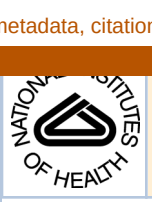

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Timing of Delivery and Pregnancy Outcomes Among Laboring Nulliparous Women

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Abstract

OBJECTIVE—To compare pregnancy outcomes by completed week of gestation after 39 weeks with outcomes at 39 weeks.

STUDY DESIGN—Secondary analysis of a multicenter trial of fetal pulse oximetry in spontaneously laboring or induced nulliparous women ≥36 weeks' gestation. Maternal outcomes included a composite (treated uterine atony, blood transfusion and peripartum infections) and cesarean delivery. Neonatal outcomes included a composite of death, neonatal respiratory and other morbidities and neonatal ICU admission.

RESULTS—Among the 4086 women studied, the risks of the composite maternal outcome (p-value for trend<0.001), cesarean delivery (p<0.001) and composite neonatal outcome (p=0.047) increased with increasing gestational age from 39 to ≥41 completed weeks. Adjusted odds ratios (95% CI) for 40 and ≥41 weeks respectively compared with 39 weeks were 1.29 (1.03–1.64) and 2.05 (1.60–2.64) for composite maternal outcome, 1.28 (1.05–1.57) and 1.75 (1.41–2.16) for cesarean delivery and 1.25 (0.86–1.83) and 1.37 (0.90–2.09) for composite neonatal outcome.

CONCLUSIONS—Risks of maternal morbidity and cesarean delivery but not neonatal morbidity increased significantly beyond 39 weeks.

Keywords

Pregnancy outcomes; Cesarean delivery; Optimal timing of delivery; Nulliparous; Labor

Introduction

We reported increasing trends in neonatal morbidities associated with delivery beyond 39 to 40 weeks' gestation in a cohort of women undergoing pre-labor elective repeat cesarean delivery [1]. The morbidities included respiratory complications, hypoglycemia, suspected or proven sepsis, and admission to the NICU. Consistent with ACOG recommendations, few women desiring a cesarean are delivered beyond the window of 39–40 weeks' gestation.[1–2] However, the potential for increased neonatal risk with increasing gestational age is of public health importance for the majority of women who anticipate a vaginal delivery, because a third of women remain pregnant beyond 39 completed weeks, and post-date induction typically is not recommended prior to the 41st week.[3–5] Furthermore, the cumulative risks and the gestational age-specific risks of stillbirth and other outcomes such as preeclampsia rise with each additional week of gestation,[6–7] and a Cochrane review of clinical trials does not support the commonly held view that cesarean rates are increased with labor induction compared with expectant management at ≥37 weeks' gestation.[8] Data from observational studies suggesting an increase in selected neonatal outcomes, cesarean delivery or maternal morbidities with later delivery at term[9–12] raise questions concerning how long a pregnancy should be managed expectantly beyond 39–40 weeks' gestation and specifically concerning the current standards of management of post-date pregnancies.[3] The majority of relevant studies are retrospective and they often examine a limited number of outcomes. The objective of this study was to compare the frequency of maternal and neonatal outcomes by gestational age at delivery in a cohort of laboring nulliparous women enrolled in a clinical trial in which data on several maternal and neonatal outcomes were prospectively collected.

Materials and Methods

We conducted a secondary analysis of a multicenter randomized trial of fetal pulse oximetry as an adjunct to fetal heart monitoring conducted at 14 academic centers of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)

Maternal Fetal Medicine Units (MFMU) Network from 2002 to 2005.[13] Nulliparous women at 36 or more weeks of gestation, with viable singleton cephalic pregnancies and who were in spontaneous or induced labor were randomly assigned to open or masked fetal pulse oximetry groups at a cervical dilatation between 2 and 6 cm. In the open group, fetal oxygen saturation values were displayed to the clinician. In the masked group, the sensor was inserted and the values were recorded, but not displayed. Exclusion criteria for the primary study included planned cesarean, intrapartum fever prior to randomization, known HIV or hepatitis infection, heart or renal disease and diabetes mellitus. We also excluded pregnancies complicated by congenital malformations and those with medical or obstetric conditions that lead to immediate delivery or early delivery at term (hypertensive diseases, suspected growth restriction, reduced fetal movement, non-reassuring antepartum fetal testing and oligohydramnios). Inductions performed for post-dates, spontaneous membrane rupture, or for elective reasons at any gestational age were not excluded. Our primary focus concerned women delivered at 39 completed weeks' gestation or later but we also examined those delivered at 36–38 weeks as one way to assess the validity of our findings.

Gestational age was categorized into completed weeks: those delivered at 39 completed weeks (i.e. $39^{0/7}$–$39^{6/7}$ weeks), those delivered at 40 completed weeks, and those delivered at or beyond 41 completed weeks. Because of relatively small numbers, those delivered at 36–38 weeks were categorized into a single gestational age group. Gestational age determination was based on standardized criteria using last menstrual period (LMP) and/or first ultrasound. Dating was based on LMP if ultrasound agreed with LMP within 7 days up to 19 6/7 weeks, within 14 days at 20–29 6/7 weeks, or within 21 days at 30 weeks or beyond. If LMP data were not available, dating was based on the first ultrasound.

Maternal outcomes included a primary composite morbidity (of chorioamnionitis, endometritis, wound infection, uterine atony and/or blood transfusion) and cesarean delivery (not included in the composite outcome). Chorioamnionitis was defined as a clinical diagnosis based on an elevated intrapartum body temperature, uterine tenderness, fetal or maternal tachycardia and malodorous or purulent vaginal discharge and no other defined infection. Postpartum endometritis was also based on a clinical diagnosis of puerperal infection in the absence of clinical or laboratory findings suggesting a non-uterine source of infection. Wound infection was based on a clinician diagnosis. Atony was defined as a clinical diagnosis based on failure of the uterus to contract after delivery or any treatment with uterotonics including 15-methyl prostaglandin F2α or methyl ergonovine.

Individual adverse neonatal outcomes included death, respiratory distress syndrome (RDS), transient tachypnea of newborn (TTN), seizure, sepsis, intraventricular hemorrhage (IVH), hypoglycemia, intubation and ventilator support, 5-min Apgar score ≤3, hypoxic ischemic encephalopathy (HIE) and neonatal ICU admission. A neonate was considered to have the primary composite adverse neonatal outcome if it experienced any one of these individual outcomes. Since some neonates (e.g. those born to women with gestational diabetes) may be admitted to the NICU for observation in the absence of complications, we examined an alternative composite neonatal outcome that excluded NICU admission less than 48 hours. Neonatal outcomes were based on diagnoses provided by the neonatology attending. RDS was based on the clinical diagnosis and need for oxygen therapy ($FIO2 \geq 0.4$) for at least 24 hours or until death. TTN required a clinician diagnosis with need for oxygen therapy and/or mechanical ventilation/CPAP during the first 24 hours of life, and no other demonstrable cause of respiratory distress such as RDS. Sepsis was defined as suspected systemic infection with positive cultures of blood, CSF, or urine (catheterized or suprapubic), or (in the absence of positive cultures) clinical evidence of cardiovascular collapse or an unequivocal X-ray confirming infection in an infant believed to be clinically septic.

Data were analyzed using SAS (SAS Institute, Cary, NC). Chi-square or Kruskal-Wallis test as appropriate was used to assess differences in maternal demographic and infant characteristics in relation to gestational age at delivery. The incidence rates of neonatal and maternal outcomes were compared by completed gestational week at birth with 39 weeks as the referent. The exact Cochran-Armitage test was used to evaluate outcomes for trends increasing weeks of gestational age from 39 weeks. Logistic regression was used to compare outcomes at each gestational age category (39 weeks as referent) adjusting for potential confounders including maternal age, ethnicity, BMI category, marital status, payor, smoking status, prenatal care in first trimester, labor type (induced vs. spontaneous/augmented) and study arm for maternal outcomes. Neonatal outcomes are adjusted additionally for mode of delivery and infant gender. We did not adjust for birth weight, labor induction, duration of labor or mode of delivery in primary analyses since these may be in the causal pathway. However, post-hoc adjustment additionally for mode of delivery and induction or labor augmentation was conducted for the composite maternal outcome. We also adjusted additionally for delivery center. P-values <0.05 were considered statistically significant and no adjustments were made for multiple comparisons. The primary study was approved by the institutional review board at each participating center.

Results

Among 5341 women in the trial, 4086 met final inclusion criteria for this secondary analysis; 981 women with indicated inductions for non-reassuring fetal testing, decreased fetal motion, growth restriction, oligohydramnios, chronic hypertension, preeclampsia/eclampsia or gestational hypertension, diabetes mellitus and/or “others”, 263 women with pre-gestational diabetes, chronic hypertension, suspected fetal growth restriction and/or preeclampsia/gestational hypertension, 10 women with major congenital malformations, and 1 woman with delivery gestational age <36 weeks were excluded.

Dating ultrasound information was available for 92.2% of the women. The characteristics of this study population by gestational age at delivery are presented in Table 1. Gestational age in completed weeks differed significantly by mean maternal age, mean pre-pregnancy body mass index (BMI) and proportion of obese women, race or ethnicity, marital status, type of insurance, prenatal care in the first trimester and type of labor. Smoking status and study arm (open vs. masked oximetry) did not differ significantly by gestational age. The frequency of oxytocin use at randomization (for both labor induction and augmentation) and mean birth weight increased with gestational age.

There were no intrapartum stillbirths, 1 neonatal death at 40 weeks’ gestation, were two cases of severe IVH at 39 and 40 weeks, and 1 case of HIE at 40 weeks. The unadjusted risks of composite and individual maternal and neonatal outcomes are presented in Table 2 (p-values are for tests of trend from 39 to ≥41 weeks). The risks of composite adverse maternal outcome and cesarean delivery increased significantly with increasing gestational age from 39 weeks to ≥41 weeks. The increasing trend in composite maternal outcome was mainly due to chorioamnionitis (which increased from 9.2% at 39 weeks to 14.9% at ≥41 weeks) and uterine atony (increasing from 2.8% to 7.3%). Both NICU admission and composite neonatal outcome were higher at 36–38 weeks’ compared to 39 weeks’ gestation. The composite adverse neonatal outcome increased from 4.4% at 39 weeks’ gestation to 6.5% at ≥41 weeks (p-value for trend test = 0.047). The alternative composite adverse neonatal outcome increased from 3.5% at 39 weeks’ gestation to 5.0% at ≥41 weeks while NICU admission increased from 3.6% to 5.0% respectively, but the trends were not statistically significant.

The incidence of composite adverse maternal and neonatal outcomes by gestational age displayed trends similar to the unadjusted overall trends when stratified by induced vs. spontaneous labor (including oxytocin augmentation) or by cesarean vs. vaginal mode of delivery (Figure 1). For each gestational age, the incidence of the composite adverse maternal outcome was higher among those who underwent spontaneous compared to induced labor and among those delivered by cesarean compared to those delivered vaginally. The incidence of chorioamnionitis (the most common outcome in the maternal composite) increased from 39 to ≥41 completed weeks among both women with spontaneous labor (10.5% to 20.7%) and induced labor (5.0% to 9.6%). The incidence of adverse neonatal outcome was higher for cesarean than for vaginal delivery but similar by type of labor.

Results for maternal outcomes after adjusting for study arm, maternal age, BMI category, ethnicity, smoking status, marital status, payor, induced vs. spontaneous labor and prenatal care in the first trimester are presented in Table 3. Findings confirmed that the odds of the composite adverse maternal outcome (mainly due to increasing uterine atony and chorioamnionitis) and cesarean delivery increased beyond 39 completed weeks. Compared to 39 completed weeks, the risk of cesarean delivery, but not adverse maternal outcomes, appeared to be lower among those in our cohort delivered prior to 39 weeks.

The results of an identical multivariable model for neonatal outcomes adjusted additionally for mode of delivery and baby gender are also presented (Table 3). Adverse neonatal outcomes were not significantly increased at 36–38, 40 or ≥41 weeks compared with 39 weeks. Cesarean delivery (OR 1.93; 95% CI 1.43, 2.61) and male infant (OR 1.49; 95% CI 1.11, 1.98) were significantly associated with the primary adverse neonatal outcome in the model.

Results stratified by center or adjusting additionally for center were consistent with the main results but were limited by small numbers and zero cells for the less frequent outcomes.

We conducted sensitivity analyses. First, we restricted analyses to women with obstetric or medical indications for delivery who were excluded from primary analyses (those whose infants had congenital malformations remained excluded). As expected, composite maternal outcome (ranging from 14.9% prior to 39 weeks to 29.8% at 41 weeks), cesarean delivery (from 25.4% to 48.0%) and neonatal morbidity (10.2% prior to 39 weeks, 7.4% at 39, 6.9% at 40 and 9.6% at 41 weeks respectively) were more frequent at each gestational age compared to those included in our primary analyses (table 2). However, the trends observed in the outcomes with increasing gestational age mirrored those observed in the primary analyses. Next, analyses combining both these excluded women and those in the primary analyses showed trends consistent with our primary results (not shown). Then, to explore the reasons for the increasing trends in composite maternal morbidity and cesarean delivery, we adjusted additionally for birth weight and duration of labor in the primary model. As anticipated, both outcomes increased with increasing birth weight and duration of labor and their addition to the primary model attenuated the association between increasing gestational age and both outcomes.

Discussion

We observed an increasing incidence of the composite adverse maternal outcome and cesarean delivery beyond 39 weeks' gestation. In contrast to the increasing incidence of composite adverse maternal outcome (ranging from 14.6% to 25.1%) in the current cohort of laboring nulliparous women, the incidence was lower at each gestational age (6.6% to 7.5% only) in a cohort of prelabor elective repeat cesarean deliveries and no trend was observed.[14] In the latter study, additional rare maternal morbidities were included in the composite. Not

surprising, chorioamnionitis, endometritis and uterine atony were key individual morbidities contributing to the increasing trend in composite maternal morbidity in our cohort of laboring nulliparous women. The observation of higher risks of chorioamnionitis and composite maternal morbidity among women in spontaneous labor compared to those induced is consistent with reports of a higher risk of histologic chorioamnionitis among term women in spontaneous (vs. induced) labor.[15] Similar to findings in women undergoing elective repeat cesarean delivery,[14] composite maternal outcome was not significantly influenced by delivery prior to 39 weeks' gestation compared to delivery in the 39th week. The incidence of cesarean delivery in our cohort was remarkably similar to risks for nulliparous women in a large US cohort.[16]

Concerning neonatal outcomes, the incidence of the composite adverse neonatal outcome presented a significant increasing trend with increasing gestational age from 39 completed weeks. Indeed, similar to prior observations among women undergoing prelabor cesarean delivery,[1,17] the relationship between each of the more frequent neonatal outcomes (composite outcome and NICU admissions) and gestational age suggested a U-shape with nadir at 39 weeks' gestation. However, after multivariable analyses comparing delivery before or after 39 weeks with delivery at 39 completed weeks, the increase in neonatal morbidity was not statistically significant. This may be due to the low incidence of the adverse neonatal outcomes and the limited power afforded by our study. Considering this limitation, our findings may support those observed in a much larger study based on US birth data which demonstrated a U-curve with a nadir at 39 weeks for various neonatal morbidities.[16]

We acknowledge additional study limitations. The primary study excluded primiparous women with cervical dilatation above 6cm. Therefore, the generalizability of our findings to primiparous women presenting late in labor (or to parous women) is limited. While these women likely have lower risks of cesarean delivery and adverse maternal outcomes, we do not expect that gestational age trends would be different than observed in our cohort. A third limitation is the lack of data on antepartum stillbirths (which do increase with increasing gestational age), since only women with viable pregnancies were eligible for the primary study. Similarly, by excluding several risk factors or conditions that cumulatively are more likely to occur with advancing gestational age (e.g., preeclampsia, oligohydramnios, non-reassuring fetal status) from primary analyses, we could have underestimated the true association between advancing gestational age and maternal and neonatal outcomes. Indeed, in supplementary analyses that including these women, we observed higher rates of the adverse outcomes at each gestational age; however, the overall trends suggesting increasing incidence beyond 39 weeks remained the same. Our findings are susceptible to bias from unmeasured factors that may be associated with both gestational age and study outcomes. While potential biases may be in either direction, our observed associations may be underestimates since women perceived to be at risk are more likely to be delivered prior to the 41st week. Although we adjusted for use of fetal pulse oximetry in half of our cohort, the lack of its use in contemporary obstetric practice in the United States is a limitation. Finally, this study involves multiple comparisons which may lead to spurious associations due to increased likelihood of type 1 error.

A large body of evidence supports recommendations to avoid delivery prior to 39 weeks' gestation in the absence of medical or obstetric indications.[1–2,14,17–21] We therefore focused our investigation on whether there is a restricted delivery window beyond 39 weeks' gestation when maternal and perinatal outcomes are optimal. Consistent with findings from prior studies of various maternal outcomes,[9,11, 17,20,22] composite adverse maternal outcome increased significantly after 39 weeks' gestation (a modest increase of 30% at 40 to 100% at ≥41weeks respectively). Although the increase occurred regardless of type of labor onset

(i.e., spontaneous or induced), the gestational age-matched incidence of adverse maternal outcome was surprisingly higher among women in spontaneous labor than in those who underwent labor induction. Women who underwent spontaneous delivery at 40 weeks or later had markedly increased composite adverse maternal outcome rates compared to those induced at 39 weeks (see figure 1). These observations suggest that induction of labor past 39 completed weeks' gestation may be associated with improved maternal outcomes compared with awaiting spontaneous labor. Furthermore, the cesarean delivery rate increased significantly with increasing gestational age regardless of the type of labor (Table 3); as expected, the magnitude of the increase appeared to be higher among those who underwent labor induction than those who entered labor spontaneously (Figure 1 – Panel C). The observed trends persisted after including women we had originally excluded because of medical or obstetric indications for early delivery. These findings are consistent with several reports suggesting that induction of labor at term, does not increase, and indeed may be associated with a lower risk of cesarean delivery compared with expectant management (which includes inductions at a later gestational age).[6,9,11,16,23–27] These observations challenge the belief that a policy of labor induction at term (vs. expectant management) is associated with an increased risk of cesarean delivery – a belief supported by data from other studies.[20,24,28–31] The discrepancy may be explained in part by design limitations, differences according to gestational age or use of the wrong comparison group. Ideally, women planning to deliver at 39 completed weeks should be compared to those planning expectant management who deliver spontaneously at 39–41 weeks or by induction in the 41st week. Ongoing fetal growth and placental maturation with expectant management may increase the risk for cesarean delivery due to dystocia or non-reassuring fetal status, and outweigh the risk of cesarean delivery associated with the alternative policy of labor induction.[23] For this reason, we did not adjust for increasing infant birth weight and duration of labor in the primary analyses since these may be intermediate factors in the causal pathway linking delivery gestational age and outcomes, particularly cesarean delivery. Adjustment for these factors in additional analyses attenuated the observed associations as anticipated for intermediate factors. Concerning neonatal outcomes, with adequate power we may expect a 20 to 40% increase in the composite outcome past 39 weeks based on our findings. Although not statistically significant, these data are supportive of studies reporting increasing adverse neonatal or infant outcomes with gestational age past 39–40 weeks (including meconium complications, macrosomia, neonatal ICU admission, low apgar or cord pH, birth injury, neonatal death and cerebral palsy).[9–12,16,32]

Considered together with increasing risk of stillbirth with pregnancy prolongation beyond 39 weeks' gestation,[33–34] our findings indicating increased maternal morbidity and cesarean delivery and a potential for increased neonatal morbidity beyond 39 weeks' gestation suggest that, maternal and perinatal outcomes may be improved by delivery soon after 39 0/7 weeks of gestation. However, we do not believe a change in practice is justifiable on the basis of this study or other observational studies considering their limitations. A policy to initiate delivery soon after 39 completed weeks will require labor induction for an increased proportion of women. The effects of such a policy may not be fully captured by observational studies. The data from systematic reviews of clinical trials though supportive of our findings are also limited – these have focused on deliveries after 41 weeks and evaluation of earlier term deliveries have combined those at 37–40 weeks.[8,23] Therefore, our findings together with those from other studies underscore the need for a large randomized trial of a policy of elective delivery at 39 weeks vs. the standard policy of expectant management until at least 41 completed weeks. Others propose an 'active management of risk' approach which tailors timing of delivery to patients' cesarean risk profile.[35] Trials should be adequately powered to detect clinically important differences in maternal outcomes including cesarean delivery and as well as perinatal outcomes. Such a study is important given the increasing inductions in the United States and the ongoing temporal

decrease in the proportion of women who deliver at 40 weeks or later from 48% in 1990 to 33% in 2007.[36]

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References

1. Tita AT, Landon MB, Spong CY, et al. Timing of Elective Repeat Cesarean at Term and Neonatal Outcomes. N Eng J Med. 2009; 360(2):111–120.
2. American College of Obstetricians and Gynecologists. Cesarean delivery on maternal request. ACOG Committee Opinion No. 394. Obstet Gynecol. 2007; 110:1501–1504. [PubMed: 18055756]

3. ACOG Committee on Practice Bulletins-Obstetrics. Management of Postterm Pregnancy. ACOG Practice Bulletin. Clinical management guidelines for obstetricians-gynecologists #55. Obstet Gynecol. 2004; 104(3):639–646. [PubMed: 15339790]
4. Cleary-Goldman J, Bettes B, Robinson JN, Norwitz E, D'Alton ME, Schulkin J. Postterm pregnancy: practice patterns of contemporary obstetricians and gynecologists. Am J Perinatol. 2006; 23(1):15–20. [PubMed: 16450267]
5. Martin, JA.; Hamilton, BE.; Sutton, PD.; Ventura, SJ.; Mathews, TJ.; Kirmeyer, S.; Osterman, MJK. Births: Final data for 2007. National vital statistics reports; vol 58 no XX. Hyattsville, MD: National Center for Health Statistics; 2010.
6. Smith GC. Life-table analysis of the risk of perinatal death at term and post-term in singleton pregnancies. Am J Obstet Gynecol. 2001; 184(3):489–496. [PubMed: 11228508]
7. Caughey AB, Stotland NE, Escobar GJ. What is the best measure of maternal complications of termpregnancy: ongoing pregnancies or pregnancies delivered? Am J Obstet Gynecol. 2003; 189(4): 1047–1052. [PubMed: 14586353]
8. Gülmezoglu AM, Crowther CA, Middleton P. Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database Syst Rev. 2006; 4:CD004945. [PubMed: 17054226]
9. Caughey AB, Musci TJ. Complications of term pregnancies beyond 37 weeks of gestation. Obstet Gynecol. 2004; 103(1):57–62. [PubMed: 14704245]
10. Caughey AB, Washington AE, Laros RK Jr. Neonatal complications of term pregnancy: rates by gestational age increase in a continuous, not threshold, fashion. Am J Obstet Gynecol. 2005; 192(1):185–190. [PubMed: 15672023]
11. Heimstad R, Romundstad PR, Eik-Nes SH, Salvesen KA. Outcomes of pregnancy beyond 37 weeks of gestation. Obstet Gynecol. 2006; 108(3 Pt 1):500–508. [PubMed: 16946207]
12. Zhang X, Kramer MS. Variations in mortality and morbidity by gestational age among infants born at term. J Pediatr. 2009; 154(3):358–362. [PubMed: 18950794]
13. Bloom SL, Spong CY, Thom E, et al. Fetal pulse oximetry and cesarean delivery. N Engl J Med. 2006; 355(21):2195–2202. [PubMed: 17124017]
14. Tita AT, Lai Y, Landon MB, Spong CY, et al. MFMU Cesarean Registry: Timing of Elective Repeat Cesarean at Term and *Maternal* Outcomes. Obstet Gynecol. 2011; 117(2 Pt 1):280–286. [PubMed: 21252740]
15. Park HS, Romero R, Lee SM, Park CW, Jun JK, Yoon BH. Histologic chorioamnionitis is more common after spontaneous labor than after induced labor at term. Placenta. 2010; 31(9):792–795. [PubMed: 20655108]
16. Cheng YW, Nicholson JM, Nakagawa S, Bruckner TA, Washington AE, Caughey AB. Perinatal outcomes in low-risk term pregnancies: do they differ by week of gestation? Am J Obstet Gynecol. 2008; 199:370.e1–370.e7. [PubMed: 18928977]
17. Bailit JL, Gregory KD, Reddy UM, et al. Maternal and neonatal outcomes by labor onset type and gestational age. Am J Obstet Gynecol. 2010; 202:245.e1–245.e12. [PubMed: 20207242]
18. Morrison JJ, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. Br J Obstet Gynaecol. 1995; 102:101–106. [PubMed: 7756199]
19. Zanardo V, Simbi AK, Franzoi M, Solda G, Salvadori A, Trevisanuto D. Neonatal respiratory morbidity risk and mode of delivery at term: influence of timing of elective caesarean delivery. Acta Paediatr. 2004; 93:643–647. [PubMed: 15174788]
20. Clark SL, Miller DD, Belfort MA, Dildy GA, Frye DK, Meyers JA. Neonatal and maternal outcomes associated with elective term delivery. Am J Obstet Gynecol. 2009; 200(2):156.e1–156.e4. [PubMed: 19110225]
21. Wilmink FA, Hukkelhoven CWPM, Lunshof S, et al. Neonatal outcome following elective cesarean section beyond 37 weeks of gestation: a 7-year retrospective analysis of a national registry. Am J Obstet Gynecol. 2010; 202:250.e1–250.e8. [PubMed: 20207243]
22. Bowers SK, MacDonald HM, Shapiro ED. Prevention of iatrogenic neonatal respiratory distress syndrome: elective repeat cesarean section and spontaneous labor. Am J Obstet Gynecol. 1982; 143:186–189. [PubMed: 7081331]

23. Caughey AB, Sundaram V, Kaimal AJ, Gienger A, et al. Systematic review: elective induction of labor versus expectant management of pregnancy. Ann Intern Med. 2009; 151(4):252–263. W53–W63. [PubMed: 19687492]
24. Caughey AB, Sundaram V, Kaimal AJ, et al. Maternal and neonatal outcomes of elective induction of labor. Evid Rep Technol Assess (Full Rep). 2009; (176):1–257. [PubMed: 19408970]
25. Caughey AB, Nicholson JM, Cheng YW, Lyell DJ, Washington AE. Induction of labor and cesarean delivery by gestational age. Am J Obstet Gynecol. 2006; 195(3):700–705. [PubMed: 16949399]
26. Osmundson SS, Ou-Yang RJ, Grobman WA. Elective induction compared with expectant management in nulliparous women with a favorable cervix. Obstet Gynecol. 2010; 116(3):601–605. [PubMed: 20733441]
27. Osmundson S, Ou-Yang RJ, Grobman WA. Elective induction compared with expectant management in nulliparous women with an unfavorable cervix. Obstet Gynecol. 2011; 117(3): 583–587. [PubMed: 21343761]
28. Glantz JC. Term labor induction compared with expectant management. Obstet Gynecol. 2010; 115(1):70–76. [PubMed: 20027037]
29. Vrouenraets FP, Roumen FJ, Dehing CJ, van den Akker ES, Aarts MJ, Scheve EJ. Bishop score and risk of cesarean delivery after induction of labor in nulliparous women. Obstet Gynecol. 2005; 105(4):690–697. [PubMed: 15802392]
30. Vardo JH, Thornburg LL, Glantz JC. Maternal and neonatal morbidity among nulliparous women undergoing elective induction of labor. J Reprod Med. 2011; 56(1–2):25–30. [PubMed: 21366123]
31. Dunne C, Da Silva O, Schmidt G, Natale R. Outcomes of elective labour induction and elective caesarean section in low-risk pregnancies between 37 and 41 weeks' gestation. J Obstet Gynaecol Can. 2009; 31(12):1124–1130. [PubMed: 20085677]
32. Moster D, Wilcox AJ, Vollset SE, Markestad T, Lie RT. Cerebral palsy among term and postterm births. JAMA. 2010; 304(9):976–982. [PubMed: 20810375]
33. Reddy UM, Bettegowda VR, Dias T, Yamada-Kushnir T, Ko CW, Willinger M. Term pregnancy: a period of heterogeneous risk for infant mortality. Obstet Gynecol. 2011; 117(6):1279–1287. [PubMed: 21606738]
34. Ananth CV, Liu S, Joseph KS, Kramer MS. Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. A comparison of foetal and infant mortality in the United States and Canada. Int J Epidemiol. 2009; 38(2):480–489. [PubMed: 18806278]
35. Nicholson JM, Parry S, Caughey AB, Rosen S, Keen A, Macones GA. The impact of the active management of risk in pregnancy at term on birth outcomes: a randomized clinical trial. Am J Obstet Gynecol. 2008; 198(5):511.e1–511.e15. [PubMed: 18455526]
36. Kirby RS. Trends in labor induction in the United States: is it true that what goes up must come down? Birth. 2004; 31(2):148–151. [PubMed: 15153136]

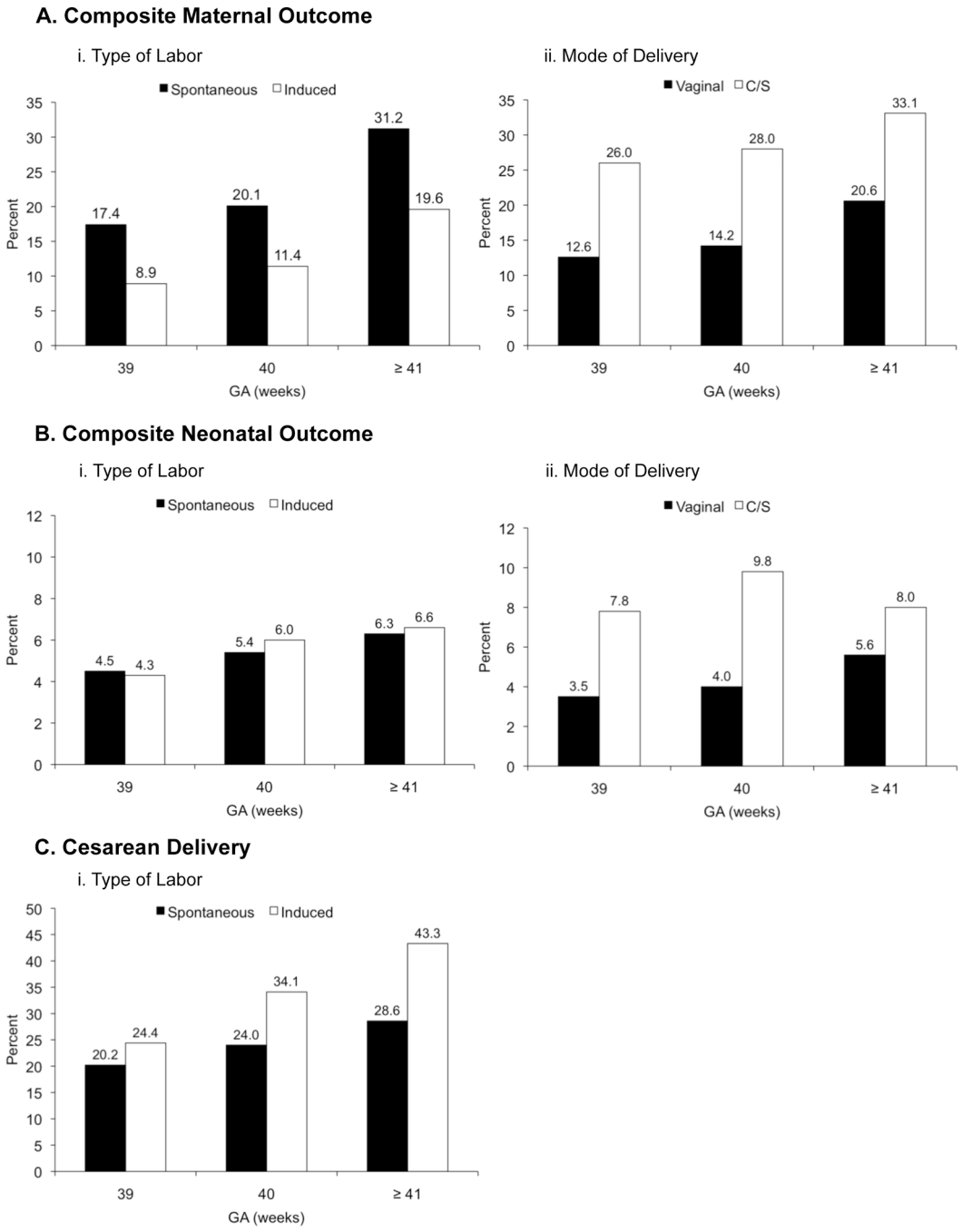

Figure 1.

Risks of adverse maternal and neonatal outcomes and cesarean delivery by completed gestational age from 39 weeks stratified by type of labor and mode of delivery

Table 1

Maternal and infant characteristics of Study Group by Timing of Delivery in Completed Weeks *

Characteristics	36–38 weeks (n=793)	39 weeks (n=1090)	40 weeks (n=1304)	≥41 weeks (n=899)	P-value ***
Maternal age – yr	23.1±5.4	23.4±5.4	23.8±5.7	23.9±5.7	0.013
<18	82 (10.3)	110 (10.1)	125 (9.6)	88 (9.8)	0.533
18–34	676 (85.3)	941 (86.3)	1111 (85.2)	763 (84.9)	
≥35	35 (4.4)	39 (3.6)	68 (5.2)	48 (5.3)	
Pre-pregnancy BMI	24.5±5.2	24.7±5.5	25.1±5.8	25.9±6.3	<0.001
Underweight (BMI<18.5)	58 (7.5)	65 (6.2)	73 (5.7)	36 (4.2)	<0.001
Normal (BMI 18.5–24.9)	423 (54.9)	605 (57.3)	686 (54.0)	448 (51.6)	
Overweight (BMI 25–29.9)	179 (23.3)	237 (22.4)	309 (24.3)	200 (23.0)	
Obese (BMI≥30)	110 (14.3)	149 (14.1)	203 (16.0)	184 (21.2)	
Race or Ethnicity					0.017
Hispanic	198 (25.0)	265 (24.3)	326 (25.0)	243 (27.0)	
Non-Hispanic White	321 (40.5)	496 (45.5)	609 (46.7)	402 (44.7)	
African American	260 (32.8)	298 (27.3)	348 (26.7)	232 (25.8)	
Other	14 (1.8)	31 (2.8)	21 (1.6)	22 (2.5)	
Unmarried	429 (54.1)	524 (48.1)	634 (48.6)	447 (49.7)	0.048
Payor					0.021
Private	297 (37.5)	475 (43.6)	548 (42.0)	347 (38.6)	
Government/Other	496 (62.5)	615 (56.4)	756 (58.0)	552 (61.4)	
Smoker **	77 (9.7)	116 (10.6)	137 (10.5)	114 (12.7)	0.223
Prenatal care (1st trimester)	556 (70.6)	791 (73.0)	960 (74.0)	603 (67.7)	0.008
Type of Labor					<0.001
Induced	121 (15.3)	258 (23.7)	334 (25.6)	469 (52.2)	
Spontaneous †	672 (84.7)	832 (76.3)	970 (74.4)	430 (47.8)	
Oxytocin use (at randomization) †	473 (59.6)	683 (62.7)	864 (66.3)	657 (73.1)	<0.001
Study arm (Open)	396 (49.9)	546 (50.1)	656 (50.3)	475 (52.8)	0.559
Infant gender (female)	336 (42.4)	521 (47.8)	625 (47.9)	436 (48.5)	0.039
Birth weight – gm	3128±413	3341±400	3482±407	3629±417	<0.001

* Data are presented as N (%) or mean±SD;

** Self-reported smoking during pregnancy;

*** Kruskal-Wallis test or chi-square test

† Includes those in spontaneous labor who were given oxytocin for augmentation

Table 2

Incidence (%) of Adverse Pregnancy Outcomes by Timing of Delivery (N=4086) *

Pregnancy outcomes (%)	36–38 wks (n=793)	39 wks (n=1090)	40 wks (n=1304)	≥41 wks (n=899)	p-value**
Maternal					
Composite	14.6 (116)	15.4 (168)	17.9 (233)	25.1 (226)	<0.001
Chorioamnionitis	8.8 (70)	9.2 (100)	10.8 (141)	14.9 (134)	<0.001
Endometritis	4.2 (33)	3.9 (42)	4.5 (59)	5.1 (46)	0.174
Wound infection	0 (0)	0.3 (3)	0 (0)	0.1 (1)	0.347
Uterine atony	1.9 (15)	2.8 (30)	3.8 (49)	7.3 (66)	<0.001
Postpartum blood transfusion	0.9 (7)	1.1 (12)	0.8 (10)	1.6 (14)	0.390
Cesarean delivery	16.4 (130)	21.2 (231)	26.6 (347)	36.3 (326)	<0.001
Neonatal					
Composite adverse outcome	5.3 (42)	4.4 (48)	5.5 (72)	6.5 (58)	0.047
Alternative composite adverse outcome†	3.7 (29)	3.5 (38)	3.8 (49)	5.0 (45)	0.097
Respiratory illness‡	1.9 (15)	2.1 (23)	1.9 (25)	2.6 (23)	0.537
Intubation for CPR	0.3 (2)	0.5 (5)	0.4 (5)	1.0 (9)	0.140
Sepsis	0 (0)	0.2 (2)	0.5 (7)	0.4 (4)	0.374
Seizures	0 (0)	0.2 (2)	0.2 (2)	0.2 (2)	>0.99
Treated hypoglycemia	0.9 (7)	0.4 (4)	0.6 (8)	0.3 (3)	>0.99
Cord pH<7.0	0.3 (2/684)	0.4 (4/939)	0.8 (9/1115)	0.5 (4/780)	0.876
5-minute Apgar ≤3	0 (0)	0.1 (1)	0.1 (1)	0.2 (2)	0.532
NICU admission	4.5 (36)	3.6 (39)	4.3 (56)	5.0 (45)	0.119

* Data are presented as % (N) – a different denominator is provided for cord pH since it was not available on for all newborns

** P-value for Exact Cochran-Armitage trend test based on 39, 40 and 41+ weeks;

† Neonatal composite excluding NICU admissions <48 hours

‡ Respiratory illness = Respiratory distress syndrome or Transient tachypnea of the newborn

Table 3

Relationship between delivery gestational age and adverse outcomes (Adjusted OR and 95% CI)

	36–38 Wks		39 Wks	40 Wks		≥41 wks	
Adverse outcomes*	**OR**	**95% CI**		**OR**	**95% CI**	**OR**	**95% CI**
Maternal composite	0.88	*(0.67, 1.16)*	Ref	1.29	*(1.03, 1.64)*	2.05	*(1.60, 2.64)*
Uterine atony	0.69	*(0.35, 1.35)*	Ref	1.55	*(0.94, 2.54)*	3.10	*(1.90, 5.06)*
Chorioamnionitis	0.94	*(0.67, 1.33)*	Ref	1.30	*(0.97, 1.73)*	2.03	*(1.49, 2.76)*
Endometritis	0.94	*(0.57, 1.54)*	Ref	1.24	*(0.81, 1.89)*	1.27	*(0.79, 2.03)*
Cesarean delivery	0.72	*(0.56, 0.93)*	Ref	1.28	*(1.05, 1.57)*	1.75	*(1.41, 2.16)*
Neonatal composite	1.20	*(0.78, 1.86)*	Ref	1.25	*(0.86, 1.83)*	1.37	*(0.90, 2.09)*
Alternative neonatal composite	1.12	*(0.68, 1.85)*	Ref	1.06	*(0.68, 1.64)*	1.27	*(0.79, 2.05)*
Respiratory illness†	0.91	*(0.47, 1.76)*	Ref	0.87	*(0.49, 1.56)*	1.03	*(0.55, 1.94)*
NICU† Admission	1.27	*(0.79, 2.05)*	Ref	1.21	*(0.79, 1.84)*	1.40	*(0.87, 2.23)*

*All outcomes are adjusted for maternal age (continuous variable), race or ethnicity, BMI category, marital status, payor, smoking, prenatal care in first trimester, labor type and study arm; neonatal outcomes are adjusted additionally for mode of delivery and infant gender

†Respiratory illness = Respiratory distress syndrome or transient tachypnea of newborn; NICU=Neonatal intensive care unit