DOI: 10.1111/1471-0528.13299
www.bjog.org

# Perinatal outcomes following an earlier post-term labour induction policy: a historical cohort study

M Hedegaard,[a] Ø Lidegaard,[a] CW Skovlund,[a] LS Mørch,[a] M Hedegaard[b]

[a] Department of Gynaecology, [b] Department of Obstetrics, Rigshospitalet, Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark

*Correspondence:* Dr Ø Lidegaard, Rigshospitalet, Blegdamsvej 9, Copenhagen, Denmark. Email Oejvind.Lidegaard@regionh.dk

*Accepted 9 December 2014. Published Online 18 February 2015.*

**Objective** To assess the changes in perinatal outcomes in children born from 37 weeks of gestation after implementation of a more proactive labour induction practice from 2009.

**Design** Register-based cohort study.

**Setting** Denmark, 2000–12.

**Population** Newborns from 37 weeks of gestation.

**Methods** Perinatal outcomes were estimated using a logistic regression analysis with adjustment for gestational age, maternal age, parity, plurality, smoking and body mass index.

**Main outcome measures** Perinatal outcomes.

**Results** A total of 770 926 infants were included. Labour induction from 37 weeks increased from 9.7% in 2000–02 to 22.5% in 2011–12. From 2003–05 to 2011–12, the risk of umbilical cord pH < 7.0 decreased by 23%; odds ratio (OR) 0.77 (95% confidence interval 0.67–0.89), and the adjusted OR of Apgar score < 7 at 5 minutes was unchanged. The risk of admission to neonatal intensive care units increased by 56%; OR 1.56 (1.47–1.66), whereas the risk of neonatal deaths decreased by 44%; OR 0.56 (0.45–0.70). The risk of cerebral palsy was from 2000–02 to 2009–10 reduced by 26%; OR 0.74 (0.60–0.90). The proportion of infants born with fetal weight ≥ 4500 g decreased by one-third; OR 0.68 (0.65–0.71). However, the risk of shoulder dystocia increased by 32%; OR 1.32 (1.21–1.44), whereas the risk of peripheral nerve injuries was reduced by 43%; OR 0.57 (0.45–0.73).

**Conclusion** The results suggest an overall improvement in perinatal outcomes as a result of a more proactive post-term labour induction practice.

**Keywords** Asphyxia, birth induction, misoprostol, perinatal outcome, post-term labour.

*Please cite this paper as:* Hedegaard M, Lidegaard Ø, Skovlund CW, Mørch LS, Hedegaard M. Perinatal outcomes following an earlier post-term labour induction policy: a historical cohort study. BJOG 2015; DOI: 10.1111/1471-0528.13299.

## Introduction

In 2008, the National Institute for Health and Clinical Excellence published a guideline on late term labour induction, stating that uncomplicated pregnancies should be induced in weeks 41–42 of gestation; this guideline was followed by a similar practice bulletin issued by the American Congress of Obstetricians and Gynaecologists in 2009.[1,2] The same year, the national Danish guidelines were changed accordingly to recommend labour induction at week 41[+3–5] for low-risk pregnant women and even earlier for high-risk pregnant women, e.g. women with body mass index > 30 kg/m$^2$, age ≥ 40 years or certain medical conditions.[3] The goal was to ensure delivery before 42 weeks of gestation.[4] The guideline was discussed and approved by representatives from all delivery units in Denmark. The new guideline led to an increase in post-term labour induction, which was followed by a significant reduction in the number of stillborn infants at term.[5] It has also been suggested that maternal morbidity may be improved by a more proactive labour induction practice.[6] However, recent meta-analyses found only a few studies addressing the impact of different induction practices on neonatal mortality and morbidity;[4,7,8] and asked for further studies.[9]

When examining rare outcomes, such as neonatal death, it is often difficult to achieve statistically significant correlations in clinical trials.[10] Under such circumstances, large observational studies may provide useful information.[11,12]

 

This study aimed to investigate the national changes in different perinatal outcomes over a period, during which a more proactive labour induction guideline was implemented.

# Methods

## Design and setting

This historical cohort study included all newborns in Denmark delivered from 1 January 2000 to 31 December 2012. To reduce the random year-to-year variation, the 13-year study period was subdivided into five intervals of 3, 3, 3, 2 and 2 years.

Data were retrieved in October 2013 from the Danish National Health Register and the Medical Birth Register, which contains information on all deliveries in Denmark since 1973.[13] Approval was obtained from the Danish Data Protection Agency (J.no: 2013-41-2063) and the National Board of Health (J.no. FSEID 00000579). According to the Danish Research Ethics Committee Law (§ 10), ethical approval is not required for register-based studies.

## Participants

All infants born from 37 weeks of gestation were included. Despite focusing on post-term labour induction, the limit for inclusion was set at >37 weeks of gestation to avoid exclusion of the outcomes of high-risk pregnancies, which are often induced before 40 weeks. Gestational age was generally calculated based on first-trimester ultrasound examinations. For the few women who did not attend this routine offer to all pregnant women in Denmark, the date of their last menstrual period was used.

Based on diagnostic and surgical codes, the study population was subdivided according to the intentional mode of delivery: (i) an induction of labour cohort, (ii) a planned spontaneous vaginal delivery cohort, and (iii) an elective caesarean section cohort. The specific codes identifying the cohorts are listed in the supplementary appendix (Table S1).

## Outcomes

Eight outcomes were defined based on different criteria or clusters of diagnosis codes from the International Classification of Diseases, 10th revision (ICD 10). The outcomes were categorised into three groups (Table S2): asphyxia indicators (umbilical cord pH $< 7.0$ and Apgar score $< 7$ at 5 minutes), potential manifestations of asphyxia (admission to neonatal intensive care units within 28 days after birth, neonatal death and cerebral palsy), and prevention of macrosomia (fetal weight $\geq 4500$ g, shoulder dystocia and peripheral nerve injury). A neonate could potentially have more than one outcome.

Before 2003, umbilical cord pH was not routinely recorded in the register. In this study we intended to use arterial pH, but in the few cases where this information was not available, either venous or unspecified pH was used. All pH values not in the range of 6.6–7.9 were considered invalid, and were consequently excluded from the analysis.

There is often a long latency from birth until cerebral palsy is potentially diagnosed. Therefore, diagnoses recorded up to 3 years after birth were included. Hence the years 2011 and 2012 were excluded from the analysis of this specific outcome because of the lack of sufficient follow-up time.

In accordance with the World Health Organization, neonatal death was defined as death within 28 days after birth.[14]

Shoulder dystocia and nerve injury were only assessed in vaginal deliveries.

## Potential confounders

To describe the influence of potential confounders, we gathered information on maternal age, parity, plurality, smoking and body mass index. The definitions are presented in the supporting information (Table S3).

## Statistical analysis

To estimate the crude and adjusted odds ratio (OR), logistic regression analyses were performed with the period 2000–02 as the reference period. Adjustments were made for maternal age, parity, plurality, gestational age and smoking. Because body mass index was not registered until 2004, we assessed the influence of body mass index in a sub-analysis restricted to the period 2004–12. Because the results changed by <5% with adjustment for body mass index, this variable was not included in the main analyses. To assess the influence of risk-factors such as intrauterine growth restriction and pre-eclampsia, a sensitivity analysis of the factors combined was performed. Finally sensitivity analysis for only singleton pregnancies was performed. Incidence rates in the total population and within the three delivery cohorts were calculated. A chi-square test was used to analyse differences in incidence rates, with a $P$-value of <0.05 considered significant.

# Results

During the 13-year study period, a total of 832 935 children were born in Denmark. Among those were 770 926 children (92.6%) born after 37 weeks of gestation, constituting the study group. Of these, 104 107 (13.5%) children were born after labour induction, 602 219 (78.1%) were born after planned vaginal delivery, and 64 600 (8.4%) were born after elective caesarean section.

Medical induction of labour from 37 weeks of gestation increased from 9.1% in 2000 to 26.0% in 2012 ($P < 0.001$)

 

(Figure 1). A steep increase was observed, especially after 2009. Correspondingly, the percentage of pregnancies that continued beyond 42 gestational weeks decreased from 8.0% in 2000 to 1.5% in 2012 ($P < 0.001$) (Figure 1).

Apart from a major decrease in the proportion of children born from 42 weeks of gestation, and a corresponding increase in children born between 41 and 42 weeks of gestation, no obvious alterations in length of gestation at delivery were observed (Figure 2).

The percentage of women with planned spontaneous vaginal delivery decreased from 84.5% in 2000–02 to 67.7% in 2011–12 ($P < 0.001$), whereas the elective caesarean section rate increased from 5.9 to 9.8% ($P < 0.001$) (Table 1).

Among women in spontaneous labour, the percentage of women undergoing emergency caesarean sections was stable (2000–02: 9%, 2003–05: 10%, 2006–08: 10%, 2009–10: 10%, 2011–12: 10%). In contrast, the percentage of women whose infants were delivered by emergency caesarean section after labour induction decreased during the most recent years, where the use of induction was highest (2000–02: 19%, 2003–05: 21%, 2006–08: 20%, 2009–10: 20%, 2011–12: 16%).

## Asphyxia indicators

The adjusted relative risk of umbilical cord pH < 7.0 decreased by 23%; OR 0.77 (95% confidence interval 0.67–0.89) when comparing 2011–12 with 2003–04 (Table 1). Low pH decreased significantly in all three cohorts and was 4.9‰ in both the induced and the planned spontaneous vaginal delivery cohorts in 2011–12 (Table 2).

Except for the changes in the crude incidence rate of Apgar scores < 7 at 5 minutes (<7/5) within the total population, all other results indicated that the rate of Apgar scores < 7/5 was stable over time and across all study groups (Tables 1 and 2; Figure S1).

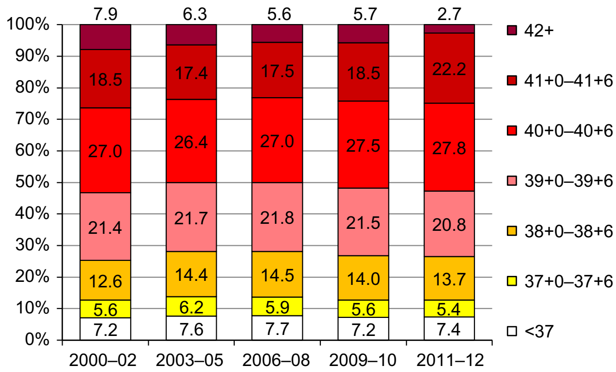


**Figure 2.** Percentage distribution of deliveries according to gestational age by time-period in Denmark from 2000 to 2012.

## Potential manifestations of asphyxia

Throughout the study period, the adjusted risk of admission to a neonatal intensive care unit increased by 56%; OR 1.56 (1.47–1.66) (Table 1). The admission rates were stable in the induced delivery cohort, whereas the rates increased significantly after planned vaginal delivery and elective caesarean section (Table 2).

The adjusted relative risk of neonatal death was almost halved; OR 0.56 (0.45–0.70) (Table 1). Although significant decreases were observed in all three cohorts, the steepest decrease from 2.7‰ in 2000–02 to 1.0‰ in 2011–12 was observed among children born after elective caesarean section ($P < 0.001$) (Table 2).

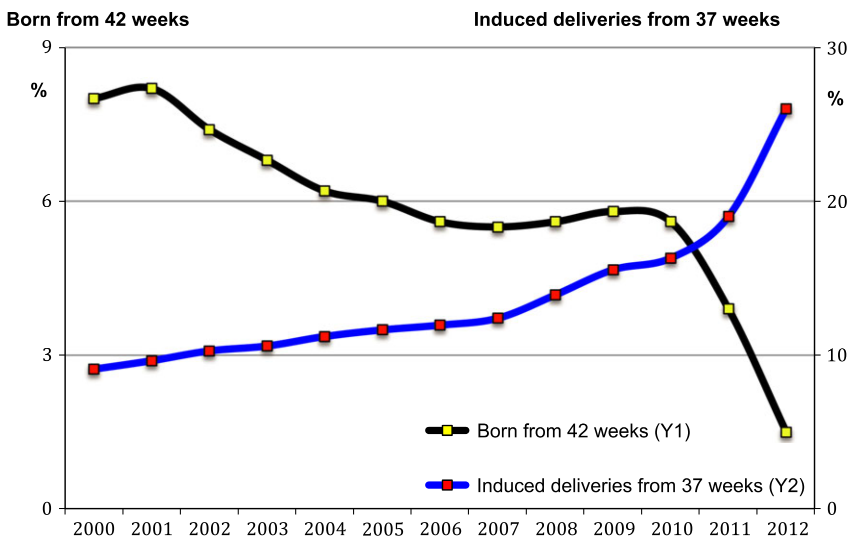


**Figure 1.** Percentages of deliveries induced after 37 weeks of gestation and of children born after 42 weeks of gestation in Denmark from 2000 to 2012.

**Table 1.** Developments in hazard ratios for adverse perinatal outcomes in children born from 37 weeks' gestation in Denmark from 2000 to 2012

| Outcome | 2000–02 | 2003–05 | 2006–08 | 2009–10 | 2011–12 |
|---|---|---|---|---|---|
| **Distribution of deliveries (%)** | | | | | |
| Induced delivery | 9.7 | 11.1 | 12.8 | 15.9 | 22.5 |
| Planned vaginal | 84.5 | 80.6 | 77.8 | 74.5 | 67.7 |
| Elective caesarean | 5.9 | 8.2 | 9.4 | 9.6 | 9.8 |
| **Umbilical cord pH < 7.0** | | | | | |
| Hazard ratio, crude | – | 1.00 | 0.88 | 0.71* | 0.76* |
| Hazard ratio, adjusted | – | 1.00 | 0.89 | 0.72* | 0.77* |
| Confidence intervals, adjusted | – | Reference | 0.77–1.02 | 0.62–0.84 | 0.67–0.89 |
| **Apgar score < 7/5 minutes** | | | | | |
| Hazard ratio, crude | 1.00 | 0.97 | 0.95 | 0.95 | 1.09 |
| Hazard ratio, adjusted | 1.00 | 0.97 | 0.93 | 0.93 | 1.07 |
| Confidence intervals, adjusted | Reference | 0.89–1.05 | 0.86–1.02 | 0.84–1.02 | 0.97–1.18 |
| **Admission to neonatal intensive care units** | | | | | |
| Hazard ratio, crude | 1.00 | 1.10* | 1.12* | 1.47* | 1.60* |
| Hazard ratio, adjusted | 1.00 | 1.08* | 1.11* | 1.45* | 1.56* |
| Confidence intervals, adjusted | Reference | 1.02–1.14 | 1.04–1.17 | 1.37–1.54 | 1.47–1.66 |
| **Neonatal death** | | | | | |
| Hazard ratio, crude | 1.00 | 0.81* | 0.71* | 0.52* | 0.54* |
| Hazard ratio, adjusted | 1.00 | 0.82* | 0.69* | 0.52* | 0.56* |
| Confidence intervals, adjusted | Reference | 0.70–0.96 | 0.59–0.82 | 0.42–0.64 | 0.45–0.70 |
| **Cerebral palsy** | | | | | |
| Hazard ratio, crude | 1.00 | 0.81* | 0.79* | 0.74* | – |
| Hazard ratio, adjusted | 1.00 | 0.81* | 0.79* | 0.74* | – |
| Confidence intervals, adjusted | Reference | 0.68–0.95 | 0.66–0.93 | 0.60–0.90 | – |
| **Birthweight ≥ 4500 g** | | | | | |
| Hazard ratio, crude | 1.00 | 0.95* | 0.81* | 0.75* | 0.65* |
| Hazard ratio, adjusted | 1.00 | 0.99 | 0.85* | 0.76* | 0.68* |
| Confidence intervals, adjusted | Reference | 0.96–1.03 | 0.82–0.88 | 0.73–0.80 | 0.65–0.71 |
| **Shoulder dystocia** | | | | | |
| Hazard ratio, crude | 1.00 | 0.97 | 1.13* | 1.34* | 1.30* |
| Hazard ratio, adjusted | 1.00 | 0.99 | 1.15* | 1.36* | 1.32* |
| Confidence intervals, adjusted | Reference | 0.91–1.07 | 1.07–1.25 | 1.25–1.48 | 1.21–1.44 |
| **Nerve injury** | | | | | |
| Hazard ratio, crude | 1.00 | 0.77* | 0.73* | 0.83 | 0.59* |
| Hazard ratio, adjusted | 1.00 | 0.77* | 0.71* | 0.80* | 0.57* |
| Confidence intervals, adjusted | Reference | 0.64–0.93 | 0.58–0.86 | 0.65–0.99 | 0.45–0.73 |

Ratios adjusted for maternal age, smoking, parity and plurality.
*Significant results.

The adjusted relative risk of cerebral palsy decreased by 26% from 2000–02 to 2009–10; OR 0.74 (0.60–0-90) (Table 1). However, this decrease was only significant in the planned vaginal delivery cohort ($P = 0.003$) (Table 2).

## Prevention of macrosomia

Throughout the study period, the adjusted risk of birthweight ≥ 4500 g decreased by one-third; OR 0.68 (0.65–0.71), from 4.2% in 2000–02 to 2.8% in 2011–12 ($P < 0.001$) (Tables 1 and 2; Figure S2).

Despite the presence of fewer children with macrosomia, the adjusted relative risk of shoulder dystocia increased by 32%; OR 1.32 (1.21–1.44) during the same period (Table 1). In contrast, the adjusted risk of peripheral nerve injury decreased by 43% overall; OR 0.57 (0.45–0.73), and the decrease was seen in both vaginal delivery cohorts; however, this was only significant in the planned vaginal delivery cohort ($P = 0.003$) (Table 2).

## Changes in potential confounders

Mean maternal age increased linearly from 30.1 years in 2000–02 to 30.9 years in 2009–10 (Table 3) but has been stable since then. The prevalence of pregnant women >40 years of age increased from 2.0% in 2000–02 to 3.5% in 2011–12 ($P < 0.001$) (Table 3).

**Table 2.** Incidence rates of morbidity indicators among children born after (i) induced delivery, (ii) planned spontaneous vaginal delivery, and (iii) elective Caesarean section from 37 weeks of gestation in Denmark from 2000 to 2012

| | 2000–02 | 2003–05 | 2006–08 | 2009–10 | 2011–12 | *P*-value | 2000–12 |
|---|---|---|---|---|---|---|---|
| **Umbilical cord pH < 7.0** | | | | | | | |
| Induced delivery | – | 8.0 | 7.9 | 5.7 | 4.9 | <0.001 | 6.3 |
| Planned vaginal | – | 6.0 | 5.1 | 4.3 | 4.9 | 0.002 | 5.0 |
| Elective caesarean | – | 2.2 | 1.5 | 0.4 | 0.5 | 0.002 | 1.0 |
| Total | – | 5.9 | 5.1 | 4.2 | 4.4 | <0.001 | 4.8 |
| **Apgar scores < 7/5 minutes** | | | | | | | |
| Induced delivery | 9.7 | 7.9 | 9.3 | 8.5 | 8.2 | 0.259 | 8.7 |
| Planned vaginal | 5.7 | 5.8 | 5.4 | 5.5 | 6.3 | 0.153 | 5.7 |
| Elective caesarean | 4.7 | 3.4 | 2.9 | 3.0 | 4.5 | 0.051 | 3.6 |
| Total | 6.0 | 5.8 | 5.7 | 5.7 | 6.5 | 0.037 | 5.9 |
| **Admission to neonatal intensive care units (%)** | | | | | | | |
| Induced delivery | 2.5 | 2.6 | 2.5 | 2.7 | 2.6 | 0.738 | 2.6 |
| Planned vaginal | 1.1 | 1.2 | 1.2 | 1.6 | 1.7 | <0.001 | 1.3 |
| Elective caesarean | 2.2 | 1.9 | 1.7 | 2.4 | 2.7 | <0.001 | 2.1 |
| Total | 1.3 | 1.4 | 1.4 | 1.9 | 2.0 | <0.001 | 1.6 |
| **Neonatal death** | | | | | | | |
| Induced delivery | 2.4 | 1.5 | 1.8 | 1.3 | 1.0 | 0.005 | 1.6 |
| Planned vaginal | 1.7 | 1.5 | 1.3 | 0.9 | 1.0 | <0.001 | 1.4 |
| Elective caesarean | 2.7 | 1.8 | 0.7 | 0.5 | 1.0 | <0.001 | 1.3 |
| Total | 1.9 | 1.5 | 1.3 | 1.0 | 1.0 | <0.001 | 1.4 |
| **Cerebral palsy** | | | | | | | |
| Induced delivery | 2.2 | 1.6 | 1.3 | 1.7 | – | 0.178 | 1.7 |
| Planned vaginal | 1.6 | 1.2 | 1.3 | 1.1 | – | 0.003 | 1.4 |
| Elective caesarean | 1.9 | 2.0 | 1.6 | 1.7 | – | 0.804 | 2.0 |
| Total | 1.7 | 1.3 | 1.3 | 1.2 | – | 0.005 | 1.5 |
| **Birth weight ≥ 4500 g (%)** | | | | | | | |
| Induced delivery | 6.2 | 5.6 | 4.6 | 4.2 | 3.7 | <0.001 | 4.8 |
| Planned vaginal | 4.0 | 3.8 | 3.3 | 3.0 | 2.5 | <0.001 | 3.5 |
| Elective caesarean | 3.7 | 3.7 | 2.9 | 3.1 | 2.6 | <0.001 | 3.2 |
| Total | 4.2 | 4.0 | 3.4 | 3.2 | 2.8 | <0.001 | 3.6 |
| **Shoulder dystocia** | | | | | | | |
| Induced delivery | 8.4 | 8.8 | 9.4 | 11.8 | 12.1 | <0.001 | 10.2 |
| Planned vaginal | 7.1 | 6.9 | 8.3 | 9.7 | 9.0 | <0.001 | 7.9 |
| Total | 6.8 | 6.6 | 7.6 | 9.1 | 8.8 | <0.001 | 7.6 |
| **Nerve injury** | | | | | | | |
| Induced delivery | 2.3 | 1.6 | 1.5 | 1.9 | 1.2 | 0.076 | 1.7 |
| Planned vaginal | 1.3 | 1.1 | 1.0 | 1.1 | 0.8 | 0.003 | 1.1 |
| Total | 1.4 | 1.1 | 1.0 | 1.1 | 0.8 | <0.001 | 1.1 |

Incidence rates are expressed per 1000 newborns unless otherwise specified.

Although statistically significant, the incidence rate of multiple pregnancies born after 37 weeks of gestation changed only minimally, ranging from 2.4 to 2.6% ($P < 0.001$). The proportion of nulliparous women increased slightly from 43.0% in 2000–02 to 44.5% in 2011–12 ($P < 0.001$) (Table 3).

The prevalence of smokers in the study population was almost halved from 21.1 to 11.6% ($P < 0.001$) (Table 3). However, logistic regression analyses with and without adjustments for smoking, maternal age and parity demonstrated that these factors could not explain the reported improvements in perinatal outcomes (Table 1). Body mass index was relatively constant, with a mean of 24.3 kg/$m^2$ (Table 3). However, the prevalence of severe maternal obesity (body mass index > 35 kg/$m^2$) increased from 3.6% in 2003–05 to 4.4% in 2011–12 ($P < 0.001$) (Table 3). Sensitivity analysis including adjustment for preeclampsia and intrauterine growth restriction did not change the trends significantly. Analyses restricted to singletons provided similar results as for all deliveries (results not shown).

 

**Table 3.** Maternal age, parity, plurality, smoking and body mass index among women pregnant from 37 weeks of gestation in Denmark from 2000 to 2012

| | 2000–02 | 2003–05 | 2006–08 | 2009–10 | 2011–12 | *P*-value | Total |
|---|---|---|---|---|---|---|---|
| **Maternal age** | | | | | | | |
| Mean maternal age, years | 30.1 | 30.6 | 30.8 | 30.9 | 30.9 | | 30.7 |
| Maternal age > 40 years (%) | 2.0 | 2.4 | 3.0 | 3.2 | 3.5 | <0.001 | 2.7 |
| **Parity** | | | | | | | |
| Nulliparas (%) | 43.0 | 42.9 | 43.0 | 43.8 | 44.5 | <0.001 | 43.3 |
| **Plurality** | | | | | | | |
| Multigravidas (%) | 2.4 | 2.6 | 2.6 | 2.6 | 2.5 | <0.001 | 2.5 |
| **Smoker** | | | | | | | |
| Smokers (%) | 21.1 | 17.5 | 14.5 | 12.9 | 11.6 | <0.001 | 16.1 |
| **Body mass index** | | | | | | | |
| Mean BMI | – | 24.1 | 24.2 | 24.4 | 24.4 | | 24.3 |
| Maternal BMI > 35 kg/m$^2$ (%) | – | 3.6 | 4.1 | 4.4 | 4.4 | <0.001 | 4.1 |

## Discussion

### Main findings

One-quarter of Danish women pregnant beyond 37 weeks of gestation now experience labour induction, and our recent study demonstrated a simultaneous halving of stillbirths.[5]

The present study demonstrates that the reduction in stillborn infants was followed by significant reductions in newborn asphyxia, neonatal mortality, newborn macrosomia and peripheral nerve injuries. The incidence rate of admission to neonatal intensive care units increased, but only in neonates born after planned vaginal delivery or elective caesarean section and not in neonates born after labour induction. Consistent with the decrease in asphyxia, the incidence rate of cerebral palsy decreased, although this was only statistically significant in the planned vaginal delivery cohort.

### Strengths and limitations

The unique personal identity number that every individual in the Nordic countries carries is the cornerstone of the Nordic medical register research.[13] We included a broad and unselected sample of individuals, to achieve a high external validity. The size of our study ensured rather precise estimates. Also the exposure information was collected before knowing outcomes, so avoiding recall bias. The limitations of register-based studies are their observational and historical design, which makes it difficult effectively to account for all potential confounders. Information about exposure is determined by the content of the registry, restricting the possibility to investigate new exposures. Moreover, data reporting improved for some variables during the study period.

### Interpretation

The reason for labour induction often involves some type of pregnancy complication and is not necessarily limited to post-term pregnancies. Second, with the proactive induction practice, the induced group has become gradually less burdened by pathological pregnancies, as more women are now induced with prolonged pregnancy as the only indication for labour induction. The size of the planned vaginal delivery group has consequently been reduced, and includes less overborne and fewer high-risk deliveries. If the decrease in adverse perinatal outcomes in the planned vaginal delivery group was associated with an increase in adverse outcomes in the induced delivery group, an earlier induction practice would be questionable. However, simultaneous reductions in adverse perinatal outcomes in both the labour induction group and in the planned spontaneous vaginal delivery group supports a more proactive induction practice.

The stable risk of Apgar scores < 7 at 5 minutes corresponds well with the findings of earlier studies.[4,15,16] A Cochrane review from 2012 also suggested no increase in newborn asphyxia with an earlier birth induction practice.[8] Although the decrease in asphyxia may have been reflected in fewer Apgar scores < 7 at 5 minutes, this outcome was also influenced by a range of other factors, such as drug use, trauma, congenital abnormalities and infections, problems that have not been resolved by an earlier labour induction policy.[17] Because umbilical cord pH is more objective than Apgar score assessment,[18] cord pH is our preferred indicator of asphyxia in newborns.[19]

The increased risk of admission to neonatal intensive care units among children born after planned vaginal delivery is worrying. Due to a centralisation of Danish deliveries into larger hospital units, the accessibility to neonatal care has improved throughout our study period. In the first part of the study period, several smaller delivery units were placed in hospitals with no neonatal intensive care unit. At the end of the study period, only three small delivery units did not have immediate access to neonatal services. As a result, a lowered threshold for transfer may explain the increase in admission, as a similar increase was observed in the elective caesarean section group. Furthermore, the increase in referrals to neonatal units was associated with a substantial reduction in the risk of neonatal deaths. Earlier studies have encountered difficulties achieving sufficient statistical power to demonstrate differences between children born after labour induction and those born after expectant management,[4,8] but recent studies suggest that labour induction significantly reduces perinatal mortality, in agreement with our results.[7,20] Nevertheless, the reduction in neonatal deaths was undoubtedly also influenced by improved neonatal care throughout the study period.[21,22] In accordance with the positive development in neonatal deaths, the corresponding rate of infant death (death within the first year of life) showed a similar decrease in adjusted relative risk of 0.57 comparing 2011 to 2000–02 (data not shown).

The reduction in cerebral palsy corroborates with the decrease in asphyxia. Through the last decade, our capacity to more precisely diagnose neurological pathologies has improved, especially with the increased use of magnetic resonance imaging.[23] The treatment regimen has also improved, resulting in enhanced neuroprotection, such as moderate hypothermia in cases of severe asphyxia.[24–27]

The proportion of newborns with birthweight $\geq$ 4500 g has increased over the last decades in Denmark.[28,29] Proactive induction practice reversed this development. Although this improvement was not the primary aim of the induction guideline, it constitutes an additional positive side effect.

In theory, the reduction in vaginal deliveries of macrosomic children should reduce the risk of shoulder dystocia.[30–33] However, we detected increases in shoulder dystocia in both vaginal delivery cohorts. The incidence rate of shoulder dystocia of 0.8% in 2006–08 is still low compared with an American study, which reported an incidence rate of shoulder dystocia of 1.6% in 2006.[34] Hence, shoulder dystocia may previously have been underreported, an explanation that is further supported by the reduction in peripheral nerve injuries. Recently, many obstetric units in Denmark have focused on the management of shoulder dystocia, resulting in a more thorough diagnosis and training of medical staff. This increased attention could explain why more cases of shoulder dystocia are being diagnosed, even though fewer children suffer from nerve injuries.

Children born after labour induction demonstrated the highest incidence rates of the majority of the adverse outcomes. If this was a consequence of the intervention itself, one would expect more complications following the increased use of labour induction. However, most adverse outcomes actually decreased in frequency with the increased induction rate. This suggests that the higher incidence rates in the labour induction cohort are a consequence of selection, with high-risk pregnant women being induced more often than women awaiting spontaneous delivery.

The improved perinatal outcomes might also be influenced by other factors not related to labour induction. Awareness of the dangers related to smoking has grown,[35] explaining the significant reduction in pregnant smokers; this reduction contributed significantly to the decrease in stillbirths but only marginally to reductions in the perinatal outcomes described in this study.[5]

The increased maternal age, greater nulliparity and higher body mass index indicated that more women were at risk according to time in our study population, suggesting that the crude results reported have underestimated the positive effect of labour induction.[36] However, adjusting for these factors only changed the results minimally.

## Conclusion

On a national level, this study assessed the changes in different perinatal outcomes over a decade during which the management of post-term pregnancies changed considerably. The results suggest an overall improvement in perinatal outcomes in children born from 37 weeks of gestation. Although smoking, maternal age and parity changed significantly over the study period, adjusting for these factors did not change the estimates substantially.

Labour induction is a simple and inexpensive intervention, but demands a closer surveillance during delivery and an infrastructure supporting such changes. The generalisability of our findings should be cautiously scrutinised before implementing national initiatives elsewhere.

### Disclosure of interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that ØL within the last 3 years received honoraria for speeches in pharmacoepidemiological issues. MH, MH, CWS and LSM did not declare any conflicts.

### Contribution to authorship

MH, MH and ØL planned the study. CWS and LSM retrieved data from The Danish National Health Register and The Medical Birth Register. LSM, CWS, MH, MH and ØL analysed the data. MH, MH and ØL wrote the manuscript. All authors revised the manuscript and accepted the final version. Morten Hedegaard is the guarantor.

## Details of ethics approval

According to the Danish Research Ethics Committee Law (§ 10), ethical approval is not required for register-based studies.

## Funding

The study was supported by a scholar grant from Rigshospitalet. Other expenses were covered by Department of Gynaecology, Rigshospitalet, University of Copenhagen.

## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Incidence rates of asphyxia indicators and their potential manifestations from 37 weeks of gestation in Denmark from 2000 to 2012.

**Figure S2.** Incidence rates of macrosomia from 37 weeks of gestation in Denmark from 2000 to 2012.

**Table S1.** Diagnosis codes defining groups of women who had a) induced delivery, b) planned spontaneous vaginal delivery, and c) elective caesarean section in Denmark from 2000 to 2012.

**Table S2.** Diagnosis codes and other criteria defining eight adverse perinatal outcomes.

**Table S3.** Criteria defining possible confounders. ■

## References

1 American Congress of Obstetricians and Gynaecologists (ACOG). Clinical management guidelines for obstetrician-gynecologists: induction of labour. Practice bulletin (107). 2009 [http://amoripat.com/_assets/acog–practice_bulletin_107_2009.pdf]. Accessed 18 March 2014.

2 National Institute for Health and Care Excellence (NICE). Induction of labour. Secondary Induction of labour. 2001, updated 2008. [http://publications.nice.org.uk/induction-of-labour-cg70]. Accessed 18 March 2014.

3 Danish Society for Obstetricians and Gynaecologists (DSOG). Guideline on prolonged pregnancy. 2009 [http://gynobsguideline.dk/files/Graviditas%20prolongata2011_endelig.pdf]. Accessed 25 January 2015.

4 Caughey AB, Sundaram V, Kaimal AJ, Cheng YW, Gienger A, Little SE, et al. Maternal and neonatal outcomes of elective induction of labor: Evidence report number 176. Prepared for Agency for Healthcare and Research Quality. 2009 [http://www.ahrq.gov/research/findings/evidence-based-reports/eil-evidence-report.pdf]. Accessed 18 March, 2014.

5 Hedegaard M, Lidegaard OE, Skovlund CW, Mørch LS, Hedegaard M. Reduction in stillbirths at term after new birth induction paradigm. Results of a national intervention. *BMJ open* 2014;4:e005785.

6 Liu S, Joseph KS, Hutcheon JA, Bartholomew S, León JA, Walker M, et al. Gestational age-specific severe maternal morbidity associated with labour induction. *Am J Obstet Gynecol* 2013;209:e1–8.

7 Grunewald C, Hakansson S, Saltvedt S, Källén K. Significant effects on neonatal morbidity and mortality after regional change in management of post-term pregnancy. *Acta Obstet Gynecol Scand* 2011;90:26–32.

8 Gulmezoglu AM, Crowther CA, Middleton P, Heatley E. Induction of labour for improving birth outcomes for women at or beyond term. *Cochrane Database Syst Rev* 2012;(6):CD004945.

9 Caughey AB. Perinatal outcomes related to induction of labour: a call for randomized trials. *Am J Obstet Gynecol* 2013;209:168–9.

10 Wennerholm UB, Hagberg H, Brorsson B, Bergh C. Induction of labour versus expectant management for post-date pregnancy: is there sufficient evidence for a change in clinical practice? *Acta Obstet Gynecol Scand* 2009;88:6–17.

11 Blenstrup LT, Knudsen LB. Danish registers on aspects of reproduction. *Scand J Public Health* 2011;39:79–82.

12 Smith GC, Pell JP, Dobbie R. Birth order, gestational age, and risk of delivery related perinatal death in twins: retrospective cohort study. *BMJ* 2002;325:1004.

13 Langhoff-Roos J, Krebs L, Klungsoyr K, Bjarnadottir RI, Källén K, Tapper A. The Nordic medical birth registers—a potential goldmine for clinical research. *Acta Obstet Gynecol Scand* 2013;93:132–7.

14 WHO. Neonatal and perinatal mortality: country, regional and global estimates. 2006;2–6 [http://whqlibdoc.who.int/publications/2006/9241563206_eng.pdf]. Accessed 18 March 2014.

15 Nielsen PE, Howard BC, Hill CC, Larson PL, Holland RHB, Smith PN. Comparison of elective induction of labour with favorable bishop scores versus expectant management: a randomized clinical trial. *J Matern Fetal Neonatal Med* 2005;18:59–64.

16 Heimstad R, Skogvoll E, Mattsson LA, Johansen OJ, Eik-Nes SH, Salvesen KÅ. Induction of labour or serial antenatal fetal monitoring in postterm pregnancy: a randomized controlled trial. *Obstet Gynecol* 2007;109:609–17.

17 Li F, Wu T, Lei X, Zhang H, Mao M, Zhang J. The Apgar score and infant mortality. *PLoS ONE* 2013;8:e69072.

18 Bharti B, Bharti S. A review of the Apgar score indicated that contextualization was required within the contemporary perinatal and neonatal care framework in different settings. *J Clin Epidemiol* 2005;58:121–9.

19 Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. *N Engl J Med* 2001;344:467–71.

20 Stock SJ, Ferguson E, Duffy A, Ford I, Chalmers J, Norman JE. Outcomes of elective induction of labour compared with expectant management: population based study. *BMJ* 2012;344:e2838.

21 Singh BS, Clark RH, Powers RJ, Spitzer AR. Meconium aspiration syndrome remains a significant problem in the NICU: outcomes and treatment patterns in term neonates admitted for intensive care during a ten-year period. *J Perinatol* 2009;29:497–503.

22 Amin HJ, Aziz K, Halamek LP, Beran TN. Simulation-based learning combined with debriefing: trainers satisfaction with a new approach to training the trainers to teach neonatal resuscitation. *BMC Res Notes* 2013;6:251.

23 Ostergaard JR, Christensen T, Schoitz PO. Magnetic resonance imaging in neuropediatrics. *Ugeskr Laeger* 2005;167:382–5.

24 Johnston MV, Fatemi A, Wilson MA, Northington F. Treatment advances in neonatal neuroprotection and neurointensive care. *Lancet Neurol* 2011;10:372–82.

25 Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM, et al. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet* 2005;365:663–70.

**26** Lando A, Jonsbo F, Hansen BM, Greisen G. Induced hypothermia in infants born with hypoxic-ischaemic encephalopathy. *Ugeskr Laeger* 2010;172:1433–7.

**27** Shankaran S. Outcomes of hypoxic-ischemic encephalopathy in neonates treated with hypothermia. *Clin Perinatol* 2014;41:149–59.

**28** Meeuwisse G, Olausson PO. Increased birth weights in the nordic countries. A growing proportion of neonates weigh more than four kilos. *Läkartidningen* 1998;95:5488–92.

**29** Orskou J, Kesmodel U, Henriksen TB, Secher NJ. An increasing proportion of infants weigh more than 4000 grams at birth. *Acta Obstet Gynecol Scand* 2001;80:931–6.

**30** Cheng YK, Lao TT, Sahota DS, Leung VKT, Leung TY. Use of birth weight threshold for macrosomia to identify fetuses at risk of shoulder dystocia among Chinese populations. *Int J Gynaecol Obstet* 2013;120:249–53.

**31** Cheng YW, Sparks TN, Laros RK, Nicholson JM, Caughey AB. Impending macrosomia: will induction of labour modify the risk of Caesarean delivery? *BJOG* 2012;119:402–9.

**32** Mollberg M, Hagberg H, Bager B, Lilja H, Ladfors L. High birthweight and shoulder dystocia: the strongest risk factors for obstetrical brachial plexus palsy in a Swedish population-based study. *Acta Obstet Gynecol Scand* 2005;84:654–9.

**33** Overland EA, Spydslaug A, Nielsen CS, Eskild A. Risk of shoulder dystocia in second delivery: does a history of shoulder dystocia matter? *Am J Obstet Gynecol* 2009;200:506 e1–6.

**34** Darney BG, Snowden JM, Cheng YW, Jacob L, Nicholson JM, Kaimal A. Elective induction of labour at term compared with expectant management: maternal and neonatal outcomes. *Obstet Gynecol* 2013;122:761–9.

**35** Wisborg K, Henriksen TB. Pregnancy and tobacco. A status article focusing on Danish conditions. *Ugeskr Laeger* 2003;165:4537–40.

**36** Timofeev J, Reddy UM, Huang CC, Driggers RW, Landy HJ, Laughon SK. Obstetric complications, neonatal morbidity, and indications for cesarean delivery by maternal age. *Obstet Gynecol* 2013;122:1184–95.