 648.2, 648.7; ICD10: O99.0) Mild infections in pregnancy or labour (ICD9: 646.5–6; ICD10: O23, O75.3) Other conditions predominantly related to pregnancy (ICD9: 646.8–9, 656.7–9, 663.3–4, 663.6, 663.8–9; ICD10: O26, O36.8–9, O69.3, O69.5, O69.8–9)
15. No diagnosis available	Neither abnormal conditions, nor indications for CS could be detected using Swedish Medical Birth Registry data

ICD, International Classification of Diseases; SD, standard deviation.
*Exceptions: congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus, single umbilical artery and preauricular tags.

Statistical methods

Statistical analyses were performed using Gauss (Gauss™; Aptec Systems Inc., Maple Valley, WA, USA; www.aptech.com). Odds ratios with 95% confidence intervals for low Apgar score or perinatal death were obtained using logistic regression analyses. For each indication, for the first caesarean delivery, the odd ratios for low Apgar score and perinatal death were computed using three different models: (a) crude odds ratio; (b) odds ratio adjusted for year of birth and maternal characteristics; and (c) odds ratio adjusted for year of birth, maternal characteristics and fetal/infant parameters. Year of birth was entered as a linear continuous variable in the logistic models. The 'maternal characteristics' were maternal age (continuous), smoking

(semi-continuous; 1, no; 2, 1–9 cigarettes per day; 3, 10 or more cigarettes per day), height (cm, continuous) and BMI (kg/m^2, continuous). The 'fetal/infant' parameters were restricted to 'hard facts', not dependent on delivery mode or hospital level: multiple birth (yes/no), preterm birth <37 weeks (yes/no), breech presentation (yes/no) and birth weight SD scores, according to a Swedish ultrasound-based growth curve[13] (continuous, second grade model). Adjustment was performed for all possible confounders valid for the second delivery.

Nonparametric tests (Mann–Whitney *U*-test) were performed in order to compare the background characteristics of the study groups (women with one previous CS versus one previous vaginal delivery).

Results

The demographic characteristics of women with one previous delivery are shown in Table 2. Compared with women with one previous vaginal delivery, women who had experienced one previous CS were more likely to give birth towards the end of the study period ($P < 0.001$), to be older ($P < 0.001$), to be shorter ($P < 0.001$), to have a higher BMI ($P < 0.001$) and to be delivered preterm (before 37 completed weeks of pregnancy) ($P < 0.001$). No apparent differences between the groups could be detected with regard to the interval between deliveries, maternal country of birth or maternal smoking. The infants of women who had experienced one previous CS were more likely to weigh less than two SDs below the expected birth weight according to gestational age ($P < 0.001$), or more than two SDs over the expected weight ($P < 0.001$), when compared with infants of women with one previous vaginal delivery. The gender distribution was similar between the groups.

In the cohort of women who gave birth at least twice (in the current study, only data from the first two deliveries were included), the overall CS rate at the first delivery was 12.4%. The CS rate was 47.6% among women with multiple births, 29.0% among women with singleton preterm births, 69.0% in term singleton breech presentation and 9.2% in deliveries with term singleton cephalic presentation. The corresponding CS rate in the second delivery was 11.2% overall, 40.6% in multiple births, 34.0% in preterm singletons, 69.1% in term singleton breech presentation and 8.8% in term singleton cephalic presentation.

The overall caesarean delivery rate among women having undergone a CS at their first delivery was 50% (increasing gradually from 46% in 1987–1992 to 55% in 2003–2007). The corresponding percentage among women with one previous vaginal delivery was 5.7%.

In Table 3, the delivery indications/conditions of all women experiencing a CS at their first delivery are shown.

Table 2. Demographic characteristics. All women with at least two deliveries in Sweden between 1987 and 2007; data from the first and second deliveries as specified

	Caesarean first delivery	Vaginal first delivery
	N* = 69 133 (%)	***N* = 487 610 (%)***
Year of delivery (second delivery)		
1987–1992	12 494 (18.1)	108 278 (22.2)
1993–1997	19 236 (27.8)	152 178 (31.2)
1998–2002	19 461 (28.2)	128 477 (26.3)
2003–2007	17 942 (26.0)	98 677 (20.2)
Maternal age (years) (second delivery)		
<20	188 (0.3)	2389 (0.5)
20–24	6846 (9.9)	72 785 (14.9)
25–29	22 243 (32.2)	191 180 (39.2)
30–34	26 081 (37.7)	163 253 (33.5)
35–39	11 761 (17.0)	51 538 (10.6)
≥40	2014 (2.9)	6465 (1.3)
Interval between deliveries (years)		
0–1	18 910 (27.4)	136 009 (27.9)
2–5	45 171 (65.3)	315 928 (64.8)
6–9	4213 (6.1)	28 860 (5.9)
≥10	839 (1.2)	6813 (1.4)
Maternal country of birth		
Sweden	60 399 (87.4)	428 585 (87.9)
Other	8734 (12.6)	59 025 (12.1)
Maternal height (cm) (second pregnancy)**		
Not known	8397 (12.1)	61 284 (12.6)
<155	3195 (5.3)	9191 (2.2)
155–164	25 185 (41.5)	142 315 (33.4)
165–174	28 328 (46.6)	232 278 (54.5)
≥175	4028 (6.6)	42 542 (10.0)
Maternal body mass index (BMI) (kg/m^2) (second pregnancy)**		
Not known	17 931 (25.9)	135 313 (27.8)
<20	4128 (8.1)	40 833 (11.6)
20–24	25 931 (50.6)	200 701 (57.0)
25–29	14 120 (27.6)	81 046 (23.0)
30–34	4909 (9.6)	22 012 (6.2)
35–39	1567 (3.1)	5896 (1.7)
≥40	547 (1.1)	1809 (0.5)
Maternal smoking (second pregnancy)**		
Not known	4436 (6.4)	26 897 (5.5)
No	56 521 (87.4)	399 432 (86.7)
<10 cigarettes per day	5504 (8.5)	41 002 (8.9)
≥10	2672 (4.1)	20 279 (4.4)
Infant gender (second delivery)		
Male	35 692 (51.6)	251 000 (51.5)
Female	33 441 (48.4)	236 610 (48.5)
Gestational length (completed weeks) (second delivery)		
<28	183 (0.3)	756 (0.2)
28–31	483 (0.7)	1786 (0.4)
32–36	3586 (5.2)	16 950 (3.5)
37–41	60 220 (87.1)	439 674 (90.2)
≥42	4661 (6.7)	28 444 (5.8)

Table 2. (*Continued*)

	Caesarean first delivery	Vaginal first delivery
	N* = 69 133 (%)	***N* = 487 610 (%)***
Birth weight deviation* (second delivery)**		
<−3SD	289 (0.4)	1020 (0.2)
−3 to −2.1SD	1600 (2.3)	6049 (1.2)
−2 to −1.1SD	7849 (11.4)	46 933 (9.6)
−1 to −0.1SD	21 048 (30.4)	158 033 (32.4)
0–1SD	22 961 (33.2)	178 004 (36.5)
1.1–2SD	10 839 (15.7)	76 158 (15.6)
2.1–3SD	3256 (4.7)	16 691 (3.4)
>3SD	1291 (1.9)	4722 (1.0)

*Percentages based on records with obtainable information.
**The pregnancy leading to the second delivery.
***Deviation in standard deviation (SD) from the expected birth weight according to Swedish growth standard curves.[13]

The recurrence of indications/conditions in the second delivery, whether vaginal or by CS, is then shown, first using all the diagnoses given for each woman at the second delivery and, second, for comparison, using the hierarchical system. In order to highlight the degree of recurrence, Table 3 also shows the crude odds ratios for second delivery conditions/diagnoses among women with the same conditions/diagnoses in both deliveries versus women having a different condition/diagnosis at the second delivery from the indication for the first-delivery CS.

For the hierarchical system, as well as for the nonhierarchical system, strong associations between the conditions/diagnoses of the first and second delivery were found. In addition to the self-evident correlation for diabetes at the first and second delivery, strong associations with odds ratios above 2.0 (according to both the hierarchical and nonhierarchical systems) were found for all conditions/diagnoses, except for congenital malformations. The strongest correlation between first and second delivery conditions/diagnoses was seen for LGA/excessive fetal growth, SGA/intrauterine growth restriction (IUGR) and placenta praevia.

Table 4 shows the risk of an Apgar score below seven at 5 minutes among second-delivery infants of women having experienced one previous CS or one previous vaginal delivery. Infants of women having undergone a CS at the first delivery (regardless of indication) were twice as likely to have a low Apgar score as were infants of women who had experienced a previous vaginal delivery. When the odds ratio was adjusted for year of birth and maternal characteristics (age, BMI, height and smoking habits), the odds ratio for a low Apgar score – previous CS versus previous vaginal delivery – was marginally lowered. The corresponding odds ratio was further reduced, but still strongly significant, when also adjusting for fetal/infant parameters (multiple birth, preterm birth, breech presentation and birth weight SD score).

When investigating the relationship between previous CS and risk of perinatal death in the second pregnancy/delivery (Table 5), it was apparent that the adjustment for maternal as well as fetal/infant characteristics had a substantial influence on the estimated odds ratio. The crude odds ratio for perinatal death, regardless of the indication for the first CS, was highly statistically significant, and was only marginally reduced after adjustment for maternal characteristics. When fetal/infant variables were also adjusted for, no statistically significant association could be detected between previous caesarean delivery and perinatal death in the second pregnancy/delivery.

Tables 4 and 5 focus on the perinatal outcome by indication for the first-delivery CS. It is evident that, among infants of women having experienced a CS at their first delivery, the outcome of the second pregnancy/delivery varied considerably with the indication for the first-delivery CS. For low Apgar score, as well as for perinatal death, the *P* value for homogeneity of the odd ratios across indications strata was $<10^{-6}$. Crude odd ratios for low Apgar score at the second delivery were increased significantly for all classes of medical indications for the previous CS, except for placenta praevia. In contrast, infants of women who had a previous CS without mention of indication, or a previous CS indicated by minor complications, did not have a significantly increased risk for low Apgar score, compared with infants of women who had experienced a previous vaginal delivery. Adjustment for the year of birth and maternal characteristics only marginally lowered the odds ratios for low Apgar score among the respective conditions/indications.

The impact of adjustment for fetal/infant parameters varied among the subgroups of indications for the previous CS; for example, the odds ratio for a low Apgar score at the second delivery was not increased significantly for infants of women who had a previous CS before 37 weeks of pregnancy when fetal parameters were considered. Among women who had diabetes as the indication for the first-delivery CS (but no indication for CS higher in the hierarchy), the odds ratio for low Apgar score at the second delivery was substantially lowered, but still significant when fetal parameters were adjusted for. For the other classes of indications, adjustment for fetal/infant parameters only marginally altered the magnitude of the association between a previous CS and the risk of a low Apgar score at the subsequent delivery.

For several indication classes, a significant association between delivery mode at the first delivery and perinatal

Table 3. Delivery indications/conditions of all women experiencing a caesarean section (CS) at their first delivery, and recurrence of indications/conditions in the second delivery, whether vaginal or by CS, first using all the conditions/diagnoses of each woman at the second delivery, and then using the hierarchical system

	Proportion with this CS indication at 1st delivery and repeated condition/diagnosis at 2nd delivery	Proportion without this CS indication at 1st delivery but with this condition/diagnosis at 2nd delivery	OR for recurrence: this indication at 1st delivery versus another indication at 1st delivery
	n/N (%)	*n/N* (%)	OR (95% CI)
Nonhierarchical system			
Multiple gestation	46/1674 (2.7)	932/67 459 (1.4)	2.0 (1.5–2.7)
Preterm birth, <37 weeks	1826/10 494 (17.4)	2426/58 639 (4.1)	4.9 (4.6–5.2)
Breech or other malpresentation, ≥37 weeks	1225/13 962 (8.8)	2104/55 171 (3.8)	2.4 (2.3–2.6)
Congenital malformations	106/2592 (4.1)	1611/66 541 (2.4)	1.7 (1.4–2.1)
Rupture of uterus	0/33 (0.0)	552/69 100 (0.8)	–
Placenta praevia	22/742 (3.0)	298/68 391 (0.4)	7.0 (4.8–10.2)
Diabetes mellitus/gestational diabetes	944/1373 (68.8)	907/67 760 (1.3)	162.2 (152.0–173.1)
SGA*/suspected IUGR	1016/7006 (14.5)	1328/62 127 (2.1)	7.8 (7.2–8.4)
LGA**/suspected LGA/>4500 g	1760/4606 (38.2)	3991/64 527 (6.2)	9.4 (8.9–9.9)
Prolonged pregnancy, ≥42 weeks	1285/8871 (14.5)	3376/60 262 (5.6)	2.9 (2.7–3.0)
Severe pregnancy complications/severe maternal disease	612/6420 (9.5)	1240/62 713 (2.0)	5.2 (4.8–5.7)
Complications during labour/delivery	15 691/38 500 (40.8)	7754/30 633 (25.3)	2.0 (2.0–2.1)
Fetal distress/death	2966/18 858 (15.7)	4787/50 275 (9.5)	1.8 (1.7–1.9)
Hierarchical system			
Multiple gestation	46/1674 (2.7)	932/67 459 (1.4)	2.0 (1.5–2.7)
Preterm birth, <37 weeks	1677/9584 (17.5)	2212/59 549 (3.7)	5.5 (5.2–5.8)
Breech or other malpresentation, ≥37 weeks	834/11 408 (7.3)	1730/57 725 (3.0)	2.6 (2.4–2.8)
Congenital malformations	50/1412 (3.5)	1320/67 721 (1.9)	1.8 (1.4–2.4)
Rupture of uterus	0/24 (0.0)	513/69 109 (0.7)	–
Placenta praevia	4/325 (1.2)	125/68 808 (0.2)	6.8 (2.9–16.2)
Diabetes mellitus/gestational diabetes	468/896 (52.2)	934/68 237 (1.4)	78.8 (72.7–85.3)
SGA/suspected IUGR	269/2871 (9.4)	1103/66 262 (1.7)	6.1 (5.4–6.9)
LGA/suspected LGA/>4500 g	1116/3474 (32.1)	3514/65 659 (5.4)	8.4 (7.8–9.0)
Prolonged pregnancy, ≥42 weeks	819/6658 (12.3)	2862/62 475 (4.6)	2.9 (2.7–3.2)
Severe pregnancy complications/severe maternal disease	91/1805 (5.0)	806/67 328 (1.2)	4.4 (3.6–5.4)
Complications during labour/delivery	5803/17 516 (33.1)	9363/51 617 (18.1)	2.2 (2.2–2.3)
Fetal distress/death	506/5701 (8.9)	2681/63 432 (4.2)	2.2 (2.0–2.4)

CI, confidence interval; IUGR, intrauterine growth restriction; OR, odds ratio; SD, standard deviation.
*Small for gestational age: birth weight below the mean – 2SDs of the Swedish growth standard curve.[13]
**Large for gestational age: birth weight above the mean + 2SDs of the Swedish growth standard curve.[13]

death at the second delivery was found. For women without a strict medical indication for CS performed at the first delivery, no association between this first delivery by CS and perinatal death at the second delivery could be detected.

Discussion

An infant being born at the second delivery to a woman having had a CS performed at the first delivery was found to have an increased risk for a low Apgar score and/or perinatal death compared with an infant born to a woman having experienced a previous vaginal delivery. The significance of a low Apgar score has been reported by others.[14] In order to examine to what extent the indication for the first CS affected the perinatal outcome of the second delivery, a hierarchical system of caesarean delivery indications and pregnancy/delivery conditions was developed. Following this hierarchy, it was revealed that, for most classes of indications, there was a substantial risk for recurrence in the second pregnancy/delivery. It became evident that the conditions/indications present at the first delivery must be considered when evaluating the impact of the mode of the first delivery on the perinatal outcome of the second delivery.

Table 4. Association between the mode of the first delivery and Apgar score below seven at 5 minutes at the second delivery. Crude and adjusted odds ratios as specified

	Apgar score at second delivery		Crude OR	Adjusted OR*	Adjusted OR**
	<7 *n* (%)	≥7	OR (95% CI)	OR (95% CI)	OR (95% CI)
First delivery vaginal (reference)	3938 (0.8)	483 672	1.0	1.0	1.0
First delivery by caesarean section (CS), regardless of indication	1108 (1.6)	68 025	2.0 (1.9–2.1)	1.8 (1.7–1.9)	1.6 (1.5–1.8)
Conditions/diagnoses, first-delivery CS (hierarchical order)					
Multiple gestation	25 (1.5)	1649	1.9 (1.3–2.8)	1.7 (1.1–2.5)	1.6 (1.0–2.3)
Preterm birth, <37 weeks	179 (1.9)	9405	2.3 (2.0–2.7)	2.2 (1.9–2.5)	1.1 (0.9–1.3)
Breech or other malpresentation, ≥37 weeks	172 (1.5)	11 236	1.9 (1.6–2.2)	1.8 (1.5–2.1)	1.7 (1.4–1.9)
Congenital malformations	28 (2.0)	1384	2.5 (1.7–3.6)	2.2 (1.5–3.1)	2.2 (1.5–3.2)
Term singleton cephalic					
All	704 (1.6)	44 351	2.0 (1.8–2.1)	1.7 (1.6–1.9)	1.8 (1.6–1.9)
Rupture of uterus	0 (0.0)	24	0 (NS)	–	–
Placenta praevia	3 (0.9)	322	1.2 (0.4–3.6)	1.1 (0.4–3.3)	0.9 (0.3–3.0)
Diabetes mellitus/gestational diabetes	21 (2.3)	875	2.9 (1.9–4.5)	2.4 (1.5–3.6)	1.8 (1.1–2.8)
SGA/suspected IUGR	64 (2.2)	2807	2.8 (2.2–3.6)	2.4 (1.9–3.1)	2.1 (1.6–2.7)
LGA/suspected LGA/>4500 g	44 (1.3)	3430	1.6 (1.2–2.1)	1.4 (1.0–1.9)	1.6 (1.2–2.2)
Prolonged pregnancy, ≥42 weeks	100 (1.5)	6558	1.9 (1.5–2.3)	1.6 (1.3–2.0)	1.9 (1.5–2.3)
Severe pregnancy complications/severe maternal disease	41 (2.3)	1764	2.9 (2.1–3.9)	2.6 (1.9–3.6)	2.4 (1.8–3.4)
Complications during labour/delivery	260 (1.5)	17 256	1.9 (1.6–2.1)	1.6 (1.4–1.8)	1.7 (1.5–1.9)
Fetal distress/death unexplained by conditions mentioned above	107 (1.9)	5594	2.3 (1.9–2.9)	2.1 (1.7–2.6)	2.2 (1.8–2.6)
CS without indication mentioned above, or mild conditions not classified elsewhere	34 (1.0)	3519	1.2 (0.8–1.7)	1.1 (0.8–1.5)	1.0 (0.7–1.5)
No diagnosis available	30 (1.3)	2202	1.7 (1.2–2.4)	1.6 (1.1–2.3)	1.5 (1.0–2.1)

CI, confidence interval; IUGR, intrauterine growth restriction; LGA, large for gestational age; OR, odds ratio; SGA, small for gestational age.
*Adjusted for year of birth and maternal characteristics (maternal age, smoking, height and body mass index), second delivery.
**Adjusted for year of birth, maternal characteristics and fetal/infant parameters (multiple birth, preterm birth, breech presentation and birth weight standard deviation score), second delivery.

The results suggested that the indication for the first caesarean delivery had a major influence on the risk for a low Apgar score or perinatal death at the second delivery. Compared with the perinatal outcome following the first vaginal delivery, the risk for a low Apgar score was more than doubled at deliveries following a first CS with a main indication of congenital malformations, suspect intrauterine growth restriction, severe pregnancy complications or unexplained fetal distress during labour. When the first delivery by CS was performed without a strict medical indication, no increased risk for a low Apgar score or perinatal death at the second delivery was found. For both outcomes, the risk estimates were close to unity. However, in spite of the large numbers, the upper confidence limits for the risk estimates for low Apgar scores and perinatal death were 1.5 and 1.4, respectively. Thus, even if unlikely, a weak association between a previous CS and an adverse outcome in the subsequent delivery could not be ruled out.

In addition to the impact of the indication for the first-delivery CS on the outcome of the second delivery, it was shown that maternal baseline characteristics had a substantial influence on the risk estimates. In concordance with the report by Taylor *et al.*,[9] women having undergone a previous caesarean delivery were older than women having experienced a previous vaginal delivery. In the present study, women having experienced a CS at their first delivery also had a higher BMI and smoked more than women giving birth vaginally.

Fetal/infant parameters were also found to have an important influence on the outcome of the second delivery. After adjusting the outcome results for year of birth and maternal characteristics, the risk was still increased for both low Apgar score and perinatal death. However, after

Table 5. Association between the mode of the first delivery and perinatal death at the second delivery. Crude and adjusted odds ratios as specified

	Perinatal outcome at second delivery		Crude OR	Adjusted OR*	Adjusted OR**
	Perinatal death, *n* (%)	Survival, 7 days	OR (95% CI)	OR (95% CI)	OR (95% CI)
First delivery vaginal (reference)	1965 (0.4)	485 645	1.0 (–)	1.0 (–)	1.0 (–)
First delivery by caesarean section (CS), regardless of indication	433 (0.6)	68 700	1.6 (1.4–1.7)	1.5 (1.3–1.6)	1.1 (0.97–1.2)
Conditions/diagnoses, first-delivery CS (hierarchical order)					
Multiple gestation	15 (0.9)	1659	2.2 (1.3–3.7)	2.1 (1.3–3.5)	1.9 (1.1–3.3)
Preterm birth, <37 weeks	110 (1.1)	9474	2.9 (2.4–3.5)	2.7 (2.2–3.3)	0.7 (0.6–0.9)
Breech or other malpresentation, ≥37 weeks	55 (0.5)	11 353	1.2 (0.9–1.6)	1.2 (0.9–1.6)	1.1 (0.8–1.4)
Congenital malformations	11 (0.8)	1401	1.9 (1.1–3.5)	1.8 (0.97–3.2)	1.8 (0.95–3.3)
Term singleton cephalic					
All	242 (0.5)	44 813	1.3 (1.2–1.5)	1.2 (1.1–1.4)	1.3 (1.1–1.5)
Rupture of uterus	0 (0.0)	24	0 (NS)	–	–
Placenta praevia	1 (0.3)	324	0.8 (0.1–5.4)	0.7 (0.1–5.3)	0.7 (0.1–5.1)
Diabetes mellitus/gestational diabetes	8 (0.9)	888	2.2 (1.1–4.5)	2.0 (0.97–3.9)	1.6 (0.8–3.4)
SGA/suspected IUGR	35 (1.2)	2836	3.1 (2.2–4.3)	2.7 (2.0–3.9)	1.4 (1.0–2.1)
LGA/suspected LGA/>4500 g	12 (0.3)	3462	0.9 (0.5–1.5)	0.8 (0.4–1.4)	1.4 (0.8–2.5)
Prolonged pregnancy, ≥42 weeks	34 (0.5)	6624	1.3 (0.9–1.8)	1.2 (0.8–1.6)	1.6 (1.1–2.3)
Severe pregnancy complications/severe maternal disease	14 (0.8)	1791	1.9 (1.1–3.3)	1.7 (1.0–3.0)***	1.4 (0.8–2.4)
Complications during labour/delivery	76 (0.4)	17 440	1.1 (0.9–1.4)	1.0 (0.8–1.3)	1.2 (0.9–1.5)
Fetal distress/death unexplained by conditions mentioned above	34 (0.6)	5667	1.5 (1.1–2.1)	1.4 (1.0–2.0) NS	1.4 (1.0–1.9) NS
CS without indication mentioned above, or mild conditions not classified elsewhere	14 (0.4)	3539	1.0 (0.6–1.7)	1.0 (0.6–1.7)	0.8 (0.5–1.4)
No diagnosis available	14 (0.6)	2218	1.6 (0.9–2.6)	1.4 (0.8–2.3)	1.3 (0.7–2.2)

CI, confidence interval; IUGR, intrauterine growth restriction; LGA, large for gestational age; NS, not significant; OR, odds ratio; SGA, small for gestational age.

*Adjusted for year of birth and maternal characteristics (maternal age, smoking, height and body mass index), second delivery.

**Adjusted for year of birth, maternal characteristics and fetal/infant parameters (multiple birth, preterm birth, breech presentation and birth weight standard deviation score), second delivery.

***$P < 0.05$.

adjusting for certain fetal/infant parameters (multiple birth, preterm birth, breech presentation and birth weight SD score), only the risk for an Apgar score below seven at 5 minutes remained significantly increased.

Despite the growing rates of caesarean delivery, there are few published studies that have focused on the perinatal outcome of deliveries following one previous CS. The available literature does not address all of the subgroups analysed in this study. Richter *et al.*[5] found a similar odds ratio for perinatal death at the second delivery (CS at first delivery versus vaginal first delivery; 1.39 from German data 1993–1995), but they did not study the outcome by indication for the CS at first delivery. After having performed a systematic review of the safety of vaginal birth after caesarean delivery, Guise *et al.*[15] stressed that the identification of high-risk and low-risk groups of women and settings for morbidity remains a key research priority.

In concordance with the results of the present study, Hemminki *et al.*[7] and Daltveit *et al.*[6] found that women with a previous caesarean delivery were more likely than women with a previous vaginal delivery to suffer from miscellaneous complications during their next pregnancy. Hemminki *et al.*[7] reported poorer infant outcome of deliveries after the first CS, even when women with persistent problems were excluded, and concluded that their findings were unlikely to be explained entirely by the CS indications. No results were presented of the perinatal outcome with regard to the indication for the previous caesarean delivery. Daltveit *et al.*[6] concluded that an increased risk of complications after a caesarean delivery might be caused by

CS itself, but could also be a result of confounding by indication. The authors stated that, in analyses of outcomes after previous CS, indications for the first CS should be considered. However, no such results were reported.

A limitation of this study was that the conditions and diagnoses presented in the medical records were lacking for some patients. Different methods of diagnosis and different indications might have been used in different regions of Sweden. We tried to diminish this problem by using as many conditions as possible determined by 'hard facts' in the medical records, rather than using the diagnoses/indications given by obstetricians. The hierarchical system was constructed to support this strategy, with the 'self-given' conditions higher up the hierarchy.

Another fact that should be kept in mind is that, in the present study, we chose to compare women with one previous CS with women who had experienced one vaginal delivery. This design might have disfavoured the results of the CS group, as a previous vaginal delivery is well known to facilitate a second delivery.[16,17] Furthermore, the putative harmful maternal effects of a first delivery by CS were not evaluated in this study.

A strength of this study is that it is population based, involving a large number of women/births from the whole country. As a low Apgar score and, especially, perinatal death are rare events in an industrialised country, large amounts of data are required to detect possible differences. As every delivery unit in Sweden sends its statistical data to the Swedish Medical Birth Registry, it was possible to analyse the results from a mixture of obstetric departments.

In the present study, the CS rate after a first delivery by CS was about 50%. Similar rates have been reported from Finland[7] and Norway,[6] but substantially different results have been reported recently from the USA, where the frequency of repeated CS was nearly 90% in 2006.[15]

The determination of the influence of the mode of the second delivery on the perinatal outcome was beyond the scope of the current study. Probably, the choice of delivery mode at the second delivery has a substantial influence on the perinatal outcome. In future studies of deliveries following one previous CS, we intend to identify women belonging to high- and low-risk groups, considering the indication for the first-delivery CS. Our results could then be used to develop evidence-based guidelines for obstetricians counselling women and their partners about the preferable mode for the second delivery. This should, in turn, provide a possibility to influence the caesarean delivery rates[17,18] without jeopardising infant health.

Conclusion

Infants of women having experienced one previous caesarean delivery had almost double the risk for a low Apgar score and perinatal death compared with infants of women with one previous vaginal delivery. The association could be explained, to some extent, by the underlying maternal and fetal baseline characteristics, as adjustments for these factors considerably lowered the overall risk estimates. However, the magnitude of the association varied significantly with the indication for the first-delivery CS. The results suggest that medical conditions, not the previous CS *per se*, contributed to the increase in risk.

Disclosure of interests

There are no interests to disclose.

Contribution to authorship

MCW performed the analyses and contributed to the writing of the manuscript, PE contributed to the writing of the manuscript, KM contributed to the writing of the manuscript and KK performed the analyses and contributed to the writing of the manuscript.

Details of ethics approval

This study was approved by the Regional Research Ethics Committee in Lund, 16 August 2007, reference number 309/2007.

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Journal club

Discussion points

1. Background: Describe the rate of caesarean section (CS) in your area/country and compare with worldwide rates and trends over time.

   Discuss the evidence from previous studies[1,2] with regard to outcome in subsequent pregnancies for women with previous CS. How is this current study different in its stated aims and approach?
2. Methods: Discuss the value of the Apgar score as a proxy marker for short- and long-term neonatal outcome; discuss its advantages and disadvantages compared with perinatal death.

   Describe the hierarchical system used by the authors to classify the indication for CS and comment on its usefulness and validity.
3. Results and implications: Describe the odds of recurrence for the maternal and fetal conditions recorded in this study.

   Discuss whether, according to this study, CS *per se* or the indication for CS is a more important risk factor for adverse outcome in subsequent pregnancies, with reference to both statistical significance and effect size.

   Will the findings of this study change the way you counsel women who are about to have their first CS, depending on the indication? Will they change your plan of care for women having a second pregnancy after a CS? ■

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Paper II

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Indications for First Caesarean and Delivery Mode in Subsequent Trial of Labour

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Abstract

Background: A previous caesarean delivery is no longer an indication *per se* for a subsequent, planned caesarean. We performed this study to identify women suitable for trial of labour after caesarean (TOLAC), investigating the association between the indication for the first caesarean and the risk of unplanned caesarean in the second pregnancy.

Methods: We identified women with their first two pregnancies registered in the Swedish Medical Birth Registry 1992–2007. The indications for caesarean in the first pregnancy were determined using a previously published hierarchical system. For each indication group, the rate of caesarean among women with a first caesarean (n = 59 643) and a TOLAC in the second pregnancy was compared with that of primiparae (parity 0) (n = 354 053).

Results: The TOLAC rate was 69.5%. Among women with TOLAC, the uterine rupture rate was 1.1%. The success rate of TOLAC varied substantially based on the indication for the first caesarean (range 51–83%). Multiple births, breech presentation, and placenta praevia in the first pregnancy were associated with marginally increased odds of unplanned caesarean in the second pregnancy when compared with primiparae (adjusted OR 1.27 [95% CI 1.10, 1.48], 1.42 [1.34, 1.51], and 1.65 [1.17, 2.31]; OR, odds ratio; CI, confidence interval). The indications based on complications during labour/delivery, macrosomia, and maternal diabetes, were associated with substantially increased OR: 3.87 [3.70, 4.06], 4.15 [3.74, 4.61], and 4.62 [3.79, 5.63], respectively.

Conclusions: Considering the indications for caesarean in the first pregnancy before recommending a TOLAC or a planned caesarean in the second pregnancy may help to lower the rate of unplanned caesarean deliveries.

Keywords: *Caesarean indication, delivery mode, trial of labour.*

A previous caesarean delivery is no longer considered an indication *per se* to perform a planned caesarean in the second pregnancy. However, it is well known that women with a first caesarean delivery are at increased likelihood of a repeat caesarean. No widely used rules exist for when to recommend a trial of labour after caesarean (TOLAC), or a planned caesarean in the second pregnancy.[1] This despite the fact that identifying the woman having an adequate chance to give birth vaginally in a TOLAC remains an obstetrical challenge.

Several investigators have reported data on outcomes related to vaginal birth or unplanned caesarean delivery in women with a TOLAC.[2–8] Only a few of these studies[2–4] have considered indications for the first caesarean delivery in broad categories (four to six indication groups), and all were based on small numbers (300–2200) of women.

When is it appropriate to recommend a TOLAC? According to Eden *et al.*,[9] a scoring model is needed that incorporates known antepartum factors and can be adjusted for current obstetrical factors and labour patterns if induction or augmentation is needed. In the present study, we focused on antepartum factors. Indications for the first caesarean performed were estimated using a previously published hierarchical classification system.[10] If the indication for the first caesarean delivery could be shown to predict a part of the success or failure rate in a subsequent TOLAC, it should be of substantial help in identifying groups of women having a fair chance of giving birth vaginally after a first caesarean delivery.

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Methods

Women having experienced their first two deliveries between 1992 and 2007 were identified using the Swedish Medical Birth Registry (MBR), comprising medical information on nearly all deliveries in Sweden.[11] Standardised record forms are used in all antenatal clinics and all delivery units in Sweden. Copies of these forms are sent to the National Board of Health where they are computerised. The obstetrical history of each woman could be tracked using the unique Swedish personal identification number. Medical diagnoses were reported by International Classification of Diseases (ICD) codes (1992–96: ICD-9; 1997 ICD-9 or ICD-10, 1998 onwards: ICD-10).

Women residing in Sweden receive free antenatal care. At the first antenatal visit, each woman is interviewed by the midwife, and maternal height, weight, and smoking habits are recorded. Thus, the available information regarding maternal body mass index (BMI) and smoking refers to the first trimester of pregnancy. All women are offered a routine ultrasound examination before 20 weeks of pregnancy for dating.

Delivery mode was defined as 'planned caesarean delivery' when a caesarean was reported to have been performed before the start of uterine contractions. All other caesareans were defined as 'unplanned'. Time for the start of contractions, birthweight and gestational age were studied using data from neonatal standard record forms. Infants weighing less than two standard deviations below expected birthweight according to gestational age were defined as small for gestational age (SGA), whereas infants weighing more than two standard deviations above the expected birthweight were regarded as large for gestational age (LGA).[12]

In the MBR, multiple diagnoses were recorded for the majority of the first caesarean deliveries. To avoid each caesarean to appear in more than one group, a hierarchical classification system was used.[10] The aim of this system was to classify the conditions/indications (hereinafter called 'indications') according to underlying factors rather than focusing on indications appearing during labour. In this way, the impact of post hoc diagnoses recorded after the delivery was minimised. Information on the medical indication for caesarean delivery was based on the reported ICD-codes and medical information obtainable from registry data. A simplified version of the hierarchical system is shown in Table 1.

Table 1. Hierarchical classification of indications for the first caesarean delivery

1	Multiple gestation
2	Preterm birth, GA <37 weeks
3	Breech or other malpresentation, GA ≥37 weeks
4	Significant congenital malformations[a]
5	Rupture of uterus
6	Placenta praevia
7	Diabetes mellitus/gestational diabetes
8	SGA[b]/suspected IUGR
9	LGA[c]/suspected LGA/BW >4500 g
10	Prolonged pregnancy, GA ≥42 weeks
11	Severe pregnancy complications/severe maternal disease
12	Complications during labour/delivery
13	Fetal distress/death unexplained by indications listed above
14	No indication listed above/mild conditions not classified elsewhere
15	No diagnosis available

[a]Exceptions: Congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus, single umbilical artery, and preauricular tags.
[b]<–2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
[c]>+2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
BW, birthweight; GA, gestational age; IUGR, intrauterine growth restriction; LGA, large for gestational age; SD-scores, standard-deviation scores; SGA, small for gestational age.

The main analyses focused on women for whom planned caesarean was not performed in the second delivery. For each indication for the first caesarean delivery, the odds for second caesarean delivery among women with TOLAC were compared with the corresponding odds among primiparae (parity 0).

Statistical analyses were performed using Gauss [Gauss™, Aptec Systems Inc., Maple Valley, WA, USA (http://www.aptech.com)]. Odds ratios (OR) with 95% confidence intervals (CI) for unplanned caesarean delivery among women with TOLAC compared with the reference group were obtained using logistic regression analyses.

For each indication for the first caesarean delivery, the OR for unplanned caesarean were computed using three different models: (1) unadjusted OR; (2) OR adjusted for year of birth and maternal characteristics; and (3) OR adjusted for year of birth, maternal characteristics, and fetal/infant parameters. Year of birth was entered as a linear, continuous variable in

Table 2. Demographic characteristics at the first delivery (primiparae) or at the second delivery (women with a caesarean first delivery)

	Primiparae (parity 0)		Caesarean first delivery		
Characteristics	*n* = 354 053	(%)[a]	*n* = 59 643	(%)[a]	*P*-value[b]
Year of delivery					<0.001
1992–1997	194 231	(54.9)	2201	(38.2)	
1998–2002	122 907	(34.7)	19 177	(32.2)	
2003–2007	36 915	(10.4)	17 665	(29.6)	
Maternal age (years)					<0.001
<20	15 217	(4.3)	129	(0.2)	
20–24	96 721	(27.3)	5123	(8.6)	
25–29	149 149	(42.1)	18 434	(30.9)	
30–34	77 707	(21.9)	23 321	(39.1)	
35–39	14 488	(4.1)	10 773	(18.1)	
40+	771	(0.2)	1863	(3.1)	
Maternal country of birth					0.03[c]
Sweden	307 030	(86.7)	51 917	(87.0)	
Other	47 023	(13.3)	7726	(13.0)	
Maternal height (cm)					<0.001
Not known	29 367		4863		
<155	8412	(2.6)	2844	(5.2)	
155–164	111 084	(34.2)	22 675	(41.4)	
165–174	173 013	(53.3)	25 585	(46.7)	
175+	32 177	(9.9)	3676	(6.7)	
Maternal body mass index, BMI (kg/m^2)					<0.001
Not known	55 573		9195		
<20	40 231	(13.5)	4070	(8.1)	
20–24	180 327	(60.4)	25 548	(50.6)	
25–29	59 056	(19.8)	13 919	(27.6)	
30–34	14 426	(4.8)	4838	(9.6)	
35–39	3560	(1.2)	1539	(3.1)	
40+	880	(0.3)	534	(1.1)	
Maternal smoking					<0.001
Not known	18 427		3742		
No	294 201	(87.7)	49 621	(88.8)	
<10 cigarettes/day	30 011	(8.9)	4320	(7.7)	
10+ cigarettes/day	11 414	(3.4)	1960	(3.5)	
Infant gender					0.37[c]
Male	182 517	(51.6)	30 805	(51.6)	
Female	171 536	(48.4)	28 838	(48.4)	
Gestational age at delivery (weeks)					<0.001
<28	765	(0.2)	152	(0.3)	
28–31	1966	(0.6)	393	(0.7)	
32–36	17 954	(5.1)	2829	(4.7)	
37–41	302 860	(85.5)	52 158	(87.5)	
42+	30 508	(8.6)	4111	(6.9)	
Birthweight SD-scores[d]					<0.001
<–3	1577	(0.4)	227	(0.4)	
–3––2.1	9304	(2.6)	1275	(2.1)	
–2––1.1	56031	(15.8)	6418	(10.8)	
–1––0.1	135 377	(38.2)	17 914	(30.0)	
0–1	109 018	(30.8)	20 033	(33.6)	
1.1–2	34 316	(9.7)	9650	(16.2)	
2.1–3	5899	(1.7)	2948	(4.9)	
>3	2531	(0.7)	1178	(2.0)	

[a]Percentages based on records with obtainable information.
[b]*P*-values for difference between groups obtained by Mann–Whitney *U*-tests, or (when specified) by chi-squared tests.
[c]Based on chi-squared test.
[d]Deviation in SD from the expected birthweight according to Swedish growth standard curves.[12]
SD-scores, standard-deviation scores.

the models. The maternal characteristics included: maternal age (continuous variable), smoking (non-smoker, 1–9 cigarettes smoked per day, 10 or more cigarettes smoked per day), height (cm), and BMI (kg/m^2). The fetal and infant parameters included: preterm birth <37 weeks, breech presentation, and birthweight standard-deviation scores (SD-scores).[12] Adjustments were performed for all possible confounders valid for the index delivery [the first delivery of the primiparae (parity 0), or the second delivery of the women with one previous caesarean].

Results

The demographic characteristics of the two groups studied – primiparae, and women with one previous caesarean delivery – are shown in Table 2. Compared with primiparae, women who had experienced one previous caesarean delivery were more likely to have given birth towards the end of the study period, they were older, shorter, and had a higher BMI.

Table 3 shows the delivery mode in the two study groups. Among women with one previous caesarean delivery, the TOLAC rate was 69.5%. The rate of uterine rupture among women that underwent a TOLAC was 1.1%. The rate of vaginal birth after caesarean was 49.6%, yielding a success rate in TOLAC of 71.4%. The overall caesarean delivery rate was just above 50%, compared with 13% in primiparae (OR 6.72, [95% CI 6.60, 6.85]).

During the study period, the frequency of trial of labour after one previous caesarean in Sweden decreased from 55% in 1992–95 to 45% 2004–07 (*P*-value for trend <0.001).

As shown in Table 4, the caesarean delivery rates among women with one previous caesarean differed substantially by the indication for the first caesarean delivery. The rate of planned caesarean delivery was highest among women with previous rupture of the uterus or with previous caesarean without any medical indication.

Table 5 shows the association between maternal characteristics and delivery mode in trial of labour, without considering the obstetrical history. There was a positive and linear association between unplanned caesarean and year of birth, maternal smoking, and increasing maternal age and BMI. For maternal height, a negative association with unplanned caesarean in trial of labour was shown.

Table 6 shows the rates of vaginal deliveries and of caesareans in trial of labour based on obstetrical history. The table also shows the OR for caesarean delivery among women with TOLAC, compared with primiparae, by indication for the first caesarean delivery. The unadjusted OR for unplanned caesarean delivery in women with one previous caesarean was 3.86 [95% CI 3.77, 3.96], regardless the indication for the first caesarean. The OR decreased significantly when adjustments were made for maternal factors, but additional adjustments for fetal factors did not further lower the estimate. The lowest OR were found for women with a previous caesarean delivery because of multiple gestations or term breech deliveries. The strongest associations between failed trial of labour and previous caesarean delivery were found for diabetes/gestational diabetes and LGA/macrosomia (birthweight >4500 g).

Comment

Unplanned caesarean delivery has repeatedly been shown to have negative consequences for both the mother and the infant.[13–15] It would be of considerable clinical importance to be able to predict and thereby

Table 3. Mode of delivery at first delivery (primiparae) or at second delivery (women with a caesarean first delivery)

	Vaginal, non-instrumental delivery		Planned caesarean delivery		Unplanned caesarean delivery		Forceps/ vacuum extraction		Total
	n	(%)	*n*	(%)	*n*	(%)	*n*	%	*n*
Primiparae (parity 0)	264 149	(74.6)	14 539	(4.1)	31 957	(9.0)	43 408	(12.3)	354 053
Caesarean first delivery	24 275	(40.7)	18 193	(30.5)	11 867	(19.9)	5308	(8.9)	59 643

Singleton pregnancies, Sweden 1992–2007.

Table 4. Mode of delivery for women with one previous caesarean, by indication for the first caesarean delivery

	Vaginal, non-instrumental delivery		Planned caesarean delivery		Unplanned caesarean delivery		Forceps/ vacuum extraction		Total
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*
Indication for the first caesarean delivery (hierarchical order)									
Multiple gestation	912	(60.9)	202	(13.5)	220	(14.7)	164	(10.9)	1498
Preterm birth, GA <37 weeks	4087	(50.8)	1902	(23.6)	1374	(17.1)	683	(8.5)	8046
Breech or other malpresentation, GA ≥37 weeks	6038	(55.5)	2224	(20.4)	1545	(14.2)	1069	(9.8)	10876
Significant congenital malformations[a]	440	(37.4)	393	(33.4)	247	(21.0)	95	(8.1)	1175
Rupture of uterus	4	(18.2)	15	(68.2)	3	(13.6)	0	(0.0)	22
Placenta praevia	145	(53.3)	47	(17.3)	46	(16.9)	34	(12.5)	272
Diabetes mellitus/gestational diabetes	160	(19.7)	372	(45.7)	217	(26.7)	65	(8.0)	814
SGA[b]/suspected IUGR	1079	(46.2)	610	(26.1)	436	(18.7)	210	(9.0)	2335
LGA[c]/suspected LGA/BW >4500 g	768	(24.9)	1404	(45.5)	701	(22.7)	215	(7.0)	3088
Prolonged pregnancy, GA ≥42 weeks	1820	(31.0)	2030	(34.6)	1427	(24.3)	596	(10.1)	5873
Severe pregnancy complications/severe maternal disease	715	(47.7)	373	(24.9)	279	(18.6)	131	(8.7)	1498
Complications during labour/delivery	4406	(30.0)	5364	(36.5)	3669	(25.0)	1262	(8.6)	14 701
Fetal distress/death unexplained by indications listed above	2155	(43.9)	1209	(24.6)	1010	(20.6)	532	(10.8)	4906
No indication listed above/mild conditions not classified elsewhere	843	(26.8)	1694	(53.9)	464	(14.8)	139	(4.4)	3140
No diagnosis available	703	(50.3)	354	(25.3)	229	(16.4)	113	(8.1)	1399
Women with caesarean first delivery, total	24 275	(40.7)	18 193	(30.5)	11 867	(19.9)	5308	(8.9)	59 643

[a]Exceptions: Congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus, single umbilical artery, and preauricular tags.
[b]<–2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
[c]>+2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
Singleton pregnancies, Sweden 1992–2007.
BW, birthweight; GA, gestational age; IUGR, intrauterine growth restriction; LGA, large for gestational age; SD-scores, standard-deviation scores; SGA, small for gestational age.

Table 5. Delivery mode in trial of labour among primiparae (parity 0), or women with one previous caesarean

	Delivery mode (%)		Odds Ratio (OR) for unplanned caesarean delivery			
			Unadjusted		Adjusted[a]	
	Vaginal	Caesarean	OR	[95% CI]	OR	[95% CI]
Year of birth						
1992–1997	95.7	4.3	–		–	
1998–2002	94.4	5.6	–		–	
2003–2007	94.0	6.0	–		–	
Continuous variable			1.06	[1.05, 1.06]	1.02	[1.01, 1.02]
Maternal age (years)						
<20	97.4	2.6	0.48	[0.45, 0.52]	0.52	[0.48, 0.56]
20–24	96.6	3.4	0.70	[0.68, 0.72]	0.72	[0.70, 0.74]
25–29	95.8	4.2	1.00	Reference	1.00	Reference
30–34	94.5	5.5	1.51	[1.48, 1.55]	1.34	[1.30, 1.37]
35–39	92.1	7.9	2.51	[2.42, 2.60]	1.84	[1.77, 1.92]
≥40	89.1	10.9	4.54	[4.09, 5.04]	2.52	[2.26, 2.82]
Maternal height (cm)						
<155	87.4	12.6	3.18	[3.03, 3.34]	3.18	[3.02, 3.34]
155–164	93.4	6.6	1.60	[1.56, 1.63]	1.58	[1.55, 1.62]
165–174	95.8	4.2	1.00	Reference	1.00	Reference
≥175	97.1	2.9	0.69	[0.66, 0.73]	0.70	[0.67, 0.73]
Maternal BMI (kg/m^2)						
<20	96.8	3.2	0.69	[0.66, 0.72]	0.76	[0.73, 0.79]
20–24	95.8	4.2	1.00	Reference	1.00	Reference
25–29	93.7	6.3	1.60	[1.56, 1.64]	1.45	[1.41, 1.48]
30–34	91.3	8.7	2.27	[2.18, 2.36]	1.98	[1.89, 2.06]
≥35	88.9	11.1	2.84	[2.66, 3.02]	2.34	[2.18, 2.50]
Maternal smoking						
No	95.0	5.0	1.00	Reference	1.00	Reference
Yes	94.6	5.4	0.93	[0.90, 0.96]	1.06	[1.02, 1.09]

[a]Model including previous caesarean delivery and all variables listed in the table.
BMI, body mass index; CI, confidence interval.

avoid most of the unplanned caesarean deliveries. By using the indications for the first caesarean delivery, we aimed to identify groups of women having a high chance of giving birth vaginally after one caesarean delivery, and groups of women who should rather be recommended a planned second caesarean delivery.

Prediction models have already been described and validated – a model described by Grobman *et al*.[8] and subsequently validated by Costantine *et al*.[16] is available on the internet for use in clinical practice. We have shown that considering the indication for the first caesarean could add valuable information, which could increase the predictability for success in TOLAC.

We found that the rate of women recommended, or requesting, a planned second caesarean delivery was 30%. The rate varied by indication for the first caesarean delivery, from 14% for multiple gestations to 54% for caesarean without medical indication. (We presume the 68% planned caesarean rate after a first caesarean for rupture of the uterus to be heavily underestimated.) Despite this high rate of planned second caesarean delivery, women who had experienced a first caesarean delivery were also found to have a high rate of unplanned second caesarean delivery (20%) as compared with primiparae (9.0%).

When the delivery mode in TOLAC was studied, 71% of the women achieved a vaginal delivery. Landon *et al*.[14] and Kwee *et al*.[7] reported 73% and 76% success for TOLAC, respectively. However, when comparing the results from the quoted articles with the current results, it should be noted that their studies included women with previous vaginal deliveries.

Table 6. Vaginal delivery rates and unplanned caesarean rates in trial of labour, and odds ratios for caesarean delivery in trial of labour among women with one previous caesarean delivery compared with primiparae, by indication for the first caesarean delivery

			Caesarean first delivery vs. primiparae					
			Unadjusted		Adjusted for maternal factors[a]		Adjusted for fetal and maternal factors[b]	
	Vaginal delivery rate in TOL (%)	Unplanned caesarean rate in TOL (%)	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
Primiparae (parity 0)	90.6	9.4	Reference		Reference		Reference	
Caesarean first delivery, total	71.4	28.6	3.86	[3.77, 3.96]	2.59	[2.53, 2.66]	2.62	[2.55, 2.69]
Indication for the first caesarean delivery (hierarchical order)								
Multiple gestation	83.0	17.0	1.97	[1.70, 2.28]	1.26	[1.09, 1.46]	1.27	[1.10, 1.48]
Preterm birth, GA <37 weeks	77.6	22.4	2.77	[2.61, 2.95]	1.95	[1.83, 2.08]	1.88	[1.76, 2.00]
Breech or other malpresentation, GA ≥37 weeks	82.1	17.9	2.09	[1.98, 2.21]	1.45	[1.37, 1.54]	1.42	[1.34, 1.51]
Significant congenital malformations[c]	68.4	31.6	4.44	[3.82, 5.17]	2.82	[2.41, 3.30]	2.92	[2.49, 3.43]
Placenta praevia	79.6	20.4	2.47	[1.79, 3.42]	1.60	[1.14, 2.22]	1.65	[1.17, 2.31]
Diabetes mellitus/gestational diabetes	50.9	49.1	9.28	[7.70, 11.19]	5.19	[4.27, 6.31]	4.62	[3.79, 5.63]
SGA[d]/suspected IUGR	74.7	25.3	3.26	[2.92, 3.63]	2.07	[1.85, 2.32]	2.37	[2.11, 2.66]
LGA[e]/suspected LGA/BW >4500 g	58.4	41.6	6.86	[6.22, 7.57]	4.55	[4.11, 5.04]	4.15	[3.74, 4.61]
Prolonged pregnancy, GA ≥42 weeks	62.9	37.1	5.68	[5.32, 6.08]	3.46	[3.22, 3.71]	3.66	[3.41, 3.92]
Severe pregnancy complications/severe maternal disease	75.2	24.8	3.18	[2.77, 3.64]	2.28	[1.98, 2.62]	2.38	[2.06, 2.74]
Complications during labour/ delivery	60.7	39.3	6.23	[5.97, 6.50]	3.82	[3.64, 3.99]	3.87	[3.70, 4.06]
Fetal distress/death unexplained by indications listed above	72.7	27.3	3.62	[3.36, 3.89]	2.36	[2.19, 2.55]	2.49	[2.30, 2.69]
No indication listed above/mild conditions not classified elsewhere	67.9	32.1	6.79	[5.78, 7.98]	5.32	[4.50, 6.30]	5.48	[4.62, 6.51]
No diagnosis available	78.1	21.9	3.26	[2.79, 3.82]	2.10	[1.79, 2.48]	2.14	[1.81, 2.52]

[a]Adjusted for year of birth and maternal characteristics (maternal age, smoking, height and body mass index).
[b]Adjusted for year of birth, maternal characteristics, and fetal/infant parameters (preterm birth, breech presentation, and birthweight SD-score).
[c]Exceptions: Congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus, single umbilical artery, and preauricular tags.
[d]<–2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
[e]>+2 birthweight SD-scores according to a Swedish ultrasound-based weight curve.[12]
Singleton pregnancies, Sweden 1992–2007.
BW, birthweight; CI, confidence interval; GA, gestational age; IUGR, intrauterine growth restriction; LGA, large for gestational age; OR, odds ratio; SGA, small for gestational age; TOL, trial of labour.

In our study, the unplanned caesarean rate varied substantially by the indication for the first caesarean delivery, 17–18% after multiple gestations or breech presentation, which is consistent with earlier reports,[2,6] to 49% after diabetes mellitus/gestational diabetes. We studied the indication for the first caesarean delivery using the hierarchical system described in the Methods section, and we found that women who had experienced a first caesarean delivery with the indications LGA or macrosomia (diabetes excluded), prolonged pregnancy or complications during labour/delivery all had an unplanned caesarean rate of about 40%. Thus, the results showed that the selection of groups of women eligible for a TOLAC was probably not optimal during the study period.

The group of women without medical indication for the first caesarean delivery, presumably having a caesarean performed on 'maternal request', had a high rate of planned second caesarean delivery (54%). Women in this group also had a high rate of unplanned caesarean (32%) in TOLAC, which possibly reflects their low motivation to accomplish a vaginal delivery.

In the current study, we compared the second delivery mode of women with a first caesarean delivery with the delivery mode of primiparae. We did not compare with women who had experienced a first vaginal delivery, as a first delivery *per vaginam* is well known to facilitate the second delivery.[5,6] However, depending on the stage of labour in which the first caesarean was performed, the subsequent delivery will, to varying degree, resemble the delivery of a woman who has given birth vaginally.[17] In the present study, the cervical dilatation at the first caesarean delivery was unknown.

A limitation of our study might be the difficulty to validate the indications used for the first caesarean delivery. Various ways of classification are used in various centres or clinics. By using the hierarchical classification of indications, we minimised the impact of variations in diagnostic code assignment.

The Swedish caesarean delivery rate was increasing during the study period, from 11% in 1990 (2 years prior to the start of the study) to 18% in 2007.[10] The TOLAC rate was 50% during the whole study period. For comparison, in the US, the caesarean delivery rate was 32% and the TOLAC rate 8% in 2007.[18] The relatively low caesarean rate and high TOLAC rate in Sweden probably reflect a tradition, an endeavour to keep caesarean rates low. However, as the primary caesarean rate did rise during the study period, complications in the subsequent delivery, especially rupture of the uterus, became apparent and the TOLAC rate somewhat decreased.

Despite the relatively low primary caesarean delivery rate in Sweden during the studied period, and the high rate of TOLAC, this study still has a high generalisability. The absolute rate of the outcome, failed TOLAC, would vary between countries, but comparisons with a control group of primiparae would yield similar OR.

The data used in the current study were retrospectively collected. However, the study was large and population-based and the information regarding indications for the first caesarean delivery was registered prospectively, years before the second delivery. Thus, the classification used could not be biased by the outcome of the second delivery.

Based on the results of the present study, it might be possible to lower the rate of unplanned second caesarean delivery by considering the indication for the first caesarean delivery before recommending a TOLAC or a planned second caesarean. In addition to the data presented here, we intend to analyse the outcome of deliveries after one caesarean, by planned delivery mode, in terms of Apgar score. By providing new evidence, these and other studies can be expected to facilitate counselling women and their partners about the suitable delivery mode after one caesarean.

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Paper III

AOGS
ACTA Obstetricia et Gynecologica Scandinavica

AOGS MAIN RESEARCH ARTICLE

Neonatal outcome after trial of labor or elective cesarean section in relation to the indication for the previous cesarean delivery

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Key words
Apgar score, cesarean section indication, elective repeat cesarean, perinatal outcome, trial of labor

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Conflicts of interest
The authors have stated explicitly that there are no conflicts of interests in connection with this article.

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Abstract

Objective. To compare the neonatal outcome after a trial of labor (TOL) with that after an elective cesarean section (CS) following one previous cesarean delivery, considering the indication for the first CS. *Design.* Population-based cohort study. *Setting.* Sweden. *Population.* Women with their first two deliveries between 1992 and 2007 registered in the Swedish Medical Birth Registry. *Methods.* The risk of low Apgar score (<7 at 5 min) after a TOL was compared with that after an elective CS among 407 159 singletons of women with one previous vaginal delivery and 59 643 singletons of women with one previous CS. The indication for the first-delivery CS was estimated using a hierarchical system. For each indication group, the odds ratio and 95% CI for low Apgar score, TOL vs. elective CS, was computed. *Main outcome measure.* Low Apgar score. *Results.* The overall risk of low Apgar score was increased in the TOL group (adjusted odds ratio 1.8, 95% CI 1.5–2.1), but the estimate differed substantially by the indication for the first CS (p-value for homogeneity = 0.0001). There was a high risk for low Apgar score after TOL and first CS indication "complications during labor/delivery" (adjusted odds ratio 2.4, 95% CI 1.7–3.4), but low risk with TOL and first CS "without medical indication" (adjusted odds ratio 0.7, 95% CI 0.2–2.1). *Conclusion.* Neonatal outcome might be improved by considering the indication for the first CS when choosing between an elective CS or a TOL for the second delivery.

Abbreviations: BMI, body mass index; CS, cesarean section; ERC, elective repeat cesarean; ICD, International Classification of Diseases; LGA, large-for-gestational age; OR, odds ratio; SGA, small-for-gestational age; TOL, trial of labor.

Introduction

The cesarean section (CS) rate has increased in most developed countries since the 1980s (1). Consequently, the number of deliveries after one CS is rising. In the pregnancy after one CS, the woman and her partner need professional advice about the safest and most convenient delivery mode – a trial of labor (TOL) after cesarean or an elective repeat cesarean (ERC).

Key Message

The risk of Apgar score <7 at 5 min in the delivery after one cesarean section might be lowered by considering the indication for the first cesarean section when choosing between a trial of labor and an elective repeat cesarean in the second pregnancy.

It is known that many of the possible indications for, or conditions at, a first CS do recur in the following pregnancy or delivery (2–4). In our first article (5), we studied the recurrence rate of the indications for the first CS, both in a nonhierarchic system and in our new hierarchic system of indications. All the studied indications show a statistically significant recurrence – from 3% for placenta praevia to 70% in diabetes mellitus/gestational diabetes. In the same study, we show considerable variations in neonatal outcome in terms of Apgar score <7 at 5 min (low Apgar score) and perinatal death by the various indications for the first-delivery CS, irrespective of the second-delivery mode.

In a subsequent article (6), focusing on delivery mode in the pregnancy following a first CS, we show that considering the indications for CS in the first pregnancy before recommending a TOL or an ERC in the second pregnancy might help to lower the rate of unplanned/emergency cesarean deliveries (failed TOL).

Several studies (6–9), scoring models (10–17), and validations of scoring models (18–20) have been published, focusing on factors associated with failure or success in a TOL after cesarean delivery and primarily aiming to lower the frequency of second-delivery CS – especially unplanned CS in failed TOL. In the present paper we aimed to reach further by combining former knowledge with new results. We wanted to facilitate the choice of second-delivery mode by comparing the neonatal outcome after a TOL with that after an ERC, considering the indication for the first CS.

Material and methods

The Swedish Medical Birth Registry (18) was used to identify women with their two first deliveries between 1992 and 2007. The registry is based on medical record forms, and medical diagnoses were reported by International Classification of Diseases (ICD) codes (1992–1997: ICD-9; 1997 onwards: ICD-10). The previous delivery mode, and medical history, of each woman was tracked as described in a previous publication (5). The Regional Research Ethics Committee in Lund, Sweden, approved the study on 16 August 2007 (reference number 309/2007).

When a CS was reported to have been performed before the start of contractions, the delivery mode was defined as planned, i.e. elective cesarean. Small-for-gestational age (SGA) was defined as birthweight less than two standard deviations below expected birthweight according to gestational age (21), and large-for-gestational age (LGA) was defined as birthweight more than two standard deviations above the expected weight for gestational age.

Information on the indication for the first cesarean delivery was based on the reported ICD codes and other medical information obtainable from registry data. For most CS deliveries, multiple diagnoses were recorded. To yield mutually exclusive indication groups, a previously published hierarchical system was used (5). The CS indication groups were classified according to underlying factors rather than to conditions appearing during labor. In this way, the impact of post hoc diagnoses recorded after the delivery was reduced.

Statistical analysis

Odds ratios (OR) with 95% CI for Apgar score at 5 min in infants of women with TOL vs. planned CS were obtained using logistic regression analyses. If the number of cases with low Apgar score within a specific indication group was sufficient (the number of independent variables did not exceed 1/10 of the number of cases), the ORs for low Apgar score were computed using three different models: (i) unadjusted OR, (ii) OR adjusted for year of birth and maternal characteristics, and (iii) OR adjusted for year of birth, maternal characteristics, and fetal/infant parameters.

All maternal/infant parameters considered were valid for the index (second) delivery. Year of birth was entered as a linear, continuous variable in the logistic models. The maternal characteristics considered were: maternal age (continuous variable), smoking (discrete variable, 1, no; 2, one to nine cigarettes per day; 3, 10 or more cigarettes per day), height (cm, continuous), and body mass index (BMI, kg/m^2, continuous). The fetal/infant parameters considered were: gestational age <37 weeks (yes/no), breech presentation (yes/no), and birthweight standard deviation scores, according to a Swedish ultrasound-based growth curve (21) (continuous, second grade model).

In the total material, all of the mentioned variables were associated (at the 0.2 level) with low Apgar score (most p-values were significantly lower than 0.2). When the numbers within the indication-groups were sufficient, we included all of the mentioned possible confounders regardless of the level of significance. Among the 15 indication groups for the first CS, seven suffered from low numbers, and the estimates could not be adjusted as explained above. Instead, forward and backward selection procedures were performed to choose the best restricted adjustment models. The final models included variables with p-values below 0.2. The final models are specified in the Results section.

Tests of homogeneity of the OR across indication groups were based on weighted sums of the squared deviations of the stratum specific log-OR from their weighted means (22).

Non-parametric tests (Mann–Whitney *U*-test) for continuous data and chi-squared tests for categorical data were performed to compare the background characteristics of the study groups (women with one previous CS vs. women with one previous vaginal delivery, or the groups defined by planned delivery mode within the previous CS group).

All statistical analyses were performed using GAUSS (Gauss™; Aptec Systems Inc., Maple Valley, WA, USA; http://www.aptech.com).

Results

Table 1 shows the maternal and fetal characteristics by planned second-delivery mode in women with a first vaginal delivery and a first CS, respectively. Compared with women with one previous vaginal delivery, women with one previous CS gave birth more towards the end of the study period, they were older, shorter, and had a higher BMI (all *p*-values <0.001). Infants of women with one previous CS rather than those of women with one prior vaginal delivery were likely to be born before 37 weeks or after 42 completed weeks of pregnancy, to be SGA, or to be LGA (all *p*-values <0.001).

Among women with one previous CS, women in the TOL group were more likely to give birth in the earlier part of the study period, to be younger (even though the rate of women <20 years old was similar), to be taller, and to have a lower BMI, compared with women in the ERC group (all *p*-values <0.001). The infants of women in the TOL group were less likely to be born preterm (*p*-value <0.001), less likely to be SGA or LGA (both *p*-values <0.001), and more likely to be male ($p = 0.006$) than infants of women with one previous CS for whom an ERC was planned.

In Table 2, the hierarchical system of indications for the first-delivery CS is explained. The sources of the indication data, and the reasons for the hierarchical order of the groups are presented. We give the percentages of indications in each group in the hierarchical and in a nonhierarchical setting, respectively.

Table 3 shows the frequencies and the ORs for low Apgar score in the TOL group vs. the planned CS group. Among women with one previous vaginal delivery, the risk of low Apgar score was considerably lower ($OR = 0.3$, $p < 10^{-6}$) in infants of women with TOL than among infants who were born after a planned CS. When adjustments were made for maternal characteristics and fetal conditions, the estimate was less extreme, but was still highly significant ($OR = 0.6$, $p < 10^{-6}$). In contrast, in the group of women who had experienced one previous CS, the risk of low Apgar score was higher in the TOL than in the planned CS group, and changed only marginally when adjustments were made.

Table 1. Maternal and fetal characteristics by obstetric history and planned mode of delivery, Sweden 1992–2007.

	Vaginal first delivery (%)			Cesarean first delivery (%)		
Characteristics (second pregnancy)	Total (n = 407 159)	Trial of labor (n = 394 565)	Elective cesarean (n = 12 594)	Total (n = 59 643)	Trial of labor (n = 41 450)	Elective cesarean (n = 18 193)
Year of delivery						
1992–1997	45.0	45.5	29.8	38.2	40.4	33.4
1998–2002	31.1	31.0	35.2	32.2	31.9	32.8
2003–2007	23.9	23.5	35.1	29.6	27.8	33.8
Maternal age						
<20 years	0.4	0.4	0.2	0.2	0.2	0.2
≥35 years	12.9	12.6	22.2	21.2	18.3	27.6
Any smoking	11.3	11.3	11.2	10.5	10.7	10.1
BMI >30 kg/m^2	7.1	7.1	9.1	11.6	10.8	13.3
Maternal height						
<160 cm	9.8	9.8	10.7	16.7	15.1	20.3
≥175 cm	9.3	9.3	9.3	6.2	6.3	5.8
Maternal origin non-Swedish	12.7	12.7	12.0	13.0	12.7	13.6
Gestational duration						
<37 weeks	3.5	3.1	16.6	5.7	4.8	7.7
≥42 weeks	5.9	6.1	1.7	6.9	8.8	2.5
Male fetal gender	51.5	51.5	50.2	51.6	51.3	52.5
SGA	1.3	1.2	5.2	2.5	2.2	3.2
LGA	4.6	4.4	8.8	6.9	5.1	11.2

BMI, body mass index; LGA, large for gestational age; SGA, small for gestational age.

Table 2. Hierarchical system of indications for cesarean delivery. Women with their two first deliveries 1992–2007 in Sweden and the first delivery by cesarean section.

Indication for the first-delivery cesarean section		Explanation of groups	Hierarchical system, %	Nonhierarchical system, %
1.	Multiple gestation	Three well-defined groups, entirely based on data from the Swedish Medical Birth Registry (no ICD codes)	2.5	2.5
2.	Preterm birth, gestational age <37 weeks		13.5	14.9
3.	Breech or other malpresentation		18.2	22.3
4.	Significant congenital malformations	Malformation diagnoses with exceptions: congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus in preterm infants, single umbilical artery, and preauricular tags	2.0	3.7
5.	Rupture of uterus	Small groups placed high in the hierarchy to make tracing of the diagnosis possible in following pregnancies. Data from ICD codes	0.0	0.0
6.	Placenta previa		0.5	1.1
7.	Diabetes mellitus/gestational diabetes	Placed high in the hierarchy to distinguish from LGA and prolonged pregnancy. Data from ICD codes	1.4	2.1
8.	SGA/suspected IUGR	Birthweight <2 SD below expected birthweight according to a Swedish ultrasound-based weight curve (21), or ICD codes	3.9	9.8
9.	LGA/suspected LGA/BW >4500 g	Birthweight >2 SD above expected birthweight according to a Swedish ultrasound-based weight curve (21), or BW >4500 g, or ICD codes	5.2	6.9
10.	Prolonged pregnancy, GA ≥42 weeks	Group refined from diabetes and LGA indications. Information on gestational length from the Swedish Medical Birth Registry	9.8	13.2
11.	Severe pregnancy complications/severe maternal disease	ICD codes for premature separation of placenta, antepartum bleeding, severe preeclampsia, eclampsia, severe maternal disease, or maternal care for known or suspected fetal abnormality/damage. Oligohydramnios or polyhydramniosis	2.5	9.0
12.	Complications during labor/delivery	The largest group, consisting of ICD codes for dystocia, prolonged labor, suspected cephalopelvic disproportion, pelvic organ abnormalities, problems associated with amniotic cavity and membranes, problems regarding induction of labor, prolapse of umbilical cord or cord entanglement with compression, or complications of obstetric surgery and procedures	24.6	56.8
13.	Fetal distress/death unexplained by indications listed above	ICD codes for fetal distress, fetal hypoxia, birth asphyxia, or intrauterine death	8.2	27.7
14.	No indication listed above/mild conditions not classified elsewhere	ICD codes for cesarean section performed on maternal request/non-medical indication, or mild conditions not likely to lead to cesarean delivery	5.3	20.8
15.	No diagnosis available	Neither abnormal conditions, nor indications for cesarean section detected using data from the Swedish Medical Birth Registry	2.3	3.9
			100	194.7[a]

BW, birthweight; GA, gestational age; ICD, International Classification of Diseases; LGA, large for gestational age; SD, standard deviation; SGA, small for gestational age.

[a]Sum >100%: more than one indication possible in a nonhierarchical system.

When women with one previous CS were divided into groups based on the indication for the first CS, it became evident that the ORs for low Apgar score, TOL vs. ERC, differed considerably between indication groups (p-value for homogeneity = 0.0001). Compared with the infants of women with an ERC, infants of women with a TOL within the groups with the following indications for the first CS in the hierarchical system: prolonged pregnancy, complications during labor/delivery, or unexplained fetal distress, were significantly, and more than twice as likely to have a low Apgar score (Table 3). Infants of women with a TOL in the group with the first CS indication "Significant congenital malformations" had a more than five-fold risk of low Apgar score compared with infants of women with an ERC. However, the estimate was based on low numbers of cases with low Apgar score (19 vs. 2 children in the TOL and the ERC groups, respectively).

Table 3. Apgar score <7 at 5 min in singletons of women with one previous vaginal delivery and in singletons of women with one previous cesarean section. The latter group was divided by indication for the first delivery cesarean. Odds ratio for trial of labor vs. elective cesarean delivery, Sweden 1992–2007.

	Trial of labor (*N*)		Elective cesarean delivery (*N*)				
	Apgar <7 at 5 min (*n*)		Apgar <7 at 5 min (*n*)		Odds ratio (95% CI)		
	n/*N*	%	*n*/*N*	%	Crude	Adjusted[a]	Adjusted[b]
Women with a vaginal first delivery	2794/394 565	0.7	324/12 594	2.6	0.3 (0.2–0.3)	0.3 (0.3–0.3)	0.6 (0.5–0.7)
Women with a cesarean first delivery, total	738/41 450	1.8	200/18 193	1.1	1.6 (1.4–1.9)	1.7 (1.5–2.0)	1.8 (1.5–2.1)
Indications for the cesarean first delivery (hierarchical order)							
1. Multiple gestation	21/1296	1.6	2/202	1.0	1.6 (0.4–7.1)	1.6 (0.4–6.7)	1.6 (0.4–6.7)
2. Preterm birth, GA <37 weeks	90/6144	1.5	57/1902	3.0	0.5 (0.3–0.7)	0.5 (0.3–0.7)	0.9 (0.7–1.4)
3. Breech or other malpresentation, GA ≥37 weeks	133/8652	1.5	24/2224	1.1	1.4 (0.9–2.2)	1.5 (1.0–2.3)[NS]	1.4 (0.9–2.2)
4. Significant congenital malformations[c]	19/782	2.4	2/393	0.5	4.9 (1.1–21.0)	4.9 (1.1–21.0)	5.4 (1.2–23.6)
5. Rupture of uterus	0/7	0.0	0/15	0.0	–	–	–
6. Placenta previa	1/225	0.4	0/47	0.0	–	–	–
7. Diabetes mellitus/ gestational diabetes	14/442	3.2	4/372	1.1	3.0 (1.0–9.2)[NS]	–	–
8. SGA/suspected IUGR	38/1725	2.2	12/610	2.0	1.1 (0.6–2.2)	1.2 (0.6–2.4)	1.7 (0.8–3.5)
9. LGA/suspected LGA/BW >4500 g	26/1684	1.5	9/1404	0.6	2.4 (1.1–5.2)	2.4 (1.1–5.2)	2.0 (0.9–4.5)
10. Prolonged pregnancy, GA ≥42 weeks	73/3843	1.9	15/2030	0.7	2.6 (1.5–4.5)	2.7 (1.5–4.7)	2.6 (1.5–4.6)
11. Severe pregnancy complications/severe maternal disease	31/1125	2.8	7/373	1.9	1.5 (0.6–3.4)	1.9 (0.8–4.5)	2.3 (1.0–5.6),NS
12. Complications during labor/delivery	182/9337	1.9	40/5364	0.7	2.6 (1.9–3.7)	2.7 (1.9–3.9)	2.4 (1.7–3.4)
13. Fetal distress/death unexplained by indications listed above	78/3697	2.1	11/1209	0.9	2.3 (1.2–4.4)	2.6 (1.4–4.9)	2.9 (1.5–5.5)
14. No indication listed above/mild conditions not classified elsewhere	13/1446	0.9	15/1694	0.9	0.8 (0.3–2.3)	0.7 (0.2–2.0)	0.7 (0.2–2.1)
15. No diagnosis available	19/1045	1.8	2/354	0.6	1.4 (0.4–4.8)	1.2 (0.3–4.0)	1.5 (0.4–5.0)

BW, birthweight; CI, confidence interval; GA, gestational age; IUGR, intrauterine growth restriction; LGA, large-for-gestational age, i.e. birthweight >2 SD above expected birthweight according to a Swedish ultrasound-based weight curve (21); OR, odds ratio; SD, standard deviation; SGA, small-for-gestational age, i.e. birthweight <2 SD below expected birthweight according to a Swedish ultrasound-based weight curve (21).

[a]Adjusted for year of birth and maternal characteristics (maternal age, smoking, height, and body mass index).

[b]Adjusted for year of birth, maternal characteristics, and fetal/infant parameters (preterm birth, breech presentation, and BW SD scores).

[c]Exceptions: Congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus in preterm infants, single umbilical artery, and preauricular tags.

Among infants of women without any medical indication for the first CS, no association between mode of delivery and low Apgar score was found.

Table 4 is a descriptive table that shows the recurrence rate of first CS indications in the second delivery, by second-delivery mode. As previously described, second pregnancy multiple gestations were excluded. Irrespective of second-delivery mode, diabetes showed the highest recurrence rate, followed by complications during labor, and LGA.

Table 4. First cesarean delivery indication according to a hierarchical system and the risk for recurrent condition, irrespective of hierarchy, Sweden 1992–2007.

	Recurrence rate					
	Irrespective of planned second delivery mode		Trial of labor		Elective repeat cesarean	
	n recurrent/*N* total	%	*n* recurrent/*N* total	%	*n* recurrent/*N* total	%
1. Multiple gestation[a]	0/1498	0.0	0/1296	0.0	0/202	0.0
2. Preterm birth, GA <37 weeks	1444/8046	17.9	764/6144	12.4	680/1902	35.8
3. Breech or other malpresentation	909/10 876	8.4	247/8652	2.9	662/2224	29.8
4. Significant congenital malformations[b]	49/1175	4.2	28/782	3.6	21/393	5.3
5. Rupture of uterus	0/22	0.0	0/7	0.0	0/15	0.0
6. Placenta previa	6/272	2.2	1/225	0.4	5/47	10.6
7. Diabetes mellitus/gestational diabetes	561/814	68.9	279/442	63.1	282/372	75.8
8. SGA/suspected IUGR	283/2335	12.1	174/1725	10.1	109/610	17.9
9. LGA/suspected LGA/BW >4500 g	1176/3088	38.1	515/1684	30.6	661/1404	47.1
10. Prolonged pregnancy, GA ≥42 weeks	894/5873	15.2	739/3843	19.2	155/2030	7.6
11. Severe pregnancy complications/severe maternal disease	117/1498	7.8	77/1125	6.8	40/373	10.7
12. Complications during labor/delivery	6625/14 701	45.1	4233/9337	45.3	2392/5364	44.6
13. Fetal distress/death	887/4906	18.1	841/3697	22.7	46/1209	3.8

BW, birthweight; CS, cesarean section; GA, gestational age; IUGR, intrauterine growth restriction; LGA, large-for-gestational age; SGA, small-for-gestational age.

[a]Second pregnancy multiples were not included in the study.

[b]Exceptions: Congenital dislocation of hip/unstable hip, undescended testicle, persistent ductus arteriosus in preterm infants, single umbilical artery, and preauricular tags

Discussion

Infants of women with one previous CS were at significantly higher risk of low Apgar score after a TOL than after an ERC. The risk increase varied substantially by indication for the first-delivery CS. Infants of women with a previous CS indication, in the hierarchical classification, of significant congenital malformations, macrosomia, prolonged pregnancy, labor complications, or unexplained fetal distress, had a more than doubled risk of low Apgar score after TOL compared with after ERC. The group with the highest OR for low Apgar score was significant congenital malformations. However, the numbers were small, and until the results have been confirmed in an independent investigation, we regard them as a random finding. With the exception of the previous macrosomia group, the risk estimates listed above remained statistically significant when adjustments were made for maternal characteristics, and maternal + fetal/infant parameters. Among infants born to women with a first-delivery CS without any medical indication, there was a low risk for low Apgar score and the risk after a TOL was similar to that after an ERC.

Our study, aiming to predict delivery outcome by studying first-delivery indications, was based on the hypothesis that conditions present at the first delivery are likely to reoccur in the following pregnancy. The exact recurrence rates are biased by the second-delivery mode, as clinicians are requested to set diagnoses in cases of operative deliveries, but not in spontaneous, vaginal deliveries. Hence, our results regarding recurrence risk (Table 4) should be interpreted cautiously.

For some of the conditions in the hierarchical system, it is possible to identify recurrence early in the second pregnancy (such as congenital malformations, diabetes and severe maternal disease). Other conditions could be, but are not always, identified in early third trimester (such as breech presentation, placenta previa, SGA, and LGA). For the remaining diagnoses, it is not possible to tell whether the condition will appear until delivery. Hence, for a minor part of the pregnancies following one CS, it would be possible to include the knowledge of a recurrent condition when planning the second-delivery mode. For the largest indication groups in the hierarchical system, however, recurrence is not known at the time of second-delivery mode planning. Therefore, we do not include information on recurrent conditions in our analyses regarding low Apgar score and first-delivery indication for CS.

To study the outcome among infants of women with a previous vaginal delivery was beyond the scope of the current study, but the results were included to allow comparison. The proportion of women with a previous vaginal delivery who had a planned CS at the second

delivery was low, and was likely to consist of high-risk pregnancies. Therefore, the high risk for low Apgar score in this group was expected.

Although the present study was based on nearly 60 000 deliveries following one CS, the numbers within the indication groups were not sufficient to study the relation between delivery mode and perinatal death. Instead, we focused on a somewhat less objective measurement – low Apgar score. The clinical importance of Apgar score has been debated, but evidence suggests that there is a significant association between low Apgar score and future health. For example, Thorngren-Jerneck and Herbst (23) have reported an increased risk of mortality and severe neurologic morbidity for term infants with low Apgar score, and Stuart et al. (24) have found an association between low Apgar score and cognitive impairment, as measured by academic achievement at 16 years of age.

The main limitation of the current study was that, despite the large population dataset, the numbers of infants with low Apgar scores in several CS indication groups were too low to detect a true low to moderate risk increase after TOL. Even though the evaluation of short-term and long-term maternal health consequences is important in a risk analysis of planned delivery mode, we did not consider this in the present study. Other authors have focused on maternal implications (7,25–27).

Previous studies have shown that TOL is associated with a greater perinatal risk than is ERC (7,26). Guise et al. (26) stated that definitive studies are lacking to identify patients who are at greatest risk for adverse outcomes. To our knowledge, no study has been published with the attempt to relate the perinatal risks involved in TOL to the indication for the first CS. The absolute risk for low Apgar score was low in the present study. However, the mere knowledge of a more than doubled risk for low Apgar score in the infants of women with a TOL compared with an ERC in certain first-delivery CS indication groups could help to increase the safety in deliveries after one CS.

During the pregnancy after one CS, the obstetrician will see the pregnant woman and her partner, aiming to counsel them about the safest, and therefore preferable, method for the second delivery: TOL or ERC. Some factors will be evident at the consultation – the woman's age, her height and weight, findings from ultrasound examinations, the indication for the first CS performed, and perhaps the couple's preferred second-delivery mode. In certain cases, based on the facts present, it may be obvious which second-delivery mode to choose. In other circumstances, it would be of much help to have knowledge about the probability of giving birth to a healthy child, given the "baseline facts" available at the time of consultation. The indication for the first CS is one of the most important factors to take into consideration. Scoring tools, aiming to facilitate the professional counseling regarding the most appropriate delivery mode after cesarean, have already been published (10–17). These tools, in combination with knowledge of maternal health consequences and our new results regarding neonatal outcome by delivery mode and indication for the first CS performed, could all be useful pieces in the obstetric patient safety jigsaw puzzle.

Conclusion

The second-delivery neonatal outcome, as measured by Apgar score, might be improved by considering the indication for the first-delivery CS when choosing between a TOL and an ERC in the second pregnancy.

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Paper IV