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Peters, Lilian L ORCID: 0000-0003-2342-0799, Thornton, Charlene ORCID: 0000-0003-4457-1799, de Jonge, Ank ORCID: 0000-0002-5384-3744, Khashan, Ali, Tracy, Mark, Downe, Soo ORCID: 0000-0003-2848-2550, Feijen-de Jong, Esther I ORCID: 0000-0001-5766-296X and Dahlen, Hannah G ORCID: 0000-0002-4450-3078 (2018) The effect of medical and operative birth interventions on child health outcomes in the first 28 days and up to 5 years of age: A linked data population-based cohort study. Birth. ISSN 0730-7659

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The effect of medical and operative birth interventions on child health outcomes in the first 28 days and up to 5 years of age: A linked data population-based cohort study

Lilian L. Peters PhD1,2,3 | Charlene Thornton RM, PhD4 | Ank de Jonge RM, PhD1,3 | Ali Khashan PhD5,6 | Mark Tracy MBBS, PhD7 | Soo Downe RM, PhD8 | Esther I. Feijen-de Jong RM, PhD1,2,3 | Hannah G. Dahlen RM, PhD9,10,11

1Department of Midwifery Science, VU University Medical Center Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, The Netherlands
2Department of General Practice & Elderly Care Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
3AVAG Midwifery Academy Amsterdam Groningen, Amsterdam/Groningen, The Netherlands
4College of Nursing and Health Sciences Adelaide, Flinders University, Adelaide, SA, Australia
5School of Public Health, University College Cork, Cork, Ireland
6School of Public Health, University College Cork (INFANT), Cork, Ireland
7Westmead Newborn Intensive Care Unit, Westmead Hospital, University of Sydney, Sydney, NSW, Australia
8University of Central Lancashire, Preston, Lancashire, UK
9School of Nursing and Midwifery Sydney, Western Sydney University, Sydney, NSW, Australia
10Affiliate of the Ingham Institute, Liverpool, NSW, Australia
11National Institute of Complementary Medicine, Western Sydney University, Sydney, NSW, Australia

Correspondence
Lilian L. Peters, VU University Medical Center Amsterdam, Department of Midwifery Science/University Medical Center Groningen, The Netherlands.
Email: L.L.Peters@umcg.nl

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Abstract
Background: Spontaneous vaginal birth rates are decreasing worldwide, while caesarean delivery, instrumental births, and medical birth interventions are increasing. Emerging evidence suggests that birth interventions may have an effect on children’s health. Therefore, the aim of our study was to examine the association between operative and medical birth interventions on the child’s health during the first 28 days and up to 5 years of age.

Methods: In New South Wales (Australia), population-linked data sets were analyzed, including data on maternal characteristics, child characteristics, mode of birth, interventions during labor and birth, and adverse health outcomes of the children (ie, jaundice, feeding problems, hypothermia, asthma, respiratory infections, gastrointestinal disorders, other infections, metabolic disorder, and eczema) registered with the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification codes. Logistic regression analyses were performed for each adverse health outcome.

Results: Our analyses included 491 590 women and their children; of those 38% experienced a spontaneous vaginal birth. Infants who experienced an instrumental
INTRODUCTION

Worldwide cesarean delivery rates are increasing, while spontaneous vaginal birth rates are decreasing. The rate of cesarean delivery has risen steadily in Europe to 25%, in Australia to 33%, and the highest rates are reported in Latin America and the Caribbean (41%). Instrumental birth (ie, forceps or vacuum) and medical birth interventions (ie, including the use of exogenous oxytocin for labor induction and/or augmentation) are increasing globally as well.

There is emerging evidence that operative birth (ie, instrumental vaginal birth or cesarean) may have an effect on children’s physical health and cognitive development in the longer term. The Extended Hygiene Hypothesis (EHH) hypothesizes that infants born by cesarean delivery have different colonization of the gut flora compared with infants born by vaginal birth. This may potentially affect the neonatal immune response. The EPIgenetic Impact of Childbirth (EPIIC) hypothesis raises concern over the effects of stress (too high and too low) caused by medical and operative birth interventions to the epigenetic regulation of gene expression in the immune system.

Studies have demonstrated that children born vaginally at term have different short- and longer-term physical health outcomes than those born by cesarean, particularly when there has been no exposure. Epidemiological studies that analyzed population-based registry data, reported conflicting associations between operative birth interventions, and the increased risk of several immune-related diseases, including asthma, type 1 diabetes, obesity, and inflammatory bowel disease. These conflicting findings may be due to different statistical methods used, differences in study population characteristics (eg, maternal age, morbidity, smoking, and gestational age), and failure to differentiate between mode of birth and medical birth interventions.

The aim of this study was to examine the associations between operative and/or medical birth interventions on children’s health outcomes in the first 28 days and up to 5 years of age, in a large population of healthy pregnant women and their children.

METHODS

The study cohort consisted of women and their children born in New South Wales (NSW), Australia, between January 1, 2000 and August 31, 2008. Children’s health was followed until August 31, 2013. The NSW Centre for Health Record Linkage utilized probabilistic data linkage techniques to merge data of the following data sets: Record Linkage from the Perinatal Data Collection (PDC), Admitted Patient Data Collection, Register of Congenital Conditions, NSW Registry of Birth Deaths and Marriages, the Australian Bureau of Statistics—Socio-Economic Indexes for Areas. Probabilistic record linkage software assigns a “linkage weight” to pairs of records. For example, records that match perfectly or nearly perfectly on first name, surname, date of birth, and address have a high linkage weight and records that match only on date of birth have a low-linkage weight. This technique has been shown to have a false-positive rate of 0.3% of records. Several studies have evaluated the validity of the NSW linkage data and reported a tendency toward underreporting of maternal medical conditions during pregnancy. However, by comparing PDC and Admitted Patient Data Collection data with women’s individual medical records, it showed that conditions and procedures regarding delivery and discharge status had high specificity, indicating that false positives were uncommon.

The study was approved by the Ethics Committee of the NSW Population and Health Services Research Committee (HREC/10/CIPHS/96). The ethics privacy statement outlines that consent is waived due to the size of the data set, retrospective nature of the data, and the inherent difficulties in obtaining consent.
2.1 | Data

Data were routinely collected from women who gave birth or had subsequent births in either a public or private hospital in NSW, Australia. Data of nulliparous and multiparous women were selected if they were low-risk pregnant women according to the guideline of the National Institute for Health and Care Excellence on intrapartum care and in alignment with methodology previously utilized on this and other linked data sets.20,25,26 This resulted in a cohort of “healthy pregnant women” who had no preexisting or pregnancy-related hypertension or diabetes, did not smoke or take drugs, were within the age range of 20-35 years, and gave birth at 37-41 weeks of gestation to a singleton baby in cephalic presentation with a birthweight of ≥2500 g. In addition, children with minor or major congenital conditions were excluded based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification codes (ICD-10-AM, Q0.0-Q99.9).25 Minor malformations could be related to more major malformations, which could be caused by genetic factors, for example, and which may become apparent some time after birth. Moreover, women and their children were excluded from the analyses if stillbirth or death had occurred during the 5-year follow-up period. By making this selection, we aimed to include a population of healthy pregnant women and their healthy born children, to reduce confounding and to increase the likelihood of finding the true association between exposure (birth interventions) and outcomes (child’s health short and longer term).

Women or children with missing data on either mode of birth, maternal age, parity, gestational age, or birthweight were also excluded from the analyses since these variables have a potential effect on children’s health. If missing data on other variables occurred, that is, country of birth, socioeconomic status, and infant gender, these variables were indicated as system missing in the linked data file and subsequently excluded from the logistic regression models.

2.2 | Variables

Mode of birth and birth interventions were collected from the PDC file and included: spontaneous vaginal birth, instrumental birth, elective cesarean delivery, and an emergency cesarean (either with or without medical birth interventions). Medical birth interventions included induction or augmentation of labor with oxytocin, prostaglandin, and/or artificial rupture of membranes.

The short-term follow-up data of infants during the first 28 days and of children up to 5 years of age included admissions to public and private hospitals located in NSW (Admitted Patient Data Collection file). The children were followed from the date of birth until their fifth birthday to identify any adverse health outcomes which occurred during this time period. The classifying diagnoses and reasons with accompanying hospital visit dates were registered with ICD-10-AM-codes. Short-term adverse health outcomes included jaundice, feeding problems, and hypothermia and often are part of the adaptation of the infant to being outside the uterus.7,27,28 The longer-term adverse health outcomes included asthma, respiratory infections (eg, common cold, pneumonia, bronchitis), gastrointestinal disorders, other infections (eg, sepsis, streptococcus, cystitis), metabolic disorder (eg, hypoglycemia, neonatal diabetes mellitus, diabetes mellitus type 1 or 2, localized adiposity), and eczema, based on the potential effect that mode of birth has on immune-related diseases.5-7,12-18 An overview of all adverse health outcomes and other covariates with corresponding ICD-10-AM codes are presented in the Supporting Information.

Potential confounders of either women or children characteristics were selected from several data files. Women’s characteristics were extracted from the PDC and NSW Registry of Birth Deaths and Marriages files and included, for example, age and country of birth. From the Socio-Economic Indexes for Areas file, the socioeconomic status of women were collected and were based on area indices of income and education using women’s postal codes and defined as low (10-30 percentiles), medium (40-60 percentiles) or high (≥70 percentiles). Pharmacological pain medication during labor and birth (ie, nitrous oxide, systematic opioid, local administered to perineum, pudendal, morphine, and pethidine), and anesthesia (ie, epidural, caudal, and spinal) were extracted from the PDC file.

Children’s characteristics were extracted from the PDC and Admitted Patient Data Collection files and included gender, gestational age, birthweight, small-for-gestational age, large-for-gestational age, and birth trauma (appendix).

2.3 | Data analyses

A retrospective analysis of prospectively collected linked data was performed. Baseline characteristics of the women and children were reported using descriptive statistics. Statistical differences in baseline characteristics in women and children in the different mode of birth and birth interventions groupings (ie, spontaneous vaginal birth, vaginal birth with induction or augmentation, instrumental birth, instrumental birth with induction or augmentation, elective cesarean delivery, emergency cesarean, and an emergency cesarean delivery after induction) were calculated with chi-square tests.

Univariate and multivariate logistic regression analyses were performed to examine the association between the exposure variable and each child outcome. Spontaneous vaginal birth without induction or augmentation of labor was used as the reference group. The logistic regression models were adjusted for maternal characteristics (maternal age, country of birth, socioeconomic status, parity), birth characteristics (pain medication during birth), and child characteristics (gender, gestational age, birthweight, small-for-gestational age, large-for-gestational age, birth trauma). Crude and adjusted odds ratios (OR) with corresponding 95% confidence
| Table 1 | Maternal, mode of birth, and child characteristics by type of birth interventions, New South Wales, Australia, 2000-2008 |
|---------|----------------------------------------------------------------------------------------------------------|
| Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation<sup>a</sup> | Instrumental birth | Cesarean elective | Cesarean emergency | Cesarean emergency after induction or augmentation | Statistical differences among groups that differed on mode of birth |
| N = 491 590 | n = 185 883 | n = 136 651 | n = 19 865 | n = 41 631 | n = 55 499 | n = 17 216 | n = 34 845 | P-value |
| 100% | 37.8% | 27.8% | 4.0% | 8.5% | 11.3% | 3.5% | 7.1% | ≤.001 |
| N (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Maternal characteristics | | | | | | | | |
| Maternal age (y) | 20-24 | 25 482 (18.6) | 2901 (14.6) | 6663 (14.6) | 4612 (8.3) | 2175 (12.6) | 5354 (14.6) | ≤.001 |
| 25-29 | 71 439 (38.4) | 7749 (39.0) | 16 514 (39.7) | 17 391 (31.3) | 6175 (35.9) | 13 658 (39.2) | | |
| 30-35 | 58 787 (43.0) | 9215 (46.4) | 19 054 (45.8) | 33 496 (60.4) | 8866 (51.5) | 15 833 (45.4) | | |
| Country of birth | | | | | | | | ≤.001 |
| Australia | 339 072 (69.0) | 13 096 (65.9) | 27 620 (66.3) | 41 191 (74.2) | 11 653 (67.7) | 23 503 (67.5) | | |
| Not Australia | 151 335 (30.8) | 36 926 (27.0) | 13 884 (33.4) | 14 124 (25.5) | 5508 (32.0) | 11 248 (32.3) | | |
| Missing | 1183 (0.2) | 293 (0.2) | 127 (0.3) | 184 (0.3) | 55 (0.3) | 94 (0.3) | | |
| Socioeconomic status<sup>b</sup> | | | | | | | | |
| Low | 123 311 (25.1) | 35 710 (26.1) | 3762 (18.9) | 7876 (18.9) | 12 449 (22.4) | 4000 (23.2) | 7328 (21.0) | ≤.001 |
| Middle | 169 198 (34.4) | 47 549 (34.8) | 6505 (32.7) | 13 325 (32.0) | 18 121 (32.7) | 5741 (33.3) | 12 065 (34.6) | | |
| High | 197 712 (40.2) | 53 037 (38.8) | 9535 (48.0) | 20 222 (48.6) | 24 816 (44.7) | 7433 (43.2) | 15 325 (44.0) | | |
| Missing | 1369 (0.3) | 355 (0.3) | 208 (0.5) | 113 (0.2) | 42 (0.2) | 127 (0.4) | | |
| Parity | | | | | | | | |
| Nulliparous | 219 951 (44.7) | 56 547 (41.4) | 15 163 (76.3) | 34 574 (83.0) | 11 560 (20.8) | 8788 (51.0) | 29 413 (84.4) | ≤.001 |
| Multiparous | 271 639 (55.3) | 80 104 (58.6) | 4702 (23.7) | 7057 (17.0) | 43 939 (79.2) | 8428 (49.0) | 5402 (15.6) | | |
| Mode of birth characteristics | | | | | | | | |
| Pain medication | | | | | | | | |
| None | 57 214 (11.6) | 13 602 (10.0) | 418 (2.1) | 305 (0.7) | – | – | – | ≤.001 |
| Pharmacological pain medication<sup>c</sup> | 231 106 (47.0) | 82 384 (60.3) | 10 080 (50.7) | 12 631 (30.3) | – | – | – | | |
| Epidural, caudal, spinal or general anesthesia | 200 942 (40.9) | 40 017 (29.3) | 9326 (46.9) | 28 666 (68.9) | 55 461 (99.9) | 17 208 (100) | 34 837 (100) | | | |
| Missing | 2328 (0.5) | 648 (0.5) | 41 (0.2) | 29 (0.1) | 38 (0.1) | 8 (0) | 8 (0) | | |
TABLE 1 (Continued)

| Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | Statistical differences among groups that differed on mode of birth |
|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|-------------------------------------------------------------|
| N = 491 590      | n = 185 883              | n = 136 651                                 | n = 19 865        | n = 41 631       | n = 55 499                                    | n = 17 216        | n = 34 845                                                   |
| 100%             | 37.8%                    | 27.8%                                       | 4.0%              | 8.5%             | 11.3%                                        | 3.5%              | 7.1%                                                        |
| n (%)            | n (%)                    | n (%)                                       | n (%)             | n (%)            | n (%)                                        | n (%)             | n (%)                                                       |

Child characteristics

Gender

| Gender | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|--------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|
| Female | 242 618 (49.3)   | 94 161 (50.9)            | 69 096 (50.6)                               | 8993 (45.3)       | 19 367 (46.5)   | 26 988 (48.6)                                | 7650 (44.4)       | ≤.001   |
| Male   | 249 242 (50.7)   | 91 237 (50.1)            | 70 617 (49.4)                               | 10 864 (54.7)     | 22 246 (53.4)   | 28 449 (51.3)                                | 9554 (55.5)       | 19 375 (55.6) |
| Missing| 180 (0)          | 30 (0)                   | 8 (0)                                       | 18 (0)            | 62 (0)          | 12 (0)                                       | 12 (0)            |         |

Gestational age

| Gestational age | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|-----------------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|
| 37-37 + 6       | 21 800 (4.4)     | 8503 (4.6)               | 5646 (4.1)                                  | 885 (4.4)         | 1251 (3.0)      | 3303 (6.0)                                   | 1358 (7.9)        | ≤.001   |
| 38-40 + 6       | 367 792 (74.8)   | 149 685 (80.5)           | 92 235 (67.5)                               | 15 646 (78.8)     | 28 202 (67.7)   | 49 328 (88.9)                                | 13 016 (75.6)     | 19 680 (56.5) |
| 41-41 + 6       | 101 998 (20.7)   | 27 695 (14.9)            | 38 770 (28.4)                               | 3334 (16.8)       | 12 178 (29.3)   | 2868 (5.1)                                   | 2842 (16.5)       | 14 311 (41.1) |

Birthweight

| Birthweight | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|-------------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|
| ≤2500 g     | 4993 (1.0)       | 1618 (0.8)               | 1496 (1.1)                                  | 174 (0.9)         | 362 (0.9)       | 729 (1.3)                                    | 218 (1.3)         | 396 (1.1) |
| 2500-3499 g | 240 896 (49.0)   | 97 316 (52.4)            | 63 789 (46.6)                               | 10 629 (53.5)     | 19 811 (47.6)   | 28 020 (50.5)                                | 8195 (47.6)       | 13 136 (37.7) |
| 3500-3999 g | 176 014 (35.8)   | 64 872 (34.9)            | 50 361 (36.9)                               | 6947 (35.0)       | 15 558 (37.4)   | 19 029 (34.3)                                | 5692 (34.6)       | 13 285 (38.1) |
| ≥4000 g     | 69 687 (14.2)    | 22 077 (11.9)            | 21 005 (15.4)                               | 2115 (10.6)       | 5900 (14.2)     | 7721 (13.9)                                  | 2841 (16.5)       | 8028 (23.0) |

Small-for-gestational age

| Small-for-gestational age | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|---------------------------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|
| 2151 (0.4)               | 720 (0.4)        | 594 (0.4)                | 88 (0.4)                                    | 170 (0.4)         | 327 (0.6)       | 177 (0.7)                                    | 135 (0.4)         | ≤.001   |

Large-for-gestational age

| Large-for-gestational age | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|--------------------------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|
| 16460 (3.3)             | 2954 (1.6)       | 2530 (1.9)               | 2570 (12.9)                                 | 5475 (13.2)       | 765 (1.4)       | 689 (4.0)                                    | 1477 (4.2)        | ≤.001   |

Birth trauma child

| Birth trauma child | Total population | Spontaneous vaginal birth | Vaginal birth with induction or augmentation* | Instrumental birth | Cesarean elective | Cesarean emergency after induction or augmentation | Cesarean emergency | P-value |
|-------------------|------------------|--------------------------|---------------------------------------------|-------------------|------------------|-----------------------------------------------|-------------------|---------|

*Induction or augmentation with oxytocin, prostaglandin, and/or artificial rupture of membranes.

bSocioeconomic status are index data of relative socioeconomic advantage and disadvantage, low (deciles 0-3), middle (deciles 4-6), high (7-10 deciles).

Pharmacological pain medication (ie, nitrous oxide, systematic opioid, local administered to perineum, pudendal, morphine, and pethidine).

Birth trauma refers to birth trauma to central or peripheral nervous system, birth trauma to scalp, birth trauma to skeleton, intracranial laceration, and hemorrhage due to birth trauma.
3 | RESULTS

The total population linked data set contained the antenatal, birth, and postnatal details of 669,880 women and 1,097,762 births which occurred in public or private hospitals during the study period 2000-2008 with a follow-up until age 5 years. A total 548,815 births (50%) were excluded due to medical or obstetric risk factors (eg, maternal morbidity, preterm birth) or substance abuse in pregnancy (eg, smoking or drug abuse). We excluded 54,254 (4.9%) children with congenital abnormalities. After applying all other exclusion criteria, mortality was recorded for 1638 (0.1%) children during the study period. There were 653 stillbirths, 353 cases of neonatal mortality, and 632 of childhood mortality. The risk of neonatal mortality was similar across the different mode of births. Finally, 1465 cases were excluded due to missing data on either maternal characteristics (ie, age, mode of birth, parity) or child characteristics (ie, gestational age, birthweight). The final study cohort consisted of 491,590 healthy pregnant women and their children.

The majority of the women were Australian born (69%) and had a mean age of 29 (SD 4) years. Fifty-five percent of the women were nulliparous. About 38% had a spontaneous vaginal birth, 28% had a vaginal birth with induction or augmentation, 4% had an instrumental birth without induction or augmentation, and 8% had an instrumental birth with induction or augmentation. Eleven percent of these women had an elective cesarean delivery, 4% had an emergency cesarean, and 7% had an emergency cesarean delivery after induction or augmentation of labor (Table 1). Overall, 43% of the women included were induced before labor, or received augmentation during labor. The majority (88%) of women received pain medication and infant’s birth trauma was experienced in 3% of the births. Maternal (eg, socioeconomic status), birth (eg, pain medication), and child characteristics (eg, gestational age) showed statistically significant differences across seven modes of the birth group ($P \leq .001$, Table 1). Missing values ranged from 0.04% (ie, infant gender) to 0.3% (ie, socioeconomic status) in the final linked data set.

3.1 | Outcomes at short-term follow-up (first 28 days)

The prevalence of jaundice, feeding problems, and hypothermia were, respectively, 4%, 3%, and 2%. Compared with infants who were born by spontaneous vaginal birth, all other infants born with either medical or operative birth interventions had significantly higher odds of jaundice and feeding problems, except for an elective cesarean delivery which was not associated with the risk of jaundice ($P = .07$). Infants born by instrumental vaginal birth after induction or augmentation showed the highest association of jaundice (crude OR 3.26 [95% CI 3.12-3.41], adjusted OR [aOR] 2.75 [95% CI 2.61-2.91]). Significantly higher odds of hypothermia were observed for infants born by all the specified cesarean groups compared with those born by spontaneous vaginal delivery (Table 2).

3.2 | Outcomes at longer-term follow-up (up to 5 years of age)

Diagnosed respiratory infections had the highest prevalence of any of the medical conditions during the 5-year follow-up period, 14%. The lowest prevalence was observed for gastrointestinal disorders, 0.5%. Other bacterial infections, sepsis, otitis, cystitis, or urethritis, were reported in 8% of the children in the study. There was no evidence to suggest an association between mode of birth and the odds of asthma. Metabolic disorder was reported in 1% of children and 3% were diagnosed with eczema. Compared with children born after spontaneous vaginal birth without induction or augmentation, all other groups had higher odds of respiratory infections, metabolic disorder, and eczema (Table 3). Odds of gastrointestinal disorders were higher among children born after vaginal birth with induction or augmentation and after elective cesarean delivery. Other infections were more prevalent among all exposure groups compared with those born after spontaneous vaginal birth without induction or augmentation. No statistical significant associations between other infections and groups born after instrumental birth either without or with induction or augmentation were observed ($P$-values .07 and .02, respectively). Compared with children born by spontaneous vaginal birth, children born by cesarean delivery had higher odds of longer-term adverse health outcomes. Birth by elective cesarean delivery aOR 2.49 (95% CI 2.19-2.82), an emergency cesarean aOR 2.63 (95% CI 2.26-3.07), and emergency cesarean delivery after induction aOR 2.41 (95% CI 2.11-2.76) was associated with increased odds of metabolic disorder.

4 | DISCUSSION

The aim of this study was to examine the association between medical birth interventions and/or operative birth interventions on short- and longer-term child health outcomes in healthy women and their children by analyzing population-based linked data. Our results showed that newborns born by instrumental birth after induction or augmentation were more likely to experience jaundice. Children born by cesarean delivery were particularly at increased risk for adverse health outcomes in the longer term, that is, respiratory infection, other infection, and metabolic disorder.
There is emerging evidence that some birth interventions may have an effect on the neonatal immune response and the child’s health in the longer term.\textsuperscript{7,29} There is evidence of short-term health impacts for the infant after a cesarean delivery, such as hypothermia, impaired lung function, altered metabolism, altered blood pressure, and altered feeding, which is consistent with our results.\textsuperscript{7,27,28} Some of these changes might be due to a lack of labor stress, associated with physiological maladaptation after birth. Some epidemiological studies have linked the mode of birth (particularly cesarean delivery) to increasing rates of asthma and gastrointestinal disorders.\textsuperscript{15,17} However, other epidemiological studies did not report higher rates of asthma, diabetes type 1, obesity, and inflammatory bowel disease for children born with birth interventions.\textsuperscript{12,16} Several studies that included meta-analyses reported that children born by cesarean delivery were at higher risk of developing obesity, diabetes, or asthma in childhood.\textsuperscript{5,6,30,31}

The EPIIC hypothesis postulated by some of the authors in this paper, proposes that nonphysiological interventions during the intrapartum period, and specifically the use of synthetic oxytocin, epidural analgesia, and cesarean delivery, may interrupt the normal stress of being born.\textsuperscript{10,11} This could have an epigenetic effect on specific genes, such as those that program immune responses, including weight regulation and metabolism. In support of an epigenetic hypothesis in this area, an association between mode of birth and DNA methylation has previously been reported.\textsuperscript{32,33} Schlinzig et al examined 37 term babies born by elective cesarean delivery (n = 16) or vaginal birth (n = 21) and found a higher global measure of DNA methylation if the infant was born by cesarean delivery. While there was a nonsignificant difference between vaginal birth and cesarean delivery at 3-5 days postpartum, the pattern did not alter in the infants born vaginally but significantly

| TABLE 2 Prevalence and associations between birth interventions and short-term child health outcomes, New South Wales, Australia, 2000-2013 |
|--------------------------------------------------|------------------|------------------|------------------|
| **Short-term adverse health outcomes**  | **Total population** | **Unadjusted OR (95% CI)** | **Adjusted\textsuperscript{a} OR (95% CI)** |
| Spontaneous vaginal birth | 5299 (2.9) | Reference | Reference |
| Vaginal birth with induction or augmentation | 4986 (3.6) | 1.28 (1.23-1.33) | 1.36 (1.31-1.42) |
| Instrumental vaginal birth without induction or augmentation | 1615 (8.1) | 3.01 (2.84-3.19) | 2.34 (2.20-2.49) |
| Instrumental vaginal birth with induction or augmentation | 3662 (8.8) | 3.26 (3.12-3.41) | 2.75 (2.61-2.91) |
| Elective cesarean | 1638 (3.0) | 1.02 (0.96-1.07) | 1.07 (1.00-1.14) |
| Emergency cesarean without induction or augmentation | 686 (4.0) | 1.39 (1.29-1.51) | 1.24 (1.14-1.36) |
| Emergency cesarean after induction or augmentation | 1375 (3.9) | 1.38 (1.30-1.46) | 1.31 (1.22-1.41) |
| Feeding problems  |  |  |  |
| Spontaneous vaginal birth | 1886 (1.0) | Reference | Reference |
| Vaginal birth with induction or augmentation | 1907 (1.4) | 1.37 (1.28-1.46) | 1.23 (1.15-1.32) |
| Instrumental vaginal birth without induction or augmentation | 513 (2.6) | 2.58 (2.34-2.85) | 1.44 (1.30-1.60) |
| Instrumental vaginal birth with induction or augmentation | 1344 (3.2) | 3.22 (3.00-3.46) | 1.73 (1.59-1.89) |
| Elective cesarean | 1095 (2.0) | 1.93 (1.79-2.08) | 1.81 (1.64-1.99) |
| Emergency cesarean without induction or augmentation | 450 (2.6) | 2.58 (2.33-2.87) | 1.82 (1.61-2.05) |
| Emergency cesarean after induction or augmentation | 1090 (3.1) | 3.10 (2.87-3.34) | 1.85 (1.67-2.04) |
| Hypothermia  |  |  |  |
| Spontaneous vaginal birth | 5537 (3.0) | Reference | Reference |
| Vaginal birth with induction or augmentation | 4484 (3.3) | 1.09 (1.05-1.14) | 1.04 (1.00-1.08) |
| Instrumental vaginal birth without induction or augmentation | 687 (3.5) | 1.16 (1.07-1.26) | 0.96 (0.88-1.04) |
| Instrumental vaginal birth with induction or augmentation | 1542 (3.7) | 1.24 (1.17-1.31) | 1.01 (0.94-1.08) |
| Elective cesarean | 2104 (3.8) | 1.26 (1.20-1.32) | 1.16 (1.08-1.24) |
| Emergency cesarean without induction or augmentation | 742 (4.3) | 1.45 (1.34-1.56) | 1.24 (1.13-1.36) |
| Emergency cesarean after induction or augmentation | 1775 (5.1) | 1.72 (1.63-1.82) | 1.43 (1.33-1.54) |

\textsuperscript{a}Adjusted for maternal characteristics (ie, maternal age, country of birth, socioeconomic status, parity), birth characteristics (ie, pharmacological pain medication or anesthesia), and child characteristics (ie, gender, gestational age, birthweight, small-for-gestational age, large-for-gestational age, birth trauma).

\textsuperscript{b}Associations reported in bold reflect a statistical significant association ($P \leq .01$).
TABLE 3 Prevalence and associations between birth interventions and longer-term child health outcomes, New South Wales, Australia, 2000-2013

| Longer-term adverse health outcomes | Total population | No. of events | Unadjusted OR (95% CI) | Adjusted\(^a\) OR (95% CI) |
|------------------------------------|-----------------|---------------|------------------------|-----------------------------|
|                                    | N (%)           |               |                        |                             |
| Asthma                             |                 |               |                        |                             |
| Spontaneous vaginal birth          | 5738 (3.1)      | Reference     | Reference              |                             |
| Vaginal birth with induction or augmentation | 4294 (3.1) | 1.01 (0.97-1.05) | 1.01 (0.96-1.05) |
| Instrumental vaginal birth without induction or augmentation | 640 (3.2) | 1.04 (0.96-1.13) | 1.07 (0.98-1.17) |
| Instrumental vaginal birth with induction or augmentation | 1201 (2.9) | 0.92 (0.87-0.98) | 0.97 (0.90-1.04) |
| Elective cesarean                  | 1868 (3.4)      | 1.07 (1.02-1.13) | 1.04 (0.97-1.11) |
| Emergency cesarean without induction or augmentation | 604 (3.5) | \(1.12 (1.03-1.23)^b\) | 1.09 (0.99-1.20) |
| Emergency cesarean after induction or augmentation | 1084 (3.1) | 0.99 (0.93-1.06) | 1.03 (0.95-1.12) |
| Respiratory infections             |                 |               |                        |                             |
| Spontaneous vaginal birth          | 22 454 (12.1)   | Reference     | Reference              |                             |
| Vaginal birth with induction or augmentation | 18 653 (13.7) | \(1.14 (1.12-1.16)\) | 1.11 (1.08-1.13) |
| Instrumental vaginal birth without induction or augmentation | 2960 (14.9) | \(1.27 (1.22-1.33)\) | 1.25 (1.20-1.31) |
| Instrumental vaginal birth with induction or augmentation | 6538 (15.7) | \(1.34 (1.30-1.38)\) | 1.31 (1.27-1.36) |
| Elective cesarean                  | 9660 (17.4)     | \(1.50 (1.46-1.54)\) | 1.35 (1.31-1.40) |
| Emergency cesarean without induction or augmentation | 3030 (17.6) | \(1.53 (1.47-1.60)\) | 1.39 (1.32-1.46) |
| Emergency cesarean after induction or augmentation | 5497 (15.8) | \(1.34 (1.30-1.38)\) | 1.29 (1.23-1.34) |
| Gastrointestinal disorders         |                 |               |                        |                             |
| Spontaneous vaginal birth          | 665 (0.4)       | Reference     | Reference              |                             |
| Vaginal birth with induction or augmentation | 665 (0.5) | \(1.35 (1.21-1.50)\) | 1.22 (1.09-1.37) |
| Instrumental vaginal birth without induction or augmentation | 97 (0.5) | \(1.36 (1.10-1.69)\) | 1.13 (0.90-1.41) |
| Instrumental vaginal birth with induction or augmentation | 181 (0.4) | \(1.20 (1.02-1.42)\) | 0.96 (0.79-1.16) |
| Elective cesarean                  | 330 (0.6)       | \(1.63 (1.43-1.86)\) | 1.21 (1.02-1.44) |
| Emergency cesarean without induction or augmentation | 101 (0.6) | \(1.62 (1.31-2.00)\) | 1.24 (0.98-1.57) |
| Emergency cesarean after induction or augmentation | 193 (0.6) | \(1.53 (1.30-1.79)\) | 1.19 (0.98-1.45) |
| Other infections                   |                 |               |                        |                             |
| Spontaneous vaginal birth          | 13 448 (7.2)    | Reference     | Reference              |                             |
| Vaginal birth with induction or augmentation | 11 750 (8.6) | \(1.20 (1.16-1.23)\) | 1.12 (1.09-1.15) |
| Instrumental vaginal birth without induction or augmentation | 1678 (8.4) | \(1.18 (1.12-1.24)\) | 1.05 (1.00-1.11) |
| Instrumental vaginal birth with induction or augmentation | 3589 (8.6) | \(1.20 (1.15-1.24)\) | 1.06 (1.01-1.10) |
| Elective cesarean                  | 5326 (9.6)      | \(1.33 (1.29-1.38)\) | 1.07 (1.03-1.12) |
| Emergency cesarean without induction or augmentation | 1630 (9.5) | \(1.32 (1.25-1.39)\) | 1.10 (1.04-1.17) |
| Emergency cesarean after induction or augmentation | 3218 (9.2) | \(1.28 (1.23-1.33)\) | 1.10 (1.05-1.16) |
| Metabolic disorder                 |                 |               |                        |                             |
| Spontaneous vaginal birth          | 1041 (0.6)      | Reference     | Reference              |                             |
| Vaginal birth with induction or augmentation | 1124 (0.8) | \(1.46 (1.34-1.59)\) | 1.35 (1.23-1.48) |
| Instrumental vaginal birth without induction or augmentation | 181 (0.9) | \(1.63 (1.39-1.91)\) | 1.28 (1.08-1.52) |
| Instrumental vaginal birth with induction or augmentation | 463 (1.1) | \(1.98 (1.77-2.21)\) | 1.54 (1.35-1.75) |
| Elective cesarean                  | 919 (1.7)       | \(2.93 (2.68-3.21)\) | 2.49 (2.19-2.82) |
| Emergency cesarean without induction or augmentation | 338 (2.0) | \(3.51 (3.10-3.97)\) | 2.63 (2.26-3.07) |
| Emergency cesarean after induction or augmentation | 653 (1.9) | \(3.34 (3.02-3.68)\) | 2.41 (2.11-2.76) |

(Continues)
TABLE 3 (Continued)

| Long-term adverse health outcomes | Total population |
|----------------------------------|-----------------|
|                                  | No. of events   | Unadjusted OR (95% CI) | Adjusteda OR (95% CI) |
| Eczema                           |                 |                 |                  |
| Spontaneous vaginal birth        | 3566 (1.9)      | Reference        | Reference        |
| Vaginal birth with induction or augmentation | 3529 (2.6) | 1.34 (1.28-1.41) | 1.16 (1.10-1.22) |
| Instrumental vaginal birth without induction or augmentation | 1171 (5.9) | 3.20 (2.99-3.42) | 2.18 (2.03-2.35) |
| Instrumental vaginal birth with induction or augmentation | 2817 (6.8) | 3.68 (3.50-3.87) | 2.30 (2.16-2.45) |
| Elective cesarean                | 1541 (2.8)      | 1.43 (1.35-1.52) | 1.11 (1.03-1.19) |
| Emergency cesarean without induction or augmentation | 1178 (6.8) | 3.71 (3.46-3.97) | 2.54 (2.35-2.75) |
| Emergency cesarean after induction or augmentation | 2476 (7.1) | 3.85 (3.65-4.06) | 2.38 (2.22-2.55) |

*aAdjusted for maternal characteristics (ie, maternal age, country of birth, socioeconomic status, parity), birth characteristics (ie, pharmacological pain medication or anesthesia), and child characteristics (ie, gender, gestational age, birthweight, small-for-gestational age, large-for-gestational age, birth trauma).

*bAssociations reported in bold reflect a statistical significant association (P ≤ .01).

decreased in infants born by cesarean delivery.\(^3^3\) Almgren et al\(^3^2\) undertook a more precise analysis, looking at DNA from hematopoietic stem cells (CD34\(^+\)). Those in specific gene sites that programmed for immune-mediated disease showed different methylation patterns in infants born by cesarean delivery than those born vaginally.\(^3^2\) Furthermore, those infants born after shorter labor showed similar DNA methylation patterns to those born by cesarean, suggesting that physiological labor stress over a certain period of time is required to program certain autoimmune responses in the neonate.

An alternative theory, the Extended Hygiene Hypothesis suggests that in utero, during a vaginal birth, and following skin-to-skin contact and breastfeeding, the infant needs to gather a community of microbes that come from the mother and the surrounding environment.\(^8^,^9\) Establishing the gut microbiota may be important in protecting the child, and later the adult, against atopic and immunological diseases.\(^10^,^3^4\) Disturbances in this process could be linked to developing infectious, inflammatory, and allergic diseases later in life.\(^10^,^3^4\)

However, some studies associate the mode of birth with differences in the child’s microbiota, other conflicting results showed that there was no effect of cesarean delivery on the early microbiota beyond the immediate neonatal period.\(^3^5\)

Despite this, there is a global awareness that cesarean delivery rates are too high. Currently, the emphasis is on labor induction to address this issue, as in, for example, a recently reported randomized controlled trial on routine induction of labor at 39 weeks in nulliparous women.\(^3^6\) Although this study showed a reduced cesarean delivery, our population level analysis shows that replacing one technical intervention with another might not improve longer-term outcomes. We suggest that those looking to reduce unnecessary intervention could consider results of systematic reviews that show that relationship-based interventions, such as continuous support in labor, or continuity of midwifery care, are associated with decreased interventions, improved rates of physiological birth, and higher levels of maternal reports of well being, without adversely affecting mortality and morbidity, and at reduced cost for women and health systems.\(^3^7^,^3^8\)

Our study had several strengths and limitations. To our knowledge, this is the first study that has provided an overview of associations between all possible birth interventions and a wide range of adverse child health outcomes within a large population of healthy pregnant women and their children. In our analyses, we adjusted for a range of confounders, including maternal characteristics, birth characteristics, and child characteristics. However, our associations could still be affected by unmeasured confounding, such as maternal body mass index, antibiotic use during pregnancy or administered during childhood until the age of 5, breast or artificial feeding, paternal characteristics, and familial environmental and genetic factors. Moreover, we were unable to control for confounding by indication since the underlying reasons for the provided medical and operative birth interventions were unknown.\(^3^9\) All of these factors may independently be associated with some of the health outcomes seen in children and therefore our findings must be interpreted with caution. It is possible that the routine use of intrapartum antibiotics also plays a role in the disturbance of the microbiome. As a consequence, the infant may experience adverse outcomes. Furthermore, experimental and laboratory-based studies are needed to determine the precise mechanism and contribution of the different factors to the outcome. While we included country of birth, we could not include ethnicity and this may also affect outcomes and associations. We were only able to examine admissions of the child to a hospital while visits to general practitioners were not incorporated, suggesting an underreporting of adverse outcomes. Unfortunately, population-based linked data are restricted to the selection of variables and limited ability to verify the accuracy of the data, but do
provide a cost-effective way of establishing incidence and association of (rare) health outcomes and can direct future research.

Further research is required to confirm or refute the findings from this study. Research ideally would include other population-based data registries, including a longer follow-up period for a wider range of adverse child health outcomes, particularly those that are found more commonly beyond 5 years of age (eg, asthma). More research is also needed to explain some of the potential mechanisms at play, including epigenetic and microbiome research.

By analyzing linked population data, we obtained insight into the association of medical and operative birth interventions and short- and longer-term child health outcomes. These results support the “Too little too late, too much too soon debate” in maternal care, in which Miller et al argued that unnecessary use of nonevidence-based interventions can be harmful for healthy women and infants, as much as a lack of lifesaving interventions is damaging for those that need them. Our results should make consumers and maternal health care professionals aware of the potential harm that birth interventions may have in the longer term, encouraging a “precautionary principle” approach that weighs the possible benefits of interventions against its potential detrimental effects for each mother and child. The aim should always be to provide the right amount of care at the right time in the right way to childbearing women, with a clear assessment of the potential consequences of just-in-case interventions.

4.1 Conclusion

Children born by spontaneous vaginal birth had fewer short- and longer-term health problems, compared with those born after birth interventions. This suggests that when examining labor interventions, researchers need to pay attention to use of exogenous oxytocin and to instrumental and operative birth, and that follow-up should be continued into the longer term.

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ORCID

Lilian L. Peters http://orcid.org/0000-0003-2342-0799
Charlene Thornton http://orcid.org/0000-0003-4457-1799
Ank de Jonge http://orcid.org/0000-0002-5384-3744

Esther I. Feijen-de Jong http://orcid.org/0000-0001-5766-296X
Hannah G. Dahlen http://orcid.org/0000-0002-4450-3078

REFERENCES

1. Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Tornoli MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. PLoS One. 2016;11:e0148343.
2. The Australian Institute of Health and Welfare. Australia’s mothers and babies 2014—in brief. Perinatal statistics. 2016;series no. 32. Cat no. PER 87 Canberra: AIHW.
3. Buchanan SL, Patterson JA, Roberts CL, Morris JM, Ford JB. Trends and morbidity associated with oxytocin use in labour in nulliparas at term. Aust N Z J Obstet Gynaecol. 2012;52:173-178.
4. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. PLoS Med. 2018;15:e1002494.
5. Huh SY, Rifas-Shiman SL, Zera CA, et al. Delivery by caesarean section and risk of obesity in preschool age children: a prospective cohort study. Arch Dis Child. 2012;97:610-616.
6. Cardwell CR, Stene LC, Joner G, et al. Caesarean section is associated with an increased risk of childhood-onset type 1 diabetes mellitus: a meta-analysis of observational studies. Diabetologia. 2008;51:726-735.
7. Hyde MJ, Mostyn A, Modi N, Kemp PR. The health implications of birth by caesarean section. Biol Rev Camb Philos Soc. 2012;87:229-243.
8. Azad MB, Konya T, Maughan H, et al. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. CMAJ. 2013;185:385-394.
9. Vidal AC, Murphy SK, Murtha AP, et al. Associations between antibiotic exposure during pregnancy, birth weight and aberrant methylation at imprinted genes among offspring. Int J Obes (Lond). 2013;37:907-913.
10. Dahlen HG, Downe S, Wright ML, Kennedy HP, Taylor JY. Childbirth and consequent atopic disease: emerging evidence on epigenetic effects based on the hygiene and EPIIC hypotheses. BMC Pregnancy Childbirth. 2016;16:4.
11. Dahlen HG, Kennedy HP, Anderson CM, et al. The EPIIC hypothesis: intrapartum effects on the neonatal epigenome and consequent health outcomes. Med Hypotheses. 2013;80:656-662.
12. Clausen TD, Bergholt T, Eriksson F, Rasmussen S, Keiding N, Lokkegaard EC. Prelabor cesarean section and risk of childhood type 1 diabetes: a register-based cohort study. Epidemiology. 2016;27:547-555.
13. Khashan AS, Kenny LC, Lundholm C, Kearney PM, Gong T, Almqvist C. Mode of obstetrical delivery and type 1 diabetes: a sibling design study. Pediatrics. 2014;134:e806-e813.
14. Almqvist C, Cnattingius S, Lichtenstein P, Lundholm C. The impact of birth mode of delivery on childhood asthma and allergic diseases—a sibling study. Clin Exp Allergy. 2012;42:1369-1376.
15. Davidson R, Roberts SE, Wotton CJ, Goldacre MJ. Influence of maternal and perinatal factors on subsequent hospitalisation...
for asthma in children: evidence from the Oxford record linkage study. *BMC Pulm Med.* 2010;10:14.

16. Black M, Bhattacharya S, Philip S, Norman JE, McLernon DJ. Planned cesarean delivery at term and adverse outcomes in childhood health. *JAMA.* 2015;314:2271-2279.

17. Tollanes MC, Moster D, Daltveit AK, Irgens LM. Cesarean section and risk of severe childhood asthma: a population-based cohort study. *J Pediatr.* 2008;153:112-116.

18. Hakansson S, Kallen K. Caesarean section increases the risk of hospital care in childhood for asthma and gastroenteritis. *Clin Exp Allergy.* 2003;33:757-764.

19. Homer CS, Thornton C, Scarf VL, et al. Birthplace in New South Wales, Australia: an analysis of perinatal outcomes using routinely collected data. *BMC Pregnancy Childbirth.* 2014;14:206.

20. Dahlen HG, Tracy S, Tracy M, Bisits A, Brown C, Thornton C. Centre for Health Record Linkage. Quality assurance report. *Lain SJ, Hadfield RM, Raynes-Greenow CH, et al. Quality of data in perinatal population health databases: a systematic review. Med Care.* 2012;50:e20.

21. Centre for Health Record Linkage. Quality assurance report. <http://www.cherel.org.au/media/24160/qa_report_2012.pdf> Web site. Updated 2012. Accessed February 19, 2018.

22. Hadfield RM, Lain SJ, Cameron CA, Bell JC, Morris JM, Roberts CL. The prevalence of maternal medical conditions during pregnancy and a validation of their reporting in hospital discharge data. *Aust N Z J Obstet Gynaecol.* 2008;48:78-82.

23. Lam MK. How good is New South Wales admitted patient data collection in recording births? *Health Inf Manag.* 2011;40:12-19.

24. National Collaborating Centre for Women’s and Children’s Health. *Intrapartum Care, Care for Healthy Women and Their Babies During Childbirth.* Commissioned by the National Institute for Health and Clinical Excellence. London: RCOG Press; 2007.

25. de Jonge A, Peters L, Geerts CC, et al. Mode of birth and medical interventions among women at low risk of complications: a cross-national comparison of birth settings in England and The Netherlands. *PLoS One.* 2017;12:e0180846.

26. Bodner K, Wierrani F, Grunberger W, Bodner-Adler B. Influence of the mode of delivery on maternal and neonatal outcomes: a comparison between elective cesarean section and planned vaginal delivery in a low-risk obstetric population. *Arch Gynecol Obstet.* 2011;283:1193-1198.

27. Saeed G, Fakhar S, Imran T, Khawaja AL. The effect of modes of delivery on infants’ feeding practices. *Iran J Med Sci.* 2011;36:128-132.

28. Polidano C, Zhu A, Bornstein JC. The relation between cesarean birth and child cognitive development. *Sci Rep.* 2017;7:11483.

29. Sutharsan R, Mannan M, Doi SA, Mamun AA. Caesarean delivery and the risk of offspring overweight and obesity over the life course: a systematic review and bias-adjusted meta-analysis. *Clin Obes.* 2015;5:293-301.

30. Huang L, Chen Q, Zhao Y, Wang W, Fang F, Bao Y. Is elective cesarean section associated with a higher risk of asthma? A meta-analysis. *J Asthma.* 2015;52:16-25.

31. Almgren M, Schlinzig T, Gomez-Cabero D, et al. Cesarean delivery and hematopoietic stem cell epigenetics in the newborn infant: implications for future health? *Am J Obstet Gynecol.* 2014;211:502.e1-502.e8.

32. Schlinzig T, Johansson S, Gunnar A, Ekstrom TJ, Norman M. Epigenetic modulation at birth—altered DNA-methylation in white blood cells after cesarean section. *Acta Paediatr.* 2009;98:1096-1099.

33. Rautava S, Ruuskanen O, Ouwehand A, Salminen S, Isolauri E. The hygiene hypothesis of atopic disease—an extended version. *J Pediatr Gastroenterol Nutr.* 2004;38:378-388.

34. Chu DM, Ma J, Prince AL, Antony KM, Seferovic MD, Aagard KM. Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery. *Nat Med.* 2017;23:314-326.

35. Grobman W. LB01: a randomized trial of elective induction of labor at 39 weeks compared with expectant management of low-risk nulliparous women. *Am J Obstet Gynecol.* 2018;218:S601.

36. Sandall J, Soltani H, Gates S, Shennan A, Devane D. Midwife-led continuity models versus other models of care for childbearing women. *Cochrane Database Syst Rev.* 2016;4:CD004667.

37. Bohren MA, Hofmeyr GJ, Sakala C, Fukuzawa RK, Cuthbert KM. Continuous support for women during childbirth. *Cochrane Database Syst Rev.* 2017;7:CD003766.

38. Danilack VA, Dore DD, Triche EW, Muri JH, Phipps MG, Savitz DA. The effect of labour induction on the risk of caesarean delivery: using propensity scores to control confounding by indication. *BIOG.* 2016;123:1521-1529.

39. Miller S, Abalos E, Chamillard M, et al. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. *Lancet.* 2016;388:2176-2192.

40. Jansen L, Gibson M, Bowles BC, Leach J. First do no harm: interventions during childbirth. *J Perinat Educ.* 2013;22:83-92.

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