Management of preterm delivery in women with abnormal fetal presentation

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Management of preterm delivery in women with abnormal fetal presentation

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Lester Anita Bergenhenegouwen
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General Introduction

Preterm birth is a major contributor to perinatal morbidity and mortality[1]. It occurs in 7.7% of the pregnancies in the Netherlands and affects around 12,000 pregnancies per year. [2] Preterm birth is defined as a delivery before 37 weeks of gestation and further divided into moderate preterm birth (between 32-37 weeks) and very preterm birth (before 32 weeks). In preterm birth, fetal malpresentation occurs more frequently than in term births.

Breech presentation is defined as a fetus in longitudinal lie with the buttocks or feet closest to the cervix. The incidence decreases with advancing gestational age from 25% at 26 weeks, 15% at 32 weeks, to 3 to 4% in term pregnancy.[3] The optimal mode of delivery in breech presentation is subject of debate. The Term Breech Trial showed that an intended caesarean delivery is safer in terms of combined short term morbidity and mortality for term breech presentation.[4] The findings of the Term Breech Trial have led to a worldwide shift towards an intended caesarean delivery. In The Netherlands the overall caesarean section rate in term breech presentation increased from 50% to 80% within three months after publication of the trial.[5] Still, 40% of the women with a term breech presentation in The Netherlands attempt a vaginal birth. It is unclear whether the Dutch management of this clinical obstetric issue is justified, and how this relatively large proportion of women is being selected for a vaginal breech delivery. The question is whether there is a favourable profile based on patient characteristics such as parity, onset of labour, type of breech presentation that can identify women with a low risk of poor perinatal outcome during planned vaginal delivery as compared to planned caesarean delivery.

For women with a preterm delivery knowledge on the optimal mode of delivery in case of breech presentation is limited, while the incidence of breech presentation in these women is much higher [6-14]. In the past, several randomized controlled trials have been started on this subject, but they have all been preliminary stopped due to recruitment difficulties [15-19]. The difficulty in recruiting women in a study concerning this topic lies in the fact that women have to be recruited during labour, obstetricians may not feel skilled in performing preterm vaginal breech deliveries anymore and women tend to accept a chance of personal risk to herself in the hope it may help her infant [20]. Subsequently, randomized controlled trials on the mode of delivery of the preterm breech presentation were unable to include enough women to draw meaningful conclusions about the optimal intended mode of delivery. This was also the conclusion of the Cochrane review on this subject by Alfirevic et al. [21].
As the preterm fetus has a relative bigger size of the fetal head as compared to the rest of the body, one could argue that there might be an increased risk of mechanical problems during vaginal birth thus making a caesarean delivery a safer mode of delivery in case of preterm breech delivery. Arguments against a preterm caesarean section are the timing of the delivery and general objections such as an increased risk of maternal morbidity, risks for future pregnancies and costs. More women will have a scarred uterus in the subsequent pregnancy, which might lead to complications in the subsequent pregnancy. Moreover, neonatal respiratory distress syndrome occurs more frequently after caesarean section compared to vaginal delivery. [22] A final argument against a planned caesarean delivery is that in women with threatened preterm delivery the exact moment of delivery is sometimes difficult to predict, thus implicating that a caesarean section might sometimes be performed too early, an event that is not the case for vaginal delivery. A preterm vaginal delivery occurs only when further delay of pregnancy was either not indicated or not possible.

The same issue on the optimal mode of delivery as mentioned above occurs in women with a twin pregnancy. Twin pregnancy occurs in 1.7% of all pregnancies in the Netherlands [5].

The Twin Birth study, a large multicenter randomized controlled trial, showed that planned caesarean section did not reduce the risk of fetal or neonatal death or serious morbidity as compared with planned vaginal delivery in twin pregnancies with the first twin in cephalic position beyond 32 weeks gestation. The risk of adverse neonatal outcome was higher for the second twin than for the first twin, however planned caesarean section did not reduce this risk. There was no difference in adverse maternal outcome between women with a planned caesarean section and a planned vaginal delivery [25]. An important comment on this study by GC Smith was that almost 50% of the women delivered preterm (32-37 weeks of gestation). Many of the primary outcomes (fetal or neonatal death or serious neonatal morbidity) in both groups of the study would have been related to preterm birth and were unlikely to be preventable by caesarean delivery[26]. In a previous study of data from England, Northern Ireland, and Wales, an analysis of 10 years of data on women with a twin pregnancy concluded that the major determinant of neonatal death was the degree of prematurity, and that the small additional risk associated with vaginal delivery was observed only at term [27].

A recent study of Roberts et al on perinatal outcome in twin pregnancy at and near term (36 weeks of gestation) showed that compared with prelabour caesarean, twins born after labour (vaginal delivery and emergency caesarean section) have an increased risk of hypoxia related complications (0.08% versus 0.75%, RR 0.10; 95% CI 0.04-0.26); furthermore, the second twin had a significantly increased mortality up to 5 years of age after an intended vaginal delivery (0.16% versus 0.14%; RR 0.41; 95% CI 0.20-0.83) [28]. However, the absolute mortality rate is low in term twin pregnancies and needs to be balanced against maternal morbidity.

Recently, a study was published on the optimal mode of delivery in preterm twin pregnancy.[29] However, this study was limited to very preterm twins with the first child in cephalic presentation. Neonatal death for the first twin was 5.2% in the planned vaginal delivery group and 6.3% in the planned caesarean delivery group (aOR 0.78; 95% CI 0.17-3.68) and 3.2% versus 6.3% for the second twin (aOR 0.44, 95% CI 0.12-1.66). Composite severe neonatal morbidity for the first twin was 32% in planned vaginal delivery and 35% in planned caesarean delivery (aOR 0.71; 95% CI 0.36-1.44) and for the second twin 23% versus 29% respectively (aOR 0.56; 95% CI 0.16-1.98). The conclusion of this study was that a policy of planned vaginal delivery of very preterm twins with the first twin in cephalic presentation does not increase neonatal mortality or severe neonatal morbidity; maternal morbidity was not reported in this study.[30]

Triplets pregnancies occur in approximately 0.03 % of all pregnancies in the Netherlands, thus concerning 45 to 50 women with a triplet pregnancy per year.[5] In women with a triplet pregnancy, the incidence of overall preterm deliveries is approximately 90%; with a risk of extreme preterm birth < 28 weeks and very preterm birth (28-32 weeks) 13-fold and almost 20-fold, respectively, when compared to singletons [31]. In women with a triplet pregnancy, the preferred mode of delivery has not yet been determined. In an effort to minimize intrapartum fetal complications, there has been a tendency to deliver triplets by the caesarean route [32].

The incidence of multiple pregnancies has increased over the past 20 years by approximately 80%, largely because of the growing use of assisted reproductive technologies and the increase in average maternal age at first childbirth. [24] This makes the issue on the optimal mode of delivery in multiple pregnancies an important topic.

In determining the optimal mode of delivery for women with a preterm breech, twin or triplet pregnancy we have to take into account possible future pregnancies, although this a difficult question in women who have a sudden preterm delivery. The responsible obstetrician has to counsel women on the mode of delivery of the preterm breech, twin or triplet pregnancy and also has to pay attention to a possible subsequent pregnancy.
Aim of the thesis

The aim of the thesis was to answer the following questions.

1. What is the optimal mode of delivery in preterm breech presentation?
2. Does an intended caesarean section reduce the risk of perinatal mortality and morbidity as compared to intended vaginal delivery in preterm breech presentation?
3. What is the effect of the mode of delivery in preterm breech presentation on perinatal and maternal outcomes in the subsequent pregnancy?
4. What is the effect of the increased elective caesarean delivery rates for term breech presentation on maternal and neonatal outcome?
5. Does a planned caesarean section improve perinatal outcome in women with twin pregnancy and a very preterm delivery as compared to planned vaginal delivery?
6. Does a caesarean section reduce the risk of adverse perinatal outcomes in women with a triplet pregnancy?

Outline of the thesis

For the majority of the studies described in this thesis we were allowed to use the data of the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 28 days after birth. The PRN database is obtained by a validated linkage of three different registries: the midwifery registry (LVR1), the obstetrics registry (LVR2) and the neonatology registry (LNR) of hospital admissions of newborns. [33] The coverage of the PRN registry is about 96% of all deliveries in the Netherlands.

Part I reports on studies concerning neonatal and maternal outcome related to the mode of delivery in (pre)term breech presentation.

In chapter 2 we describe the results of a systematic review and meta-analysis of the available cohort studies on preterm breech presentation according to the mode of delivery. We identified seven articles reporting on 3,557 women that met the eligibility criteria.

Chapter 3 contains the results of a nationwide cohort study in the Netherlands in which we compared perinatal morbidity and mortality according to the intended mode of delivery as well as the actual mode of delivery in women with a preterm breech delivery. We identified 8,356 women who delivered between 2000 and 2011 preterm (26-37 weeks of gestation) in breech presentation.

In chapter 4 we describe the results of a nationwide cohort study on the effect of the intended mode of delivery in preterm breech presentation on the subsequent pregnancy. We identified 1,543 women with a preterm breech delivery and a subsequent delivery in the years 1999-2007. We compared perinatal outcome in both pregnancies according to the intended mode of the index pregnancy (preterm breech delivery).

Chapter 5 describes the effect of the increased caesarean section rate on perinatal mortality and morbidity in women with a term breech delivery in a nationwide retrospective cohort study in the years 1999-2007. We studied 58,320 women with a term breech delivery. Furthermore this study describes whether a favourable profile for women with an intended vaginal delivery can be identified.

Part II contains studies that report on neonatal and maternal outcome related to the mode of delivery in preterm delivery of multiple pregnancies.

Chapter 6 contains the results of a nationwide cohort study on the mode of delivery in 1,655 women with a twin pregnancy and a very preterm delivery (<32 weeks of gestation) in terms of perinatal and maternal outcome in the years 2000-2010 in the Netherlands. Perinatal outcomes were paired taking into account the dependency between the children of the same twin pregnancy and were also analysed for each child separately.

In chapter 7 we study the effect of the mode of delivery on perinatal outcome in women with a triplet pregnancy. We identified therefore all women with a triplet pregnancy who delivered in the years 1998-2008 in the Netherlands, which resulted in a study on 386 women with a triplet pregnancy. We analysed perinatal outcome according to the intended mode of delivery as well as the actual mode of delivery.

In chapter 8 we summarise the results of the studies presented in this thesis and give clinical implications and implications for future research in this field.
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Breech presentation
Vaginal delivery versus caesarean section in preterm breech delivery: a systematic review

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Abstract

There is controversy on the preferred mode of delivery (vaginal delivery (VD) versus caesarean section (CS)) in preterm breech delivery in relation to neonatal outcome. While CS is supposed to be more safe for the fetus, arguments against CS can be the increased risk of maternal morbidity, risks for future pregnancies and costs. Moreover, neonatal respiratory distress syndrome occurs more frequently after CS compared to VD.

In the past, several RCT’s have been started on this subject, but they were all preliminary stopped due to recruitment difficulties. As the Cochrane review of these RCT’s reported on 116 women only, knowledge on the effectiveness of CS and VD can at present only be obtained from non-randomised studies.

We performed a systematic review and meta-analysis of non-randomised studies that assesses the association between mode of delivery and neonatal mortality in women with preterm breech presentation. We therefore searched Pubmed, Embase and The Cochrane library for articles comparing neonatal mortality after VD versus CS in preterm breech presentation (gestational age 25+0 till 36+6 weeks). The weighted risk of neonatal mortality was 3.8% in the CS group and 11.5% in the VD group. (Pooled RR 0.63 (95% CI 0.48 to 0.81)). We conclude that cohort studies indicate that CS reduces neonatal mortality as compared to VD.

Introduction

Preterm delivery, defined as delivery before 37 weeks of gestation, is associated with a high prevalence of breech presentation. Nearly 25-30% of the fetuses present in breech presentation at 28 weeks of gestation. This percentage decreases to 4% in term pregnancies.1, 2

Since publication of the Term Breech Trial in the year 2000, planned Caesarean Section (CS) is the preferred mode of delivery for term breech presentation in most countries.3, 4 In the Netherlands CS rates in term breech presentation increased from 50% to over 80% after publication of this trial.5

In preterm breech presentation, the mode of delivery is controversial. In many countries, CS is applied for preterm breech presentation. In the Netherlands, women with preterm labour and a child in breech position deliver more often vaginally as compared to other developed countries.5, 6

While CS is supposed to be the safer route for the fetus, arguments against CS can be the increased risk of maternal morbidity, risks for future pregnancies and costs.5 Moreover, neonatal respiratory distress syndrome occurs more frequently after CS compared to VD.7

A final argument is that in women with threatened preterm delivery the exact moment of delivery is sometimes difficult to predict, thus implicating that a CS is sometimes performed to early, an event that is not the case for vaginal delivery.

In the past, several randomized controlled trials (RCT’s) have been started on this subject, but they were all preliminary stopped due to recruitment difficulties.3, 9, 10 The Cochrane review on these RCT’s, published by Alfierivc et al in 201211 could therefore only report on a total of 116 women from six trials with a sample size varying between 12 and 38. The difference between the two groups with regard to perinatal deaths was not significant (0.29, 95% CI 0.07 to 1.14; three trials, 89 women), as were the reports on neonatal morbidity. The conclusion of this review was therefore that there is not enough evidence to evaluate the use of a policy of planned immediate caesarean section for preterm babies. In the absence of RCT’s with a large number of women included, evidence should be obtained from observational studies. We performed a systematic review and meta-analysis of these non-randomised studies to investigate the association between the mode of delivery and perinatal mortality in preterm breech presentation.
Methods

Searching and selection
We searched the electronic databases Pubmed (Medline), Embase and The Cochrane Library from inception until 1st September 2011. The medical literature was searched for RCT’s and cohort studies studying the effect of the mode of delivery on neonatal mortality in preterm breech presentation. The following terms were used: ((“Breech Presentation”[Mesh]) OR (breech)) AND ((“Obstetric Labor, Premature”[Mesh]) OR (“Premature Birth”[Mesh]) OR (preterm) OR (premature)) AND ((vaginal delivery) OR (cesarean) OR (abdominal delivery) OR (“Cesarean Section”[Mesh])) AND (“Mortality”[Mesh]) OR (mortality) OR (death)) AND (Humans[Mesh]). We also performed a manual search of reference lists from the retrieved studies.

Publication date restriction was imposed on studies published before 1980, since perinatal care and interventions have greatly improved over the years. Language restrictions were not applied. Two authors (LB and LM) independently performed the search and screened the abstracts of identified studies. Disagreement between reviewers was resolved by consensus, and if needed the judgement of a third author was decisive.

Study population and eligibility criteria
All studies that compared the relation between the mode of delivery and neonatal mortality in preterm breech presentation were eligible. Preterm delivery was defined as delivery between a gestational age between 25th – and 36th – weeks. Studies that solely used low-birth-weights as inclusion criterion were excluded from this review. Primary outcome was neonatal mortality. Secondary outcomes were neonatal morbidity (low Apgar scores, respiratory distress syndrome, ventilatory support, low umbilical artery pH, cerebral haemorrhage, infection, bronchopulmonary dysplasia and survival without disability), and maternal morbidity (duration of hospital recording and puerperal fever). Two reviewers independently performed eligibility assessment.

Quality assessment and data extraction
Data extraction was independently completed by LB and LM using a prespecified data extraction form. The following data were extracted from the selected studies: (1) methods of study (including study design, data collection and time-period of the study); (2) characteristics of trial participants (including number of participants, setting and country) and the inclusion and exclusion criteria; (3) type of intervention (VD versus CS); (4) type of outcome measures (perinatal and/or neonatal mortality, secondary outcomes); (5) statistical methods.

To ascertain the validity of eligible observational studies, the reviewers independently determined the adequacy of inclusion and exclusion criteria, characteristics of study participants, inception cohort, selection bias, interventions and co-interventions, outcome measurement, confounders, subgroup analyses and follow-up.

To explore the heterogeneity in study results the following hypothesis was specified before conducting the analysis. The reviewers hypothesized that the intention for the individual interventions (CS or VD) may differ in the studies leading to confounding by indication.

Data analysis
We constructed two by two tables comparing the mode of delivery and neonatal mortality in women preterm delivering a child in breech presentation. Relative risks (RR’s) and their 95% confidence intervals were calculated for the outcome neonatal mortality and total mortality (intrapartum and neonatal death). Overall estimates of effect were calculated with the Mantel-Haenszel method.

The random-effects model was used in advance, as this method takes into account the variation between studies. Heterogeneity was tested with the chi-squared (P= 0.10) and Tau test. Inconsistency (I²) was measured, because this method does not inherently depend on the number of studies and is accompanied by an uncertainty interval. A subgroup analysis was performed to address whether the summary effects vary in relation to gestational age. RR’s and their 95% confidence intervals were also calculated for the secondary outcomes where possible. Statistical analysis was carried out using Review Manager software (RevMan version 5.0, The Cochrane Collaboration).

Results

Selected studies
Our search strategy identified 723 studies (Figure 1). Of these studies, 706 were discarded after screening the abstracts and titles, because they did not meet the eligibility criteria. Three studies could not be included because their full text was not available online or in the university depot and the authors e-mail addresses were unknown. The full texts of the remaining 14 studies were assessed in detail. Seven studies did not meet the eligibility criteria: three did not define the gestational age period12-14, two studies were performed before 198015-16, one study was terminated because of insufficient patient recruitment17 and one study included both preterm and low birth weight infants.17 References of the 14 full text studies revealed no new relevant papers. Finally, seven studies met the eligibility criteria and were included in this systematic review. 18-24
Description of studies

The seven selected studies involved a total of 3557 women (range 88–2674 women per study) delivering preterm of a fetus in breech presentation. All studies were retrospective studies published in English. Detailed information on the characteristics of the included studies is provided in Figure 2.

The data sources of five of the seven included studies were maternal and neonatal charts, while the other two studies used hospital databases. All participants were recruited in a hospital setting, mostly tertiary care centres. The main inclusion criteria entailed women who delivered preterm singleton fetuses in breech presentation. The gestational age was different in the selected studies, varying from 25+0 weeks as the lower limit to 36+6 weeks as the upper limit. All studies excluded cases of antepartum death and lethal congenital malformations. Three studies had more narrow exclusion criteria.

Four studies were single centre, and two studies were multi-centre.
multicentre[19, 21] and one study was nationwide. All studies compared CS and VD. The sample size of almost all studies was relatively small, except for the study performed by Herbst et al., which included 2674 women.

Neonatal mortality

Neonatal mortality was defined differently in the studies: neonatal mortality in the first 7 days after birth, neonatal mortality in first 28 days after birth and neonatal mortality in the period from birth till discharge from the hospital. Two studies, Malhotra et al. and Herbst et al., reported a significant lower neonatal mortality after CS (RR 0.52 (95% CI 0.32-0.84) and RR 0.50 (95% CI 0.31-0.81)). The other studies showed a trend favouring CS, except for the study of Wolf et al., which was the only study that showed a non-significant trend favouring VD, RR 1.3 (95% CI 0.64-2.6).

The pooled analysis showed that CS reduced the risk of neonatal mortality by 37% (pooled RR 0.63 (95% CI 0.48-0.81)) compared to VD (Figure 3). The absolute risks were 3.6% for CS and 11.5% for VD respectively, corresponding with a number needed to treat to prevent one neonatal death in the overall group of 13.

Total perinatal mortality, i.e. intrapartum and neonatal mortality, was reported in six of the seven studies. Total perinatal mortality was significantly different in two studies favouring CS, RR 0.49 (95% CI 0.30-0.80) and RR 0.50 (95% CI 0.27-0.96). The other studies, except the study of Wolf et al., showed a non-significant trend favouring CS. The pooled analysis for total mortality indicated a RR of 0.63 (95% CI 0.44-0.92) favouring CS (Figure 4).

Only two of seven studies explicitly mentioned intention to treat analysis. The study of Kayem et al. showed a non-significant trend in favour of CS for the outcome neonatal mortality, RR 0.85 (95% CI 0.30-2.42) and for total mortality, RR 0.66 (95% CI 0.25-1.77).

Neonatal morbidity

Neonatal morbidity was reported in all studies, but analysis was hampered since the included studies used different morbidity outcomes. The Apgar scores were variably.

Figure 3 Comparison of CS versus VD for preterm breech presentation, Outcome Neonatal mortality

In this study, in the planned VD group 49% delivered by CS, whereas in the planned CS group 5.9% delivered vaginally. The study of Wolf et al. was also analysed according intention to treat, and showed a non-significant trend in favour of vaginal delivery for the outcome neonatal mortality, RR 1.29 (95% CI 0.64-2.60), and for total mortality, RR 1.27 (95% CI 0.66-2.45). This study however only included women with gestational age 26-32 weeks. The other five included studies did not use an intention to treat analysis, these studies described the number of VD compared to the number of CS.

A subgroup analysis for neonatal mortality according to gestational age and mode of delivery was also performed. Outcomes in different gestational age groups were reported in two of the seven studies. Herbst et al. showed a significant difference for neonatal mortality in gestational age 25-28 weeks favouring CS, RR 0.30 (95% CI 0.18-0.49) and there was a non-significant trend favouring CS for gestational age 28-33 weeks and 34-37 weeks (Figure 5). The study of Warke et al. showed a non-significant trend towards VD for gestational age 30-34 weeks, (RR 1.1; 95% CI 0.32-3.8) and a non-significant trend favouring CS for 34-37 weeks of gestation (RR 0.67; 95% CI 0.19-2.4). Data stratified for gestational age could not be pooled since the studies did not analyse the same subgroups of gestational age. The study of Kayem et al. was limited to preterm breech deliveries between 26-29.6 weeks of gestation. This study showed a non-significant trend favouring CS for the outcome neonatal mortality (RR 0.85; 95% CI 0.30-2.4) and total mortality (RR 0.66; 95% CI 0.25-1.8).

Neonatal morbidity

Neonatal morbidity was reported in all studies, but analysis was hampered since the included studies used different morbidity outcomes. The Apgar scores were variably.

Figure 4 Comparison of CS versus VD for preterm breech presentation, Outcome Total mortality (intrapartum and neonatal death)
reported as low 1-min and 5-min Apgar scores. A low 1-min Apgar score was significantly different favouring CS in the study of Herbst et al.\(^21\) (44, RR 0.73, 95% CI 0.53-0.94) and in Malhotra et al.\(^23\) (0.3, RR 0.68, 95% CI 0.47-0.97). The low 1-min Apgar score was similar between the two groups as reported in Malhotra et al.\(^23\) (6, RR 0.80, 95% CI 0.64-1.01), Van Eyk et al.\(^24\) (66, RR 0.98, 95% CI 0.53-1.82) and Ziadeh et al.\(^18\) (66, RR 0.95, 95% CI 0.73-1.23).

The incidence of a low 5-min Apgar scores occurred significantly more frequent in the VD Group, as published by Herbst et al.\(^21\) (56, RR 0.50, 95% CI 0.31-0.81), Kayem et al.\(^22\), (66, RR 0.33, 95% CI 0.16-0.69) and Malhotra et al.\(^23\) (66, RR 0.62, 95% CI 0.41-0.92). The low 5-min Apgar scores were similar between the two groups as reported by Ziadeh et al.\(^18\) (66, RR 0.88, 95% CI 0.52-1.50) and Malhotra et al.\(^23\) (46, RR 0.63, 95% CI 0.36-1.09). In the study of Warke et al.\(^20\) infants above 30 weeks of gestation had statistically lower 5-min Apgar scores in the VD group as compared to the CS group (≤6, RR 0.88 95% CI 0.52-1.50). The study of Wolf et al.\(^19\) described no Apgar scores.

The number of infants on artificial ventilation was significantly higher in the CS group as published by Wolf et al.\(^19\) (13, RR 0.49 95% CI 0.20-1.2). The number of days that the infants needed ventilation was significantly higher in the CS group as reported by Wolf et al.\(^19\) (VD 7.5 ± 15.1 and CS 6.2 ± 12.5, median [range]), but similar between the two groups in the study of Kayem et al.\(^22\) (VD 7.5 ± 15.1 and CS 6.2 ± 12.5, mean ± SD).

Herbst et al.\(^21\) found that the risk of respiratory distress syndrome was significantly higher after CS (RR 2.0, 95% CI 1.4-2.7), however Malhotra et al.\(^23\) and Wolf et al.\(^19\) found no significant difference (RR 0.55, 95% CI 0.24-1.3) and RR 0.98 (95% CI 0.61-1.6). No significant differences were found in umbilical pH\(^22\), risk of bronchopulmonary dysplasia\(^19,22\), risk of cerebral haemorrhage\(^21,24\) and risk of infection\(^19,22,23\).

Also, no significant difference in survival without disability or handicap was found in the two studies with follow-up of two years, as reported in Wolf et al.\(^19\) (RR 0.59, 95% CI 0.07-5.06) and Warke et al.\(^20\) (RR 0.16, 95% CI 0.01-2.82).

It was impossible to pool the neonatal morbidity data, because the studies used different parameters for morbidity and the data were too limited.

### Maternal morbidity

Maternal morbidity was only reported in the study of Wolf et al.\(^19\). The duration of hospital stay was significantly longer in the CS group (mean 8.4 days versus mean 6.3 days). The incidence of puerperal fever was not different (CS 9% versus VD 3%, RR 2.93, 95% CI 0.68-12.5). No major maternal complications were described in the studies.

### Discussion

This systematic review assesses the mode of delivery for women preterm (gestational age 25\(^{th}\) and 36\(^{th}\) weeks) delivering a fetus in breech presentation. We retrieved no randomized studies and seven non-randomized studies. The absolute risk for neonatal mortality was 3.8% in the CS group and 11.5% in the VD group. The pooled RR was 0.63 (95% CI 0.48 to 0.81) for neonatal mortality after CS compared to VD.

Neonatal mortality was chosen as main outcome for this review since this outcome is relevant and easy to measure, and therefore often reliably reported. Morbidity, although also important, is much more difficult to define. For neonatal morbidity, the included studies used different types of neonatal outcomes whereby it was impossible to pool these data and to draw valid conclusions. Besides, especially in preterm infants, short term morbidity is not always correlated to a long-term adverse outcome.

The data on maternal morbidity had insufficient power to draw valid conclusions. This review demonstrates that neonatal mortality is significantly reduced by 37% (pooled RR 0.63 95% CI 0.48-0.81) performing a CS as compared to VD in preterm breech presentation in gestational age 25\(^{th}\) till 36\(^{th}\) weeks. As these data origin from non-randomised studies, some comments have to be highlighted.

An important issue in studies on this subject is that the intention of the mode of delivery often is not clearly described. Consequently, in most studies there is only a description of the number of women who delivered vaginally and the number of women that delivered by CS. This is also the case in studies identified for this review, as only two of seven studies clearly described the intention of the mode of delivery and used intention to treat analysis.\(^19,22\) Not analysing according to intention to treat
analysis implicates that in women with expected adverse outcome (severe growth restriction or a “non intervention” policy) or rapid progress of labour a VD possibly is more common. On the other hand, emergency CS are included in the CS group and the outcome of the infants who were “intended” to deliver vaginally may be worse, suggesting an even better outcome in planned CS. Planning a CS in the preterm period is however also not without risks. If an incorrect diagnosis of unavoidable preterm birth is made, the fetus might be delivered at an earlier gestational age than necessary. However, the impact of CS is so strong that we do not expect that the individual women, who would have delivered later if VD would be awaited, will compensate for this difference.

Another problem of this review is that the included studies had different subgroups of gestational age, whereby we were unable to pool these data and conclude which subgroup of gestational age has the most benefit by delivering by CS. Obviously, in neonates born very preterm the baseline risk of neonatal mortality will be higher than in neonates born late preterm. Consequently, the relative benefit of a CS will be stronger in neonates born late preterm.

Ideally, of course, an RCT would reveal the best management for preterm breech presentation, taking gestational age in account as a treatment prediction marker.

Although several attempts have been made for a RCT, including women into such a trial is very difficult and all RCT’s were stopped before reaching the calculated sample size due to recruitment difficulties. The Cochrane review on this subject could include only 116 women, the authors concluded that there is not enough evidence to evaluate the use of a policy of planned immediate caesarean delivery for preterm babies. Further studies are needed in this area, but adequate recruitment has proven to be difficult. Therefore evidence should be obtained from a review of cohort studies: on this subject the best available evidence. Although this is a very important topic, we believe that it is very unlikely that a new large RCT on preterm breech presentation, the mode of delivery and neonatal mortality will be performed in the near future.

Conclusion

We found no large randomised controlled studies addressing the optimal mode of delivery in women delivering a fetus in breech presentation preterm. The available cohort studies indicate that CS reduces neonatal mortality by 37% as compared to VD in preterm breech delivery. This conclusion should carefully be interpreted, concerning the lack of intention to treat analysis and other bias that is inevitably in cohort studies. However, we have summarized the best available data on the subject. Further studies on this subject are necessary, but a large randomized controlled trial is unlikely to be performed in the near future.

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Disclosure of interests
No relevant financial, personal, political, intellectual or religious interests were disclosed.

Contribution to authorship
LB is the first and main author of the manuscript. LM was the second reviewer; she independently screened titles and abstracts of dentified studies and independently performed the data extraction using the data extraction form and contributed an essential part to the writing of the manuscript. HS participated as the third independent reviewer when disagreement occured and contributed to the writing of the manuscript. JS, JN and BM contributed to the writing of the manuscript and to the methodology and statistic co-analysis.

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References

5. LVR data (nationwide perinatal database in The Netherlands)
Preterm Breech Presentation: A Comparison of Intended Vaginal and Intended Cesarean Delivery
Abstract

Objective: To study the association of the intended mode of delivery and perinatal morbidity and mortality among breech fetuses who are delivered preterm.

Methods: We conducted a nationwide cohort study of women with a singleton pregnancy in breech presentation who delivered preterm (26+0 – 36+6 weeks of gestation) in the years 2000-2011. We compared perinatal outcomes according to the intended and actual mode of delivery using multivariate logistic regression analysis. We performed subgroup analyses of gestational age and parity.

Results: We studied 8,356 women with a preterm singleton breech delivery. Intended cesarean delivery (n=1,935) was not associated with a significant reduction in perinatal mortality compared to intended vaginal delivery (n=6,421) (1.3% versus 1.5%, (aOR 0.97; 95% CI 0.60-1.57)). However, the composite of perinatal mortality and morbidity was significantly reduced in the intended cesarean delivery group (8.7% versus 10.4% (aOR 0.77; 95% CI 0.63-0.93). In the sub-group of women delivering at 28-32 weeks, intended caesarean delivery was associated with a 1.7% risk of perinatal mortality, compared to 4.1% with intended vaginal delivery (aOR 0.27; 95% CI 0.10-0.77) and significantly reduced composite mortality and severe morbidity from, 5.9% compared to 10.1% (aOR 0.37; 95% CI 0.20-0.68).

Conclusions: In women delivering a preterm breech fetus, cesarean delivery is associated with reduced perinatal mortality and morbidity.

Introduction

The incidence of breech presentation varies according to gestational age, with an incidence of 25% at 26 weeks, 15% at 32 weeks, declining to 3 to 4% in term pregnancy. [1] The Term Breech Trial showed that intended cesarean delivery is safer in terms of combined short term morbidity and mortality for term breech presentation. This has led to a worldwide shift towards an intended caesarean delivery, which has been associated with a sustained reduction of neonatal mortality and morbidity in the Netherlands. [3] Unfortunately, knowledge on the optimal mode of delivery in case of preterm breech presentation is limited, while the incidence of breech presentation in these women is much higher. [4-12]

Too few women have been enrolled in randomized trials of mode of delivery of the preterm breech fetus to draw meaningful conclusions about the optimal intended mode of delivery. [13-18] Therefore, the aim of the present study was to evaluate the association of intended mode of delivery and perinatal mortality and morbidity in a large national cohort of women who delivered preterm breech fetuses.

Materials and Methods

This retrospective cohort study was performed using data from the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 28 days after birth. The PRN database is obtained by a validated linkage of three different registries: the midwife registry (LVR 1), the obstetricians registry (LVR 2) and the neonatology registry (LNR) of hospital admissions of newborn infants. [19]

The coverage of the PRN is approximately 96% of all deliveries in the Netherlands and currently includes over 1.9 million records derived from deliveries in the last decade.

All PRN data are voluntarily recorded by the caregivers during prenatal care, delivery, and the neonatal period. The data are annually sent to the national registry office, where a number of range and consistency checks are conducted. Institutional review board approval was not necessary since the data were used anonymous, thus exempting ethics approval in the Netherlands.

From this database, we identified all women who delivered a singleton fetus in breech presentation between 26+0 and 36+6 weeks of gestation in the period 2000 and 2011. Exclusion criteria were (lethal) congenital abnormalities, antepartum stillbirth, placental abruption (antenatally), unknown gestational age, small for gestational age.
problems that unequivocally were not associated with the mode of delivery. To do so, we obtained permission of the PRN to approach gynaecologists to study the case(s) of perinatal death that took place in their hospital. We asked the obstetricians to check the maternal and neonatal chart of the concerning case(s) and asked them to fill in a form on the exact data of the mode of delivery and the cause of perinatal death. We excluded cases of perinatal death if either the neonatal chart was lacking or if data were not complete enough to allow appropriate judgement.

Secondary perinatal outcome was a composite outcome of perinatal mortality and morbidity, in which morbidity was defined as 5-minute Apgar-score <7, birth trauma (facial nerve paralysis, cephalo hemaetoma, brachial plexus injuries, clavicle fracture, humerus fracture and asphyxia related morbidity (intra-ventricular haemorrhage, IRDS, hypoxic-ischemic encefalopathy, neonatal hypotonia, cerebral ischemia and neonatal seizures). Finally, we analysed a composite measure of perinatal mortality and severe morbidity, in which severe morbidity was defined as asphyxia related morbidity, intra-ventricular haemorrhage, IRDS, hypoxic-ischemic encefalopathy, cerebral ischemia and neonatal seizures.

We compared intrapartum and neonatal mortality and morbidity according to intended mode of delivery: i.e., women who delivered by intended cesarean compared with women who delivered vaginally or after an emergency cesarean delivery. Subsequently, we repeated this analysis for the actual mode of delivery: vaginal delivery, intended cesarean delivery and emergency cesarean delivery.

Analysis was done for the total study group and then separately for different subgroups of gestational age (26+0 to 27+6 weeks, 28+0 to 31+6 weeks and 32+0 to 36+6 weeks). We performed a logistic regression analysis with women who delivered vaginally as reference group. First, we calculated an unadjusted odds ratio. Subsequently, we adjusted the risk estimates in a logistic regression analysis (enter method) to show the association of level of care in relation to other factors with neonatal outcomes. The 95% confidence intervals (CI) were estimated to determine the precision of each odds ratio. We adjusted for the following confounders: nulliparity, gestational age (weeks), ethnicity, prolonged rupture of membranes (≥ 24 hours), birth weight and delivery in a secondary or a tertiary hospital.

To visualize the outcomes by week of gestation moving average was used. Because of the rare outcome a moving average is used, this means that for each week of gestation the two adjacent weeks (one week before and one week after the week in question) are combined and an average outcome is calculated for these three weeks together. In a subgroup analysis we assessed nulliparous and parous women separately as the mechanics of vaginal breech delivery might be different in nulliparous and in parous women.

(defined as a birth weight below the 10th percentile), maternal hypertension (defined as DBP ≥ 95 mmHg), gestational and type 1 or 2 diabetes and preeclampsia (defined as hypertension with proteinuria). We excluded women with severe maternal co-morbidity as the cesarean section might have been performed for another reason than the breech presentation. We excluded women who delivered before 26+0 weeks of gestation because in the time period under study babies born in this time frame did not in general receive resuscitative care. Specific management data including the use of tocolytic medication, fetal lung maturation with corticosteroids, antibiotic treatment and antenatal transfer to a third level care facility were not available from the database. According to the national guidelines then in effect, tocolytics (atosiban or nifedipine) and antenatal corticosteroids to enhance fetal lung maturity were recommended from 25+0 till 33+6 weeks of gestation for a period of 48 hours in women with symptoms of threatened preterm birth, but magnesium sulphate for fetal neuroprotection was not. Women in the study were treated according to these national guidelines.

Threatened preterm birth is defined as preterm contractions combined with dilatation or cervical length shortening below 25 mm, or preterm premature rupture of membranes (PPROM). Women at risk for preterm delivery before 32 weeks of gestation are referred to tertiary centres that are equipped with Neonatal Intensive Care Units (NICU). After 32 weeks delivery typically occurred in a general hospital (secondary care). Preterm breech delivery is considered as a high risk delivery in the Netherlands and always takes place in hospital setting with a responsible obstetrician.

During the study period, the decision for intended cesarean delivery or intended vaginal delivery in preterm breech presentation was made by the pregnant woman and her responsible obstetrician. In line with Dutch guidelines, women were often counselled towards a vaginal delivery.

The actual mode of delivery was either by vaginal delivery, intended, or emergency cesarean delivery. The directions of the national database collection state that women who intend to deliver by cesarean delivery are registered as “intended caesarean section.” Thus, women who opted for a cesarean delivery were recorded as a intended cesarean delivery, even if the delivery took place when labour already started. Women who underwent an emergency (unplanned) cesarean delivery were assumed to have had an intention to deliver vaginally. The type of breech presentation was not registered in the database. The type of breech, however, generally did not influence the mode of delivery decision.

The primary outcome of the present study was intrapartum and neonatal mortality defined as fetal death during labor and neonatal death within the first 28 days after birth. We reviewed every perinatal death on case-level to ensure that the perinatal death was not caused by other factors such as congenital abnormalities or other
Results

Of the 146,885 women who delivered preterm in the Netherlands between 2000 and 2011, 23,303 (16%) had a fetus in breech presentation. After exclusions, 8,356 women were included in the study cohort (Figure 1 and Table 1). In the overall study cohort, perinatal mortality was not significantly different for intended cesarean delivery and intended vaginal delivery after adjustment for parity, gestational age, delivery in a tertiary hospital, PPROM, birth weight and ethnicity (aOR 0.97; 95% CI 0.60-1.57). In the analysis according to subgroups of gestational age, perinatal mortality was significantly lower in the intended cesarean delivery subgroup of gestational age 28-32 weeks (aOR 0.27; 95% CI 0.10-0.77).

In the whole study population, composite perinatal mortality and morbidity occurred significantly less in intended cesarean delivery compared to vaginal delivery (aOR 0.77; 95% CI 0.63-0.93) and in the gestational age subgroups of 26-28 weeks (aOR 0.57; 95% CI 0.33-0.99) and 28-32 weeks (aOR 0.58; 95% CI 0.41-0.83).

In the subgroup analysis for parity, testing for interaction between parity and mode of (breech) delivery showed a statistically non-significant interaction (p= 0.64). In the whole study population composite perinatal mortality and morbidity in nulliparous women was significantly lower in the intended cesarean delivery group as compared to intended vaginal delivery group (OR 0.71; 95% CI 0.54-0.93). Subgroup analysis of gestational age 28-32 weeks of composite mortality and severe morbidity in nulliparous women showed the same trend (OR 0.39; 95% CI 0.16-1.00). All other outcomes according to parity were not statistically different (Table 3).

Table 4 shows the data on perinatal mortality and morbidity according to the actual mode of delivery. The overall perinatal mortality was 2.3% (79 of 3,426) in women who delivered vaginally, 1.3% (26 of 1,935) in women who delivered by intended cesarean delivery while for emergency cesarean delivery the overall neonatal mortality was 0.63% (19 of 2,995).

Perinatal mortality was significantly lower in emergency cesarean delivery for the whole study group (aOR 0.47; 95% CI 0.28-0.79). In the subgroups by gestational age there was a similar trend but differences were not statistically different (26-28 weeks; aOR 0.43; 95% CI 0.18-1.01); (28-32 weeks (aOR 0.48; 95% CI 0.21-1.13)); (32-37 weeks (aOR 0.45; 95% CI 0.16-1.29)).

Emergency cesarean delivery was not associated with a reduced risk of composite perinatal mortality and severe morbidity as compared to vaginal delivery (aOR 0.76; 95% CI 0.58-0.99) for the whole study-group. This applied also for the subgroup of 32-37 weeks of gestation favouring emergency cesarean delivery (aOR 0.76; 95% CI 0.58-0.99).

Figure 2 shows the moving average on perinatal mortality according to the intended mode of delivery. Before 32 weeks of gestation the risk of perinatal mortality is higher among women with a intended vaginal delivery. After 32 weeks of gestation, the perinatal mortality risk between the two groups become comparable. Figure 3 shows moving average on perinatal mortality according to the actual mode of delivery. Perinatal mortality is low among very preterm infants (31 weeks of gestation) delivered by emergency cesarean delivery.
### Table 1 Characteristics of preterm singleton births with a fetus in breech presentation in The Netherlands from 2000-2010 according to the mode of delivery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Intended Cesarean Delivery</th>
<th>Intended Vaginal Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population, N, %</td>
<td>1935 (23.2%)</td>
<td>6421 (76.8%)</td>
</tr>
<tr>
<td>Number of previous deliveries, 0, n (%)</td>
<td>1049 (54.2%)</td>
<td>4018 (62.2%)</td>
</tr>
<tr>
<td>≥1, n (%)</td>
<td>886 (45.8%)</td>
<td>2403 (37.4%)</td>
</tr>
<tr>
<td>Maternal age, &lt;25 years, n (%)</td>
<td>172 (8.9%)</td>
<td>707 (11.0%)</td>
</tr>
<tr>
<td>25-29 years, n (%)</td>
<td>513 (26.5%)</td>
<td>2403 (37.4%)</td>
</tr>
<tr>
<td>30-34 years, n (%)</td>
<td>884 (45.7%)</td>
<td>2879 (44.8%)</td>
</tr>
<tr>
<td>35 years, n (%)</td>
<td>366 (18.9%)</td>
<td>900 (14.1%)</td>
</tr>
<tr>
<td>Ethnicity, Caucasian, n (%)</td>
<td>1673 (86.5%)</td>
<td>5620 (87.5%)</td>
</tr>
<tr>
<td>Non-Caucasian, n (%)</td>
<td>262 (13.5%)</td>
<td>801 (12.5%)</td>
</tr>
<tr>
<td>Socio-economic status, High/middle, n (%)</td>
<td>1436 (74.2%)</td>
<td>4949 (77.1%)</td>
</tr>
<tr>
<td>Low, n (%)</td>
<td>499 (25.8%)</td>
<td>1472 (22.9%)</td>
</tr>
<tr>
<td>Birth weight, mean (±SD) grams</td>
<td>2219 (±720)</td>
<td>2312 (±588)</td>
</tr>
<tr>
<td>Gestational age in days, mean (±SD)</td>
<td>238 (±18)</td>
<td>240 (±18)</td>
</tr>
<tr>
<td>Female fetal sex, n (%)</td>
<td>1099 (56.8%)</td>
<td>3086 (48.1%)</td>
</tr>
<tr>
<td>Male Fetal sex, n (%)</td>
<td>836 (43.2%)</td>
<td>3335 (51.9%)</td>
</tr>
<tr>
<td>Antenatal Corticosteroids, Yes, n (%)</td>
<td>115 (5.9%)</td>
<td>978 (50.6%)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>978 (50.6%)</td>
<td>3165 (49.3%)</td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>842 (43.5%)</td>
<td>2896 (45.2%)</td>
</tr>
<tr>
<td>Gestational age, 26-27+6 weeks, n (%)</td>
<td>76 (3%)</td>
<td>319 (5.0%)</td>
</tr>
<tr>
<td>28+0-31+6 weeks, n (%)</td>
<td>290 (15.0%)</td>
<td>806 (12.8%)</td>
</tr>
<tr>
<td>32-36+6 weeks, n (%)</td>
<td>1569 (81.1%)</td>
<td>5286 (82.4%)</td>
</tr>
<tr>
<td>PPROM, Yes, &gt; 24 hours, n (%)</td>
<td>206 (10.4%)</td>
<td>1245 (19.7%)</td>
</tr>
<tr>
<td>No, &gt;24 hours, n (%)</td>
<td>1739 (89.4%)</td>
<td>5240 (80.3%)</td>
</tr>
<tr>
<td>Location of delivery NICU hospital, n (%)</td>
<td>601 (31.1%)</td>
<td>1558 (24.7%)</td>
</tr>
<tr>
<td>General hospital, n (%)</td>
<td>1334 (68.9%)</td>
<td>4863 (75.2%)</td>
</tr>
<tr>
<td>Previous CS, Yes, n (%)</td>
<td>300 (15.5%)</td>
<td>519 (8.1%)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>1635 (84.5%)</td>
<td>5502 (91.9%)</td>
</tr>
<tr>
<td>Reason for intrapartum CS - No intrapartum CS</td>
<td>1889 (97.6%)</td>
<td>2440 (38.2%)</td>
</tr>
<tr>
<td>- Fetal distress</td>
<td>27 (1.4%)</td>
<td>777 (12.3%)</td>
</tr>
<tr>
<td>- Failure to progress</td>
<td>0</td>
<td>824 (12.9%)</td>
</tr>
<tr>
<td>- Fetal distress and FTP</td>
<td>0</td>
<td>177 (2.9%)</td>
</tr>
<tr>
<td>- other reasons</td>
<td>19 (1.0%)</td>
<td>2203 (34.7%)</td>
</tr>
</tbody>
</table>

### Table 2 Neonatal Morbidity and Perinatal Mortality According to the Intended Mode of Delivery in Preterm Breech Presentation

<table>
<thead>
<tr>
<th>Intended Mode of Delivery</th>
<th>Perinatal Mortality</th>
<th>Composite Mortality and Morbidity</th>
<th>Composite Mortality and Severe Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (26-36 weeks)</td>
<td>26/1935 (1.3%)</td>
<td>98/1935 (5.2%)</td>
<td>66/1935 (3.4%)</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>26/1935 (1.3%)</td>
<td>98/1935 (5.2%)</td>
<td>66/1935 (3.4%)</td>
</tr>
<tr>
<td>Composite mortality and morbidity</td>
<td>26/1935 (1.3%)</td>
<td>98/1935 (5.2%)</td>
<td>66/1935 (3.4%)</td>
</tr>
<tr>
<td>Composite mortality and severe morbidity</td>
<td>26/1935 (1.3%)</td>
<td>98/1935 (5.2%)</td>
<td>66/1935 (3.4%)</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval. Adjusted for: nulliparity, gestational age (weeks), NICU center, prolonged rupture of membranes (≥24 hours), birth weight (grams) and ethnicity.
Table 3 Neonatal Morbidity and Perinatal Mortality According to the Intended Mode of Delivery in Preterm Breech Presentation According to Parity

<table>
<thead>
<tr>
<th>Intended Cesarean Delivery</th>
<th>Intended Vaginal Delivery (Vaginal Delivery + Emergency Cesarean Delivery)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI) *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall (26-36 weeks), n</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality nulliparous, n (%)</td>
<td>15/1177 (1.3%)</td>
<td>57/4239 (1.3%)</td>
<td>0.95 (0.53-1.68)</td>
</tr>
<tr>
<td>Perinatal mortality parous, n (%)</td>
<td>11/758 (1.5%)</td>
<td>41/2182 (1.9%)</td>
<td>0.77 (0.39-1.55)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity nulliparous, n (%)</td>
<td>87/1177 (7.4%)</td>
<td>389/4239 (9.2%)</td>
<td>0.79 (0.62-1.01)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity parous, n (%)</td>
<td>82/758 (10.8%)</td>
<td>279/2182 (12.8%)</td>
<td>0.83 (0.64-1.08)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity nulliparous, n (%)</td>
<td>30/1177 (2.5%)</td>
<td>147/4239 (3.5%)</td>
<td>0.73 (0.49-1.08)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity parous, n (%)</td>
<td>32/758 (4.2%)</td>
<td>117/2182 (5.4%)</td>
<td>0.78 (0.52-1.16)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>26+0-27+6 weeks, n</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal mortality nulliparous, n (%)</td>
<td>8/40 (20.0%)</td>
<td>33/175 (18.9%)</td>
<td>1.08 (0.45-0.82)</td>
</tr>
<tr>
<td>Perinatal mortality parous, n (%)</td>
<td>7/36 (19.4%)</td>
<td>15/144 (10.4%)</td>
<td>2.08 (0.78-5.55)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity nulliparous, n (%)</td>
<td>16/40 (40%)</td>
<td>86/175 (49%)</td>
<td>0.69 (0.34-1.39)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity parous, n (%)</td>
<td>13/36 (35.6%)</td>
<td>63/144 (43.8%)</td>
<td>0.97 (0.26-3.42)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity nulliparous, n (%)</td>
<td>10/40 (25%)</td>
<td>50/175 (28.6%)</td>
<td>0.83 (0.38-1.83)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity parous, n (%)</td>
<td>8/36 (22.2%)</td>
<td>28/144 (19.4%)</td>
<td>1.18 (0.49-2.88)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>28+0-31+6 weeks, n</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Perinatal mortality nulliparous, n (%)</td>
<td>3/159 (1.9%)</td>
<td>14/471 (3.0%)</td>
<td>0.63 (0.18-2.21)</td>
</tr>
<tr>
<td>Perinatal mortality parous, n (%)</td>
<td>2/131 (1.5%)</td>
<td>19/335 (5.7%)</td>
<td>0.26 (0.06-1.12)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity nulliparous, n (%)</td>
<td>34/159 (21.3%)</td>
<td>119/471 (25.3%)</td>
<td>0.81 (0.52-1.24)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity parous, n (%)</td>
<td>28/131 (21.4%)</td>
<td>95/335 (28.4%)</td>
<td>0.81 (0.52-1.32)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity nulliparous, n (%)</td>
<td>8/159 (5.0%)</td>
<td>40/471 (8.5%)</td>
<td>0.57 (0.26-1.25)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity parous, n (%)</td>
<td>9/131 (6.9%)</td>
<td>41/335 (12.2%)</td>
<td>0.53 (0.25-1.12)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>32+0-36+6 weeks, n</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal mortality nulliparous, n (%)</td>
<td>4/978 (0.4%)</td>
<td>10/3593 (0.3%)</td>
<td>1.47 (0.46-4.70)</td>
</tr>
<tr>
<td>Perinatal mortality parous, n (%)</td>
<td>2/591 (0.3%)</td>
<td>7/1703 (0.4%)</td>
<td>0.82 (0.17-3.97)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity nulliparous, n (%)</td>
<td>37/978 (3.8%)</td>
<td>184/3593 (5.1%)</td>
<td>0.73 (0.51-1.05)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity parous, n (%)</td>
<td>43/591 (7.3%)</td>
<td>121/1703 (7.1%)</td>
<td>1.01 (0.72-1.47)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity nulliparous, n (%)</td>
<td>12/978 (1.2%)</td>
<td>57/3593 (1.6%)</td>
<td>0.77 (0.41-1.44)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity parous, n (%)</td>
<td>15/591 (2.5%)</td>
<td>48/1703 (2.8%)</td>
<td>0.90 (0.50-1.62)</td>
</tr>
</tbody>
</table>

*Adjusted for: NICU center, gestational age (weeks), prolonged rupture of membranes (≥24 hours), birth weight (grams) and ethnicity.
## Table 4  Neonatal Morbidity and Perinatal Mortality in Preterm Singleton Births
With a Breech Presentation in Subgroups of Gestational Age According to the Actual Mode of Delivery

<table>
<thead>
<tr>
<th></th>
<th>Intended Cesarean Delivery</th>
<th>Vaginal Delivery</th>
<th>Emergency Cesarean Delivery</th>
<th>OR (unadjusted) 95%CI</th>
<th>OR (unadjusted) 95%CI</th>
<th>OR (Adjusted 95%CI)*</th>
<th>OR (Adjusted 95%CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (26-36 weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, n (%)</td>
<td>26/1935 (1.3%)</td>
<td>79/3426 (2.3%)</td>
<td>19/2995 (0.6%)</td>
<td>0.58 (0.37–0.90)</td>
<td>0.27 (0.16–0.45)</td>
<td>0.79 (0.48–1.30)</td>
<td>0.47 (0.28–0.79)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity, n (%)</td>
<td>169/1935 (8.7%)</td>
<td>419/3426 (12.2%)</td>
<td>249/2995 (8.3%)</td>
<td>0.63 (0.52–0.77)</td>
<td>0.65 (0.55–0.77)</td>
<td>0.74 (0.60–0.92)</td>
<td>0.93 (0.77–1.11)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity, n (%)</td>
<td>62/1935 (3.2%)</td>
<td>180/3426 (5.3%)</td>
<td>84/2995 (2.8%)</td>
<td>0.60 (0.44–0.80)</td>
<td>0.52 (0.40–0.68)</td>
<td>0.69 (0.50–0.84)</td>
<td>0.76 (0.58–0.99)</td>
</tr>
<tr>
<td>26+0-27+6 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, n (%)</td>
<td>15/76 (19.7%)</td>
<td>41/234 (17.5%)</td>
<td>7/85 (8.2%)</td>
<td>1.16 (0.60–2.24)</td>
<td>0.42 (0.18–0.98)</td>
<td>0.95 (0.46–1.96)</td>
<td>0.43 (0.18–1.01)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity, n (%)</td>
<td>27/76 (35.5%)</td>
<td>107/234 (45.7%)</td>
<td>42/85 (49.4%)</td>
<td>0.65 (0.38–1.12)</td>
<td>1.16 (0.71–1.91)</td>
<td>0.59 (0.33–1.04)</td>
<td>1.15 (0.69–1.92)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity, n (%)</td>
<td>18/76 (23.7%)</td>
<td>64/234 (27.4%)</td>
<td>14/85 (16.5%)</td>
<td>0.82 (0.45–1.51)</td>
<td>0.52 (0.28–0.99)</td>
<td>0.72 (0.37–1.39)</td>
<td>0.51 (0.26–0.99)</td>
</tr>
<tr>
<td>28+0-31+6 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, n (%)</td>
<td>5/290 (1.7%)</td>
<td>26/528 (4.9%)</td>
<td>7/278 (2.5%)</td>
<td>0.34 (0.13–0.89)</td>
<td>0.50 (0.21–1.16)</td>
<td>0.22 (0.08–0.64)</td>
<td>0.48 (0.21–1.13)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity, n (%)</td>
<td>62/290 (21.4%)</td>
<td>134/528 (25.4%)</td>
<td>80/278 (28.8%)</td>
<td>0.80 (0.57–1.11)</td>
<td>1.19 (0.86–1.65)</td>
<td>0.62 (0.42–0.90)</td>
<td>1.18 (0.85–1.63)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity, n (%)</td>
<td>17/290 (5.9%)</td>
<td>58/528 (11.0%)</td>
<td>23/278 (8.3%)</td>
<td>0.51 (0.29–0.88)</td>
<td>0.73 (0.44–1.21)</td>
<td>0.33 (0.18–0.62)</td>
<td>0.71 (0.43–1.19)</td>
</tr>
<tr>
<td>32+0-36+6 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, n (%)</td>
<td>6/1569 (0.4%)</td>
<td>12/2664 (0.5%)</td>
<td>5/2632 (0.2%)</td>
<td>0.85 (0.32–2.27)</td>
<td>0.42 (0.15–1.20)</td>
<td>0.81 (0.30–2.21)</td>
<td>0.45 (0.16–1.29)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity, n (%)</td>
<td>80/1569 (5.1%)</td>
<td>178/2664 (6.7%)</td>
<td>127/2632 (4.8%)</td>
<td>0.75 (0.57–0.98)</td>
<td>0.71 (0.56–0.90)</td>
<td>0.69 (0.52–0.91)</td>
<td>0.77 (0.61–0.98)</td>
</tr>
<tr>
<td>Composite mortality &amp; severe morbidity, n (%)</td>
<td>27/1569 (1.7%)</td>
<td>58/2664 (2.2%)</td>
<td>47/2632 (1.8%)</td>
<td>0.79 (0.50–1.25)</td>
<td>0.82 (0.55–1.21)</td>
<td>0.74 (0.46–1.18)</td>
<td>0.89 (0.60–1.18)</td>
</tr>
</tbody>
</table>

* Adjusted for: nulliparity, gestational age (weeks), hospital equipped NICU center, prolonged rupture of membranes (≥24 hours), birth weight (grams) and ethnicity.
Discussion

This population-based cohort study shows that in women with a preterm breech presentation, intended cesarean delivery is associated with reduced perinatal mortality and morbidity as compared to intended vaginal delivery. In the sub-group of women delivering at 28-32 weeks, intended caesarean delivery was associated with a 1.7% risk of perinatal mortality, compared to 4.1% with intended vaginal delivery (aOR 0.27; 95% CI 0.10-0.77). Analysis according to actual mode of delivery showed that emergency cesarean delivery was associated with the highest reduction in perinatal mortality and morbidity.

The main and important strength of our study is that we report on a very large cohort of women with an intended vaginal preterm breech delivery and analyse outcomes by intended mode of delivery in addition to actual mode of delivery. We found this important, as the intended vaginal delivery group then getting an emergency cesarean delivery had better outcomes than the intended cesarean delivery group. This may indicate selection bias in this non-randomised study in favour of the group with intended vaginal delivery.

Obstetric practice in the Netherlands is likely to differ from practice in for example the US. For instance in the US more often active management will be performed in babies born at very early gestational ages. We excluded women delivering below a gestational age of 26 weeks from our analysis. Otherwise, we think that active management in terms of steroids, antibiotics and NICU facilities between the US and the Netherlands will be comparable. Routine use of magnesium sulphate for neuroprotection was only introduced after our study period, but this is unlikely to interfere with our outcome measures. The relatively high vaginal delivery rate in The Netherlands gave us the unique opportunity to study the effect of the mode of delivery in preterm breech delivery. Obviously, the impact of our study on current Dutch practice will be strong, whereas our findings will probably more or less confirm current US policy.

Overall, in terms of perinatal mortality and morbidity the results of this study correspond with the findings of most smaller cohort studies that were summarized in our recent review ([20]). The current study is based on a larger number of women who delivered vaginally, thus increasing the power of our findings. A potential disadvantage of cesarean delivery in women with threatened preterm labor is timing of the delivery. Obviously, when vaginal delivery occurs further delay of pregnancy was either not indicated or not possible. In cesarean delivery, however, one is not sure whether the preterm birth would actually occur. As our dataset only registered the exact moment of delivery, we could not correct for the potential advantage of a further delay of pregnancy with some days. This might explain why the emergency cesarean had the...
most favourable neonatal outcome in the analysis according to actual mode of delivery.

All studies concerning preterm breech presentation and perinatal mortality and morbidity according to the mode of delivery are pointing in the same direction: cesarean delivery reduces perinatal mortality and morbidity compared to vaginal delivery. However, the treatment effect seems smaller than has been found after the randomized controlled trial for term breech delivery. Ideally, the exact treatment effect would be assessed by a large RCT. A (new) RCT will however face the same problem in recruiting women as the RCT’s published until now. Consequently, in absence or expectation of a large RCT, clinical decision-making should be based on the current best available evidence from large cohort studies such as ours. We therefore conclude that in women presenting with a preterm breech presentation cesarean delivery is associated with reduced perinatal mortality and morbidity. This information should be used in counselling of women and their families.

References

1) NVOG guideline “term breech pregnancy” www.nvog.nl/richtlijn
Subsequent pregnancy outcome after preterm breech delivery, a population based cohort study

Lester Bergenhenegouwen
Sabine Ensing
Anita Ravelli
Jelle Schaaf
Marjolein Kok
Ben Willem Mol

Accepted Journal Maternal-Fetal and Neonatal Medicine
**Abstract**

**Objective** To investigate the effect of the mode of delivery in women with preterm breech presentation on neonatal and maternal outcome in the subsequent pregnancy.

**Methods** Nationwide population based cohort study in the Netherlands of women with a preterm breech delivery and a subsequent delivery in the years 1999 to 2007. We compared planned caesarean section versus planned vaginal delivery for perinatal outcomes in both pregnancies.

**Results** We identified 1,543 women in the study period, of whom 259 (17%) women had a planned caesarean section and 1,284 (83%) women had a planned vaginal delivery in the first pregnancy. In the subsequent pregnancy, perinatal mortality was 1.1% (3/259) for women with a planned caesarean section in the first pregnancy and 0.5% (6/1284) for women with a planned vaginal delivery in the first pregnancy, (aOR 1.8; 95% CI 0.31-10.1). Composite adverse neonatal outcome was 2.3% (6/259) versus 1.5% (19/1284), (aOR 1.5; 95% CI 0.55-4.2). The average risk of perinatal mortality over two pregnancies was 1.9% (10/518) for planned caesarean section and 2.0% (51/2568) for planned vaginal delivery, (OR 0.98; 95% CI 0.49-1.9).

**Conclusion** In women with a preterm breech delivery planned caesarean section does not reduce perinatal mortality, perinatal morbidity or maternal morbidity rate over the course of two pregnancies.

**Keywords** Subsequent pregnancy, neonatal morbidity and mortality, maternal morbidity and mortality, preterm breech presentation, caesarean section

**Introduction**

Breech presentation occurs in 3-4% of all term pregnancies, but it occurs more frequently in preterm delivery [1]. In term breech presentation, the Term Breech Trial [2] reported a decrease in poor perinatal outcome in case of an elective caesarean delivery compared to a trial of labour (1.6 vs. 5.5%, RR 0.33; 95% CI 0.19-0.56). This finding was confirmed in a recent systematic review reporting on 27 studies that had studied more than 250,000 pregnancies, and in which perinatal mortality rates were 0.3% after planned vaginal delivery and 0.05% after elective caesarean delivery [3].

In a recent Dutch study, we confirmed the positive impact of planned caesarean section for term breech delivery, as the shift towards elective caesarean section resulted in a decrease of perinatal mortality and morbidity among women delivering a child in breech at term [4]. In the controversy on term breech delivery, it can be concluded that the risks of poor neonatal outcome after vaginal delivery are low, but can be improved by caesarean section, and that this information should be used in a process of counselling and shared decision making involving women with a child in breech position at term.

In case of preterm breech delivery, there is also controversy on the optimal mode of delivery. Randomized controlled trials failed to achieve the planned number of recruited women, thus leaving wide uncertainty among the estimates of treatment effect [5]. In the absence of adequately powered randomised clinical trials, the best available evidence has to be obtained from cohort studies. A recent review of cohort studies indicated a caesarean section to be safer for the fetus and reduces neonatal mortality as compared to vaginal delivery [6]. In addition, we recently studied perinatal outcome in preterm breech deliveries in The Netherlands in the years 2000-2011, a population of 8,356 women with an intended vaginal delivery rate of 77%. We concluded that in women delivering a preterm breech fetus, intended caesarean delivery is associated with reduced perinatal mortality and morbidity [7].

An important disadvantage of a caesarean section is its impact on future pregnancies: more women will have a scarred uterus in subsequent pregnancies with accompanying risks of complicated placentaion, uterine rupture and renewed caesarean section, resulting in maternal and fetal mortality and morbidity [8,9]. In a recent comparison among women with a baby in breech presentation at term, we studied a policy of elective caesarean delivery followed by repeat elective caesarean delivery as compared to intended vaginal delivery. We found that elective caesarean delivery resulted in the lowest perinatal mortality and morbidity rates when studied over two pregnancies [10].

The question of the impact of the mode of delivery in preterm breech delivery on the next pregnancy has by our knowledge not been addressed. Here, we report the
impact of mode of delivery in women with a preterm breech presentation on the outcome of the first and the subsequent pregnancy.

Methods

This study was performed using data from a retrospective national cohort registered in the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 28 days after birth.

The PRN database is obtained by a validated linkage of three different registries: the midwife registry (LVR 1), the obstetricians registry (LVR 2) and the neonatology registry (LNR) of hospital admissions of newborn infants. The coverage of the PRN is approximately 96% of all deliveries in the Netherlands and currently includes over 1.9 million records derived from deliveries in the last decade. All PRN data are recorded by the caregivers during prenatal care, delivery and the neonatal period. The data are annually sent to the national registry office, where a number of range and consistency checks are conducted.

In order to identify the second pregnancy of women who had a preterm breech delivery in their first pregnancy, we used a longitudinal linkage procedure. This was necessary, because the records that are included in the PRN registry are entered at the level of the child, and there is no unique maternal identifier available in the registry to follow-up on outcomes of the subsequent pregnancy of the same mother. Details of procedure for this longitudinal linkage method are described by Schaaf et al.

All nulliparous women with a singleton fetus in breech presentation who delivered preterm in the years 1999-2007, and had a subsequent pregnancy in the same period, were selected for the present study. Exclusion criteria were antepartum fetal death, a child with major congenital malformations, preeclampsia and fetal growth restriction (growth < P5).

We analysed the outcomes of the first pregnancy (from women delivering in preterm breech presentation) and the subsequent pregnancy in the same woman according to the intended mode of the first delivery. Outcome measures were perinatal mortality (defined as fetal death during labour and neonatal death within the first 28 days after birth) and neonatal morbidity, defined as a 5-minute Apgar score < 4 and birth trauma (which included intracerebral bleeding, cephalic hematoma, facial nerve paresis, brachial plexus lesion, fracture of clavicle, humerus or femur and other trauma). Adverse neonatal outcome was defined as a composite measure of mortality and morbidity.

Maternal outcome measures were maternal mortality and maternal morbidity. Maternal morbidity was defined as uterine rupture, postpartum haemorrhage (PPH >1000 ml, according to Dutch guidelines) and need for a blood transfusion. Adverse maternal outcome was defined as a composite measure of maternal mortality and morbidity.

Statistical Analysis

We compared the groups for the following baseline characteristics: gestational age at first delivery, maternal age, maternal ethnicity, socio-economic status and mean birth weight of the first child. We also reported inter pregnancy interval, gestational age and mean birth weight at subsequent delivery. We then calculated the incidence of adverse pregnancy outcomes in the index and the subsequent pregnancy for both groups. As outcomes of the index pregnancy have been presented previously, we report here on the subsequent pregnancy and of the two pregnancies combined. Odds ratios and their 95% confidence interval (CI) were calculated for these outcomes. We also performed multivariate analysis, in which we adjusted for maternal age, gestational age (first pregnancy), mode of delivery, birth weight of the first child and interpregnancy interval. To assess the combined outcome of the index pregnancy and the subsequent pregnancy we calculated the average neonatal and maternal composite outcome scores over the two pregnancies. Also, we described every case of perinatal death in the subsequent pregnancy on case-level.

Furthermore, we performed a sensitivity analysis in which we excluded women with pre-eclampsia or severe growth restriction (IUGR <P5) in the subsequent pregnancy. To mimic a scenario, in which women who had had a caesarean delivery in the first pregnancy always delivered by caesarean section in the second pregnancy, we did a sensitivity analysis in which all women with a trial of labour after a caesarean section in the first pregnancy were excluded. Data were analysed using SAS statistical software package version 9.2 (SAS Institute Inc, Cary, NC, USA).

Results

There were 272,551 women who delivered during the study period and of whom the outcome of the first and the second pregnancy could be linked. Of these, 271,008 were excluded: 258,013 because these women did not have a preterm breech delivery in their first pregnancy, 7,480 women because of a multiple pregnancy, 4,730 women...
because their child had severe congenital abnormalities, 203 women because of fetal death before onset of labour and 582 for preeclampsia or severe fetal growth restriction in the first pregnancy. Thus, we were able to include 1,543 women in this study, 259 of whom had a planned caesarean section and 1,284 of whom had a planned vaginal delivery.

Baseline characteristics are summarized in table 1. There were no significant or clinically relevant differences between the two groups. Median gestational age at first delivery was 34.5 weeks for both planned caesarean section and planned vaginal delivery (p=0.94), and mean maternal age was 29.2 versus 28.9 years for planned caesarean section and planned vaginal delivery, respectively (p=0.23). Also, mean interval to the second pregnancy (30.5 versus 31.0 months) as well as characteristics of the second pregnancy were comparable.

All 259 women in the planned caesarean section group had a caesarean section. In the planned vaginal delivery group, 740 out of the 1,284 (58%) women had a vaginal delivery, while 544 women had a planned caesarean delivery. Perinatal mortality in the index pregnancy was 38.2 (2.2) (p=0.55) versus 28.9 (3.8) (p=0.22) for planned caesarean section and planned vaginal delivery, respectively.

Table 1. Baseline characteristics of the cohort of preterm breech deliveries and subsequent pregnancy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Planned Caesarean Section N = 259</th>
<th>Planned Vaginal Delivery N = 1,284</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean maternal age at first delivery in years (SD)</td>
<td>29.2 (4.2)</td>
<td>28.9 (3.8)</td>
<td>0.23</td>
</tr>
<tr>
<td>Median gestational age at first delivery in weeks (SD)</td>
<td>34.5 (2.7)</td>
<td>34.5 (2.4)</td>
<td>0.94</td>
</tr>
<tr>
<td>Mean birth weight first baby in grams (SD)</td>
<td>2332 (677)</td>
<td>2380 (565)</td>
<td>0.22</td>
</tr>
<tr>
<td>Western ethnicity, n (%)</td>
<td>247 (95.4%)</td>
<td>1202 (93.5%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Low socio-economic status, n (%)</td>
<td>46 (17.8%)</td>
<td>228 (17.8%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Median interval to subsequent pregnancy in months (SD)</td>
<td>30.5 (13.8)</td>
<td>31.0 (13.7)</td>
<td>0.55</td>
</tr>
<tr>
<td>Mean maternal age at second delivery in years (SD)</td>
<td>31.8 (4.1)</td>
<td>31.5 (3.9)</td>
<td>0.33</td>
</tr>
<tr>
<td>Median gestational age at second delivery in weeks (SD)</td>
<td>38.5 (2.5)</td>
<td>38.2 (2.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Mean birth weight second baby in grams (SD)</td>
<td>3213 (680)</td>
<td>3193 (579)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

The outcomes of the subsequent pregnancy according to the intended mode of delivery in the first pregnancy are summarized in table 2. Caesarean section rates were 39% (100/259) versus 19% (244/1284) (aOR 3.7, 95% CI 2.5-5.5), respectively. Perinatal mortality was 1.1% (3/259) in women with a planned caesarean section in the index pregnancy versus 0.5% (6/1284) in women with a planned vaginal delivery in the index pregnancy (aOR 1.8, 95% CI 0.31-10.1). Composite adverse neonatal outcome in the second pregnancy was 2.3% (6/259) versus 1.5% (19/1284) (aOR 1.5; 95% CI 0.55-4.2). The risk of preterm birth (< 37 weeks of gestation) was 15.8% (41/259) versus 20.8% (267/1284) (aOR 0.49; 95% CI 0.29-0.84).

The rate of HPP > 1,000 ml in the subsequent pregnancy was 7.0% (18/259) in the planned caesarean section versus 5.4% (69/1284) in the planned vaginal delivery group (aOR 1.4; 95% CI 0.85-2.2), uterine rupture 0.4% (1/259) versus 0% respectively. Composite adverse maternal outcome in the second pregnancy was 7.3% (19/259) for planned caesarean section versus 5.4% (69/1284) for planned vaginal delivery (aOR 1.5; 95% CI 0.86-2.5). There were no cases of maternal mortality in both groups. There were nine women who suffered perinatal death in the subsequent pregnancy, four below 28 weeks, three between 30 and 37 weeks and two after delivery at term. Five baby’s died intrapartum and four neonatally. All six women who suffered perinatal death in the subsequent pregnancy after intended vaginal delivery in the index pregnancy, had an emergency caesarean section in the index pregnancy and a vaginal delivery in the subsequent pregnancy.

We performed a sensitivity analysis in which we excluded women with preeclampsia and women with a fetus with severe growth restriction (growth < P5) in the subsequent pregnancy in which we excluded 145 women (45 women in the planned caesarean section group and 100 women of the planned vaginal delivery group), leaving 1,398 for this analysis. The risk of preterm birth before 37 weeks was 14.5% for planned caesarean section versus 0.5% (6/1284) in women with a planned vaginal delivery in the index pregnancy (aOR 1.8; 95% CI 0.31-10.1). Composite adverse neonatal outcome in the second pregnancy was 2.3% (6/259) versus 1.5% (19/1284) (aOR 1.5; 95% CI 0.55-4.2). The risk of preterm birth (< 37 weeks of gestation) was 15.8% (41/259) versus 20.8% (267/1284) (aOR 0.49; 95% CI 0.29-0.84).

To mimic the scenario of “once a caesarean section always a caesarean” we also performed a subgroup analysis in which we excluded women with a trial of labour in the subsequent pregnancy after a caesarean delivery in the first pregnancy. To do so, we excluded 738 women (194 women in the planned caesarean section group and 544 in the planned vaginal delivery group). There were no cases of perinatal mortality or severe morbidity in the subsequent pregnancy in both groups.
Finally, we calculated the average maternal and neonatal composite outcome scores over the two pregnancies (Table 3). The average risk of perinatal mortality over two pregnancies was 1.9% (10/518) for planned caesarean section and 2.0% (51/2568) for planned vaginal delivery in the first pregnancy, (OR 0.98; 95% CI 0.49-1.9). The average risk of perinatal morbidity was 5.2% (27/518) in the planned caesarean section group and 5.4% (138/2568) in the planned vaginal delivery group (OR 0.97; 95% CI 0.64-1.5). The average risk of maternal morbidity was 5.4% (28/518) for planned caesarean section and 3.8% (97/2568) for planned vaginal delivery (OR 1.5; 95% CI 0.95-2.2).

Table 2 Outcome and complications in subsequent pregnancy after preterm breech delivery: according to the intended mode of delivery in the first pregnancy

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Planned caesarean section (N = 259)</th>
<th>Planned vaginal delivery (N = 1284)</th>
<th>Odds Ratio (95%CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CS</td>
<td>65 (25.1%)</td>
<td>123 (9.6%)</td>
<td>3.7 (2.5-5.5)</td>
</tr>
<tr>
<td>Spontaneous vaginal</td>
<td>132 (51%)</td>
<td>933 (72.7%)</td>
<td>0.36 (0.26-0.49)</td>
</tr>
<tr>
<td>Vacuum or forceps delivery</td>
<td>26 (10%)</td>
<td>101 (7.9%)</td>
<td>1.4 (0.87-2.2)</td>
</tr>
<tr>
<td>Breech extraction</td>
<td>1 (0.4%)</td>
<td>6 (0.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Emergency CS</td>
<td>35 (13.5%)</td>
<td>121 (9.4%)</td>
<td>1.4 (0.90-2.1)</td>
</tr>
</tbody>
</table>

Table 3 Neonatal and maternal outcomes of first and second pregnancy in nulliparous women with a preterm breech presentation in the first pregnancy

<table>
<thead>
<tr>
<th>Outcome first pregnancy</th>
<th>Planned CS in first pregnancy n, (%)</th>
<th>Planned VD in first pregnancy n, (%)</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of births</td>
<td>259</td>
<td>1284</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>7 (2.7%)</td>
<td>45 (3.5%)</td>
<td>0.76 (0.34-1.7)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity</td>
<td>21 (8.1%)</td>
<td>119 (9.3%)</td>
<td>0.86 (0.53-1.4)</td>
</tr>
<tr>
<td>Maternal morbidity</td>
<td>9 (3.5%)</td>
<td>28 (2.2%)</td>
<td>1.6 (0.75-3.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome first and second pregnancy</th>
<th>Planned CS in first and second pregnancy (n, %)</th>
<th>Planned VD in first and second pregnancy (n, %)</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of births</td>
<td>518</td>
<td>2568</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>10 (1.9%)</td>
<td>51 (2.0%)</td>
<td>0.98 (0.49-1.9)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity</td>
<td>27 (5.2%)</td>
<td>138 (5.4%)</td>
<td>0.97 (0.64-1.5)</td>
</tr>
<tr>
<td>Maternal morbidity</td>
<td>28 (5.4%)</td>
<td>97 (3.8%)</td>
<td>1.5 (0.95-2.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome first and second pregnancy (exclusion PE/IUGR second pregnancy)</th>
<th>Planned CS in first and second pregnancy (n, %)</th>
<th>Planned VD in first and second pregnancy (n, %)</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of births</td>
<td>473</td>
<td>2468</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>10 (2.1%)</td>
<td>51 (2.1%)</td>
<td>1.02 (0.52-2.0)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity</td>
<td>27 (5.7%)</td>
<td>138 (5.4%)</td>
<td>1.02 (0.67-1.6)</td>
</tr>
<tr>
<td>Maternal morbidity</td>
<td>28 (5.9%)</td>
<td>97 (3.9%)</td>
<td>1.5 (0.99-2.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome first and second pregnancy with exclusion of trial of labour</th>
<th>Planned CS in first and second pregnancy (n, %)</th>
<th>Planned VD in first and second pregnancy (n, %)</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of births</td>
<td>324</td>
<td>2024</td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>7 (2.2%)</td>
<td>45 (2.2%)</td>
<td>0.97 (0.43-2.2)</td>
</tr>
<tr>
<td>Composite mortality &amp; morbidity</td>
<td>22 (6.8%)</td>
<td>126 (6.2%)</td>
<td>1.1 (0.69-1.8)</td>
</tr>
<tr>
<td>Maternal morbidity</td>
<td>13 (4.0%)</td>
<td>62 (3.1%)</td>
<td>1.3 (0.72-2.4)</td>
</tr>
</tbody>
</table>
Discussion

We analysed the impact of mode of delivery in women with a preterm breech delivery on the first and subsequent pregnancy. Analysis was performed according to the intended mode of the first delivery: planned caesarean section versus planned vaginal delivery.

Perinatal mortality rates in the subsequent pregnancy were not significantly different for planned caesarean section as compared to planned vaginal delivery in the first pregnancy, and the same applied for neonatal and maternal morbidity rates. The risk of recurrent preterm delivery after 32 weeks was decreased in women with a planned caesarean section in the index pregnancy.

Strengths and limitations of our study

Our study is the first study that compares neonatal and maternal outcomes in the subsequent pregnancy after a pregnancy complicated by preterm breech presentation. An important strength of our study is that it reports on a large cohort of women with an intended vaginal breech delivery, which gave us the unique opportunity to study the effect of the mode of delivery in preterm breech presentation and the subsequent pregnancy.

We acknowledge that some of the outcomes that we used in this study (such as uterine rupture and maternal mortality) are rare, thus hampering the capacity of our study to find statistical significant differences for some outcomes. However, most outcomes of this study are not so rare and a sample size of 1,500 women generated sufficient power.

The decreased risk of recurrent preterm delivery after 32 weeks of gestation in women who delivered by planned caesarean section in their first pregnancy was even lower as might be expected. In view of an overall recurrence rate of preterm delivery of 20% [14] the recurrence rate of 15% among women who delivered preterm in breech presentation by planned caesarean section in our study is low.

An explanation for this lower incidence of recurrent preterm birth might be that because of the caesarean section in the first pregnancy there was less dilatation of the cervix whereby it remains stronger than in case of a vaginal delivery with full cervical dilatation. The combined adverse neonatal outcome and the combined adverse maternal outcome were not significantly different for both groups.

The caesarean section rate in the subsequent pregnancy in women with a planned vaginal delivery in the first pregnancy is 19%. This high percentage might be partly due to the 15% recurrence rate of breech presentation in the subsequent pregnancy and due to the relatively high emergency caesarean section rate in the first pregnancy.

The scenario “once a caesarean section, always a caesarean” in our study did not lead to an improved combined perinatal outcome of the first and subsequent pregnancy; although there were no perinatal deaths in the subsequent pregnancy in this scenario. An explanation might be that by excluding all women with a trial of labour, the number of women that remain for analysis in this scenario becomes too small to reach statistical significance.

Overall, the average risk of perinatal mortality, neonatal morbidity or maternal morbidity over the two pregnancies were not significantly different for both groups.

Based on the results of our present study we conclude that in nulliparous women with a preterm breech delivery in their first pregnancy, planned caesarean section does not lead to a significantly different average perinatal mortality, neonatal morbidity or maternal morbidity rate over the two pregnancies. This should be taken into account when counselling women on the mode of delivery in preterm breech presentation. The decision on the optimal mode of delivery should be a shared decision of the pregnant woman, her partner and the responsible obstetrician in which possible future pregnancies are also an important factor. The rates produced by this study might be helpful in such a process.

Declaration of interest

The authors report no declarations of interest.
References

Term breech deliveries in the Netherlands: did the increased cesarean rate affect neonatal outcome? A population based cohort study

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Abstract

Objective The aim of this study was to evaluate the effect of the increased cesarean rate for term breech presentation on neonatal outcome. We also investigate whether the clinical case selection for vaginal delivery applied by Dutch obstetricians led to an optimization of neonatal outcome, or if there is still room for improvement in terms of perinatal outcome.

Setting the Netherlands.

Population Singleton term breech deliveries from 37 0/7 to 41 6/7 weeks, excluding fetus with congenital malformations or antenatal death.

Method We used data from the Dutch national perinatal registry from 1999 up to 2007.

Main outcome measures Perinatal mortality and morbidity.

Result We studied 58,320 women with a term breech delivery. There was an increase in the elective cesarean rate (from 24% to 60%). As a consequence, overall perinatal mortality decreased (1.3 vs. 0.7‰; OR 0.51 (95% CI 0.28 – 0.93)), while it remained stable in the planned vaginal birth group (1.7 vs. 1.6‰; OR 0.96 (95% CI 0.52 – 1.76)). The number of cesareans to prevent one perinatal death was 338.

Conclusions Adjustment of the national guidelines after publication of the Term Breech Trial resulted in a shift towards elective cesarean and a decrease of perinatal mortality and morbidity among women delivering a child in breech at term. Still 40% of these women attempt vaginal birth. The relative safety of an elective cesarean should be weighed against the consequences of a scarred uterus in future pregnancies.

Introduction

The term breech trial was the largest randomized controlled trial to investigate the effect of mode of delivery for term breech deliveries on neonatal and maternal outcomes.¹ The study reported a highly significant decrease in combined perinatal mortality and morbidity scores among women undergoing a planned cesarean compared to those planned to deliver vaginally (5.0 vs. 16.0‰), RR 0.33; 95%CI 0.19-0.56). The relative benefit of a planned cesarean was strongest in countries with a perinatal mortality rate below 2.0% (57.0 vs. 4.0‰), RR 0.07; 95%CI 0.02-0.29). However, planned cesarean delivery was not associated with a reduction in risk of death or neurodevelopmental delay in children at 2 years of age.² The authors suggested that the fact that only 44% of children from the initial trial were investigated in the follow up may have limited of statistical power to detect differences at age 2. Maternal outcomes immediately postpartum and at 2 years were similar after planned cesarean section and planned vaginal birth for the singleton breech fetus at term.³,⁴

Publication of the term breech trial had a worldwide impact on clinical practice. An Australian population study reported an increase of elective cesarean rate for breech deliveries up to 76.6% and an overall cesarean rate of 96.3% in 2005.⁵ A Danish study reported an increase of overall cesarean rate up to 94.2% in 2008.⁶ Within the latter cohort, intrapartum and early neonatal mortality was reduced from 1.3‰ (1997 - 2000) to 0.5‰ in (2001 - 2008) (RR 0.38; 95%CI 0.15-0.98).

In the Netherlands, the overall cesarean rate increased from 50 to 78% within three months after publication of the term breech trial, mainly due to an increase of elective cesareans.⁷ This resulted in a significant decrease of neonatal death (OR 0.53; 95%CI 0.33-0.83) and neonatal trauma (OR 0.26, 95%CI 0.14-0.50) between 1998 and 2002. However, the most recent ‘Dutch report of perinatal care’ from 2008 showed that after the initial rise in elective cesareans, there was no further increase, and the overall cesarean rate remained stable at 80%.⁸

The difference in cesarean rate for term breech presentation between the Netherlands and other countries is remarkable and can only be explained in a multifactorial way. Factors potentially influencing the difference in clinical care are; interpretation of research findings presented in published articles (reflected by differences in content and style of phrasing of guidelines and translation of guidelines to women by their attending physician), claim culture, jurisdiction and organization of obstetric care.

The aim of this study is to evaluate the effect of the rise in cesarean rate for term breech delivery on neonatal outcome up to 2007. Furthermore, in order to investigate whether the Dutch management of the clinical obstetric issue of safe term breech delivery is justified, we wondered whether the clinical case selection for vaginal
delivery applied by Dutch obstetricians, resulting in a relatively large proportion of women (40%) with a term breech being selected for vaginal delivery, led to an optimization of neonatal outcome, or if there is still room for improvement in terms of perinatal mortality and morbidity.

**Material and methods**

This study was performed in a population based cohort using the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 7 days after birth. The PRN database is obtained by a validated linkage of three different registries: the midwifery registry (LVR 1), the obstetric registry (LVR 2) and the neonatology registry (LNR) of hospital admissions of newborns. The coverage of the PRN registry is about 96% of all deliveries in the Netherlands. All data contained in the PRN are voluntarily recorded by the caregiver during prenatal care, delivery and the neonatal period. Data on neonatal admissions are registered in 53-58% of hospitals in The Netherlands. The neonatal follow up, up to 28 days after birth, is provided by 80% of neonatal care units to the PRN. The data are sent to the national registry office annually, where a number of range and consistency checks are conducted. For this study all births between 1 January 1999 (inception of the PRN registry) and 31 December 2007 (the most recent, validated and linked year available at start of the analyses for this study) were selected. The PRN gave approval for anonymous use of requested data for this analyses. No ethical approval or informed consent was required for this retrospective cohort study as the use of the data was within the confines pose by Dutch law on the use of registry data.

We studied pregnant women with singleton breech presentations who delivered between 37 0/7 and 41 6/7 weeks of gestation. Exclusion criteria were antepartum death and major congenital malformations. Major congenital malformations were defined as lethal congenital malformations (e.g. trisomy 18, Potter’s syndrome, central nervous system abnormalities (meningomyelocele, exencephaly, anencephaly, hydrocephaly and microcephaly) and infants with multiple congenital malformations (including spina bifida, intestinal atresias and congenital heart disease). To validate the perinatal mortality we verified all causes of mortality through the hospital charts.

Planned vaginal birth was defined as initially intended vaginal birth; the combination of actual vaginal birth and emergency cesarean delivery, including both failure to progress and fetal distress as indications for a cesarean delivery. Elective cesarean section was defined as all women opting for a planned cesarean delivery.

The primary outcome was perinatal mortality, defined as intrapartum death or death within 28 days after birth. Secondary outcomes were; a five-minute Apgar score below 7, neonatal trauma (defined as a composite of intracerebral bleeding, cephalic hematoma, facial nerve paresis, brachial plexus lesion, fracture of clavicle, humerus or femur and other trauma), and poor neonatal outcome was defined as perinatal mortality, five-minute Apgar score below 7 and neonatal trauma.

We analyzed trends of mode of delivery and neonatal outcomes over the years and differences in neonatal outcomes before and after publication of the term breech trial (before October 2000 and after November 2000). We performed univariate analysis and provided outcomes for different subgroups: parity (nulliparous/multiparous), birth weight (≤3500 / >3500 gram), type of breech (complete/frank), and onset of labor (spontaneous vs. induced or augmented).

Furthermore, we looked at the difference in elective cesarean delivery rate in relation to neonatal outcomes among Dutch hospitals. We not only compared neonatal outcome before and after November 2000, but also the impact of planned vaginal delivery and elective cesarean delivery. All statistical analyses were carried out with SAS 9.2 (SAS Institute, Cary, NC).

**Results**

There were 1.4 million singleton term deliveries in the nine year study period, of which 4.4% were breech deliveries. We excluded 161 cases of antenatal death (0.27%) and 642 cases with major congenital abnormalities (0.09%) from the analysis, leaving 58320 women in the study.

Figure 1 shows the trend in the mode of delivery for breech presentation between 1999 and 2007. Publication of the term breech trial led to an increase in elective cesareans from 24% before publication of the study to 60% after. Figure 2 shows the impact on the neonatal outcome. The increase in elective cesarean rate resulted in a decrease in perinatal death (1.3‰ before Oct 2000 vs. 0.7‰ after Nov 2000, OR 0.51; 95%CI 0.28-0.93), a decrease in low Apgar score (20.2 vs. 9.6‰, OR 0.47; 95%CI 0.34-0.63), and a decrease in neonatal trauma (4.8 vs. 2.2‰, OR 0.46 95%CI 0.34-0.63) (Table 1).

Subgroup analysis showed a smaller increase in elective cesarean rate among multiparous compared to nulliparous (31 vs. 39%). The increase of 31% in elective cesarean delivery within the multiparous group did not result in statistically significant decrease of overall perinatal mortality rate among multiparous women, although there was also in this group a positive trend (0.8‰ before Oct 2000 vs. 0.6‰ after Dec 2000, OR 0.69; 95%CI 0.22-2.20) (Table 2).
Despite the increased emergency cesarean rate (from 34 to 45%) within the planned vaginal birth group after publication of the term breech trial, the perinatal mortality rate within the planned vaginal breech group remained stable (1.7 before October 2000 vs. 1.6‰ after December 2000, OR 0.96; 95% CI 0.52-1.76). The prevalence of low Apgar score (25.1 vs. 20.3‰, OR 0.81; 95% 0.68-0.95) and of neonatal trauma (6.4 vs. 4.1‰, OR 0.65; 95% 0.46-0.92) improved in women with a planned vaginal delivery after publication of the term breech trial (Table 2). Of the 46 cases of perinatal mortality, breech presentation had not been diagnosed until birth in 9 cases (19.1%).

Table 3 shows the gain in neonatal outcome by performing an elective cesarean delivery. There was no perinatal mortality in the elective cesarean group, compared to 1.6‰ in the planned vaginal birth group. Elective cesarean delivery was associated with a lower risk of poor neonatal outcome compared to planned vaginal birth (OR 0.14, 95% CI 0.11 to 0.18), including a lower risk of low Apgar score (OR 0.12, 95% CI 0.09 to 0.16), and a lower risk of neonatal trauma (OR 0.24, 95% CI 0.15 to 0.37).

Exclusion of the nine women with breech presentation not diagnosed until labor, who were all included in the planned vaginal birth group, did not alter the difference in perinatal mortality between the two groups (1.3‰ in the planned vaginal birth group vs. none in the elective cesarean group).

Table 4 shows the relation between mode of delivery and neonatal outcome for different subgroups. Elective cesarean led to a strong decrease in neonatal morbidity and mortality regardless of parity, type of breech, birth weight, or onset of labor.

In stratified analysis results for parity, type of breech, birth weight and onset of labor, did not change the strong relationship between mode of delivery and poor neonatal outcome. There was no interaction between parity and mode of delivery for poor neonatal outcome. Birth weight below 3500gr was related to a poorer outcome compared to higher birth weight (>3500gr). Complete breech was related to a poorer outcome compared to frank breech presentation and induced or augmented labor to a worse outcome compared to spontaneous birth (table 4).
Data from 99 different hospitals are registered in the PRN registry. The total number of breech births within seven years after the term breech trial varied from 9 to 739 per hospital with a median of 381. The elective cesarean rate in these women varied from 14 to 80% between the hospitals. Perinatal death (n=30) occurred in 24 hospitals (24%), with a maximum of 9.4‰ (3 of 318 breech deliveries in seven years).

Correlation analyses did neither demonstrate an association between hospital elective

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Neonatal outcome following term breech delivery before and after publication of the Term Breech Trial (TBT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>n 12,383 45,937</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>n 7,677 28,871</td>
</tr>
<tr>
<td>Multiparous</td>
<td>n 4,706 17,066</td>
</tr>
</tbody>
</table>

^ Intrapartum death and neonatal mortality up to 7 days
* Five-minute Apgar score <7
~ Composite score of: intracerebral bleeding, cephalic haematoma, facial nerve paresis, brachial plexus, lesion, fracture of clavicle, humerus or femur and other trauma
^{j} Percentage of pursued vaginal birth

### Table 2 | Neonatal outcome in case of term breech delivery according to mode of delivery

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Neonatal outcome in case of term breech delivery according to mode of delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective cesarean (%)</td>
<td>24</td>
</tr>
<tr>
<td>Emergency cesarean (%)</td>
<td>34</td>
</tr>
</tbody>
</table>

^ Intrapartum death and neonatal mortality up to 7 days
* Five-minute Apgar score <7
~ Composite score of: intracerebral bleeding, cephalic haematoma, facial nerve paresis, brachial plexus, lesion, fracture of clavicle, humerus or femur and other trauma
Table 3  Neonatal outcomes per mode of delivery: Elective cesarean delivery compared to pursued vaginal breech delivery since publication of the Term Breech Trial

<table>
<thead>
<tr>
<th></th>
<th>Pursued vaginal birth5 (Dec 2000 – 2007) (%)</th>
<th>Elective cesarean delivery (Dec 2000 – 2007) (%)</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor neonatal outcome6</td>
<td>424 (23.1)</td>
<td>92 (3.3)</td>
<td>0.14 (0.11 – 0.18)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Perinatal death^6</td>
<td>30 (1.6)</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Low Apgar score*</td>
<td>374 (20.3)</td>
<td>65 (2.5)</td>
<td>0.12 (0.09 – 0.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neonatal Trauma~</td>
<td>76 (4.1)</td>
<td>27 (1.0)</td>
<td>0.24 (0.15 – 0.37)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* Composite of perinatal death, low Apgar score and neonatal trauma
^ Intrapartum death and neonatal mortality up to 7 days

Table 4  Neonatal outcomes for planned vaginal breech vs. elective cesarean delivery since publication of the term breech trial for different subgroups

<table>
<thead>
<tr>
<th></th>
<th>Perinatal death^6 (Incidences) (%)5</th>
<th>Low Apgar score* (Odds ratio (95%CI))</th>
<th>p-value</th>
<th>Neonatal trauma (Incidences) (%)5</th>
<th>Odds ratio (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>(1.8 vs. 0%)</td>
<td>0.11 (0.08 – 0.15)</td>
<td>&lt;0.0001</td>
<td>0.23 (0.13 – 0.39)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>(1.4 vs. 0%)</td>
<td>0.13 (0.09 – 0.20)</td>
<td>&lt;0.0001</td>
<td>0.25 (0.12 – 0.54)</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>Type of breech</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>(3.2 vs. 0%)</td>
<td>0.11 (0.07 – 0.17)</td>
<td>&lt;0.0001</td>
<td>0.19 (0.08 – 0.46)</td>
<td>0.0002</td>
<td></td>
</tr>
<tr>
<td>Frank</td>
<td>(1.2 vs. 0%)</td>
<td>0.11 (0.08 – 0.15)</td>
<td>&lt;0.0001</td>
<td>0.23 (0.14 – 0.39)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Birth weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3500 grams</td>
<td>(2.0 vs. 0%)</td>
<td>0.11 (0.08 – 0.15)</td>
<td>&lt;0.0001</td>
<td>0.25 (0.15 – 0.42)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>&gt;3500 grams</td>
<td>(0.8 vs. 0%)</td>
<td>0.13 (0.08 – 0.21)</td>
<td>&lt;0.0001</td>
<td>0.50 (0.29 – 0.87)</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td>Onset of labor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>(1.5 vs. 0%)</td>
<td>0.15 (0.12 – 0.20)</td>
<td>0.008</td>
<td>0.39 (0.23 – 0.65)</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>Induced / augmented</td>
<td>(2.1 vs. 0%)</td>
<td>0.09 (0.06 – 0.11)</td>
<td>&lt;0.0001</td>
<td>0.15 (0.09 – 0.25)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

^ Intrapartum death and neonatal mortality up to 7 days. No odds ratios could be calculated for neonatal mortality since there was no mortality in the planned cesarean group.
5 No odds ratio could be calculated due to no events in the elective cesarean delivery group.
6 Five-minute Apgar score 7

cesarean rate and perinatal death, low Apgar score, neonatal trauma, or poor neonatal outcome, nor was there an association between the volume of breech births and the neonatal outcome.

Since publication of the term breech trial, 1 692 more cesarean deliveries (combined elective and emergency cesarean) were performed annually. This led to an annual reduction of five neonatal deaths (number needed to treat (NNT) 338), 126 neonates with low Apgar scores (NNT 13), and 30 neonates with birth traumata (NNT 66).

If all women who nowadays still undergo a planned vaginal breech birth, would receive an elective cesarean, 6 490 more elective CS would be performed. This would lead to an additional annual reduction of 10 neonatal mortalities, 116 neonates with low Apgar scores and 20 neonates with birth traumata.

Breech deliveries account for 5.8% (10 of 172 per year) of the perinatal and neonatal mortality up to 28 days post partum among term singleton deliveries in the Netherlands. A policy of elective cesarean for all term breech deliveries could lower the overall term neonatal mortality in term deliveries with 6.8% from 172 to 162 cases per year.

Discussion

In this analysis of almost a decade of term breech deliveries in the Netherlands, we found a significant improvement of neonatal outcomes most likely due to the increased elective cesarean rate that occurred after publication of the Term Breech Trial. Nulliparous women benefitted more from the change in policy than multiparous women as elective cesarean rates were higher in the first group. Despite the lower percentage of women opting for or offered a vaginal delivery, and despite a higher emergency cesarean rate during vaginal breech birth, neonatal outcome within the planned vaginal birth group did not improve.

This study on breech birth is unique in its size, and the Dutch setting makes it possible to evaluate the effect of an increase, though not complete chance in daily practice of elective cesarean for breech presentation at term. We showed that based on patient characteristics including parity, onset of labor, type of breech presentation and birth weight, no subgroup of women could be identified with a low risk of poor neonatal outcome during planned vaginal delivery compared to elective cesarean.

Several other studies tried to identify a subgroup of patients with low risk at adverse perinatal outcome during vaginal breech delivery. Most of these studies have a lack of power to detect a significant difference on for instance perinatal mortality.8,10 There is one large prospective cohort trial from the PREMODA study group, who evaluated the birth outcome of 2 502 planned vaginal deliveries and 5 573 planned cesarean
deliveries and could not find a significant difference in fetal and neonatal mortality or serious neonatal morbidity. Women were found eligible for planned vaginal delivery according to the CNGOF guideline and trial of labor was guided according to advices from national guidelines as well. The composite poor neonatal outcome was 16.0‰ in the planned vaginal delivery group vs. 14.5‰ in the planned cesarean group (OR 1.10, (95%CI 0.75-1.61)). Their rates of low Apgar scores and birth trauma are higher in the cesarean section group, but much lower in the planned vaginal breech group, compared to the data presented in this study. Their explanation of the non-significant results is partly the quality advantages of a prospective study design compared to all the significant results in retrospective studies. Similar to this prospective cohort study, we have evaluated the cause of all perinatal mortalities, which improves the reliability of our outcomes compared to those of other retrospective studies. Secondly, the authors state that the regulated selection procedure for planned vaginal delivery and intrapartum management might explain the non-significant results. Although evidence based proof of these antenatal examinations is lacking, they assume that special attention to the decision on mode of delivery might be an explanation of the low poor neonatal outcome rate in the vaginal delivery group. The potential effectiveness of application of a consensus guidelines is also seen in a study by Vendittelli et al. with less neonatal complications in centers working according to these guidelines compared to other centers (OR 0.27 (95%CI 0.09-0.85)). Since vaginal breech delivery is still common practice in the Netherlands, the high poor neonatal outcome rates in comparison to other countries, should be focus of research and training of obstetricians.

In this study, we choose to use a cut off level of birth weight of 3500 grams and not small for gestational age. The correlation of small for gestational age and adverse neonatal outcome is reported in several studies. Concerning breech presentation, there is discussion among clinicians whether a term fetus below or above a certain birth weight could be more at risk for breech birth related adverse outcome. For instance in the previously mentioned PREMODA study, the estimated fetal weight should not exceed 3800 grams to qualify for planned vaginal breech delivery.

An important strength of this study is the well-maintained, population-based national registry, covering 96% of all births. The missing 4% are deliveries supervised by general practitioners and midwives practices that did not contribute data to the PRN. Since breech presentation is an indication for hospital birth, we do not expect that these missing data would influence our outcomes. Neonatal morbidity of admitted children is not measured in all of the neonatal departments of the 99 hospitals. When analyses were restricted to the hospitals with complete neonatal admission registration, similar results were found.

Analyzing data of a population-based national registry presented some disadvantages as well. Only data up to 2007 were available for analysis. However, a recent survey among 24 hospitals in the Netherlands showed similar elective cesarean rates for breech presentation at term in 2011 and 2012. Second, we were not able to perform a complete intention to treat analysis for mode of delivery. Women who opted for elective cesarean, but underwent a vaginal birth (for instance due to unexpected start of delivery and fast progression), could not be included in the cesarean group. In the term breech trial, 9.7% of women with a planned cesarean in fact had a vaginal delivery. Evaluation of the perinatal mortalities in hospital files revealed that 19.1% breech presentations was not diagnosed until birth. We did not have this information for the whole study population, consequently there will be a misclassification of women in the planned vaginal birth group, who were simply not aware of the breech presentation. Thus the positive outcome of elective cesarean might be overestimated.

The high percentage of women opting for a planned vaginal breech birth is remarkable compared to other countries. We have no explanation for this high rate of trial of labor in case of breech presentation. It is probably a combination of a doctor and patient driven decision. The large intra hospital variation of planned cesarean rates (14-80%) reveal a large variety in management of breech presentation among hospitals. This might be a result of population differences and attitudes of obstetricians towards vaginal breech delivery.

When performing elective cesarean sections, attention should be paid to the gestational age at which these are planned in order to minimize neonatal morbidity related to elective cesarean sections such as respiratory distress syndrome. The downside of increased cesarean rates is the increased maternal morbidity and mortality. In our database, only two maternal deaths were reported within the study group. A previous study by the Dutch Maternal Mortality Committee, reported four maternal deaths after elective cesarean for term singleton breech delivery (0.47‰) from 2000-2002. Other studies report maternal mortality rates of 0.04‰ for elective cesarean and 0.15‰ for repeat cesarean. These data support the presumption of underreporting of maternal mortality and morbidity in the database. Therefore we cannot comment on the effects of modes of delivery on maternal outcomes in our cohort.

A frequently mentioned argument against a policy of elective cesarean delivery is the lower exposure of the health care professional to vaginal breech delivery, and thus a loss of expertise in this field. However, in our opinion, training of the professional is no reason to expose healthy fetuses to high risks. Experience should be gained by simulation training, as is current practice with other uncommon events such as shoulder dystocia, postpartum hemorrhage and newborn life support.
Our results can be used by clinicians during counseling of women with a term breech presentation for mode of delivery. In the current patient information leaflets of the Dutch Society of Obstetrics and Gynecology is written that there is no difference in mortality or development at the age of two between vaginal and elective cesarean deliveries (based on the two year follow up of the Term Breech Trial). This information needs to be revised in the light of our findings with the significant difference in mortality rate. To properly inform patients, a combination of risk presentations (absolute risks, relative risks and figures) is necessary to enable individual informed decision making. 22,23 For example, absolute numbers on a vaginal breech delivery should be mentioned as well: 55% of all planned breech deliveries lead to a vaginal birth and the chance of a normal neonatal outcome without any additional neonatal care, is 97% in case of planned vaginal birth in our study population.

During the study period, the percentage of breech presentation at birth remained stable around 4%. This suggests that there is still room for improvement of the implementation of external cephalic version, as this relative safe treatment can significantly improve neonatal outcome by preventing breech presentation at birth.

Due to a rise in cesarean delivery rate in case of term breech presentation, there was a significant improvement of neonatal outcome. However, 40% of term breech deliveries in the Netherlands are still planned vaginal deliveries and these deliveries generate a tenfold fetal mortality rate compared to elective cesarean delivery. Subgroup analysis could not identify antepartum parameters which could distinguish between women with low versus high risk vaginal breech birth. These facts need to be discussed when women opt for a vaginal breech delivery.

References


Multiple pregnancies
The impact of mode of delivery on the outcome in very preterm twins

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CHAPTER 6

Abstract

Objective  Studies on the optimal mode of delivery in women with a twin pregnancy <32 weeks are scarce. We studied the effects of the mode of delivery on perinatal and maternal outcomes in very preterm twin pregnancy.

Design and Setting  Population-based cohort study including all women with twin pregnancy who delivered very preterm (26-32 weeks of gestation) in the Netherlands between January 2000 and December 2010.

Methods  We compared perinatal mortality and neonatal and maternal morbidity according to the intended mode of delivery as well as to the actual mode of delivery. Perinatal outcomes were paired taking into account the dependency between the children of the same twin pregnancy and were also analysed for each child separately. We used logistic regression to correct for possible confounding factors.

Results  Perinatal mortality was significantly higher in planned caesarean section 22/212 (10.4%) as compared to planned vaginal delivery 94/1443 (6.5%) (aOR 2.5; 95% CI 1.5-4.2) in the whole study population. The same applied for perinatal morbidity 140/212 (66.0%) versus 905/1443 (62.7%) (aOR 1.5; 95% CI 1.1-2.0), maternal morbidity 36/212 (17.0%) versus 71/1443 (4.9%), (aOR 4.0; 95% CI 2.6-6.3) and for perinatal mortality for the second twin 15/212 (7.1%) versus 51/1443 (3.5%) (aOR 2.9; 95% CI 1.7-5.2).

Conclusion  In very preterm delivery of twins a policy of planned caesarean section increases perinatal mortality and neonatal and maternal morbidity.

Keywords  Very preterm twin pregnancy, intrapartum and neonatal mortality, maternal morbidity, neonatal morbidity, mode of delivery, vaginal delivery, caesarean section

Introduction

The incidence of twin pregnancies has increased due to the growing use of assisted reproductive technologies and due to the increased maternal age at first pregnancy[1]. Twin pregnancies have a higher risk of complications such as preterm birth, intrauterine growth restriction and perinatal mortality and morbidity. In the high-resourced countries approximately one third of the very preterm deliveries (before 32 weeks of gestation) concerns a twin pregnancy [1,2].

The Twin Birth study, a large multicenter randomized controlled trial, showed that planned caesarean section did not reduce the risk of fetal or neonatal death or serious morbidity as compared with planned vaginal delivery in twin pregnancies beyond 32 weeks gestation. The risk of adverse neonatal outcome was higher for the second twin than for the first twin, however planned caesarean section did not reduce this risk [3]. This study has been criticized for randomising women from 32 weeks onwards, thus introducing higher morbidity and mortality rates at these lower gestational ages, and mimicking a potential protective effect of caesarean section at term. [4]

Currently, there are only a few smaller studies that report on the preferred mode of delivery in women with a twin pregnancy and a delivery before 32 weeks of gestation[5-7]. Recently, a study limited to very preterm twins with the first child in cephalic presentation showed that a policy of planned vaginal delivery of very preterm twins with the first twin in cephalic presentation does not increase perinatal mortality (aOR 0.78; 95% CI 0.17-3.68) or severe neonatal morbidity (aOR 0.71; 95% CI 0.36-1.44) [8].

The purpose of our study is to analyse the association between the intended mode of delivery and perinatal and maternal outcomes in very preterm twin pregnancies (26-32 weeks of gestation).

Material and methods

This study was performed using data from a national cohort registered in the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 28 days after birth.

The PRN database is obtained by a validated linkage of three different registries: the midwife registry (LVR 1), the obstetricians registry (LVR 2) and the neonatology registry (LNR) of hospital admissions of newborn infants. [9]

The coverage of the PRN is approximately 96% of all deliveries in the Netherlands and currently includes over 1.9 million records derived from deliveries in the last decade.
CHAPTER 6
THE IMPACT OF THE MODE OF DELIVERY ON THE OUTCOME IN VERY PRETERM TWINS

All PRN data are recorded by the caregivers during prenatal care, delivery and the neonatal period. The data are annually sent to the national registry office, where a number of range and consistency checks are conducted. Institutional review board approval was not necessary since the data were used anonymous, thus exempting ethics approval in the Netherlands.

For this study we identified all women with a twin pregnancy who delivered between 26 and 32 weeks of gestation between January 1st 2000 and December 31st 2010.

Women with a pregnancy complicated by congenital abnormalities, placental abruption, intra-uterine fetal death before onset of labour, fetal growth restriction (birthweight <P5), twin-to-twin-transfusion syndrome (TTTS), maternal hypertension (maternal systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) or preeclampsia (high blood pressure and proteinuria; ≥300 mg protein loss in 24-hours urine sample) were excluded. We also excluded women who delivered before 26+0 weeks of gestation because in the time period under study active management between 24 to 26 weeks was not general practice in the Netherlands.

We compared perinatal and maternal outcomes according to the intended mode of delivery, i.e. intended caesarean section versus intended vaginal delivery (vaginal delivery of both twins, emergency caesarean section of both twins and vaginal delivery of first twin and emergency caesarean section of the second twin) as well as according to the actual mode of delivery. We performed a subgroup analysis according to fetal presentation (cephalic/cephalic, cephalic/other, breech/cephalic, breech/other). We compared intrapartum and neonatal mortality (within the first 28 days after birth) and maternal and neonatal morbidity between these groups. Neonatal morbidity was defined as any neonatal mortality. We also analysed perinatal mortality and morbidity as a composite outcome “adverse perinatal outcome”. Maternal morbidity was defined as uterine rupture, postpartum haemorrhage > 1,000 ml and the need for blood transfusion.

We used logistic regression to correct for possible confounding factors. McNamee’s traditional criteria for identifying confounders were used to determine whether a covariate was a confounder or not.[10] In the multivariate analyses we corrected for: nulliparity, gestational age (weeks), admission child to NICU center, non-western ethnicity, prolonged rupture of membranes (≥ 24 hours) and birth weight (grams). The correlation structure between the paired twins was taken into account by analysing the data as clustered data. Perinatal outcomes were analysed as pairs (“any mortality”, “any morbidity”, “any composite adverse perinatal outcome”) and for each child separately.

Specific management data including the use of tocolytic medication, fetal lung maturation with corticosteroids, antibiotic treatment and antenatal transfer to a third level care facility were not available from the database. According to the national guidelines at that time, tocolytics (atosiban or nifedipine) and antenatal corticosteroids to enhance fetal lung maturity were recommended from 25+6 till 33+6 weeks of gestation for a period of 48 hours in women with symptoms of threatened preterm birth. Magnesium sulphate for fetal neuroprotection was not recommended to administer at that time. Women in the study were treated according to these national guidelines. Threatened preterm birth is defined as preterm contractions combined with dilatation or cervical length shortening below 25 mm or preterm premature rupture of membranes (PPROM). Women at risk for preterm delivery before 32 weeks of gestation are referred to tertiary centres that are equipped with Neonatal Intensive Care Units (NICU).

The decision for caesarean section or vaginal delivery was made by the responsible obstetrician and the patient. In case of cephalic presentation of the first twin, it is common practice in The Netherlands to counsel women towards a vaginal delivery. In case of the first twin in breech presentation the absence of clear data and guidelines on this subject results in practice variation.

Data selection was done in SAS version 9.3 and all analyses were performed in R version 0.98.1091 (The R Foundation for Statistical Computing).

Results

During the study period between January 2000 and December 2010, 146,885 women delivered preterm in The Netherlands, of which 1,653 women delivered very preterm of a twin pregnancy. Of these 1,653 women, 212 (13%) women delivered by planned caesarean section and 1,443 women (87%) by planned vaginal delivery. Table 1 shows the baseline characteristics of the two groups. Multiparity, previous caesarean section and delivery in a NICU hospital occurred more often in the caesarean section group, while women with PPROM delivered more often vaginally. Also, women with a planned caesarean section had a higher gestational age, and surprisingly, their babies were more often both female.

Perinatal and maternal outcomes according to the intended mode of delivery are listed in table 2. In the whole study population, any perinatal mortality was significantly higher in women with a planned caesarean section 22/212 (10.4%) as compared to women with a planned vaginal delivery 94/1443 (6.5%), (aOR 2.5; 95% CI 1.5-4.2). The same applied for any neonatal morbidity 140/212 (66.0%) versus 905/1443 (62.7%),
The impact of the mode of delivery on the outcome in very preterm twins

(aOR 1.5; 95% CI 1.1-2.0) and any composite adverse perinatal outcome 141/212 (66.5%) versus 918/1443 (63.6%), (aOR 1.4; 95%CI 1.0-2.0). In the subgroup analysis for each child separately perinatal mortality of the first twin was not significantly different for

| Table 1 Baseline characteristics of 1655 women with a twin pregnancy and a very preterm delivery (26-32 weeks of gestation) in The Netherlands from 2000-2010 according to the intended mode of delivery |
|---------------------------------|-----------------|-----------------|------------------|
|                                  | Planned CS (n=212) | Planned vaginal delivery (n=1443) | p-value |
| Parity                          |                  |                  |                  |
| Nulliparous, n (%)              | 125 (59.0%)      | 989 (69%)        | 0.0127 |
| Primiparous*, n (%)             | 7 (3.3%)         | 25 (1.7%)        |        |
| Parous, n (%)                   | 80 (38%)         | 429 (30%)        |        |
| Previous CS                     |                  |                  |                  |
| Yes, n (%)                      | 12 (5.7%)        | 41 (2.8%)        | 0.029  |
| No, n (%)                       | 200 (94%)        | 1402 (97%)       |        |
| Mean maternal age, years (SD)   | 31.1 (4.7)       | 30.4 (4.5)       | 0.45   |
| Mean birth weight (SD)          |                  |                  |        |
| Fetus 1                         | 1396 (295)       | 1376 (294)       | 0.90   |
| Fetus 2                         | 1358 (318)       | 1354 (304)       | 0.37   |
| Mean gestational age at delivery, Weeks (SD) | 29.6 (1.4) | 29.2 (1.6) | 0.013 |
| Gestational age                 |                  |                  |        |
| 26-28 weeks                     | 19 (9%)          | 253 (18%)        | 0.002  |
| 29-32 weeks                     | 193 (91%)        | 1190 (83%)       |        |
| Ethnicity                       |                  |                  |        |
| Western, n (%)                  | 180 (85%)        | 1251 (87%)       | 0.48   |
| Non-western, n (%)              | 32 (15%)         | 192 (13%)        |        |
| Socio economic status           |                  |                  |        |
| Low, n (%)                      | 61 (29%)         | 350 (24%)        | 0.155  |
| Medium/ high, n (%)             | 151 (71%)        | 1093 (76%)       |        |
| PPROM                            |                  |                  |        |
| Yes, > 24 hours, n (%)          | 22 (10%)         | 294 (20%)        | 0.0005 |
| No, (+ <24 hours), n (%)        | 190 (90%)        | 1149 (80%)       |        |
| Location of delivery            |                  |                  |        |
| NICU equipped hospital, n (%)   | 167 (79%)        | 959 (67%)        | 0.0003 |
| General hospital, n (%)         | 45 (21%)         | 484 (34%)        |        |
| Fetal sex                       |                  |                  |        |
| Both female, n (%)              | 89 (42%)         | 431 (30%)        | 0.0001 |
| Both male, n (%)                | 78 (37%)         | 521 (36%)        |        |
| Female/ male, n (%)             | 45 (21%)         | 469 (34%)        |        |

* Previous caesarean section

(aOR 1.7; 95% CI 1.0-2.7) and any composite adverse perinatal outcome 150/212 (69.9%) versus 1427/1443 (98.9%), (aOR 2.0; 95%CI 1.1-3.6). In the subgroup analysis for each child separately perinatal mortality of the first twin was not significantly different for

| Table 2 Perinatal mortality, morbidity** and maternal morbidity*** in 1655 women with a twin pregnancy and a very preterm delivery (26-32 weeks of gestation) according to the intended mode of delivery |
|---------------------------------|-----------------|-----------------|------------------|
|                                  | Planned CS (n=212) | Planned vaginal delivery (n=1443) | OR (95% CI) Adjusted*** |
| Overall (26-32weeks)             |                  |                  |                  |
| Any perinatal mortality, n (%)   | 22 (10%)         | 140 (66%)        | 2.5 (1.5-4.2) |
| Any maternal morbidity, n (%)    | 140 (66%)        | 927 (64%)        | 1.7 (1.0-2.9) |
| Any composite adverse perinatal |                  |                  |                  |
| (first twin), n (%)              | 25 (11.8%)       | 153 (10.5%)      | 1.3 (0.72-2.4) |
| (second twin), n (%)             | 15 (11.3%)       | 102 (7.0%)       | 2.1 (1.1-4.0) |
| Perinatal death of the first twin, n (%) | 11 (5.2%) | 57 (3.9%) | 2.0 (1.0-4.0) |
| Perinatal death of the second twin, n (%) | 15 (11.3%) | 102 (7.0%) | 2.1 (1.1-4.0) |
| Composite adverse perinatal first twin, n (%) | 1 (0.5%) | 7 (0.5%) | 1.1 (0.1-10.9) |
| Composite adverse perinatal second twin, n (%) | 1 (0.5%) | 7 (0.5%) | 1.1 (0.1-10.9) |
| Composite adverse perinatal both twins, n (%) | 1 (0.5%) | 7 (0.5%) | 1.1 (0.1-10.9) |
| Material morbidity, (n%)         | 36 (17%)         | 77 (5.4%)        | 4.0 (2.6-6.3) |

** Neonatal morbidity is defined as: 5-minute Apgar score <4, intraventricular haemorrhage, cephalo hemaetoma, facial nerve paralysis, brachial plexus injury, asphyxia related morbidity: hypoxic-ischemic encephalopathy, neonatal hypoglycaemia, neonatal hypothermia.

*** Maternal morbidity defined as uterine rupture, HPP > 1000 ml or bloodtransfusion, Other means breech or transverse presentation. Other means breech or transverse presentation.
Table 3 Perinatal mortality* and maternal morbidity** in 1655 women with a twin pregnancy and a very preterm delivery according to the intended mode of delivery and presentation at birth ***

<table>
<thead>
<tr>
<th>Planned Caesarean Section</th>
<th>Planned vaginal delivery</th>
<th>OR (95% CI) Unadjusted</th>
<th>OR (95% CI) Adjusted***</th>
</tr>
</thead>
<tbody>
<tr>
<td>26-32 weeks, n (%)</td>
<td>N= 73</td>
<td>N= 585</td>
<td></td>
</tr>
<tr>
<td>Cephalic/Cephalic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any perinatal mortality, n (%)</td>
<td>14 (19%)</td>
<td>29 (5.0%)</td>
<td>4.6 (2.9-7.1)</td>
</tr>
<tr>
<td>Any neonatal morbidity, n (%)</td>
<td>47 (6%)</td>
<td>367 (63%)</td>
<td>1.1 (0.81-1.4)</td>
</tr>
<tr>
<td>Any composite adverse perinatal, n (%)</td>
<td>48 (66%)</td>
<td>370 (63%)</td>
<td>1.1 (0.85-1.5)</td>
</tr>
<tr>
<td>Perinatal death of the first twin, n (%)</td>
<td>7 (9.6%)</td>
<td>20 (3.4%)</td>
<td>3.0 (1.6-5.6)</td>
</tr>
<tr>
<td>Perinatal death of the second twin, n (%)</td>
<td>9 (12%)</td>
<td>15 (2.6%)</td>
<td>5.3 (1.9-13.9)</td>
</tr>
<tr>
<td>Neonatal morbidity of the first twin, n (%)</td>
<td>41 (56%)</td>
<td>235 (40%)</td>
<td>1.9 (1.5-2.5)</td>
</tr>
<tr>
<td>Neonatal morbidity of the second twin, n (%)</td>
<td>41 (56%)</td>
<td>313 (54%)</td>
<td>1.1 (0.85-1.5)</td>
</tr>
<tr>
<td>Composite adverse perinatal first twin, n (%)</td>
<td>41 (56%)</td>
<td>238 (41%)</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Composite adverse perinatal second twin, n (%)</td>
<td>43 (59%)</td>
<td>316 (54%)</td>
<td>1.2 (0.93-1.6)</td>
</tr>
<tr>
<td>Maternal morbidity, n (%)</td>
<td>12 (16%)</td>
<td>32 (5.5%)</td>
<td>3.4 (1.7-6.9)</td>
</tr>
<tr>
<td>26-32 weeks, n (%)</td>
<td>N= 67</td>
<td>N= 516</td>
<td></td>
</tr>
<tr>
<td>Cephalic/Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any perinatal mortality, n (%)</td>
<td>6 (9.0%)</td>
<td>41 (7.9%)</td>
<td>6 (0.62-8.2)</td>
</tr>
<tr>
<td>Any neonatal morbidity, n (%)</td>
<td>46 (6%)</td>
<td>331 (64%)</td>
<td>1.2 (0.72-2.1)</td>
</tr>
<tr>
<td>Any composite adverse neonatal, n (%)</td>
<td>46 (69%)</td>
<td>337 (65%)</td>
<td>1.2 (0.67-2.1)</td>
</tr>
<tr>
<td>Perinatal death of the first twin, n (%)</td>
<td>4 (6.0%)</td>
<td>20 (3.9%)</td>
<td>16 (0.52-8.8)</td>
</tr>
<tr>
<td>Perinatal death of the second twin, n (%)</td>
<td>4 (6.0%)</td>
<td>28 (5.4%)</td>
<td>11 (0.38-3.1)</td>
</tr>
<tr>
<td>Neonatal morbidity of the first twin, n (%)</td>
<td>38 (57%)</td>
<td>236 (46%)</td>
<td>16 (0.93-2.6)</td>
</tr>
<tr>
<td>Neonatal morbidity of the second twin, n (%)</td>
<td>34 (51%)</td>
<td>279 (54%)</td>
<td>0.88 (0.53-1.5)</td>
</tr>
<tr>
<td>Composite adverse perinatal first twin, n (%)</td>
<td>38 (57%)</td>
<td>241 (47%)</td>
<td>1.1 (0.66-2.0)</td>
</tr>
<tr>
<td>Composite adverse perinatal second twin, n (%)</td>
<td>35 (52%)</td>
<td>248 (48%)</td>
<td>1.2 (0.64-2.0)</td>
</tr>
<tr>
<td>Maternal morbidity, n (%)</td>
<td>13 (19.4%)</td>
<td>26 (5.0%)</td>
<td>5.5 (2.52-12.3)</td>
</tr>
<tr>
<td>26-32 weeks, n (%)</td>
<td>N= 26</td>
<td>N= 140</td>
<td></td>
</tr>
<tr>
<td>Breech/Cephalic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any perinatal mortality, n (%)</td>
<td>1 (3.9%)</td>
<td>6 (4.3%)</td>
<td>11 (0.64-2.3)</td>
</tr>
<tr>
<td>Any neonatal morbidity, n (%)</td>
<td>17 (65%)</td>
<td>81 (58%)</td>
<td>12 (0.72-2.1)</td>
</tr>
<tr>
<td>Any composite adverse neonatal, n (%)</td>
<td>17 (65%)</td>
<td>83 (59%)</td>
<td>1.3 (0.54-3.1)</td>
</tr>
<tr>
<td>Perinatal death of the first twin, n (%)</td>
<td>0</td>
<td>4 (2.9%)</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death of the second twin, n (%)</td>
<td>1 (3.9%)</td>
<td>2 (1.4%)</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal morbidity of the first twin, n (%)</td>
<td>14 (54%)</td>
<td>67 (48%)</td>
<td>1.3 (0.55-3.1)</td>
</tr>
<tr>
<td>Neonatal morbidity of the second twin, n (%)</td>
<td>14 (54%)</td>
<td>68 (48%)</td>
<td>1.2 (0.55-3.1)</td>
</tr>
<tr>
<td>Composite adverse perinatal first twin, n (%)</td>
<td>1 (3.9%)</td>
<td>62 (44%)</td>
<td>0.92 (0.49-2.2)</td>
</tr>
<tr>
<td>Composite adverse perinatal second twin, n (%)</td>
<td>14 (54%)</td>
<td>68 (48%)</td>
<td>1.2 (0.55-3.1)</td>
</tr>
<tr>
<td>Maternal morbidity, n (%)</td>
<td>7 (27%)</td>
<td>6 (4.3%)</td>
<td>-</td>
</tr>
<tr>
<td>26-32 weeks, n (%)</td>
<td>N= 46</td>
<td>N= 202</td>
<td></td>
</tr>
<tr>
<td>Breech/Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any perinatal mortality, n (%)</td>
<td>1 (2.2%)</td>
<td>18 (8.9%)</td>
<td>0.23 (0.03-1.8)</td>
</tr>
<tr>
<td>Any neonatal morbidity, n (%)</td>
<td>30 (65%)</td>
<td>126 (62%)</td>
<td>1.1 (0.58-2.2)</td>
</tr>
<tr>
<td>Any composite adverse neonatal, n (%)</td>
<td>30 (65%)</td>
<td>128 (63%)</td>
<td>1.1 (0.55-2.1)</td>
</tr>
<tr>
<td>Perinatal death of the first twin, n (%)</td>
<td>0</td>
<td>11 (6.4%)</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death of the second twin, n (%)</td>
<td>1 (2.2%)</td>
<td>6 (3.0%)</td>
<td>0.73 (0.09-6.2)</td>
</tr>
<tr>
<td>Neonatal morbidity of the first twin, n (%)</td>
<td>25 (54%)</td>
<td>87 (45%)</td>
<td>1.6 (0.83-2.1)</td>
</tr>
<tr>
<td>Neonatal morbidity of the second twin, n (%)</td>
<td>26 (52%)</td>
<td>108 (54%)</td>
<td>0.95 (0.51-1.8)</td>
</tr>
<tr>
<td>Composite adverse perinatal first twin, n (%)</td>
<td>25 (54%)</td>
<td>90 (45%)</td>
<td>1.5 (0.78-2.1)</td>
</tr>
<tr>
<td>Composite adverse perinatal second twin, n (%)</td>
<td>24 (52%)</td>
<td>109 (54%)</td>
<td>0.91 (0.49-1.8)</td>
</tr>
<tr>
<td>Maternal morbidity, n (%)</td>
<td>9 (20%)</td>
<td>7 (3.5%)</td>
<td>6.8 (2.3-19.3)</td>
</tr>
</tbody>
</table>

O.R. = Odds Ratio
* Neonatal morbidity is defined as: 5-minute Apgar score <4; intraventricular haemorrhage; cephalo hemaetoma, facial nerve paralysis, brachial plexus injuries, clavicle fracture, humerus fracture, IRDS and asphyxia related morbidity: hypoxic ischemic encephalopathy, neonatal hypotonia, neonatal seizures
**Maternal morbidity defined as uterine rupture, HPP > 1000 ml or blood transfusion
Other means breech or transverse presentation
***adjusted for: nulliparity, gestational age (weeks), NICU center, prolonged rupture of membranes (≥24 hours), birth weight (grams) and non-western ethnicity.
planned caesarean section 11/212 (5.2%) as compared to planned vaginal delivery 57/1443 (4.0%), (aOR 2.0; 95% CI 1.0-4.0), while neonatal morbidity of the first twin (54.3% versus 42.9%) and composite adverse perinatal outcome (54.3% versus 42.9%) were significantly higher in planned caesarean section as compared to planned vaginal delivery (aOR 1.9; 95% CI 1.4-2.6) and (aOR 1.9; 95% CI 1.4-2.5).

For the second twin perinatal mortality was significantly higher in planned caesarean section 15/212 (7.1%) versus planned vaginal delivery 51/1443 (3.5%), (aOR 2.9; 95% CI 1.7-5.2), while neonatal morbidity (53.3% versus 53.2%) and composite adverse perinatal outcome (54.7% versus 53.8%) were not significantly different (aOR 1.2; 95% CI 0.89-1.6) and (aOR 1.3; 0.94-1.7) respectively. Maternal morbidity was higher in women who delivered by planned caesarean section (17%) as compared to planned vaginal delivery (4.9%), (aOR 4.0; 95% CI 2.6-6.3). There were no cases of maternal mortality or uterine rupture, therefore maternal morbidity consisted of haemorrhage postpartum > 1000 ml and need for blood transfusion.

We also analysed the perinatal outcomes according to fetal presentation (table 3).

**Cephalic/cephalic presentation**
In women with a twin pregnancy with both children in cephalic presentation any neonatal mortality was significantly higher for the planned caesarean section group 14/73 (19.2%) as compared to the planned vaginal delivery group 29/585 (5.0%) (aOR 5.8; 95% CI 2.6-12.9). Any neonatal morbidity and any perinatal morbidity and morbidty was not significantly different (aOR 1.2; 95% CI 0.66-2.0) and (aOR 1.2; 95% CI 0.68-2.1) respectively. In the subgroup analysis for every child separately perinatal mortality was significantly higher for both the first and the second twin in planned caesarean section as compared to planned vaginal delivery, (aOR 3.8; 95% CI 1.4-10.5) and (aOR 5.4; 95% CI 2.1-13.9). Neonatal morbidity was also significantly higher for the first twin (aOR 2.0; 95% CI 1.2-3.5). Maternal morbidity was significantly higher in planned caesarean section as compared to planned vaginal delivery (aOR 3.2; 95% CI 1.5-7.1).

**Cephalic/breech or transverse presentation**
Any perinatal mortality, or mortality of the first or second twin were not significantly different for planned caesarean as compared to planned vaginal delivery. Neonatal morbidity of the first twin was significantly higher in planned caesarean section as compared to planned vaginal delivery (aOR 2.3; 95% CI 1.3-3.9). The same applied for maternal morbidity (aOR 5.5; 95% CI 2.5-12.3).

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Planned Vaginal Delivery</th>
<th>Planned Caesarean Delivery</th>
<th>Planned Caesarean Delivery vs Planned Vaginal Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any perinatal mortality (%)</td>
<td>14/1035 (1.3%)</td>
<td>11/212 (5.2%)</td>
<td>4.0; 95% CI 2.6-6.3</td>
</tr>
<tr>
<td>Any neonatal mortality (%)</td>
<td>11/1035 (1.0%)</td>
<td>11/212 (5.2%)</td>
<td>4.9; 95% CI 2.6-6.3</td>
</tr>
<tr>
<td>Any composite adverse perinatal outcome (%)</td>
<td>12/1035 (1.2%)</td>
<td>15/212 (7.1%)</td>
<td>5.9; 95% CI 2.3-14.6</td>
</tr>
<tr>
<td>Perinatal death of first twin (%)</td>
<td>7/1035 (0.7%)</td>
<td>11/212 (5.2%)</td>
<td>7.0; 95% CI 2.9-16.7</td>
</tr>
<tr>
<td>Perinatal death of second twin (%)</td>
<td>7/1035 (0.7%)</td>
<td>4/212 (1.9%)</td>
<td>2.0; 95% CI 0.6-6.8</td>
</tr>
<tr>
<td>Neonatal morbidity of first twin (%)</td>
<td>111/1035 (10.8%)</td>
<td>115/212 (54.3%)</td>
<td>4.0; 95% CI 2.6-6.3</td>
</tr>
<tr>
<td>Neonatal morbidity of second twin (%)</td>
<td>111/1035 (10.8%)</td>
<td>115/212 (54.3%)</td>
<td>4.0; 95% CI 2.6-6.3</td>
</tr>
<tr>
<td>Composite adverse perinatal outcome (%)</td>
<td>122/1035 (11.8%)</td>
<td>150/212 (71.6%)</td>
<td>5.7; 95% CI 3.8-8.7</td>
</tr>
<tr>
<td>Maternal morbidity (%)</td>
<td>13/1035 (1.3%)</td>
<td>11/212 (5.2%)</td>
<td>4.0; 95% CI 2.6-6.3</td>
</tr>
</tbody>
</table>

**Note:** All perinatal outcomes were adjusted for nulliparity, gestational age (weeks), NICU center, prolonged rupture of membranes (>24 hours), birth weight (grams) and non-Western ethnicity.

**Adverse perinatal outcome:** Any neonatal morbidity or any composite adverse perinatal outcome was defined as any neonatal morbidity and any composite adverse perinatal outcome respectively.
Breech/cephalic presentation
There were no statistically significant outcomes for perinatal mortality or neonatal morbidity in women who delivered by planned caesarean section as compared to planned vaginal delivery.

Breech/ breech or transverse presentation
Any perinatal mortality was not significantly different, the same applied for perinatal mortality of the first or second twin. Neonatal morbidity of the first twin was significantly higher for planned caesarean section as compared to planned vaginal delivery (aOR 2.3, 95% CI 1.1-4.6). Maternal morbidity was also higher for planned caesarean section (aOR 9.0, 95% CI 2.9-28.0).

Analysis according to the actual mode of delivery
We performed a subgroup analysis in which we compared perinatal and maternal outcomes for planned caesarean section of both twins, vaginal delivery of both twins, emergency caesarean section of both twins and vaginal delivery of the first twin followed by emergency caesarean of the second twin. There were no differences in perinatal or maternal outcomes in emergency caesarean of both twins and vaginal delivery; the same applied for vaginal delivery of the first twin followed by emergency caesarean section of the second twin as compared to vaginal delivery. Planned caesarean section showed a higher perinatal mortality and morbidity rate and a higher maternal morbidity rate as compared to vaginal delivery (table 4).

Discussion
In our study of women with a twin pregnancy suffering very preterm birth, perinatal mortality and morbidity were higher after a planned caesarean section compared to a planned vaginal delivery. Maternal morbidity was also significantly higher after a planned caesarean delivery. Subgroup analysis according to fetal presentation showed that in women with a twin pregnancy with both children in cephalic presentation a policy of planned caesarean section has a higher risk of neonatal mortality and morbidity as compared to planned vaginal delivery. In twins with the first fetus in breech position perinatal morbidity of the first twin is significantly higher in case of a planned caesarean section. All other perinatal outcomes differed not statistically significant. Maternal morbidity was significantly higher in almost all subgroup analyses according to gestational age.

By our knowledge this is thus far the first study that reports on a large cohort of women with a very preterm twin delivery between 26 to 32 weeks. A strength of this study is that it reports on a large cohort of women with an intended vaginal delivery. Furthermore, we analysed perinatal outcomes according to the intended as well as the actual mode of delivery. Another strength is the subgroup analysis according to fetal presentation, since most clinicians take this into consideration in counselling women for a caesarean section or a vaginal delivery. Moreover, we report on both paired and separate outcomes of the offspring.

A limitation of our study is that we excluded all women with obstetric complications other than very preterm delivery such as fetal growth restriction, preeclampsia and maternal hypertension. We did this because co-morbidity might influence perinatal and maternal outcomes and might influence the decision on the mode of delivery.

Another limitation of our study is the fact that it is a retrospective cohort study where a randomised study would be desirable. Recruitment difficulties in studies on subjects like this makes it very unlikely that a RCT will be done in the near future, since recruitment will face the same problems as studies that compare perinatal outcomes in preterm breech presentation [11—16].

In our study maternal morbidity was higher in planned caesarean section as compared to vaginal delivery; which was not the case in women who delivered by emergency caesarean section or women who delivered vaginally followed by emergency caesarean section as compared to vaginal delivery. There were no cases of maternal mortality or uterine rupture in the whole study group; therefore maternal morbidity consisted of haemorrhage postpartum > 1000 ml and need for blood transfusion. When we compare the maternal morbidity rate in planned caesarean section in our study to the maternal morbidity rate in other studies such as the Twin Birth Study [3], the risk of postpartum haemorrhage after planned caesarean section is not as high as in our study. The fact that the higher maternal morbidity rates occurred in women with planned caesarean section and not in women with an emergency caesarean section, suggests that there might have been more women with co-morbidity such as placenta previa in the planned caesarean section group. We excluded severe co-morbidity (lethal congenital abnormalities, placental abruption, intra-uterine fetal death before onset of labour, fetal growth restriction (birthweight <P5), twin-to-twin-transfusion syndrome (TTTS), maternal hypertension (maternal systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) or preeclampsia (high blood pressure and proteinuria)) to eliminate confounders for which the multivariate analysis did not control, however some bias in a retrospective cohort study is inevitable.

In preterm breech presentation of women with a singleton pregnancy planned caesarean delivery is associated with an improved perinatal outcome. [13,14] An explanation for not finding this benefit in case of a planned caesarean section in women with a very preterm delivery of a twin pregnancy might be that when the first
child is delivered vaginally malpresentation of the second child is not such a problem due to the fact that the first baby has already passed the birth channel. We conclude that in women with a twin pregnancy delivering very preterm (<32 weeks), a planned caesarean section does not improve perinatal outcome.

References
Perinatal outcomes according to the mode of delivery in women with a triplet pregnancy in The Netherlands

Lester Bergenhenegouwen
Joost Velzel
Lidewij van de Mheen
Marjolein Kok
Ben Willem Mol
Abstract

Objective In women with a triplet pregnancy, there is debate on the preferred mode of delivery. We performed a nationwide cohort study to assess the impact of mode of delivery on perinatal outcome in women with a triplet pregnancy.

Methods Nationwide cohort study on women with a triplet pregnancy who delivered between 26-0 to 40-0 weeks of gestation in the years 1999-2008. We compared perinatal outcomes according to the intended mode of delivery and the actual mode of delivery. Outcome measures were perinatal mortality and neonatal morbidity. Perinatal outcomes were analysed taking into account the dependency between the children of the same triplet pregnancy (“any mortality” and “any morbidity”) and were also analysed separately per child.

Results We identified 386 women with a triplet pregnancy in the study period. Mean gestational age at delivery was 33.1 weeks (SD 2.5 weeks; range 26.0-40.0 weeks). Perinatal mortality was 2.3% for women with a planned caesarean section and 2.4% in women with a planned vaginal delivery (aOR 0.37; 95% CI 0.09-1.5) and neonatal morbidity was 26.0% versus 36.0%, (aOR 0.88; 95% CI 0.51-1.4) respectively. In the subgroup analyses according to gestational age and in the analysis of perinatal outcomes per child separately there were also no large differences in perinatal outcomes. The same applied for perinatal outcomes according to the actual mode of delivery.

Conclusion In this large cohort study among women with a triplet pregnancy, we did not find large differences in perinatal mortality and neonatal morbidity between caesarean delivery and vaginal delivery.

Keywords
Triplet pregnancy, perinatal mortality, neonatal morbidity, mode of delivery, caesarean section, vaginal delivery

Introduction

Multiple gestation has increased over the years, mainly due the growing use of assisted reproductive technologies and due to the increased maternal age at first pregnancy [1]. This increase in multiple gestation is a concern in obstetrical practice, as multiple pregnancies result in poorer maternal and perinatal outcomes than singleton pregnancies, mainly due to prematurity [2]. In women with a triplet pregnancy, the incidence of overall preterm deliveries is approximately 90%; with a risk of extreme preterm birth (<28 weeks and very preterm birth (28-32 weeks) 13-fold and almost 20-fold, respectively, when compared to women with a singleton pregnancy [3].

Another issue in women with a multiple pregnancy is the mode of delivery. In women with a twin pregnancy, a recent large randomised clinical trial found no difference between planned caesarean section and planned vaginal delivery [4]. That study has been criticized, as women were randomised from 32 weeks onwards and the mortality and morbidity rates in the study were mainly driven by those babies delivered at 32, 33 and 34 weeks [5]. Indeed, in the subgroup of women randomised after 37 weeks, the Twin birth study showed non-significant benefit of caesarean section (RR 0.3; 95% CI 0.06 to 1.4). Also, a recent Australian cohort study showed a clear better perinatal outcome of caesarean section in women with a twin pregnancy at term [6].

In women with a triplet pregnancy, the preferred route of delivery has not been determined [7]. In an effort to minimize intrapartum fetal complications, there has been a tendency to caesarean delivery in women with a triplet pregnancy [8]. There are studies that report an improved outcome by planned caesarean section, but also studies that suggest a lower perinatal morbidity following vaginal delivery [9-19] (Table 1). In an very large series of 7000 women, Vintzileos et al. showed an increase in intrapartum death and neonatal mortality after vaginal delivery. Other studies showed absolute risks to be small, thus also allowing a policy of vaginal delivery if the woman opted to do so.

The aim of the present study was to evaluate the association of (intended) mode of delivery and perinatal mortality and morbidity in a large national cohort of women who delivered a triplet pregnancy in The Netherlands.

Material and methods

This study was performed using data from a retrospective national cohort registered in the Netherlands Perinatal Registry (PRN). The PRN consists of population-based data containing information on pregnancies, deliveries and (re)admissions until 28 days after birth.
The PRN database is obtained by a validated linkage of three different registries: the midwife registry (LVR 1), the obstetricians registry (LVR 2) and the neonatology registry (LNR) of hospital admissions of newborn infants. [20] The coverage of the PRN is approximately 96% of all deliveries in the Netherlands and currently includes over 1.9 million records derived from deliveries in the last decade.

All PRN data are recorded by the caregivers during prenatal care, delivery and the neonatal period. The data are annually sent to the national registry office, where a number of range and consistency checks are conducted. Institutional review board approval was not necessary since the data were used anonymous, thus exempting ethics approval in the Netherlands.

For this study we included all women with a triplet pregnancy who delivered beyond 26 weeks between January 1st 1999 and December 31st 2008. Women were included independently of chorionicity and mode of conception. Exclusion criteria were severe congenital abnormalities and intrauterine fetal death.

Neonatal outcomes were intrapartum death and neonatal death up to 28 days after birth. Neonatal morbidity was defined as NICU admission, neonatal sepsis, intraventricular haemorrhage (IVH), bronchopulmonary dysplasia (BPD) and infant respiratory distress syndrome (IRDS). We excluded women who delivered before 26+0 weeks of gestation because in the time period of the study active management between 24+0 till 26+6 weeks was not general practice in the Netherlands. According to the national guidelines in that period, tocolytics (Atosiban or Nifedipine according to the Dutch guidelines) and antenatal corticosteroids to enhance fetal lung maturity were recommended from 25+0 till 33+6 weeks of gestation for a period of 48 hours in women with symptoms of threatened preterm birth. Threatened preterm birth is defined as preterm contractions combined with dilatation or cervical length shortening below 25 mm or preterm premature rupture of membranes (PPROM).

Women at risk for preterm delivery before 32 weeks of gestation are referred to tertiary centres that are equipped with Neonatal Intensive Care Units (NICU). After 32

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**Table 1** Description of the studies on women with a triplet pregnancy according to the mode delivery

<table>
<thead>
<tr>
<th>Authors</th>
<th>Period</th>
<th>Number of patients included</th>
<th>Main outcome of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loucopoulos A and Jewelewicz R.</td>
<td>1965-1981</td>
<td>35</td>
<td>Study includes also quadruplets and quintuplets. Overall mortality 14.8%</td>
</tr>
<tr>
<td>Feingold M et al.</td>
<td>1977-1986</td>
<td>15</td>
<td>Lower combined perinatal mortality and morbidity in CS as compared to VD.</td>
</tr>
<tr>
<td>Crowther CA and Hamilton RA.</td>
<td>1975-1984</td>
<td>105</td>
<td>Study in Zimbabwe, mortality for triplet one 0/15 (0%) in CS versus 22/72 (30.6%) in VD, mortality of triplet two in CS 1/17 (5.9%) and for VD 22/72 (30.6%); triplet three 2/17 (11.8%) versus 27/70 (38.6%)</td>
</tr>
<tr>
<td>Vintzielos AM et al.</td>
<td>1995-1998</td>
<td>7067</td>
<td>95% caesarean section. Vaginal delivery was associated with increased risk stillbirth RR 5.7; neonatal death &lt; 28 days RR 2.8 and infant death 1 year RR 2.3</td>
</tr>
<tr>
<td>Ron-El R et al.</td>
<td>1970-1978</td>
<td>25</td>
<td>Triplets (9) and quadruplets (6)</td>
</tr>
<tr>
<td>Clarke JP, Roman JD</td>
<td>1981-1992</td>
<td>19</td>
<td>44% caesarean delivery; no differences in perinatal outcome.</td>
</tr>
<tr>
<td>Wildschut Hl et al.</td>
<td>1989-2001</td>
<td>69</td>
<td>63% caesarean delivery; perinatal death 6/36 (17%) in CS and 0/21 (0%) in VD; greater maturity of the infants delivered vaginally appeared to be the major factor for the lower neonatal mortality.</td>
</tr>
<tr>
<td>Alran S et al.</td>
<td>1994-1999</td>
<td>41</td>
<td>84% caesarean delivery; perinatal mortality significantly higher in caesarean section P= 0.02</td>
</tr>
<tr>
<td>Grobman WA et al.</td>
<td>1993-1997</td>
<td>66</td>
<td>71% vaginal deliveries; no differences in perinatal outcome: 9/234 (3.8%) in CS and 0/45 (0%) in VD. Neonatal deaths were not related to the mode of delivery.</td>
</tr>
<tr>
<td>Machtinger R et al.</td>
<td>1997-2005</td>
<td>73</td>
<td>49% caesarean section; perinatal mortality 30.0% in caesarean section and 22.2% in vaginal delivery.</td>
</tr>
<tr>
<td>Alamia et al.</td>
<td>1995-1997</td>
<td>23</td>
<td>50% caesarean delivery. In both groups 0% perinatal mortality and no differences in perinatal and maternal morality</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Perinatal mortality 4/78 (5.1%) in VD and 0/141 (0%) in CS. Composite adverse neonatal outcome 29/78 (37.2%) and 45/141 (31.9%) respectively</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No cases of perinatal mortality in planned CS and planned VD, no differences in neonatal morbidity.</td>
</tr>
</tbody>
</table>
weeks of gestation delivery can take place in a general hospital (secondary care). Magnesium sulphate for fetal neuroprotection was not common practice in the Netherlands during the study period.

Analysis

We studied the impact of the intended mode of delivery, i.e. planned caesarean section versus planned vaginal delivery and of the actual mode of delivery, i.e. planned caesarean section, vaginal delivery, emergency caesarean section, and vaginal delivery of one or two children followed by emergency caesarean section. The coding in the PRN is such that women who never have the intention to deliver vaginally are coded as a planned caesarean section, and women who intend to deliver vaginally but who then have a caesarean section are coded as an emergency caesarean section. Perinatal outcomes were clustered: taking into account the dependency between the children of the same mother/same triplet pregnancy. These clustered outcome measures are “any mortality”, “any morbidity” and “any mortality or morbidity”. Furthermore we analysed perinatal outcomes separately per child. We calculated odds ratios with 95% confidence intervals (CI) to determine the precision of each odds ratio. We adjusted for gestational age (weeks). We also made a subgroup analysis according to gestational age, which was divided into the following classes: 26-32 weeks, 32-37 weeks and > 37 weeks. We used statistical software SPSS® for analysis.

Results

We identified 386 women with a triplet pregnancy in our nationwide database who delivered between 1999-2008, delivering 1,158 children. Mean gestational age at delivery was 33.1 weeks (SD 2.5 weeks, range 26.0 - 40.0 weeks). (figure 1).

There were 219/386 women (57%) with a planned caesarean section and 167/386 women (43%) with a planned vaginal delivery. The baseline characteristics of these women are listed in table 2. The planned caesarean delivery group contained more nulliparous women (129/219; 59%) as compared to the planned vaginal delivery group (77/167; 46%) (p=0.06). Mean gestational age at delivery was higher in women with a planned caesarean section (33.5 weeks) as compared to women with a planned vaginal delivery (32.4 weeks) (p<0.001). The same applied for mean birth weight of all children (1962 g versus 1769 g, p= 0.001), (1910 g versus 1768 g, p= 0.005) and (1900 g versus 1746 g, p= 0.002) for the first, second and third child respectively.

Table 2 Baseline characteristics of women with a triplet pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Planned CS (N=219)</th>
<th>Planned VD (N=167)</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean maternal age, years (SD)</td>
<td>32.5 (4.1)</td>
<td>31.7 (4.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous, n (%)</td>
<td>129 (59%)</td>
<td>77 (46%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Parous, n (%)</td>
<td>90 (41%)</td>
<td>90 (54%)</td>
<td></td>
</tr>
<tr>
<td>Chorionicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCTA, n (%)</td>
<td>87 (40%)</td>
<td>70 (42%)</td>
<td>0.45</td>
</tr>
<tr>
<td>DCTA, n (%)</td>
<td>65 (30%)</td>
<td>47 (28%)</td>
<td></td>
</tr>
<tr>
<td>MCTA, n (%)</td>
<td>11 (5%)</td>
<td>6 (4%)</td>
<td></td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>56 (26%)</td>
<td>44 (26%)</td>
<td></td>
</tr>
<tr>
<td>Conception</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous, n (%)</td>
<td>69 (31%)</td>
<td>63 (38%)</td>
<td>0.71</td>
</tr>
<tr>
<td>ART, n (%)</td>
<td>148 (68%)</td>
<td>103 (61%)</td>
<td></td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>2 (1%)</td>
<td>3 (1%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western, n (%)</td>
<td>206 (94%)</td>
<td>160 (96%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Non-western, n (%)</td>
<td>13 (6%)</td>
<td>7 (4%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>39 (18%)</td>
<td>25 (15%)</td>
<td>0.55</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>180 (82%)</td>
<td>142 (85%)</td>
<td></td>
</tr>
<tr>
<td>Maternal Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>2 (1%)</td>
<td>1 (1%)</td>
<td>0.45</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>154 (70%)</td>
<td>127 (76%)</td>
<td></td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>63 (29%)</td>
<td>39 (23%)</td>
<td></td>
</tr>
<tr>
<td>Mean birth weight, grams (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetus 1</td>
<td>1962 (432)</td>
<td>1769 (492)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fetus 2</td>
<td>1910 (482)</td>
<td>1768 (499)</td>
<td>0.005</td>
</tr>
<tr>
<td>Fetus 3</td>
<td>1900 (476)</td>
<td>1764 (501)</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean gestational age at delivery, weeks (SD)</td>
<td>33.5 (2.1)</td>
<td>32.4 (2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26+0 - 31+6 weeks, n (%)</td>
<td>27 (12%)</td>
<td>55 (33%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>32+0 - 36+6 weeks, n (%)</td>
<td>183 (84%)</td>
<td>107 (64%)</td>
<td></td>
</tr>
<tr>
<td>37+0 - 40+0 weeks, n (%)</td>
<td>9 (4%)</td>
<td>5 (3%)</td>
<td></td>
</tr>
</tbody>
</table>

TCTA = trichorionic triamniotic
DCTA = dichorionic triamniotic
MCTA = monochorionic triamniotic
ART = assisted reproductive technologies
### Table 3: Perinatal mortality* and neonatal morbidity** in women with a triplet pregnancy according to the intended mode of delivery

<table>
<thead>
<tr>
<th></th>
<th>Planned CS N = 219</th>
<th>Planned VD N = 167</th>
<th>OR (95% CI)</th>
<th>aOR (95% CI)***</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall 26-40 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any mortality</td>
<td>5/219</td>
<td>4/167</td>
<td>0.95 (0.25 - 3.4)</td>
<td>0.37 (0.09 - 1.3)</td>
</tr>
<tr>
<td>Any morbidity</td>
<td>56/219</td>
<td>60/167</td>
<td>0.61 (0.40-0.95)</td>
<td>0.88 (0.53 - 1.4)</td>
</tr>
<tr>
<td>Any mortality or morbidity</td>
<td>55/219</td>
<td>56/167</td>
<td>0.66 (0.43-1.04)</td>
<td>1.2 (0.72 - 2.2)</td>
</tr>
<tr>
<td>Perinatal death first child, n%</td>
<td>3/219</td>
<td>4/167</td>
<td>0.57 (0.32 - 0.93)</td>
<td>1.6 (0.32 - 8.3)</td>
</tr>
<tr>
<td>Perinatal death second child, n%</td>
<td>2/219</td>
<td>1/167</td>
<td>1.5 (0.14-17.0)</td>
<td>3.7 (0.30 - 44.9)</td>
</tr>
<tr>
<td>Perinatal death third child, n%</td>
<td>1/219</td>
<td>2/167</td>
<td>0.38 (0.03-4.2)</td>
<td>1.16 (0.10 - 11.7)</td>
</tr>
<tr>
<td>Neonatal morbidity first child, n %</td>
<td>31/219</td>
<td>35/167</td>
<td>0.62 (0.37-1.1)</td>
<td>0.78 (0.41 - 1.5)</td>
</tr>
<tr>
<td>Neonatal morbidity second child, n%</td>
<td>35/219</td>
<td>40/167</td>
<td>0.65 (0.39-1.1)</td>
<td>0.91 (0.50 - 1.7)</td>
</tr>
<tr>
<td>Neonatal morbidity third child, n%</td>
<td>39/219</td>
<td>39/167</td>
<td>0.71 (0.43-1.2)</td>
<td>0.73 (0.40 - 1.3)</td>
</tr>
<tr>
<td><strong>26-31+6 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any mortality</td>
<td>3/27</td>
<td>4/55</td>
<td>1.6 (0.3377)</td>
<td>3.5 (0.05 - 22.5)</td>
</tr>
<tr>
<td>Any morbidity</td>
<td>21/27</td>
<td>43/55</td>
<td>0.02 (0.00-0.11)</td>
<td>0.78 (0.24 - 2.5)</td>
</tr>
<tr>
<td>Any mortality or morbidity</td>
<td>21/27</td>
<td>40/55</td>
<td>1.3 (0.44-3.9)</td>
<td>1.7 (0.05 - 55)</td>
</tr>
<tr>
<td>Perinatal death first child, n%</td>
<td>2/27</td>
<td>4/55</td>
<td>1.02 (0.17-5.9)</td>
<td>2.0 (0.27 - 15.0)</td>
</tr>
<tr>
<td>Perinatal death second child, n%</td>
<td>1/27</td>
<td>1/55</td>
<td>2.1 (0.12-35.4)</td>
<td>3.5 (0.19 - 64.4)</td>
</tr>
<tr>
<td>Perinatal death third child, n%</td>
<td>1/27</td>
<td>2/55</td>
<td>1.02 (0.09-11.8)</td>
<td>1.7 (0.13 - 21.4)</td>
</tr>
<tr>
<td>Neonatal morbidity first child, n %</td>
<td>16/27</td>
<td>28/55</td>
<td>1.0 (0.55-3.9)</td>
<td>0.48 (0.17 - 1.4)</td>
</tr>
<tr>
<td>Neonatal morbidity second child, n%</td>
<td>15/27</td>
<td>31/55</td>
<td>0.97 (0.48-2.0)</td>
<td>0.83 (0.37 - 2.0)</td>
</tr>
<tr>
<td>Neonatal morbidity third child, n%</td>
<td>13/27</td>
<td>30/55</td>
<td>1.0 (0.31-9.0)</td>
<td>0.96 (0.34 - 2.7)</td>
</tr>
<tr>
<td><strong>32-36+6 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any mortality</td>
<td>2/183</td>
<td>0/107</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Any morbidity</td>
<td>34/183</td>
<td>16/107</td>
<td>1.3 (0.62-2.5)</td>
<td>0.74 (0.37 - 1.5)</td>
</tr>
<tr>
<td>Any mortality or morbidity</td>
<td>33/183</td>
<td>15/107</td>
<td>1.3 (0.70-2.4)</td>
<td>1.4 (0.70 - 2.9)</td>
</tr>
<tr>
<td>Perinatal death first child, n%</td>
<td>1/183</td>
<td>0/107</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death second child, n%</td>
<td>1/183</td>
<td>0/107</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death third child, n%</td>
<td>6/183</td>
<td>0/107</td>
<td>-</td>
<td>1.01 (0.34 - 3.1)</td>
</tr>
<tr>
<td>Neonatal morbidity first child, n %</td>
<td>15/183</td>
<td>6/107</td>
<td>1.5 (0.57-4.0)</td>
<td>0.64 (0.24 - 1.7)</td>
</tr>
<tr>
<td>Neonatal morbidity second child, n%</td>
<td>19/183</td>
<td>9/107</td>
<td>1.3 (0.33-2.9)</td>
<td>0.77 (0.23 - 2.3)</td>
</tr>
<tr>
<td>Neonatal morbidity third child, n%</td>
<td>25/183</td>
<td>9/107</td>
<td>1.7 (0.77-3.8)</td>
<td>0.56 (0.24 - 1.3)</td>
</tr>
<tr>
<td><strong>&gt; 37 weeks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any mortality</td>
<td>0/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Any morbidity</td>
<td>1/9</td>
<td>1/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Any mortality or morbidity</td>
<td>1/9</td>
<td>1/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death first child, n%</td>
<td>0/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death second child, n%</td>
<td>0/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal death third child, n%</td>
<td>0/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal morbidity first child, n %</td>
<td>0/9</td>
<td>1/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal morbidity second child, n%</td>
<td>1/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal morbidity third child, n%</td>
<td>1/9</td>
<td>0/5</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Perinatal mortality is defined as intrapartum mortality and neonatal mortality < 28 days.

** Neonatal morbidity is defined as NICU admission, neonatal sepsis, IHI, BPD and IRDS.

*** Adjusted for gestational age in weeks.

---

**CHAPTER 7 TRIPLET PREGNANCIES AND NEONATAL OUTCOMES ACCORDING TO THE MODE OF DELIVERY**
<table>
<thead>
<tr>
<th></th>
<th>Planned CS</th>
<th>VD</th>
<th>Emergency CS</th>
<th>VD + ECS</th>
<th>OR (95% CI)***</th>
<th>OR (95% CI)***</th>
<th>OR (95% CI)***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 219</td>
<td>N = 74</td>
<td>N = 70</td>
<td>N = 23</td>
<td>CS vs VD</td>
<td>ECS vs VD</td>
<td>VD+ECS vs VD</td>
</tr>
<tr>
<td>Any mortality</td>
<td>5/219</td>
<td>1/74</td>
<td>1/70</td>
<td>2/23</td>
<td>4.2 (0.47 - 40.9)</td>
<td>0.78 (0.04 - 13.9)</td>
<td>5.8 (0.39 - 85.6)</td>
</tr>
<tr>
<td>Any morbidity</td>
<td>56/219</td>
<td>24/74</td>
<td>26/70</td>
<td>10/23</td>
<td>0.89 (0.38 - 2.1)</td>
<td>0.99 (0.34 - 2.8)</td>
<td>0.64 (0.15 - 2.7)</td>
</tr>
<tr>
<td>Any mortality or morbidity</td>
<td>55/219</td>
<td>23/74</td>
<td>24/70</td>
<td>9/23</td>
<td>1.3 (0.66 - 2.7)</td>
<td>0.98 (0.42 - 2.3)</td>
<td>1.05 (0.27 - 4.0)</td>
</tr>
</tbody>
</table>

**Perinatal death first child, n%**

- Overall 26-40 weeks
  - Planned CS: 3/219
  - VD: 1/74
  - Emergency CS: 1/70
  - OR (95% CI): 2.5 (0.23 - 28.4)
  - Adjusted OR: 0.78 (0.4 - 13.9)
  - OR: 5.8 (0.39 - 85.6)

**Neonatal morbidity first child, n%**

- Overall 26-40 weeks
  - Planned CS: 35/219
  - VD: 16/74
  - Emergency CS: 12/70
  - OR (95% CI): 1.3 (0.5 - 3.4)
  - Adjusted OR: 1.05 (0.27 - 4.0)
  - OR: 0.64 (0.15 - 2.7)

**Neonatal death second child, n%**

- Overall 26-40 weeks
  - Planned CS: 2/219
  - VD: 0/74
  - Emergency CS: 1/70
  - OR (95% CI): 1.2 (0.22 - 6.8)
  - Adjusted OR: 1.05 (0.53 - 2.3)
  - OR: 0.64 (0.15 - 2.7)

**Neonatal death third child, n%**

- Overall 26-40 weeks
  - Planned CS: 3/219
  - VD: 1/74
  - Emergency CS: 1/70
  - OR (95% CI): 1.3 (0.5 - 3.4)
  - Adjusted OR: 1.05 (0.53 - 2.3)
  - OR: 0.64 (0.15 - 2.7)

**Perinatal death first child, n%**

- Overall 26-40 weeks
  - Planned CS: 2/219
  - VD: 0/74
  - Emergency CS: 1/70
  - OR (95% CI): 1.2 (0.22 - 6.8)
  - Adjusted OR: 1.05 (0.53 - 2.3)
  - OR: 0.64 (0.15 - 2.7)

**Neonatal morbidity first child, n%**

- Overall 26-40 weeks
  - Planned CS: 35/219
  - VD: 16/74
  - Emergency CS: 12/70
  - OR (95% CI): 1.3 (0.5 - 3.4)
  - Adjusted OR: 1.05 (0.53 - 2.3)
  - OR: 0.64 (0.15 - 2.7)

**Neonatal death second child, n%**

- Overall 26-40 weeks
  - Planned CS: 1/219
  - VD: 0/74
  - Emergency CS: 1/70
  - OR (95% CI): 1.2 (0.22 - 6.8)
  - Adjusted OR: 1.05 (0.27 - 4.0)
  - OR: 0.64 (0.15 - 2.7)

**Neonatal death third child, n%**

- Overall 26-40 weeks
  - Planned CS: 3/219
  - VD: 1/74
  - Emergency CS: 1/70
  - OR (95% CI): 1.3 (0.5 - 3.4)
  - Adjusted OR: 1.05 (0.27 - 4.0)
  - OR: 0.64 (0.15 - 2.7)

---

*Perinatal mortality is defined as intrapartum mortality and neonatal mortality < 28 days.
**Neonatal morbidity is defined as NICU admission, neonatal sepsis, IVH, BPD and IRDS.
***Adjusted for AD in weeks.
The clustered data (taking into account the dependency between children of the same mother/triplet pregnancy) according to the intended mode of delivery showed in the overall group a mortality rate of 2.3% in planned caesarean section versus 2.4% in planned vaginal delivery, (aOR 0.37, 95% CI 0.09-1.5); any morbidity in 26% versus 36%, (aOR 0.88, 95% CI 0.51-1.4) and any mortality and morbidity of 25% for planned caesarean section as compared to 34% for planned vaginal delivery (aOR 1.2, 95% CI 0.72-2.2). In the subgroup analysis according to gestational age there were also no large differences for any mortality, any morbidity and any mortality or morbidity in planned caesarean section as compared to planned vaginal delivery.

When we compared the first, second or third child separately, there were no statistically significant differences in perinatal mortality (1.4% vs 2.4%, aOR 1.6; 95% CI 0.32-8.3), (0.91% vs 0.60%, aOR 3.7; 95% CI 0.30-44.9) and (0.46% vs 1.2%, aOR 1.6; 95% CI 0.10-13.7), respectively, for planned caesarean section as compared to planned vaginal delivery. Neonatal morbidity per child also showed no significantly different outcomes for the first, second and third child ((14% vs 21%, aOR 0.78; 95% CI 0.41-1.5), (16% vs 24%,aOR 0.91; 95% CI 0.50-1.7) and (18% vs 23%, aOR 0.73; 95% CI 0.40-1.3) for planned caesarean section as compared to planned vaginal delivery. The same applied for all perinatal outcomes according to gestational age (Table 3).

In the analysis according to the actual mode of delivery in the whole study population any mortality was not significantly different in women who delivered by planned caesarean section, emergency caesarean section, vaginal delivery of one or two children followed by emergency caesarean section as compared to vaginal delivery (2.3% vs 1.4%, aOR 4.2; 95% CI 0.43-40.9), (1.4% vs 1.4%, aOR 0.78; 95% CI 0.04-13.9) and (8.7% vs 1.4%, aOR 5.8; 95% CI 0.39-85.6) respectively.

The same applied for any morbidity (26% vs 32%, aOR 0.89,95% CI 0.38-2.1) for women who delivered by planned caesarean section, for women who delivered by emergency caesarean section (37% vs 32%, aOR 0.99; 95% CI 0.34-2.8) and for women who delivered by vaginal delivery and emergency caesarean section (44% vs 32%, aOR 0.64, 95% CI 0.15-2.7) as compared to vaginal delivery. The subgroup analysis according to gestational age also showed no large differences in perinatal outcomes. The analysis for every child of the triplet pregnancy separately showed a significantly increased risk for perinatal morbidity of the third child in emergency caesarean section as compared to vaginal delivery (17% vs 27%, aOR 3.8; 95% CI 1.3-11.4). All other perinatal outcomes were not significantly different. (Table 4)

Discussion

This population based cohort study of perinatal outcomes in women with a triplet pregnancy in the Netherlands shows an overall perinatal mortality rate of 2.3% in planned caesarean section versus 2.4% in planned vaginal delivery and a neonatal morbidity rate of 26% versus 36% respectively. Perinatal mortality for the first child was 1.4% versus 2.4%, for the second child 0.9% versus 0.60% and for the third child 0.46% versus 1.2%. There is a trend towards improved perinatal outcomes in women with a planned caesarean section, which however does not reach significance.

In many countries women with a triplet pregnancy deliver by planned caesarean section. [21]. The high vaginal delivery rate in The Netherlands gave us the unique opportunity to study the effect of the mode of delivery on perinatal outcomes in women with a triplet pregnancy. In our study population of 386 women with a triplet pregnancy, almost half of the women had an intended vaginal delivery. Of these women with an intended vaginal delivery 44% had an actual vaginal delivery, while 56% had an emergency caesarean section after vaginal birth of one or two children. Mean gestational age at delivery in our study was 33.1 weeks, which is comparable with other studies on perinatal outcomes in women with a triplet pregnancy [13,17]. Remarkable in our cohort is that we identified a relatively high percentage of women with a triplet pregnancy who delivered beyond 37 weeks of gestation (16/386, 4.1%).

A limitation of this study is that due to the fact that this is a retrospective cohort study with different baseline characteristics for both groups, with a significantly higher mean gestational age at delivery and higher mean birth weight of all children in women who delivered by planned caesarean section as compared to planned vaginal delivery.

Another limitation is that from our database we were not able to determine what criteria were used in the decision of the mode of delivery: what was the profile of women who were allowed to deliver vaginally and what were the reasons for a planned caesarean section.

A potential disadvantage of caesarean delivery in women with threatened preterm labour is timing of the delivery. In case caesarean delivery is done preterm, one is never sure whether preterm delivery actually would occur. As our dataset only registered the exact moment of delivery, we could not correct for the potential advantage of a further delay of pregnancy with some days. Obviously, caesarean delivery should be delayed as much as possible, specifically in women at very low gestational ages.

When we compare our study to the studies that have been published until now, our study describes a relatively large cohort. The largest study that was published by Vintzileos et al compared perinatal outcomes in a cohort of more than 7,000 women...
with a triplet pregnancy [12]. Of these women, 95% delivered by caesarean section. Perinatal mortality was significantly higher in vaginal delivery as compared to caesarean section. Therefore, the authors concluded that vaginal delivery should be avoided in women with a triplet pregnancy. All other studies published until now are much smaller, with sample sizes varying from 15 till 105 women. Three of these studies favour caesarean section [9-11], six studies favour vaginal delivery [8, 14-18] and three studies concluded that the preferable mode of delivery cannot be stated. [13, 19]

Obviously, possible future pregnancies should play a role in the decision, especially at lower gestational ages where the chance of fetal loss is high.

We conclude that in relatively large cohort study among women with a triplet pregnancy, we did not find large differences in perinatal mortality and neonatal morbidity between caesarean delivery and vaginal delivery. Although larger studies indicate an advantage for elective caesarean section, obstetricians should consider vaginal delivery in women with a triplet pregnancy. Obviously, the final decision should be a shared decision, taking into account the opinion of the woman.

References


Summary and General Discussion
Summary

This thesis addresses the optimal mode of delivery in women with a preterm and term breech presentation and in women with a multiple pregnancy. We analysed perinatal and maternal outcomes according to the intended as well as the actual mode of delivery in nationwide cohort studies using data from the Netherlands Perinatal Registry (PRN). This chapter summarises and discusses the findings from our research. Furthermore, clinical and future research implications are put forward.

Chapter 1 contains a general introduction on preterm delivery, abnormal fetal presentation and multiple pregnancy and presents the outline of the thesis. In preterm birth, fetal malpresentation occurs more frequently than in term births. Breech presentation is defined as a fetus in longitudinal lie with the buttocks or feet closest to the cervix. For term breech delivery the Term Breech Trial [1] showed that an intended caesarean delivery is safer in terms of combined short term morbidity and mortality which has led to a shift to planned caesarean delivery. Breech presentation occurs more frequently at lower gestational ages, with an incidence of 25% at 26 weeks, 15% at 32 weeks, declining to 3 to 4% in term pregnancy [2]. For women with a preterm delivery in breech presentation knowledge on the optimal mode of delivery is limited. Randomised controlled trials were stopped before reaching large sample size due to recruitment difficulties and were therefore too small to draw meaningful conclusions about the optimal mode of delivery [3-8].

The incidence of multiple pregnancies has increased over the past 20 years by approximately 80%, largely because of the growing use of assisted reproductive technologies and the increase in average maternal age at first childbirth [9]. This makes the issue on the optimal mode of delivery in multiple pregnancies an important topic. However, studies on the optimal mode of delivery in women with a twin pregnancy and a very preterm delivery (< 32 weeks) are limited, the same applies for women with a triplet pregnancy.

Chapter 2 describes the results of a systematic review and meta-analysis of non-randomised studies that assesses the association between mode of delivery and neonatal mortality in women with preterm breech presentation. We therefore searched Pubmed, Embase and The Cochrane library for articles comparing neonatal mortality after vaginal delivery versus caesarean section in preterm breech presentation (gestational age 25+0 and 36+6 weeks). Seven studies met the eligibility criteria and were included in this systematic review, thus including a total of 3,557 women with a preterm delivery of a child in breech presentation. The weighted risk of neonatal...
mortality was 3.8% in the caesarean section group and 11.5% in the vaginal delivery group (pooled RR 0.63; 95% CI 0.48 to 0.81). In conclusion, we found no large randomised controlled studies addressing the optimal mode of delivery in women delivering a preterm fetus in breech presentation for this review; the available cohort studies indicate that caesarean section is associated with a reduced neonatal mortality as compared to vaginal delivery. This conclusion should however be carefully interpreted, concerning the lack of intention to treat analysis and other bias that is inevitably in cohort studies.

Chapter 3 provides the results of a nationwide cohort study in the Netherlands on women with a singleton pregnancy in breech presentation who delivered preterm (26+0 and 36+6 weeks of gestation) in the years 2000-2011. We compared perinatal outcomes according to the intended mode of delivery as well as the actual mode of delivery using multivariate logistic regression analysis. We studied a total of 8,356 women with a singleton preterm breech delivery. Intended caesarean delivery (n=1,935) was not associated with a significant reduction in perinatal mortality compared to intended vaginal delivery (n=6,421) (1.3% versus 1.5%, aOR 0.97; 95% CI 0.60-1.57). However, the composite of perinatal mortality and morbidity was significantly reduced in the intended caesarean delivery group (8.7% versus 10.4% (aOR 0.77; 95% CI 0.63-0.93). In the sub-group of women delivering at 28-32 weeks, intended caesarean delivery was associated with a significant reduction of perinatal mortality, from 4.1% after an intended vaginal delivery to 1.7% after a planned caesarean delivery (aOR 0.27; 95% CI 0.10-0.77) and a significantly reduced composite mortality and severe morbidity from 10.1% after a planned vaginal delivery to 5.9% after a planned caesarean delivery (aOR 0.37; 95% CI 0.20-0.68). We concluded therefore that in women with a preterm delivery of a fetus in breech presentation caesarean section is associated with a reduced perinatal mortality and morbidity as compared to vaginal delivery.

In chapter 4 we provide the results of a nationwide population based cohort study on the effect of the mode of delivery in women with a preterm breech delivery on perinatal and maternal outcome of the subsequent pregnancy. We identified all women with a preterm breech delivery (26+0 and 36+6 weeks of gestation) and a subsequent delivery in the years 1999 to 2007 in the Netherlands. We compared perinatal outcomes in both pregnancies according to the intended mode of the index pregnancy (preterm breech presentation). We included 1,543 women in the study period, of whom 259 (47%) women had a planned caesarean section and 1,284 (83%) women had a planned vaginal delivery in the first pregnancy. In the subsequent pregnancy, perinatal mortality was 1.1% for women with a planned caesarean section in the first pregnancy and 0.5% for women with a planned vaginal delivery in the first pregnancy, (aOR 1.8; 95% CI 1.3-10.1). Composite adverse neonatal outcome was 2.3% versus 1.5%, (aOR 1.5; 95% CI 0.55-4.2). We also calculated the average risk of perinatal mortality over the two pregnancies, which was 1.9% for planned caesarean section and 2.0% for planned vaginal delivery, (OR 0.98; 95% CI 0.49-1.9). In conclusion, in women with a preterm breech delivery planned caesarean section does not reduce perinatal mortality, perinatal morbidity or maternal morbidity rate over the course of two pregnancies.

Chapter 5 describes the results of a nationwide cohort study which showed that after publication of the Term Breech Trial there was a shift towards elective caesarean delivery up to 80% of breech birth in the Netherlands. This increase in elective caesarean delivery led to a decrease in perinatal mortality and morbidity among women delivering a child in breech presentation at term. Still, 40% of the women with a term breech presentation attempt a vaginal birth. Presumed risk selection of the women attempting vaginal breech birth since the Term Breech Trial, has not led to better outcome of the planned vaginal deliveries. We were not able to select a subgroup of women based on parity, type of breech, birth weight and onset of labour, with a low risk of adverse neonatal outcome during planned vaginal breech delivery, compared to an elective caesarean delivery.

In chapter 6 we present the results of a population-based cohort study including all women with a twin pregnancy who delivered very preterm (26-32 weeks of gestation) in the Netherlands between January 2000 and December 2010. Perinatal outcomes (mortality and morbidity) were paired taking into account the dependency between the children of the same twin pregnancy and were also analysed for each child separately. We studied 1,655 women with a very preterm twin delivery (3,310 children). Perinatal mortality was higher after a planned caesarean section as compared to planned vaginal delivery (10% versus 6.5%, aOR 2.5; 95% CI 1.5-4.2). The same applied for perinatal morbidity (63% versus 66%, aOR 1.5; 95% CI 1.1-2.0). Maternal morbidity was also significantly higher in women who delivered by planned caesarean section (17%) as compared to planned vaginal delivery (9.9%, (aOR 4.0; 95% CI 2.6-6.3). We concluded therefore that there is not much place for a planned caesarean section for women with a twin pregnancy delivering very preterm (<32 weeks).

Chapter 7 contains the results of a study on perinatal outcomes in women with a triplet pregnancy in the Netherlands in the years 1999-2008. We identified 386 women (1,158 children), of whom we compared perinatal mortality and morbidity according to...
the intended as well as actual mode of delivery. Perinatal mortality was 2.3% for women with a planned caesarean section and 2.4% in women with a planned vaginal delivery (aOR 0.37; 95% CI 0.09-1.5) and neonatal morbidity was 26.0% versus 36.0%, (aOR 0.88; 95% CI 0.51-1.4) respectively. In the subgroup analyses according to gestational age and in the analysis of perinatal outcomes per child separately there were also no large differences in perinatal outcomes. The same applied for perinatal outcomes according to the actual mode of delivery. This is one of the largest cohort studies described until now on women with a triplet pregnancy and perinatal outcomes according to the mode of delivery. We did not find large differences in perinatal mortality and neonatal morbidity between caesarean delivery and vaginal delivery.
General Discussion
General Discussion

Clinical implications
The optimal mode of delivery in case of fetal malpresentation is an important obstetric issue for both obstetricians as well as the women involved. The obstetric labour ward provides a unique setting in which rapid clinical judgement and decision-making skills are important for a safe outcome for both mother and child. The safety and optimal outcome for the baby is often, but not always directly, linked to the outcome of the mother and can lead to conflicting interests. Women have a natural desire to put their babies health before their own, but the anticipated morbidity and mortality for both mother and baby must be carefully weighed and considered in the actions we take at delivery in case of fetal malpresentation. Randomized controlled trials on this subject would therefore be helpful.

A typical example of the possible effect that publication of such a randomized controlled trial can have on daily clinical practice is the publication of the Term Breech Trial [1]. In this trial of 2083 women with a term breech delivery it was shown that perinatal mortality or serious neonatal morbidity was significantly lower for women with a planned caesarean section (17/1039; 1.6%) as compared to women with a planned vaginal delivery (52/1039 (5.0%); RR 0.33; 95% CI 0.19-0.56). Within three months after publication of this trial the elective caesarean section rate doubled in the Netherlands and eventually increased up to 90% in some countries [2,3]. In chapter 5 we showed that this increase in elective caesarean delivery led to a decrease in perinatal mortality from 1.3‰ to 0.7‰ (OR 0.51 (95% CI 0.28 – 0.93)) among women delivering a child in breech presentation at term in The Netherlands. However, still 40% of the women with a term breech presentation attempt a vaginal birth. Subgroup analysis could not identify antepartum parameters that could distinguish between women with a low versus a high risk vaginal breech birth. In view of this relatively large percentage of women attempting term vaginal breech birth it is important that obstetricians are aware of the fact that risk selection is not possible based on patient characteristics. Women opting for a vaginal delivery remain therefore at increased risk and both women and clinicians should be aware of this risk.

In preterm birth, fetal malpresentation occurs more frequently than in term births, with an incidence of breech presentation as high as 25% at 26 weeks. Randomized controlled trials to assess the optimal mode of delivery in case of preterm breech presentation were not as successful as the term counterpart in terms of recruitment of participants; all studies were stopped before reaching the targeted sample size [4-7].
The largest randomized controlled trial on this topic contained 38 women. The optimal mode of delivery in preterm breech presentation therefore cannot be concluded based on these studies, and the optimal mode of delivery remains controversial and subject of debate. In lack of randomized controlled trials we have to rely on evidence available from cohort studies.

The relatively high vaginal delivery rate in The Netherlands gave us the unique opportunity to study the effect of the mode of delivery in preterm breech delivery in a nationwide cohort study. All studies, including our study and a systematic review, are pointing in the same direction: caesarean delivery reduces perinatal mortality and morbidity as compared to vaginal delivery. However, the treatment effect seems smaller than has been found after the randomized controlled trial for term breech delivery by Hannah et al.[1] Women with a preterm breech delivery between 28-32 weeks seem to benefit most from a caesarean delivery, with a 1.7% risk of perinatal mortality as compared to 4.1% in women with an intended vaginal delivery (aOR 0.27; 95% CI 0.10-0.77). An explanation for this could be that in this gestational period there is a more unfavourable abdominal circumference versus head circumference ratio.[8]

In women with a preterm delivery the major determinant of neonatal death is the degree of prematurity, and the additional risk associated with a vaginal delivery is small. This might explain why the health benefit of a caesarean delivery in case of preterm breech delivery for the offspring is smaller than in term delivery. When the subsequent pregnancy is taken into account, the perinatal mortality and morbidity rate over the two pregnancies are equal for women with a planned caesarean section and a planned vaginal delivery in the first pregnancy (with the preterm breech presentation). Therefore the effect on possible future pregnancies should be part of counselling on the optimal mode of delivery. This might be a difficult subject at the moment of an unexpected and overwhelming event such as a preterm delivery for the pregnant woman and her partner. In a very short period of time, the delivery can suddenly take place very rapidly, they have to be able to understand the meaning of having a (very) preterm child, think about the optimal mode of delivery for this pregnancy and take into account what the consequences of the mode of delivery might be on possible future pregnancies.

In women with a multiple pregnancy, dynamics in birth (preterm and term) are different than in singleton pregnancies and fetal malpresentation occurs more often.[9] After vaginal birth of the first child, malpresentation of the subsequent child(ren) is different from malpresentation in a singleton pregnancy, as one child has already passed the birth channel. This potentially reduces the problem of the passing of the fetal head as compared to in women with a preterm delivery of a singleton in breech presentation as described above.

In women with a very preterm delivery below 32 weeks of gestation our study of 1,655 women showed a higher perinatal mortality in women with a planned caesarean section (10.4%) as compared to women with a planned vaginal delivery (6.5%) (aOR 2.5; 95% CI 1.5-4.2). In this very preterm period, the degree of prematurity is the major determinant of neonatal mortality. To find a difference in perinatal outcome according to the mode of delivery sample size of the study probably has to be larger. A potential disadvantage of caesarean delivery in women with threatened preterm labour is timing of the delivery. Obviously, when vaginal delivery occurs further delay of pregnancy was either not indicated or not possible. In caesarean delivery, however, one is not sure whether the preterm birth would actually occur. If the caesarean section is performed too early, the problem of prematurity addressed above has become even larger, which is an important factor in gestational age below 32 weeks. Maternal morbidity (hemorrhage postpartum > 1,000 ml) was higher in women with a planned caesarean delivery in our study, however since this was not the case in other studies we have to be careful to draw firm conclusions on this specific topic. Taking into account that perinatal outcome does not improve by a planned caesarean section and might lead to adverse maternal outcome there is not much place for a planned caesarean delivery in women with a twin pregnancy delivering before 32 weeks of gestation.

In women with a triplet pregnancy the same issue on the mode of delivery occurs. In an effort to minimize intrapartum fetal complications, there has been a tendency to a caesarean delivery in women with a triplet pregnancy. This was also the case in the largest study on women with a triplet pregnancy and perinatal outcome according to the mode of delivery: in this study of 7067 women in the U.S. caesarean section rate was 95%. This study concluded that vaginal delivery was associated with increased risk of stillbirth (RR 3.7); newborn death < 28 days (RR 2.8) and infant death < 1 year (RR 2.3). The high vaginal delivery rate in the Netherlands gave us the unique opportunity to study the relation between the mode of delivery and perinatal outcome, and we found in our national cohort study 386 women (vaginal delivery rate of 43%) that perinatal mortality was equal for planned caesarean section (2.3%) as compared to planned vaginal delivery (2.4%). Based on the large differences in women attempting a vaginal delivery, an important question is whether we are able to identify criteria for the decision on the mode of delivery: what is the profile of women who are allowed to deliver vaginally. Since this is still unclear, obstetricians are challenged to discuss all these factors with women with a triplet pregnancy, and the decision on the mode of delivery has to be a shared decision.
Future research implications

In this thesis we present the results of nationwide cohort studies, which are all based on data derived from Netherlands Perinatal Registry (PRN). In retrospective cohort studies we have to be careful to draw firm conclusions. These studies can however help us to find associations between for example the mode of delivery and perinatal outcome, and in the absence of large randomised clinical trials we simply do not have better data to underpin our practice. Furthermore, we have to be aware that some bias is inevitable. Ideally, the exact treatment effect of the mode of delivery on perinatal outcomes in preterm breech, twin and triplet pregnancies would be assessed by large randomized controlled trials. These trials will probably face the same recruitment difficulties as other trials on the subject. However, in view of the high vaginal delivery rates we found in our cohort studies in the Netherlands and the large number of clinical trials that were successfully conducted in the Dutch obstetric research consortium we might be able to successfully conduct such a trial in the Netherlands. On the other hand, the PRN data might already have helped to solve particular questions, such as the optimal mode of delivery in women with a preterm breech baby (chapter 3). The better outcome that we observed after caesarean section might affect existing equipoise, thus hampering recruitment in a randomised clinical trial.

We have to realise that a nationwide database like the PRN is very valuable and contains an incredible amount of information, which is used too little to address research questions. One can question whether it is ethical that data presented in chapter 3 only were analysed now, and not 5 or 10 years earlier. Suboptimal use of the information of such nationwide databases does question the effort of registration of the course and outcome of all pregnancies in the Netherlands, and, more importantly, denies important information to women and their babies who face delivery in malpresentation.

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8) NVOG guideline “fetal growth restriction” www.nvog.nl/richtlijn
Samenvatting

Dit proefschrift gaat over de optimale manier van bevallen voor vrouwen met een (premature) stuitligging, premature tweeling en drielings zwangerschap. Wij hebben de uitkomsten voor moeder en kind onderzocht in relatie met de modus partus, dat wil zeggen een geplande keizersnede of een geplande vaginale baring. Deze onderzoeken hebben wij gedaan met data uit de Perinatale Registratie Nederland (PRN), een nationale database van alle bevallingen in Nederland.

Hoofdstuk 1 bevat een algemene introductie over premature bevallingen, stuitligging en meerlingzwangerschappen. Daarnaast bespreken we het doel van dit proefschrift. In het geval van vroeggeboorte liggen meer kinderen in stuitligging dan bij een a terme geboorte. Stuitligging heeft een prevalentie van 25% bij 26 weken, 15% bij 32 weken en neemt verder af naar 3 tot 4% bij een a terme zwangerschap. Studies waarin de relatie tussen de wijze van bevallen en de uitkomst voor het kind in het geval van een vroeggeboorte van een kind in stuitligging is onderzocht zijn schaars. Gerandomiseerde onderzoeken die tot heden gedaan zijn, zijn allemaal voortijdig gestopt vanwege problemen met het werven van patiënten voor dit type onderzoek. Dit heeft geleid tot studies met zo danig kleine aantallen dat er geen belangrijke conclusie uit getrokken kon worden met betrekking tot de optimale manier van bevallen. In het geval van een a terme bevalling met een kind in stuitligging heeft de Term Breech Trial aangetoond dat een geplande keizersnede veiliger is en op korte termijn leidt tot lagere mortaliteit en morbiditeit, waardoor het aantal geplande keizersneden bij een a terme stuitligging flink is gestegen.

De incidentie van meerlingzwangerschappen is de afgelopen 20 jaar enorm gestegen (met ongeveer 80%), met name doordat veel meer vrouwen zwanger zijn geworden met geassisteerde voortplanting en door de gestegen gemiddelde leeftijd van vrouwen als ze hun eerste kind krijgen. De toename van het aantal meerlingzwangerschappen maakt de optimale manier van bevallen voor deze vrouwen een belangrijk onderwerp. Het aantal studies naar de relatie tussen modus partus en perinatale uitkomst voor vrouwen met een tweeling zwangerschap die voor 32 weken bevallen is beperkt. Hetzelfde geldt voor studies omtrent de optimale manier van bevallen bij vrouwen met een drielings zwangerschap.

Hoofdstuk 2 beschrijft de uitkomsten van een systematische review en meta-analyse van de studies die gedaan zijn over de modus partus en neonatale sterfte bij vrouwen die prematuur zijn bevallen van een kind in stuitligging. We hebben daarvoor gezocht op Pubmed, Embase en Cochrane Library naar studies die de relatie onderzochten.
tussen neonatale sterfte en een vaginale baring versus een keizersnede bij vrouwen met een premature bevalling (tussen de 25e en 36e weken zwangerschap) van een kind in stuitligging. We evalueren zeven onderzoeken met in totaal 3.557 vrouwen die we konden opnemen in ons review en meta-analyse. Het gewogen risico op neonatale sterfte was 3.8% voor vrouwen die bevielen middels een keizersnede en 11.5% voor vrouwen die vaginaal bevallen zijn (pooled RR 0.63; 95% CI 0.48 to 0.81). Concluderend vonden wij geen grote gerandomiseerde onderzoeken met als onderwerp neonatale uitkomsten bij vrouwen met een premature bevalling in stuitligging, de beschikbare studies zijn cohort-studies en deze geven aan dat een keizersnede leidt tot een lagere neonatale sterfte. Deze conclusie moet echter zorgvuldig geinterpreteerd worden omdat we geen intention-to-treat analyse konden doen en enige bias onvermijdelijk is in retrospectieve cohort-onderzoeken.

Hoofdstuk 3 bevat de resultaten van een nationaal cohort onderzoek in Nederland naar de neonatale uitkomsten van vrouwen die prematuur (zwangerschapsduur 26e-36 weken) bevallen zijn tussen 2000 en 2011 van een kind in stuitligging. We hebben perinatale uitkomsten vergeleken in relatie tot de geplande manier van bevallen en de daadwerkelijke manier van bevallen door middel van een multivariate logistische regressie analyse. We onderzochten de uitkomst van in totaal 8.356 vrouwen met een eenling in stuitligging en een premature bevalling. Een geplande keizersnede (n= 1.955) leidde niet tot een significante afname van de perinatale mortaliteit in vergelijking met een geplande vaginale bevalling (n= 6.421) (1.3% versus 1.5%, (aOR 0.97; 95% CI 0.60-1.57)). Echter de samengestelde uitkomst van perinatale mortaliteit en morbiditeit was wel significant lager bij vrouwen met een geplande keizersnede (8.7% versus 10.4% (aOR 0.77; 95%CI 0.63-0.93)). In de subgroep van vrouwen die tussen de 28-32 weken zijn bevallen was een keizersnede geassocieerd met 1.7% risico op perinatale mortaliteit vergeleken met 4.1% voor vrouwen met een vaginale baring (aOR 0.27; 95% CI 0.10-0.79). Er was ook een significante afname van de samengestelde uitkomst van mortaliteit en ernstige morbiditeit: 5.9% in de groep met een geplande keizersnede en 10.1% in de groep met een geplande vaginale bevalling (aOR 0.37; 95% CI 0.20-0.68). De conclusie van dit onderzoek is derhalve dat bij vrouwen met een premature bevalling van een kind in stuitligging een geplande keizersnede geassocieerd is met een lagere perinatale mortaliteit en morbiditeit vergeleken met een geplande vaginale bevalling.

In hoofdstuk 4 beschrijven we de resultaten van een nationale cohort studie naar het effect van de modus partus bij vrouwen met een premature bevalling van een kind in stuitligging op de uitkomst van moeder en kind in de daaropvolgende zwangerschap. We onderzochten de uitkomsten van alle vrouwen die in Nederland prematuur bevallen zijn van een kind in stuitligging en een volgende bevalling in de jaren 1999-2007. We vergeleken de perinatale uitkomsten in beide zwangerschappen naar de geplande manier van bevallen van de eerste zwangerschap (prematuur met kind in stuitligging). We incluerden 1.543 vrouwen in dit onderzoek, waarvan 259 vrouwen (17%) een geplande keizersnede ondergingen en 1.284 vrouwen (83%) een geplande vaginale baring ondergingen in de eerste zwangerschap. In de daaropvolgende zwangerschap was de perinatale mortaliteit 1.1% voor vrouwen met een geplande keizersnede in de eerste zwangerschap en 0.5% voor vrouwen met een geplande vaginale baring in de eerste zwangerschap (aOR 1.8; 95% CI 0.31-10.1). De samengestelde adverse neonatale uitkomst was 2.3% versus 1.5%, (aOR 1.5; 95% CI 0.55-4.2). De berekende uitkomst van het gemiddelde risico op perinatale mortaliteit over beide zwangerschappen samen was 1.9% voor de vrouwen met een geplande keizersnede in de eerste zwangerschap versus 2.0% voor de vrouwen met een geplande vaginale baring, (OR 0.98; 95% CI 0.49-1.9). De conclusie van dit onderzoek is derhalve dat voor vrouwen met een premature bevalling van een kind in stuitligging een geplande keizersnede het risico op mortaliteit en morbiditeit voor moeder en kind niet verlaagd over het totaal van beide zwangerschappen samen.

In hoofdstuk 5 presenteren we de uitkomsten van een studie met data uit de Perinatale Registratie Nederland. Deze studie laat zien dat in een periode van drie maanden na publicatie van de Term Breech Trial (2000), waarin de keizersnede als meest veilige manier van bevallen bij een stuitligging werd geadviseerd, het percentage geplande keizersneden steeg van 30% naar 60%. De relatieve veiligheid van een keizersnede moet worden afgewogen tegen de gevolgen van een litteken in de baarmoeder voor de volgende zwangerschap. Veronderstelde risicoselectie bij vrouwen die een volgende zwangerschap willen proberen (ongeveer 40%) heeft niet geleid tot betere uitkomsten. Op basis van patiëntkarakteristieken (pariteit, soort stuitligging, geboortegewicht en start bevalling) kon geen subgroep gedefinieerd worden omdat we konden opnemen in ons review en meta-analyse. Het gewogen risico op slechte perinatale uitkomsten tijdens en na een vaginale stuitbevalling in vergelijking met een keizersnede is 0.49-1.9. De conclusie van dit onderzoek is derhalve dat voor vrouwen met een premature bevalling van een kind in stuitligging een geplande keizersnede het risico op mortaliteit en morbiditeit voor moeder en kind niet verlaagd over het totaal van beide zwangerschappen samen.

Hoofdstuk 6 bevat de resultaten van een population-based-cohort studie naar de uitkomsten van de zwangerschap van vrouwen die prematuur (26-32 weken zwangerschap) bevallen zijn van een tweeling in Nederland tussen januari 2000 en december 2010. Perinatale uitkomsten (mortaliteit en morbiditeit) werden gecorrigeerd rekening houdend met de afhankelijkheid van beide kinderen van dezelfde tweelingzwangerschap, en tevens voor elk kind afzonderlijk. We onderzochten de uitkomsten van 1,655

We onderzochten de uitkomsten van alle vrouwen die in Nederland prematuur bevallen zijn van een kind in stuitligging en een volgende bevalling in de jaren 1999-2007. We vergeleken de perinatale uitkomsten in beide zwangerschappen naar de geplande manier van bevallen van de eerste zwangerschap (prematuur met kind in stuitligging). We incluerden 1.543 vrouwen in dit onderzoek, waarvan 259 vrouwen (17%) een geplande keizersnede ondergingen en 1.284 vrouwen (83%) een geplande vaginale baring ondergingen in de eerste zwangerschap. In de daaropvolgende zwangerschap was de perinatale mortaliteit 1.1% voor vrouwen met een geplande keizersnede in de eerste zwangerschap en 0.5% voor vrouwen met een geplande vaginale baring in de eerste zwangerschap (aOR 1.8; 95% CI 0.31-10.1). De samengestelde adverse neonatale uitkomst was 2.3% versus 1.5%, (aOR 1.5; 95% CI 0.55-4.2). De berekende uitkomst van het gemiddelde risico op perinatale mortaliteit over beide zwangerschappen samen was 1.9% voor de vrouwen met een geplande keizersnede in de eerste zwangerschap versus 2.0% voor de vrouwen met een geplande vaginale baring, (OR 0.98; 95% CI 0.49-1.9). De conclusie van dit onderzoek is derhalve dat voor vrouwen met een premature bevalling van een kind in stuitligging een geplande keizersnede het risico op mortaliteit en morbiditeit voor moeder en kind niet verlaagd over het totaal van beide zwangerschappen samen.
vrouwen met een tweelingzwangerschap (3,310 kinderen). Perinatale mortaliteit was hoger bij een geplande keizersnede (10% versus 6.5%) ten opzichte van een geplande vaginale baring (aOR 2.5; 95% CI 1.5-4.2). Perinatale morbiditeit was ook hoger bij een geplande keizersnede (66% versus 63%) ten opzichte van een vaginale baring (aOR 1.5; 95% CI 1.1-2.0). Hetzelfde gold voor morbiditeit van de moeder (17% versus 4.9%, aOR 4.0; 95% CI 2.6-6.3). De conclusie van dit onderzoek is dat voor vrouwen met een vroeg premature bevalling (26-32 weken) van een tweelingzwangerschap een geplande keizersnede niet leidt tot betere uitkomsten van moeder en kind.

Hoofdstuk 7 bevat de resultaten van een onderzoek naar perinatale uitkomsten bij vrouwen met een drielingzwangerschap. Dit onderzoek werd verricht met data uit de PRN in de jaren 1999-2008. Er werden 386 vrouwen geïncludeerd (1,158 kinderen) waarvan de perinatale mortaliteit en morbiditeit werd vergeleken naar de geplande en de daadwerkelijke manier van bevallen. Perinatale mortaliteit was 2.3% voor vrouwen met een geplande keizersnede en 2.4% voor vrouwen met een geplande vaginale baring (aOR 0.37, 95% CI 0.09-1.5), en neonatale morbiditeit was 26% versus 36% (aOR 0.88; 95% CI 0.51-1.4). In de subgroep analyse naar zwangerschapsduur en in de analyse van perinatale uitkomsten per kind separaat vonden we geen grote verschillen. Hetzelfde was het geval voor de perinatale uitkomsten naar de daadwerkelijke modus partus. Onze studie is een van de grootste cohort studies naar perinatale uitkomsten in relatie tot modus partus bij vrouwen met een drielingzwangerschap. We hebben geen grote verschillen gevonden in perinatale mortaliteit en morbiditeit tussen een geplande keizersnede en een geplande vaginale baring.
List of co-authors
List of publications
PhD portfolio
Dankwoord
Curriculum Vitae
List of co-authors and their contribution to the manuscript

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L. Bergenhenegouwen: Study concept and design, acquisition of the data, data analysis, interpretation of the data, drafting the manuscript, final approval of the manuscript
L. J. Meertens: Study concept and design, acquisition of the data, data analysis, interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
J. Schaaf: Data analysis, final approval of the manuscript
J. G. Nijhuis: Critically reviewing the manuscript, final approval of the manuscript
B. W. J. Mol: Study concept and design, critically reviewing the manuscript, final approval of the manuscript
M. Kok: Study concept and design, critically reviewing the manuscript, final approval of the manuscript
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F. Vlemmix: Study concept and design, acquisition of the data, data analysis, interpretation of the data, drafting the manuscript, final approval of the manuscript
L. Bergenhenegouwen: Study concept and design, acquisition of the data, data analysis, interpretation of the data, drafting the manuscript, final approval of the manuscript
J.M. Schaal: data analysis, final approval of the manuscript
S. Ensing: data analysis, final approval of the manuscript
A.N. Rosman: interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
A.C.J. Ravelli: Supervision of data acquisition and analysis, critically reviewing the manuscript, final approval of the manuscript
B.W.J. Mol: Interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
M. Kok: Study concept and design, supervision of data acquisition and analysis, interpretation of the data, critically reviewing the manuscript, final approval of the manuscript

The impact of the mode of delivery on the outcome in very preterm twins

L. Bergenhenegouwen: Study concept and design, acquisition of the data, data analysis, interpretation of the data, drafting the manuscript, final approval of the manuscript
S. Ensing: Study concept and design, acquisition of the data, data analysis, interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
A.C.J. Ravelli: Supervision of data acquisition and analysis, critically reviewing the manuscript, final approval of the manuscript
B.W.J. Mol: Interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
M. Kok: Study concept and design, supervision of data acquisition and analysis, interpretation of the data, critically reviewing the manuscript, final approval of the manuscript

Triplet pregnancies and neonatal outcomes according to the mode of delivery

L. Bergenhenegouwen: Study concept and design, acquisition of the data, data analysis, interpretation of the data, drafting the manuscript, final approval of the manuscript
J. Velzel: Study concept and design, data analysis, critically reviewing the manuscript, final approval of the manuscript
L. van de Mheen: acquisition of the data, final approval of the manuscript
M. Kok: Supervision of data acquisition and analysis, critically reviewing the manuscript, final approval of the manuscript
B.W.J. Mol: Study concept and design, supervision of data acquisition and analysis, interpretation of the data, critically reviewing the manuscript, final approval of the manuscript
List of publications


Bergenhenegouwen L, Ensing S, Ravelli ACJ, Mol BW, Kok M. The impact of the mode of delivery on the outcome in very preterm twins

Bergenhenegouwen L, Velzel J, van de Mheen L, Kok M, Mol BW. Triplet pregnancies and neonatal outcomes according to the mode of delivery
# PhD Portfolio

Name PhD student: L. Bergenhenegouwen

PhD period: January 2010 – September 2015

Name PhD supervisor: Prof. dr. B.W.J. Mol, dr. M. Kok

## 1. PhD training

<table>
<thead>
<tr>
<th>Year</th>
<th>Workload (Hours/ECTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-2015</td>
<td>3.5</td>
</tr>
<tr>
<td>2012</td>
<td>3.5</td>
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</tbody>
</table>

### Seminars, workshops and master classes
- Department seminars dept. Obstetrics & Gynecology AMC
- Consortium training Days, Veldhoven

### Presentations
- Oral Presentation European Congres Perinatal Medicine
  - Mode of delivery in preterm breech presentation
  - 2012: 0.5
- Poster presentation SMFM San Francisco
  - Preterm breech presentation and neonatal mortality
  - 2013: 0.5
- Oral Presentation Doelencongres Rotterdam
  - Mode of delivery in preterm breech presentation
  - 2013: 0.5

### (Inter)national conferences
- European Congres Perinatal Medicine, Granada
- European Congres Perinatal Medicine, Paris
- SMFM’s 33rd Annual Pregnancy Meeting, San Francisco
- European Congres Perinatal Medicine, Florence

## 2. Teaching

<table>
<thead>
<tr>
<th>Year</th>
<th>Workload (Hours/ECTS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012-2014</td>
<td>0.1</td>
</tr>
</tbody>
</table>

### Tutoring, Mentoring
- Skills Education to medical students
  - 2012-2014: 0.1
Dankwoord

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DANKWOORD

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Curriculum Vitae
