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SMFM Statement

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SMFM Statement on Elective Induction of Labor in Low-Risk Nulliparous Women at Term: the ARRIVE Trial

Society of Maternal-Fetal (SMFM) Publications Committee

A Randomized Trial of Induction Versus Expectant Management (ARRIVE) was conducted by the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network from March 2014 to August 2017.This large multicenter, unmasked, randomized controlled trial was performed to test the hypothesis that elective IOL at 39 weeks of gestation, compared with expectant management among low-risk nulliparous women, reduces the risk of a composite outcome of perinatal death or severe neonatal morbidity. Nulliparous women with reliable dating and no obstetric or medical complications were eligible, regardless of favorability of cervical examination. The purpose of this document is to review the findings of the recent randomized trial and to provide guidance for implementation of the study findings.

Historically, elective induction of labor (IOL) has been regarded as harmful, with an increased risk of cesarean delivery and worse perinatal outcomes than spontaneous labor. This perception results from older observational cohort studies in which women who were induced were compared with women in spontaneous labor at the same gestational age.[1–4] Over time, investigators recognized that this was not an appropriate comparison, because spontaneous labor is not an option that can be chosen. Rather, the available clinical options are IOL vs expectant management with either the onset of spontaneous labor or IOL for obstetric indications at a later date. During a period of expectant management, complications can arise that may make an uncomplicated vaginal birth less likely.[5–7] When women who underwent IOL were compared with those who were treated expectantly in observational cohorts, IOL was associated with similar or lower rates of cesarean delivery and perinatal morbidity.[8–11] Given these observational data, the need for a randomized trial that would compare outcomes among low-risk nulliparous women whose labor was induced at 39 weeks of gestation with those expectantly managed became apparent.

The purpose of this document is to review the findings of a recent randomized trial of IOL vs expectant management in low-risk nulliparous women at 39 weeks of gestation and to provide guidance for implementation of the study findings. The primary outcome of the study was a composite of perinatal death or severe neonatal morbidity; the principal secondary outcome was cesarean delivery.

A Randomized Trial of Induction Versus Expectant Management (ARRIVE) was conducted by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network from March 2014 to August 2017.[12] ARRIVE was a large multicenter, unmasked, randomized controlled trial to test the hypothesis that elective IOL at 39 weeks of gestation, compared with expectant management among low-risk nulliparous women, reduces the risk of a composite outcome of perinatal death or severe neonatal morbidity.

Nulliparous women with reliable dating and no obstetric or medical complications were eligible, regardless of favorability of cervical examination. Of the 22,533 women who were eligible for participation, 27% (n=6106) enrolled. Recruitment occurred at 41 academic and community-based hospitals, with 3062 women randomly assigned to the IOL group and 3044 women randomly assigned to the expectant treatment group. Randomization occurred between 38 weeks 0 days and 38 weeks 6 days of gestation; women in the IOL group planned to undergo induction from 39 weeks 0 days through 39 weeks 4 days of gestation. Women in the expectant management group were asked to undergo induction only if medically indicated at <40 weeks 5 days of gestation, and all women were to be delivered by 42 weeks 2 days of gestation.

Most of the enrolled women (63%) had an unfavorable cervix, which was defined as a modified Bishop score <5, at the time of randomization. A cervical ripening agent was requested to be used for women with an unfavorable cervix,

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but the method of ripening and management of the first and second stages of labor were not specified in the protocol. If there was no acute maternal or fetal indication for delivery, providers were asked to allow at least 12 hours after completion of cervical ripening, rupture of membranes, and use of a uterine stimulant before considering cesarean delivery for the indication of "failed" induction with the patient in the latent phase. However, labor management was ultimately at the discretion of the obstetric care providers, including the decision and time for cesarean delivery for any indication.

The primary outcome was a composite of perinatal death or severe neonatal morbidity, which included perinatal death, need for respiratory support within 72 hours, Apgar score ≤3 at 5 minutes, hypoxic ischemic encephalopathy, seizures, confirmed sepsis or pneumonia, meconium aspiration syndrome, birth trauma, intracranial or subgaleal hemorrhage, or hypotension that required support. The prespecified major maternal outcome was cesarean delivery. Other secondary outcomes included cesarean delivery indication, operative vaginal delivery and indication, third- or fourth-degree lacerations, gestational hypertension/preeclampsia, chorioamnionitis, postpartum hemorrhage, and intensive care unit admission.

Women in the IOL group were delivered earlier than those in the expectant management group, at a mean gestational age of 39.3 weeks vs 40.0 weeks ($P<.001$). Almost all women adhered to their allocated treatment group (94% in the IOL group and 95% in the expectant management group). Although the primary neonatal composite outcome of perinatal death or severe morbidity was lower in the IOL group vs the expectant management group (4.3% IOL group vs 5.4% expectant treatment group; RR, 0.80; 95% confidence interval, 0.64−1.00; P=.049), this difference did not reach the probability value threshold of .046 that was preset to account for an interim analysis. There were, however, differences in maternal outcomes, which included cesarean delivery in the IOL group compared with the expectant management group (18.6% vs 22.2%; RR, 0.84; 95% confidence interval, 0.76−0.93; $P<.001$). In addition, the incidence of hypertensive disorders of pregnancy (preeclampsia and gestational hypertension) was lower in the IOL group (9.1% vs 14.1%; RR, 0.64; 95% confidence interval, 0.56−0.74; $P<.001$). To prevent 1 cesarean delivery, the investigators concluded that 28 low-risk nulliparous women would need to undergo elective IOL at 39 weeks of gestation.

In conclusion, the ARRIVE investigators evaluated outcomes for IOL vs expectant management in otherwise healthy low-risk nulliparous women with no medical or obstetric indication for IOL and found no statistically significant difference in their primary perinatal outcomes. However, the reductions in the rate of primary cesarean delivery and in hypertensive disorders of pregnancy were notable findings. Given the findings of this study, it is reasonable to offer elective IOL to women who meet study eligibility criteria. Because there was no difference in the primary neonatal outcome between groups, women can be reassured that both elective IOL and expectant management are reasonable options at 39 weeks of gestation. It is unknown whether the findings can be extrapolated to multiparous women. In addition, women with medical or obstetric conditions that necessitate IOL should continue to be delivered at a time that is consistent with standard recommendations and guidelines for each condition.[13,14]

Shared decision-making when counseling women about elective IOL is critical. For some women, the benefits of decreased cesarean delivery rates and decreased risk of gestational hypertension/preeclampsia will be sufficient reason to choose an elective IOL. For others, expectant treatment with the possibility of entering spontaneous labor will be preferred. Although there was a high degree of satisfaction with IOL among the trial participants, this information may not be generalizable, because women who enrolled in the trial were willing to be assigned randomly to the IOL arm.

If elective IOL is implemented in practice for low-risk nulliparous women, providers must consider the circumstances under which the trial was conducted. Importantly, all women in this trial had dating confirmed by early ultrasonography. For women who were sure of their last menstrual period, ultrasonography for confirmation of dating occurred at <21 weeks of gestation. In cases of an uncertain last menstrual period, only women with a first-trimester ultrasound examination for dating were enrolled. Confidence in the estimated date of delivery with the use of early ultrasonography will be imperative in clinical practice to avoid an iatrogenic early term or preterm delivery for women who elect IOL at 39 weeks of gestation. Early term neonates (37 weeks 0 days to 38 weeks 6 days of gestation) have an increased risk of respiratory morbidity,[15] and elective IOL at <39 weeks of gestation should not be undertaken.

Other questions remain, including how generalizable these findings will be to settings outside of a clinical trial or to institutions with cesarean delivery rates that are lower or higher than those of the participating centers. In addition,

Summary of Recommendations

	Recommendations
1	It is reasonable to offer elective induction of labor to low-risk nulliparous women ≥39 weeks 0 days of gestation. We recommend that providers who choose this approach ensure that women meet eligibility criteria of the ARRIVE trial.
2	We recommend against offering elective induction of labor to women under circumstances that are inconsistent with the ARRIVE study protocol unless performed as part of research or quality improvement.
3	We recommend that further research be conducted to measure the impact of this practice in settings other than a clinical trial.

there is concern from centers about how to accommodate women who desire elective IOL when all induction slots are taken by women who have medical or obstetric indications for delivery. Finally, the cost implications of elective IOL are not yet known but will become available with planned secondary analyses. Offering elective IOL will depend not only on patient preferences but also on the capacity of the facility and available staff, including nurses and anesthesiologists. More data about the impact of implementation on resource use in different clinical settings and practices across the United States are needed.

Despite these remaining questions, this large trial demonstrates that IOL in low-risk nulliparous women at 39 weeks of gestation does not have adverse neonatal effects and provides maternal benefit, with a decrease in rates of cesarean delivery and gestational hypertension/preeclampsia.

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From the Society for Maternal-Fetal Medicine, Washington, DC.

All authors and committee members have filed a conflict of interest disclosure delineating personal, professional, and/or business interests that might be perceived as a real or potential conflict of interest in relation to this publication. Any conflicts have been resolved through a process approved by the executive board. The Society for Maternal-Fetal Medicine has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

This document has undergone an internal peer review through a multilevel committee process within the Society for Maternal-Fetal Medicine (SMFM). This review involves critique and feedback from the SMFM Publications and Document Review Committees and final approval by the SMFM Executive Committee. SMFM accepts sole responsibility for document content. SMFM publications do not undergo editorial and peer review by the American Journal of Obstetrics & Gynecology. The SMFM Publications Committee reviews publications every 18-24 months and issues updates as needed. Further details regarding SMFM Publications can be found at www.smfm.org/publications.

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The American College of Obstetricians and Gynecologists (ACOG) endorses this document.

  https://doi.org/10.1016/j.ajog.2018.08.009