Received: 2 September 2023 | Revised: 27 December 2023 | Accepted: 7 January 2024

DOI: 10.1111/aogs.14785

ORIGINAL RESEARCH ARTICLE

Likelihood of primary cesarean section following induction of labor in singleton cephalic pregnancies at term, compared with expectant management: An Australian population-based, historical cohort study

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Abstract

Introduction: There has been increased use of both induction of labor (IOL) and cesarean section for women with term pregnancies in many high-income countries, and a trend toward birth at earlier gestational ages. Existing evidence regarding the association between IOL and cesarean section for term pregnancies is mixed and conflicting, and little evidence is available on the differential effect at each week of gestation, stratified by parity.

Material and methods: To explore the association between IOL and primary cesarean section for singleton cephalic pregnancies at term, compared with two definitions of expectant management (first: at or beyond the week of gestation at birth following IOL; and secondary: only beyond the week of gestation at birth following IOL), we performed analyses of population-based historical cohort data on women who gave birth in one Australian state (Queensland), between July 1, 2012 and June 30, 2018. Women who gave birth before 37^{+0} or after 41^{+6} weeks of gestation, had stillbirths, no-labor, multiple births (twins or triplets), non-cephalic presentation at birth, a previous cesarean section, or missing data on included variables were excluded. Four sub-datasets were created for each week at birth (37–40). Unadjusted relative risk, adjusted relative risk using modified Poisson regression, and their 95% confidence intervals were calculated in each sub-dataset. Analyses were stratified by parity (nulliparas vs. parous women with a previous vaginal birth). Sensitivity analyses were conducted by limiting to women with low-risk pregnancies.

Results: A total of 239 094 women were included in the analysis, 36.7% of whom gave birth following IOL. The likelihood of primary cesarean section following IOL in a Queensland population-based cohort was significantly higher at 38 and 39 weeks, compared with expectant management up to 41^{+6} weeks, for both nulliparas and

Abbreviations: aRR, adjusted relative risk; CI, confidence interval; CS, cesarean section; EM, expectant management; IOL, induction of labor; RR, unadjusted relative risk.

paras with singleton cephalic pregnancies, regardless of risk status of pregnancy and definition of expectant management. No significant difference was found for nulliparas at 37 and 40 weeks; and for paras at 40 weeks.

Conclusions: Future studies are suggested to investigate further the association between IOL and other maternal and neonatal outcomes at each week of gestation in different maternal populations, before making any recommendation.

KEYWORDS
birth, cesarean section, expectant management, induction of labor, maternity care

1 | INTRODUCTION

There has been a trend toward birth earlier in gestation and increased use of both induction of labor (IOL) and cesarean section (CS) for women with term pregnancies in high-income countries.[1] The average rate of CS in high-income countries has increased from 12% to 27% between 1990 and 2018, and is estimated to reach 37% by 2030.[2] Similarly, the average rate of IOL has increased from 20% in 1990[3–5] to 30% in 2019[6–9] in high-income countries. Alongside these trends toward increasing use of provider-initiated birth, the average gestational age at birth has declined – for example, US and Australian data show a shift in average gestational age at birth from 40 to 39 weeks.[10,11] Australia has higher rates of IOL and CS than the average for high-income countries. In Australia between 2010 and 2020, the proportion of women who had IOL out of women who gave birth at term increased from 25% to 37%, and the proportion of women who gave birth at term by CS increased from 31% to 36%.[9] By 2030, a published modeling exercise has predicted that the Australian CS rate could reach 45%.[2]

Performing a CS (with or without a clinical indication) is associated with an increased risk of adverse health outcomes for women (eg uterine rupture[12] and hysterectomy[12,13]) and children (eg obesity,[12,14] asthma,[12,14] and autism spectrum disorders[15]). The rising rate of CS has significant financial consequences for individuals and the healthcare systems. The World Health Organization estimated that US$ 2.32 billion of global healthcare expenditure could be avoided if medically unnecessary CS were not performed.[16] These financial burdens are compounded if additional treatments for CS-related complications are required.[6] Strategies that can avoid unnecessary CS will lead to health and economic benefits, and are therefore a global priority.[16]

Previously, several studies (both observational[17–19] and interventional[20]) have been conducted to explore the likelihood of CS among women who had IOL at term, compared with expectant management (EM). However, these findings are mixed in the magnitude and direction of the association; little evidence is available on the differential effect at each week of gestation between 37 and 40 weeks, stratified by parity.[21] In addition, observational studies comparing IOL with EM outside the USA are scant. This study aimed to explore the likelihood of primary CS following IOL for women with singleton cephalic pregnancies at each week of gestation from 37 to 40, compared with EM.

Key message

In our Queensland population-based cohort, the likelihood of primary cesarean section following induction of labor was significantly higher at 38 and 39 weeks, compared with expectant management up to 41^{+6} weeks, for both nulliparous and parous women with singleton cephalic pregnancies.

For each comparison group at each index week, our null hypothesis was that IOL in the index week would not be associated with a difference in the likelihood of primary CS, compared with EM.

2 | MATERIAL AND METHODS

2.1 | Data set and analysis population

A historical cohort study was designed using an existing population-based administrative data set from the Queensland Perinatal Data Collection,[22] which covers all live births, and stillbirths of at least 20 weeks of gestation and/or at least 400 g in weight that occurred in one Australian state (Queensland) between July 1, 2012 and June 30, 2018. Variables used in our study are maternal demographics and clinical characteristics occurring before and during pregnancy, labor, and birth. Definitions of these variables are available in Appendix S1. This data set has a high degree of completeness and accuracy. The data quality statement is available here.[23]

We limited the data set to women with a singleton pregnancy with fetal presentation at birth that was cephalic (includes cephalic, vertex, face or brow presentations), who gave birth between 37^{+0} and 41^{+6} weeks, had a live birth, had a vaginal birth (spontaneous or instrumental assisted with forceps or vacuum) or CS after labor and did not have a previous CS and missing data on included variables (Figure 1). Women who gave birth after 41^{+6} weeks were removed from the analysis population, because it is not common practice to continue EM beyond that gestational age. We also excluded women who previously gave birth by CS to avoid overestimating the likelihood of CS due to the increased likelihood of a CS in a subsequent pregnancy, and the known low rates of vaginal birth after CS.[24–26]

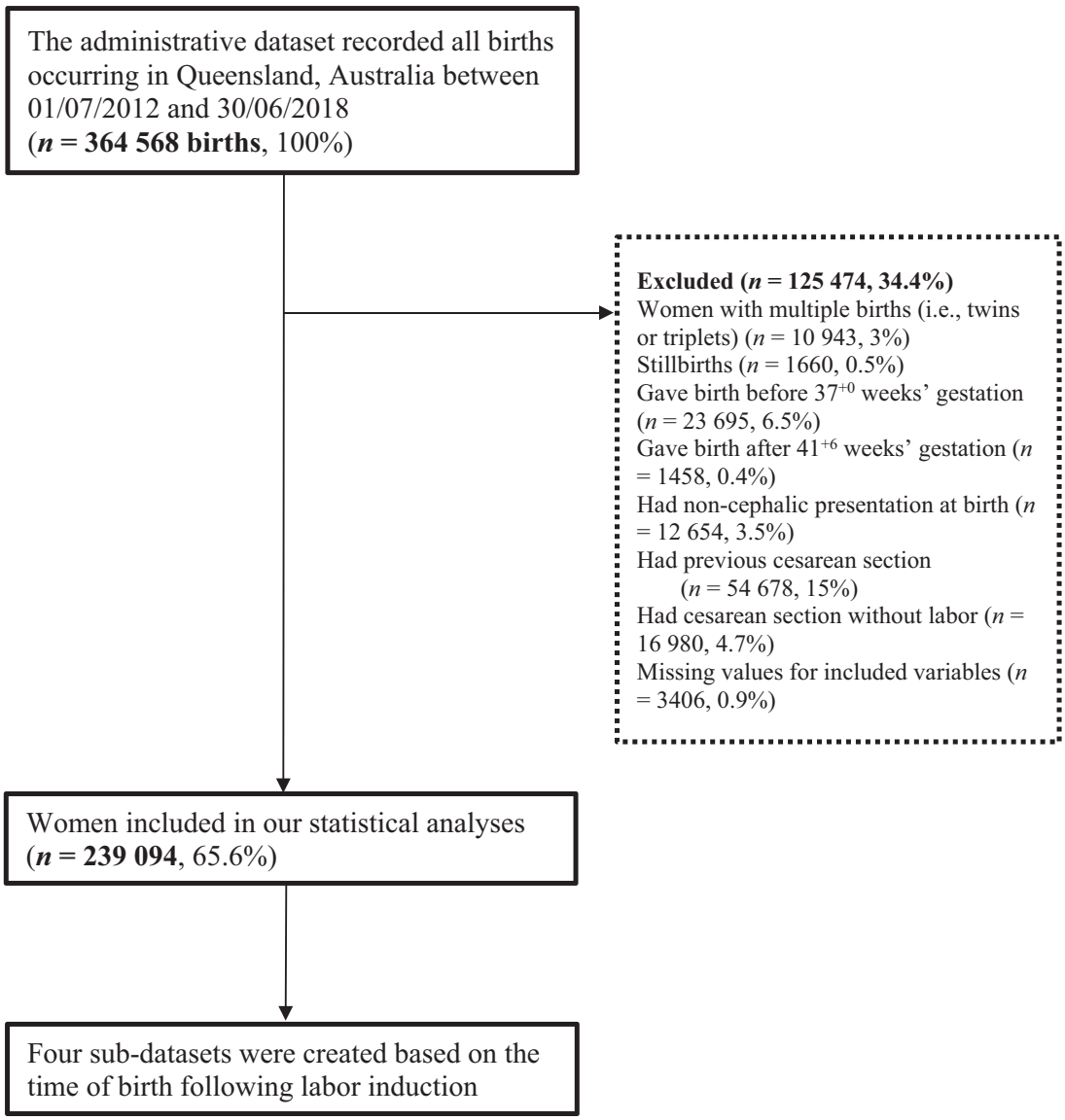

FIGURE 1 A flow diagram of data selection.

Women who had a pre-labor CS (i.e. no labor) were not included in the EM group to be consistent with previous studies[18,27,28] and considering IOL attempts to achieve a vaginal birth.[29]

2.2 | Exposure group—women who gave birth following IOL

The exposure group for this analysis is women who gave birth following IOL. Any attempted induction, including failed IOL, for any reason, was included. Women who gave birth following IOL were identified and classified separately based on the week of gestation at birth following IOL. Each week includes zero to 6 days. We considered the weeks of gestation at birth following IOL, rather than the timing of IOL, to be the index week for this analysis, because no relevant data with certainty were available in our routinely collected data set.

2.3 | Reference group—women who had EM

The reference group for women who gave birth following IOL in each index week was women who experienced EM in the same index week. This reference group included women who experienced spontaneous onset of labor in the same weeks of gestation, or whose pregnancy progressed to a later week of gestation ("at or above"). For example, for the exposure group of women who gave birth following IOL at 38 weeks, the reference group was women who gave birth following spontaneous onset of labor at 38 weeks and women who gave birth following IOL or spontaneous onset of labor from 39^{+0} weeks onwards. This definition is used as suggested in previous cohort studies.[28,30,31]

A secondary analysis was performed using a different reference group that only included pregnancies that progressed to a later week of gestation ("above"). In our above example, the new reference group was women who gave birth from 39^{+0} weeks onward. In order

to identify the exposure and reference group at each index week, four sub-datasets were created based on different time of birth following IOL (37, 38, 39, and 40 weeks).

2.4 | Outcome—primary CS

The outcome of this analysis was primary CS after labor (either IOL or spontaneous onset of labor).

2.5 | Statistical analyses

We separated all analyses by parity (nulliparas vs. parous women with a previous vaginal birth). Potential confounders including sociodemographic, medical, and obstetric variables were selected based on univariate analyses and expert consultation. This included mother's age, pre-pregnancy body mass index (BMI), country of birth, indigenous status, residential area of socio-economic disadvantage, whether the birth was at a public or private hospital, and medical risk status of pregnancy (detailed definition is given in the "Methods" section of Appendix S1). A period effect based on the year of birth event was also analyzed.

Unadjusted relative risk (RR) and adjusted relative risk (aRR) were calculated for each comparison group, stratified by parity. The modified Poisson regression was used to calculate aRR with robust error variance estimation to account for the correlation between repeated births from the same woman.[32] Wald statistics and 95% confidence interval (CI) were calculated for each RR and aRR.

Sensitivity analyses were conducted by limiting both exposure and reference group to women who had low-risk pregnancies only, which enabled us to explore the possible effects of a woman's risk status (which is related to underlying medical indications of IOL) on the results.

All analyses were performed using SAS V9.4.

TABLE 1 Sociodemographic characteristics of included women, births in Queensland, Australia, 2012–2013 to 2017–2018.

Characteristics *N* (%)	Total 239 094
Mother's age (years)	
≤19	8726 (3.65%)
20–34	186 719 (78.09%)
≥35	43 649 (18.26%)
Mean ± standard deviation	29.37 ± 5.56
Pre-pregnancy BMI (kg/m^2)	
≤18.4 (underweight)	14 381 (6.01%)
18.5–24.9 (normal weight)	128 603 (53.79%)
25.0–29.9 (overweight)	53 312 (22.30%)
≥30.0 (obesity)	42 798 (17.90%)
Mean ± standard deviation	25.15 ± 5.89
Mother's country of birth (grouped in regions)	
Australia	174 557 (73.01%)
Oceania (excludes Australia)	17 465 (7.30%)
Asia	26 514 (11.09%)
Europe	11 359 (4.75%)
The Americas	3672 (1.54%)
Africa	5527 (2.31%)
Mother's Indigenous status (Aboriginal and/or Torres Strait Islander)	
Yes	14 160 (5.92%)
No	243 934 (94.08%)
Residential area of socioeconomic disadvantage (SEIFA)	
1st quintile (the most disadvantaged)	45 230 (18.92%)
2nd quintile	40 240 (16.83%)
3rd quintile	61 442 (25.70%)
4th quintile	57 881 (24.21%)
5th quintile (the least disadvantaged)	34 301 (14.35%)

Abbreviations: BMI, body mass index; SEIFA, Socio-Economic Indexes for Areas.

3 | RESULTS

In all, 239 094 women were eligible for our analyses (Figure 1). These women had a mean gestational age at birth of 39.3 weeks, a mean age of 29.4 years and a mean BMI of 25.2 kg/m^2. Seventy-three percent of these women were born in Australia, 5.9% were identified as Aboriginal and/or Torres Strait Islander, 48.2% were nulliparous, 30.1% were classified as having a high-risk pregnancy, and 32.5% gave birth in a private facility. In total, 87 776 (36.7%) women gave birth following IOL and 17 491 (19.9%) of them had a CS (Tables 1 and 2).

For women with high-risk or low-risk pregnancies, the unadjusted likelihood of primary CS following IOL was significantly higher in both nulliparous and parous women with singleton cephalic pregnancies at each index week between 37 and 40 weeks, compared with women who had EM (at or beyond the gestation of birth following IOL, up to 41^{+6} weeks). After adjusting for potential confounding factors, similar increased likelihood of primary CS following IOL was found at 37 weeks (paras: aRR = 1.52, 95% CI 1.35–1.71), at 38 weeks (nulliparas: aRR = 1.15, 95% CI 1.11–1.19; paras: aRR = 1.43, 95% CI 1.31–1.56), at 39 weeks (nulliparas: aRR = 1.20, 95% CI 1.16–1.24; paras: aRR = 1.42, 95% CI 1.29–1.57), and at 40 weeks (nulliparas: aRR = 1.29, 95% CI 1.25–1.34; paras: aRR = 1.55, 95% CI 1.39–1.74); no significant difference was found at 37 weeks for nulliparous women (aRR = 1.04, 95% CI 0.99–1.10). Sensitivity analyses limited to women with low-risk pregnancies only (n = 167 105, 69.9% of 239 094) showed similar results at each index week.

For the secondary analyses of a different reference group (only beyond the gestation of birth following IOL, up to 41^{+6} weeks), an increased likelihood of CS was found at 38 weeks (aRR = 1.12, 95% CI 1.08–1.16) and 39 weeks (aRR = 1.09, 95% CI 1.05–1.12) for nulliparas, and at 37 weeks (aRR = 1.53, 95% CI 1.37–1.73), 38 weeks (aRR = 1.44, 95% CI 1.32–1.57) and 39 weeks (aRR = 1.26, 95%

TABLE 2 Obstetric characteristics of included women, births in Queensland, Australia, 2012–2013 to 2017–2018.

Characteristics *N* (%)	Total 239 094
Birthplace of child	
Public hospital	161 449 (67.53%)
Private hospital	77 645 (32.47%)
Risk status of pregnancy	
Low-risk	167 105 (68.89%)
High-risk	71 989 (30.11%)
Parity	
Nulliparous	115 210 (48.19%)
Parous with a previous vaginal birth	123 884 (51.91%)
Onset of labor	
Spontaneous onset of labor	151 318 (63.29%)
Vaginal birth following spontaneous onset of labor	137 547 (90.90%)
Cesarean section following spontaneous onset of labor	13 771 (9.10%)
Induction of labor	87 776 (36.71%)
Vaginal birth following induction of labor	70 285 (80.07%)
Cesarean section following induction of labor	17 491 (19.93%)
Mode of birth	
Vaginal birth	207 832 (86.92%)
Cesarean section	31 262 (13.08%)
Weeks of gestation at birth	
37^{+0}–37^{+6}	17 817 (7.45%)
38^{+0}–38^{+6}	44 571 (18.64%)
39^{+0}–39^{+6}	68 094 (28.48%)
40^{+0}–40^{+6}	72 209 (30.20%)
41^{+0}–41^{+6}	36 403 (15.23%)
Mean ± standard deviation	39.27 ± 1.15
Year of birth event	
2012	20 417 (8.54%)
2013	41 091 (17.19%)
2014	40 877 (17.10%)
2015	39 567 (16.55%)
2016	39 679 (16.60%)
2017	38 131 (15.95%)
2018	19 332 (8.09%)

CI 1.14–1.40) for paras (Figures 2 and 3). Sensitivity analyses of women with low-risk pregnancies also showed similar results at each index week.

4 | DISCUSSION

Our analyses of a state-wide (Queensland, Australia) observational data set demonstrated that the likelihood of primary CS following IOL was significantly higher at 38 and 39 weeks, compared with EM up to 41^{+6} weeks of gestation, in women with singleton cephalic pregnancies, regardless of parity, risk status of pregnancy, and definition of EM ("at or above" or "above"). No significant difference was found for nulliparas at 37 and 40 weeks; and for paras at 40 weeks.

Compared with other historical cohort studies that used the same definition of the "at or above" EM analysis, our findings are consistent with a 2010 US study that reported an increased likelihood of CS at 38 and 39 weeks in women with singleton, vertex presentations pregnancies.[31] Conversely, our findings are not aligned with a 2016 US study that reported an increased likelihood of CS at 40 weeks in women with singleton, vertex presentation pregnancies, but decreased likelihood between 37 and 39 weeks after propensity score matching.[33]

In comparison with findings from other comparable observational studies, the results of our secondary analysis ("above" EM) are supported by a 2020 observational study conducted in Austria, which reported a higher likelihood of CS following non-medically indicated IOL at 38 and 39 weeks for nulliparous women with singleton pregnancies; and at 37 and 38 weeks for parous women with previous vaginal birth.[27] Although the decreased likelihood of CS was found at 40 weeks of gestation for both nulliparous and parous women, which contradicts with our nonsignificant results at the same index week.[27] Additionally, our findings do not support a 2021 US nationwide study that reported IOL among low-risk women as being associated with a lower likelihood of CS at 39 weeks of gestation.[34] The most recent (2020) Cochrane systematic review and meta-analysis of 31 randomized clinical trials showed a decreased likelihood of CS for women at low risk of complications and planned IOL between 37 and 40 weeks of gestation.[20] Although our results did not align with those meta-analysis results based on clinical trials and some studies conducted in the USA, the differences are probably attributed to different methodological approaches and differences in the women included and the setting where they gave birth. Our focus is on the association between IOL and CS outside a clinical research setting, including all women regardless of parity and risk status, giving birth at any birth place (home, birth center, and hospital) in Queensland with presumed provider-level differences regarding the decisions of whether, why, and when to perform IOL.

The conflicting findings as discussed above may reflect differences in clinical practice of IOL[35–37] among different settings and raise the concern of external validity regarding the findings of previous studies. In 2020, 22% of women who had IOL gave birth by CS in Australia.[9] Unnecessary CS is associated with substantial financial burden to families and governments[6,38,39] and an increased risk of adverse health outcomes; for these reasons, optimizing its use in clinical practice is an international health priority.[40] Outcomes can include the experience of psychological trauma and depression for women,[41] as well as increased risk of adverse outcomes in children born following CS (chronic health conditions including allergies, asthma, diabetes, gastroenteritis, autism, and attention deficit/hyperactivity disorder).[15,42] As such, considering the increased likelihood of CS following IOL as demonstrated in our study and the

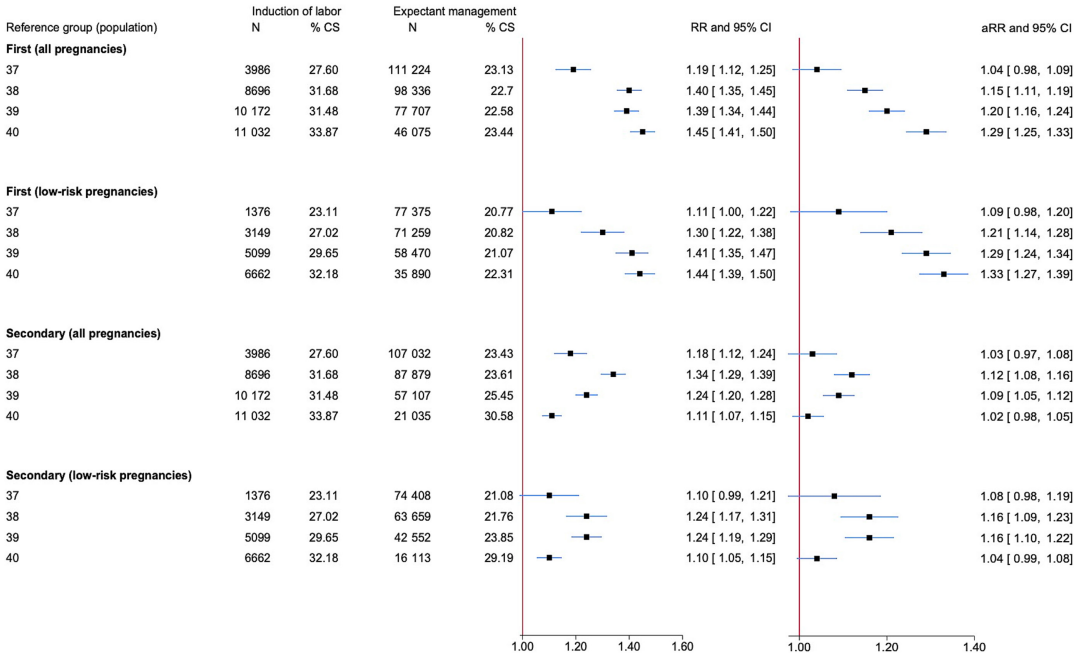

FIGURE 2 Relative risk of primary CS for nulliparous women who had IOL, compared with women who had expectant management. First: compared with women who gave birth at or beyond the week of gestation at birth following IOL. Secondary: compared with women who gave birth only beyond the week of gestation at birth following IOL. All pregnancies: aRR were adjusted for mother's age, pre-pregnancy BMI, country of birth, indigenous status, residential area of socioeconomic disadvantage, whether the birth was at a public or private hospital, medical risk status of pregnancy, and year of birth event. Low-risk pregnancies: aRR were adjusted for mother's age, pre-pregnancy BMI, country of birth, indigenous status, residential area of socioeconomic disadvantage, whether the birth was at a public or private hospital, and year of birth event. Abbreviations: aRR, adjusted relative risk; BMI, body mass index; CI, confidence interval; CS, cesarean section; IOL, induction of labor; RR, unadjusted relative risk.

potential harms of unnecessary CS reported in current literature, it is important to consider these clinical and financial risks when discussing labor options with women.[19,43]

In addition to the likelihood of CS following IOL, it is suggested that the association between IOL at term and other maternal outcomes (eg morbidity) and neonatal outcomes (eg morbidity or neonatal intensive care unit admission) should be further analyzed at each week of gestation to explore the potential benefits and harms of IOL. Apart from these factors, women's preferences, experiences, accessible resources, and available support also affect the decision being made around IOL.[44] Economic evaluation between IOL and EM should also be conducted to further inform policy changes. Given the complexity of the decision-making process and the development of clinical practice guidelines, further analysis and discussion are needed before suggesting any substantial practice change. There is a need to develop strategies to optimize the use and timing of provider-initiated birth, ensuring that the benefits clearly outweigh any potential harm.

A key strength of our study is that we drew on data from a whole-of-population routine administrative data set, which allows us to perform a week-to-week analysis by creating four sub-datasets with a large number of women. This provides new evidence of how each additional week would affect the likelihood of CS among women being managed expectantly. Furthermore, we were able to analyze all births from all clinical settings, which broadened the applicability of our findings. Another strength is that we conducted multiple analyses by comparing two definitions of EM and including different maternal populations (i.e. low-risk status only), which improves the robustness of our findings. Considering there is not a widely agreed appropriate definition of the reference group for IOL in a retrospective cohort study, both definitions of the EM group have their weaknesses. The "above" EM excludes women who gave birth within the same index week, which might artificially bias the results in favor of IOL, because more CS were conducted at later gestational ages as demonstrated in our study. However, the gestation at birth is recorded with certainty only in completed weeks, and not in weeks and days. Therefore, in the "at or above" EM group, some women may have had a spontaneous onset of labor at an earlier gestational length than the IOL group, which may introduce a selection bias by including them in the EM group. This might distort the results in favor of EM.

In addition, our study is subject to other inherent limitations of historical data. For example, we used the weeks of gestation at birth following IOL, rather than the timing of IOL, to be the index week for this analysis, which might introduce small non-random misclassifications of exposure. Furthermore, when defining "low-risk pregnancies", we excluded women with new conditions developed during pregnancy and immediately preceding labor and delivery, which might include conditions being diagnosed after the index week and

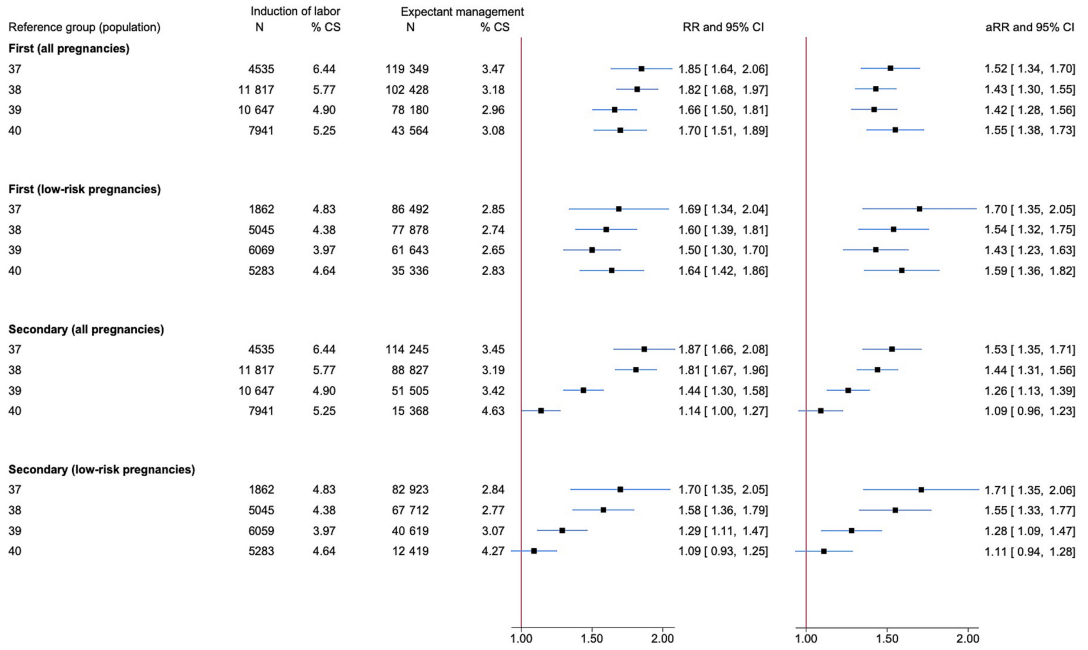

FIGURE 3 Relative risk of primary CS for parous women who had IOL, compared with women who had expectant management. First: compared with women who gave birth at or beyond the week of gestation at birth following IOL. Secondary: compared with women who gave birth only beyond the week of gestation at birth following IOL. All pregnancies: aRR were adjusted for mother's age, pre-pregnancy BMI, country of birth, indigenous status, residential area of socioeconomic disadvantage, whether the birth was at a public or private hospital, medical risk status of pregnancy, and year of birth event. Low-risk pregnancies: aRR were adjusted for mother's age, pre-pregnancy BMI, country of birth, indigenous status, residential area of socioeconomic disadvantage, whether the birth was at a public or private hospital, and year of birth event. Abbreviations: aRR, adjusted relative risk; BMI, body mass index; CI, confidence interval; CS, cesarean section; IOL, induction of labor; RR, unadjusted relative risk.

should not be used for exclusion of women in the EM group. This limitation may introduce a selection bias affecting the results. Another limitation is that we were unable to differentiate between IOL with, and without, a clinical indication. This limitation might lead to an overestimation of the likelihood of CS among the IOL group, considering many of these indications are independently associated with a higher likelihood of CS. Our sensitivity analysis and adjusted relative risks, however, serve to partially adjust for the effect of these indications. Although our sample size is relatively large, it was collected from one state (Queensland) in Australia. It should be acknowledged that despite the existence of statewide clinical guidelines,[45] the actual practice of IOL between sites could vary, and so affect the external validity of the results. Finally, there is potential that other important clinical factors not available in our data set (eg indication for induction, cervical length, and BMI before birth) affecting the association were not included in our multivariate analyses due to the nature of our routinely collected data set.

5 | CONCLUSION

This study assessed the association between IOL and primary CS at different weeks of gestation at birth in different maternal populations giving birth in Queensland. In our population-based cohort, the likelihood of primary CS following IOL was significantly higher at 38 and 39 weeks of gestation, compared with EM up to 41^{+6} weeks, for both nulliparas and paras with singleton cephalic pregnancies, regardless of the risk status of the pregnancy and the definition of EM. The findings of this study are only applicable to singleton cephalic pregnancies in countries with comparable healthcare systems and clinical practice. Future studies are suggested to investigate further the association between IOL and other maternal and neonatal outcomes at each week of gestation.

AUTHOR CONTRIBUTIONS

Yanan Hu led the study design, data selection and analyses, and drafting of the manuscript, supervised by Emily J. Callander, Valerie Slavin, and Joanne Enticott. Caroline S. E. Homer, David Ellwood, Valerie Slavin, Joshua P. Vogel, Joanne Enticott, and Emily J. Callander contributed to the study design, interpretation of the results, and editing of the final manuscript. All authors read and approved the final manuscript.

ACKNOWLEDGMENTS

The authors acknowledge the data linkage team of the Statistical Services Branch (SSB), Queensland Health for linking the data sets used for this project. Open access publishing facilitated by University of Technology Sydney, as part of the Wiley - University of Technology Sydney agreement via the Council of Australian University Librarians.

FUNDING INFORMATION

EJC, CSEH, and JPV receive salary support from the National Health and Medical Research Council (NHMRC) through fellowship schemes. YH receives support from the Australian Government Research Training Programme (RTP) Scholarship.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

ETHICS STATEMENT

The data used in this study were de-identified before use. All methods were performed in accordance with the Declaration of Helsinki. The Townsville Hospital and Health Service Human Research Ethics Committee (HREC; HREC/16/QTHS/223) and the Australian Institute of Health and Welfare HREC (EO2017-1-338) granted permission to access the raw data used in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Hu Y, Homer CSE, Ellwood D, et al. Likelihood of primary cesarean section following induction of labor in singleton cephalic pregnancies at term, compared with expectant management: An Australian population-based, historical cohort study. *Acta Obstet Gynecol Scand*. 2024;103:946-954. doi:10.1111/aogs.14785