Coronavirus disease 2019 pandemic and pregnancy and neonatal outcomes in general population: A living systematic review and meta-analysis (updated Aug 14, 2021)

Jie Yang | Rohan D’Souza | Ashraf Kharrat | Deshayne B. Fell | John W. Snelgrove | Kellie E. Murphy | Prakesh S. Shah

1Department of Pediatrics, Mount Sinai Hospital, Toronto, Ontario, Canada
2Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada
3Lunenfeld Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada
4Children’s Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
5School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada
6Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada

Correspondence
Prakesh S. Shah, Department of Pediatrics, Mount Sinai Hospital, 19-231, 600 University Avenue, Toronto, ON M5G 1X5, Canada.
Email: Prakeshkumar.shah@sinaihealth.ca

Funding information
Although no specific funding was received for this study, the Canadian Preterm Birth Network is funded by a grant from the Canadian Institutes of Health Research (PBN 150642).

Abstract

Introduction: Conflicting reports of increases and decreases in rates of preterm birth (PTB) and stillbirth in the general population during the coronavirus disease 2019 (COVID-19) pandemic have surfaced. The objective of our study was to conduct a living systematic review and meta-analyses of studies reporting pregnancy and neonatal outcomes by comparing the pandemic and pre-pandemic periods.

Material and methods: We searched PubMed and Embase databases, reference lists of articles published up until August 14, 2021 and included English language studies that compared outcomes between the COVID-19 pandemic time period and the pre-pandemic time periods. Risk of bias was assessed using the Newcastle–Ottawa scale. We conducted random-effects meta-analysis using the inverse variance method.

Results: Forty-five studies with low-to-moderate risk of bias, reporting on 1 843 665 pregnancies during the pandemic period and 23 564 552 pregnancies during the pre-pandemic period, were included. There was significant reduction in unadjusted estimates of PTB (35 studies, unadjusted odds ratio [uaOR] 0.95, 95% CI 0.92–0.98), but not in adjusted estimates (six studies, adjusted OR [aOR] 0.95, 95% CI 0.80–1.13). This reduction was noted in studies from single centers/health areas (25 studies, uaOR 0.90, 95% CI 0.86–0.96) but not in regional/national studies (10 studies, uaOR 0.99, 95% CI 0.95–1.02). There was reduction in spontaneous PTB (six studies, uaOR 0.89, 95% CI 0.81–0.96) and induced PTB (five studies, uaOR 0.89, 95% CI 0.81–0.97). There was no difference in the odds of stillbirth between the pandemic and pre-pandemic time periods (24 studies, uaOR 1.11, 95% CI 0.97–1.26 and four studies, aOR 1.06, 95% CI 0.81–1.38). There was an increase in mean birthweight during the pandemic period compared with the pre-pandemic period (six studies, mean difference 17 g, 95% CI 7–28 g). The odds of maternal mortality were increased (four studies, uaOR...
1 | INTRODUCTION

Most pregnancies end with healthy mothers and healthy children, but a small proportion result in adverse outcomes for the mother, fetus, or neonate. Among others, such outcomes include stillbirth, preterm birth (PTB), neonatal mortality, and maternal mortality—all of which can have devastating and long-lasting effects on families. Preterm birth (birth before 37 weeks of gestation) is a major determinant of neonatal and morbidities with long-term adverse consequences during childhood and adulthood. Medical, social, psychological, environmental, and economic factors have all been implicated in the etiopathogenesis of PTB and other adverse pregnancy outcomes.

The coronavirus disease 2019 (COVID-19) pandemic has had an unprecedented impact on society worldwide and provided a natural experiment allowing us to study the effects of these factors on adverse pregnancy outcomes. During the early stages of the pandemic, reports emerged describing reduced PTB rates in Denmark and Ireland. However, these were followed by reports of increased PTB rates (births between 28 and 32 weeks of gestation) in Nepal and no changes in PTB rates in the UK and Sweden. At the same time, increases in stillbirth rates were reported from the UK and Nepal with or without changes in PTB rates, whereas no change in the stillbirth rate was reported from Ireland.

In light of these mixed reports, it is uncertain whether or not the COVID-19 pandemic has affected pregnancy outcomes at the population level. Inconsistency among conclusions from different studies and a lack of evidence to inform the creation of evidence-based population health guidance prompted us to undertake a comprehensive review of the influence of the COVID-19 pandemic on pregnancy outcomes. Our objective was to systematically review and meta-analyze studies reporting defined local, regional, or national population-based rates for maternal, fetal, and neonatal outcomes during the pandemic period compared with the pre-pandemic period.

2 | MATERIAL AND METHODS

The review was conducted using standardized methods for systematic reviews of observational studies and reported according to the Preferred Reporting Items in Systematic Reviews and Meta-analyses guidelines. No ethical approval was obtained because all data used for these analyses were published previously. The review protocol was registered in PROSPERO (CRD42021234036). This is update #1 of a previously published review.

2.1 | Data sources: Search strategy and selection criteria

We searched PubMed and Embase databases, reference lists of included articles, and personal files for studies published up to August 14, 2021. The search strategy used a combination of the
MeSH terms “preterm” or “stillbirth” AND “Covid19” or “SARS-CoV-2” and included any type of study design published in the English language (Appendix S1). As this is a living systematic review, it will be updated 3-monthly for the duration of the pandemic, using the same search strategy. Studies were included if they compared pregnancy outcomes between the COVID-19 pandemic period and pre-pandemic time periods and reported on any of the outcomes of interest. We excluded studies that only reported outcomes of pregnant women with COVID-19. Screening of articles was conducted by two authors (PS and JY) and disagreements were resolved through discussion (JY, RD and PS) and consensus. As we were interested in overall pregnancy outcomes, we did not restrict studies based on plurality (including both singleton and multiple pregnancies).

2.2 Exposure

In most studies, the pandemic period was defined as the period beginning from the date or month of the implementation of emergency lockdown measures in relevant countries or states or cities, or when there was an emergence of cases or a surge of cases in the population studied. Some studies assessed “post-lockdown” period which for the purpose of this study was included as “pandemic” period as we are still not out of the pandemic yet. The pre-pandemic period was defined either as the period ending immediately before lockdown measures were implemented or before the emergence of the first case or high case numbers in the population, or as a historical period, such as births in the same population in previous year(s). The lengths of these periods varied across studies.

We included studies that reported outcomes of pregnancy in general population. The review was not designed to evaluate outcomes of pregnancies where only women affected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were reported.

2.3 Outcomes

The primary outcomes in this study were rates of PTB and stillbirth. Secondary outcomes included mean birthweight (continuous) and rates of low birthweight (LBW), spontaneous PTB, medically indicated PTB, and neonatal, perinatal, or maternal mortality. We contacted authors to obtain data on stillbirth and neonatal mortality when the outcomes were reported as “intrauterine fetal death” and “perinatal mortality”. The outcomes of intrauterine fetal death and perinatal mortality, though specified in the protocol, were not included ultimately in the review (deviation from protocol). Outcomes were defined as follows:

1. Preterm birth: Live births between 22+0 and 36+6 weeks of gestation were classified as PTB. Data on PTB at <28 weeks, <32 weeks, and <34 weeks of gestation were reported separately in some studies and were analyzed independently.

2. Stillbirth: Death before the complete expulsion or extraction from the parturient of a product of human conception at or after 20 weeks of gestation.14

3. Birthweight: Infant weight in grams, measured as soon as possible after live birth. Birthweight <2500 g was defined as LBW, birthweight <1500 g was defined as very low birthweight (VLBW), and birthweight <1000 gram was defined as extremely low birthweight (ELBW).

4. Spontaneous PTB: Birth of a baby between 22+0 and 36+6 weeks of gestation following spontaneous preterm labor or preterm prelabor rupture of membranes.3

5. Medically indicated PTB: Preterm birth initiated by a healthcare provider for maternal or fetal indications.3

6. Neonatal mortality: Death of a newborn due to any cause before 28 days of age.

7. Maternal mortality: Death of a woman either during pregnancy or childbirth from any cause related to or aggravated by pregnancy or its management, or within 42 days of end of pregnancy, irrespective of the duration and site of the pregnancy.7

2.4 Data extraction and risk of bias assessment

Data from the eligible studies were independently extracted by two authors (JY and PS) using a predefined, standardized extraction form. Disagreements between the authors were resolved by consensus and involving a third author (RD). The information extracted included details of the publication, study setting and size, pre-pandemic period definition, pandemic period definition, and rates of the reported outcomes in pre-pandemic and pandemic time periods. We relied only on published information.

We anticipated that primarily observational studies would be included in this review, so we used the Newcastle–Ottawa Scale15 for cohort studies to assess risk of bias. This scale assesses risk of bias in the domains of selection, comparability, and outcomes, and assigns a maximum score of 9. Studies with scores of 0 to 3 were considered to have high risk of bias, those with scores of 4 to 6 had moderate risk of bias, and those with scores of 7 to 9 had low risk of bias.

2.5 Statistical analyses

We planned for meta-analyses of studies that reported similar outcomes and were methodologically homogeneous. For binary outcomes, we calculated the summary unadjusted odds ratios (uaOR), adjusted OR (aOR) when available and 95% CI, whereas for birthweight we calculated the mean difference and 95% CI. Statistical heterogeneity was assessed using Cochran’s Q statistic and quantified by calculating the I² values. We expected clinical and methodological heterogeneity between studies, so planned a priori for random effect meta-analyses using the inverse variance method. We planned to meta-analyze adjusted estimates from studies that reported them, understanding that studies will have adjusted for different factors.
based on data availability and baseline differences. We also expected that the duration of the "pre-pandemic" period would vary across studies, so we conducted meta-regression on the variable "duration of the pre-pandemic period" as a covariate to explain any heterogeneity in the results. Post-hoc subgroup analyses were conducted for the two primary outcomes after dividing studies into single-center (or selected hospitals/centers in an area), regional (statewide or province-wide) or national in scope. Publication bias was assessed qualitatively, using funnel plots, and quantitatively, by calculating Egger’s regression intercept when more than 10 studies were included in the meta-analyses. For the Egger test, values less than 0.10 were considered indicative of publication bias. Meta-analyses were conducted using STATA v11.0 (StataCorp, College Station, TX, USA) and REVIEW MANAGER v5.3 (Cochrane Collaboration).

3 | RESULTS
3.1 | General study characteristics

Of 9953 records in the initial search, 45 articles were eligible for inclusion, of which 44 were used in the quantitative synthesis2,6–10,16–53 (Figure 1). Twenty-six full-text reports were excluded: reasons for the exclusions are provided in Appendix S2. For one study conducted in the Netherlands by Been et al.54 data were presented using multiple cut-offs to define the pre- and post-pandemic periods, with several different comparisons, making it difficult to select one comparison that aligned well with the other studies; we, therefore, included this study in the systematic review but not in meta-analyses. Khalil et al.9 had overlapping data for stillbirth outcome with another study; however, preterm birth data were not overlapping, so only preterm birth data were used in this review. Study characteristics are reported in Table 1: eight studies were national in scope, 11 were regional, and 24 were local, including single-center studies. Two studies did not report data settings. One study included in the previous version of this review, by Simpson et al.55 was replaced by data from a new study Shah et al.49 because the latter contained a larger pandemic and pre-pandemic period from the same province of Ontario, Canada. Liu et al.41 published another study from Canada, including data from Ontario. As they reported Ontario data separately and for an overlapping period with Shah et al.49, we extracted the data for Canada excluding Ontario from Liu et al. to avoid double counting of data. Across the included studies, totals of 1 843 665 pregnancies during the pandemic period (excluding numbers from Been et al.54) and 23 564 552 pregnancies during the pre-pandemic period were
| First author, Country | Population level | Neonatal | Exposed cohort (Pandemic period) | Non-exposed cohort (Pre-pandemic period) | Outcomes | Statistical approach | Factors adjusted for if any |
|-----------------------|------------------|----------|----------------------------------|------------------------------------------|----------|----------------------|----------------------------|
| Arnaez16 Spain        | 13 regional hospitals | Singleton | March 15–May 3, 2020 | March 15–May 3, 2015–2019 | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks; Stillbirth; LBW; VLBW; ELBW | Join-point regression analysis; Multivariate binomial logistic regression models | Hospital, sex, type of delivery and multiples |
| Been54 Netherlands    | Nationwide | Singleton | 1 month, 2 months, 3 months and 4 months after March 9, 2020; 1 month, 2 months, 3 months and 4 months after March 15, 2020; 1 month, 2 months, 3 months and 4 months before March 23, 2020 | 1 month, 2 months, 3 months and 4 months before March 9, 2020; 1 month, 2 months, 3 months and 4 months before March 15, 2020; 1 month, 2 months, 3 months and 4 months before March 23, 2020 | PTB <37 weeks; PTB <32 weeks | Difference-in-regression-discontinuity analysis | |
| Berghella27 USA       | Single center | Singleton | March 1–July 31, 2020 | March 1–July 31, 2019 | PTB <37 weeks; PTB <34 weeks; PTB <28 weeks; Stillbirth; Spontaneous PTB; Medically indicated PTB | Chi-squared test; multivariable logistic regression | |
| Bian,18 China         | Single center | Singleton | 2020 | 2014–2019 | PTB <37 weeks; PTB <32 weeks; Stillbirth | Chi-squared test; Student’s t-test; logistic regression | Maternal age, pre-pregnant body mass index, education, insurance status, type of conception, parity, maternal chronic medical conditions, pregnancy complications, gender of fetus |
| Briozzo,19 Uruguay    | Not reported | Not reported | March 15–September 30, 2020 | March 15–September 30, 2019 | PTB <37 weeks; LBW | Not reported | |
| Caniglia20 Botswana   | Nationwide | Singleton | April 3–July 20, 2020 | April 3–July 20, 2017–2019 | PTB <37 weeks; PTB <32 weeks; Stillbirth; Neonatal mortality | Difference-in-differences | |
| De Curtis21 Italy     | Single center | Singleton | March–May, 2020 | March–May, 2019 | PTB <37 weeks; PTB <32 weeks; Stillbirth | Z-test | |
| Dell’Utri22 Italy     | Single center | Not reported | February 23–June 24, 2020 | February 23–June 24, 2019 | Stillbirth | Chi-squared test; | |

(Continues)
| First author, Country | Population level | Neonatal | Exposed cohort (Pandemic period) | Non-exposed cohort (Pre-pandemic period) | Outcomes | Statistical approach | Factors adjusted for if any |
|-----------------------|------------------|----------|--------------------------------|------------------------------------------|----------|---------------------|----------------------------|
| Du23 China            | Single center    | Singleton | January 20–July 31, 2020       | May 20–November 30, 2019                | PTB <37 weeks; Stillbirth; LBW           | Chi-squared test; t-test; Univariate and multivariate log-binomial regression models | Age, ethnicity, occupation, education, gravidity, parity, h/o miscarriage, h/o induced abortion, BMI, GWG, f/h chronic diseases, prenatal visits |
| Einarsdóttir,24 Iceland | Nationwide      | Singleton | 2020                          | 2016–2019                                | PTB <37 weeks; PTB <32 weeks; Spontaneous PTB; Medically indicated PTB | Generalized linear mixed models (proc glimmix) with binomial distribution and logit link | Parity (primipara/multipara), maternal age (continuous), country of origin (Iceland, other), residential area (capital area, outside capital area), cohabitation (yes/no), employment (employed/student/homemaker/disability pension/unemployed), essential hypertension (yes/no), and pre-existing diabetes mellitus (yes/no) |
| Gallo25 Australia     | Single center    | Singleton | March 30–May 1, 2020           | March 30–May 1, 2013–2019               | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks | Analysis of variance (ANOVA) (scale); chi-squared testing (categorical); Logistic regressions | Maternal age, body mass index, ethnicity, parity, socioeconomic status, and history of or current asthma, diabetes mellitus, and/or hypertensive disorder |
| Goyal26 India         | Single center    | Not reported | April 1–August 30 2020        | October 1 2019–February 29, 2020       | Maternal mortality                      | Chi-squared test; Student’s t-test | |
| Greene27 USA          | Single center    | Not reported | March–April, 2020             | January–February, 2020                 | PTB <37 weeks                           | Student’s t-test; Wilcoxon test; chi-squared test; Fisher’s exact test | |
| Gu28 China            | Single center    | Not reported | January–February, 2020        | January–February, 2019                 | PTB <37 weeks; Stillbirth; Birthweight | t test; Chi-squared test | |
| Handley29 USA         | 2 Penn Medicine hospitals in Philadelphia | Singleton | March–June, 2020              | March–June, 2018–2019                  | PTB <37 weeks; Stillbirth; Spontaneous PTB; Medically indicated PTB | Fisher’s exact test | |

(Continues)
| First author, Country | Population level | Neonatal | Exposed cohort (Pandemic period) | Non-exposed cohort (Pre-pandemic period) | Outcomes | Statistical approach | Factors adjusted for if any |
|-----------------------|------------------|----------|----------------------------------|------------------------------------------|----------|----------------------|----------------------------|
| Harvey, USA           | Regionwide       | Not reported | March 22–April 30, 2020 | March 22–April 30, 2015–2019 | PTB <37 weeks; PTB <32 weeks; LBW; VLBW | Logistic regression models | Maternal age, education, race/ethnicity, diabetes, and hypertension |
| Hedermann, Denmark     | Nationwide       | Singleton | March 12–April 14, 2020 | March 12–April 14 of 2015–2019 | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks | Logistic regression | |
| Huseynova, Saudi Arabia | Single health authority | Singleton | March 1–June 30, 2020 | March 1–June 30, 2017–2019 | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks | One-sample test for binomial proportion; Chi-squared test, Fisher’s exact test; Poisson regression model | |
| Janevic, USA          | Single center    | Not reported | March 28–July 31, 2020 | March 28–July 31, 2019 | PTB <37 weeks; PTB <32 weeks | Log binomial regression | |
| Justman, Israel       | Single center    | Not reported | March-April, 2020 | March-April, 2019 | PTB <37 weeks; PTB <32 weeks; Stillbirth; Birthweight | Chi-squared and t-test or Mann-Whitney U test | |
| Kassie, Ethiopia       | Regionwide       | Not reported | March–June, 2020 | March–June, 2019 | Stillbirth; Neonatal mortality | t test | |
| Kasuga, Japan         | Single center    | Not reported | April 1–June 30, 2020 | April 1–June 30, 2017–2019 | PTB <37 weeks | Not reported | |
| KC, Nepal             | 9 hospitals across seven provinces | Not reported | March 21–May 30, 2020 | January 1–March 20, 2020 | PTB <37 weeks; Stillbirth; LBW; Neonatal mortality | Generalized linear model with Poisson regression; Pearson’s chi-squared test | Ethnicity, maternal age, and complication during admission |
| Khalil, UK            | Single center    | Singleton; twin; triplet | February 1–June 14, 2020 | October 1, 2019–January 31, 2020 | PTB <37 weeks; PTB <34 weeks; Stillbirth* | Mann–Whitney and Fisher’s exact tests | |
| Kirchengast, Austria  | Single center    | Singleton | March to July, 2020 | March to July, 2005–2019 | PTB <37 weeks; PTB <32 weeks; LBW; VLBW; ELBW | t test; Chi-squared test; Linear regression | |
| Kumar, India          | Not reported     | Not reported | March to September, 2020 | March to September, 2019 | Stillbirth; LBW; ELBW; VLBW | Fisher’s exact test | |
| Kumari, India         | 4 regional hospitals | Not reported | March 25 June 2, 2020 | January 15–March 24, 2020 | Stillbirth; Maternal mortality | Not reported | |

(Continues)
TABLE 1 (Continued)

| First author, Country | Population level | Neonatal | Exposed cohort (Pandemic period) | Non-exposed cohort (Pre-pandemic period) | Outcomes | Statistical approach | Factors adjusted for if any |
|-----------------------|------------------|----------|----------------------------------|------------------------------------------|----------|----------------------|-----------------------------|
| Lemon39 USA           | Single center    | Singleton| April 1–October 27, 2020          | January 1, 2018–January 31, 2020         | PTB <37 weeks; PTB <34 weeks; PTB <28 weeks; PTB <28 weeks; Spontaneous PTB; Medically indicated PTB | Pearson chi-squared or t tests |
| Li40 China            | Single center    | Not reported | January 23–March 24, 2020          | January 1, 2019–January 22, 2020         | PTB <37 weeks; Birthweight | Chi-squared, t test and Fisher's exact |
| Liu41 Canada          | Nationwide       | Singleton| March–August, 2020                | March–August, 2015–2019                  | PTB <37 weeks; PTB <34 weeks; PTB <32 weeks; PTB <28 weeks; Stillbirth | Not reported |
| Llorca42 Spain        | Single center    | Not reported | May 26–October 22, 2020            | January 1–August 31, 2018                 | PTB <37 weeks; PTB <34 weeks; LBW | Goodman–Kruskal γ test; Chi-squared test; Logistic regression | Age at delivery, educational level, and occupational status |
| Lumbrares–Marquez43 Mexico | Nationwide | Not reported | January 1–August 9, 2020          | 2011–2019                                 | Maternal mortality | Not reported |
| Main44 USA            | Statewide        | Singleton| April–July, 2020                  | April–July, 2016–2019                     | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks | Logistic regression |
| Matheson45 Australia  | 3 regional hospitals | Singleton and multiple pregnancies | July–September, 2019 | July–September, 2020 | PTB <37 weeks; PTB <34 weeks; PTB <28 weeks; Stillbirth; Spontaneous PTB; Medically indicated PTB | Interrupted time-series analysis; Auto-regressive integrated moving average (ARIMA) model |
| McDonnell7 Ireland    | Single center    | Not reported | January–July, 2020                | January–July, 2018–2019                   | PTB <37 weeks; Stillbirth | Pearson correlation; chi-squared, Fisher’s exact test |
| Meyer 146 Israel      | Single center    | Singleton| March 20–June 27, 2020            | March 20–June 27, 2011–2019              | PTB <37 weeks; PTB <34 weeks; PTB <32 weeks; Birthweight; Neonatal mortality | Multivariate regression |
| Meyer 247 Israel      | Single center    | Not reported | February–March, 2020              | February–March, 2019                      | PTB <37 weeks; PTB <34 weeks; Birthweight | Chi-squared; Fisher’s exact test; Mann-Whitney U test |

(Continues)
| First author, Country | Population level | Neonatal | Exposed cohort (Pandemic period) | Non-exposed cohort (Pre-pandemic period) | Outcomes | Statistical approach | Factors adjusted for if any |
|-----------------------|------------------|----------|---------------------------------|------------------------------------------|----------|----------------------|----------------------------|
| Morv | Single center | Singleton | February 21–April 30, 2020 | February 21–April 30, 2017–2019 | PTB <37 weeks; PTB <34 weeks; PTB <28 weeks; Stillbirth; Birthweight | Chi-squared test or Fisher’s exact test | |
| Pastemak | Nation-wide | Singleton | April 1-May 31, 2020 | April 1-May 31, 2015–2019 | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks; Stillbirth | Logistic regression | Maternal age, birth country, parity, body mass index and smoking |
| Philip | Region-wide | Not reported | January–April, 2020; And March–June, 2020 | January–April of 2001–2019; And March–June 2016–2019 | Stillbirth; LBW; ELBW; VLBW | Poisson regression | |
| Shah | Regionwide | All births | January 1–December 31, 2020 | July 1, 2002–December 31, 2019 | PTB <37 weeks; PTB <32 weeks; PTB <28 weeks; Stillbirth | Laney control P’ charts; the interrupted time-series analysis; | |
| Shakespeare | Single center | Not reported | April–June, 2020 | January–March, 2020 | Stillbirth; Neonatal mortality; Maternal mortality | Not reported | |
| Stowe | Nation-wide | Not reported | April–June, 2020 | April–June, 2019 | Stillbirth | Fisher’s exact test | |
| Sun | Single center | March 11–June 11, 2020 | March 11–June 11, 2019 | PTB <37 weeks; LBW | Not reported | |
| Wood | 4 level 3 or 4 neonatal intensive care units | Singleton | April–July, 2020 | April–July, 2019 | PTB <37 weeks; PTB <34 weeks; PTB <32 weeks; PTB <28 weeks; Spontaneous PTB | Not reported | |

Abbreviations: ELBW, extremely low birthweight; GWG, gestational weight gain; LBW, low birthweight, PTB, preterm birth, VLBW, very low birthweight.

aData not used because of overlapping cohort.
| First Author | Selection | Comparability | Outcome |
|--------------|-----------|---------------|---------|
| Arnaez16     | ☆         | ☆             | ☆       |
| Been54       | ☆         | ☆             | ☆       |
| Berghella17   | ☆         | ☆             | ☆       |
| Bian18       | ☆         | ☆             | ☆       |
| Briozzo19    | ☆         | ☆             | ☆       |
| Caniglio20   | ☆         | ☆             | ☆       |
| De Curtis21   | ☆         | ☆             | ☆       |
| Dell’Utri22   | ☆         | ☆             | ☆       |
| Du23         | ☆         | ☆             | ☆       |
| Einarsdóttir24 | ☆ | ☆             | ☆       |
| Gallo75      | ☆         | ☆             | ☆       |
| Goyal26      | ☆         | ☆             | ☆       |
| Greene27     | ☆         | ☆             | ☆       |
| Gu28         | ☆         | ☆             | ☆       |
| Handley29    | ☆         | ☆             | ☆       |
| Harvey30     | ☆         | ☆             | ☆       |
| Hedermann5   | ☆         | ☆             | ☆       |
| Huseynova31  | ☆         | ☆             | ☆       |
| Janevic32    | ☆         | ☆             | ☆       |
| Justman33    | ☆         | ☆             | ☆       |
| Kassic34     | ☆         | ☆             | ☆       |
| Kasuga35     | ☆         | ☆             | ☆       |
| KC8          | ☆         | ☆             | ☆       |
| Khalil9      | ☆         | ☆             | ☆       |
| Kirchengast36 | ☆ | ☆         | ☆       |
| Kumar37      | ☆         | ☆             | ☆       |
| Kumari38     | ☆         | ☆             | ☆       |
| Lemon39      | ☆         | ☆             | ☆       |

(Continues)
| First Author                  | Selection | Comparability | Outcome |
|------------------------------|-----------|---------------|---------|
| Liu                          | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 8       |
| Li                           | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Llorca                       | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 7       |
| Lumbreras-Marquez            | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Main                         | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 7       |
| Matheson                     | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 5       |
| McDonnell                    | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Meyer 1                      | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Meyer 2                      | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Mor                          | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |
| Pastemak                     | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 8       |
| Philip                       | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 7       |
| Shakespeare                  | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 5       |
| Shah                         | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 7       |
| Stowe                        | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 8       |
| Sun                          | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 5       |
| Wood                         | ☆         | ☆             | ☆       | ☆       | ☆             | ☆       | 6       |

**Note:** A study can be awarded a maximum of one star for each item within the Selection and Outcome categories. A maximum of two stars can be given for comparability.
studied. The duration of the “pandemic period” studied varied from 4 weeks to 12 months, and the duration of the “pre-pandemic period” varied from 2 months to 19 years across studies. The risk of bias scores for the included studies ranged from 5 to 9 (Table 2). Twenty-two studies had moderate risk of bias and 23 studies had low risk of bias. Thirty-three studies included pregnant populations from local/regional/national data, which may have included those with COVID-19, whereas eight studies specifically excluded women known to have COVID-19. However, it is difficult to be completely certain as testing on pregnant women was not universally applied in any of the studies.

### 3.2 Synthesis: Outcomes

#### 3.2.1 Preterm birth and its subgroups

Thirty-five studies including 462,772 women during the pandemic period and 3,788,270 women in the pre-pandemic period reported PTB <37 weeks of gestation; there was a small reduction in the unadjusted odds of PTB during the pandemic period compared with the pre-pandemic period (pooled uaOR 0.95, 95% CI 0.95–0.98, I² = 70%, Figure 2). Subgroup analyses revealed no differences in odds of PTB during the pandemic period in national or regional studies (pooled uaOR
0.99, 95% CI 0.95–1.02; I² = 78%); however, there was a reduction in odds of PTB in single-center studies (pooled uaOR 0.90, 95% CI 0.86–0.96, I² = 52%, subgroup differences p = 0.008, Figure 2). Six of the studies examining PTB reported adjusted estimates (with different factors adjusted, reported in Table 1) and pooled analyses did not show any significant differences in the odds of PTB during the pandemic, though the magnitude of the adjusted pooled estimate was the same as the unadjusted pooled estimate (pooled aOR 0.95, 95% CI 0.80–1.13; I² = 92%; Figure 3). There was no reduction in the unadjusted odds of PTB <34 weeks (Table 3, Appendix S3), <32 weeks (Table 3, Appendix S4), or <28 weeks (Table 3, Appendix S5) of gestation. Meta-analysis of six studies reporting data on spontaneous PTB (Table 3, Appendix S6) and six studies of medically indicated PTB and five studies of spontaneous PTB revealed reductions in unadjusted odds of PTB during the pandemic period of similar magnitude (Table 3, Appendix S7).

Although most of the studies presented data for the entire pregnant population, some explicitly excluded individuals with a known confirmed diagnosis of COVID-19. When such studies were included in meta-analyses, we identified no difference in the odds of PTB or stillbirth— for PTB: regional/national data from two studies had pooled uaOR of 1.14 (95% CI 0.58–2.22), whereas four single-center studies had uaOR of 1.97 (95% CI 0.85–4.55).

### Stillbirth

Twenty-five studies of 498 231 women during the pandemic period and 3 569 667 women in the pre-pandemic period assessed stillbirth. There was no difference in the odds of stillbirth between the pandemic and pre-pandemic periods (pooled uaOR 1.10, 95% CI 0.98–1.24, I² = 54%, Figure 4). Subgroup analyses also revealed no difference in stillbirth during the pandemic period compared with the pre-pandemic period in single-center studies and regional/national studies (Figure 4). Meta-analysis of adjusted estimates from four studies revealed no difference in stillbirth between pandemic and pre-pandemic periods (aOR 1.06, 95% CI 0.81–1.38; I² = 72%; Appendix S8).

### Birthweight

Seven studies of 13 871 women during the pandemic period and 49 152 women in the pre-pandemic period reported...
birthweight. There was a small increase in mean birthweight during the pandemic compared with the pre-pandemic period (pooled mean difference 17 g, 95% CI 7–28g, $I^2 = 0\%$) (Table 3, Appendix S9). There was no difference in the odds of LBW (Table 3, Appendix S10), VLBW (Table 3, Appendix S11), or ELBW (Table 3, Appendix S12).

### 3.2.4 Neonatal mortality

Six studies of 99,364 neonates during the pandemic period did not show any difference in neonatal mortality between the pandemic and pre-pandemic periods (pooled unadjusted OR 1.56, 95% CI 0.98–2.49, $I^2 = 94\%$, Table 3, Appendix S13), however, the heterogeneity of

---

**FIGURE 4** Forest plot for odds of stillbirth in pandemic vs pre-pandemic periods. IV, inverse variance

**FIGURE 5** Forest plot for odds of maternal mortality in pandemic vs pre-pandemic periods. IV, inverse variance
results across studies was very high. One national study from nine hospitals in Nepal\(^5\) reported a higher neonatal mortality rate during the pandemic period, which may reflect significant local impact on access to care during the lockdown period.

### 3.2.5 Maternal mortality

Four studies reported on maternal mortality. Three reported no significant difference in maternal mortality; however, one study from Mexico\(^53\) reported a significant increase in maternal mortality during the pandemic period (Figure 5). The study from Mexico contributed to 98.7% of the weight in this meta-analysis and it also reported that a significant portion of excess mortality was due to respiratory infections including COVID-19.

In meta-regression analyses, duration of the pre-pandemic study period did not emerge as a significant covariate for any outcome ($p > 0.05$ for all outcomes). We found evidence of publication bias for PTB (Egger’s $p = 0.002$, Appendix S14) but not for stillbirth (Appendix S15), with fewer studies reporting higher rates of PTB during the pandemic period.

### 4 DISCUSSION

In this updated systematic review and meta-analysis, we identified a 5% reduction in the unadjusted odds of PTB in pandemic compared with pre-pandemic time periods, in both spontaneous PTB and medically indicated PTB. However, in subgroup analyses, a significant reduction in PTB was only observed in single-center studies, not in regional or national studies. Although there was no statistically significant difference in the pooled adjusted odds of PTB, the magnitude of the pooled estimate was the same as the pooled unadjusted estimate. We identified no difference in any other fetal/neonatal outcomes, including stillbirths and neonatal mortality, and only a marginal increase of 17 g in mean birthweight during the pandemic period compared with the pre-pandemic period. The increased incidence of maternal mortality noted in our meta-analysis was mostly driven by one study from Mexico\(^43\) that included deaths due to COVID-19; these were the leading cause of maternal mortality during the pandemic period.

This review was designed to evaluate the impact of the COVID-19 pandemic on pregnancy and neonatal outcomes and not to evaluate studies that report only on maternal COVID-19 itself, which has been discussed in other reviews.\(^56-58\) We specifically excluded studies that only reported outcomes of pregnant individuals infected with COVID-19. We identified conflicting evidence from the included studies based on whether they were single-center or regional/national studies. There could be several reasons for this. In addition to potential referral bias, other potential explanations include variation in sample sizes, outcome definitions, lengths of the pandemic and pre-pandemic periods, differences in timing and enforcement of lockdown orders, failure of some studies to account for natural variation in pregnancy outcomes over time, and dissimilarities among COVID-19 mitigation strategies.\(^8,10,20,29,47\) Moreover, the study populations were heterogeneous; for example, baseline PTB rates ranged from 4.8% to 16.7% during the pre-pandemic period across the included studies; however, the change in PTB rate between periods was not baseline rate dependent. Although we did not observe any differences in subgroups of PTB using different gestational age cut-offs (ie <34, <32, and <28 weeks), not all studies contributed to these analyses.

Recently, Chmielewska\(^59\) et al reported results from a systematic review and meta-analyses including studies evaluating studies assessing population-level impact during the pandemic period published up to January 8, 2021. They reported no difference in the PTB rate (15 studies, $uaOR \, 0.94, \, 95\% \, CI \, 0.87–1.02$) and an increase in stillbirth (12 studies, $uaOR \, 1.28, \, 95\% \, CI \, 1.07–1.54$) and maternal mortality. With the availability of data from 13 more studies on PTB and nine more studies for stillbirth, the results have remarkably changed, although this could also partly relate to minor differences in study inclusion criteria and data extraction. The larger number of subjects included in pooled analyses in our review has improved the precision of pooled estimates, increasing confidence in the findings particularly for less common secondary outcomes. However, this is the main reason for conducting this as a living systematic review, so that the information can be updated regularly.

The effects of lockdowns and mitigation strategies had contrasting effects in high-income vs low- and middle-income countries.\(^59\) Reports from low-resource settings described increased fear and stress among pregnant individuals, reluctance to access in-hospital care during a pandemic, financial or employment issues, childcare or home schooling challenges, maternity staff shortages, reduced access to in-hospital care, and perceived or actual reductions in available obstetric services, resulting in a significant reduction in institutional births.\(^8,9,20,37,38\) Some reports noted a reduction in PTB and attributed this to a number of social and health behaviors associated with the pandemic,\(^2,7\) including decreased physical and mental stress due to better work-life balance,\(^6,17,46\) better support systems and financial assistance,\(^17,35\) improved nutrition, better hygiene,\(^8,12\) reduced physical activity,\(^6,17,35,40\) reduced exposure to infection,\(^8,17,46,60\) lower incidence of smoking and drug use due to reduced access and being indoors,\(^57\) lower pollution exposure and levels in environment,\(^17,61\) and fewer medical interventions secondary to reduced antenatal surveillance.\(^7,17,46,54\) The differences in PTB findings between single-center/adjacent hospitals studies and national/regional studies could reflect a change in referral patterns due to reduced access or the fact that pregnant individuals opted to give birth in hospitals with lower prevalence of COVID-19 or in non-COVID designated hospitals.\(^33\) Future studies are needed to explore these differences.

Although we did not observe an overall change in the odds of stillbirth during the pandemic period, several individual studies, mostly single center in scope, reported increased odds of stillbirth compared with pre-pandemic time periods. The increase in stillbirth reported by these studies was attributed to reduced antenatal surveillance, a
reductance to access in-hospital care due to increased stress and anxiety,
9,21,37,40,48 or missed appointments due to rapid changes in maternity services during the pandemic.60 These reasons may also explain an increase in maternal mortality identified in Mexico;43 however, according to the authors the data from the government website were preliminary in scope and may change as more data are available. This could be a signal to be vigilant in attending the mother–fetus dyad during difficult public health emergency situations.

We did not find any significant differences between the pandemic and pre-pandemic periods for other outcomes, except for a marginal difference in birthweight. As these data came from only five studies, further studies are needed to clarify this association, as a difference of 17 g is unlikely to be of clinical significance. Other factors that could be responsible for the differences between study findings include variations in the etiology of adverse pregnancy outcomes in different countries,2,20 initiatives by local governments to provide support to those at risk for higher stress,7 and changes to national legislation on pregnancy termination during the study period potentially influencing the incidences of stillbirth and PTB.2,7

A key strength of our review was the inclusion of large populations from 18 countries, mainly arising from national or state/provincial data. Most included studies came from registries or similar types of data sets. In addition, we only included studies that reported on temporal changes in outcomes in the overall population, and not data specifically from women affected by COVID-19. However, our study also has limitations. There may be other relevant studies that are not yet published (and so not included) as the pandemic is still ongoing and many countries are facing additional waves of infections and associated public health restrictions. There was clinical and methodological heterogeneity across studies regarding pandemic and pre-pandemic period definitions, population bases (single center/adjacent hospitals vs. regional/national), and choices of statistical methodologies. To overcome these limitations, we planned a priori to include pre-pandemic duration in meta-regression analyses, and we conducted post-hoc subgroup analyses on type of studies. We were able to explain statistical heterogeneity to an extent for both of our primary outcomes. Some studies included the entire population of pregnant women, comprising those who did and did not have COVID-19 in their sample. When studies that categorically excluded women with COVID-19 were included in our review, we identified no difference in PTB or stillbirth. Finally, there were insufficient studies to assess some of the pre-specified outcomes, including maternal mortality.

The COVID-19 pandemic has affected many countries with very high case numbers, such as India, Brazil, the UK, and Italy, but large, population-based estimates on pregnancy outcomes from these countries are lacking in this review. National registries from these and other countries would be ideally suited to investigate the impact of the pandemic on perinatal health at a population level. A harmonization of methodological approaches would also facilitate the assessment of the effects of the pandemic period on fetal, neonatal, and maternal outcomes, as high methodological heterogeneity makes direct comparisons challenging. One important point to consider going forward will be that the rates of these outcomes fluctuate with natural variation over time. We hope to capture these fluctuations through further 3-monthly updates of this living systematic review. Future investigations should use approaches that can elucidate whether any fluctuation observed in a particular setting during the pandemic period is outside the range of expected natural variation.

5 CONCLUSION

In pooled analyses, we observed reductions in the unadjusted odds of PTB between the pandemic and pre-pandemic periods; in both induced and spontaneous PTB. However, this finding was driven by single-center studies. There was no difference in analyses of adjusted estimates of PTB or within subgroups of PTB. Although we did not observe meaningful differences in other outcomes, including odds of stillbirth, the data were more limited and precluded a robust assessment. Higher maternal mortality reported from Mexico indicates that further studies from low- and middle-income regions highly affected by COVID-19 are needed where drastic changes in the healthcare access, healthcare availability, and personal, social, and environmental factors contributed disproportionately to adverse pregnancy outcomes. As the findings have changed between the review published recently and this current review, there is a need for this type of living systematic review that can be updated regularly.

ACKNOWLEDGMENTS

We thank Heather McDonald Kinkaid, PhD, for editorial support in preparing this manuscript. Dr Kinkaid is a scientific writer employed with the Maternal-infant Care Research Centre (MiCare) at Mount Sinai Hospital in Toronto, Ontario, Canada, and receives a salary for her work. MiCare is supported by Sinai Health and the participating hospitals, and in turn provides organizational support for the Canadian Preterm Birth Network.

CONFLICT OF INTEREST

None.

ORCID

Rohan D’Souza https://orcid.org/0000-0002-4049-2017
John W. Snelgrove https://orcid.org/0000-0002-7128-8916
Prakesh S. Shah https://orcid.org/0000-0002-9920-0488

REFERENCES

1. Ohlsson A, Shah PS. Effects of the September 11, 2001 disaster on pregnancy outcomes: a systematic review. Acta Obstet Gynecol Scand. 2011;90:6-18.
2. Philip RK, Purtill H, Reidy E, et al. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a ‘natural experiment’ allowing analysis of data from the prior two decades. BMJ Glob Health. 2020;5:e003075.
3. Stout MJ, Busam R, Macones GA, Tuuli MG. Spontaneous and indicated preterm birth subtypes: Interobserver agreement and accuracy of classification. Am J Obstet Gynecol MFM. 2014;211:530.e531-530.e5304.
4. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385:430-440.

5. Crump C. An overview of adult health outcomes after preterm birth. *Early Hum Dev*. 2020;150:105187.

6. Hedemann G, Hedley PL, Bækvad-Hansen M, et al. Danish preterm birth rates during the COVID-19 lockdown. *Arch Dis Child Fetal Neonatal Ed*. 2021;106:93-95.

7. McDonnell S, McNamee E, Lindow SW, O’Connell MP. The impact of the Covid-19 pandemic on maternity services: a review of maternal and neonatal outcomes before, during and after the pandemic. *Eur J Obstet Gynecol Reprod Biol*. 2020;255:172-176.

8. Kc A, Gurung R, Kinney MV, et al. Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study. *Lancet Glob Health*. 2020;8:e1273-e1281.

9. Khalil A, von Dadelszen P, Ugwumadu A, O’Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA*. 2020;324:705-706.

10. Pasternak B, Neovius M, Söderling J, et al. Preterm birth and stillbirth during the COVID-19 pandemic in Sweden: a nationwide cohort study. *Ann Intern Med*. 2021;174:873-875. doi:10.7326/M20-6367

11. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PloS Medicine*. 2009;6:e1000097.

12. Yang J, Shah PS. COVID-19 pandemic and population level pregnancy and neonatal outcomes: a systematic review. Available online at: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021234036 (Accessed September 5, 2021).

13. Yang J, O’Souza R, Kharrat A, et al. COVID-19 pandemic and population level pregnancy and neonatal outcomes: a living systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2021;100:1756-1770.

14. Statistics Canada. Deaths 2004: Vital Statistics—Stillbirth or neonatal mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Available online at: https://www150.statcan.gc.ca/n1/pub/84F0211x/2004000/4068009-eng.htm (Accessed September 5, 2021).

15. Wells GA, Shea B, O’Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available online at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (Accessed September 5, 2021)

16. Arnaez J, Ochoa-Sangrador C, Caserio S, et al. Lack of changes in quality of nonrandomised studies in meta-analyses. Available online at: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021234036 (Accessed September 5, 2021).

17. Berghella V, Boelig R, Roman A, Burd J, Anderson K. Decreased incidence of preterm birth during coronavirus disease 2019 pandemic. *Am J Obstet Gynecol MFM*. 2020;2:100258.

18. Bian Z, Qu X, Ying H, Liu X. Are COVID-19 mitigation measures reducing preterm birth rate in China? *BMJ Glob Health*. 2021;6:e006359.

19. Bríozzo L, Tomasso G, Viroga S, Nozar F, Bianchi A. Impact of mitigation measures against the COVID 19 pandemic on the perinatal incidence of the reference maternity hospital in Uruguay. *J Matern Fetal Neonatal Med*. 2021;1-6.

20. Caniglia EC, Magosi LE, Zash R, et al. Modest reduction in adverse birth outcomes following the COVID-19 lockdown. *Am J Obstet Gynecol*. 2020;32574-32576.

21. De Curtis M, Villani L, Polo A. Increase of stillbirth and decrease of late preterm infants during the COVID-19 pandemic lockdown. *Arch Dis Child Fetal Neonatal Ed*. 2021;106:456.

22. Dell’Utri C, Manzoni E, Cipriani S, et al. Effects of SARS Cov-2 epidemic on the obstetrical and gynecological emergency service accesses. What happened and what shall we expect now? *Eur J Obstet Gynecol Reprod Biol*. 2020;254:64-68.

23. Du M, Yang J, Han N, Liu M, Liu J. Association between the COVID-19 pandemic and the risk for adverse pregnancy outcomes: a cohort study. *BMJ Open*. 2021;11:e047900.

24. Einarsdóttir K, Swift EM, Zoega H. Changes in obstetric interventions and preterm birth during COVID-19: a nationwide study from Iceland. *Acta Obstet Gynecol Scand*. 2021;100:1924-1930.

25. Gallo LA, Gallo TF, Borg DJ, Moritz KM, Clifton VL, Kumar S. A decline in planned, but not spontaneous, preterm birth rates in a large Australian tertiary maternity centre during COVID-19 mitigation measures. *Aust N Z J Obstet Gynaecol*. 2021. doi: 10.1111/ajo.13406. Epub ahead of print.

26. Goyal M, Singh P, Singh K, Shekhar S, Agrawal N, Misra S. The effect of the COVID-19 pandemic on maternal health due to delay in seeking health care: experience from a tertiary center. *Int J Gynaecol Obstet*. 2021:152:231-235.

27. Greene NH, Kilpatrick SJ, Wong MS, Ozimek JA, Naqvi M. Impact of labor and delivery unit policy modifications on maternal and neonatal outcomes during the coronavirus disease 2019 pandemic. *Am J Obstet Gynecol MFM*. 2020;2:100234.

28. Gu XX, Chen K, Lu H, Liang Y, Chen H, Chen Y. How to prevent inhospital COVID-19 infection and reassure women about the safety of pregnancy: experience from an obstetric center in China. *J Int Med Res*. 2020;48:300060520939337.

29. Handley SC, Mullin AM, Elowitz MA, et al. Changes in preterm birth phenotypes and stillbirth at 2 Philadelphia Hospitals during the SARS-CoV-2 pandemic, March-June 2020. *JAMA*. 2021;325:87-89.

30. Harvey EM, McNeer E, McDonald MF, et al. Association of preterm birth rate with COVID-19 statewide stay-at-home orders in Tennessee. *JAMA Pediatr*. 2021;175:635-637.

31. Huseynova R, Bin Mahmoud L, Abdelrahim A, et al. Prevalence of preterm birth rate during COVID-19 lockdown in a Tertiary Care Hospital. *Riyadh. Cureus*. 2021;3:e13634.

32. Janevic T, Glazer KB, Vieira L, et al. Racial/ethnic disparities in very preterm birth and preterm birth before and during the COVID-19 pandemic. *JAMA Netw Open*. 2021;4:e211816.

33. Justman N, Shahak G, Gutzeit O, et al. Lockdown with a price: the impact of the COVID-19 pandemic on prenatal care and perinatal outcomes in a tertiary care center. *Isr Med Assoc J*. 2020;22:533-537.

34. Kassie A, Wale A, Yismaw W. Impact of coronavirus diseases-2019 (COVID-19) on utilization and outcome of reproductive, maternal, and newborn health services at governmental health facilities in South West Ethiopia, 2020: comparative cross-sectional study. *Int J Womens Health*. 2021;13:479-488.

35. Kasuga Y, Tanaka M, Ochiai D. Preterm delivery and hypertensive disorder of pregnancy were reduced during the COVID-19 pandemic: a single hospital-based study. *J Obstet Gynaecol Res*. 2020. doi: 10.1111/jog.14518. Epub ahead of print.

36. Kirchengast S, Hartmann B. Pregnancy outcome during the first COVID 19 lockdown in Vienna, Austria. *Int J Environ Res Public Health*. 2021;18:3782.

37. Kumar M, Puri M, Yadav R, et al. Stillbirths and the COVID-19 pandemic: looking beyond SARS-CoV-2 infection. *Int J Gynaecol Obstet*. 2021;153:76-82.

38. Kumari V, Mehta K, Choudhary R. COVID-19 outbreak and decreased hospitalisation of pregnant women in labour. *Lancet Glob Health*. 2020;8:e1116-e1117.

39. Lemon L, Edwards RP, Simhan HN. What is driving the decreased incidence of preterm birth during the coronavirus disease 2019 pandemic? *Am J Obstet Gynecol MFM*. 2021;3:100330.

40. Li M, Yin H, Jin Z, et al. Impact of Wuhan lockdown on the indications of cesarean delivery and newborn weights during the epidemic period of COVID-19. *PloS One*. 2020;15:e0237420.

41. Liu S, Dzakpasu S, Nelson C, et al. Pregnancy outcomes during the COVID-19 pandemic in Canada, March to August 2020. *J Obstet Gynaecol Can*. 2021;51701-2163(21)00581-8. doi: 10.1016/j.jogc.2021.06.014. Epub ahead of print.
42. Llorca J, Lechosa-Muñiz C, Frank de Zulueta P, et al. Results of pregnancy control before and during the COVID-19 Pandemic: a comparison of two cohorts. *Int J Environ Res Public Health*. 2021;18:8182.

43. Lumbreras-Marquez MI, Campos-Zamora M, Seifert SM, et al. Excess maternal deaths associated with coronavirus disease 2019 (COVID-19) in Mexico. *Obstet Gynecol*. 2020;136:1114-1116.

44. Main EK, Chang SC, Carpenter AM, et al. Singleton preterm birth rates for racial and ethnic groups during the coronavirus disease 2019 pandemic in California. *Am J Obstet Gynecol*. 2021;224:239-241.

45. Matheson A, McGannon CJ, Malhotra A, et al. Prematurity rates during the coronavirus disease 2019 (COVID-19) pandemic lockdown in Melbourne, Australia. *Obstet Gynecol*. 2021;137:405-407.

46. Meyer R, Bart Y, Tsur A, et al. A marked decrease in preterm deliveries during the coronavirus disease 2019 pandemic. *Am J Obstet Gynecol*. 2021;224:234-237.

47. Meyer R, Levin G, Hendin N, Katorza E. Impact of the COVID-19 outbreak on routine obstetrical management. *Isr Med Assoc J*. 2020;22:483-488.

48. Mor M, Kugler N, Jauniaux E, et al. Impact of the COVID-19 pandemic on excess perinatal mortality and morbidity in Israel. *Am J Perinatol*. 2021;38:398-403.

49. Shah PS, Ye XY, Yang J, Campitelli MA. Preterm birth and stillbirth rates during the COVID-19 pandemic: a population-based cohort study. *CMAJ*. 2021;193:E1164-E1172.

50. Shakespeare Clare DH, Moyo S, Ngwenya S. Resilience and vulnerability of maternity services in Zimbabwe: a comparative analysis of the effect of Covid-19 and lockdown control measures on maternal and perinatal outcomes at Mpilo Central Hospital. Available online at: https://www.researchsquare.com/article/rs-52159/v1 (Accessed September 5, 2021).

51. Stowe J, Smith H, Thurland K, Ramsay ME, Andrews N, Ladhani SN. Stillbirths during the COVID-19 pandemic in England. April-June 2020. *JAMA*. 2021;325:86-87.

52. Sun SY, Guazzelli CAF, de Morais LR, et al. Effect of delayed obstetric labor care during the COVID-19 pandemic on perinatal outcomes. *Int J Gynaecol Obstet*. 2020;151:287-289.

53. Wood R, Sinnott C, Goldfarb I, Clapp M, McElrath T, Little S. Preterm birth during the coronavirus disease 2019 (COVID-19) pandemic in a large hospital system in the United States. *Obstet Gynecol*. 2021;137:403-404.

54. Been JV, Burgos Ochoa L, Bertens LCM, Schoenmakers S, Steegers EAP, Reiss IKM. Impact of COVID-19 mitigation measures on the incidence of preterm birth: a national quasi-experimental study. *Lancet Public Health*. 2020;5:e604-e611.

55. Simpson AN, Snelgrove JW, Sutradhar R, Everett K, Liu N, Baxter NN. Perinatal outcomes during the COVID-19 pandemic in Ontario, Canada. *JAMA Netw Open*. 2021;4:e2110104.

56. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320.

57. Yuan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol*. 2020;56:15-27.

58. Smith V, Seo D, Warty R, et al. Maternal and neonatal outcomes associated with COVID-19 infection: a systematic review. *PLoS One*. 2020;15:e0234187.

59. Chmielewska B, Barratt I, Townsend R, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021;9:e759-e772.

60. Coxon K, Turienzo CF, Kweekel L, et al. The impact of the coronavirus (COVID-19) pandemic on maternity care in Europe. *Midwifery*. 2020;88:102779.

61. Bauwens M, Compernolle S, Stavarakou T, et al. Impact of coronavirus outbreak on NO(2) pollution assessed using TROPOMI and OMI observations. *Geophys Res Lett*. 2020;e2020GL087978.

**SUPPORTING INFORMATION**

Additional supporting information may be found in the online version of the article at the publisher’s website.

**How to cite this article:** Yang J, D’Souza R, Kharrat A, et al. Coronavirus disease 2019 pandemic and pregnancy and neonatal outcomes in general population: A living systematic review and meta-analysis (updated Aug 14, 2021). *Acta Obstet Gynecol Scand*. 2022;101:7–24. [https://doi.org/10.1111/aogs.14277](https://doi.org/10.1111/aogs.14277)