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Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis

Barbara Chmielewska, Imogen Barratt, Rosemary Townsend, Erkan Kalafat, Jan van der Meulen, Ipek Gurol-Urganci, Pat O'Brien, Edward Morris, Tim Draycott, Shakila Thangaratinam, Kirsty Le Doare, Shamez Ladhani, Peter von Dadelszen, Laura Magee, Asma Khalil

Summary

Background The COVID-19 pandemic has had a profound impact on health-care systems and potentially on pregnancy outcomes, but no systematic synthesis of evidence of this effect has been undertaken. We aimed to assess the collective evidence on the effects on maternal, fetal, and neonatal outcomes of the pandemic.

Methods We did a systematic review and meta-analysis of studies on the effects of the pandemic on maternal, fetal, and neonatal outcomes. We searched MEDLINE and Embase in accordance with PRISMA guidelines, from Jan 1, 2020, to Jan 8, 2021, for case-control studies, cohort studies, and brief reports comparing maternal and perinatal mortality, maternal morbidity, pregnancy complications, and intrapartum and neonatal outcomes before and during the pandemic. We also planned to record any additional maternal and offspring outcomes identified. Studies of solely SARS-CoV-2-infected pregnant individuals, as well as case reports, studies without comparison groups, narrative or systematic literature reviews, preprints, and studies reporting on overlapping populations were excluded. Quantitative meta-analysis was done for an outcome when more than one study presented relevant data. Random-effects estimate of the pooled odds ratio (OR) of each outcome were generated with use of the Mantel-Haenszel method. This review was registered with PROSPERO (CRD42020211753).

Findings The search identified 3592 citations, of which 40 studies were included. We identified significant increases in stillbirth (pooled OR 1·28 [95% CI 1·07–1·54]; I^2=63%; 12 studies, 168 295 pregnancies during and 198 993 before the pandemic) and maternal death (1·37 [1·22–1·53; I^2=0%, two studies [both from low-income and middle-income countries], 1 237 018 and 2 224 859 pregnancies) during versus before the pandemic. Preterm births before 37 weeks' gestation were not significantly changed overall (0·94 [0·87–1·02]; I^2=75%; 15 studies, 170 640 and 656 423 pregnancies) but were decreased in high-income countries (0·91 [0·84–0·99]; I^2=63%; 12 studies, 159 987 and 635 118 pregnancies), where spontaneous preterm birth was also decreased (0·81 [0·67–0·97]; two studies, 4204 and 6818 pregnancies). Mean Edinburgh Postnatal Depression Scale scores were higher, indicating poorer mental health, during versus before the pandemic (pooled mean difference 0·42 [95% CI 0·02–0·81; three studies, 2330 and 6517 pregnancies). Surgically managed ectopic pregnancies were increased during the pandemic (OR 5·81 [2·16–15·6]; I^2=26%; three studies, 37 and 272 pregnancies). No overall significant effects were identified for other outcomes included in the quantitative analysis: maternal gestational diabetes; hypertensive disorders of pregnancy; preterm birth before 34 weeks', 32 weeks', or 28 weeks' gestation; iatrogenic preterm birth; labour induction; modes of delivery (spontaneous vaginal delivery, caesarean section, or instrumental delivery); post-partum haemorrhage; neonatal death; low birthweight (<2500 g); neonatal intensive care unit admission; or Apgar score less than 7 at 5 min.

Interpretation Global maternal and fetal outcomes have worsened during the COVID-19 pandemic, with an increase in maternal deaths, stillbirth, ruptured ectopic pregnancies, and maternal depression. Some outcomes show considerable disparity between high-resource and low-resource settings. There is an urgent need to prioritise safe, accessible, and equitable maternity care within the strategic response to this pandemic and in future health crises.

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See Comment page e722

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Introduction

The SARS-CoV-2 pandemic has had profound effects on health-care systems, societal structures, and the world economy.[1] The adverse effects of the COVID-19 pandemic on maternal and perinatal health are not limited to the morbidity and mortality caused directly by the disease itself. Nationwide lockdowns, disruption of health-care services, and fear of attending health-care facilities might also have affected the wellbeing of pregnant people and their babies.[2,3]

Emerging evidence suggests that rates of stillbirth and preterm birth might have changed substantially during the pandemic.[4,5] A reduction in health-care-seeking behaviour, as well as reduced provision of maternity services, has been suggested as a possible cause.[6] Robust estimates of the indirect maternal health effects of the

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Research in context

Evidence before this study

Before conducting this study, we electronically searched MEDLINE and Embase from Jan 1, 2020, to Jan 8, 2021, with no language restriction, to identify any previous systematic reviews and meta-analyses. Search terms included stillbirth, perinatal mortality, maternal mortality and morbidity, preterm birth, obstetric complications, mode of delivery, and COVID-19. Large systematic reviews have consistently reported that pregnant individuals infected with SARS-CoV-2 are more likely to require intensive care treatment and experience preterm birth. Although individual studies have reported pandemic-associated changes in pregnancy outcomes in the general maternity population, particularly for preterm birth and stillbirth, no global synthesis of this kind has previously been reported.

Added value of this study

This review provides a comprehensive assessment of the global effects of the COVID-19 pandemic on maternal, fetal, birth, and neonatal outcomes. We identified significant increases in maternal and fetal mortality (particularly in low-income and middle-income countries [LMICs]), ruptured ectopic pregnancies, and maternal symptoms of depression. Moreover, we found a reduction in preterm birth in high-income countries during the pandemic epoch.

Implications of all the available evidence

The disruption caused by the COVID-19 pandemic has led to avoidable deaths of both mothers and babies. Policy makers and health-care leaders must urgently investigate robust strategies for preserving safe and respectful maternity care, even during the ongoing global emergency. Our findings highlight a disproportionate impact on LMICs. Immediate action is required to avoid rolling back decades of investment in reducing mother and infant mortality in low-resource settings. There is also an unprecedented opportunity to investigate the mechanisms underlying the observed reduction in preterm birth and generate novel preventive interventions.

pandemic can be derived from historical cohorts by examining the change in outcomes and calculating the excess event rate.[7] This before–after approach applied to key pregnancy outcomes can be used to estimate the indirect effects of the COVID-19 pandemic.

We aimed to assess the collateral effects on maternal, fetal, and neonatal outcomes of the global COVID-19 pandemic.

Methods

Overview

We did a systematic review and meta-analysis of studies on the effects of the pandemic on maternal, fetal, and neonatal outcomes. The review was registered with PROSPERO (CRD42020211753) and reported according to PRISMA guidelines.[8] The study protocol is available online.

For the study protocol see https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=211753

Search strategy, selection criteria, and data extraction

We electronically searched the MEDLINE and Embase databases from Jan 1, 2020, to Jan 8, 2021. The search included relevant medical subject heading terms, keywords, and word variants for stillbirth, perinatal mortality, maternal mortality and morbidity, preterm birth, obstetric complications, mode of delivery, and COVID-19 (appendix p 4). No language restrictions were applied. One article, which was subsequently excluded, was translated from Mandarin.

See Online for appendix

Abstracts and potentially relevant full texts were reviewed independently by three authors (BC, IB, and RT) with any conflicts resolved by consensus. Case-control studies, cohort studies, and brief reports were eligible for inclusion. Case reports, studies without comparison groups, narrative or systematic literature reviews, preprint papers, and studies reporting on overlapping populations were excluded. Studies of only SARS-CoV-2-infected women were excluded.

For Covidence software see https://www.covidence.org/

Data were extracted with use of Covidence systematic review software (version 2, Veritas Health Innovation, Melbourne, VIC, Australia). The following data were extracted: author's name, publication date, study design, sampling period, study period, study population, and location. The total number of pregnant women and the sum of adverse events in each group were extracted for categorical outcomes (eg, stillbirth, caesarean section). Mean, standard deviation, and the total number of pregnant women in each outcome group were extracted for outcomes reported on a continuous scale (Edinburgh Postnatal Depression Scale [EPDS] scores).

Outcomes of interest included maternal and perinatal mortality, maternal morbidity, pregnancy complications, and intrapartum and neonatal outcomes. We planned to record any additional maternal and offspring outcomes identified. Where papers described service configuration or resource-use changes without clinical outcomes, we excluded them from the analysis.

Pandemic mitigation response measures were extracted from the Oxford COVID-19 Government Response Tracker.[9] We recorded the maximum restrictions implemented during the study timeframe. Quantitative assessment of the severity of mitigation measures was recorded according to the Government Response Stringency Index (GRSI) developed by the Blavatnik School of Government at the University of Oxford (Oxford, UK).[9]

Quality assessment

Each study was scored according to the Newcastle-Ottawa Scale[10] independently by two assessors (BC, IB)

on three broad characteristics: selection of study groups, comparability of groups, and ascertainment of the outcome of interest.

Statistical analysis

Quantitative meta-analysis was done for an outcome when more than one study presented relevant data. We excluded individual outcomes from studies reporting no adverse outcomes in one or both groups, and studies not satisfying the normality assumption for continuous variables. We divided studies according to World Bank classifications into high-income or low-income and middle-income contexts.

A random-effects estimate of the pooled odds of each outcome was generated with use of the Mantel-Haenszel method. Between-study heterogeneity was explored using the I^2 statistic, with substantial heterogeneity defined as an I^2 value greater than 50%. Meta-regression analyses were done for outcomes with substantial heterogeneity to investigate the relative contribution of the WHO Healthcare Efficiency Index[11] and the stringency of lockdown measures (quantified with the GRSI).[9] GRSI scores were scaled and regression coefficients corresponded to one standard unit change in the respective covariate. Positive regression coefficients indicate an increase in the effect size whereas negative coefficients show a decrease. We reported p values and the amount of accounted heterogeneity for each covariate. Potential publication bias was assessed with Egger's test and funnel plots for visual inspection when sufficient studies (n>10) were available.

Analyses were done with R software (version 4.0.2).

Role of the funding source

There was no funding source for this study.

Results

Of 3592 abstracts screened, 192 were relevant for full-text review and 40 met the inclusion criteria for systematic review (figure 1).[4,5,12–49] A list of excluded studies with reasons for exclusion is provided in the appendix (p 6). Reporting on resource use or service reconfiguration outcomes is summarised in the appendix (p 27). Of the 40 included studies, 31 for which comparable outcomes were also reported in at least one other study were included in the meta-analysis.[4,12,14–21,24–28,30–34,37,38,40,42,45–49] Table 1 shows the characteristics of the 40 included studies, all of which used a historical cohort design. 17 countries were represented, with substantial variation in pandemic mitigation measures among countries. No study reported data from countries in the lowest WHO Healthcare Efficiency Index quartile, and the majority (28 studies)[4,5,12,14,16,17,19,20,22,23,28–37,39,40,42,44–46,48,49] reported data from countries in the highest quartile (table 2). 21 of the 31 studies included in the quantitative analysis were from high-income countries (HICs) according to the World Bank classification.[4,12,14,16,17,19,20,23,28,30–34,42,45,46,49] The

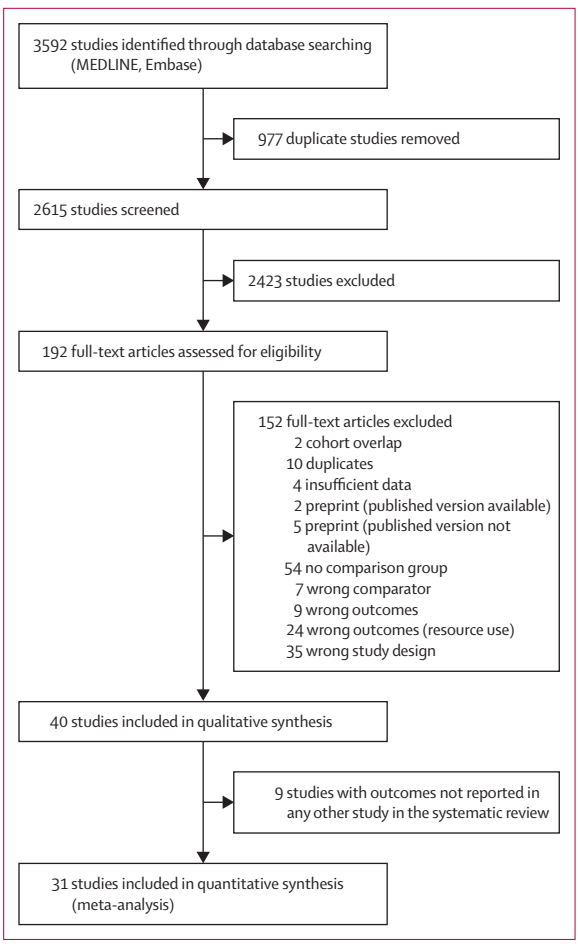


Figure 1: **PRISMA flow chart**

reported outcomes and outcome measures are listed with the relevant studies in the appendix (p 31).

The majority of the included studies were of moderate methodological rigour (ie, 6–8 stars on the Newcastle-Ottawa Scale; table 1; appendix p 35). The main weaknesses were inconsistent definition and reporting of outcomes, inconsistency in selection of control groups, and retrospective study design. For example, although 18 papers[4,5,14–17,19–21,26,28,30–33,38,47,49] reported on preterm birth, variation in the gestational age cutoffs and use of ranges limited their comparability.

There were five reports from national registries,[5,17,27,37,47] six regional reports,[28,37,41,43–45] and four multicentre studies;[16,21,25,46] the remaining 25 were single-centre studies. 11 studies[12,15,19,23,24,33,38,39,42,45,49] had a comparison group from the equivalent period in 2019, the year preceding the pandemic. Nine studies[16,17,20,28,30–32,35,47] had a comparison group of annually matched periods from several preceding years (table 1). 18 studies[4,5,13,14,18,21,22,25–27,29,36,37,41,43,44,46,48] had a comparison group from immediately before the lockdown period in the respective country. Exposed sample sizes varied from nine to 56 720 pregnancies (table 2). Only 19 studies[5,14–16,19,21,22,24,26,28,30,33,34,39,41,42,47] adjusted for

	Country	Study population	Reported outcome categories	Sample size of exposed cohort	Total sample size	Data collection period		Newcastle-Ottawa Scale score
						Pandemic group	Control group	
Ayaz et al, 2020[22]	Turkey	Single centre	Maternal anxiety and depression	63	NR	April 12 to May 27, 2020	June 1, 2018, to April 11, 2020	6
Been et al, 2020[5]	Netherlands	National	Preterm birth	56 720	1 599 547	March 9 to July 16, 2020	Oct 9, 2010, to March 8, 2020	9
Berghella et al, 2020[33]	USA	Single centre	Overall preterm birth, spontaneous preterm birth, iatrogenic preterm birth, caesarean section, vaginal delivery, perinatal death	1197	2108	March 1 to July 31, 2020	March 1 to July 31, 2019	8
Berthelot et al, 2020[44]	Canada	Regional (Quebec province)	Maternal emotions and concerns	1258	1754	April 2 to April 23, 2020	April 1, 2018, to March 1, 2020	6
Bhatia et al, 2020[45]	UK	Regional (northwest England)	Caesarean rate	8381	17 424	April 1 to July 1, 2020	Similar period in 2019	7
Bornstein et al, 2020[46]	USA	Multicentre	Vaginal delivery, caesarean section	5877	11 770	March 15 to June 20, 2020	Dec 8, 2019, to March 14, 2020	7
Caniglia et al, 2020[47]	Botswana	National	Stillbirth, preterm birth, neonatal death	10 751	68 448	April 3 to July 20, 2020	Annual matched periods, 2017–19	9
Casadio et al, 2020[48]	Italy	Single centre	Ectopic pregnancy	9	201	March 1 to April 30, 2020	Jan 1, 2014, to Feb 29, 2020	7
De Curtis et al, 2020[49]	Italy	Single centre	Preterm birth, caesarean section, stillbirth	7755	16 808	March 1 to May 31, 2020	March 1 to May 31, 2019	6
Dell'Utri et al, 2020[12]	Italy	Single centre	Ectopic pregnancy, vaginal delivery, induction of labour, stillbirth	3647	9291	Feb 23 to June 24, 2020	Feb 23 to June 24, 2019	7
Goyal et al, 2021[13]	India	Single centre	Maternal death	633	1749	April 1 to Aug 31, 2020	Oct 1, 2019, to Feb 29, 2020	8
Greene et al, 2020[14]	USA	Single centre	Vaginal delivery, caesarean section, instrumental delivery, NICU admission, 5-min Apgar score, cord blood gas, preterm birth	920	1936	March 1 to April 30, 2020	Jan 1 to Feb 29, 2020	9
Gu et al, 2020[15]	China	Single centre	Gestational hypertension, gestational diabetes, preterm birth, caesarean section, vaginal delivery, stillbirth, 5-min Apgar score, NICU admission, maternal anxiety	271	582	Jan 1 to Feb 29, 2020	Jan 1 to Feb 28, 2019	5
Handley et al, 2021[16]	USA	Multicentre	Stillbirth, overall preterm birth, spontaneous preterm birth, iatrogenic preterm birth	3007	8914	March 1 to June 30, 2020	Annual matched periods, 2018–19	9
Hedermann et al, 2021[17]	Denmark	National	Preterm birth	5162	31 180	March 12 to April 14, 2020	Annual matched periods, 2015–19	7
Hui et al, 2020[18]	Hong Kong	Single centre	Vaginal delivery, caesarean section, instrumental delivery, post-partum depression	954	4531	Jan 5 to April 30, 2020	Jan 1, 2019, to Jan 4, 2020	5
Justman et al, 2020[19]	Israel	Single centre	Gestational hypertension, gestational diabetes, induction of labour, caesarean section, instrumental delivery, preterm birth, 5-min Apgar score, NICU admission, stillbirth, post-partum haemorrhage	610	1352	March 1 to April 30, 2020	March 1 to April 30, 2019	9
Kasuga et al, 2020[20]	Japan	Single centre	Preterm birth, gestational hypertension	153	713	April 1 to June 30, 2020	Annual matched periods, 2017–19	7
Kc et al, 2020[21]	Nepal	Multicentre	Induction of labour, caesarean section, preterm birth, stillbirth, neonatal death	7165	20 354	March 21 to May 30, 2020	Jan 1 to March 20, 2020	9
Khalil et al, 2020[4]	UK	Single centre	Gestational hypertension, gestational diabetes, stillbirth, preterm birth, caesarean section, NICU admission	1718	3399	Feb 1 to June 14, 2020	Oct 1, 2019, to Jan 31, 2020	7
Kugelman et al, 2020[23]	Israel	Single centre	NICU admission, umbilical cord blood pH, 5-min Apgar score	398	942	March 15 to April 12, 2020	March 15 to April 12, 2019	7
Kumar et al, 2021[24]	India	Single centre	Stillbirth	3610	9771	March 1 to Sept 30, 2020	March 1 to Sept 30, 2019	9
Kumari et al, 2020[25]	India	Multicentre	Caesarean section, maternal death, stillbirth	3527	9736	March 25 to June 2, 2020	Jan 15 to March 24, 2020	5

(Table 1 continues on next page)

	Country	Study population	Reported outcome categories	Sample size of exposed cohort	Total sample size	Data collection period		Newcastle-Ottawa Scale score
						Pandemic group	Control group	
(Continued from previous page)								
Li et al, 2020[26]	China	Single centre	Preterm birth, caesarean section	3432	10 591	Jan 23 to March 24, 2020	Jan 1, 2019, to Jan 22, 2020	9
Lumbreras-Marquez et al, 2020[27]	Mexico	National	Maternal death, post-partum haemorrhage	523*	7747*	Jan 1 to Aug 9, 2020	2011–19	7
Main et al, 2020[28]	USA	Regional (California)	Preterm birth	132 853	713 567	April 1 to July 31, 2020	Annual matched periods, 2016–19	9
Matvienko-Sikar et al, 2020[29]	Ireland	Single centre	Pregnancy-specific stress	235	445	June 16 to July 17, 2020	May 1, 2019, to Feb 29, 2020	5
McDonnell et al, 2020[30]	Ireland	Single centre	Preterm birth, stillbirth, neonatal death, caesarean section, instrumental delivery, induction of labour, gestational hypertension, post-partum haemorrhage	2488	4309	April 1 to July 31, 2020	Annual matched periods, 2018–19	8
Meyer et al, 2020[31]	Israel	Single centre	Induction of labour, preterm birth, vaginal delivery, instrumental delivery, caesarean section, stillbirth, 5-min Apgar score, NICU admission	2594	34 022	March 20 to June 27, 2020	Annual matched periods, 2011–19	7
Mor et al, 2020[32]	Israel	Single centre	Gestational diabetes, gestational hypertension, stillbirth, preterm birth, vaginal delivery, caesarean section, instrumental delivery, induction of labour, birthweight, 5-min Apgar score, umbilical cord blood pH, NICU admission	1556	6120	Feb 21 to April 30, 2020	Annual matched periods, 2017–19	7
Pariente et al, 2020[34]	Israel	Single centre	Gestational diabetes, gestational hypertension, post-partum depression, maternal depression and suicidal ideation	223	346	March 18 to April 29, 2020	Nov 1, 2016, to April 30, 2017	5
Philip et al, 2020[35]	Ireland	Regional	Birthweight	1381	30 705	Jan 1 to April 30, 2020	Annual matched periods, 2001–19	7
Silverman et al, 2020[36]	USA	Single centre	Postpartum depression	155	485	March 12 to June 12, 2020	Feb 2 to March 11, 2020	6
Stowe et al, 2021[37]	UK	National	Stillbirth	131 218	270 963	April 1 to June 30, 2020	April 1, 2019, to June 30, 2020	7
Sun et al, 2020[38]	Brazil	Single centre	Preterm birth, vaginal delivery, instrumental delivery, caesarean section, 5-min Apgar score	40	81	March 11 to June 11, 2020	March 11 to June 11, 2019	6
Suzuki et al, 2020[39]	Japan	Single centre	Maternal depression and anxiety	117	251	March 11 to April 13, 2020	March 9 to April 11, 2019	8
Werner et al, 2020[40]	USA	Single centre	Ectopic pregnancy	12	63	March 15 to May 17, 2020	2019–20 interval before pandemic	7
Wu et al, 2020[41]	China	Regional (ten provinces in China)	Postpartum depression, maternal anxiety	1285	4124	Jan 21 to Feb 9, 2020	Jan 1 to Jan 20, 2020	9
Xie et al, 2021[43]	China	Regional (Zhejiang)	Maternal depression, maternal anxiety	689	3348	Jan 1 to Aug 31, 2020	March 1 to Dec 31, 2019	5
Zanardo et al, 2020[42]	Italy	Single centre	Postpartum depression	91	192	March 8 to May 3, 2020	March 8 to May 3, 2019	7

NR=not reported. NICU=neonatal intensive care unit. *Maternal deaths.

Table 1: **Characteristics of included studies**

socioeconomic status, ethnic background, comorbidities, or other confounding factors.

A summary of the findings from included studies is shown in table 2. Meta-analysis was done for 21 outcomes for which more than one study was available for quantitative synthesis (table 3).

Three studies[13,25,27] included data on maternal death, all of which reported an increase during the pandemic compared with before the pandemic, although this increase was statistically significant in only one study.[25] Two studies in which statistical analysis was done, from India and Mexico, were included in the meta-analysis (1 237 018 pregnancies during and 2 224 859 before the pandemic), which showed a significant increase in maternal death during the pandemic (OR 1·37 [95% CI 1·22–1·53]; I^2=0%; table 3, figure 2A), with findings dominated by a single study.[27]

	Government Response Stringency Index[12]	WHO Healthcare Efficiency Index[14]	Outcomes		
			Statistically significant increase during pandemic	Statistically significant decrease during pandemic	Statistically non-significant change
Ayaz et al, 2020[22]	77·78	0·734	Maternal anxiety (IDAS II score), moderate and severe maternal anxiety (BAI score)	No maternal anxiety (BAI score), mild maternal anxiety (BAI score)	None
Been et al, 2020[5]	79·63	0·928	None	Preterm birth before 37 weeks' gestation post mitigation measures introduced on March 9	Preterm birth before 37 weeks' gestation post mitigation measures introduced on March 15–23
Berghella et al, 2020[33]	72·69	0·838	None	Overall preterm birth before 37 weeks' gestation, preterm birth before 34 weeks' gestation, preterm birth before 28 weeks' gestation	Caesarean section, vaginal delivery, stillbirth, iatrogenic preterm birth before 37 weeks' gestation, spontaneous preterm birth before 37 weeks' gestation
Berthelot et al, 2020[44]	74·54	0·881	Depressive and anxiety symptoms, dissociative symptoms, symptoms of post-traumatic stress disorder, negative affectivity	Positive affectivity	None
Bhatia et al, 2020[45]	79·63	0·925	Caesarean section	None	None
Bornstein et al, 2020[46]	72·69	0·838	None	None	Caesarean section, vaginal delivery
Caniglia et al, 2020[47]	86·11	0·388	None	Preterm birth before 37 weeks' gestation, preterm birth before 32 weeks' gestation	Neonatal death, stillbirth
Casadio et al, 2020[48]	93·52	0·991	Ruptured ectopic pregnancy (needing surgical intervention)	None	None
De Curtis et al, 2020[49]	93·52	0·991	Stillbirth	Preterm birth before 37 weeks' gestation	Caesarean section
Dell'Utri et al, 2020[12]	75·46	0·991	Stillbirth, induction of labour	None	Vaginal delivery, surgical management of ectopic pregnancy
Goyal et al, 2021[13]	100·0	0·617	None	None	Maternal death
Greene et al, 2020[14]	72·69	0·838	None	None	Vaginal delivery, caesarean section, instrumental delivery, NICU admission, 5-min Apgar score <7, umbilical cord blood pH
Gu et al, 2020[15]	81·02	0·485	Gestational hypertension, gestational diabetes	None	Caesarean section, stillbirth, gestational diabetes, vaginal delivery, NICU admission, mean Apgar score
Handley et al, 2021[16]	72·69	0·838	None	None	Stillbirth, preterm birth before 37 weeks' gestation, spontaneous preterm birth, iatrogenic preterm birth
Hedermann et al, 2021[17]	72·22	0·862	Preterm birth before 28 weeks' gestation	None	Preterm birth at 28–32 weeks' gestation, preterm birth at 32–36 weeks' gestation
Hui et al, 2020[18]	66·67	0·485	Postnatal depression (EPDS score ≥10 1 day after delivery)	None	Vaginal delivery, caesarean section, instrumental delivery, postnatal depression (EPDS score)
Justman et al, 2020[19]	94·44	0·884	Gestational diabetes, gestational hypertension	None	Caesarean section, induction of labour, instrumental delivery, stillbirth, preterm birth before 37 weeks' gestation and before 32 weeks' gestation, post-partum haemorrhage, 5-min Apgar score <7, umbilical cord blood pH, NICU admission
Kasuga et al, 2020[20]	47·22	0·957	None	Gestational hypertension, preterm birth before 27 weeks' gestation	Preterm birth (gestation not specified)
Kc et al, 2020[21]	96·3	0·457	Caesarean section, induction of labour, stillbirth, neonatal death, preterm birth before 37 weeks' gestation	None	Vaginal delivery, birthweight <2·5 kg
Khalil et al, 2020[4]	79·63	0·925	Stillbirth	Gestational hypertension	Caesarean section, preterm birth before 37 weeks' gestation and before 34 weeks' gestation, gestational diabetes, NICU admission
Kugelman et al, 2020[23]	94·44	0·884	None	None	NICU admission, umbilical cord blood pH <7·1, 5-min Apgar score <7
Kumar et al, 2021[24]	100·0	0·617	Stillbirth	None	None
Kumari et al, 2020[25]	100·0	0·617	Caesarean section, maternal death, stillbirth	None	None
Li et al, 2020[26]	81·94	0·485	Caesarean section	None	None

(Table 2 continues on next page)

	Government Response Stringency Index[12]	WHO Healthcare Efficiency Index[14]	Outcomes		
			Statistically significant increase during pandemic	Statistically significant decrease during pandemic	Statistically non-significant change
(Continued from previous page)					
Lumbreras-Marquez et al, 2020[27]	82·41	0·755	No statistical analysis done	No statistical analysis done	No statistical analysis done
Main et al, 2020[28]	72·69	0·838	Preterm birth at 28–32 weeks' gestation	None	Preterm birth before 28 weeks' gestation, at 32–37 weeks' gestation, before 37 weeks' gestation (combined)
Matvienko-Sikar et al, 2020[29]	90·74	0·924	None	None	Pregnancy-specific stress (NuPDQ score)
McDonnell et al, 2020[30]	90·74	0·924	None	None	Birthweight <2·5 kg, stillbirth, neonatal death (early and late), caesarean section, instrumental delivery (vacuum and forceps), vaginal delivery, induction of labour, gestational hypertension, pre-eclampsia, post-partum haemorrhage, preterm birth before 37 weeks' gestation, preterm birth before 26 weeks' gestation
Meyer et al, 2020[31]	94·44	0·884	None	Preterm birth before 34 weeks' gestation, NICU admission	Induction of labour, preterm birth before 37 weeks' gestation and before 32 weeks' gestation, vaginal delivery, instrumental delivery, caesarean section, stillbirth, 5-min Apgar score <7
Mor et al, 2020[32]	94·44	0·884	Stillbirth, induction of labour, 5-min Apgar score <7	None	Gestational hypertension, gestational diabetes, vaginal delivery, instrumental delivery, caesarean section, umbilical artery pH <7·1, NICU admission
Pariente et al, 2020[34]	94·44	0·884	None	Postpartum depression (EPDS score)	Gestational hypertension, pre-eclampsia, maternal suicidal ideations (EPDS question 10 positive)
Philip et al, 2020[35]	90·74	0·924	None	Very low birthweight (<1500 g)	Extremely low birthweight (<1000 g)
Silverman et al, 2020[36]	72·69	0·838	None	Postnatal depression (EPDS score)	None
Stowe et al, 2021[37]	79·63	0·925	None	None	Stillbirths
Sun et al, 2020[38]	81·02	0·573	No statistical analysis done	No statistical analysis done	No statistical analysis done
Suzuki et al, 2020[39]	47·22	0·957	Maternal depression (Whooley questions)	None	None
Werner et al, 2020[40]	72·69	0·838	No statistical analysis done	No statistical analysis done	No statistical analysis done
Wu et al, 2020[41]	77·31	0·485	Postnatal depression (EPDS score), maternal anxiety (EPDS-3A score)	None	None
Xie et al, 2021[43]	81·94	0·485	Maternal depression, maternal anxiety (SCL-90-R score)	None	None
Zanardo et al, 2020[42]	93·52	0·991	Postnatal depression (EPDS score)	None	Caesarean section

IDAS-II=Inventory of Depression and Anxiety Symptoms, Expanded Form. BAI=Beck Anxiety Inventory. NICU=neonatal intensive care unit. EDPS=Edinburgh Postnatal Depression Scale. NuPDQ=Revised Prenatal Distress Questionnaire. SCL-90-R=Symptom Checklist 90 Revised.

Table 2: **Summary of findings of included studies**

14 studies from nine countries provided data on the incidence of stillbirth during (168 295 births) and before the pandemic (165 118 births).[4,12,15,16,19,21,24,25,30–32,37,47,49] Two of these studies were excluded (Gu et al[15] because no adverse outcomes were reported and Khalil et al[4] because of cohort overlap with another larger study in the analysis[37]). Meta-analysis of the remaining 12 studies found a significant increase in the rate of stillbirth (pooled OR 1·28 [95% CI 1·07–1·54]; I^2=63%; table 3, figure 2B). A subgroup analysis according to study setting produced similar findings, but only the subgroup of low-income and middle-income countries (LMICs) reached statistical significance (1·29 [1·06–1·58]; I^2=64%), whereas HICs did not (1·38 [0·94–2·02]; I^2=52%). Funnel plot asymmetry testing did not show a significant publication bias effect (p=0·12; appendix p 42). One study reported on antepartum and intrapartum stillbirth separately and found no difference in the proportion of antenatally diagnosed stillbirth, despite an overall increase in stillbirth in this tertiary centre in India.[24] One study excluded antepartum stillbirth by definition because only women carrying a live fetus at admission were enrolled.[21]

Three studies reported on neonatal death. The largest, from Nepal,[21] found a statistically significant increase, but two smaller studies[30,47] identified no significant change. The pooled OR for studies included in the meta-analysis (detailing 13 214 births during and 22 570 before the pandemic) was 1·01 (95% CI 0·38–2·67; I^2=85%;

	Studies	Pandemic		Pre-pandemic		Odds ratio or mean difference*	p value	I^2
		Events	Pregnancies	Events	Pregnancies			
Maternal and perinatal death								
Stillbirth	12	1099	168 295	1325	198 993	1·28 (1·07–1·54)	0·0082	63%
HICs only	8	625	150 404	640	165 118	1·38 (0·94–2·02)	0·099	52%
LMICs only	4	474	17 891	685	33 875	1·29 (1·06–1·58)	0·012	64%
Neonatal death	3	62	13 214	120	22 570	1·01 (0·38–2·67)	0·98	85%
HICs only	1	5	2538	6	1262	0·41 (0·13–1·36)	0·14	NA
LMICs only	2	57	10 676	114	21 308	1·37 (0·42–4·46)	0·59	90%
Maternal death	2	530	1 237 018	698	2 224 859	1·37 (1·22–1·53)	<0·0001	0%
HICs only	0	NA	NA	NA	NA	NA	NA	NA
LMICs only	2	530	1 237 018	698	2 224 859	1·37 (1·22–1·53)	<0·0001	0%
Maternal morbidity and complications								
Gestational diabetes	6	697	6946	954	10 137	1·01 (0·86–1·19)	0·85	45%
HICs only	5	667	6675	920	9826	1·02 (0·85–1·22)	0·86	56%
LMICs only	1	30	271	34	311	1·01 (0·60–1·71)	0·95	NA
Hypertensive disorders of pregnancy	6	293	6946	434	10 137	1·16 (0·75–1·79)	0·50	81%
HICs only	5	279	6675	431	9826	0·99 (0·67–1·46)	0·95	77%
LMICs only	1	14	271	3	311	5·59 (1·59–19·7)	0·0073	NA
EPDS score	3	NA	2330	NA	6517	0·42 (0·02–0·81)	0·038	79%
HICs only	1	NA	91	NA	101	2·16 (0·92–3·40)	0·0006	NA
LMICs only	2	NA	2239	NA	6416	0·22 (0·21–0·23)	<0·0001	0%
Early pregnancy outcomes								
Surgical treatment of ectopic pregnancy	3	27	37	73	272	5·81 (2·16–15·6)	0·0005	26%
HICs only	3	27	37	73	272	5·81 (2·16–15·6)	0·0005	26%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Delivery outcomes								
Spontaneous vaginal delivery	11	17 305	26 494	27 011	40 639	0·98 (0·93–1·02)	0·25	25%
HICs only	6	9675	14 632	11 288	16 362	0·99 (0·94–1·05)	0·80	4%
LMICs only	5	7630	11 862	15 723	24 277	0·96 (0·90–1·04)	0·33	37%
Caesarean section	17	15 304	48 550	20 656	67 442	1·03 (0·99–1·07)	0·14	46%
HICs only	11	10 091	33 161	10 824	36 956	1·01 (0·97–1·04)	0·76	10%
LMICs only	6	5213	15 389	9832	30 486	1·07 (0·99–1·16)	0·071	55%
Induction of labour	7	4860	16 459	5208	24 592	1·15 (0·81–1·64)	0·43	98%
HICs only	6	2578	9294	2950	11 403	1·03 (0·90–1·19)	0·64	76%
LMICs only	1	2282	7165	2258	13 189	2·26 (2·12–2·42)	<0·0001	NA
Instrumental delivery	7	1045	16 287	1492	27 066	1·06 (0·97–1·15)	0·22	0%
HICs only	5	728	8168	740	10 300	1·07 (0·95–1·20)	0·88	0%
LMICs only	2	317	8119	752	16 766	1·02 (0·82–1·26)	0·25	0%
Preterm birth before 37 weeks' gestation	15	13 466	170 640	49 596	656 423	0·94 (0·87–1·02)	0·13	75%
HICs only	12	11 600	159 987	46 149	635 118	0·91 (0·84–0·99)	0·035	63%
LMICs only	3	1866	10 653	3447	21 305	1·05 (0·81–1·35)	0·73	88%
Preterm birth before 34 weeks' gestation	4	141	7039	210	9872	0·76 (0·42–1·36)	0·35	85%
HICs only	4	141	7039	210	9872	0·76 (0·42–1·36)	0·35	85%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Preterm birth before 32 weeks' gestation	6	2297	152 422	6679	627 344	0·95 (0·64–1·39)	0·77	90%
HICs only	5	2198	148 974	6409	619 269	0·96 (0·61–1·52)	0·87	86%
LMICs only	1	99	3448	270	8075	0·85 (0·68–1·08)	0·18	NA

(Table 3 continues on next page)

	Studies	Pandemic		Pre-pandemic		Odds ratio or mean difference*	p value	I^2
		Events	Pregnancies	Events	Pregnancies			
(Continued from previous page)								
Preterm birth before 28 weeks' gestation	3	605	135 606	2603	586 189	0·84 (0·46–1·53)	0·56	57%
HICs only	3	605	135 606	2603	586 189	0·84 (0·46–1·53)	0·56	86%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Iatrogenic preterm birth, any week	2	208	4204	358	6818	0·92 (0·77–1·10)	0·38	0%
HICs only	2	208	4204	358	6818	0·92 (0·77–1·10)	0·38	0%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Spontaneous preterm birth, any week	2	192	4204	374	6818	0·81 (0·67–0·97)	0·020	0%
HICs only	2	192	4204	374	6818	0·81 (0·67–0·97)	0·020	0%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Postpartum haemorrhage	2	603	3098	318	1978	1·02 (0·87–1·19)	0·82	0%
HICs only	2	603	3098	318	1978	1·02 (0·87–1·19)	0·82	0%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Neonatal outcomes								
5-min Apgar score <7	4	35	5701	45	9081	1·15 (0·62–2·15)	0·95	44%
HICs only	4	35	5701	45	9081	1·15 (0·62–2·15)	0·95	44%
LMICs only	0	NA	NA	NA	NA	NA	NA	NA
Birthweight <2500 g	3	919	9743	1510	14 492	0·99 (0·90–1·08)	0·75	0%
HICs only	1	144	2538	78	1262	0·91 (0·69–1·21)	0·53	NA
LMICs only	2	775	7205	1432	13 230	0·99 (0·91–1·09)	0·90	0%
NICU admission	7	446	8072	1604	37 557	0·90 (0·80–1·01)	0·084	0%
HICs only	6	413	7801	1555	37 246	0·91 (0·80–1·03)	0·14	0%
LMICs only	1	33	271	49	311	0·74 (0·46–1·19)	0·21	NA

Data are n or point estimate (95% CI). HICs=high-income countries. LMICs=low-income and middle-income countries. NA=not applicable. EPDS=Edinburgh Postnatal Depression Scale. NICU=neonatal intensive care unit. *Random-effects estimates calculated by Mantel-Haenszel method for during versus before pandemic; all values are odds ratios, except the estimate for EPDS scores (mean difference).

Table 3: **Results of the quantitative synthesis**

table 3, appendix p 45). The substantial statistical heterogeneity (table 3) was explained by neither WHO Healthcare Efficiency Index quartile nor GRSI score (appendix p 39).

Quantitative synthesis was possible for gestational diabetes (OR 1·01 [95% CI 0·86–1·19]; I^2=45%)[4,15,19,31,32,34] and hypertensive disorders of pregnancy (1·16 [0·75–1·79]; I^2=81%),[4,15,19,31,32,34] which were not significantly different during the pandemic compared with before the pandemic (table 3, appendix p 48). The statistical heterogeneity in the meta-analysis of hypertensive disorders of pregnancy was partly explained by WHO Healthcare Efficiency Index quartile (p=0·023) but not GRSI score (p=0·89; appendix p 39).

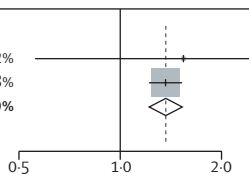
Two studies[19,30] reported on post-partum haemorrhage. Meta-analysis (including 3098 pregnancies during and 1978 before the pandemic) found no significant difference associated with the pandemic (OR 1·02 [95% CI 0·87–1·19]; I^2=0%; table 3, appendix p 48).

11 studies reported on measures of maternal mental health.[15,18,22,29,34,36,39,41–44] Assessment tools included the Generalised Anxiety and Depression Scale, EPDS, Generalised Anxiety Disorder 7 questionnaire, Inventory of Depression and Anxiety Symptoms (Expanded Form), Symptom Checklist 90 Revised, and Patient Health Questionnaire 9. Four studies[18,36,41,42] gave mean EPDS scores (on a scale of 0–30). One study violated the normality assumption and was excluded from quantitative synthesis.[36] For the remaining three studies, the pooled mean difference was 0·42 (95% CI 0·02–0·81; I^2=79%; table 3, appendix p 49). There was significant statistical heterogeneity, not explained by either the WHO Healthcare Efficiency Index quartile (p=0·62) or GRSI score (p=0·057; appendix p 39). When subdivided according to country income status, there was a statistically significant increase in mean EPDS score in LMICs (0·22 [0·21 to 0·23]). Of the 11 studies reporting on maternal mental health, seven reported a statistically significant increase in postnatal depression, maternal anxiety, or both.

Three studies[12,40,48] reported on the surgical management of ectopic pregnancy. Meta-analytical summary of three studies found increased odds for surgical treatment of ectopic pregnancy during the pandemic (OR 5·81

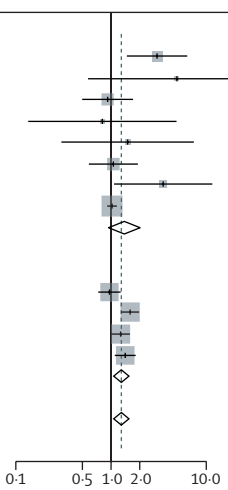
A

	Pandemic		Pre-pandemic		Weight	OR (95% CI)
	Events	Pregnancies	Events	Pregnancies		
LMIC subgroup*						
Kumari et al, 2020[25]	7	3527	8	6209	1·2%	1·54 (0·56–4·25)
Lumbreras-Marquez et al, 2020[27]	523	1233491	690	2218650	98·8%	1·36 (1·22–1·53)
Overall total	**530**	**1237018**	**698**	**2224859**	**100·0%**	**1·37 (1·22–1·53)**
Heterogeneity: τ^2=0; χ^2=0·06, df=1 (p=0·81); I^2=0%						
Residual heterogeneity: τ^2=NA; χ^2=0·06, df=1 (p=0·81); I^2=0%						



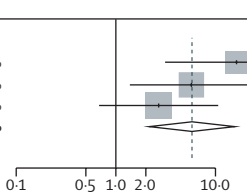
B

HIC subgroup						
De Curtis et al, 2020[49]	26	7755	10	9053	4·8%	3·04 (1·47–6·31)
Dell'Utri et al, 2020[12]	5	1126	1	1103	0·7%	4·92 (0·57–42·14)
Handley et al, 2021[16]	15	3007	32	5907	6·2%	0·92 (0·50–1·70)
Justman et al, 2020[19]	2	610	3	742	1·0%	0·81 (0·13–4·87)
McDonnell et al, 2020[30]	6	2538	2	1262	1·2%	1·49 (0·30–7·41)
Meyer et al, 2020[31]	22	2594	22	2742	6·5%	1·06 (0·58–1·91)
Mor et al, 2020[32]	6	1556	5	4564	2·1%	3·53 (1·08–11·58)
Stowe et al, 2021[37]	543	131218	565	139745	18·3%	1·02 (0·91–1·15)
Subgroup total	**625**	**150404**	**640**	**165118**	**40·9%**	**1·38 (0·94–2·02)**
Heterogeneity: τ^2=0·1200; χ^2=14·71, df=7 (p=0·04); I^2=52%						
LMIC subgroup						
Caniglia et al, 2020[47]	76	3589	183	8316	13·9%	0·96 (0·73–1·26)
Kc et al, 2020[21]	153	7165	179	13189	15·5%	1·59 (1·28–1·97)
Kumar et al, 2021[24]	134	3610	183	6161	15·2%	1·26 (1·00–1·58)
Kumari et al, 2020[25]	111	3527	140	6209	14·4%	1·41 (1·09–1·81)
Subgroup total	**474**	**17891**	**685**	**33875**	**59·1%**	**1·29 (1·06–1·58)**
Heterogeneity: τ^2=0·0272; χ^2=8·42, df=3 (p=0·04); I^2=64%						
Overall total	**1099**	**168295**	**1325**	**198993**	**100·0%**	**1·28 (1·07–1·54)**
Heterogeneity: τ^2=0·0445; χ^2=29·48, df=11 (p<0·01); I^2=63%						
Residual heterogeneity: τ^2=NA; χ^2=23·14, df=10 (p=0·01); I^2=57%						



C

HIC subgroup*						
Werner et al, 2020[40]	10	12	12	51	28·0%	16·25 (3·12–84·64)
Casadio et al, 2020[48]	6	9	52	201	35·1%	5·73 (1·38–23·74)
Dell'Utri et al, 2020[12]	11	16	9	20	36·8%	2·69 (0·68–10·65)
Overall total	**27**	**37**	**73**	**272**	**100·0%**	**5·81 (2·16–15·61)**
Heterogeneity: τ^2=0·1980; χ^2=2·70, df=2 (p=0·26); I^2=26%						
Residual heterogeneity: τ^2=NA; χ^2=2·70, df=2 (p=0·26); I^2=26%						



D

HIC subgroup						
Berghella et al, 2020[33]	118	1197	115	911	5·1%	0·76 (0·58–0·99)
De Curtis et al, 2020[49]	419	7755	587	9053	9·8%	0·82 (0·72–0·94)
Greene et al, 2020[14]	66	920	91	1016	4·0%	0·79 (0·56–1·09)
Handley et al, 2021[16]	283	3007	617	5907	9·1%	0·89 (0·77–1·03)
Hedermann et al, 2021[17]	249	5162	1317	26018	9·4%	0·95 (0·83–1·09)
Justman et al, 2020[19]	39	610	48	742	2·6%	0·99 (0·64–1·53)
Kasuga et al, 2020[20]	5	153	50	560	0·7%	0·34 (0·13–0·88)
Khalil et al, 2020[4]	127	1692	113	1655	5·3%	1·11 (0·85–1·44)
Main et al, 2020[28]	9843	132853	42630	580714	13·3%	1·01 (0·99–1·03)
McDonnell et al, 2020[30]	195	2488	83	1236	5·3%	1·18 (0·91–1·54)
Meyer et al, 2020[31]	174	2594	220	2742	6·9%	0·82 (0·67–1·01)
Mor et al, 2020[32]	82	1556	278	4564	5·6%	0·86 (0·67–1·10)
Subgroup total	**11600**	**159987**	**46149**	**635118**	**77·1%**	**0·91 (0·84–0·99)**
Heterogeneity: τ^2=0·0104; χ^2=29·92, df=11 (p<0·01); I^2=63%						
LMIC subgroup						
Caniglia et al, 2020[47]	518	3448	1316	8075	10·6%	0·91 (0·81–1·01)
Kc et al, 2020[21]	1342	7165	2125	13189	11·9%	1·20 (1·11–1·29)
Sun et al, 2020[38]	6	40	6	41	0·4%	1·03 (0·30–3·51)
Subgroup total	**1866**	**10653**	**3447**	**21305**	**22·9%**	**1·05 (0·81–1·35)**
Heterogeneity: τ^2=0·0339; χ^2=16·7, df=2 (p<0·01); I^2=88%						
Overall total	**13466**	**170640**	**49596**	**656423**	**100·0%**	**0·94 (0·87–1·02)**
Heterogeneity: τ^2=0·0120; χ^2=55·25, df=14 (p<0·01); I^2=75%						
Residual heterogeneity: τ^2=NA; χ^2=46·62, df=13 (p<0·01); I^2=72%						

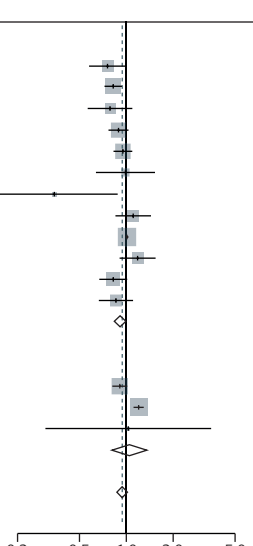


***Figure 2*: Forest plot of pooled ORs for maternal death (A), stillbirth (B), surgical management of ectopic pregnancy (C), and preterm birth before 37 weeks' gestation (D)**
ORs are random-effects estimates calculated by Mantel-Haenszel method. HIC=high-income country. LMIC=low-income and middle-income country. NA=not applicable. OR=odds ratio. *All studies investigating this outcome fell into a single subgroup (either LMIC or HIC); therefore, the subgroup totals are the same as the overall totals.

[95% CI 2·16–15·6]; I^2=26%; table 3, figure 2C), most of which were due to ruptured ectopic pregnancy.

On the basis of 11 studies,[14,15,18,21,26,30–33,38,46] there was no significant change in the rate of spontaneous vaginal delivery (OR 0·98 [95% CI 0·93–1·02]; I^2=25%; appendix p 51) during versus before the pandemic. 17 studies,[6,14,15,18,19,21,25,26,30–33,38,42,45,46,49] including 48 550 pregnancies during and 67 442 before the pandemic, showed no significant change in caesarean section rate (1·03 [0·99–1·07]; I^2=46%; table 3, appendix p 52), with consistent findings when subdivided into HICs and LMICs. Additionally, on the basis of seven studies,[14,18,19,21,30–32] rates of instrumental delivery did not differ during versus before the pandemic (1·06 [0·97–1·15]; I^2=0%; table 3, appendix p 53). The funnel plot asymmetry tests showed no significant publication bias in the included studies for vaginal birth (p=0·53) or caesarean section (p=0·61; appendix pp 64–65).

Seven studies,[12,14,19,21,30–32] including 16 459 pregnancies during and 24 592 before the pandemic, showed no significant difference in the rate of induction of labour (OR 1·15 [95% CI 0·81–1·64]; I^2=98%; table 3, appendix p 54). The very high statistical heterogeneity was explained by WHO Healthcare Efficiency Index scores, with countries in the fourth quartile having lower induction rates (estimate –0·783, p<0·0001) than countries in the second quartile (appendix p 39). The only LMIC study[21] included in the meta-analysis reported a significant increase in induction of labour (2·26 [2·12–2·42]).

There was a significant decrease in preterm birth in specific subgroups. Preterm birth was reported in 18 articles[4,5,14–17,19–21,26,28,30–33,38,47,49] with varying gestational age thresholds, and conflicting findings. Several large studies reported a local decrease in preterm birth, mostly in western European countries.[5,31,33,47,49] One large study reported an increase in preterm birth in Nepal.[21] Pooled analysis showed no overall effect for preterm birth before 37 weeks' gestation (OR 0·94 [95% CI 0·87–1·02]; I^2=75%; 15 studies; table 3, figure 2D). However, subgroup analysis of 12 studies (including 159 987 pregnancies during the pandemic and 635 118 pre-pandemic) suggested that there might be a significant decrease in HICs (0·91 [0·84–0·99]; I^2=63%). There was no overall effect on preterm birth before 34 weeks' gestation (0·76 [0·42–1·36]; I^2=85%; four studies), 32 weeks' gestation (0·95 [0·64–1·39]; I^2=90%; six studies) or 28 weeks' gestation (0·84 [0·46–1·53]; I^2=57%; three studies; table 3, appendix pp 55–57). In a meta-regression analysis for preterm birth before 37 weeks' gestation, neither WHO Healthcare Efficiency Index quartile (p=0·97) nor GRSI scores (p=0·17) adequately explained the statistical heterogeneity (appendix p 39). The funnel plot asymmetry test showed no significant publication bias in the included studies for preterm birth before 37 weeks' gestation (p=0·13; appendix p 66). Two studies reported on iatrogenic and spontaneous preterm birth before 37 weeks' gestation, both in HICs;[16,33] meta-analysis showed a significant decrease in spontaneous preterm birth (0·81 [0·67–0·97]; I^2=0%) but no difference in iatrogenic preterm birth (0·92 [0·77–1·10]; I^2=0%; table 3, appendix pp 59–60).

One study[35] reported on the incidence of very low (<1500 g) and extremely low (<1000 g) birthweight as a proxy for preterm birth. This study reported a 73% reduction in very low birthweight infants, consistent with the reduction in preterm birth found in the meta-analysis. Three studies reported on the incidence of birthweight of less than 2500 g[21,30,38] and found no significant difference associated with the pandemic (OR 0·99 [95% CI 0·90–1·08]; I^2=0%; table 3, appendix p 61).

Seven studies reported on neonatal intensive care unit admissions. Meta-analysis (including 8072 pregnancies during and 37 557 before the pandemic) found no overall difference in the rate of neonatal intensive care unit admissions (OR 0·90 [95% CI 0·80–1·01]; I^2=0%; table 3, appendix p 62).[4,14,15,19,23,31,32]

There were no significant differences in other neonatal outcomes between pandemic and pre-pandemic cohorts (table 3). Justman and colleagues[19] reported no difference in the proportion of pregnancies with shoulder dystocia (p=0·26) or umbilical arterial pH below 7·0 (p>0·99). Seven studies assessed 5-min Apgar scores (tables 1, 2).[14,15,19,23,31,32,38] We excluded from the meta-analysis the studies by Gu and colleagues[15] (scores reported as mean rather than binary [<7 *vs* ≥7]), Kugelman and colleagues[23] (no adverse events reported), and Sun and colleagues[38] (no statistical analysis done). Meta-analysis of the remaining four studies[14,19,31,32] showed no change in the proportion of pregnancies with 5-min Apgar scores of less than 7 (OR 1·15 [95% CI 0·62–2·15]; I^2=44%; table 3, appendix p 63). Li and colleagues[26] found no significant change in the proportion of pregnancies in which neonatal asphyxia was recorded (p=0·12). Meyer and colleagues[31] reported on a composite score for adverse neonatal outcomes and found no difference between pandemic and pre-pandemic cohorts (p=0·12).

Discussion

This systematic review summarises the available global data on the effects of the COVID-19 pandemic on maternal and perinatal outcomes. We found increased maternal mortality and stillbirth, maternal stress, and ruptured ectopic pregnancies during the pandemic compared with before the pandemic. Stillbirth might be particularly increased in LMIC settings. There was no overall difference in preterm birth, but analyses of HIC data only suggested that both preterm birth before 37 weeks' gestation and spontaneous preterm birth might be reduced. WHO Healthcare Efficiency Index explained some of the observed between-study heterogeneity, but GRSI scores did not. This finding suggests that the increased rate of adverse outcomes might be driven mainly by the inefficiency of health-care systems and

their inability to cope with the pandemic, rather than by the stringency of pandemic mitigation measures.

The strengths of this review include the comprehensive search not restricted by language, and the inclusion and synthesis of a broad range of literature. We used meta-regression to adjust for between-study heterogeneity in important outcomes, and analysed HIC and LMIC settings separately to clarify the differential effects of the pandemic by country income.

The main limitations are the retrospective design of the included studies, as well as the heterogeneity of the study populations and the definitions and ways of measuring outcomes, thereby limiting the comparability of results. There were fewer studies from LMIC settings than from HIC settings, which is concerning because our analysis showed substantial variation in outcomes between high-income and low-income settings. With regard to stillbirth, only one study reported on antepartum and intrapartum stillbirth separately, limiting our ability to speculate on the probable mechanism of this change. Few studies reported both stillbirth and preterm birth in the same cohort, which would be necessary to ascertain whether the cost of a reduction in preterm birth was an increase in stillbirth. Finally, we could not exclude the risk of publication bias against studies reporting negative findings, although funnel plot asymmetry testing for such bias was negative.

Early evidence suggested that the pandemic period was marked by a substantial decrease in preterm birth. Our findings from HICs supported this decrease, whereas those from LMICs did not. The report of a significant reduction in very low birthweight birth in Ireland further supports the hypothesis that preterm birth in HICs was reduced during the pandemic.[35] Although no significant overall difference in neonatal death was observed, the data suggested that neonatal death might be increased in LMICs and decreased in HICs, consistently with the observed trends in preterm birth, a leading cause of neonatal mortality. This reduction in HICs appears to be driven by a reduction in spontaneous preterm birth, and is, therefore, not likely to be explained by reduced iatrogenic delivery. It is more likely that changes in health-care delivery and population behaviours are contributing factors. If a decrease in preterm birth has been achieved without a corresponding increase in fetal loss in some regions, there are valuable lessons to be learned from understanding the mechanisms underlying this effect.

The observed increase in maternal death is based only on data from LMICs. However, our findings are particularly concerning because these areas already carry the majority of the global burden of maternal mortality. This finding is supported by national data from Kenya not yet formally published,[50] and we call for further investigation of maternal mortality as a matter of urgency, particularly in LMIC settings. Data from the MBRRACE-UK rapid report show that; in the first wave of the pandemic (March–May, 2020), there were 16 maternal deaths (ten associated with SARS-CoV-2) of an estimated 162 344 births, corresponding to a maternal mortality rate of 9·9 per 100 000,[51] compared with a pre-pandemic rate of 9·7 per 100 000 in 2016–18.

One proposed explanation for the increase in adverse pregnancy outcomes is that such outcomes could be linked to reduced access to care. Although maternal anxiety was consistently shown to be increased during the pandemic, health-care providers around the world have reported reduced attendance for routine[6,13,15,52–55] and unscheduled pregnancy care.[6,12,13,15,19,56] This reduction could be driven by concern about the risk of acquiring COVID-19 in health-care settings, governmental advice to stay at home, or reduced public transport and childcare access during lockdowns.[13,52] In HICs, much of routine care was rapidly restructured and delivered remotely using diverse models, including telephone or video-based appointments. Although technology can provide a COVID-19-secure path to continuity of antenatal care, there remains inequality of access for people without regular access to high-speed internet or privacy in their living space.[57,58] In LMICs, where remote consultations are less feasible, people might simply miss out on preventive antenatal care entirely.[13,53] In all settings, the impact is greatest on the most vulnerable individuals in the population: in Nepal, hospital deliveries decreased, most markedly among disadvantaged groups;[21] and in the UK, 88% of pregnant women who died during the first wave of the pandemic were from black and minority ethnic groups.[51]

Reduced access to care is not the sole factor to consider in our continuing response to this global emergency. During its peak prevalence, maternity staff have been redeployed to support critical care and medical teams, reducing the staffing available for maternity care. Following the first wave in the UK, the Royal College of Obstetricians and Gynaecologists argued strongly for excluding maternity staff from redeployment wherever possible. We strongly recommend the prioritisation of safe staffing for maternity services throughout all phases of the pandemic response and in response to future health system shocks.

Wider societal changes are also echoed in observed changes in maternal health. Intimate-partner violence, already a leading cause of maternal death, has increased during the pandemic[59] and has already been highlighted[51] as a contributor to increased maternal mortality. Women have been disproportionately more likely to both become unemployed[60] and take on more childcare because of nursery and school closures. The resultant financial and time constraints are likely to have far-reaching consequences for mothers' physical, emotional, and financial health during pregnancy and in the future.

Health-care providers planning for service delivery in the ongoing pandemic must consider how to establish robust antenatal care pathways that explicitly reach out to vulnerable individuals and communities. Public health

messaging must emphasise the importance of antenatal care, and provide avenues of support for those at risk of intimate-partner violence. National governments must consider how to support financially vulnerable and socially isolated individuals, considering that each intersecting vulnerability magnifies risk across all contexts.[51,61,62]

It is clear that pregnant individuals and babies have been subjected to harm during the pandemic, and the onus is on the academic community, health-care providers, and policy-makers to learn from it. Women's health-care is often adversely affected in humanitarian disasters[63] and our findings highlight the central importance of planning for robust maternity services in any emergency response.

There remain opportunities to be seized as well as challenges to be faced as we work to end the grip of the pandemic on our global community. Rapid restructuring of maternity care has shown that high-quality remote care can be facilitated, reductions in hospital stay can be achieved, and apparently intractable and entrenched problems can be transformed by the concerted application of funding, scientific enquiry, and political will. We can prioritise safe and accessible maternity care during the pandemic and the aftermath, while planning for a future of radically inclusive and equitable maternity care that will draw on the lessons of this pandemic to reduce preterm birth, stillbirth, and maternal mortality worldwide.

Contributors

BC, IB, RT, EK, and AK participated in the data curation, formal analysis, and validation. LM, JvdM, IG-U EM, TD, ST, KLD, and SL participated in the investigation and visualisation. PvD and PO'B participated in the investigation, validation, and visualisation. All authors participated in the conceptualisation, visualisation, and writing, reviewing, and editing of the manuscript, and have read and agreed to the published version of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. BC, IB, RT, and EK accessed and verified the data underlying the study.

Declaration of interests

We declare no competing interests.

Data sharing

All datasets generated and analysed, including the study protocol, search strategy, list of the included and excluded studies, data extracted, analysis plans, quality assessment, and assessment of the publication bias, are available in the Article and upon request from the corresponding author.

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