

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



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## 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); postpartum 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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## Introduction

The SARS-CoV-2 pandemic has had profound effects on health-care systems, societal structures, and the world economy.<sup>1</sup> 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.<sup>2,3</sup>

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

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prospero/display\\_record.  
php?RecordID=211753](https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=211753)

See Online for appendix

## 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,

pandemic can be derived from historical cohorts by examining the change in outcomes and calculating the excess event rate.<sup>7</sup> 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.<sup>8</sup> The study protocol is available online.

### 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.

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

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.

papers, and studies reporting on overlapping populations were excluded. Studies of only SARS-CoV-2-infected women were excluded.

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.<sup>9</sup> 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).<sup>9</sup>

### Quality assessment

Each study was scored according to the Newcastle-Ottawa Scale<sup>10</sup> 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<sup>11</sup> and the stringency of lockdown measures (quantified with the GRSI).<sup>9</sup> 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).<sup>4,5,12-49</sup> 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.<sup>4,12,14-21,24-28,30-34,37,38,40,42,45-49</sup> 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)<sup>4,5,12,14,16,17,19,20,22,23,28-37,39,40,42,44-46,48,49</sup> 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.<sup>4,12,14,16,17,19,20,23,28,30-34,42,45,46,49</sup> The

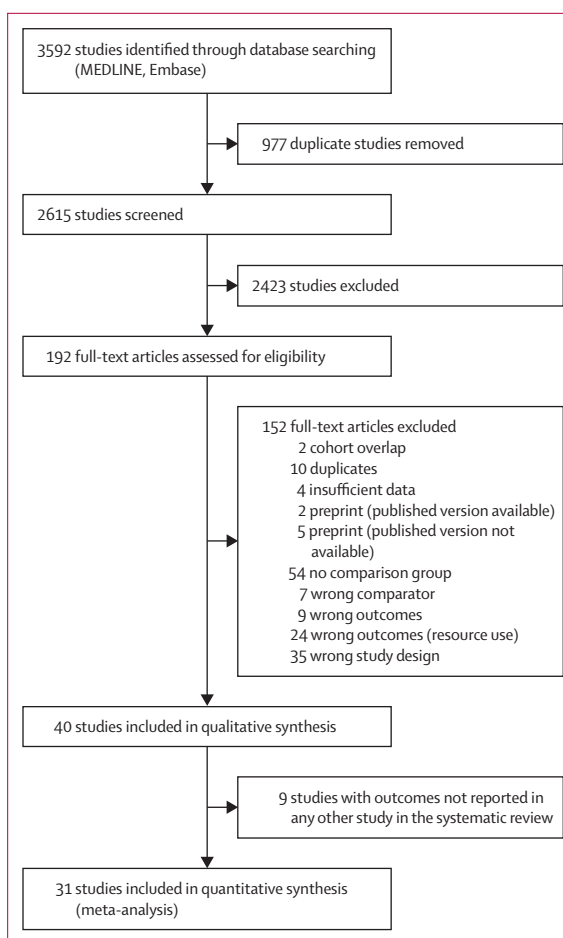


Figure 1: PRISMA flow chart

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<sup>4,5,14-17,19-21,26,28,30-33,38,47,49</sup> reported on preterm birth, variation in the gestational age cutoffs and use of ranges limited their comparability.

There were five reports from national registries,<sup>5,17,27,37,47</sup> six regional reports,<sup>28,37,41,43-45</sup> and four multicentre studies;<sup>16,21,25,46</sup> the remaining 25 were single-centre studies. 11 studies<sup>12,15,19,23,24,33,38,39,42,45,49</sup> had a comparison group from the equivalent period in 2019, the year preceding the pandemic. Nine studies<sup>16,17,20,28,30-32,35,47</sup> had a comparison group of annually matched periods from several preceding years (table 1). 18 studies<sup>4,5,13,14,18,21,22,25-27,29,36,37,41,43,44,46,48</sup> had a comparison group from immediately before the lockdown period in the respective country. Exposed sample sizes varied from nine to 56720 pregnancies (table 2). Only 19 studies<sup>5,14-16,19,21,22,24,26,28,30,33,34,39,41,42,47</sup> 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 <sup>22</sup>      | 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 <sup>5</sup>       | 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 <sup>33</sup> | 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 <sup>44</sup> | 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 <sup>45</sup>    | UK          | Regional (northwest England) | Caesarean rate   | 8381                          | 17 424            | April 1 to July 1, 2020    | Similar period in 2019          | 7                            |
| Bornstein et al, 2020 <sup>46</sup> | 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 <sup>47</sup>  | 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 <sup>48</sup>   | 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 <sup>49</sup> | 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 <sup>12</sup> | 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 <sup>13</sup>     | 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 <sup>14</sup>    | 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 <sup>15</sup>        | 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 <sup>16</sup>   | 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 <sup>17</sup> | Denmark     | National                     | Preterm birth  | 5162                          | 31 180            | March 12 to April 14, 2020 | Annual matched periods, 2015–19 | 7                            |
| Hui et al, 2020 <sup>18</sup>       | 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 <sup>19</sup>   | 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 <sup>20</sup>    | 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 <sup>21</sup>        | 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 <sup>4</sup>     | 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 <sup>23</sup>  | 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 <sup>24</sup>     | India       | Single centre                | Stillbirth   | 3610                          | 9771              | March 1 to Sept 30, 2020   | March 1 to Sept 30, 2019        | 9                            |
| Kumari et al, 2020 <sup>25</sup>    | 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 <sup>26</sup>                | China   | Single centre                     | Preterm birth, caesarean section  | 3432                          | 10591             | Jan 23 to March 24, 2020   | Jan 1, 2019, to Jan 22, 2020     | 9                            |
| Lumbreras-Marquez et al, 2020 <sup>27</sup> | Mexico  | National                          | Maternal death, post-partum haemorrhage   | 523*                          | 7747*             | Jan 1 to Aug 9, 2020       | 2011–19                          | 7                            |
| Main et al, 2020 <sup>28</sup>              | USA     | Regional (California)             | Preterm birth   | 132 853                       | 713567            | April 1 to July 31, 2020   | Annual matched periods, 2016–19  | 9                            |
| Matvienko-Sikar et al, 2020 <sup>29</sup>   | 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 <sup>30</sup>         | 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 <sup>31</sup>             | Israel  | Single centre                     | Induction of labour, preterm birth, vaginal delivery, instrumental delivery, caesarean section, stillbirth, 5-min Apgar score, NICU admission   | 2594                          | 34022             | March 20 to June 27, 2020  | Annual matched periods, 2011–19  | 7                            |
| Mor et al, 2020 <sup>32</sup>               | 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                            |
| Pariante et al, 2020 <sup>34</sup>          | 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 <sup>35</sup>            | Ireland | Regional                          | Birthweight   | 1381                          | 30705             | Jan 1 to April 30, 2020    | Annual matched periods, 2001–19  | 7                            |
| Silverman et al, 2020 <sup>36</sup>         | USA     | Single centre                     | Postpartum depression   | 155                           | 485               | March 12 to June 12, 2020  | Feb 2 to March 11, 2020          | 6                            |
| Stowe et al, 2021 <sup>37</sup>             | 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 <sup>38</sup>               | 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 <sup>39</sup>            | 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 <sup>40</sup>            | USA     | Single centre                     | Ectopic pregnancy   | 12                            | 63                | March 15 to May 17, 2020   | 2019–20 interval before pandemic | 7                            |
| Wu et al, 2020 <sup>41</sup>                | 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 <sup>43</sup>               | 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 <sup>42</sup>           | 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<sup>13,25,27</sup> 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.<sup>25</sup> Two studies in which statistical analysis was done, from India and Mexico, were included in the meta-analysis (1237018 pregnancies during and 2224859 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.<sup>27</sup>

|                                     | Government Response Stringency Index <sup>22</sup> | WHO Healthcare Efficiency Index <sup>24</sup> | Outcomes   |  |  |
|-------------------------------------|--|---|--|--|--|
|                                     |  |   | Statistically significant increase during pandemic   | Statistically significant decrease during pandemic   | Statistically non-significant change   |
| Ayaz et al, 2020 <sup>22</sup>      | 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 <sup>5</sup>       | 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 <sup>33</sup> | 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 <sup>44</sup> | 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 <sup>45</sup>    | 79-63  | 0-925   | Caesarean section  | None   | None   |
| Bornstein et al, 2020 <sup>46</sup> | 72-69  | 0-838   | None   | None   | Caesarean section, vaginal delivery  |
| Caniglia et al, 2020 <sup>47</sup>  | 86-11  | 0-388   | None   | Preterm birth before 37 weeks' gestation, preterm birth before 32 weeks' gestation   | Neonatal death, stillbirth   |
| Casadio et al, 2020 <sup>48</sup>   | 93-52  | 0-991   | Ruptured ectopic pregnancy (needing surgical intervention)   | None   | None   |
| De Curtis et al, 2020 <sup>49</sup> | 93-52  | 0-991   | Stillbirth   | Preterm birth before 37 weeks' gestation   | Caesarean section  |
| Dell'Utri et al, 2020 <sup>52</sup> | 75-46  | 0-991   | Stillbirth, induction of labour  | None   | Vaginal delivery, surgical management of ectopic pregnancy   |
| Goyal et al, 2021 <sup>53</sup>     | 100-0  | 0-617   | None   | None   | Maternal death   |
| Greene et al, 2020 <sup>54</sup>    | 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 <sup>55</sup>        | 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 <sup>56</sup>   | 72-69  | 0-838   | None   | None   | Stillbirth, preterm birth before 37 weeks' gestation, spontaneous preterm birth, iatrogenic preterm birth  |
| Hedermann et al, 2021 <sup>57</sup> | 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 <sup>58</sup>       | 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 <sup>59</sup>   | 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 <sup>60</sup>    | 47-22  | 0-957   | None   | Gestational hypertension, preterm birth before 27 weeks' gestation   | Preterm birth (gestation not specified)  |
| Kc et al, 2020 <sup>61</sup>        | 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 <sup>64</sup>    | 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 <sup>63</sup>  | 94-44  | 0-884   | None   | None   | NICU admission, umbilical cord blood pH <7.1, 5-min Apgar score <7   |
| Kumar et al, 2021 <sup>64</sup>     | 100-0  | 0-617   | Stillbirth   | None   | None   |
| Kumari et al, 2020 <sup>65</sup>    | 100-0  | 0-617   | Caesarean section, maternal death, stillbirth  | None   | None   |
| Li et al, 2020 <sup>66</sup>        | 81-94  | 0-485   | Caesarean section  | None   | None   |

(Table 2 continues on next page)

|   | Government Response Stringency Index <sup>22</sup> | WHO Healthcare Efficiency Index <sup>24</sup> | Outcomes  |  |  |
|---|--|---|---|--|--|
|   |  |   | Statistically significant increase during pandemic                  | Statistically significant decrease during pandemic       | Statistically non-significant change   |
| (Continued from previous page)              |  |   |   |  |  |
| Lumbreras-Marquez et al, 2020 <sup>27</sup> | 82.41  | 0.755   | No statistical analysis done  | No statistical analysis done                             | No statistical analysis done   |
| Main et al, 2020 <sup>28</sup>              | 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 <sup>29</sup>   | 90.74  | 0.924   | None  | None   | Pregnancy-specific stress (NuPDQ score)  |
| McDonnell et al, 2020 <sup>30</sup>         | 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 <sup>31</sup>             | 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 <sup>32</sup>               | 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   |
| Pariante et al, 2020 <sup>34</sup>          | 94.44  | 0.884   | None  | Postpartum depression (EPDS score)                       | Gestational hypertension, pre-eclampsia, maternal suicidal ideations (EPDS question 10 positive)   |
| Philip et al, 2020 <sup>35</sup>            | 90.74  | 0.924   | None  | Very low birthweight (<1500 g)                           | Extremely low birthweight (<1000 g)  |
| Silverman et al, 2020 <sup>36</sup>         | 72.69  | 0.838   | None  | Postnatal depression (EPDS score)                        | None   |
| Stowe et al, 2021 <sup>37</sup>             | 79.63  | 0.925   | None  | None   | Stillbirths  |
| Sun et al, 2020 <sup>38</sup>               | 81.02  | 0.573   | No statistical analysis done  | No statistical analysis done                             | No statistical analysis done   |
| Suzuki et al, 2020 <sup>39</sup>            | 47.22  | 0.957   | Maternal depression (Whooley questions)                             | None   | None   |
| Werner et al, 2020 <sup>40</sup>            | 72.69  | 0.838   | No statistical analysis done  | No statistical analysis done                             | No statistical analysis done   |
| Wu et al, 2020 <sup>41</sup>                | 77.31  | 0.485   | Postnatal depression (EPDS score), maternal anxiety (EPDS-3A score) | None   | None   |
| Xie et al, 2021 <sup>43</sup>               | 81.94  | 0.485   | Maternal depression, maternal anxiety (SCL-90-R score)              | None   | None   |
| Zanardo et al, 2020 <sup>42</sup>           | 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. EPDS=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).<sup>4,12,15,16,19,21,24,25,30–32,37,47,49</sup> Two of these studies were excluded (Gu et al<sup>15</sup> because no adverse outcomes were reported and Khalil et al<sup>4</sup> because of cohort overlap with another larger study in the analysis<sup>37</sup>). 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.<sup>24</sup> One study excluded antepartum stillbirth by definition because only women carrying a live fetus at admission were enrolled.<sup>21</sup>

Three studies reported on neonatal death. The largest, from Nepal,<sup>21</sup> found a statistically significant increase, but two smaller studies<sup>30,47</sup> 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 <sup>2</sup> |
|---|---------|----------|-------------|--------------|-------------|--------------------------------|---------|----------------|
|   |         | Events   | Pregnancies | Events       | Pregnancies |                                |         |                |
| <b>Maternal and perinatal death</b>         |         |          |             |              |             |                                |         |                |
| 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        | 2 538       | 6            | 1 262       | 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%             |
| <b>Maternal morbidity and complications</b> |         |          |             |              |             |                                |         |                |
| Gestational diabetes                        | 6       | 697      | 6 946       | 954          | 10 137      | 1.01 (0.86–1.19)               | 0.85    | 45%            |
| HICs only                                   | 5       | 667      | 6 675       | 920          | 9 826       | 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      | 6 946       | 434          | 10 137      | 1.16 (0.75–1.79)               | 0.50    | 81%            |
| HICs only                                   | 5       | 279      | 6 675       | 431          | 9 826       | 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       | 2 330       | NA           | 6 517       | 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       | 2 239       | NA           | 6 416       | 0.22 (0.21–0.23)               | <0.0001 | 0%             |
| <b>Early pregnancy outcomes</b>             |         |          |             |              |             |                                |         |                |
| 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             |
| <b>Delivery outcomes</b>                    |         |          |             |              |             |                                |         |                |
| Spontaneous vaginal delivery                | 11      | 17 305   | 26 494      | 27 011       | 40 639      | 0.98 (0.93–1.02)               | 0.25    | 25%            |
| HICs only                                   | 6       | 9 675    | 14 632      | 11 288       | 16 362      | 0.99 (0.94–1.05)               | 0.80    | 4%             |
| LMICs only                                  | 5       | 7 630    | 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       | 5 213    | 15 389      | 9 832        | 30 486      | 1.07 (0.99–1.16)               | 0.071   | 55%            |
| Induction of labour                         | 7       | 4 860    | 16 459      | 5 208        | 24 592      | 1.15 (0.81–1.64)               | 0.43    | 98%            |
| HICs only                                   | 6       | 2 578    | 9 294       | 2 950        | 11 403      | 1.03 (0.90–1.19)               | 0.64    | 76%            |
| LMICs only                                  | 1       | 2 282    | 7 165       | 2 258        | 13 189      | 2.26 (2.12–2.42)               | <0.0001 | NA             |
| Instrumental delivery                       | 7       | 10 45    | 16 287      | 1 492        | 27 066      | 1.06 (0.97–1.15)               | 0.22    | 0%             |
| HICs only                                   | 5       | 7 28     | 8 168       | 740          | 10 300      | 1.07 (0.95–1.20)               | 0.88    | 0%             |
| LMICs only                                  | 2       | 3 17     | 8 119       | 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       | 1 866    | 10 653      | 3 447        | 21 305      | 1.05 (0.81–1.35)               | 0.73    | 88%            |
| Preterm birth before 34 weeks' gestation    | 4       | 141      | 7 039       | 210          | 9 872       | 0.76 (0.42–1.36)               | 0.35    | 85%            |
| HICs only                                   | 4       | 141      | 7 039       | 210          | 9 872       | 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       | 2 297    | 152 422     | 6 679        | 627 344     | 0.95 (0.64–1.39)               | 0.77    | 90%            |
| HICs only                                   | 5       | 2 198    | 148 974     | 6 409        | 619 269     | 0.96 (0.61–1.52)               | 0.87    | 86%            |
| LMICs only                                  | 1       | 99       | 3 448       | 270          | 8 075       | 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 <sup>2</sup> |
|--|---------|----------|-------------|--------------|-------------|--------------------------------|---------|----------------|
|  |         | 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             |
| <b>Neonatal outcomes</b>   |         |          |             |              |             |                                |         |                |
| 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). |         |          |             |              |             |                                |         |                |
| <b>Table 3: Results of the quantitative synthesis</b>  |         |          |             |              |             |                                |         |                |

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).

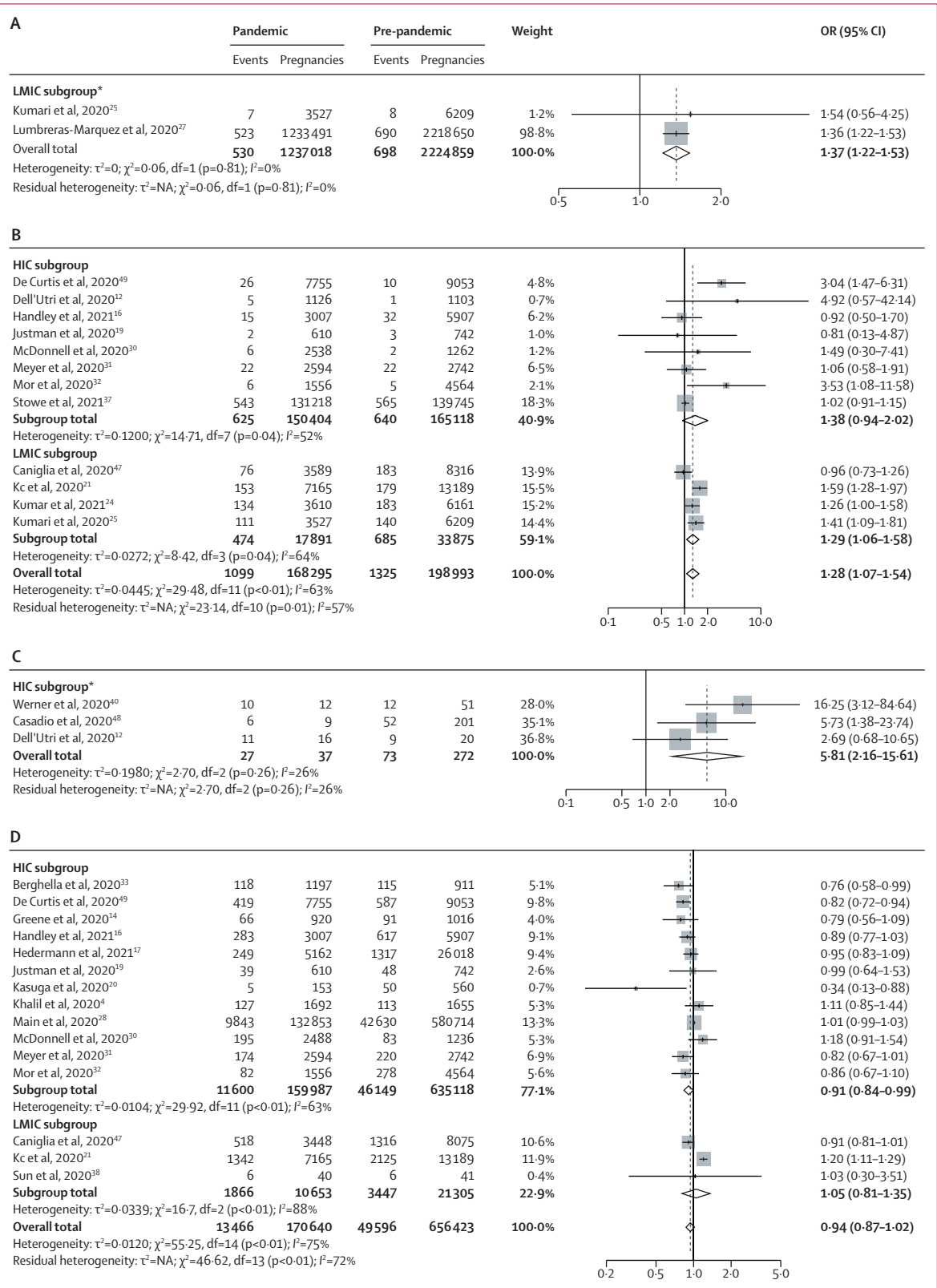
Quantitative synthesis was possible for gestational diabetes (OR 1.01 [95% CI 0.86–1.19];  $I^2=45%$ )<sup>4,15,19,31,32,34</sup> and hypertensive disorders of pregnancy (1.16 [0.75–1.79];  $I^2=81%$ ),<sup>4,15,19,31,32,34</sup> which were not significantly different during the pandemic compared with 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<sup>19,30</sup> 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.<sup>15,18,22,29,34,36,39,41–44</sup> 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<sup>18,36,41,42</sup> gave mean EPDS scores (on a scale of 0–30). One study violated the normality assumption and was excluded from quantitative synthesis.<sup>36</sup> 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<sup>12,40,48</sup> 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



**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,<sup>14,15,18,21,26,30–33,38,46</sup> 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,<sup>6,14,15,18,19,21,25,26,30–33,38,42,45,46,49</sup> 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,<sup>14,18,19,21,30–32</sup> 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,<sup>12,14,19,21,30–32</sup> 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<sup>21</sup> 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<sup>4,5,14–17,19–21,26,28,30–33,38,47,49</sup> with varying gestational age thresholds, and conflicting findings. Several large studies reported a local decrease in preterm birth, mostly in western European countries.<sup>5,31,33,47,49</sup> One large study reported an increase in preterm birth in Nepal.<sup>21</sup> 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;<sup>16,33</sup> 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<sup>35</sup> 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<sup>21,30,38</sup> 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).<sup>4,14,15,19,23,31,32</sup>

There were no significant differences in other neonatal outcomes between pandemic and pre-pandemic cohorts (table 3). Justman and colleagues<sup>19</sup> 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).<sup>14,15,19,23,31,32,38</sup> We excluded from the meta-analysis the studies by Gu and colleagues<sup>15</sup> (scores reported as mean rather than binary [ $<7$  vs  $\geq 7$ ]), Kugelman and colleagues<sup>23</sup> (no adverse events reported), and Sun and colleagues<sup>38</sup> (no statistical analysis done). Meta-analysis of the remaining four studies<sup>14,19,31,32</sup> 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<sup>26</sup> found no significant change in the proportion of pregnancies in which neonatal asphyxia was recorded ( $p=0.12$ ). Meyer and colleagues<sup>31</sup> 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.<sup>35</sup> 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,<sup>50</sup> 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,<sup>51</sup> 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<sup>6,13,15,52–55</sup> and unscheduled pregnancy care.<sup>6,12,13,15,19,56</sup> 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.<sup>13,52</sup> 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.<sup>57,58</sup> In LMICs, where remote consultations are less feasible, people might simply miss out on preventive antenatal care entirely.<sup>13,53</sup> 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;<sup>21</sup> and in the UK, 88% of pregnant women who died during the first wave of the pandemic were from black and minority ethnic groups.<sup>51</sup>

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<sup>59</sup> and has already been highlighted<sup>51</sup> as a contributor to increased maternal mortality. Women have been disproportionately more likely to both become unemployed<sup>60</sup> 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.<sup>51,61,62</sup>

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<sup>63</sup> 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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