Risk factors and prognostic models for preterm birth
Schaaf, J.M.

Citation for published version (APA):

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CHAPTER 2

Trends in preterm birth: singleton and multiple pregnancies
The Netherlands 2000 through 2007

Jelle M Schaaf
Ben Willem J Mol
Ameen Abu-Hanna
Anita CJ Ravelli

Published in the British Journal of Obstetrics and Gynaecology, 2011
Abstract

Objective
Several studies have reported increasing trends in preterm birth in developed countries, mainly attributable to an increase in medically indicated preterm births. Our aim was to describe trends in preterm birth among singleton and multiple pregnancies in the Netherlands.

Design
Prospective cohort study.

Setting
Nationwide study.

Population
We studied 1,451,246 pregnant women, from 2000 to 2007.

Methods
We assessed trends in preterm birth. We subdivided preterm birth in spontaneous preterm birth after premature prelabour rupture of membranes (pPROM), medically indicated preterm birth, and spontaneous preterm birth without pPROM. We performed analyses separately for singletons and multiples.

Main outcome measures
Primary outcome was preterm birth defined as birth before 37 weeks of gestation, with very preterm birth (<32 weeks of gestation) being a secondary outcome.

Results
Risk of preterm birth was 7.7% and risk of very preterm birth was 1.3%. In singleton pregnancies, the preterm birth risk significantly decreased from 6.4 to 6.0% (p<0.0001), mainly due to a decrease in spontaneous preterm births without pPROM (3.6 to 3.1%, p<0.0001). In multiple pregnancies, the preterm birth risk increased significantly (47.3% to 47.7%, p=0.047), mostly due to the subtype of medically indicated preterm birth which increased from 15.0 to 17.9% (p<0.0001).

Conclusion
In The Netherlands, the preterm birth risk in singleton pregnancies significantly decreased over the years. The trend of increasing preterm birth risk reported in other countries was only observed in (medically indicated) preterm birth in multiple pregnancies.
Preterm birth, defined as birth before 37 completed weeks of gestation, is strongly related to perinatal morbidity and mortality. In the developed countries, it accounts for 75% of perinatal mortality and more than half of the long-term neurocognitive, ophthalmologic and respiratory morbidity. Preterm birth is a multifactorial and heterogeneous outcome of pregnancy. It might result from a series of disorders, but in a considerable amount of cases the cause is unknown. Furthermore, preterm birth can be medically indicated when maternal and/or fetal conditions enforce induction of labour or primary caesarean section. Such might be the case in women suffering from hypertensive disorder or pregnancies complicated by intra uterine growth restriction (IUGR).

Many developed countries have reported an increase in the risk of preterm birth during the last two decades. A recent study in the United States, where the overall incidence of preterm birth was high (13%), showed that the increase in risk of preterm birth was mainly caused by an increase in medically indicated deliveries, whereas spontaneous preterm birth risk showed a decrease. Scottish data showed an overall increase in preterm birth risk that was caused by both an increase in medically indicated and spontaneous deliveries. In the latter study the risk of medically indicated preterm deliveries showed the largest increase. Recent research showed that the level of proactive treatment leading to medically indicated preterm birth has great variations between several European countries due to varying socio-cultural and organisational factors and thus varying doctor’s behaviour. The contributions of the subtypes of preterm births to all preterm births appeared to vary by ethnic group and gestational age.

More recent data were provided by the European Peristat project, which monitors perinatal health in Europe. In the years 1998/99 as well as in 2004 several countries and regions contributed data for analysis. In the report on 2004, incidence of preterm birth ranged between 5.4% in Lithuania and 11.4% in Austria. The report showed the incidence of preterm birth in The Netherlands (7.4%) was about average compared to the rest of Europe. The two Peristat reports showed that the incidence of preterm birth increased in the majority of the contributing countries and regions. However, the Peristat data were insufficient for the analysis of possible trends in preterm birth risk. Furthermore, the European Peristat project showed that perinatal mortality in The Netherlands is relatively high when compared to other European countries. The pathways leading to this relatively high perinatal mortality risk in the Netherlands are not clear and under investigation.

The aim of this study is to describe in detail recent trends in preterm birth in The Netherlands among singleton and multiple pregnancies. We focused on the different subtypes of preterm birth (spontaneous after premature prelabour rupture of membranes (pPROM), medically indicated, or spontaneous without pPROM).
Methods

This study was performed in a prospective national cohort using 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. The midwifery and obstetrics data collection starts at the booking visit and contain complete perinatal data from 20 gestational weeks onwards. The neonatal registry contains data on only 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. The data are annually sent to the national registry office, where a number of range and consistency checks are conducted. For this study all births between 1 January 2000 and 31 December 2007 were selected.

Preterm birth was defined as birth before 37 completed weeks of gestation (< 259 days). Stillbirths were included in the analyses. Very preterm birth was defined as birth before 32 completed weeks of gestation. Following the international literature on preterm birth, all pregnancies that ended before 22.0 weeks of gestation, pregnancies with unknown gestational age and pregnancies resulting in the birth of a child weighing less than 500 grams were excluded. Gestational age data were predominantly based on the date of last menstrual period and/or crown rump length (CRL) measured during early pregnancy ultrasound. The technique for measuring gestational age was consistent over the total study period. Preterm birth was classified in three subtypes: [1] Spontaneous preterm birth after premature prelabour rupture of membranes (pPROM) which was defined as a birth (due to spontaneous start of labour) after an interval > 24 hours between rupture of membranes and time of birth, [2] medically indicated preterm birth which was defined as delivery caused by iatrogenic intervention (primary caesarean section or induction of labour) and all other preterm deliveries were defined as [3] spontaneous preterm birth without pPROM. The latter is a category which contains all pregnancies not included in category 1 or 2.

We examined records of singleton and multiple births in the Netherlands between 2000 and 2007. Because of their known varying course of pregnancy, singleton and multiple pregnancies were also analysed separately. Secondly we investigated to what extent preterm birth and its subtypes contribute to the overall incidence of perinatal mortality in The Netherlands and to what extent risk of perinatal mortality changed over the investigated years. Perinatal mortality was defined as the number of fetal deaths from 22.0 weeks onwards (stillbirths) and neonatal deaths in the first week of life. We analysed incidence and trends in all preterm birth, as well as in the three distinct subtypes of preterm birth.
We performed an additional analysis for the following clinically relevant subgroups of gestational age: 22-23 wks, 24-27 wks, 28-29 wks, 30-31 wks, 32-33 wks and 34-36 weeks. Finally, nulliparous and multiparous women were analysed separately. To check for possible confounding factors we repeated the analyses for Caucasian women only, accounting for 84% of the total births.

To investigate whether there is a trend in preterm birth risk over time we performed a Cochran-Armitage trend test with year as the independent variable and preterm birth risk as the dependent variable. The same test was performed to check for trends in perinatal mortality risk during the same time period. Subsequently we repeated the trend analysis by fitting a linear regression model for each series. We tested whether the regression coefficient (beta) of the fitted linear model statistically significantly deviated from 0 using the t-test. The statistical significance levels for both types of trend test were set at the 0.05 level. We repeated this procedure to test for temporal trends in the three preterm birth subtypes. We repeated the main trend analyses on Caucasian women only. All statistical analyses were carried out with SAS 9.2 (SAS Institute, Cary, NC). Permission for record use and analysis of data for the purpose of this study was obtained from the Netherlands Perinatal Registry (registered as data petition 09.79).

Results

There were 1,451,246 births over the 8-year study period, of which 1,394,714 singleton births and 56,532 multiple births. Table 1 shows that of all births in the Netherlands 7.7% are preterm and 1.3% are very preterm. Among the singleton pregnancies 6.0% resulted in preterm and 0.9% in very preterm deliveries. Preterm birth among singletons consisted of spontaneous preterm birth after pPROM (0.9%), medically indicated preterm birth (1.7%) and spontaneous preterm birth without pPROM (3.4%). In multiple pregnancies the total incidence of preterm and very preterm birth was respectively 48.1 and 8.7%. Table 2 shows the contribution of preterm birth to the overall perinatal mortality rates. In singleton pregnancies the contribution of preterm birth was 62% whereas for multiple pregnancies this was even 87%. Rates of late preterm births were 5.1% among singletons with a mortality risk of 33 per 1000 whereas among multiples the rates were 39% with a lower mortality risk of 15 per 1000. In all subgroups of gestational age the subtype of medically indicated preterm birth gives the highest risk of perinatal mortality. Figure 1 shows that the total preterm birth risk for all pregnancies (singletons and multiples) decreased from 8.0% to 7.4% whilst the perinatal risk in the same study period also decreased (9.7‰ to 7.4‰). Trend analysis showed both declines to be significant (Cochran-Armitage trend test p<0.0001).
**Table 1.** Total preterm births and very preterm births among singleton and multiple pregnancies: the Netherlands, 2000–2007

<table>
<thead>
<tr>
<th></th>
<th>All pregnancies</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Total number of deliveries</td>
<td>1 451 246</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Total preterm</td>
<td>111 416</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>16 222</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Medically indicated</td>
<td>32 570</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>62 624</td>
<td>4.3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Singleton pregnancies</th>
<th>Multiple pregnancies</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Total number of deliveries</td>
<td>1 394 714</td>
<td>100</td>
<td>56 532</td>
</tr>
<tr>
<td>Total preterm (22–36 weeks)</td>
<td>84 233</td>
<td>6.0</td>
<td>27 134</td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>13 177</td>
<td>0.9</td>
<td>3 045</td>
</tr>
<tr>
<td>Medically indicated</td>
<td>23 633</td>
<td>1.7</td>
<td>8 937</td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>47 423</td>
<td>3.4</td>
<td>15 201</td>
</tr>
<tr>
<td>Total very preterm (22–31 weeks)</td>
<td>13 618</td>
<td>0.9</td>
<td>4 896</td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>1 407</td>
<td>0.1</td>
<td>609</td>
</tr>
<tr>
<td>Medically indicated</td>
<td>6 345</td>
<td>0.4</td>
<td>999</td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>5 866</td>
<td>0.4</td>
<td>3 288</td>
</tr>
</tbody>
</table>

pPROM, premature prelabour rupture of membranes.

The Cochran-Armitage trend test for the total of singleton pregnancies resulted in p<0.0001. For the subtypes of preterm birth the p-values were: 0.70 (spontaneous after pPROM [1]), 0.84 (medically indicated [2]) and <0.0001 (spontaneous without pPROM [3]). The multiple pregnancies also showed a significant trend according to the Cochran-Armitage test with p=0.047. The tests resulted is p=0.14 [1], p<0.0001 [2], and p=0.48 [3] for the subtypes of preterm birth in their respective order above.

**Regression models**

Risk of preterm birth in singleton pregnancies significantly decreased from 6.4 to 6.0% (p=0.049) over the years (figure 2A), which means a decrease of approximately 700 preterm deliveries per year. This decline is mainly due to significantly decreasing risk of spontaneous preterm births without pPROM from 3.6 to 3.1% (p=0.00038). There were no significant changes in risk of neither medically indicated preterm births nor spontaneous preterm birth after pPROM in singleton pregnancies. Figure 2B shows the results for multiple pregnancies. Risk of preterm birth in multiple pregnancies increased not significantly from 47.3% in the year 2000 to 47.7% in 2007 (an increase of approximately 30 preterm deliveries per year). Medically indicated preterm birth risk did show a significant increase over the years (15.0 to 17.9%), whereas spontaneous preterm birth risk (with or without pPROM) showed no significant trend.

**Figure 1.** Risk of preterm birth and perinatal mortality in all pregnancies (singleton and multiple): the Netherlands 2000-2007.
<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Incidence n (%)</th>
<th>Perinatal mortality n (%)</th>
<th>Contribution %</th>
<th>Incidence n (%)</th>
<th>Perinatal mortality n (%)</th>
<th>Contribution %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total preterm (22–27 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>4859 (0.4)</td>
<td>3 096 (637)</td>
<td>28</td>
<td>1 582 (2.8)</td>
<td>743 (469)</td>
<td>52</td>
</tr>
<tr>
<td>Medically indicated</td>
<td>556 (0.04)</td>
<td>318 (672)</td>
<td>2.8</td>
<td>232 (0.4)</td>
<td>117 (504)</td>
<td>8.2</td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>1 974 (0.1)</td>
<td>1 407 (713)</td>
<td>13</td>
<td>179 (0.3)</td>
<td>97 (542)</td>
<td>6.8</td>
</tr>
<tr>
<td><strong>Total preterm (28–31 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>8 759 (0.6)</td>
<td>1 555 (178)</td>
<td>14</td>
<td>3 314 (5.9)</td>
<td>169 (51)</td>
<td>12</td>
</tr>
<tr>
<td>Medically indicated</td>
<td>851 (0.1)</td>
<td>76 (89)</td>
<td>0.7</td>
<td>377 (0.7)</td>
<td>9 (24)</td>
<td>0.6</td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>4 371 (0.3)</td>
<td>1 041 (238)</td>
<td>9.3</td>
<td>820 (1.5)</td>
<td>80 (98)</td>
<td>5.7</td>
</tr>
<tr>
<td><strong>Total preterm (32–36 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous after pPROM</td>
<td>70 615 (5.1)</td>
<td>2 329 (33)</td>
<td>21</td>
<td>22 287 (39.4)</td>
<td>329 (15)</td>
<td>23</td>
</tr>
<tr>
<td>Medically indicated</td>
<td>11 770 (0.8)</td>
<td>1 56 (13)</td>
<td>1.4</td>
<td>2 436 (4.3)</td>
<td>38 (16)</td>
<td>2.7</td>
</tr>
<tr>
<td>Spontaneous without pPROM</td>
<td>17 228 (1.2)</td>
<td>1 300 (75)</td>
<td>12</td>
<td>7 938 (14.0)</td>
<td>159 (20)</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total term (≥37 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of deliveries</td>
<td>1 310 481 (94.0)</td>
<td>4 193 (3.2)</td>
<td>38</td>
<td>29 349 (51.9)</td>
<td>184 (6.3)</td>
<td>13</td>
</tr>
<tr>
<td><strong>Total number of deliveries</strong></td>
<td>1 394 714 (100)</td>
<td>11 173 (8.0)</td>
<td>100</td>
<td>56 532 (100)</td>
<td>1425 (25)</td>
<td>100</td>
</tr>
</tbody>
</table>

pPROM, premature prelabour rupture of membranes

When considering subgroups of gestational age we found that in singleton pregnancies (figure 3A) the overall decrease in preterm birth risk is mostly a reflection of decreases in the 32-33 (0.8 to 0.7%) and 34-36 (4.6 to 4.2%) weeks subgroups. A similar subgroup analysis for gestational age was performed for multiple pregnancies (figure 3B). When focussing on the preterm birth subtypes in multiple pregnancies we find an increase in medically indicated preterm birth over the years in the 34-36 weeks group (11.8 to 13.0%). Finally we performed an analysis with subgroups based on parity. In singleton pregnancies the preterm birth risk was higher for nulliparous (figure 4A) than for multiparous (figure 4B) women. For nulliparous women with singleton pregnancies the total preterm birth risk decreased from 8.0% in 2000 to 7.7% in 2007, whereas for multiparous women the proportions ranged between 4.8 and 4.5%. In nulliparous and multiparous women, we found the same trend as in the overall analysis in singleton pregnancies: a significant decrease in preterm birth without pPROM.
Figure 2. Risk of preterm birth per year in singleton (A) and multiple (B) pregnancies and subtypes: the Netherlands, 2000–2007. Different scales are used in (A) and (B). Beta values of trend analysis are presented for total preterm birth risk and all subtypes. pPROM, premature prelabour rupture of membranes.

However the total preterm birth risk was not significant after subdividing for parity. Figures 4C and 4D show the results of the parity subgroup analysis in multiple pregnancies. The total preterm birth risk was higher for nulliparous than for multiparous women. In nulliparous women with a multiple pregnancy the total preterm birth risk showed no significant trend over the years (54.0 to 54.4%, beta 0.48769, p=0.11) However, there was a significant increase in medically indicated preterm births (17.5 to 21.0%, beta 0.47551, p=0.024). In multiparous women with multiple pregnancies no significant trends were found. To check for possible confounding we repeated all analyses in a selection of the 1,220,489 Caucasian women (84%) and found similar trends as were found in the presented total population.
Figure 3. Risk of preterm birth per year in singleton (A) and multiple (B) pregnancies with subgroups for gestational age: the Netherlands 2000–2007 pPROM, premature prelabour rupture of membranes.
Figure 4. Risk of preterm birth per year in primiparous and multiparous singleton (A, B) and multiple (C, D) pregnancies with subtypes: the Netherlands, 2000–2007. Beta values of trend analyses are presented for total preterm birth risk and all subtypes. Trend analysis for preterm birth after premature prelabour rupture of membranes (pPROM) in (B) resulted in beta + 0.0033 ($P = 0.60$).
Discussion

Principal findings
Our study shows a significant decrease in as total preterm birth risk as well as total perinatal mortality risk in the Netherlands between 2000 and 2007. For singleton pregnancies this was due to a significant decrease in spontaneous preterm birth without pPROM. This decrease was mostly seen in late preterm birth at the 32-33 and 34-36 weeks of gestational age. Risk of total preterm birth and its subtypes were higher in nulliparous women compared to multiparous women.

For multiple pregnancies there was no significant trend in total preterm birth risk although the subtype of medically indicated preterm birth did increase significantly. This trend towards increasing iatrogenic preterm birth was pronounced in the 34-36 weeks subgroup of gestational age. We observed a large contribution of preterm birth to overall incidence of perinatal mortality (68% of all perinatal deaths).

Strengths and weaknesses
Our study comprises data of a large population-based well-maintained national registry and therefore provides a reliable overview of the problem of preterm birth in the Netherlands. The sample size is large, as the PRN database consists of about 96% of all pregnancy and birth characteristics in the Netherlands. Furthermore, our study is unique in its size and design as we also investigated trends in preterm births for multiple pregnancies. To our knowledge, the latter was rarely investigated before in a population-based setting. After repeating the analyses for Caucasians only we found similar results.

The method of determining gestational age can influence the outcome of preterm birth. Nowadays the vast majority of women in the Netherlands receive an early pregnancy ultrasound to confirm or change the estimated gestational age by last menstrual period so the effect of miscalculated gestational age on the studied outcome of preterm birth should be marginal. This strategy did not change over the study period.

Four percent of all births are missing in the national perinatal registry. This is due to the 2% general practitioners and a few missing midwives practices (2%) who do not contribute data to the PRN database. However, as preterm birth is an indication for referral to an obstetrical equipped hospital (of which 99% contribute to the PRN registry), these missing data could not have influenced our results to a large degree.

Our study was performed on the available linked PRN registry data between 2000 and 2007. There are no linked LVR1, LVR2 and LNR data available yet containing information in the period before 2000. In some cases there was only little overlap in the years we investigated with respect to the previously published studies. This hinders comparison.
Relationship to other studies
The Peristat project\textsuperscript{15} showed that the incidence of preterm birth in the Netherlands (7.4\%) is average when compared to other European countries (5.4-11.4\%). Ananth et al.\textsuperscript{3} showed that the incidence in the United States is much higher (10.2\%). More recently Kuehn et al.\textsuperscript{15} reported an even higher incidence of preterm birth (13\%) in the United States. Our findings on decreasing trends in preterm birth in nearly 10 years of registration do not concord with previously published studies about trends in preterm births in other developed countries. Other studies, like those performed by Ananth et al.\textsuperscript{3} and Norman et al.\textsuperscript{10}, showed significant increasing trends in preterm birth risk through the past decades, whereas our study does not show these trends in the Netherlands. Furthermore the risk of medically indicated preterm births was only shown to increase in multiple pregnancies in our population. However, recently published data show that, after 30 years of increase, a trend of decreasing risk of preterm birth in the United States in the years 2007, 2008, and 2009.\textsuperscript{25} Data on the incidence of preterm birth in the years after 2009 are not available yet, but these results mark the first 3-year decline (12.8\% to 12.2\%) in the preterm birth risk in nearly 30 years.

The Mosaic study reviewing very preterm birth in several European countries showed that the proportion of very preterm birth is ten times larger in twin pregnancies than in singleton pregnancies.\textsuperscript{26} Our results are in accordance with this finding. A recently published study considering trends in preterm birth in Flanders (Belgium) also showed a significant increase in medically indicated preterm birth in multiple pregnancies. The study showed a similar increasing risk of preterm birth in singleton pregnancy which again is in contrast with our findings.\textsuperscript{27} Most other studies reviewing trends in preterm birth address only singleton pregnancies.

Meaning of the results
We can assume, especially in light of the relatively high perinatal mortality risk in the Netherlands\textsuperscript{18,19}, that the Dutch women do not have a lower risk profile for preterm birth than women in other developed countries.

The lack of increasing trend in premature birth risk may be attributable to our different infrastructure for and attitude towards perinatal care. For instance, in the case of premature prelabour rupture of membranes or hypertensive disorders between 34-37 weeks, we conjecture that there is a relatively expectant approach in the Netherlands when it comes to medical intervention. In contrast, management in these conditions tends to be more proactive in most other developed countries. For instance, in the United States the risk preterm birth due to medical interventions steadily increased over the last two decades. This increase was most pronounced in the late preterm birth group (34-36 weeks).\textsuperscript{28} Preterm obstetric care is complicated as the caregiver needs to weigh conflicting risks; The neonatal/maternal risk of progressive morbidity or even mortality when continuing pregnancy versus the neonatal risk of morbidity or mortality after being born preterm.
The risk of neonatal mortality when born after 34 weeks is relatively low. Nevertheless there is an increasing amount of evidence emphasising that infants born late preterm are less healthy than babies born later in pregnancy.²⁹-³⁴

Our relatively expectant approach was underlined by the Peristat report.³⁶ Combined proportion of induction of labour and primary caesarean section in the Netherlands was relatively low (21.2%) when compared to a more proactive approach presented European countries (range 14.4-52.4%).

Recent research comparing primary and secondary caesarean section rates in very preterm birth (28-31 weeks) also showed a wide range (49-88%) amongst ten developed European regions.³⁶ This comparison was conducted after correcting for differences in risk of preterm preeclampsia and intra uterine growth restriction. The authors of that study suggested that the observed variation is a result of socio-cultural and organisational factors and thus doctor’s behaviour. The Netherlands had the lowest risk of caesarean section (49% of all very preterm births between 28-31 weeks) in that study. It is also possible that differences between guidelines pertaining neonatal care play a role in our deviating findings. Furthermore, clinician behaviour and optimism (or lack thereof) about neonatal care might lower or raise the thresholds for medical intervention, which in turn, influence the incidence of preterm birth. This hypothesis merits testing in future research.

Differences in socio-cultural and organisational factors, resulting in varying doctor’s behaviour, may at least partly explain the deviation of our results from trends in preterm birth described elsewhere.

However, this may change. We have shown that in multiple pregnancies, which are generally at higher risk than singleton pregnancies, the risk of medically indicated preterm birth significantly rose over the investigated years. Our results might indicate that, due the heightened awareness to risk, the doctor’s attitude towards multiple pregnancies has become more proactive.

Fortunately we found parallel to the decreasing risk of preterm birth a decrease in the risk of perinatal mortality. Similar results were found in a previous performed study on trends in perinatal mortality in the Netherlands.²¹ The exact role of decreasing preterm birth risk in the decline of perinatal mortality risk should be investigated in future research.

The fact that multiparous women have lower risk of preterm birth than nulliparous women is probably due to the fact that a risk selection has taken place. Ante partum care for multiparous women with a complicated obstetric history often differs from the care provided to nulliparous women. For instance, a selection of women with a history of spontaneous preterm birth is treated (following the national guideline³⁵) with a cerclage or progesterone. Care is more likely to be provided by gynaecologists instead of midwives. Finally, some women with a complicated obstetric history might have chosen not to get pregnant again. The result is a lower proportion of preterm birth in multiparous women.
Proposals for future research

The main scope of our article was preterm birth as a clinically important outcome of pregnancy. The lower risk of medically indicated preterm birth among singletons reported in this article in combination with the higher risk of perinatal mortality seems to be paradoxical. Perhaps the more expectant treatment strategies in the Netherlands play a role in this matter. On the other hand, the scientific evidence for a more proactive intervening approach is limited. In contrast, the more proactive or sometimes even aggressive approach may lead to poorer neonatal outcome.  

At present, major randomized controlled trials investigate the best treatment regime for patients with premature prelabour rupture of membranes (PPROMEXIL study\textsuperscript{36}, PROMPT study\textsuperscript{37}) and hypertensive disorders (HYPITAT II study\textsuperscript{38}) between 34 and 37 weeks of gestation. The outcome of these studies might influence doctor’s behaviour in the future.

In order to contribute to the discussion on relatively high perinatal mortality risk in the Netherlands we also aim on describing perinatal outcome after preterm birth in more detail.

Conclusions

Our study reported a significant decreasing trend in total preterm birth risk in singleton pregnancies in the Netherlands. This is in contrast with observations in many other developed countries where increasing medically indicated preterm birth led to an increasing trend of total preterm birth risk. We conjecture that our deviating findings are due to socio-cultural and organisational factors influencing the doctor’s attitude towards interventions.
References


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