Of the 1.5 million nulliparous women who deliver annually in the United States, more than 50% are low-risk pregnancies. Among clinicians, there is a hesitancy to offer elective induction of labor to low-risk nulliparous women, mainly due to early observational studies that noted an association between elective induction of labor and higher rates of cesarean delivery (CD) and other adverse maternal and perinatal outcomes.1-3 This reluctance over time has permeated throughout the ObGyn specialty and is culturally embedded in contemporary practice. The early observational studies lacked proper comparison groups because outcomes of women undergoing induction (elective and medically indicated) were compared to those in spontaneous labor. Since women who are being induced do not have the option to be in spontaneous labor, the appropriate comparator group for women undergoing elective induction is women who are being managed expectantly.

ARRIVE addresses appropriate comparator groups

Challenging this pervaded practice, in August 2018, Grobman and colleagues published the findings of the ARRIVE trial (A Randomized Trial of Induction Versus Expectant Management).4 This trial, conducted by Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, recruited participants from 41 geographically dispersed centers in the United States. Nulliparous women with low-risk pregnancies between 34 0/7 and 38 6/7 weeks were randomly assigned to either induction of labor at 39 0/7 to 39 4/7 weeks or to expectant management, which was defined as delaying induction until 40 5/7 to 42 2/7 weeks. The objective of the ARRIVE trial was to determine if, among low-risk nulliparous women, elective induction of labor at 39 weeks, compared with expectant management, would reduce the rate of adverse outcomes.

The primary outcome was a composite: perinatal death or severe neonatal complications (need for respiratory support within 72 hours of birth, Apgar score of ≤ 3 at 5 minutes, hypoxic-ischemic encephalopathy, seizures, infection [confirmed sepsis or pneumonia], meconium aspiration syndrome, birth trauma [bone fracture, neurologic injury, or retinal damage], intracranial or subgaleal hemorrhage, or hypotension requiring vasopressor support). The secondary outcomes included CD, hypertensive disorders of pregnancy, number of hours in the labor and delivery (L&D) unit, length of postpartum hospital stay, and assessment of satisfaction with labor process.

Mothers induced at 39 weeks fared better, while neonatal outcomes were similar. Of 22,533 eligible women, 6,106 (27%) were randomized: 3,062 were assigned to the induction group, and 3,044 to the expectant management group. The primary composite outcome—perinatal death or severe neonatal complications—was similar in both groups (4.3% in the induction group vs 5.4% in the expectant management group).

However, women who were induced had significantly lower rates of:

- CD (18.6% with induction vs 22.2%
The primary outcome was composite neonatal morbidity that included maternal and neonatal morbidity, the risk of composite neonatal morbidity was significantly higher for those delivered at 40 (adjusted RR [aRR], 1.22; 95% CI, 1.19–1.25) and 41 weeks (aRR, 1.53; 95% CI, 1.49–1.58).

The secondary outcome, the overall rate of composite maternal morbidity, was 2.8 per 1,000 live births. As with composite neonatal morbidity, the risk of composite maternal morbidity was also significantly higher for those delivered at 40 (aRR, 1.19; 95% CI, 1.14–1.25) and 41 weeks’ gestation (aRR, 1.56; 95% CI, 1.47–1.65) than at 39 weeks.

Thus, among low-risk nulliparous pregnancies, there is an incremental increase in the rates of composite neonatal and maternal morbidity from 39 to 41 weeks.

Is induction of labor at 39 weeks feasible?
As the evidence demonstrating multiple benefits of 39-week inductions increases, concerns regarding the feasibility and cost of implementation in the current US health care system mount. A planned secondary analysis of the ARRIVE trial evaluated medical resource utilization among low-risk nulliparous women randomly assigned to elective induction at 39 weeks or expectant management. Resource utilization was compared between the 2 groups during the antepartum period, delivery admission, and from discharge to 8 weeks postpartum.

For the antepartum period, women in the induction group were significantly less likely than women undergoing expectant management to have at least 1: office visit for routine prenatal care (32.4% vs 68.4%), unanticipated office visit (0.5% vs 2.6%), urgent care/emergency department/triage visit (16.2% vs 44.3%), or hospital admission (0.8% vs 2.2%). When admitted for delivery, as expected, women in the induction group spent significantly more time on the L&D unit (14 hours vs 20 hours) and were more likely to receive interventions for induction (cervical ripening, oxytocin, intrauterine pressure catheter placement). However, they required magnesium sulfate and antibiotics significantly less frequently. For the postpartum group comparison, women in the induction group and their neonates had a significantly shorter duration of hospital stay.

In summary, the investigators found that, compared to women undergoing expectant management, women undergoing elective induction spent longer duration in L&D units and utilized more resources, but they required significantly fewer antepartum clinic and hospital visits, treatments for hypertensive disorders or chorioamnionitis, and had shorter duration of postpartum length of stay.

Is induction of labor at 39 weeks cost-effective?
Hersh and colleagues performed a cost-effectiveness analysis for induction of labor at 39 weeks versus expectant management for low-risk nulliparous women. Based on 2016 National Vital Statistics Data, there were 3.5 million term births in the United States. Following the exclusion of high-risk pregnancies and term parous low-risk pregnancies, a theoretical cohort of 1.6 million low-risk nulliparous women was included in the analysis. A decision-tree
analytic model was created, in which the initial node stratified low-risk nulliparous women into 2 categories: elective induction at 39 weeks and expectant management. Probabilities of maternal and neonatal outcomes were derived from the literature.

Maternal outcomes included hypertensive disorders of pregnancy and delivery mode. Neonatal outcomes included macrosomia, shoulder dystocia, brachial plexus injury, stillbirth, and neonatal death. Costs of clinic and triage visits, induction of labor, modes of delivery, and maternal and neonatal outcomes were derived from previous studies and adjusted for inflation to 2018 dollars. Finally, quality-adjusted life years (QALYs) were calculated for mothers and neonates and were then used to estimate the incremental cost-effectiveness ratio (ICER) of elective induction of labor at 39 weeks. Following accepted standards, the threshold for cost-effectiveness was set at $100,000/QALY or less.

**Induction at 39 weeks comes in lower cost-wise than the standard threshold for QALY.** In their analysis, the investigators found that if all 1.6 million women in their theoretical cohort underwent an elective induction of labor at 39 weeks (rather than expectant management), there would be approximately 54,498 fewer CDs, 79,152 fewer cases of stillbirth, and 795 fewer CDs, 79,152 fewer cases of stillbirth, and 11 fewer neonatal deaths. Due to the decreased CD rates, the investigators did project an estimated 86 additional cases of neonatal brachial plexus injury. Using these estimates, costs, and utilities, the authors demonstrated that, compared with expectant management, elective induction of labor at 39 weeks was marginally cost-effective with an ICER of $87,692 per QALY, which was lower than the cost-effectiveness threshold of $100,000 per QALY.

Based on additional sensitivity analyses, the authors concluded that cost-effectiveness of elective induction of labor varied based on variations in model inputs. Specifically, the authors demonstrated that cost-effectiveness of induction of labor varied based on labor induction techniques, modes of delivery, and fluctuations in the rates of CD in induction versus expectant management groups.

Despite these theoretically imputed findings, the authors acknowledged the limitations of their study. Their cost-effectiveness model did not account for costs associated with long-term health impact of CD and hypertensive disease of pregnancy. Additionally, their model did not account for an increase in cost and resource utilization associated with increased time on L&D units to accommodate women undergoing induction. Furthermore, the analysis did not take into account the bundled payments for vaginal versus CDs, which are increasing in prevalence. Lastly, the analysis did not consider the incremental increase in severe neonatal and maternal morbidity from 39 to 41 weeks that Chen et al found in their study.

**Will ARRIVE finally arrive?**

Cognizant of the medical and economic benefits of 39-week inductions, the Society for Maternal-Fetal Medicine and the American College of Obstetricians and Gynecologists published a joint practice advisory recommending “shared decision-making” when counseling low-risk women about induction. While more research is needed to validate the aforementioned findings, particularly in regard to resource utilization, the ARRIVE trial and its associated analyses suggest that a reconsideration to deliver term low-risk nulliparous women at 39 weeks is warranted.

In summary, the overwhelming evidence suggests that, among low-risk nulliparous women there are maternal and neonatal benefits with delivery at 39 weeks, as compared with expectant management. Logistic concerns should not interfere with women’s desideratum for optimal outcomes.

### References


