

# Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies



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**BACKGROUND:** Elective induction of labor at 39 weeks among low-risk nulliparous women has reduced the chance of cesarean and other adverse maternal and perinatal outcomes in a randomized trial, although its clinical effectiveness in nonresearch settings remains uncertain.

**OBJECTIVE:** To perform a systematic review of observational studies that compared elective induction of labor at 39 weeks among nulliparous women with expectant management and to use meta-analytic techniques to estimate the association of elective induction with cesarean delivery, as well as other maternal and perinatal outcomes.

**STUDY DESIGN:** Studies were eligible for this meta-analysis only if they: (1) were observational; (2) compared women undergoing labor induction at 39 weeks with women undergoing expectant management beyond that gestational age; (3) included women in the induction group only if they had no other indication for labor induction at 39 weeks; and (4) provided data specifically for nulliparous women. The predefined primary outcome was cesarean delivery, and secondary outcomes representing other maternal and perinatal morbidities also were evaluated. Outcome data from different studies were combined to estimate pooled relative risks with 95% confidence intervals using random-effects models.

**RESULTS:** Of 375 studies identified by the initial search, 6 cohort studies, which included 66,019 women undergoing elective labor induction at 39 weeks and 584,390 undergoing expectant management, met inclusion criteria. Elective induction of labor at 39 weeks was associated with a significantly lower frequency of cesarean delivery (26.4% vs 29.1%; relative risk, 0.83; 95% confidence interval, 0.74–0.93), as well as of peripartum infection (2.8% vs 5.2%; relative risk, 0.53; 95% confidence interval, 0.39–0.72). Neonates of women in the induction group were less likely to have respiratory morbidity (0.7% vs 1.5%; relative risk, 0.71; 95% confidence interval, 0.59–0.85); meconium aspiration syndrome (0.7% vs 3.0%; relative risk, 0.49; 95% confidence interval, 0.26–0.92); and neonatal intensive care unit admission (3.5% vs 5.5%; relative risk, 0.80; 95% confidence interval, 0.72–0.88). There also was a lower risk of perinatal mortality (0.04% vs 0.2%; relative risk, 0.27; 95% confidence interval, 0.09–0.76).

**CONCLUSION:** This meta-analysis of 6 cohort studies demonstrates that elective induction of labor at 39 weeks, compared with expectant management beyond that gestational age, was associated with a significantly lower risk of cesarean delivery, maternal peripartum infection, and perinatal adverse outcomes, including respiratory morbidity, intensive care unit admission, and mortality.

**Key words:** cesarean delivery, elective labor induction, labor induction, low risk, maternal complications, nulliparity, nulliparous, observational studies, perinatal complications

For many years, elective labor induction among low-risk nulliparous women at full term was thought to increase the chance of cesarean delivery.<sup>1–3</sup> However, this belief was founded on observational studies in which women undergoing labor induction were not compared with those undergoing the actual clinical alternative of expectant management, but inappropriately, with those in spontaneous labor.<sup>4</sup>

Randomized trials, however, have not supported the association between labor induction in nulliparous women and the risk of cesarean delivery. Hannah et al found that women randomized to planned induction of labor at 41 weeks had a significantly lower risk of cesarean delivery as compared with women managed expectantly beyond this gestation.<sup>5</sup> In subsequent trials by Miller et al (N = 162) and Walker et al (N = 619), no increase in cesarean delivery frequency was found for nulliparous women randomized to planned induction at 39 weeks.<sup>6,7</sup> In the A Randomized Trial of Induction Versus Expectant Management (ARRIVE) study, published in 2018, more than 6000 women were randomized to planned induction at 39 weeks or expectant management.<sup>8</sup> This study demonstrated a significant decrease in the cesarean delivery rate, as well as in the frequency of other adverse outcomes such as hypertensive disorders of pregnancy and neonatal respiratory complications.

After publication of the ARRIVE trial, the American College of Obstetricians and Gynecologists produced a Practice

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Received Dec. 13, 2018; revised Feb. 18, 2019; accepted Feb. 20, 2019.

The authors report no conflict of interest.

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## AJOG at a Glance

### Why was the study conducted?

In the “A Randomized Trial of Induction Versus Expectant Management” trial, women randomized to induction at 39 weeks (vs expectant management) had a significant decreased frequency of cesarean delivery, hypertensive disorders of pregnancy, and neonatal respiratory complications. However, there has been concern whether the results are generalizable to clinical practice outside of a research trial.

### Key findings

In this meta-analysis of observational studies, including 66,019 nulliparous women undergoing elective labor induction at 39 weeks and 584,390 undergoing expectant management, induction at 39 weeks was associated with a significantly lower frequency of cesarean delivery and peripartum infection, as well as of neonatal respiratory morbidity, meconium aspiration syndrome, neonatal intensive care unit admission, and perinatal mortality.

### What does this add to what is known?

These results provide evidence that results from the “A Randomized Trial of Induction Versus Expectant Management” trial do not appear to be particular to a research trial or setting.

Advisory, endorsed by the Society of Maternal–Fetal Medicine (SMFM), stating that it was “reasonable for obstetricians and health-care facilities to offer elective induction of labor to low-risk nulliparous women at 39 weeks gestation.”<sup>9</sup> In a document with additional guidance, the SMFM also noted that this recommendation may be conditional on “the setting in which the intervention will be implemented,” given the concern whether the results are generalizable to clinical practice outside of a research trial.<sup>10</sup>

One approach to understanding the consequences of elective induction in typical clinical practice is through observational analyses that are conducted in a broad range of clinical settings. The goals of our study, therefore, were to identify observational studies that compared elective induction of labor at 39 weeks among nulliparous women with expectant management, and to estimate, using meta-analytic techniques, the association of elective induction with cesarean delivery, as well as other maternal and perinatal outcomes.

## Methods

### Search strategy

A literature search was performed that used PubMed, EMBASE, and the

Cochrane Library to identify articles based on the keywords and phrases “labor,” “induction,” and “expectant.” The search was not limited by time, and no language restrictions were imposed. The reference lists from each article were further reviewed to identify other relevant articles that had not been uncovered by the initial database search.

### Study selection

To be eligible for inclusion in this meta-analysis, studies had to meet several criteria. Specifically, studies were included only if they: (1) were observational; (2) compared women undergoing labor induction at 39 weeks with women undergoing expectant management beyond that gestational age; (3) included women in the induction group only if they had no other indication for labor induction at 39 weeks; and (4) either included only nulliparous women or, when women of varying parity were analyzed, provided results stratified by parity such that results specific for nulliparous women could be ascertained. Studies were excluded if they were randomized trials, or were observational studies that did not provide data for nulliparous women specifically, or had women in the induction group with other medical indication for delivery or

with gestational ages beyond 39 weeks that overlapped with the gestational ages of women in the expectant management group.

Studies identified through the literature search had their abstracts examined by one author (W.A.G.) to determine whether they were potentially eligible for inclusion. Those studies that clearly were not eligible (eg, randomized trials, observational studies that compared women undergoing induction with those in spontaneous labor) were not evaluated further, whereas those that remained had their full text reviewed independently by both authors (W.A.G., A.B.C.) to ensure applicability for the present analysis. Any disagreements that arose in this full-text review were resolved by discussion.

### Outcome measures

The predefined primary outcome in this study was the frequency of cesarean delivery. Secondary maternal outcomes included peripartum infection, postpartum hemorrhage, and third- or fourth-degree perinatal laceration. Secondary perinatal outcomes included respiratory morbidity (defined by the need for additional respiratory support such as continuous positive airway pressure, high-flow oxygen, or mechanical ventilation), meconium aspiration syndrome, hyperbilirubinemia, neonatal intensive care unit admission, and perinatal death.

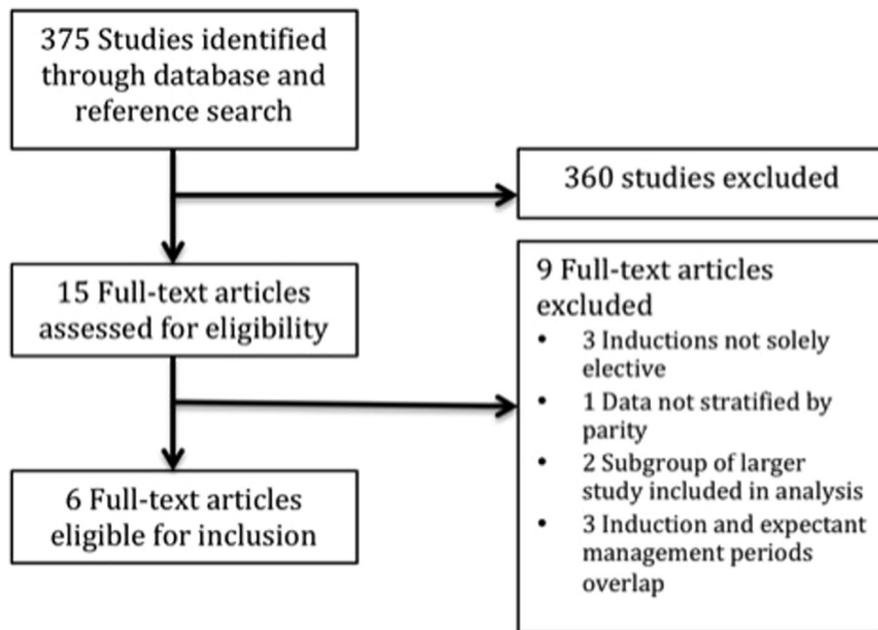
### Risk of bias assessment

Risk of bias was assessed using the Newcastle Ottawa scale.<sup>11</sup> This scale evaluates 3 quality parameters (selection, comparability, and outcome) divided into 8 specific items, each which garners a point if it is considered adequate. Studies with scores lower than 5 points were categorized as having a high risk of bias. All studies were assessed by both authors (W.A.G. and A.B.C.) with discussion used to resolve any discrepancies.

### Data extraction and synthesis

Data from studies were extracted by one author (W.A.G.) and checked for accuracy by the other (A.B.C.). Outcome data from different studies were combined to

**FIGURE 1**  
Flow diagram of study selection process



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estimate pooled relative risks (RRs) with 95% confidence intervals (CIs) using random-effects models. Heterogeneity was assessed using the  $I^2$  statistic, with a value greater than 75% considered an indication of high heterogeneity.<sup>12</sup> It was planned that publication bias would be evaluated using funnel plots and sensitivity analysis would be performed to interrogate potential sources of heterogeneity if at least 10 eligible studies were available.

Statistical analyses were performed with Review Manager, version 5.3 (Cochrane, London, UK). A  $P < .05$  was used to define statistical significance and all tests were 2-tailed. This study was exempt from institutional review board approval, given that only publicly available data were used. This meta-analysis was registered on PROSPERO (CRD42018115093).

## Results

### Study selection and characteristics

Of 375 studies identified by the initial search, only 15 met the criteria for full-text review.<sup>13–27</sup> Of these studies, an

additional 7 were determined to be ineligible because the indications for delivery in the induction group were not solely elective,<sup>13–15</sup> outcome data were not stratified by parity,<sup>16</sup> or the elective inductions performed occurred throughout the period during which women underwent expectant management.<sup>17–19</sup> The remaining 8 cohort studies were potentially eligible for inclusion in this analysis (Figure 1). Two of these studies,<sup>20,21</sup> however, were analyses of subgroups (ie, women older than the age of 35 years or who were obese) derived from a general population that had been evaluated in its entirety in another study,<sup>22</sup> and thus these 2 subgroup studies were excluded. Also, 2 studies had overlapping study populations—1 of these studies<sup>23</sup> evaluated the same population, but over a shorter time frame, as another eligible study.<sup>24</sup> However, not all reported outcomes were identical in the 2 studies. Thus, when a given outcome was reported in both studies, only data from the larger study were used in the meta-analysis; alternatively, if an outcome was only

reported in the smaller study, then those data were included.

Table 1 provides characteristics of the eligible studies, which included 66,019 women undergoing elective labor induction at 39 weeks and 584,390 women undergoing expectant management beyond 39 weeks of gestation. All studies were in English, from the United States, and included women from multiple institutions. Four studies relied on data from administrative databases,<sup>22–24,26</sup> whereas 2 used data that had been concurrently collected according to specific research protocols.<sup>22,26</sup> No study stratified results by baseline cervical status before the exposure (ie, before induction of labor or expectant management). One study stratified cesarean delivery (but not other outcomes) by cervical status at admission for delivery<sup>24</sup>; in the present meta-analysis, data for cesarean were combined such that data for the overall study population were used. Four of the studies evaluated a general obstetric population,<sup>22,25–27</sup> whereas 2 focused on women with obesity.<sup>23,24</sup> All 6 studies, according to the scores derived from the Newcastle Ottawa scale, were noted to have a low risk of bias.

### Primary outcome

All studies provided data for the primary outcome of cesarean delivery. Figure 2, A presents the forest plot with pooled RRs and 95% CIs for this outcome. There was significant heterogeneity for this outcome among studies as indicated by the high  $I^2$  value. Elective induction of labor at 39 weeks was associated with a significantly lower frequency of cesarean (26.4% vs 29.1%; RR, 0.83; 95% CI, 0.74–0.93;  $P = .002$ ). Based on these data, 1 cesarean delivery would be avoided for every 37 women who underwent elective labor induction at 39 weeks.

### Secondary outcomes

Results for maternal secondary outcomes are presented in Figure 2, B–D. The outcome of peripartum infection had an  $I^2$  that indicated high heterogeneity, whereas the other 2 maternal outcomes did not have high

**TABLE 1**  
**Characteristics of included studies**

Author, year	Data source	Years of study	39-week induction (N)	Expectant management (N)	Restrictions to study population <sup>a</sup>	Risk of bias
Bailit et al, 2015 <sup>22</sup>	APEX study	2008-2011	815	23,212	None	Low
Cheng et al, 2012 <sup>27</sup>	Vital Statistics birth certificate registry	2005	42,769	278,578	None	Low
Darney et al, 2013 <sup>25</sup>	California linked birth data	2006	6809	144,898	None	Low
Gibbs et al., 2018 <sup>24</sup>	California linked birth data	2007-2011	13,568	95,094	Prepregnancy BMI $\geq 30$ kg/m <sup>2</sup>	Low
Gibson et al, 2014 <sup>26</sup>	Consortium on Safe Labor	2002-2008	1576	26,605	None	Low
Lee et al, 2016 <sup>23</sup>	California linked birth data	2007	482	16,003	Prepregnancy BMI $\geq 30$ kg/m <sup>2</sup>	Low

APEX, Assessment of Perinatal Excellence; BMI, body mass index.

<sup>a</sup> Other than the eligibility restrictions of nulliparous women with singleton gestations without medical indication for delivery at 39 weeks.

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heterogeneity. Elective labor induction was associated with a reduced chance of peripartum infection (2.8% vs 5.2%; RR, 0.53; 95% CI, 0.39–0.72;  $P < .0001$ ). Conversely, the risks of postpartum hemorrhage (5.2% vs 4.0%; RR, 0.87; 95% CI, 0.54–1.41;  $P = .46$ ) as well as third- or fourth-degree perineal laceration (6.7% vs 6.4%; RR, 0.91; 95% CI, 0.78–1.07;  $P = .26$ ) were similar between groups.

Results for neonatal secondary outcomes are presented in Figure 3, A–E. Respiratory morbidity was reported in 5 studies, whereas other neonatal outcomes were reported in a smaller number of studies. The only perinatal outcome with a high level of heterogeneity was meconium aspiration syndrome. Elective labor induction at 39 weeks was associated with lower frequencies for 4 of the 5 neonatal morbidities that were evaluated: respiratory morbidity (0.7% vs 1.5%; RR, 0.71; 95% CI, 0.59–0.85;  $P < .001$ ); meconium aspiration syndrome (0.7% vs 3.0%; RR, 0.49; 95% CI, 0.26–0.92;  $P = .03$ ); neonatal intensive care unit admission (3.5% vs 5.5%; RR, 0.80; 95% CI, 0.72–0.88;  $P < .0001$ ); and perinatal mortality (0.04% vs 0.2%; RR, 0.27; 95% CI, 0.09–0.76;  $P = .01$ ). There was no difference in the

frequency of hyperbilirubinemia (12.6% vs 12.2%; RR, 1.13; 95% CI, 0.89–1.44;  $P = .31$ ).

## Discussion

### Main findings

In this study, we identified 6 cohort studies that compared women undergoing elective (ie, nonmedically indicated) labor induction at 39 weeks with expectant management beyond that gestational age.<sup>21–26</sup> Summary RRs demonstrate that induction of labor at 39 weeks was associated with a significantly lower risk of cesarean delivery as well as peripartum infection, and no difference in postpartum hemorrhage or severe perineal lacerations. In addition, perinatal benefits associated with labor induction included less respiratory morbidity, intensive care unit admission, and mortality.

This meta-analysis only included observational studies, in an effort to discern whether the results would be similar to those of a recent large randomized trial that compared women randomly assigned to planned labor induction at 39 weeks with those assigned to expectant management.<sup>8</sup> Evaluation of such observational studies is important to better understand whether the efficacy of an

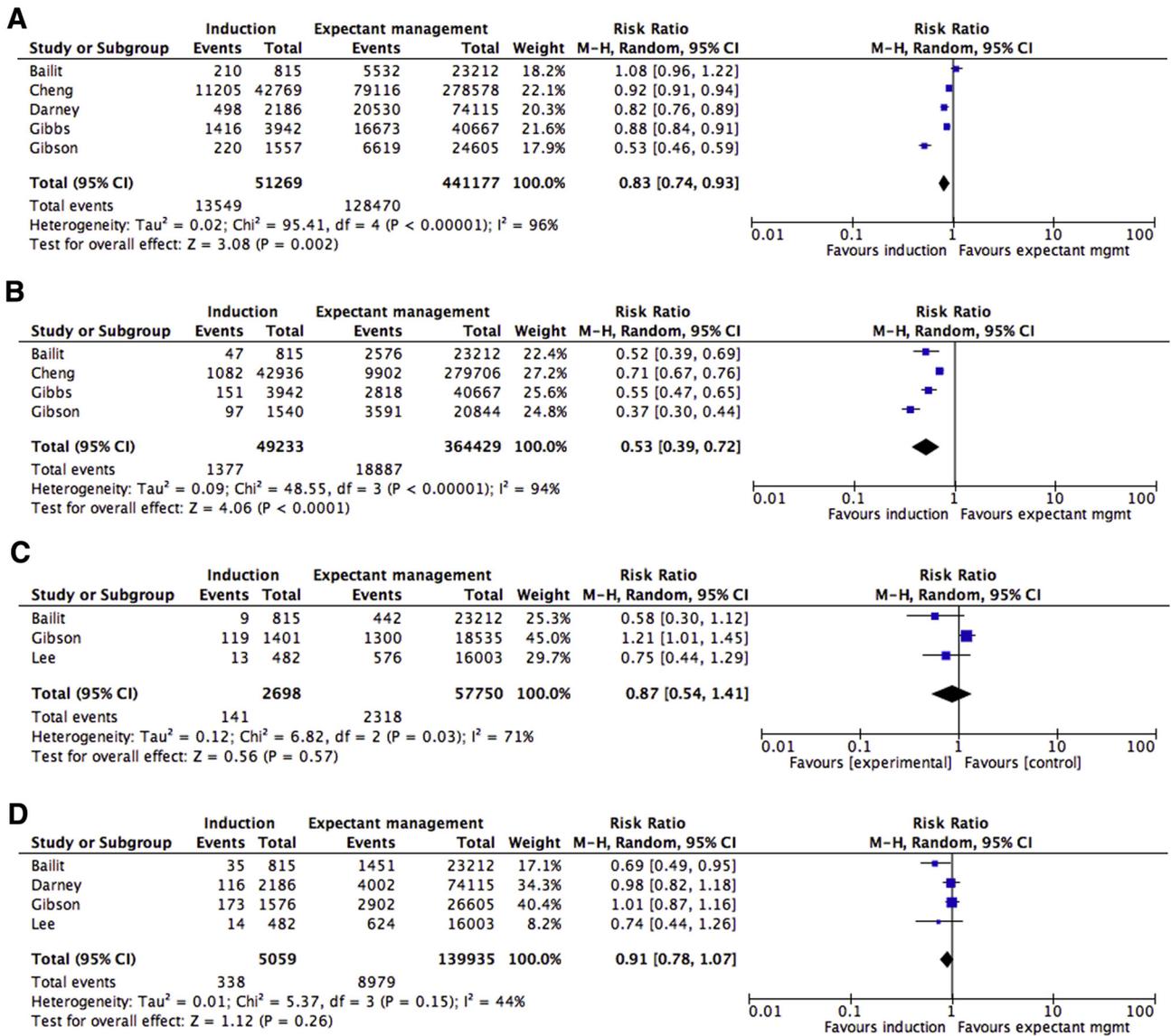
intervention in a trial setting may translate into effectiveness in more generalized settings. For example, the studies in this meta-analysis included patients from both academic and community centers, as well as from many different geographic areas within the United States.

### Comparison with existing literature

Indeed, the summary results of this meta-analysis have a substantial similarity to those of the trial. For example, the RR of cesarean delivery in the setting of labor induction is almost identical in this meta-analysis (0.83; 95% CI, 0.74–0.93) to that in the trial itself (0.84; 95% CI, 0.76–0.93). The similarity of RRs can be seen with regard to the RRs of neonatal respiratory support as well (meta-analysis: 0.71 [95% CI, 0.59–0.85]; ARRIVE trial 0.71 [95% CI 0.55–0.93]). The meta-analysis also demonstrated that labor induction was associated with significant reductions in other maternal and neonatal morbidities that were not significantly different between the 2 groups in the ARRIVE trial. However, this meta-analysis had a study population several thousand times larger than that of the trial, providing a greater ability to discern differences in less common outcomes. Of note, the point

**FIGURE 2**

**Forest plots for associations of elective labor induction at 39 weeks with maternal outcomes**



**A**, Cesarean delivery. **B**, Peripartum infection. **C**, Postpartum hemorrhage. **D**, Third- or fourth-degree perineal laceration.

CI, confidence interval; M-H, Mantel-Haenszel.

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estimates for the RRs for these morbidities in the ARRIVE trial were in the direction of benefit (and often similar in magnitude to those of the meta-analysis).

**Strengths and limitations**

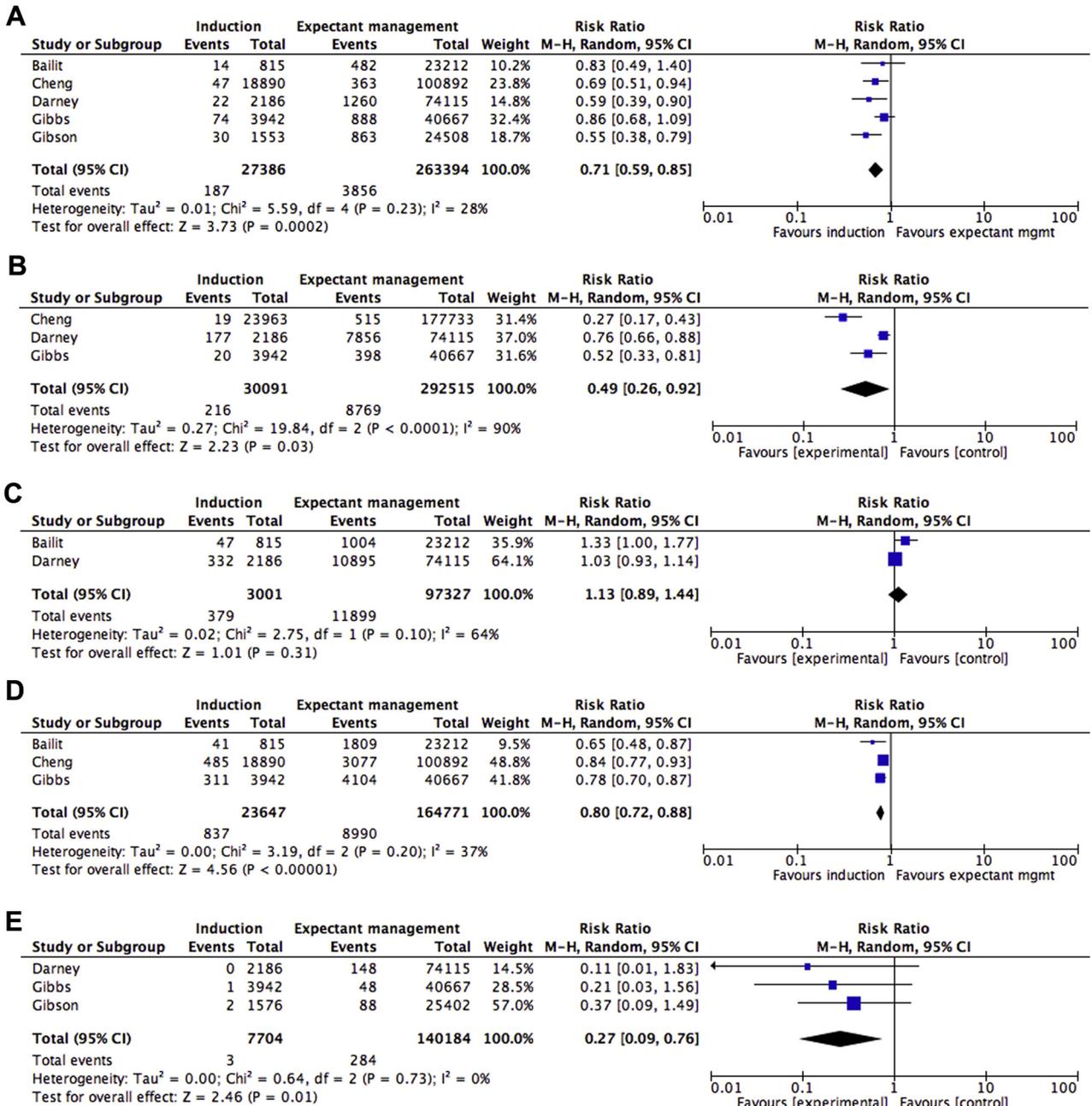
Limitations of the meta-analysis should be recognized. Because these were observational studies, the data used to generate the summary RRs may be

affected by confounding bias. Nevertheless, when multivariable adjustment was performed in the individual studies, results were often similar to those presented in the meta-analysis. For example, after multivariable adjustment, elective induction of labor remained associated with a lower chance of cesarean delivery in 5 of the 6 studies,<sup>23–27</sup> and with no difference in the risk of cesarean in the remaining study.<sup>22</sup> As with

all observational studies, the possibility of other biases, such as ascertainment or selection bias, also remains. This may be relevant for studies regarding labor induction that use administrative datasets, given that identification of this intervention in general, and of elective induction specifically, may be imprecise.<sup>28</sup> Nevertheless, one third of the studies in this meta-analysis were based on data derived directly from medical records in

**FIGURE 3**

**Forest plots for associations of elective labor induction at 39 weeks with perinatal outcomes**



**A**, Respiratory morbidity. **B**, Meconium aspiration syndrome. **C**, Hyperbilirubinemia. **D**, Neonatal intensive care unit admission. **E**, Perinatal mortality. CI, confidence interval; M-H, Mantel-Haensel.

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the context of a research protocol, and the results from these studies are generally aligned with the results of the meta-analysis overall.

There was a significant degree of heterogeneity for several outcomes. This

may be, at least partly, due to the fact that some studies evaluated general populations whereas others evaluated specific subpopulations—such as obese women—without other indications for labor induction. Also, definitions of several

outcomes varied somewhat as well. For example, in some studies perinatal infection was solely chorioamnionitis, whereas in others it included endometritis and wound infection. This differing approach also has implications for

interpretation of summary frequency estimates, as these may not fully reflect the frequencies that would be expected in a general population that was not enriched for women with obesity or in which the outcome was defined differently.

### Conclusions and Implications

In summary, the results of this meta-analysis of observational studies, which collectively included more than 650,000 women who delivered across multiple regions and hospital settings in the United States, are consistent with the results generated by the recently-published ARRIVE randomized trial,<sup>8</sup> and demonstrate that elective labor induction at 39 weeks is associated with improvements in several maternal and perinatal outcomes. These results provide evidence that the results from the trial do not appear to be particular to a research trial or setting per se, and should support the guidelines published by American College of Obstetricians and Gynecologists and SMFM, which stress the importance of information provision and shared decision-making between women and their obstetric providers regarding timing of delivery. ■

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