Women with a preterm cesarean have high rates of successful trial of labor in a subsequent pregnancy.


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ABSTRACT

Objective
The rate of cesareans has increased worldwide. Therefore, an increasing number of women has to decide how to deliver in a subsequent pregnancy. Individualized information on risks and success chances is helpful. This study investigates the effect of a preterm cesarean on success of subsequent term trial of labor.

Study Design
Ten-year Dutch cohort (2000–2009) of women with one previous cesarean and a subsequent term trial of labor. Subgroups were made based on gestational age at first cesarean delivery (25–28, 28–30, 30–32 and 32–34 weeks) and stratified based the way in which second delivery started. Rates of vaginal deliveries, maternal, and neonatal outcomes were compared with women who had a first-term cesarean (37–43 weeks).

Results
Four thousand three-hundred forty-two women delivered by preterm cesarean in the first pregnancy. These women had high rates of successful trial of labor, both after spontaneous onset (86.2–96.2%) and induction (72.8–75.4%). Rates of adverse outcomes were low and similar compared with women with a previous term cesarean.

Conclusion
In this 10-year nationwide cohort, women with a preterm first cesarean who opt for trial of labor in a subsequent pregnancy had high rates of successful trial of labor.
OBJECTIVE
Worldwide, the rate of cesarean deliveries is increasing, from 6.7 percent in 1990 to 19.1 percent in 2014. Consequently, women and gynecologists are increasingly confronted with the question how to deliver in a subsequent pregnancy. Both trial of labor after cesarean and planned cesarean delivery have certain risks and benefits. Trial of labor carries, amongst others, the maternal risk of uterine rupture and the neonatal risk of hypoxic-ischemic encephalopathy. Cesarean deliveries are associated with a higher maternal risk of infection, puerperal venous thromboembolism and anesthetic complications, and a higher neonatal risk of respiratory distress syndrome, as compared to vaginal delivery. The decision on how to deliver in a postcesarean pregnancy is usually made by the woman, her partner and her obstetrician. The American as well as Dutch guidelines describe women who are good candidates for planned trial of labor to be women in whom the balance between risks and success chance is acceptable to both herself and the obstetrician. In this regard, individualized information on the chance of success is desired. Many factors are described to influence success rate of trial of labor, such as maternal age, body mass index, ethnicity, mode of onset of labor, history of vaginal delivery and neonatal birthweight. The role of a previous preterm cesarean has also been investigated as a possible influencer of trial of labor success. Prematurity in a previous cesarean is presumed to negatively influence vaginal birth success chance. Theoretically, the damage that is done when an incision is made in a preterm, undeveloped lower uterine segment might be more extended in than in a term, fully developed lower uterine segment. This additional damage, might prompt (the suspicion of) uterine rupture during a next trial of labor. Up until now, studies on this subject include small samples or lack a subdivision into multiple gestational age groups. Therefore, to include gestational age of the previous cesarean in antepartum counselling and intrapartum decision-making, more detailed information is needed. This study aims to assess the effect of a previous preterm cesarean on chance of success of a trial of labor in a subsequent pregnancy.

MATERIALS AND METHODS
Study population
We studied women with one previous cesarean and no history of vaginal birth who opted for a trial of labor in their subsequent, term, pregnancy. Women who had a previous preterm cesarean were compared to women who had a previous term cesarean. Data were extracted from the Netherlands Perinatal Registry (PRN). In this database, information about pregnancies, deliveries and neonatal outcomes until 28 days after birth is collected. All data in the PRN are registered routinely by caregivers during prenatal care, delivery and the neonatal period. Women are informed their information is recorded in the database and they may opt out. Data are sent to a national office for several consistency checks. The data of approximately 95% of all pregnancies and deliveries in the Netherlands are registered in the PRN. The PRN is divided in three registries, a midwifery registry, an obstetrics registry and a neonatology registry. A validated linkage procedure was used to link the three different registries. Due to the fact that the information about pregnancies, deliveries and neonatal outcomes is registered on child level, there is no maternal identifier available. Consequently, an additional step was necessary to follow-up on outcome of next pregnancies of the same mother. To achieve this, a longitudinal probabilistic linkage procedure was used to link all pregnancies and children of one mother. The linkage procedure is described by Schaaf et al. This procedure was completed up until December 31st, 2009 at the moment of our analysis. Thus, in our analysis, both the first and second pregnancy and delivery were between January 1st, 2000 and December 31st, 2009.
in the Netherlands. The PRN approved usage of the database for our study (approval number 16.75).

We excluded women with twin pregnancies in first or second pregnancy, fetal congenital anomalies in first or second delivery, antepartum fetal death in second delivery, breech position in second delivery, a first cesarean before 25 and after 37 weeks of gestational for the study population and a first cesarean before 37 weeks and after 42+6 weeks of gestational for the reference group, a second delivery before 37 or after 42+6 weeks of gestational, and an elective repeat cesarean in second delivery. The study population was divided in subgroups based on gestational age at first cesarean delivery: 25+0 till 27+6 weeks, 28+0 till 29+6, 30+0 till 31+6, 32+0 till 33+6 and 34+0 till 36+6. The sixth group was the reference group with a gestational age of 37+0 till 42+6 weeks. The first group was chosen based on the assumption that the lower uterine segment has not yet been formed during the late second and the early third trimester of pregnancy, so a cesarean during this period could be considered a corporeal incision. Because it is unclear if there is a certain gestational age at which the effect on a following trial of labor is comparable with a cesarean in the term period, we decided to break the remaining group up in subgroups of two weeks. We stratified for mode of start of delivery (either spontaneous or by induction), since induction is strongly associated with decreased trial of labor success. Baseline characteristics were maternal age at second delivery, ethnicity, socioeconomic status, cesarean performed during labor in first pregnancy, induction of labor at second delivery, gestational age at second delivery, macrosomia (birthweight above 4500grams) at second pregnancy. The primary outcome was vaginal delivery, either spontaneously or assisted by vacuum/forceps. Secondary maternal outcomes were uterine rupture and postpartum hemorrhage. Secondary neonatal outcomes were defined as Apgar score <7 after 5 min, perinatal death and respiratory distress syndrome. These outcomes were chosen for their clinical importance and accurate listing in the database, an exception being uterine rupture, which was not compulsory to score.

**Statistical analysis**

Statistical Analysis Software 9.2 (SAS Institute Inc., Cary, NC, USA) was used to analyze the results. We tested for statistically significant differences in patients’ characteristics by using an ANOVA test for continuous data and the chi-square test for discrete data. For comparing the success rate of trial of labor between the subgroups a multivariate logistic regression analysis was performed, adjusting for maternal age at second delivery, ethnicity, socio-economic status and macrosomia in second delivery. To compare the maternal and neonatal outcomes, we combined the groups of 25+0 till 27+6 weeks, 28+0 till 29+6, 30+0 till 31+6 into one group of 25+0 till 31+6 weeks. This was done in order to increase power. We used the chi-square test. P-values less than 0.05 were considered statistically significant.
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RESULTS

Incidence of preterm cesarean and subsequent term trial of labor

Figure 1 shows the flow diagram of data extraction of our study population from the Netherlands Perinatal Registry. Our cohort consisted of 41,745 pregnant women with a previous cesarean between 25 and 43 weeks of gestation and a trial of labor in their second delivery between 37 and 43 weeks. As depicted in figure 1, in subgroups with a first preterm cesarean, 77.6 to 88.0 percent had a trial of labor.

Figure 1. Extraction of study population from the PRN
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Demographic characteristics

Table 1 reports demographic characteristics, obstetrical history and characteristics of the second pregnancy for each of the six gestational age subgroups. All characteristics differed significantly between the groups.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Gestational age at first cesarean delivery (weeks)</th>
<th>25 - 28 (n=111)</th>
<th>28 - 30 (n=270)</th>
<th>30 - 32 (n=447)</th>
<th>32 - 34 (n=824)</th>
<th>34 - 37 (n=2690)</th>
<th>37 - 43 (n=37403)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal characteristics at 2nd delivery</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Age in years, mean (SD)</td>
<td>30.3 (4.26)</td>
<td>30.6 (4.75)</td>
<td>31.0 (4.39)</td>
<td>31.2 (4.28)</td>
<td>31.6 (4.20)</td>
<td>31.9 (4.04)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Caucasian ethnicity</td>
<td>101 (91.0)</td>
<td>232 (85.9)</td>
<td>408 (91.3)</td>
<td>743 (90.2)</td>
<td>2451 (91.1)</td>
<td>33364 (89.20)</td>
<td>0.01</td>
</tr>
<tr>
<td>Low SES</td>
<td>28 (25.2)</td>
<td>70 (25.9)</td>
<td>95 (21.3)</td>
<td>173 (21.0)</td>
<td>494 (18.4)</td>
<td>7439 (19.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>First delivery characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean during labor</td>
<td>24 (21.6)</td>
<td>27 (10)</td>
<td>40 (8.9)</td>
<td>169 (20.5)</td>
<td>1293 (48.1)</td>
<td>26626 (71.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Second pregnancy &amp; delivery characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induction of labor</td>
<td>59 (53.2)</td>
<td>139 (51.5)</td>
<td>239 (53.5)</td>
<td>431 (52.3)</td>
<td>1178 (43.8)</td>
<td>16030 (42.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>GA 2nd delivery, weeks</td>
<td>39.0 (1.30)</td>
<td>39.1 (1.20)</td>
<td>39.2 (1.25)</td>
<td>39.2 (1.28)</td>
<td>39.2 (1.30)</td>
<td>39.7 (1.19)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Macrosomia a</td>
<td>3 (2.70)</td>
<td>2 (0.74)</td>
<td>5 (1.12)</td>
<td>14 (1.70)</td>
<td>48 (1.78)</td>
<td>1527 (4.08)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Suspected fetal distress</td>
<td>30 (27.0)</td>
<td>62 (23.0)</td>
<td>99 (22.2)</td>
<td>177 (21.5)</td>
<td>560 (20.8)</td>
<td>8329 (22.3)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data are presented as number (percentage) unless indicated otherwise. SES: socio-economic status, GA: gestational age, HD: hypertensive disorder *Birth weight above 4500 grams

Table 2. Association between gestational age at first delivery and success of TOLAC in second delivery, stratified by type of labor onset

<table>
<thead>
<tr>
<th>Gestational age at first cesarean (weeks)</th>
<th>Total (n=41745)</th>
<th>Total (n=23669)</th>
<th>Spontaneous TOLAC (n=18076)</th>
<th>Spontaneous TOLAC (n=10876)</th>
<th>Induction TOLAC (n=18076)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>93 (83.8)</td>
<td>1.98 (1.19 – 3.30)</td>
<td>50 (96.2)</td>
<td>8.54 (2.07 – 35.2)</td>
<td>43 (72.9)</td>
</tr>
<tr>
<td>Successful TOLAC</td>
<td>217 (80.4)</td>
<td>1.57 (1.16 – 2.13)</td>
<td>113 (86.3)</td>
<td>2.06 (1.25 – 3.39)</td>
<td>104 (74.8)</td>
</tr>
<tr>
<td>Spontaneous TOLAC</td>
<td>359 (80.5)</td>
<td>1.54 (1.22 – 1.95)</td>
<td>185 (88.9)</td>
<td>2.68 (1.74 – 4.15)</td>
<td>174 (72.8)</td>
</tr>
<tr>
<td>Successful TOLAC</td>
<td>670 (81.3)</td>
<td>1.67 (1.40 – 2.00)</td>
<td>348 (88.6)</td>
<td>2.61 (1.91 – 3.58)</td>
<td>322 (74.7)</td>
</tr>
<tr>
<td>Successful TOLAC</td>
<td>2191 (81.4)</td>
<td>1.69 (1.53 – 1.87)</td>
<td>1303 (86.2)</td>
<td>2.08 (1.79 – 2.42)</td>
<td>888 (75.4)</td>
</tr>
<tr>
<td>Successful TOLAC</td>
<td>26702 (71.4)</td>
<td>Reference</td>
<td>15859 (74.2)</td>
<td>Reference</td>
<td>10843 (67.6)</td>
</tr>
</tbody>
</table>

Data are presented as number (percentage). TOLAC: trial of labor after cesarean, aOR: adjusted odds ratio, CI: confidence interval *Multivariate models included the following covariates: maternal age in second delivery, low socio-economic status (yes/no), Caucasian ethnicity (yes/no), macrosomia in second pregnancy (yes/no).
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Success rates of trial of labor
Table 2 reports success rates of trial of labor per first cesarean gestational age group for the whole group, the group with spontaneous labor onset and the induced group. Success rates were 80.4 to 83.8 percent for women with a preterm first cesarean. When considering women with spontaneous labor onsets only, success rates were 86.2 to 96.2 percent, higher than success rates for women who were induced (72.8 to 75.4 percent). As compared to women with a previous term cesarean, success rates differed significantly, except for the induced women with a history of preterm cesarean between 25 and 32 weeks. Multivariate analysis, used to adjust for known confounders, showed no differences in these effects. Table 3 shows maternal and neonatal outcomes of trial of labor after cesarean in second pregnancy per gestational age in first delivery. Adverse outcomes were rare and no statistically significant differences in adverse outcomes were found between term or preterm first cesareans.

Table 3. Maternal and neonatal outcomes of TOLAC in second pregnancy per gestational age in first delivery

<table>
<thead>
<tr>
<th>Gestational age at cesarean delivery (weeks)</th>
<th>25 - 32 (n=828)</th>
<th>32 - 34 (n=824)</th>
<th>34 - 37 (n=2690)</th>
<th>37 - 43 (n=37403)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine rupture</td>
<td>3 (0.36)</td>
<td>0 (0.00)</td>
<td>7 (0.26)</td>
<td>72 (0.19)</td>
<td>0.34</td>
</tr>
<tr>
<td>HPPa</td>
<td>49 (5.92)</td>
<td>49 (5.95)</td>
<td>173 (6.43)</td>
<td>2374 (6.35)</td>
<td>0.92</td>
</tr>
<tr>
<td>Neonatal outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-min Apgar &lt;7</td>
<td>7 (0.85)</td>
<td>11 (1.33)</td>
<td>36 (1.34)</td>
<td>443 (1.18)</td>
<td>0.68</td>
</tr>
<tr>
<td>Perinatal deathb</td>
<td>0 (0.00)</td>
<td>1 (0.12)</td>
<td>1 (0.04)</td>
<td>42 (0.10)</td>
<td>0.52</td>
</tr>
<tr>
<td>IRDS</td>
<td>5 (0.60)</td>
<td>1 (0.12)</td>
<td>13 (0.48)</td>
<td>188 (0.50)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Data are presented as number (percentage) aHPP: haemorrhage postpartum (defined as > 1L blood loss)
bDeath during delivery

COMMENT
Main findings
In this large nationwide 10-year cohort study, we demonstrated that women in a term pregnancy who opt for trial of labor after a previous preterm cesarean have high success rates, that vary between 72.8 and 96.2 percent, depending on gestational age at first cesarean and the way in which the second delivery started (either spontaneous or by induction).

Interpretation
Previous smaller studies evaluated the effect of a preterm cesarean on trial of labor. Binder et al. found that in a group of 166 women with a previous high placed U-incision between weeks 25 and 29, 72 percent had a successful vaginal delivery after previous preterm cesarean.9 Kwee et al. found a success rate of 86 percent in a group of 93 women who attempted vaginal delivery after a cesarean between 26 and 34 weeks.10 Harper et al. compared success rates of 508 women who had a first cesarean before 34 weeks to 12 027 women with first cesareans after 34 weeks. The rate of successful vaginal birth in the preterm group was 82 percent, compared to 75 percent in the term group.11 Our study adds the subdivision into multiple subcategories of prematurity with a fair amount of cases in each group, contributing to the robustness of the finding that preterm cesarean does not prompt lower success rates of subsequent trial of labor.

The explanation for the higher success rates in comparison to women with a previous term cesarean might be the indication for the first cesarean. The reference group of women with a
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term first cesarean contained relatively more women with a first cesarean that was performed during labor, for instance for lack of progress. They thus have lower a priori chances on delivering vaginally as compared to women who did not (have the chance to) try to deliver vaginally. Unfortunately, in our database, the indication for the first cesarean is not registered on a level any further than whether the cesarean was performed before or during labor. However, besides considering the relative success chances, it is just as informative to look at the absolute success chances of women with a previous preterm cesarean. They have fairly high success chances, with roughly four in every five women succeeding in vaginal birth.

It is notable that in the group of women with a preterm first cesarean between 28+0 and 31+6 weeks who opt for trial of labor in a next term pregnancy, only 9 to 10 percent had a previous cesarean during labor. This means that the other 90 percent had a previous cesarean before labor started. An explanation for this observation cannot be found in selection bias, since 86 percent of women in this group opted for trial of labor in the next term pregnancy. In the PRN, it is compulsory to score if a woman was in labor or not. This observation raises the question how care providers declare a woman to be in labor and what the reasons were for performing cesarean in this group.

Since both success rates and risk of complications are taken into account when counselling women on the intended mode of birth, we analysed the occurrence of adverse outcomes, showing no differences between the groups. Harper et al. also found no differences in uterine rupture rates between prior cesarean before or after 34 weeks. Rochelson et al. analysed 25 cases of uterine rupture in a case-control design and found that a previous cesarean before or at 36 weeks is associated with a five times higher risk of uterine rupture as compared to previous term cesarean. However, the cases and controls differed on more characteristics than only the history of preterm cesarean that may explain these differences. In the PRN database, uterine rupture is not a compulsory item to score, so we are unable to draw any firm conclusion on the specific rate of uterine ruptures. However, rates of postpartum haemorrhage, low Apgar scores and neonatal deaths, which can be direct outcomes of uterine rupture, did not differ.

**Strength and limitations**

A research question as ours can only be answered by large observational cohort studies. The strength of our study is that it includes the largest amount of pregnancies as compared to studies that have been conducted on this subject so far, enabling us to provide more detailed information in counselling the specific group of women who are pregnant after having had a preterm cesarean. A limitation of this study is that our data stem from a database with a confined set of items. The first disadvantage we experienced was not being able to include all possible confounders in the multivariate analysis, such as body mass index and smoking, and not being able to report on all possible outcomes reliably, such as uterine rupture. Secondly, as already mentioned, reasons for obstetrical interventions cannot be deduced from the database. It would be informative to learn more about the indications for caesareans as well as indications for the relatively high induction rate. A possible explanation is that care providers filling out the database entry form saw the use of uterotonics during labor a means of labor induction, while in fact it was used for labor augmentation. Thirdly, we were not able to rule out selection bias. The decision on how to deliver is made by the woman, her partner and her obstetrician. Patients who attempted vaginal birth after cesarean in our cohort, might be the ones encouraged by obstetricians who estimated these women to have fairly good success
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chances. However, the fact that approximately four in every five women in our cohort opted for trial of labor, means there will by definition be heterogeneity in this group, which pleads against a strong selection bias.

CONCLUSION
In current obstetric practice, individualized information on the chance of success of trial of labor after cesarean is desired by women and obstetricians. The effect of a preterm cesarean on subsequent trial of labor has been assessed by studies with relatively small sample sizes or no division in subgroups. This study included 4 342 women with a previous preterm cesarean who opted for a subsequent trial of labor, showing that success rates are high and rates of adverse outcomes are low.
REFERENCES


