THE IMPACT AND COST-EFFECTIVENESS OF ELECTIVE INDUCTION OF LABOR IN OBESE WOMEN

By

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A THESIS

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ABSTRACT

Introduction: Maternal obesity is common in pregnancy and increases the risk of several adverse perinatal outcomes. Many such outcomes are also related to gestational age at delivery, making the timing of delivery in obese women of particular concern. The objective of this study is to investigate the relationship between term elective induction of labor (eIOL) and perinatal outcomes in obese women and determine the optimal timing and cost-effectiveness of eIOL in the setting of maternal obesity.

Methods: We performed a retrospective cohort study comparing eIOL versus expectant management in deliveries among obese women in California in 2007. Comparisons were made for 37, 38, 39, and 40 weeks of gestation. Our primary outcome was cesarean delivery, and several additional maternal and neonatal morbidities were examined. We also built a cost-effectiveness model comparing outcomes and costs following eIOL at 37-41 weeks in a theoretic cohort of 800,000 obese women.

Results: The odds of cesarean delivery were lower among nulliparous women with eIOL at 37 weeks and 39 weeks compared to expectant management. Among multiparous women with a prior vaginal delivery, eIOL at 37, 38, and 39 weeks was associated with lower odds of cesarean. Additionally, eIOL at 38, 39, and 40 weeks was associated with lower odds of macrosomia, and there were no differences in the odds of operative vaginal delivery, lacerations, brachial plexus injury, or respiratory distress syndrome. Decision analysis revealed that eIOL at 38 weeks would maximize total quality-adjusted life years. Delivery at 38 weeks was an incrementally cost-effective strategy compared to expectant management until a later gestational age in the majority of scenarios.

Conclusion: In obese women, eIOL is not associated with an increased risk of cesarean delivery or adverse perinatal outcomes when compared with expectant management. Balancing the gestational age-related risks of stillbirth and neonatal morbidities, the optimal timing of delivery is at 38 weeks in obese women, and eIOL at 38 weeks is a cost-effective strategy.

INTRODUCTION

The Obesity Problem

Obesity is defined as a body mass index (BMI) of 30 kg/m^2 or greater, and can be further sub-classified into Class I (BMI 30-34.9), Class II (BMI 35-39.9), and Class III (BMI ≥40) obesity (Mission et al 2013). Recently, Class III has been further subdivided into super obesity (BMI >50). The prevalence of obesity has increased dramatically in the United States over the past several decades: currently two thirds of Americans are overweight or obese, and the public health implications of this epidemic are far-reaching, significant, and costly (Caughey 2015). Obesity has undeniably impacted the pregnant population as well. Trends in pre-pregnancy obesity have followed those seen in the general population: data from the Pregnancy Risk Assessment Monitoring System (PRAMS) survey have shown that the prevalence of obesity in pregnancy has increased from 17.6% in 2003 to 20.5% in 2009 (Fisher et al 2013).

Obesity in Pregnancy

Obese women are at increased risk of a wide range of complications throughout pregnancy. There is a robust body of literature demonstrating the relationship between maternal obesity and the development of gestational diabetes mellitus and hypertensive disorders during the antepartum period. A prospective multicenter cohort study of 16,000 patients found that compared to patients with a BMI less than 30, obesity (BMI 30-34.9) and morbid obesity (BMI ≥35 in this study) were significantly associated with gestational hypertension (odds ratios [ORs] 2.5 and 3.2, respectively), preeclampsia (ORs 1.6 and 3.3), and gestational diabetes (ORs 2.6 and 4.0) (Weiss et al 2004). Several systematic reviews and meta-analyses have corroborated these findings and reported similar measures of association (O'Brien et al 2003, Chu et al 2007, Torloni et al 2009).

Maternal obesity is also associated with a number of complications during labor and delivery. Obese and morbidly obese women have 0.57 and 0.43 lower odds of spontaneous labor at term compared to normal-weight women (Denison et al 2008). Several studies have also demonstrated that obesity is associated with longer duration of induced labor, longer first stage of labor, higher oxytocin requirements, and higher rates of failed induction (Mission et al 2013, Heslehurst et al 2008).

In a 2008 meta-analysis of 16 studies, Heslehurst and colleagues found that compared to normal-weight women with a BMI 18-25, obese women had twofold higher odds of cesarean delivery (OR 2.00, 95% CI 1.87—2.15) (Heslehurst et al 2008). Several studies have also reported a dose-response effect of increasing cesarean delivery rates with increasing BMI (Dietz et al 2005, Lynch et al 2008, Mantakas & Farrell 2008). Such an effect has been corroborated in two meta-analyses: a 2007 meta-analysis of 33 studies found the odds of cesarean delivery were 1.46 (95% CI 1.34-1.60), 2.05 (95% CI 1.86-2.27), and 2.89 (95% CI 2.28-3.79) higher for overweight, obese, and severely obese women, respectively (Chu et al 2007). A 2009 meta-analysis looking exclusively at nulliparous women found a similar trend of increasing odds ratios (Poobalan et al 2009). Additionally, longer operative times, higher rates of postoperative wound infections, and lower vaginal birth after cesarean rates have been described in obese women (Mission et al 2013). This increased risk of cesarean delivery among obese women carries great clinical and public health significance. As most women with a prior cesarean will undergo repeat cesarean delivery in subsequent pregnancies, the higher rates of cesarean delivery in the obese population portends a large burden of maternal morbidity and health care costs.

Following delivery, obese women are at increased risk of postpartum hemorrhage. In the largest study exploring this relationship to date, Blomberg examined postpartum hemorrhage in a population-based cohort of 1.1 million women in Sweden and found that the risk of atonic postpartum hemorrhage increased with increasing BMI (Blomberg 2011). Heslehurst and colleagues reviewed seven studies and found that obese women have approximately 25% higher odds of postpartum hemorrhage compared to normal-weight women (Heslehurst et al 2008). This same meta-analysis did not find a significant relationship between maternal obesity and severe perineal lacerations (Heslehurst et al 2008).

Several studies have demonstrated an association between maternal obesity and stillbirth. Chu and colleagues conducted a meta-analysis of nine studies and found that the odds of stillbirth were 2.07 (95% CI 1.59-2.74) times higher for obese women compared to normal-weight women (Chu et al 2007). Additionally, several cohort studies have reported even higher odds of stillbirth among morbidly obese women (Cedergren 2004, Mantakas & Farrell 2010). Of note, the association between maternal obesity and stillbirth has been demonstrated in women with and without diabetes, as well as in fetuses without congenital anomalies, suggesting that obesity in and of itself is truly a risk factor for stillbirth (Roman et al 2011, Tennant et al 2011).

The association between maternal obesity and perinatal mortality has been observed beyond the antepartum period. Kristensen and colleagues evaluated the association between obesity and perinatal mortality in a population-based cohort of

24,505 pregnancies in Denmark and found that after controlling for key confounders, maternal obesity more than doubled the risk of neonatal death (OR 2.6, 95% CI 1.2-5.8) (Kristensen et al 2005). A 2009 population-based case-control study found that obese women had 1.46 (95% CI 1.23-1.73) greater odds of infant death compared to normal-weight women, and when gestational weight gain was taken into consideration, a J-shaped curve was seen in obese women with the highest weight gain associated with the highest risk of infant death (Chen et al 2009).

The offspring of obese women are at increased risk of several neonatal morbidities. Obesity is a well-established risk factor for macrosomia, even after adjusting for gestational diabetes (Ehrenberg et al 2004). Several studies have reported a two- to threefold increased risk of macrosomia in obese women; a 2008 meta-analysis of 15 studies found an odds ratio of 2.36 (95% CI 2.29-2.42) compared to normal-weight women (Heslehurst 2008). Additionally, some retrospective cohort studies have found that obese women have an increased incidence of shoulder dystocia (Mazouni et al 2006, Usha Kiran et al 2005). However, the literature surrounding maternal obesity and shoulder dystocia is still conflicting: three large studies and a meta-analysis have not demonstrated a significantly increased risk of this complication among obese women, but some of these studies corrected for birth weight, which may not be appropriate as macrosomia is on the causal pathway between obesity and shoulder dystocia (Heslehurst 2008, Mission et al 2013). Finally, although neonatal brachial plexus injury, commonly referred to as Erb’s palsy, is a largely unpredictable complication without reliable risk factors, it does occur more frequently in the settings of both shoulder dystocia and macrosomia and thus clinicians may have heightened concern for Erb's palsy in obese women (Chauhan et al 2014, Ouzounian 2014).

Timing of Delivery in Obese Women

Maternal obesity is a significant risk factor for several antepartum, intrapartum, and postpartum complications. Many of these complications are also related to gestational age. For example, Cheng et al conducted a retrospective cohort study of low-risk term pregnancies and found that delivery at 40 or 41 weeks was associated with greater risks of birth weight >4500g, neonatal injury, and meconium aspiration syndrome, whereas earlier delivery at 37 weeks conferred higher rates of pulmonary morbidity and need for mechanical ventilation; several subsequent studies have corroborated such increased morbidities in early term infants (Cheng et al 2008, Tita et al 2009, Sengupta et al 2013). Rosenstein and colleagues examined all singleton, non-anomalous deliveries in California between 1997 and 2006 and found that the risk of term stillbirth increases from 2.1 to 10.8 per 10,000 ongoing pregnancies between 37 and 42 weeks' gestation (Rosenstein et al 2012). This study also examined infant death risk by gestational age and found a U-shaped curve, with a nadir of infant deaths at 39 weeks (Rosenstein et al 2012). In particular, women with an increased BMI are at increased risk of experiencing a late term or post-term pregnancy (Mission et al 2013). There is evidence of a BMI-based dose-response effect on prolonging pregnancy (Stotland et al 2007, Halloran et al 2012).

Therefore, determining the timing of delivery in the obese population of particular concern: an obstetric provider must balance the *in utero* risks of stillbirth, progression to significant maternal morbidity such as preeclampsia, and neonatal complications associated with large for gestational age infants against the respiratory morbidities and other neonatal risks associated with early term delivery at 37-38 weeks. Some studies that have just considered the impact of stillbirth and infant mortality have demonstrated that mortality alone is minimized by delivery by 39 weeks' gestation (Rosenstein et al 2012). However, these studies do not take into account all of the neonatal morbidity, nor the potential clinical impact of induction of labor as a way to effect delivery at 39 weeks' gestation.

Induction of Labor

Induction of labor (IOL) is a common obstetric intervention performed when the benefits of an expedient vaginal delivery outweigh the risks of continuing pregnancy. Induction of labor occurred in 23.1% of all live births in the United States in 2008 (Cheng et al 2012). Induction of labor in the absence of a medical indication is deemed *elective induction of labor* (eIOL) and may occur in the context of relieving physical discomfort, concern over the patient's expedient access to care should spontaneous labor progress rapidly, ending the risk for ongoing maternal or neonatal complications, or other nonmedical reasons. Zhang and colleagues have demonstrated that the rate of clinically indicated IOL is increasing more slowly than the rate of IOL as a whole, suggesting that the rate of non-medically indicated IOL is rising particularly rapidly in the United States (Zhang et al 2002).

Induction of Labor and Cesarean Delivery

The evidence surrounding IOL and mode of delivery remains inconclusive. For obstetric providers staffing a labor and delivery unit, it is common to compare induction of labor to spontaneously laboring women, as those are the two types of labor onset. Perhaps this is the reason why the majority of studies to date have compared IOL with spontaneous labor and found an increase in the risk of cesarean delivery after IOL (Glantz 2005, Vahratian et al 2005). However, clinically, the actual options for management are induction of labor and expectant management with delivery at a later date. Expectant management includes spontaneous labor at a later gestational age as well as the development of potential complications that may require induction of labor. Randomized trials necessarily compare IOL to expectant management, the only other alternative. The majority of these trials were conducted at 41 weeks' gestation and beyond and have found a reduction in the risk of cesarean delivery with induction of labor (Caughey et al 2009). Given the lack of consensus around the impact of term IOL, there have been calls for a randomized controlled trial (Caughey 2013).

Given that the appropriate comparison to IOL is expectant management, which is what has been used in prospective randomized trials, there is a need to use a similar comparison in retrospective studies. This can be accomplished by comparing women who are induced at one gestational age and comparing them to all women who progress beyond that gestational age. In contrast with studies using the spontaneous labor comparison group, the first study describing and utilizing this technique found that IOL was associated with lower odds of cesarean compared to expectant management (Caughey et al 2006).

Since that time, several studies have analyzed maternal and neonatal outcomes of elective IOL compared with expectant management of term pregnancy. Stock and colleagues demonstrated that for gestations between 37-41 weeks, eIOL is associated with increased odds of NICU admission but decreased odds of overall perinatal mortality compared to expectant management of pregnancy (Stock et al 2012). The same study found no difference in the odds of vaginal delivery and actually observed decreased odds of maternal complications in some groups, suggesting that elective induction of labor at term can reduce perinatal mortality without increasing the risk of operative delivery or adverse maternal outcomes (Stock et al 2012).

More recently, Darney and colleagues conducted a retrospective cohort study of deliveries using a California perinatal database to compare elective IOL at each term gestational age with expectant management. In this study, the odds of Cesarean delivery were lower among women with elective induction compared with expectant management across all GAs; there were no significant differences in the odds of severe lacerations, operative deliveries, NICU admissions, or perinatal death (Darney et al 2013).

Elective Induction of Labor Versus Expectant Management in Obese Women

Evidence-based protocols for managing induction of labor in pregnancies complicated by maternal obesity remain absent. Only one study to date has examined eIOL specifically in obese women. Wolfe and colleagues analyzed women with a BMI ≥30 from a single institution and found that eIOL between 39-41 weeks conferred significantly higher rates of Cesarean delivery and neonatal intensive care unit admission compared to expectant management (Wolfe et al 2014). Rates of maternal morbidities were similar between groups. However, their study had a relatively small sample size, only examined nulliparous women with an unfavorable cervical exam performed between 38 and 39 weeks, and they did not stratify by obesity class nor perform any multivariable analyses to control for potential confounding factors. Thus, additional studies and more rigorous analyses are needed before providers and obese patients can make informed choices about eIOL.

Cost-Effectiveness Considerations

Health policy in the United States has focused on achieving the Triple Aim of increasing access to care, improving quality, and reducing health care costs (Berwick et al 2008). Given that nearly half of all births in the United States are paid for with public dollars, and given that obesity is estimated to cost the health care system over $90 billion annually and is a common condition in pregnancy, obesity and delivery together represent a significant portion of public health care resources (Sonfield & Kost 2013, Tsai et al 2011). Therefore, it behooves providers and policymakers to understand the costs and benefits, both in terms of clinical outcomes and health care spending, associated with delivery in obese women.

Decision analyses and cost-effectiveness analyses can aid evidence-based decision-making in that they integrate epidemiologic uncertainty, gaps in evidence, and tradeoffs between competing strategies (Rodriguez & Caughey 2013). These methods are particularly useful in obstetrics, where many clinical questions cannot be ethically studied using a randomized controlled trial, or the outcomes of interest are too rare (e.g., perinatal mortality) to achieve adequate power in a population-based study. Additionally, they are important when an intervention might improve outcomes, but is more expensive than the alternative management. For example, a previous cost-effectiveness study comparing IOL versus expectant management at 41 weeks' gestation found that the benefits of IOL outweighed the risks and further, that induction of labor cost more than expectant management, but that it was cost-effective (Kaimal et al 2011).

As previously discussed, gestational age-related tradeoffs in a variety of perinatal outcomes must be weighed when considering the timing of delivery in obese women. A decision analysis can synthesize multiple tradeoffs to determine an optimal gestational age for delivery, and building costs into such a model will assess whether scheduled eIOL at that gestational age would be cost-effective compared to the current practice of expectant management in such pregnancies. Cost-effectiveness analyses can estimate whether elective IOL at a particular week of gestation is a dominant strategy, that is, a strategy leading to lower costs and better outcomes on average. If eIOL at a particular gestational age is dominant, this practice should be adopted; however, for strategies that cost more but result in better outcomes, cost-effectiveness analyses can closely evaluate the differences between strategies and inform clinicians and policymakers in the efficient allocation of resources.

RESEARCH QUESTIONS

Given this background, this study sought to answer the following questions: In pregnancies complicated by maternal obesity, is term eIOL associated with cesarean delivery and other adverse perinatal outcomes compared with expectant management? Additionally, from a societal standpoint, is there an optimal and cost-effective gestational age at which to perform eIOL in obese women? To that end, our study has three specific aims:

1. Determine the impact of term eIOL, compared to expectant management, on mode of delivery and maternal and neonatal outcomes in a large population of obese women.

Hypothesis: In nulliparous obese women, there will be no significant differences between eIOL and expectant management groups in the proportions of women undergoing cesarean delivery at any term gestational age. In multiparous women with a prior vaginal delivery, eIOL will be associated with lower odds of primary cesarean delivery compared to expectant management across all term gestational ages. Regarding our secondary outcomes, we anticipate that eIOL will not be associated with increased odds of perinatal morbidities and mortality compared to expectant management, regardless of parity or obesity class.

2. Identify the optimal gestational age of delivery to perform eIOL in obese women that would maximize maternal and neonatal quality-adjusted life years (QALYs).

Hypothesis: The lowest rates of infant death and cerebral palsy will be associated with delivery at 39 weeks, whereas rates of stillbirth and Erb's palsy will be lowest at 37 weeks. The cesarean section rate will increase with increasing gestational age. Balancing these outcomes, we anticipate that delivery at 38 weeks will maximize total QALYs, and that the risks of stillbirth and infant death will be key drivers of the model.

3. Determine whether planned term eIOL in obese women is a cost-effective intervention compared to expectant management until 41 weeks' gestation.

Hypothesis: Induction of labor at 38 weeks' gestation, the optimal timing of delivery in our decision analysis, will be a dominant strategy—that is, it will lead to better outcomes and lower costs—compared to expectant management and IOL at 41 weeks. The hospital costs of IOL, the cesarean delivery rate, and the cost of cesarean delivery will be key drivers of our CEA.

RETROSPECTIVE COHORT STUDY

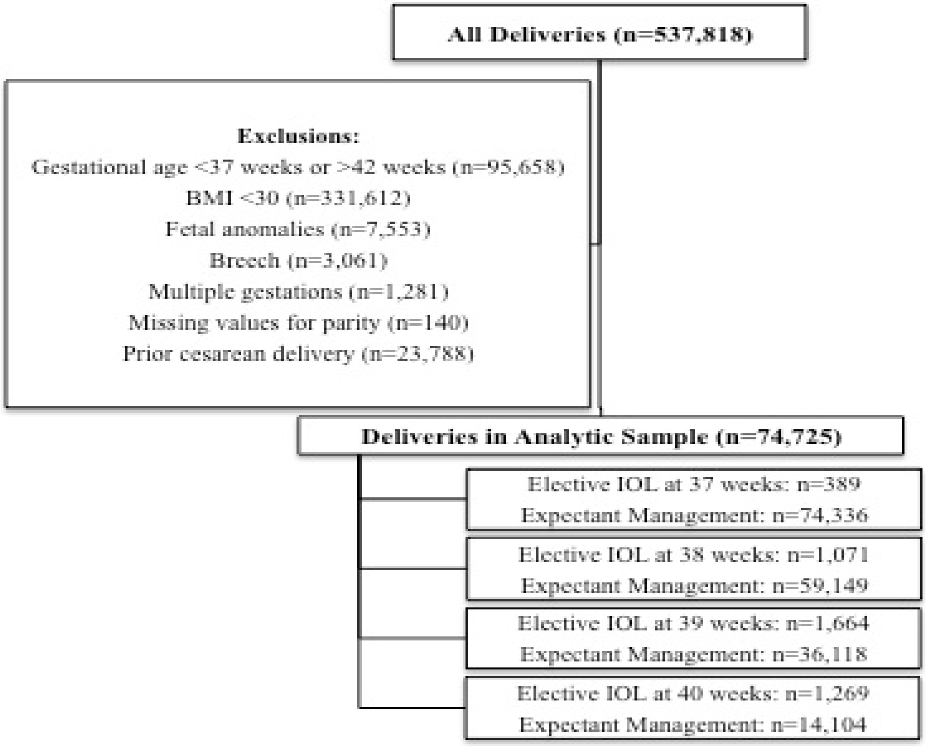
Methods

This is a retrospective cohort study using 2007 California Department of Health Services vital statistics and hospital discharge data. The database contains de-identified linked birth records and patient discharge data for maternal and neonatal pairs and includes all deliveries in the given year. We obtained human subjects approval from the Institutional Review Board at Oregon Health & Science University, the California Office of Statewide Health Planning and Development, and the California Committee for the Protection of Human Subjects. Informed consent was exempted from this study, as the data did not contain any potential patient identification information.

We arrived at our analytic sample after a series of exclusions. Preterm (<37 weeks) and postterm (>42 weeks) pregnancies (n=95,658), multiparous women with a prior cesarean delivery (n=23,788), records with missing values for parity (n=140), multiple gestations (n=1,281), fetal anomalies (n=7,553), and breech presentation (n=3,061), were excluded from this analysis. Additionally, we restricted the sample to women with a self-reported pre-pregnancy BMI greater than or equal to 30.

In the elective induction group, we included women who delivered between 37 and 40 completed weeks of gestation. To define elective induction, we used the Joint Commission criteria of indications possibly justifying delivery before 39 weeks of gestation (Appendix A) (Joint Commission). Women who underwent an induction of labor as noted by ICD-9 codes, but who did not also have an ICD-9 code matching one of the Joint Commission indications, were therefore classified as being electively induced in our study. We compared electively induced women with those who were expectantly managed at a given gestational age. For example, at 37 weeks, the comparison is eIOL at 37 weeks versus expectant management and delivery between 38 and 42 weeks. Of note, the expectant management group includes women who will go on to spontaneous labor or an indicated induction of labor at a later gestational age. Furthermore, as we cannot assess temporality in these data, this classification scheme assumes that all medical indications were known before the decision to induce; as a result, deliveries with ICD-9 codes for conditions that could have arisen during the intrapartum period, such as abnormal fetal heart rate, were included in the expectant management group (Darney et al 2013). A list of such intrapartum indications is found in Appendix B. Our sample determination and comparison groups are further delineated in Figure 1.

Figure 1: Sample Determination and Comparison Groups for Comparing Term eIOL to Expectant Management in Obese Women



Outcomes

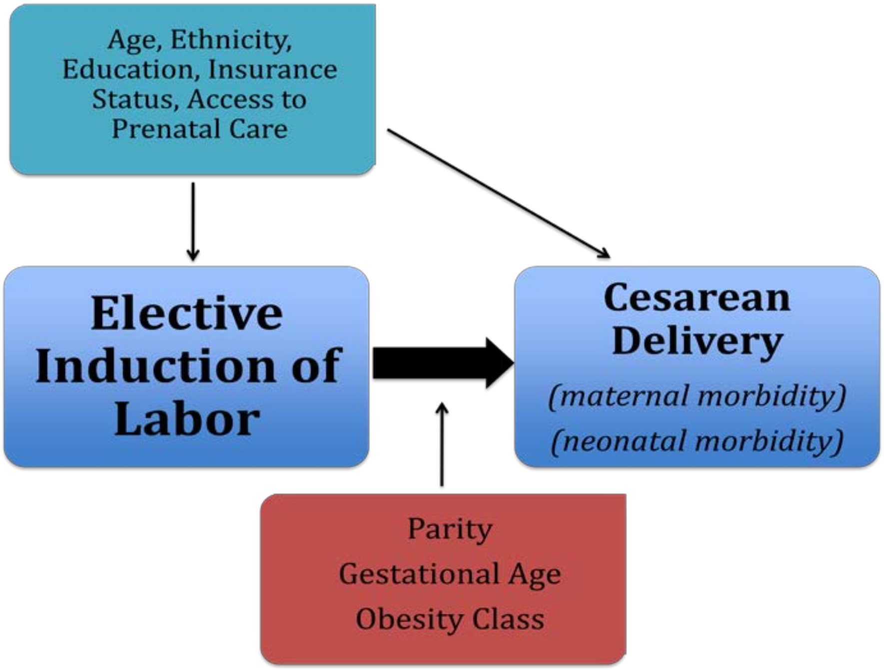
Our primary outcome of interest was cesarean delivery. Secondary outcomes included operative vaginal delivery, severe perineal lacerations, postpartum hemorrhage, chorioamnionitis, macrosomia, shoulder dystocia, brachial plexus injury, and respiratory distress syndrome. Outcome definitions are further presented in Table 1. Because the dataset only linked hospital discharge data with live birth certificates, we were unable to examine stillbirth or perinatal mortality in this study.

Table 1: Perinatal Outcomes of eIOL Versus Expectant Management in Retrospective Cohort Study

Outcome	Description	Location in Database
Cesarean delivery		Birth certificate
Operative vaginal delivery	Vaginal delivery assisted by vacuum or forceps	Birth certificate
Perineal laceration	3rd- or 4th-degree perineal laceration	ICD-9 codes 664.2, 664.20, 664.21, 664.24
Postpartum hemorrhage	Blood loss >500ml following vaginal delivery or >1000ml following cesarean delivery	ICD-9 codes 666.0, 666.1, 666.2, 666.3
Chorioamnionitis	Inflammation of the fetal membranes, diagnosed clinically in the setting of maternal fever and at least two of the following: maternal leukocytosis, maternal tachycardia, fetal tachycardia, uterine tenderness, or foul-smelling amniotic fluid	ICD-9 codes 658.4, 762.7
Macrosomia	Birth weight recorded as >4000g	Birth certificate
Shoulder dystocia	Obstetric emergency in which the fetal shoulders fail to deliver shortly after the fetal head	ICD-9 codes 660.4, 660.40, 660.41, 660.43
Brachial plexus injury	Loss or movement or weakness of the arm due to injury to the C5-T1 spinal nerves	ICD-9 code 767.6
Respiratory distress syndrome	Neonatal syndrome caused by insufficient surfactant production and/or structural immaturity of the lungs	ICD-9 codes 769, 770, 770.89, 770.84, 770.9

Covariates abstracted from hospital discharge or birth certificate files included maternal age at delivery (15-19; 20-24; 25-29; 30-34; 35-44; 45-49), insurance status (private; public or none), maternal education (did not finish high school; high school diploma; some college; college graduate or above), maternal ethnicity (Caucasian; African-American; Hispanic; Asian; Other), and initiation of prenatal care in the first trimester (yes or no). A directed acyclic graph of our exposure, outcomes, and covariates is found in Figure 2.

Figure 2: Directed Acyclic Graph Depicting the Relationship Between eIOL and Perinatal Outcomes



Analysis

We first compared the proportions of our primary and secondary outcomes between eIOL and expectant management groups using a two-sample test of proportions. Comparisons were made at 37, 38, 39, and 40 weeks. We stratified our results by parity (nulliparous; multiparous with a prior vaginal delivery), and we examined both obese women as a whole and by subgroups of WHO obesity class (Class I obesity, BMI 30-34.9; Class II obesity, BMI 35-39.9; Class III obesity, BMI ≥40).

We used multivariate logistic regression to estimate the association between eIOL and perinatal outcomes adjusted for the previously listed covariates. Separate models were built to test the association between eIOL and each outcome at 37, 38, 39, and 40 weeks. Again, results were stratified by parity, and we analyzed the association first for the entire obese cohort and then built additional multiple logistic regression models for each WHO obesity class. All analyses were conducted using STATA 13 (StataCorp, College Station, TX).

Results

The analytic sample included 74,725 obese women (40.8% nulliparas, 59.2% multiparas with a prior vaginal delivery). At nearly every term week of gestation, women who were electively induced were older and more likely to be Caucasian, multiparous, have some college education, have private insurance, and initiate prenatal care in the first trimester (Table 2).

Table 2: Demographic Characteristics of Analytic Sample

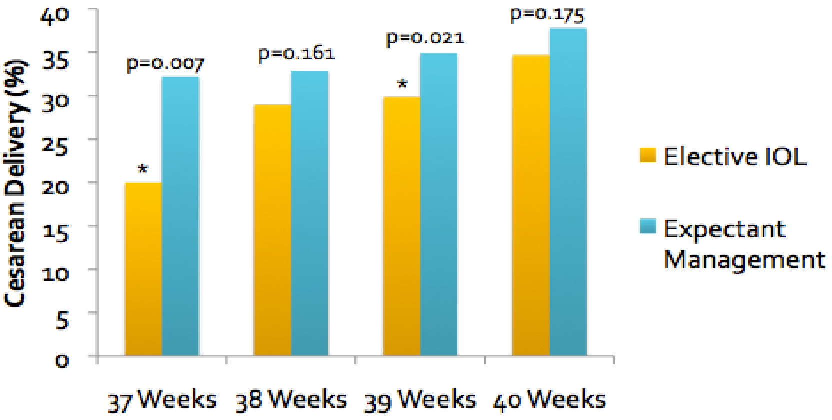
	37 weeks N=74,725		**38 weeks N=60,220**		**39 weeks N=37,782**		**40 weeks N=15,373**	
Characteristic	eIOL	Exp mgmt	eIOL	Exp mgmt	eIOL	Exp mgmt	eIOL	Exp mgmt
Parity								
Nulliparous	27.3%	40.9%	28.1%	41.8%	29.4%	44.3%	38.0%	46.7%
Multip w Prior VD	72.7%	59.1%	71.9%	58.2%	70.6%	55.6%	62.0%	53.3%
Obesity Class								
BMI 30-35	41.9%	35.8%	43.6%	36.1%	40.6%	36.7%	41.2%	36.9%
BMI 35-39	12.6%	12.8%	16.5%	12.9%	16.3%	13.4%	14.9%	14.2%
BMI 40+	45.5%	51.4%	39.9%	51.0%	43.1%	50.0%	43.9%	48.9%
Maternal age								
15-19	8.2%	10.1%	7.5%	10.2%	5.7%	10.6%	7.6%	10.8%
20-24	21.8%	27.3%	24.3%	27.7%	23.5%	28.6%	28.0%	29.3%
25-29	30.1%	29.3%	28.9%	29.4%	33.1%	29.5%	29.3%	29.8%
30-34	23.9%	21.1%	25.0%	20.8%	23.6%	20.2%	22.0%	19.9%
35-44	15.7%	12.1%	14.3%	11.8%	14.0%	10.9%	13.0%	10.1%
45-49	0.26%	0.11%	0.09%	0.11%	0.06%	0.11%	0%	0.11%
Ethnicity								
White	31.6%	25.5%	33.7%	25.8%	33.8%	26.3%	33.3%	27.4%
Black	3.3%	5.5%	4.2%	5.4%	4.4%	5.4%	5.0%	5.1%
Hispanic	57.6%	58.3%	51.6%	58.3%	52.2%	58.1%	51.5%	57.8%
Asian	2.6%	5.6%	3.9%	5.4%	4.1%	5.0%	4.0%	4.5%
Other	5.0%	5.1%	6.5%	5.1%	5.3%	5.2%	6.1%	5.3%
Education								
Did not finish HS	11.9%	12.6%	8.3%	12.5%	8.6%	12.2%	8.4%	12.0%
High school diploma	48.5%	51.2%	47.7%	51.3%	46.7%	51.5%	48.5%	52.0%
Some college	36.1%	32.2%	39.4%	32.3%	40.7%	32.5%	39.5%	32.2%
College grad or above	3.4%	3.9%	4.5%	3.9%	4.1%	3.8%	3.6%	3.8%
Prenatal care								
First trimester	83.6%	82.3%	85.3%	81.9%	85.7%	81.1%	83.1%	79.2%
Later than 1st tri	16.4%	17.7%	14.7%	18.1%	14.3%	18.9%	16.9%	20.8%
Insurance Status								
Private	48.3%	43.2%	50.1%	43.2%	51.0%	43.0%	47.8%	42.6%
Public or none	51.7%	56.8%	49.9%	56.8%	49.0%	57.0%	52.2%	57.4%

Maternal Bivariate Outcomes

Maternal bivariate analyses for the entire cohort of obese women are presented in Table 3. Full subgroup analyses by WHO obesity class are found in Appendix C. Overall, the cesarean delivery rate was 18% in our sample (n=13,518; 32.18% among nulliparous women, 8.42% among multiparous women with a prior vaginal delivery). Among all nulliparous obese women, there was either no difference or a lower cesarean delivery rate in the eIOL groups than in the expectant management groups (Figure 3).

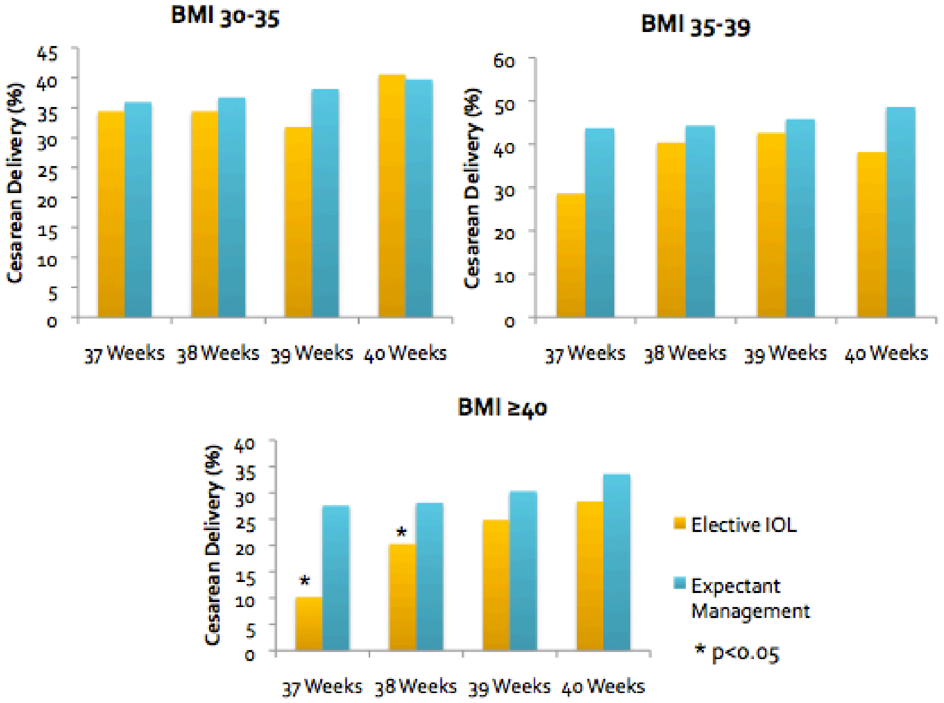
Elective induction of labor at 37 weeks was associated with a significantly lower cesarean rate compared to expectant management (20.0% vs. 32.2%, p=0.007), as did eIOL at 39 weeks compared to expectant management (29.9% vs. 34.9%, p=0.021). There were no differences in the proportions of cesarean delivery between eIOL and expectant management groups at 38 weeks (29.0% vs. 32.9%, p=0.161) or 40 weeks (34.7% vs. 37.8%, p=0.175).

Figure 3: eIOL and Cesarean Delivery in Nulliparous Obese Women



Subgroup analysis by WHO obesity class revealed that with the exception of nulliparous women with a BMI ≥40 who underwent eIOL at 37 or 38 weeks, where eIOL was associated with lower proportions of cesarean delivery (37 weeks: 10.2% vs. 27.6%, p=0.003; 38 weeks: 20.3% vs. 24.9%, p=0.045), there was no difference in cesarean delivery following eIOL compared to expectant management (Figure 4, Appendix C).

Figure 4: Subgroup Analyses: Cesarean Delivery in Nulliparous Obese Women



Among multiparous obese women with a prior vaginal delivery, elective IOL was associated with lower cesarean rates compared to expectant management at 38 weeks (3.6% vs. 8.5%, p<0.0001), 39 weeks (4.5% vs. 8.6%, p<0.0001), and 40 weeks (5.6% vs. 9.3%, p=0.001) (Figure 5). Again, in subgroup analyses by WHO obesity class, cesarean delivery rates were either no different or lower with eIOL compared to expectant management at each week of term gestation (Figure 6, Appendix C).

Figure 5: Cesarean Delivery in Multiparous Obese Women with a Prior Vaginal Delivery

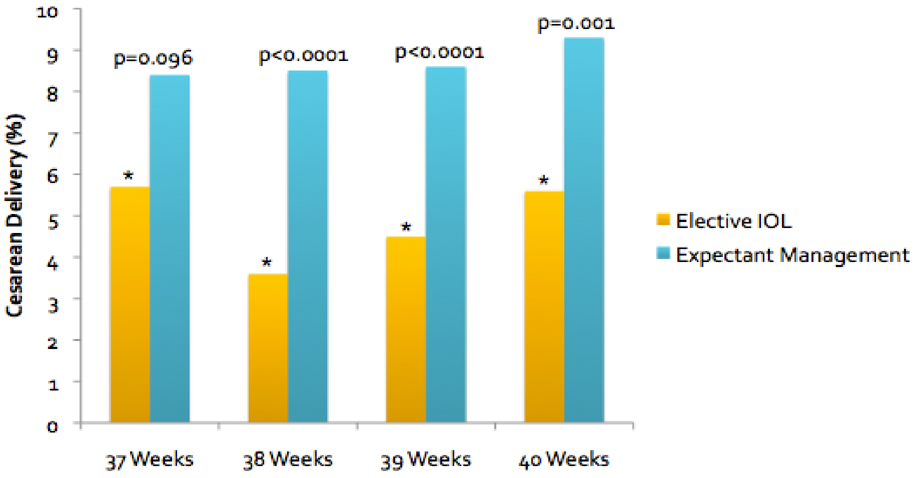
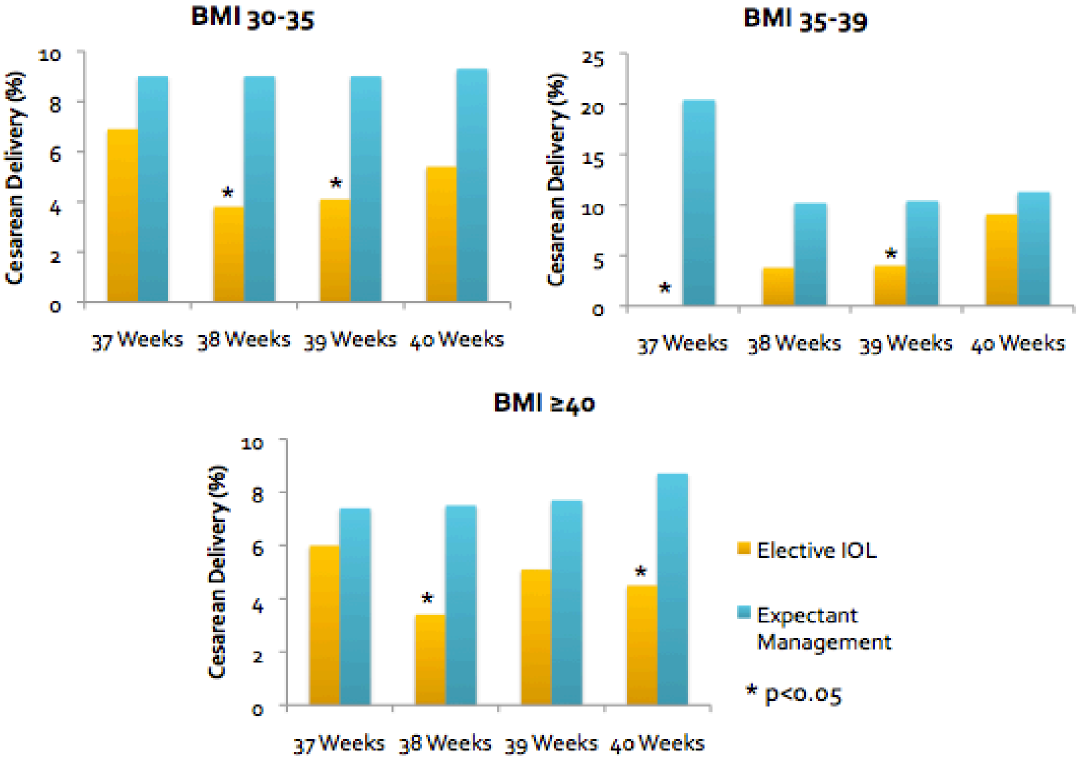


Figure 6: Subgroup Analyses: Cesarean Delivery in Multiparous Obese Women with a Prior Vaginal Delivery



The proportions of operative vaginal delivery were not statistically significantly different between eIOL and expectant management groups at any gestational age, regardless of parity or BMI category.

There were no significant differences or appreciable trends in the proportions of severe perineal lacerations between eIOL and expectant management groups in all nulliparous obese women. Subgroup analyses by WHO obesity class demonstrated that among nulliparous women with a BMI 30-35, eIOL at 39 weeks resulted in a significantly greater proportion of severe perineal lacerations compared to expectant management (5.8% vs. 2.9%, p=0.028). However, in morbidly obese women, this pattern was reversed, with eIOL at 39 weeks leading to significantly lower proportions of lacerations compared to expectant management in this subpopulation (1.7% vs. 5.0%, p=0.018). Among multiparous women with a prior vaginal delivery, eIOL at 40 weeks in women with a BMI 30-35 was associated with a greater proportion of severe perineal lacerations (1.8% vs. 0.6%, p=0.012).

Among nulliparous obese women, the proportions of postpartum hemorrhage were not statistically significantly different between eIOL and expectant management groups at any gestational age, regardless of BMI category. Among multiparous obese women with a prior vaginal delivery, eIOL was associated with lower proportions of postpartum hemorrhage compared to expectant management in all gestational age groups; these differences were statistically significant with eIOL 38 weeks (1.3% vs. 2.4%, p=0.044) and 40 weeks (1.1% vs. 2.7%, p=0.009).

The proportions of nulliparous obese women who developed chorioamnionitis were lower in eIOL groups across all gestational age comparisons. These differences were statistically significant at 38 weeks (1.6% vs. 4.0%, p=0.037), 39 weeks (1.2% vs. 4.6%, p<0.0001), and 40 weeks (2.1% vs. 5.1%, p=0.003). Subgroup analysis by obesity class revealed that eIOL at 39 weeks was associated with lower proportions of chorioamnionitis in women with a BMI ≥40 (0% vs. 4.3%, p=0.001). In multiparous obese women with a prior vaginal delivery, eIOL at 40 weeks was associated with lower proportions of chorioamnionitis compared to expectant management (0% vs. 0.7%, p=0.017), but there were no significant differences in subgroup analyses by obesity class, likely due to the rarity of this outcome.

Table 3: Unadjusted Maternal Outcomes of Term Elective Induction of Labor Compared to Expectant Management

	Comparison Group	N	Cesarean Delivery (%)	Operative Vaginal Delivery (%)	3^{rd} and 4^{th} Degree Perineal Laceration (%)	Postpartum Hemorrhage (%)	Chorioamnionitis (%)
			Nulliparous				
37 Weeks	eIOL	105	20.0*	4.7	4.8	0	0.9
	exp mgmt	30344	32.2	5.9	3.7	3.3	3.8
38 Weeks	eIOL	296	29.0	5.7	2.0	2.7	1.6*
	exp mgmt	24704	32.9	5.9	3.8	3.4	4.0
39 Weeks	eIOL	482	29.9*	5.0	2.9	2.7	1.2**
	exp mgmt	16003	34.9	5.9	3.9	3.6	4.6
40 Weeks	eIOL	473	34.7	6.3	3.6	3.1	2.1*
	exp mgmt	6580	37.8	6.0	4.0	4.1	5.1
			Multiparous with a Prior Vaginal Delivery				
37 Weeks	eIOL	282	5.7	1.4	0.3	1.4	0
	exp mgmt	43900	8.4	2.6	0.7	2.3	0.6
38 Weeks	eIOL	767	3.6**	3.0	1.0	1.3*	0.4
	exp mgmt	34375	8.5	2.7	0.7	2.4	0.6
39 Weeks	eIOL	1163	4.5**	2.5	0.5	1.7	0.7
	exp mgmt	20075	8.6	2.6	0.8	2.6	0.7
40 Weeks	eIOL	785	5.6*	1.9	1.1	1.1*	0
	exp mgmt	7511	9.3	2.6	0.8	2.7	0.7*

**p<0.05, **p<0.0001*

Maternal Multivariable Outcomes

Multivariable models for maternal outcomes adjusting for maternal age, ethnicity, education, initiation of prenatal care, and insurance status are presented in Table 4. Further subgroup analyses by WHO obesity class are fully presented in Appendix D. Among nulliparous obese women, the significant differences in the proportions of cesarean delivery following eIOL at 37 and 39 weeks persisted after controlling for key confounders. Elective IOL at 37 weeks was associated with 45% lower odds of cesarean delivery (OR 0.55, 95% CI 0.34-0.90), and elective IOL at 39 weeks was associated with 23% lower odds of cesarean delivery (OR 0.77, 95% CI 0.63-0.95) compared to expectant management. Furthermore, in nulliparous morbidly obese women, eIOL at 37 and 38 weeks was associated with significantly lower odds of cesarean delivery compared to expectant management (OR [95% CI] at 37 weeks: 0.32 [0.14-0.75]; 38 weeks: 0.62 [0.39-0.98]).

Among multiparous obese women with a prior vaginal delivery, eIOL at 38, 39, or 40 weeks was associated with lower odds of cesarean delivery compared to expectant management (OR [95% CI] for 38 weeks 0.42 [0.29-0.62]; 39 weeks 0.44 [0.33-0.60]; 40 weeks 0.57 [0.42-0.79]). In subgroup analyses by obesity class, women with a BMI 30-35 who were electively induced at 38, 39, or 40 weeks had lower odds of cesarean delivery compared to expectant management. Among multiparous women with a BMI 35-39, eIOL at 38 weeks and 39 weeks were associated with lower odds of cesarean delivery. Multiparous women with a BMI of ≥40 had lower odds of cesarean delivery with eIOL at 38 weeks or 40 weeks compared to expectant management.

After controlling for key confounders, the odds of operative vaginal delivery were lower among nulliparous morbidly obese women electively induced at 40 weeks compared to those who were expectantly managed (OR 0.44, 95% CI 0.21-0.95). There were no differences in the odds of operative vaginal delivery in the eIOL versus expectant management groups at any gestational age or BMI category among multiparous obese women with a prior vaginal delivery.

Elective IOL at 39 weeks in morbidly obese nulliparous women was associated with lower odds of severe perineal lacerations compared to expectant management (OR 0.33, 95% CI 0.12-0.88). There were no differences in the odds of lacerations in multiparous women with a prior vaginal delivery.

In nulliparous obese women, eIOL was associated with similar odds of postpartum hemorrhage compared to expectant management, but among multiparous women with a BMI ≥ 40, eIOL at 40 weeks was associated with lower odds of postpartum hemorrhage compared to expectant management (OR 0.45, 95% CI 0.23-0.88). Additionally, nulliparous obese women electively induced at 39 and 40 weeks had lower odds of chorioamnionitis compared to women expectantly managed at those gestational ages (39 weeks: OR 0.27, 95% CI 0.12-0.61; 40 weeks: OR 0.32, 95% CI 0.17-0.69). There were no differences in the odds of chorioamnionitis between eIOL and expectant management groups among multiparous obese women with a prior vaginal delivery.

Table 4: Multiple Logistic Regression—Association of eIOL Compared to Expectant Management with Maternal Outcomes

Gestational Age Group	Cesarean Delivery	Operative vaginal delivery	3rd/4th degree laceration	Postpartum hemorrhage	Chorioamnio-nitis
Nulliparous					
37 Weeks	0.55 (0.34-0.90)	0.82 (0.33-2.02)	1.34 (0.55-3.31)	-	0.24 (0.04-1.74)
38 Weeks	0.83 (0.64-1.09)	1.0 (0.60-1.66)	0.54 (0.24-1.22)	0.83 (0.41-1.69)	0.42 (0.17-1.03)
39 Weeks	0.77 (0.63-0.95)	0.78 (0.51-1.22)	0.69 (0.40-1.21)	0.70 (0.39-1.24)	0.27 (0.12-0.61)
40 Weeks	0.85 (0.70-1.05)	1.05 (0.71-1.57)	0.95 (0.57-1.56)	0.76 (0.44-1.31)	0.34 (0.17-0.69)
Multiparous with a Prior Vaginal Delivery					
37 Weeks	0.65 (0.39-1.08)	0.55 (0.20-1.49)	-	0.64 (0.24-1.72)	-
38 Weeks	0.42 (0.29-0.62)	1.04 (1.03-1.18)	1.43 (0.70-2.91)	0.52 (0.30-1.05)	0.60 (0.19-1.88)
39 Weeks	0.44 (0.33-0.60)	1.01 (0.69-1.49)	0.67 (0.29-1.52)	0.66 (0.42-1.05)	0.99 (0.48-2.04)
40 Weeks	0.57 (0.42-0.79)	0.78 (0.46-1.33)	1.42 (0.70-2.93)	0.45 (0.23-0.88)	-

**Adjusted for maternal age, ethnicity, education level, initiation of prenatal care in the first trimester, and insurance status. Hyphen indicates that cell sizes are too small to perform multiple logistic regression.*

Neonatal Bivariate Outcomes

Neonatal outcomes are displayed for the entire obese cohort in Table 5, with additional results stratified by WHO obesity class presented in Appendix E. At each gestational age comparison, elective induction of labor was associated with lower proportions of macrosomia compared to expectant management in nulliparous women. These differences were statistically significant with eIOL at 37 weeks (2.9% vs. 9.8%, p=0.017), 38 weeks (7.1% vs. 10.9%, p=0.037), and 39 weeks (9.1% vs. 12.5%, p=0.027), but did not reach statistical significance at 40 weeks (14.2% vs. 14.4%, p=0.878) (Figure 7). The same pattern was seen in multiparous obese women with a prior vaginal delivery. In this group, eIOL at 37, 38, or 39 weeks was associated with significantly lower proportions of macrosomia compared to expectant management (37 weeks: 6.4% vs. 13.5%, p=0.001; 38 weeks: 11.2% vs. 14.9%, p=0.005; 39 weeks: 13.2% vs. 17.1%, p=0.001) (Figure 8). In subgroup analyses of multiparous women, eIOL at 37, 38, or 39 weeks in women with a BMI of 30-35 and eIOL at 38 or 39 weeks in women with a BMI of 35-39 were associated with lower proportions of macrosomia compared to expectant management (Appendix E).

Figure 7: eIOL and Macrosomia in Nulliparous Obese Women

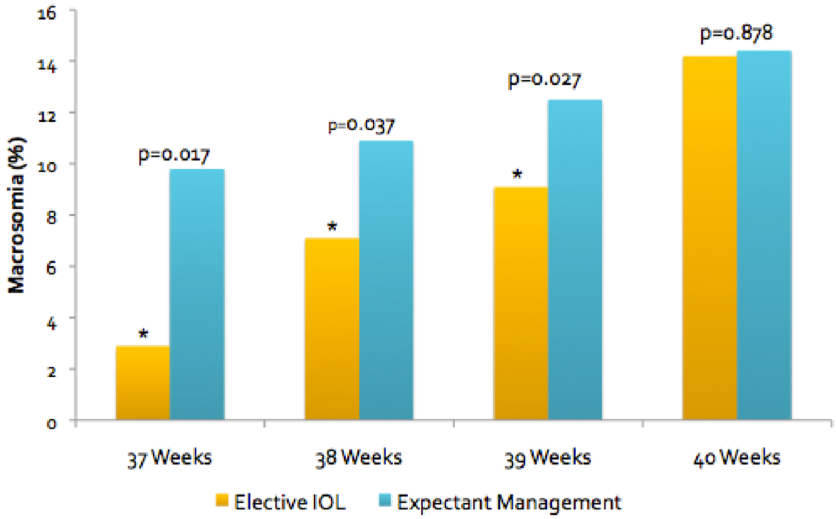
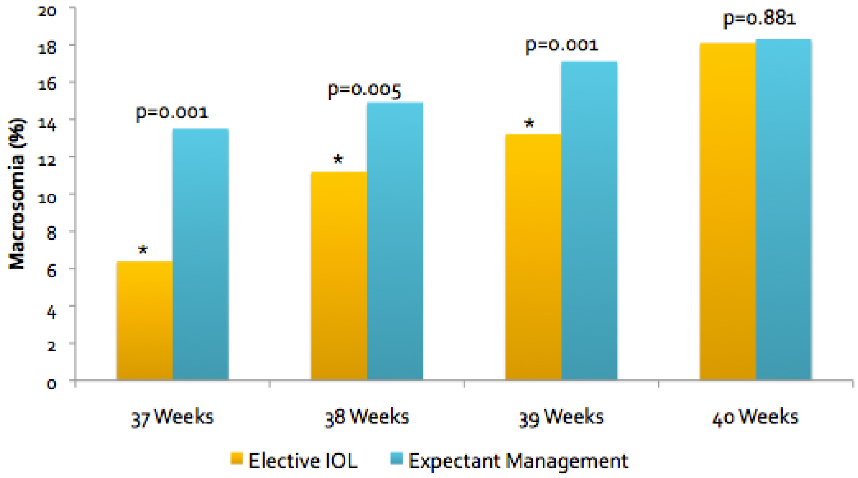


Figure 8: eIOL and Macrosomia in Multiparous Obese Women with a Prior Vaginal Delivery



There were no significant differences in the proportions of shoulder dystocia across any gestational age comparisons, regardless of parity or obesity class subgroups. Among nulliparous women with a BMI 35-39, eIOL at 40 was associated with a greater proportion of brachial plexus injury (2.9% vs. 0.1%, $p<0.0001$). Additionally, nulliparous women with a BMI ≥40 who were electively induced at 38 weeks had higher rates of brachial plexus injury compared to expectant management (0.7% vs. 0.1%, $p=0.048$). Among multiparous women with a prior vaginal delivery, the only subgroup in which rates of brachial plexus injury were different between eIOL and expectant management groups was in the morbidly obese women—in this subgroup, eIOL at 37 weeks had a greater proportion of BPI (0.9% vs. 0.1%, $p=0.018$).

There were no significant differences in the proportions of RDS between eIOL and expectant management groups at any gestational age in nulliparous obese women. In multiparous obese women without a prior vaginal delivery, eIOL at 38 weeks was associated with a higher proportion of RDS compared to expectant management (0.5% vs. 0.2%, $p=0.016$). In subgroup analyses of these multiparous women, eIOL at 38 weeks in women with a BMI 30-35 and at 37 or 39 weeks in women with a BMI 35-39 were associated with significantly greater proportions of RDS compared to expectant management.

Table 5: Unadjusted Neonatal Outcomes of Term Elective Induction of Labor Compared to Expectant Management

	eIOL or Expectant Management Group	N	Macrosomia (%)	Shoulder Dystocia (%)	Brachial Plexus Injury (%)	Respiratory Distress Syndrome (%)
Nulliparous						
37 Weeks	eIOL	105	2.9*	0	0	0
	exp mgmt	30344	9.8	1.1	0.1	0.3
38 Weeks	eIOL	296	7.1*	2.0	0.3	0.3
	exp mgmt	24704	10.9	1.1	0.2	0.3
39 Weeks	eIOL	482	9.1*	1.7	0.2	0
	exp mgmt	16003	12.5	1.3	0.1	0.3
40 Weeks	eIOL	473	14.2	0.8	0.6	0
	exp mgmt	6580	14.4	1.4	0.2	0.4
Multiparous with a Prior Vaginal Delivery						
37 Weeks	eIOL	282	6.4*	2.5	0.3	0.3
	exp mgmt	43900	13.5	1.9	0.1	0.2
38 Weeks	eIOL	767	11.2*	1.2	0	0.5*
	exp mgmt	34375	14.9	2.0	0.1	0.2
39 Weeks	eIOL	1163	13.2*	1.7	0.2	0.3
	exp mgmt	20075	17.1	2.3	0.2	0.2
40 Weeks	eIOL	785	18.1	1.7	0	0
	exp mgmt	7511	18.3	2.5	0.2	0.2

*$p<0.05$, **$p<0.01$, ***$p<0.0001$

Neonatal Multivariable Outcomes

Multivariable models for neonatal outcomes adjusting for maternal age, ethnicity, education, initiation of prenatal care, and insurance status are presented in Table 6, with additional subgroup analyses by WHO obesity class fully displayed in Appendix F. Elective induction of labor at 37, 38, or 39 weeks in nulliparous obese women was associated with lower odds of macrosomia compared to expectant management after controlling for key confounders (OR [95% CI] at 37 weeks: 0.26 [0.08-0.83], 38 weeks: 0.57 [0.35-0.92], 39 weeks: 0.66 [0.48-0.91]). Elective induction of labor at 40 weeks was associated with similar odds of macrosomia. Among nulliparous women with a BMI 30-35, eIOL at 38 weeks was associated with lower odds of macrosomia compared to expectant management (OR 0.39, 95% CI 0.17-0.88) (Appendix F).

In obese multiparous women with a prior vaginal delivery, eIOL at 37, 38, or 39 weeks was associated with lower odds of macrosomia compared to expectant management (OR [95% CI] at 37 weeks: 0.39 [0.24-0.64], 38 weeks: 0.65 [0.51-0.82], 39 weeks: 0.67 [0.56-0.81]). Elective IOL at 40 weeks' gestation also resulted in slightly lower odds of macrosomia but this was not statistically significant. Subgroup analysis by WHO obesity class revealed a similar pattern in women with a BMI 30-35; in this group, eIOL at 37, 38, and 39 weeks was associated with lower odds of macrosomia (OR [95% CI] 0.22 [0.09-0.53] for 37 weeks, 0.56 [0.40-0.80] for 38 weeks, 0.65 [0.50-0.84] for 39 weeks). Among women with a BMI 35-39, eIOL was associated with lower odds of macrosomia compared to expectant management at 38 weeks (OR 0.39, 95% CI 0.21-0.72) and 39 weeks (OR 0.62, 95% CI 0.41-0.93). In morbidly obese multiparous women, multivariate analyses revealed that eIOL at 39 weeks was associated with lower odds of macrosomia compared to expectant management (OR 0.70, 95% CI 0.42-0.94).

There were no differences in the odds of shoulder dystocia with eIOL compared to expectant management in obese nulliparous women at any term gestational age. However, in multiparous obese women with a prior vaginal delivery, after controlling for key confounders, eIOL at 38 weeks in both the entire cohort (OR 0.42, 95% CI 0.20-0.89) and in the BMI 30-35 subgroup (OR 0.24, 95% CI 0.06-0.96) was associated with lower odds of shoulder dystocia compared to expectant management.

The odds of brachial plexus injury were not different between eIOL and expectant management groups at any gestational age comparison, regardless of parity of obesity class, in population of obese women. However, it is worth noting that brachial plexus injury was a rare outcome with zero cases in many comparisons, thus making the cell sizes too small to build multiple logistic regression models.

Elective IOL was associated with similar odds of RDS in nulliparous obese women across all gestational age comparisons and obesity classes. In multiparous women, although eIOL was associated with significantly greater proportions of RDS in some subgroups, these differences did not persist after controlling for key confounders.

Table 6: Multiple Logistic Regression—Association of eIOL Compared to Expectant Management with Neonatal Outcomes

Gestational Age Group	Macrosomia	Shoulder dystocia	Brachial Plexus Injury	Respiratory Distress Syndrome
Nulliparous				
37 Weeks	0.26 (0.08-0.83)	-	-	-
38 Weeks	0.57 (0.35-0.92)	1.87 (0.83-4.24)	2.00 (0.27-14.62)	1.43 (0.20-10.36)
39 Weeks	0.66 (0.48-0.91)	1.14 (0.53-2.44)	1.51 (0.20-11.29)	-
40 Weeks	0.93 (0.70-1.23)	0.60 (0.22-1.66)	3.36 (0.95-11.94)	-
Multiparous with a Prior Vaginal Delivery				
37 Weeks	0.39 (0.24-0.64)	1.29 (0.61-2.75)	2.32 (0.32-16.87)	2.13 (0.29-15.43)
38 Weeks	0.65 (0.51-0.82)	0.42 (0.20-0.89)	-	2.61 (0.81-8.46)
39 Weeks	0.67 (0.56-0.81)	0.75 (0.48-1.18)	0.94 (0.22-3.94)	1.84 (0.55-6.12)
40 Weeks	0.95 (0.78-1.15)	0.65 (0.37-1.15)	-	-

**Adjusted for maternal age, ethnicity, education level, initiation of prenatal care in the first trimester, and insurance status. Hyphen indicates that cell sizes are too small to perform multiple logistic regression.*

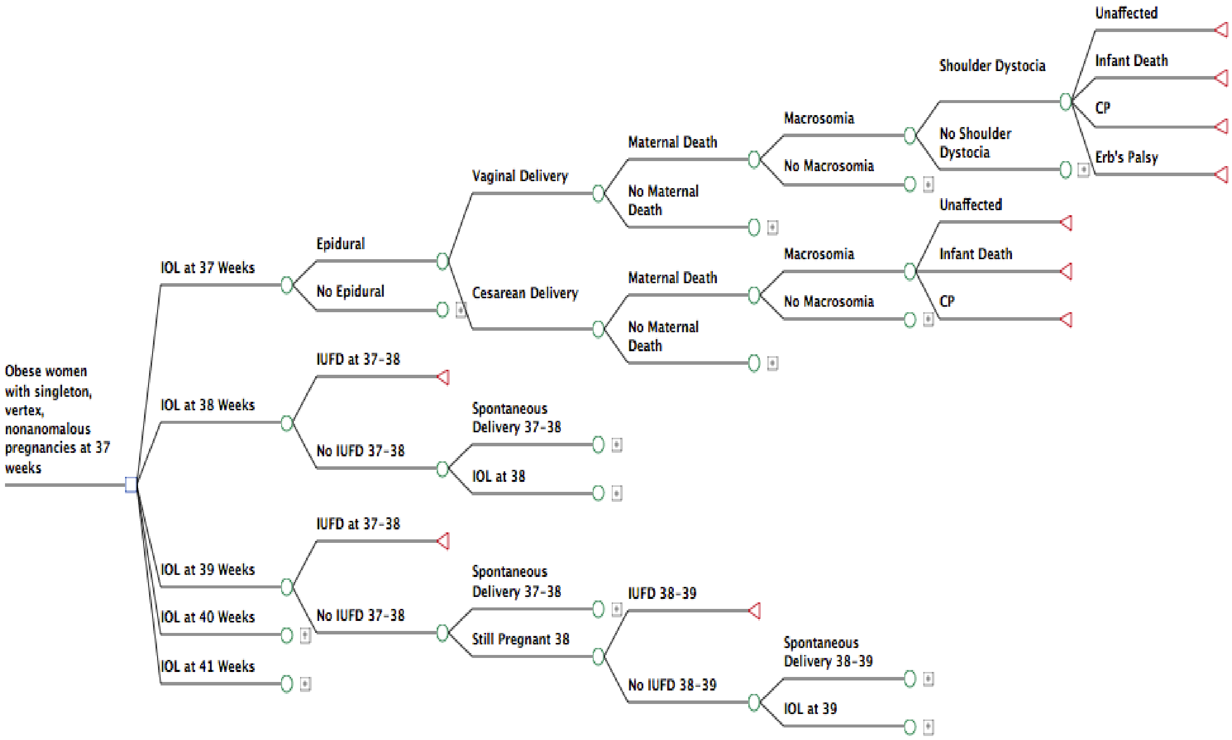
DECISION ANALYSIS AND COST-EFFECTIVENESS ANALYSIS

Methods

A decision-analytic model was built using TreeAge Pro software (2013 version, Williamstown, MA) to compare outcomes and costs for a cohort of obese women undergoing delivery at 37, 38, 39, 40, or 41 weeks. Our theoretical cohort included 800,000 women with a BMI of 30 or greater, representing approximately 20% of the nearly 4 million total births recorded in the USA in 2013 (Martin et al 2015). Aside from prepregnancy obesity, these pregnancies were low-risk; multiple gestations, fetal anomalies, and maternal complications complicating pregnancy such as gestational diabetes or chronic hypertension were not considered in this model. As no human subjects were involved in creating this decision-analytic model, this portion of the study was exempt from institutional review board approval.

The model begins with a woman at 37 weeks' gestation undergoing induction of labor at 37 weeks or being expectantly managed until induction and delivery at 38, 39, 40, or 41 weeks' gestation (Figure 9). Strategies involving expectant management accounted for the probabilities of stillbirth, spontaneous delivery, indicated IOL for preeclampsia, or scheduled eIOL for maternal obesity at each successive week of gestation; these events were cumulative for each week of continuing pregnancy. Maternal outcomes included mode of delivery and maternal death. Neonatal outcomes included stillbirth, permanent brachial plexus injury, cerebral palsy, and infant death. Costs included the hospital costs of induction of labor, epidural, and cesarean or vaginal delivery, as well as the lifetime costs of care for an infant with cerebral palsy or Erb's palsy and the opportunity costs associated with a maternal or neonatal death.

Figure 9: Schematic of Decision-Analytic Model



**Not all branches are open to facilitate display. Branches that do not terminate in a triangle are collapsed to facilitate display and are the same as branches that are already open.*

Probabilities

All probabilities were derived from the literature (Table 7). The probabilities of spontaneous delivery at each week of gestation were taken from National Center for Health Statistics data (Pilliod et al 2012). The probabilities of an epidural following IOL or spontaneous labor were based on previously published rates from a single institution (Caughey et al 2009). Cesarean delivery rates by gestational age following IOL or expectant management were derived from a retrospective cohort study of over 19,000 women at a single institution (Caughey et al 2006). These baseline rates were multiplied by the odds ratio for cesarean delivery in obese women reported in a large meta-analysis (Heslehurst et al 2008). The risks of stillbirth and infant death stratified by gestational age were taken from a retrospective cohort study of term deliveries in California, and these baseline rates were similarly multiplied by the odds ratios of stillbirth and infant death in obese versus normal-weight women (Rosenstein et al 2012, Chu et al 2007, Chen et al 2009). The probabilities of maternal death after a vaginal or cesarean delivery were derived from a retrospective cohort study of maternal deaths between 2000 and 2006 within a large health care delivery system (Clark et al 2008). Macrosomia rates by gestational age were based on a large cohort study of low-risk pregnancies, and these rates were multiplied by the increased odds of macrosomia in obese women reported in a 2008 meta-analysis (Cheng et al 2008, Heslehurst et al 2008). Shoulder dystocia was built into our model following vaginal delivery and was conditioned on the probability of macrosomia (Esakoff et al 2009). Similarly, the probability of Erb's palsy following shoulder dystocia was conditioned on the probability of macrosomia (Volpe et al 2012). Finally, rates of cerebral palsy by gestational age were taken from a cerebral palsy registry published in the United Kingdom (Surman et al 2009).

Table 7: Probabilities used in Cost-Effectiveness Analysis

Name	Value	Reference
Spontaneous Delivery		
37-38 weeks	0.102	Pilliod et al 2012
38-39 weeks	0.253	
39-40 weeks	0.471	
40-41 weeks	0.688	
Epidural		
With IOL	0.814	Caughey et al 2009
With spontaneous labor	0.720	
Cesarean Delivery after IOL		
37 weeks	0.119	Caughey et al 2006
38 weeks	0.119	
39 weeks	0.143	
40 weeks	0.204	
41 weeks	0.243	
Cesarean Delivery after Expectant Management		Caughey et al 2006
37 weeks	0.133	
38 weeks	0.133	
39 weeks	0.15	
40 weeks	0.19	
41 weeks	0.26	
Odds of Cesarean Delivery in Obese vs. Normal-Weight Women	2.005	Heslehurst et al 2008
Maternal Death, Vaginal Delivery	0.00035	Clark et al 2008
Maternal Death, Cesarean Delivery	0.000092	Clark et al 2008
Stillbirth		
37-38 weeks	0.0087	Rosenstein et al 2012
38-39 weeks	0.0010	
39-40 weeks	0.0011	
40-41 weeks	0.0012	
Odds of Stillbirth in Obese vs. Normal-Weight Women	2.04	Chu et al 2007
Infant Death		
37 weeks	0.00141	Rosenstein et al 2012
38 weeks	0.00105	
39 weeks	0.00088	
40 weeks	0.00095	
41 weeks	0.00108	
Odds of Infant Death in Obese vs. Normal-Weight Women	1.46	Chen et al 2009
Macrosomia		
37 weeks	0.045	Cheng et al 2008
38 weeks	0.101	
39 weeks	0.168	
40 weeks	0.254	
41 weeks	0.359	
Odds of Macrosomia in Obese vs. Normal-Weight Women	2.357	Heslehurst et al 2008

Shoulder Dystocia Macrosomic Not macrosomic	 0.06 0.009	Esakoff et al 2009
Erb's Palsy Following Shoulder Dystocia Macrosomic Not macrosomic	 0.061 0.029	Volpe et al 2012
Cerebral Palsy 37 weeks 38 weeks 39 weeks 40 weeks 41 weeks	 0.0023 0.0012 0.0009 0.001 0.001	Surman et al 2009

Costs

All costs in the model were in 2014 US dollars and adjusted using the medical care component of the consumer price index (Table 8). The cost of an induction of labor was set at a baseline of $1,498.03 based on a 2003 cost analysis of patients attempting vaginal delivery (Bost 2003). The cost of an epidural in labor, a vaginal delivery, and a cesarean delivery were derived from the same cost analysis (Bost 2003). The lifetime cost of maternal death was estimated from several sources and assumed maternal death at age 25, a life expectancy past age 25 of 56.75 years, an average yearly wage for women of all educational levels of $35,505, and an average retirement age of 62 (Arias 2014, Bureau of Labor Statistics, Munnell 2015). The cost of a neonatal demise was taken from a 2006 study estimating the costs of neonatal care (Phibbs & Schmitt 2006). For neonatal morbidities, the adjusted published lifetime costs were $1,262,654 for cerebral palsy and $17,769 for Erb's palsy (MMWR 2004, Ohno et al 2011).

Table 8: Costs used in Cost-Effectiveness Analysis

Name	**Value (2014 US $)**	**Reference**
Induction of labor	1,498.03	Kaimal et al 2011, Phibbs & Schmitt 2006
Epidural	954.28	Bost 2003
Vaginal delivery	8,375.09	Kaimal et al 2011, Bost 2003
Cesarean delivery	13,432.63	Kaimal et al 2011, Bost 2003
Maternal death	1,352,220.12	Arias 2014, Bureau for Labor Statistics, Munnell 2015
Neonatal death	92,352.39	Kaimal et al 2011, Phibbs & Schmitt 2006
Cerebral palsy	1,262,654.16	MMWR 2004
Erb's palsy	17,768.76	Ohno et al 2011

Utilities

Utilities were included from the maternal and neonatal perspectives and were derived from the literature (Table 9). In decision analyses, utilities are a measure of the well-being derived from various health states and are applied to life expectancies to generate quality-adjusted life years (QALYs). Utilities are obtained via the standard gamble or time-tradeoff methods in existing literature and are measured on a scale of 0-1, with 0 representing death and 1 representing perfect health (Caughey et al 2010). These utility values are then multiplied by the number of years spent in that particular health state to generate QALYs (Caughey 2010). Because the value of time spent in a given health state is decreased in future time periods compared to the present, we discounted future utilities at a rate of 3% to calculate QALYs over the entire life expectancy of the mother and the neonate (Caughey 2010).

Maternal death by definition was set to a utility of 0. Cesarean delivery was set to a baseline utility of 0.99 based on prior literature (Caughey et al 2003). The utility of a stillbirth from the maternal perspective was set to 0.92 based on the published utility of a procedure-related miscarriage (Kuppermann et al 2000). From the maternal perspective, the utility of a neonatal death was set to 0.76 and the utility of cerebral palsy was 0.73 (Grobman et al 2002). The utility of an infant with permanent Erb's palsy was estimated from the utility of mild cerebral palsy and was set to 0.78 (Grobman et al 2002). If multiple health states existed for a given outcome in the model, for instance if a mother underwent Cesarean delivery and the neonate was affected with cerebral palsy, the utilities were multiplied together.

From the neonatal perspective, the utility of being affected with cerebral palsy was set to 0.6119 based on published literature (Carroll & Downs 2006). Again, the utility of permanent Erb's palsy was estimated from the utility of mild cerebral palsy; this has been reported as 0.88 from the neonatal perspective (Carroll & Downs 2006). By definition, the utility of a neonatal death is 0 and the utility of an uncomplicated infant is 1 from the neonatal perspective. All utilities were applied over the course of the remaining maternal life expectancy (56.9 years, assuming delivery at 25 years) and neonatal life expectancy (78.7 years in normal neonates and 66.6 years in those affected by cerebral palsy) at a discount rate of 3% to calculate total QALYs associated with each strategy (Arias 2014, Blair et al 2011, Siegel et al 1996).

Table 9: Utilities used in Cost-Effectiveness Analysis

Name	Value	Reference
IUFD		
Maternal perspective	0.92	Kuppermann et al 2000
Neonatal perspective	0	Assumed
Vaginal delivery	1	Assumed
Cesarean delivery	0.99	Caughey et al 2003
Maternal death	0	Assumed
Normal neonate		Assumed
Maternal perspective	1	
Neonatal perspective	1	
Neonatal death		
Maternal perspective	0.76	Grobman et al 2002
Neonatal perspective	0	Assumed
Cerebral palsy*		
Maternal perspective	0.733	Grobman et al 2002
Neonatal perspective	0.612	Carroll & Downs 2009
Erb’s Palsy**		
Maternal perspective	0.78	Grobman et al 2002
Neonatal perspective	0.88	Carroll & Downs 2009

*Calculated as a weighted average of the utilities and frequencies of each level of cerebral palsy (mild, moderate, severe). **Estimated from the utility of mild cerebral palsy.

Analysis

We first performed baseline analysis comparing the rates of maternal and neonatal outcomes following delivery at 37-41 weeks. Next, we estimated total costs and QALYs for each strategy to determine the optimal timing of delivery from a societal perspective. We also calculated the incremental cost-effectiveness ratio (ICER) to compare competing strategies. The ICER compares the change in costs to the incremental benefits of a particular intervention and is calculated as:

$$(Cost_A - Cost_B) / (QALYs_A - QALYs_B)$$

The conventional range of what is considered cost-effective is $50,000-100,000/QALY in the United States. Therefore, we considered any ICER less than $50,000/QALY as cost-effective, ICERs between $50,000-100,00/QALY as marginally cost-effective, and ICERs over $100,000/QALY as not cost-effective (Caughey 2005).

Sensitivity analysis is a decision-analytic tool that allows an estimation of how variation in parameters such as the rates of stillbirth, infant death, costs of induction, or other variables impact results. To test the robustness of the model, univariate sensitivity analyses were performed on every input in order to investigate key drivers of the model and determine the threshold value beyond which the results of the model would change. We also performed bivariate sensitivity analyses in order to examine whether interactions between two variables significantly affected our results.

In order to incorporate additional uncertainty into the baseline model, a Monte Carlo simulation was performed using 10,000 trials to simultaneously vary all model inputs. One trial represents a woman undergoing one of the five delivery strategies in the model, and its inputs are randomly chosen from pre-specified distributions. All probabilities and utilities were given a beta distribution, and all costs were given a gamma distribution (Little et al 2010). This simulation is repeated 10,000 times with a different set of randomly chosen values within the input distribution and the aggregate represents a theoretic cohort of women.

Results

In our theoretic cohort of 800,000 pregnancies in obese women, IOL at 37 weeks resulted in the lowest cesarean section rate (Table 10). 21.3% of deliveries at 37 weeks would occur via cesarean section, and this rate would increase with each additional week of expectant management to a high of 28.1% with IOL at 41 weeks. Because the risk of maternal death is greater following cesarean delivery, our model's results for maternal death followed a similar pattern, with earlier delivery minimizing the risk of maternal death. IOL at 37 or 38 weeks both conferred 120 maternal deaths in our theoretic cohort; delivery at 39 weeks would result in six more maternal deaths while delivery at 40 or 41 weeks would lead to 14 additional maternal deaths.

As expected, delivery at later gestational ages also increased the risk of stillbirth. Immediate delivery at 37 weeks would prevent all subsequent stillbirths. Delivery at 38, 39, 40, or 41 weeks would result in 697, 1412, 1980, and 2317 stillbirths, respectively, in our theoretic cohort of 800,000 women.

Expectant management with scheduled IOL at 39 weeks minimized the risks of infant death and cerebral palsy. Compared to delivery at 41 weeks, IOL at 39 weeks would prevent 28 cases of cerebral palsy and 45 infant deaths in our theoretic cohort of 800,000 women. Cases of Erb's palsy were minimized with immediate delivery at 37 weeks, which is to be expected given that the risk of macrosomia and subsequent shoulder dystocia increases with increasing gestational age.

In our theoretic cohort of 800,000 women, eIOL at 38 weeks maximized total QALYs. Compared to delivery at 41 weeks, eIOL at 38 weeks conferred 62,000 more QALYs in our theoretic cohort. In other words, weighing the risks of early term morbidity and mortality against the risks of stillbirth, adverse maternal outcomes, and macrosomia-related complications, the optimal gestational age to deliver obese women is at 38 weeks if one considers clinical outcomes alone.

Because IOL is an intervention associated with hospitalization, higher rates of epidural use, and higher rates of infant death and cerebral palsy in our model, it follows that routine eIOL at 37 weeks was the most expensive strategy. Inducing our entire theoretic cohort of 800,000 women would cost $12.25 billion; costs decreased with each additional week of expectant management, with a nadir of $10.06 billion associated with expectant management until 41 weeks' gestation.

Although delivery at 41 weeks was the least expensive strategy, delivery at 37, 38, 39, or 40 weeks all conferred more total QALYs and were incrementally cost-effective compared to delivery at 41 weeks with ICERs of $38,652, $16,652, $14,663, and $25,673, respectively. Similarly, comparing earlier delivery to expectant management until 40 weeks, eIOL at 37, 38, or 39 weeks all resulted in more QALYs and were incrementally cost-effective at $9,965, $14,521, and $42,092, respectively. Delivery at 37 weeks resulted in 17,000 more QALYs than delivery at 39 weeks, but it would cost an additional $1.6 billion; therefore, eIOL at 37 weeks was only marginally cost-effective with an ICER of $94,831 per QALY. However, eIOL at 38 weeks yields more QALYs and is incrementally cost-effective, at $20,173 per QALY, compared to delivery at 39 weeks. Delivery at 38 weeks is also a dominant strategy compared to eIOL at 37 weeks, as it leads to greater total QALYs and lower costs.

Overall, balancing the costs and clinical outcomes associated with these five delivery strategies, at a willingness-to-pay threshold of $100,000/QALY, 38 weeks was the optimal gestational age for delivery in obese women, and it is a cost-effective strategy compared to both earlier term eIOL and expectant management until a later gestational age.

Table 10: Cost-Effectiveness Analysis Outcomes in a Theoretic Cohort of 800,000 Women

	Deliver at 37 Weeks	Deliver at 38 Weeks	Deliver at 39 Weeks	Deliver at 40 Weeks	Deliver at 41 Weeks
Cesarean rate	21.3%	21.5%	24.5%	28.0%	28.1%
Stillbirth	0	697	1412	1980	2317
Maternal Death	120	120	126	134	134
Infant Death	1646	1268	1134	1162	1179
Cerebral Palsy	1840	1049	888	916	916
Erb's Palsy	265	371	503	617	635
Cost (US $, Billions)	12.25	11.10	10.65	10.37	10.06
QALYs (Millions)	45.620	45.625	45.603	45.575	45.563
ICER (US $/QALY)	$38,652 $42,092 $94,831 (dominated)	$16,652 $14,521 $20,173 (ref)	$14,663 $9,965 (ref)	$25,673 (ref)	(ref)

Sensitivity Analysis

To further investigate whether any particular variables were driving our results, univariate sensitivity analyses were conducted on all probabilities, costs, and utilities in the model. The model was robust across all reasonable ranges of each variable, with a few exceptions.

In our decision analysis, delivery at 38 weeks was the optimal strategy until the odds ratio of stillbirth in obese versus normal-weight women increased from our baseline of 2.04 to 2.53; after this threshold, eIOL at 37 weeks maximized total QALYs (Figure 10). Additionally, eIOL at 38 weeks was the optimal strategy until the odds ratio of infant death fell from our baseline of 1.46 to below 1.05, after which delivery at 37 weeks was optimal, or rose above 9.14, when delivery at 39 weeks became preferred (Figure 11).

Figure 10: One-Way Sensitivity Analysis on Odds of Stillbirth

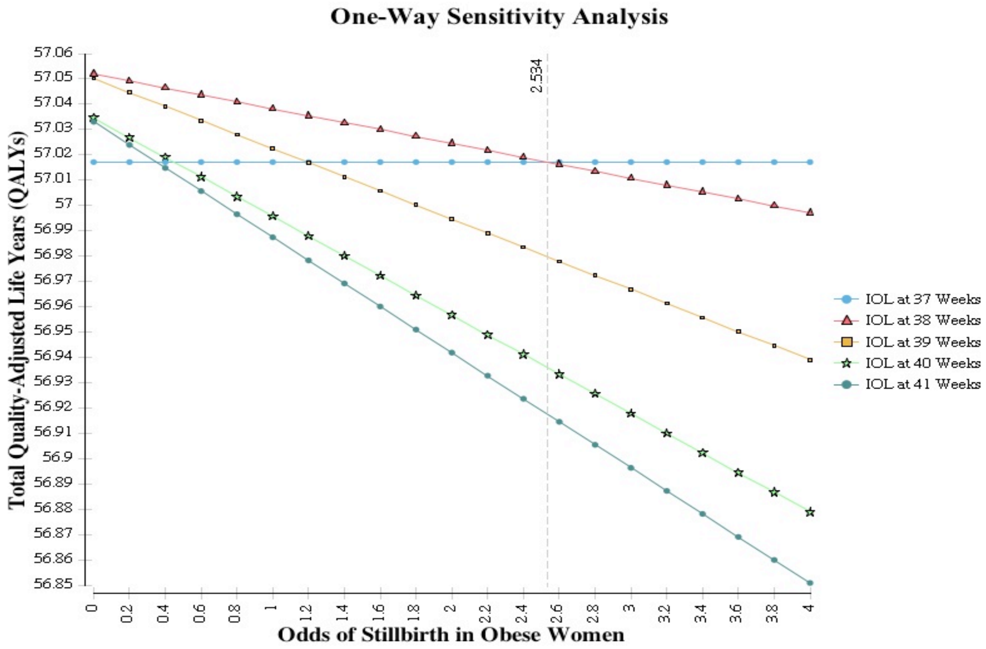
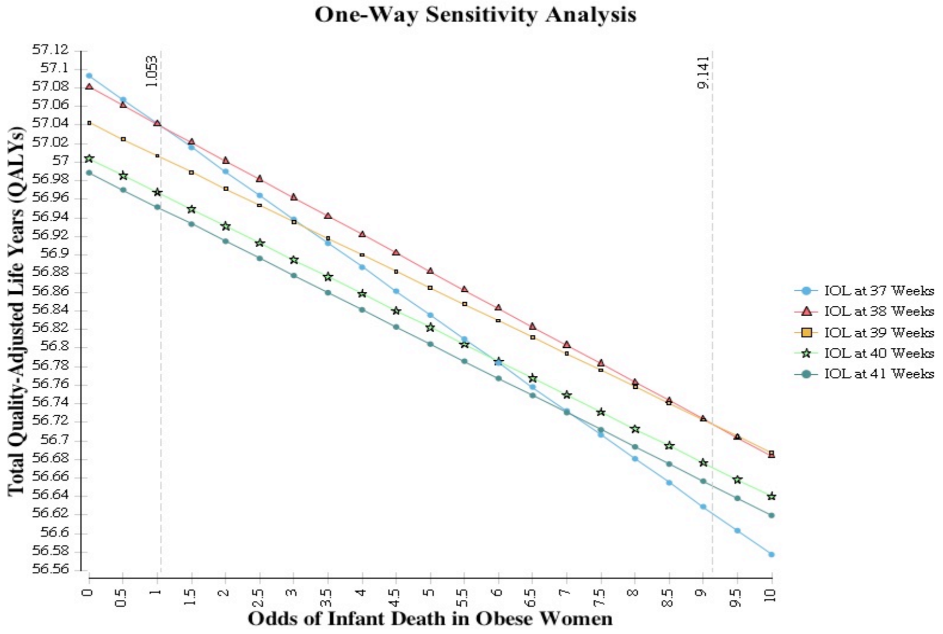


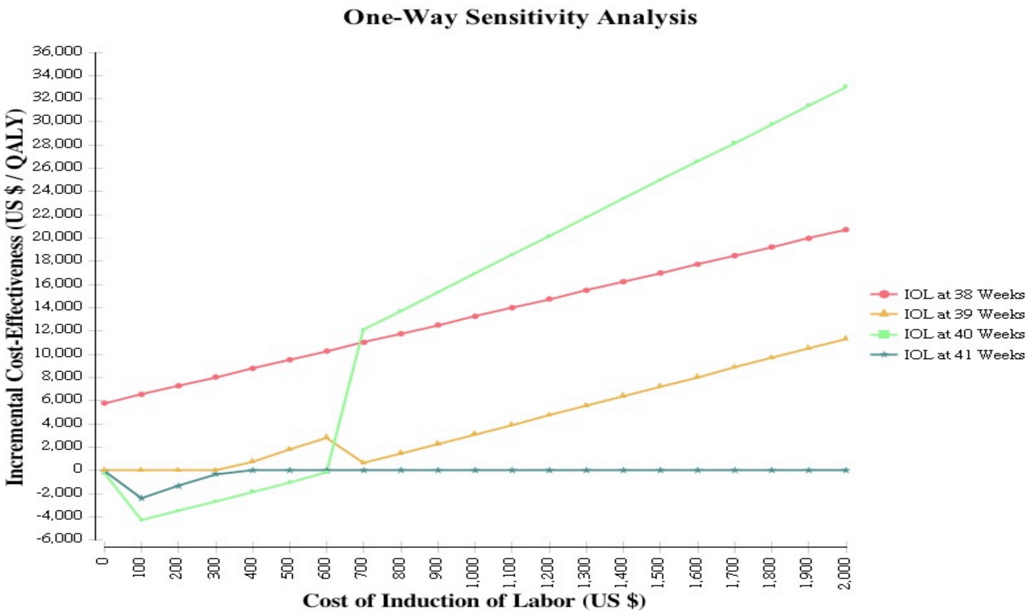
Figure 11: One-Way Sensitivity Analysis on Odds of Infant Death



Elective induction of labor at 38 weeks remained optimal until the probability of shoulder dystocia rose above 26.6% and the probability of Erb's palsy following shoulder dystocia rose above 27.1% in macrosomic pregnancies, after which delivery at 37 weeks maximized QALYs. The rates of shoulder dystocia and Erb's Palsy in non-macrosomic pregnancies were not significant drivers of the model.

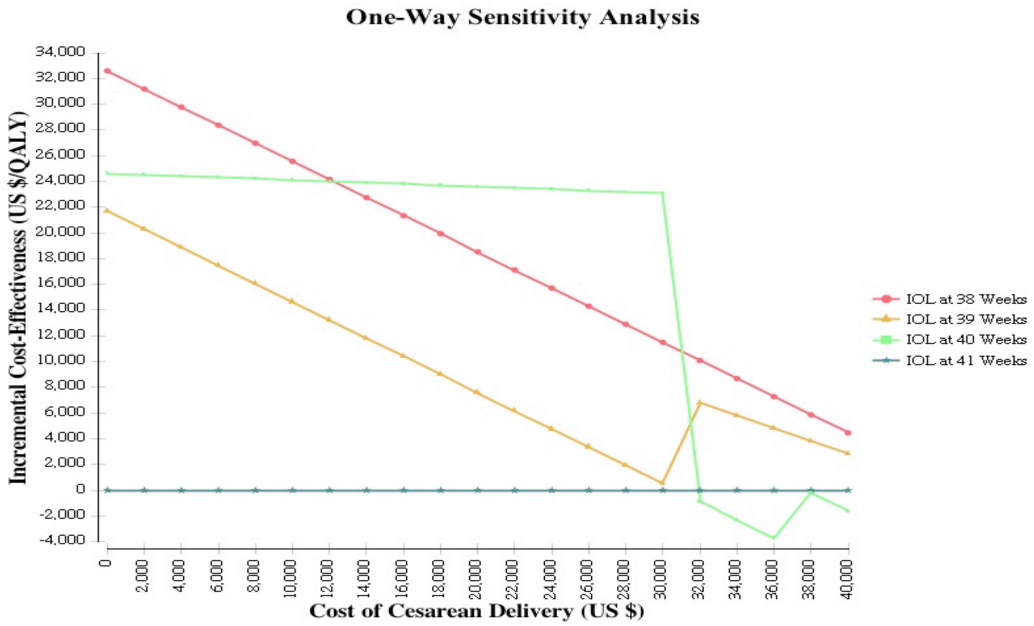
Sensitivity analyses on the cost-effectiveness portion of the model only compared delivery at 38, 39, 40, and 41 weeks, as delivery at 37 weeks was dominated. Figure 12 shows a univariate sensitivity analysis on the cost of induction of labor. At a baseline cost of $1,498, eIOL at 38, 39, and 40 weeks were all cost-effective compared to expectant management until 41 weeks. As the cost of induction of labor increases, the ICER comparing eIOL at 38 weeks to 41 weeks also increases linearly, but delivery at 38 weeks remains cost-effective as the ICER does not exceed $100,000/QALY. When the cost of induction falls below $300, delivery at both 40 and 41 weeks becomes dominated; eIOL at 38 weeks is still incrementally cost-effective at $8,000/QALY compared to delivery at 39 weeks.

Figure 12: One-Way Sensitivity Analysis on Cost of Induction of Labor



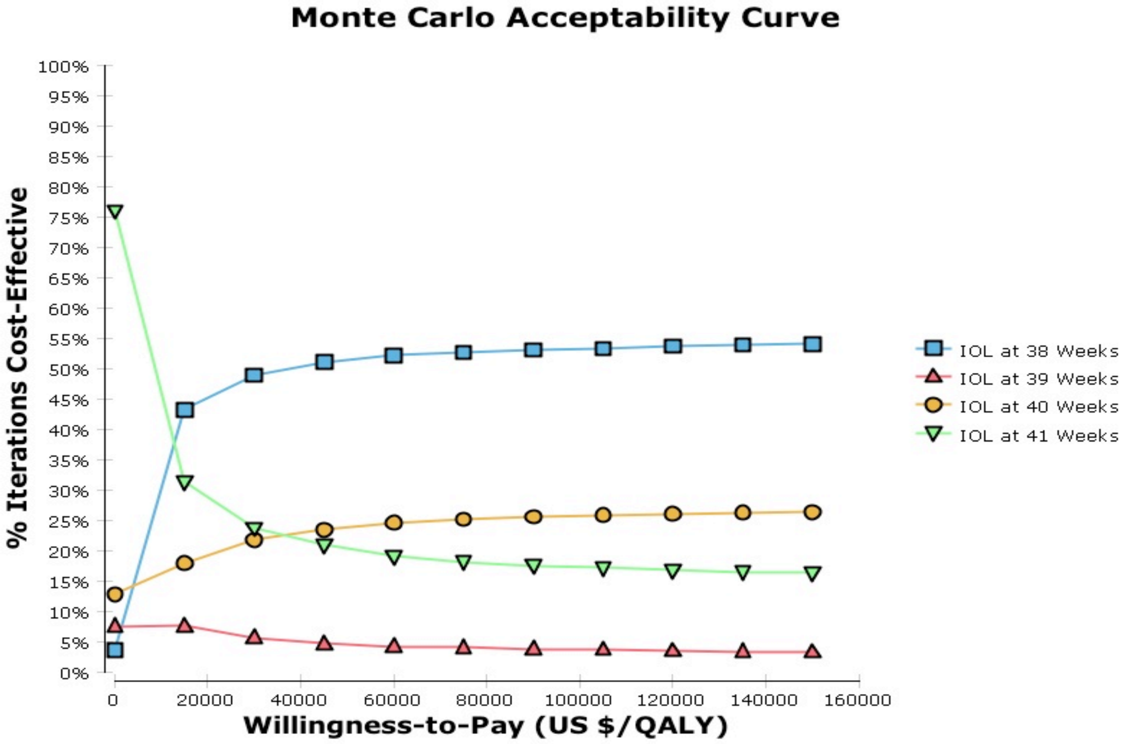
Sensitivity analysis on the cost of cesarean delivery showed that eIOL at 38 weeks remained incrementally cost-effective across a wide range of inputs. As the cost of cesarean delivery increased from our baseline of $13,432, the ICER for eIOL at 38 weeks compared to delivery at 41 weeks decreased linearly. On the opposite end of the spectrum, when the cost of cesarean was very inexpensive, the ICER for eIOL at 38 weeks increased but never crossed the $100,000/QALY threshold, indicating that delivery at 38 weeks remained incrementally cost-effective compared to delivery at 41 weeks regardless of the cost of cesarean.

Figure 13: One-Way Sensitivity Analysis on Cost of Cesarean Delivery



Monte Carlo probabilistic sensitivity analysis was performed to simulate the outcome of 10,000 random women, with all model inputs simultaneously varied within prespecified distributions. Based on these analyses, delivery at 38 weeks was cost-effective in 53.3% of scenarios at a willingness-to-pay threshold of $100,000/QALY. At a willingness-to-pay threshold of $50,000/QALY, delivery at 38 weeks was cost-effective 51.4% of the time. An acceptability curve displaying the Monte Carlo results with varying willingness-to-pay thresholds is presented in Figure 14.

Figure 14: Monte Carlo Simulation



DISCUSSION

Insights into Elective Induction of Labor and Perinatal Outcomes in Obese Women

This retrospective study demonstrated that elective induction of labor in obese women is not associated with increased risk of adverse perinatal outcomes. In fact, among nulliparous obese women, eIOL at 37 and 39 weeks was associated with lower odds of cesarean delivery compared to expectant management. Further, eIOL at 38, 39, or 40 weeks was associated with lower odds of cesarean delivery among mulitiparous women with a prior vaginal delivery.

The finding that eIOL was not associated with an increase in the risk of cesarean delivery compared to expectant management is important due to existing controversy in the literature surrounding eIOL and cesarean delivery (Macones 2009). Our findings showing an association between eIOL and either no change or a decrease in cesarean delivery among obese women is concordant with the body of literature comparing induction of labor compared to expectant management (Caughey et al 2009, Stock et al 2012, Darney et al 2013).

There is a dearth of literature on eIOL in the obese population. Only one prior study to date has examined elective induction of labor specifically in obese women. This study found that eIOL between 39-41 weeks of gestation in nulliparous obese women with an unfavorable cervix was associated with significantly higher rates of cesarean delivery compared to expectant management, whereas rates of other maternal and neonatal morbidities were similar between groups (Wolfe et al 2014). Our results regarding cesarean delivery contrast with this work, and provide new evidence in that we were able to examine multiple levels of parity, examine weekly differences in eIOL by gestational age, and account for key confounders by performing multivariable analyses.

Additionally, in morbidly obese nulliparous women, early term eIOL at 37 or 38 weeks was associated with decreased risk of cesarean delivery. In morbidly obese multiparous women, eIOL at 38 and 40 weeks was associated with decreased risk of cesarean delivery. This finding is interesting and suggests that morbidly obese women possibly represent a group where eIOL at 38 weeks of gestation may be beneficial when compared to expectant management. Perhaps in morbidly obese women, the risk of developing some condition (such as gestational diabetes, preeclampsia, or fetal distress) that increases the risk of cesarean delivery following expectant management is particularly high, so planned early term induction serves to mitigate these risks. Additional studies focusing on induction of labor in the morbidly obese population is needed to further explore our findings in this subgroup.

The finding that term eIOL in obese women was associated with either no change or a decrease in the risk of cesarean delivery, without a concomitant increase in the risk of operative vaginal delivery or severe perineal lacerations, is important as clinicians may worry that obese women may have more complicated vaginal deliveries. Our results contradict such obstetric myths as we have demonstrated that in the setting of term elective induction of labor, obese women were not at increased risk of operative vaginal delivery, severe lacerations, shoulder dystocia, or postpartum hemorrhage as compared to expectant management. This is generally consistent with literature on eIOL versus expectant management in the general obstetric population, so clinicians may be reassured that electively inducing an obese patient at term is not associated with poor maternal outcomes following vaginal delivery.

Additionally, eIOL was associated with lower odds of postpartum hemorrhage and chorioamnionitis in some subgroups, although it should be noted that the overall incidence of those outcomes was low in our study population. Regarding neonatal outcomes, eIOL at 37, 38, and 39 weeks of gestation was associated with decreased odds of macrosomia compared to expectant management in both nulliparas and multiparas with a prior vaginal delivery. Aside from eIOL at 38 weeks of gestation being associated with lower odds of shoulder dystocia in multiparous obese women with a prior vaginal delivery, there were no significant differences in the odds of other neonatal morbidities between eIOL and expectant management groups at any term gestational age.

Elective induction of labor at 37, 38 and 39 weeks was associated with lower odds of macrosomia, which makes sense given that continued fetal growth is a consequence of expectant management. Macrosomia is a well-established risk factor for shoulder dystocia and birth trauma, but although we report a decreased risk of macrosomia following eIOL, the proportions of shoulder dystocia and brachial plexus injury were not significantly different between eIOL and expectant management groups. The null findings in our study underscore the fact that these are rare and multifactorial outcomes.

Aside from eIOL at 38 weeks of gestation being associated with lower odds of shoulder dystocia in multiparous obese women with a prior vaginal delivery, there were no significant differences in the odds of other neonatal morbidities between eIOL and expectant management groups at any term gestational age. This is largely consistent with the study by Darney and colleagues showing that term eIOL was not associated with significantly higher odds of shoulder dystocia, respiratory distress syndrome, neonatal intensive care unit (NICU) admission, or perinatal death as compared with expectant management in the general obstetric population (Darney et al 2013). Stock and colleagues found that eIOL at 37-41 weeks in low-risk pregnancies was associated with decreased risk of extended perinatal mortality compared to expectant management, with the caveat that eIOL appeared to increase the risk of NICU admission (Stock et al 2012). Our findings are encouraging in that we did not observed an increased risk of certain neonatal morbidities, but more research is needed to better elucidate the relationship between eIOL and more serious neonatal morbidities and morality in obese women. Knowing that perinatal morbidity and mortality rates are greater in the early term period compared with delivery at 39-40 weeks of gestation, future studies should continue to characterize these risks in the obese population so clinicians and patients can make informed management decisions about elective induction of labor.

Insights into Delivery Timing and Cost-Effectiveness of Elective Induction of Labor

Our decision-analytic model showed that balancing the risks of early term delivery against the risks associated with expectant management and continued fetal growth, eIOL at 38 weeks in the setting of maternal obesity was the optimal delivery strategy, maximizing maternal and neonatal QALYs. Whereas eIOL at 37 weeks of gestation would minimize the rates of cesarean delivery, stillbirth, and brachial plexus injury, these benefits are offset by an increase in neonatal death and cerebral palsy, both of which were minimized following eIOL at 39 weeks.

While eIOL at 38 weeks was the optimal strategy from an outcomes standpoint, this was not the cheapest delivery strategy. However, eIOL at 38 weeks was incrementally cost-effective compared to later delivery at 39-41 weeks and a dominant strategy compared to earlier delivery at 37 weeks; therefore we can conclude that at a willingness to pay threshold of $100,000 per QALY, eIOL at 38 weeks would be cost-effective delivery strategy in obese women.

The risks of stillbirth and infant death, as well as the costs of induction of labor and cesarean delivery, were key drivers of the model. Our decision-analytic model was robust to variation in these and a variety of other inputs. For example, earlier delivery at 37 weeks only became optimal when the odds of stillbirth in obese women was 25% higher than our baseline input, and eIOL at 39 weeks would only maximize QALYs if obese women had over nine-fold higher odds of infant death compared to normal weight women, which clinically is highly implausible. Further, eIOL at 38 weeks remained incrementally cost-effective despite wide variations in the costs of care, reaffirming that delivering obese women at 38 weeks is a reasonable strategy from both an outcomes and a costs standpoint. However, in the Monte Carlo simulation eIOL at 38 weeks was cost-effective only 53% of the time, so delivery at this gestational age should not necessarily be a blanket management strategy when multiple levels of randomness and uncertainty are considered.

Limitations and Strengths

Strengths of our retrospective cohort study include the large sample size, clearly defined comparison groups, and stratified analyses by parity and gestational age.

Additionally, this is among the first large population-based observational studies to examine eIOL in obese women, which carries public health significance given the burden of maternal obesity.

Our analyses are subject to the inherent limitations of retrospective designs. We rely on vital statistics and hospital discharge data, which cannot assess temporality during the labor course. Additionally, there may be errors in self-reported pre-pregnancy BMI or gestational age dating, especially as dating ultrasounds can be more challenging in obese women, but we would expect these misclassifications to be equally likely in eIOL and expectant management groups, thus biasing our results toward the null and making our estimated measures of association more conservative. We have controlled for measured potential confounding variables in our multivariate analyses, but there could be additional unmeasured confounding variables (e.g., cervical status), and we could not control for other clinical factors such as usual care at each hospital and provider-level differences regarding induction of labor and delivery timing in obese women.

We were underpowered to examine rare secondary outcomes such as brachial plexus injury and respiratory distress syndrome in our multivariable analyses. However, bivariate analyses showed that the overall incidence of such outcomes was quite low in both eIOL and expectant management groups, so differences in the risks of these rare outcomes are not likely to be clinically significant. Furthermore, we were unable to examine perinatal mortality due to linkage with only live birth certificates in this dataset. Future studies on eIOL in the obese population should analyze samples large enough to adequately examine perinatal mortality, especially given the baseline increased risk of stillbirth and infant death in obese women (Chu et al 2007, Chen et al 2009).

Decision analysis is inherently unable to perfectly represent all clinical scenarios or include all the factors that may influence patients, clinicians, and health systems regarding delivery timing and costs of care. Our model offers a view of some of the major outcomes that could be impacted by the timing of eIOL in obese women and a policy of routinely inducing all obese women, but we did not include milder or more transient perinatal morbidities such as postpartum hemorrhage or neonatal hypoglycemia. These outcomes could certainly impact quality of life and cost the health care system. Despite this, we did consider the impact on severe and permanent morbidity and mortality that would be influenced by timing of eIOL and gestational age at delivery.

Additionally, all decision-analytic models rely on previously published literature, which may not be reflective of current clinical practice, subject to bias, or underpowered to examine rare perinatal outcomes. However, we attempted to account for this uncertainty through sensitivity analyses and Monte Carlo simulation. Through these analyses, we found that our results were robust across a wide range of model inputs.

CONCLUSION

Clinical and Public Health Implications

Maternity care is a major public health concern in the United States: as more women enter pregnancy with preexisting obesity, chronic disease, and other high-risk conditions, severe maternal morbidity and maternal mortality rates are steadily increasing, prompting calls to develop a more focused approach to improving maternal health outcomes in this country (Callaghan et al 2012, D’Alton 2010). Clinicians, researchers, and policymakers must collaborate to determine best practices for optimizing obstetric care, especially among obese and other high-risk women.

Given the host of perinatal risks associated with maternal obesity and our findings suggesting that eIOL does not increase the risk of harm, and is in fact associated with a decreased risk of cesarean delivery and macrosomia in some situations, it begs the question: should induction of labor for maternal obesity still be considered “elective”? Currently, maternal obesity in and of itself is not a medical indication for induction of labor, so the standard of care is to expectantly manage these pregnancies. Our study found that induction of labor in the setting of maternal obesity does not appear to increase the risk of harm, and is actually associated with lower proportions of cesarean delivery and complications such as chorioamnionitis and macrosomia in some scenarios.

Although our findings are intriguing, we believe that there is still not enough evidence to definitively say that the benefits of eIOL outweigh risks of expectant management insofar as to recommend that maternal obesity should become a Joint Commission indication criteria for IOL at this time. Additionally, although our decision analytic models suggest a benefit associated with eIOL at 38 weeks, a larger body of evidence is needed before recommending an optimal gestational age of delivery in obese women. However, our study is among the first to examine eIOL in a large population of obese women, so additional research is certainly needed to corroborate our findings and inform future guidelines for managing labor and delivery in obese women.

Regardless of whether policies on delivery timing in obese women change in the future, clinicians should counsel patients on the risks and benefits associated with induction of labor compared to expectant management at term. Obese women who are expectantly managed at term should receive adequate antepartum monitoring, such as fetal non-stress tests, in order to minimize the risk of stillbirth, and women should be adequately counseled on the risks of macrosomia that accompany advancing gestational age.

Our findings can inform policy debates on the costs of obesity in pregnancy as well. Induction of labor for maternal obesity will cost the health system more money compared to expectant management, but our model demonstrated that it is ultimately cost-effective as expectant management until 41 weeks resulted in more cesarean deliveries, maternal deaths, and other long-term sequelae. Whether health care institutions, policymakers, and insurance providers should endorse a policy of routine eIOL in obese women is worth debating, and stakeholders in these discussions should consider the costs of care as health systems across the United States move toward achieving the Triple Aim.

Finally, it is important to consider the value of primary prevention of maternal obesity. Obese women are at an increased risk of several perinatal complications, and of course obesity is associated with poor health outcomes outside of pregnancy. Although clinicians can work to prevent downstream complications of obesity, ultimately reducing the burden of obesity among women of reproductive age will more effectively improve maternal health. Preconception counseling on the perinatal risks associated with maternal obesity and programs to promote maintaining a healthy weight throughout a woman’s reproductive years should be a public health priority.

Future Research

While our retrospective cohort study examined the relationship between term eIOL and perinatal outcomes in a large sample of obese women, there are still groups where this question has not been adequately studied. For example, our retrospective cohort study excluded women with a prior cesarean delivery, but certainly research is needed on the impact of eIOL versus expectant management in this group of obese women. There is a burgeoning body of literature on outcomes following induction of a trial of labor after cesarean (TOLAC) compared to expectant management, and recent data suggests that induction of labor at 39 weeks increases the odds of a vaginal birth after cesarean but also of uterine rupture (Palatnik & Grobman 2015). However, little is known about the risks and outcomes of TOLAC induction compared to expectant management in the obese population.

Future studies should also investigate the optimal timing of delivery and cost-effectiveness of eIOL in morbidly obese and super-obese (BMI ≥50) women. Given the observed dose-response effect between BMI and several adverse perinatal outcomes in prior literature, women with a BMI ≥40 may represent a particularly high-risk group where optimizing delivery timing would be of value. Indeed, our retrospective results suggest that eIOL at 38 weeks is associated with lower odds of cesarean delivery in women with a BMI ≥40, but there were largely no differences in the odds of adverse neonatal outcomes between eIOL and expectant management groups. Additional studies are needed to characterize gestational age-related risks and investigate whether induction of labor could offer benefit in morbidly obese women.

Although our research suggests that eIOL does not increase the risk of cesarean delivery or other adverse perinatal morbidities, ultimately a large, prospective, randomized controlled trial is necessary to fully answer this pressing question in obstetrics. This study design would be able to standardize differences in hospital- and physician-level practice patterns, collect data prospectively that will more accurately characterize the labor course in obese women, and provide the highest level of evidence to definitively study this topic. The Eunice Kennedy Shriver National Institute of Child Health and Development is currently recruiting participants into such a trial, and clinicians, public health practitioners, and patients will surely benefit from this important research (NIH).

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Appendix A: Joint Commission List of Conditions Possibly Justifying Elective Delivery Prior to 39 Weeks Gestation

ICD-9 Code and Shortened Description	
042: Human immunodeficiency virus	651.71: Multiple gestation w/ fetal reduction
641.01, 641.11: Placenta previa	651.81, 651.91: Multiple gestation
641.21: Premature separation of placenta	652.01: Unstable lie
641.31: Coagulation deficiency, hemorrhage	652.61 Multiple gestation, malpresentation
641.81, 641.91: Antepartum hemorrhage	655.01: Fetal central nervous system malformation
642.01, 642.02: Essential hypertension	655.11: Fetal chromosomal abnormality
642.11, 642.12: Renal hypertension	655.31: Fetal damage due to virus
642.21, 642.22: Old hypertension	655.41: Fetal damage due to disease
642.31, 642.32: Transient hypertension	655.51: Fetal damage due to drug
642.41, 642.42: Mild preeclampsia	655.61: Radiat fetal damage
642.51, 642.52: Severe preeclampsia	655.81: Fetal abnormalities
642.61, 642.62: Eclampsia	656.01: Fetal-maternal hemorrhage
642.71, 642.72: Toxemia w/ old hypertension	656.11: Rh isoimmunization
642.91, 642.92: Hypertension	656.21: ABO isoimmunization
645.11: Post-term pregnancy	656.31: Fetal distress
646.21, 646.22: Renal disease	656.41: Intrauterine death
646.71: Liver/biliary tract disorder	656.51: Poor fetal growth
648.01: Diabetes	657.01: Polyhydramnios
648.51, 648.52: Congenital cardiovascular disease	658.01: Oligohydramnios
648.61, 648.62: Cardiovascular disease	658.11: Premature rupture of membranes
648.81, 648.82: Abnormal glucose tolerance	658.21: Prolonged rupture of membranes
649.31, 649.32: Coagulation defect	658.41: Amniontic infection
651.01: Twin pregnancy	659.71: Abnormal fetal heart rate/rhythm
651.11: Triplet pregnancy	663.51: Vasa previa
651.21: Quadruplet pregnancy	V08: Asymptomatic HIV infection
651.31, 651.41, 651.51, 651.61: Twins, triplets, quadruplets, or other multiple gestation with fetal loss	V23.5: Pregnant with poor reproductive history
	V27.1: Delivered single stillborn

Appendix B: List of Intrapartum Indications for Possible Induction of Labor

ICD-9 Code and Shortened Description	
641.21: Premature separation of placenta	641.31: Coagulation deficiency, hemorrhage
641.81, 641.91: Antepartum hemorrhage NEC	642.31, 642.32: Transient hypertension
642.41, 642.42: Mild preeclampsia	642.51, 642.52: Severe preeclampsia
642.61, 642.62: Eclampsia	642.91, 642.92: Hypertension
645.11: Post-term pregnancy	646.71: Liver/biliary tract disorder
649.31: Coagulation defect	656.01: Fetal-maternal hemorrhage
656.11: Rh isoimmunization	656.21: ABO isoimmunization
656.31: Fetal distress	656.41: Intrauterine death
657.01: Polyhydramnios	658.01: Oligohydramnios
658.11: Premature rupture of membranes	658.21: Prolonged rupture of membranes
659.1: Abnormal fetal heart rate/rhythm	V23.5: Pregnancy with poor reproductive history
V27.1: Delivered- single stillborn	

Appendix C: Maternal Bivariate Outcomes by WHO Obesity Class

	Comparison group	N	Cesarean Delivery (%)	Operative Vaginal Delivery (%)	3rd and 4th Degree Perineal Laceration (%)	Postpartum Hemorrhage (%)	Chorioamnionitis (%)
Nulliparous Women							
BMI 30-35							
37 Weeks	eIOL	32	34.4	6.3	3.1	0	0
	Exp Mgmt	9985	35.9	5.8	2.9	2.8	4.3
38 Weeks	eIOL	116	34.4	6.9	0	2.6	2.5
	Exp Mgmt	8246	36.7	5.8	3.0	4.0	4.5
39 Weeks	eIOL	173	31.8	6.3	5.8*	2.3	2.3
	Exp Mgmt	5521	38.1	5.6	2.9	4.3	4.8
40 Weeks	eIOL	187	40.6	4.8	2.1	3.7	2.1
	Exp Mgmt	2302	39.7	5.5	3.0	4.7	5.0
BMI 35-39							
37 Weeks	eIOL	14	28.6	0	0	0	0
	Exp Mgmt	3558	43.7	4.7	2.0	3.5	4.3
38 Weeks	eIOL	47	40.4	4.3	2.1	0	0
	Exp Mgmt	2937	44.3	4.9	2.1	3.7	4.4
39 Weeks	eIOL	68	42.6	5.9	0	4.1	2.9
	Exp Mgmt	1976	45.8	4.8	2.1	3.9	5.2
40 Weeks	eIOL	68	38.2	4.4	2.9	1.5	0
	Exp Mgmt	901	48.6	5.0	2.4	3.8	5.9
BMI 40+							
37 Weeks	eIOL	59	10.2**	5.1	6.8	0	1.7
	Exp Mgmt	16812	27.6	6.1	4.6	2.9	3.5
38 Weeks	eIOL	133	20.3*	5.3	3.8	3.8	1.5
	Exp Mgmt	13530	28.1	6.1	4.7	3.0	3.6
39 Weeks	eIOL	241	24.9	3.7	1.7*	2.5	0**
	Exp Mgmt	8513	30.3	6.4	5.0	3.1	4.3
40 Weeks	eIOL	218	28.4	8.3	5.0	3.2	2.7
	Exp Mgmt	3379	33.6	6.6	5.1	3.8	5.0
Multiparous Women with a Prior Vaginal Delivery							
BMI 30-35							
37 Weeks	eIOL	131	6.9	2.3	0.8	0.8	0
	exp mgmt	16616	9.0	2.7	0.7	2.5	0.7
38 Weeks	eIOL	346	3.8**	3.5	1.4	0.9*	0.6
	exp mgmt	13094	9.0	2.7	0.7	2.6	0.7
39 Weeks	eIOL	493	4.1***	2.8	0.8	2.2	0.8
	exp mgmt	7721	9.0	2.7	0.7	2.8	0.8
40 Weeks	eIOL	332	5.4*	1.8	1.8*	1.8	0
	exp mgmt	2904	9.3	2.6	0.6	2.9	0.6
BMI 35-39							
37 Weeks	eIOL	35	0*	0	0	2.9	0
	exp mgmt	5943	10.4	2.7	0.5	2.5	0.7
38 Weeks	eIOL	130	3.8*	4.6	0.8	3.1	0
	exp mgmt	4705	10.2	2.5	0.5	2.6	0.7
39 Weeks	eIOL	200	4.0**	2.5	1.0	1.5	0.5
	exp mgmt	2849	10.5	2.3	0.4	2.8	0.9
40 Weeks	eIOL	121	9.1	2.5	0.8	0.8	0
	exp mgmt	1100	11.3	2.5	0.5	3.0	1.0
BMI 40+							

37 Weeks	eIOL	116	6.0	0.9	0	1.7	0
	exp mgmt	21343	7.4	2.5	0.8	2.1	0.5
38 Weeks	eIOL	291	3.4**	1.7	0.7	1.0	0.3
	exp mgmt	16578	7.5	2.7	0.8	2.2	0.6
39 Weeks	eIOL	470	5.1*	2.1	0	1.3	0.6
	exp mgmt	9507	7.7	2.6	0.9	2.5	0.6
40 Weeks	eIOL	332	4.5**	1.8	0.6	0.6*	0
	exp mgmt	3507	8.7	2.5	1.0	2.4	0.7

Appendix D: Maternal Multivariate Outcomes by WHO Obesity Class

Gestational Age Group	Cesarean Delivery	Operative vaginal delivery	3rd/4th Degree Perineal Laceration	Postpartum Hemorrhage	Chorioamnio-nitis
Nulliparous					
BMI 30-35					
37 Weeks	1.0 (0.48-2.12)	1.11 (0.26-4.69)	1.09 (0.14-8.04)	-	-
38 Weeks	0.91 (0.62-1.36)	1.28 (0.62-2.67)	-	0.65 (0.21-2.08)	0.54 (0.17-1.72)
39 Weeks	0.72 (0.51-1.01)	1.21 (0.65-2.27)	1.99 (0.99-3.99)	0.55 (0.20-1.49)	0.50 (0.18-1.35)
40 Weeks	1.02 (0.75-1.41)	0.95 (0.47-1.91)	0.76 (0.27-2.11)	0.83 (0.38-1.82)	0.44 (0.16-1.22)
BMI 35-39					
37 Weeks	0.52 (0.16-1.68)	-	-	-	-
38 Weeks	0.82 (0.45-1.51)	0.89 (0.21-3.7)	1.00 (0.13-7.44)	-	-
39 Weeks	0.78 (0.47-1.30)	1.28 (0.45-3.62)	-	1.15 (0.35-3.79)	0.57 (0.14-2.36)
40 Weeks	0.63 (0.37-1.06)	0.93 (0.28-3.12)	1.25 (0.28-5.50)	0.39 (0.05-2.95)	-
BMI 40+					
37 Weeks	0.32 (0.14-0.75)	0.84 (0.26-2.71)	1.52 (0.55-4.22)	-	0.48 (0.06-3.46)
38 Weeks	0.62 (0.39-0.98)	0.80 (0.35-1.83)	0.86 (0.35-2.11)	1.42 (0.58-3.51)	0.45 (0.11-1.83)
39 Weeks	0.77 (0.57-1.04)	0.44 (0.21-0.95)	0.33 (0.12-0.88)	0.71 (0.29-1.74)	-
40 Weeks	0.77 (0.55-1.06)	1.18 (0.70-2.02)	1.09 (0.58-2.05)	0.79 (0.34-1.82)	0.40 (0.15-1.10)
Multiparous with a Prior Vaginal Delivery					
BMI 30-35					
37 Weeks	0.71 (0.36-1.41)	0.86 (0.27-2.71)	-	0.32 (0.04-2.30)	-
38 Weeks	0.40 (0.23-0.70)	1.22 (0.66-2.26)	1.73 (0.59-4.30)	0.34 (0.11-1.06)	0.68 (0.17-2.80)
39 Weeks	0.32 (0.19-0.53)	1.12 (0.64-1.95)	1.04 (0.37-2.91)	0.75 (0.40-1.44)	0.99 (0.35-2.74)
40 Weeks	0.53 (0.32-0.87)	0.78 (0.33-1.82)	3.06 (1.18-7.98)	0.66 (0.28-1.53)	-
BMI 35-39					
37 Weeks	-	-	-	1.18 (0.16-8.75)	-
38 Weeks	0.35 (0.14-0.86)	1.96 (0.84-4.56)	1.49 (0.20-11.3)	1.21 (0.44-3.34)	-
39 Weeks	0.31 (0.14-0.66)	1.20 (0.47-3.05)	1.70 (0.37-7.84)	0.58 (0.18-1.85)	0.64 (0.08-4.78)
40 Weeks	0.84 (0.43-1.61)	1.05 (0.31-3.61)	1.12 (0.13-9.68)	0.31 (0.04-2.29)	-
BMI 40+					
37 Weeks	0.82 (0.38-1.78)	0.34 (0.05-2.45)	-	0.86 (0.21-3.51)	-
38 Weeks	0.46 (0.25-0.88)	0.51 (0.19-1.39)	0.94 (0.23-3.83)	0.50 (0.16-1.58)	0.64 (0.09-4.65)
39 Weeks	0.67 (0.44-1.03)	0.85 (0.44-1.62)	-	0.58 (0.25-1.31)	1.19 (0.37-3.83)
40 Weeks	0.51 (0.30-0.87)	0.70 (0.30-1.63)	0.62 (0.15-2.62)	0.25 (0.06-1.04)	-

Appendix E: Neonatal Bivariate Outcomes by WHO Obesity Class

	eIOL or Expectant Management Group	N	Macrosomia (%)	Shoulder Dystocia (%)	Brachial Plexus Injury (%)	Respiratory Distress Syndrome (%)
Nulliparous						
BMI 30-35						
37	eIOL	32	3.1	0	0	0
	exp mgmt	9985	11.7	1.4	0.2	0.4
38	eIOL	116	5.2*	3.4	0	0
	exp mgmt	8246	13.0	1.4	0.2	0.4
39	eIOL	173	9.2*	1.2	0.6	0
	exp mgmt	5521	14.8	1.8	0.2	0.4
40	eIOL	187	19.2	1.1	0.5	0
	exp mgmt	2302	17.2	2.1	0.2	0.6
BMI 35-39						
37	eIOL	14	14.3	0	0	0
	exp mgmt	3558	13.9	1.2	0.1	0.4
38	eIOL	47	17.0	0	0	2.1
	exp mgmt	2937	15.2	1.3	0.2	0.4
39	eIOL	68	10.3	2.9	0	0
	exp mgmt	1976	16.8	1.6	0.2	0.4
40	eIOL	68	11.8	2.9	2.9***	0
	exp mgmt	901	18.0	1.5	0.1	0.4
BMI 40+						
37	eIOL	59	0*	0	0	0
	exp mgmt	16812	7.8	0.9	0.1	0.2
38	eIOL	133	5.3	1.5	0.7*	0
	exp mgmt	13530	8.7	0.9	0.1	0.2
39	eIOL	241	8.7	1.7	0	0
	exp mgmt	8513	10.0	0.9	0.1	0.2
40	eIOL	218	10.5	0	0	0
	exp mgmt	3379	11.6	0.9	0.2	0.2
Multiparous with a Prior Vaginal Delivery						
BMI 30-35						
37	eIOL	131	4.6*	0.8	0	0
	exp mgmt	16616	14.7	2.0	0.2	0.2
38	eIOL	346	10.7*	0.9	0	0.9*
	exp mgmt	13094	16.2	2.2	0.2	0.2
39	eIOL	493	13.6*	1.2	0	0
	exp mgmt	7721	18.1	2.5	0.2	0.1
40	eIOL	332	17.8	1.8	0	0
	exp mgmt	2904	19.6	2.9	0.3	0.1
BMI 35-39						
37	eIOL	35	11.4	0	0	2.9*
	exp mgmt	5943	17.2	2.3	0.2	0.3
38	eIOL	130	8.5*	0.8	0	0.8
	exp mgmt	4705	18.4	2.3	0.2	0.3
39	eIOL	200	14.5*	2.5	0	1.0*
	exp mgmt	2849	21.0	2.5	0.2	0.2
40	eIOL	121	19.0	1.6	0	0
	exp mgmt	1100	24.3	3.3	0.1	0.2
BMI 40+						
37	eIOL	116	6.9	5.2	0.9*	0

	exp mgmt	21343	11.5	1.6	0.1	0.1
38	eIOL	291	13.1	1.7	0	0
	exp mgmt	16578	12.9	1.8	0.1	0.1
39	eIOL	470	12.1	1.9	0.4	0
	exp mgmt	9507	15.0	2.0	0.1	0.2
40	eIOL	332	18.1	1.5	0	0
	exp mgmt	3507	15.3	1.9	0.1	0.2

Appendix F: Neonatal Multivariate Outcomes by WHO Obesity Class

Gestational Age Group	Macrosomia	Shoulder dystocia	Brachial Plexus Injury	Respiratory Distress Syndrome
Nulliparous				
BMI 30-35				
37 Weeks	0.23 (0.03-1.71)	-	-	-
38 Weeks	0.39 (0.17-0.88)	2.55 (0.92-7.05)	-	-
39 Weeks	0.63 (0.37-1.06)	0.36 (0.05-2.62)	-	-
40 Weeks	1.13 (0.75-1.68)	0.56 (0.13-2.36)	-	-
BMI 35-39				
37 Weeks	1.0 (0.22-4.52)	-	-	-
38 Weeks	1.03 (0.46-2.33)	-	-	5.15 (0.62-42.37)
39 Weeks	0.55 (0.25-1.23)	1.64 (0.38-7.08)	-	-
40 Weeks	0.51 (0.23-1.14)	2.01 (0.43-9.42)	-	-
BMI 40+				
37 Weeks	-	-	-	-
38 Weeks	0.47 (0.19-1.16)	1.81 (0.44-7.42)	6.97 (0.90-53.72)	-
39 Weeks	0.74 (0.46-1.20)	1.84 (0.66-5.12)	-	-
40 Weeks	0.88 (0.55-1.41)	-	-	-
Multiparous with a Prior Vaginal Delivery				
BMI 30-35				
37 Weeks	0.22 (0.09-0.53)	0.36 (0.05-2.63)	-	-
38 Weeks	0.56 (0.40-0.80)	0.24 (0.06-0.96)	-	4.02 (0.92-17.51)
39 Weeks	0.65 (0.50-0.84)	0.49 (0.21-1.11)	-	-
40 Weeks	0.84 (0.62-1.14)	0.66 (0.28-1.52)	-	-
BMI 35-39				
37 Weeks	0.67 (0.23-1.93)	-	-	9.41 (1.18-74.86)
38 Weeks	0.39 (0.21-0.72)	0.31 (0.04-2.25)	-	2.84 (0.35-22.98)
39 Weeks	0.62 (0.41-0.93)	0.87 (0.35-2.20)	-	4.57 (0.87-24.05)
40 Weeks	0.69 (0.43-1.12)	0.42 (0.10-1.77)	-	-
BMI 40+				
37 Weeks	0.54 (0.26-1.10)	3.15 (1.37-7.24)	7.49 (0.98-56.91)	-
38 Weeks	0.91 (0.64-1.31)	0.76 (0.28-2.05)	-	-
39 Weeks	0.70 (0.42-0.94)	0.98 (0.49-1.92)	3.74 (0.80-17.43)	1.43 (0.18-11.16)
40 Weeks	1.20 (0.88-1.12)	0.76 (0.30-1.90)	-	-