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# Effectiveness and safety of COVID-19 vaccines on maternal and perinatal outcomes: a systematic review and meta-analysis

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## ABSTRACT

**Objective** To assess the effects of COVID-19 vaccines in women before or during pregnancy on SARS-CoV-2 infection-related, pregnancy, offspring and reactogenicity outcomes.

**Design** Systematic review and meta-analysis.

**Data sources** Major databases between December 2019 and January 2023.

**Study selection** Nine pairs of reviewers contributed to study selection. We included test-negative designs, comparative cohorts and randomised trials on effects of COVID-19 vaccines on infection-related and pregnancy outcomes. Non-comparative cohort studies reporting reactogenicity outcomes were also included.

**Quality assessment, data extraction and analysis** Two reviewers independently assessed study quality and extracted data. We undertook random-effects meta-analysis and reported findings as HRs, risk ratios (RRs), ORs or rates with 95% CIs.

**Results** Sixty-seven studies (1 813 947 women) were included. Overall, in test-negative design studies, pregnant women fully vaccinated with any COVID-19 vaccine had 61% reduced odds of SARS-CoV-2 infection during pregnancy (OR 0.39, 95% CI 0.21 to 0.75; 4 studies, 23 927 women; $I^2$=87.2%) and 94% reduced odds of hospital admission (OR 0.06, 95% CI 0.01 to 0.71; 2 studies, 868 women; $I^2$=92%). In adjusted cohort studies, the risk of hypertensive disorders in pregnancy was reduced by 12% (RR 0.88, 95% CI 0.82 to 0.92; 2 studies; 115 085 women), while caesarean section was reduced by 9% (OR 0.91, 95% CI 0.85 to 0.98; 6 studies; 30 192 women). We observed an 8% reduction in the risk of neonatal intensive care unit admission (RR 0.92, 95% CI 0.87 to 0.97; 2 studies; 54 569 women) in babies born to vaccinated versus not vaccinated women. In general, vaccination during pregnancy was not associated with increased risk of adverse pregnancy or perinatal outcomes. Pain at the injection site was the most common side effect reported (77%, 95% CI 52% to 94%; 11 studies; 27 195 women).

**Conclusion** COVID-19 vaccines are effective in preventing SARS-CoV-2 infection and related complications in pregnant women.

**PROSPERO registration number** CRD42020178076.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Pregnant women with COVID-19 are at high risk of severe disease and death.
⇒ Pregnant women were not included in vaccine trials, resulting in a lack of data on efficacy and safety leading to vaccine hesitancy.
⇒ Existing reviews of observational studies do not account for confounding effects when combining studies, resulting in biased estimates and decreased confidence in findings.

## INTRODUCTION

Pregnant and recently pregnant women with SARS-CoV-2 infection are more likely to have severe COVID-19 disease and related mortality

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### WHAT THIS STUDY ADDS

⇒ Analysis of adjusted data by confounding variables implies the control of sources of bias, such as the differences in healthcare-seeking behaviour.

⇒ Fully vaccinated pregnant women are at reduced risk of having SARS-CoV-2 infection and being admitted to the hospital compared with unvaccinated pregnant women.

⇒ Unvaccinated pregnant women are more likely to experience hypertensive disorders and caesarean sections, and their neonates are more likely to be admitted to a neonatal unit.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Pregnant women should be counselled and reassured about the safety and benefits of COVID-19 vaccination during pregnancy, both for their own health and that of their babies.

⇒ As the pace of the pandemic continues to evolve, the effectiveness of COVID-19 vaccines against new variants and the duration of protection they provide should be monitored.

and morbidity than non-pregnant women of reproductive age.[1] Globally, vaccination has been the most important intervention in preventing COVID-19-related mortality and morbidity in the general population.[2] However, most phase III trials of COVID-19 vaccines excluded pregnant women, resulting in a lack of trial data on the safety and efficacy of these vaccines during pregnancy.[3] Additionally, concerns about maternal and offspring outcomes have contributed to pregnant women's reluctance to receive COVID-19 vaccination, despite current recommendations that pregnant women should receive the vaccine.[4 5]

Early observational studies on vaccine effectiveness focused on reporting the effects of any COVID-19 vaccine in pregnancy on maternal SARS-CoV-2 infection.[6–8] Subsequent reviews reporting pregnancy outcomes varied in their inclusion of studies, overlapped their search periods by only a few months and were rapidly outdated, limiting their relevance.[9–12] Some reviews only included studies from specific regions or countries and did not provide a global outlook.[13] Existing reviews on the effects of vaccines on pregnant women only included aggregate data and did not adjust for confounding variables, which implied they were not controlled for some sources of bias such as the differences in healthcare-seeking behaviour.[9 13]

We undertook a systematic review to comprehensively assess the effects of any COVID-19 vaccines administered to pregnant women before or during pregnancy on infection-related, pregnancy-related maternal and offspring and reactogenicity outcomes.

## METHODS

Our prospectively registered protocol (PROSPERO CRD42020178076) on effects of SARS-CoV-2 in pregnancy was extended to evaluate the effects of COVID-19 vaccines on infection-related and pregnancy-related maternal and offspring outcomes.[14] We report our review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance (see online supplemental appendix 1).

### Literature search

We searched major databases, preprint servers and websites that serve as repositories for COVID-19 studies, including Medline, Embase, Cochrane database, WHO COVID-19 database, Living Overview of the Evidence platform, China National Knowledge Infrastructure and Wanfang databases for relevant studies on COVID-19 in pregnant women (1 December 2019 to 30 January 2023). We coordinated our search efforts with the WHO Library, and the Cochrane Gynaecology and Fertility group. We contacted established groups coordinating or conducting surveillance and studies in pregnant women receiving COVID-19 vaccination, such as the US Centers for Disease Control and Prevention and the European Centre for Disease Prevention and Control, for information on published and upcoming data. Additional searches of preprint servers, blogs, websites that serve as repositories, social media, guidelines and reference lists of included studies were conducted.[15] No language restrictions were applied. Online supplemental appendix 2 provides details of the search strategies and databases.

### Study selection

Nine pairs of independent reviewers selected studies using a two-stage process. The reviewers first screened the titles and abstracts of studies and then assessed the full text of the selected studies in detail for eligibility. Disagreements between reviewers were resolved through discussion with a third reviewer (ST, JA or SF-G). We included test-negative design studies, and comparative cohorts reporting adjusted and unadjusted effects of any COVID-19 vaccine received by women before or during pregnancy on infection-related, pregnancy-related maternal and offspring outcomes, and the rates of reactogenicity outcomes. In test-negative design studies, the source population was pregnant women with COVID-19-like illness, and outcomes of interest were maternal SARS-CoV-2 infection, severe disease and maternal hospital admission outcomes. In neonates with COVID-19-like illness, our outcome was neonatal SARS-CoV-2 infection. SARS-CoV-2 infection was diagnosed by laboratory testing. Those who tested positive were considered as cases, and those who tested negative were controls, and their vaccination status assessed. For infection-related outcomes, we only included studies where women received a complete schedule of the COVID-19 vaccine during pregnancy; for pregnancy-related maternal and offspring outcomes, women were included if they received at least one dose during pregnancy, except for miscarriage outcome where women vaccinated before pregnancy were included. We additionally included non-comparative cohort and case-control studies with a minimum of 10 participants if they reported on reactogenicity outcomes of COVID-19

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vaccines in women vaccinated during pregnancy. We excluded case reports and case series, and studies where women were vaccinated after pregnancy.

### Study quality assessment and data extraction

Two independent reviewers (SF-G, LdC-A) assessed the quality of the comparative cohort studies and test-negative design case-control studies in our primary analysis using the 'Risk of Bias in Non-Randomised Studies of Interventions' (ROBINS-I) tool.[16] We used a prepiloted form to extract information on study design, recruitment period, predominant circulating SARS-CoV-2 variant at the time of study, setting (hospital, country), World Bank region, details of key adjustment variables (age, body mass index (BMI), gestational age, education, diabetes, chronic hypertension), the vaccine platform and vaccine product administered, the number of doses and time of vaccination (before or during pregnancy and trimester). The number of doses was assumed to be 'at least one dose' when the number received was unclear or when women included had received different doses. We considered the group to be 'partially vaccinated' when women received only one dose of two-dose vaccines and 'fully vaccinated' when they received one dose of single-dose vaccines or two doses of vaccines requiring two doses for immunogenicity. When women received three doses, we considered the group as 'booster dose'.

We extracted data on the adjusted estimate of the effect of COVID-19 vaccines, the number of vaccinated and non-vaccinated pregnant women and the number of events for infection-related maternal outcomes such as diagnosis of maternal SARS-CoV-2 infection before delivery, maternal hospital admission, maternal death and maternal severe COVID-19 disease defined as admission to the intensive care unit (ICU), hospitalisation due to severe disease or as defined by study authors; infection-related offspring outcomes like offspring SARS-CoV-2 infection up to 6 months after delivery; pregnancy-related maternal outcomes included miscarriage, preterm birth <37 weeks, caesarean section, postpartum haemorrhage, gestational diabetes and hypertensive disorders and offspring outcomes included stillbirth, neonatal death, neonatal intensive care unit (NICU) admission, low 5 min Apgar score (<7) and small-for-gestational-age baby. We extracted data on the number of vaccinated pregnant women who reported reactogenicity outcomes such as headache, fever, myalgia, fatigue and pain at injection site from comparative and non-comparative cohorts and case-control studies. We did not consider the booster doses for reactogenicity outcomes.

### Statistical analysis

Our primary analysis was based on test-negative design and comparative cohort studies with adjusted analyses reporting the effects of COVID-19 vaccines on infection-related, and pregnancy-related maternal and offspring outcomes. We pooled the adjusted estimates using random effects meta-analysis and summarised the findings as HRs, risk ratios (RRs) or ORs with 95% CIs.

For the secondary analysis, we pooled data from all included comparative cohort studies with unadjusted estimates and summarised the findings of infection-related and pregnancy-related maternal and offspring outcomes as ORs with 95% CIs. We calculated the rates of reactogenicity outcomes from non-comparative studies as proportions with 95% CIs using DerSimonian and Laird random-effects meta-analysis, after transforming data using Freeman-Tukey double-arcsine transformation. Heterogeneity was reported using $I^2$. All statistical analyses were performed using Stata (V.18).

### Patient and public involvement

This study is supported by Katie's team, a dedicated patient and public involvement group in women's health. The team was involved in the interpretation and reporting of this systematic review through participation in virtual meetings. Findings will be made available on our website in a format more suitable for patients and members of the public (www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/index.aspx).

## RESULTS

We included 67 studies (1 813 947 women) from 1 326 315 identified articles (figure 1). Twenty-four were included in the primary analysis, with eight performing adjusted analysis (185 955 women) for SARS-CoV-2 infection-related outcomes.[6–8 17–21] Six of them reported maternal SARS-CoV-2 infection, three reported maternal hospital admission and two reported severe COVID-19 disease and neonatal SARS-CoV-2 infection. Sixteen performed adjusted analysis for pregnancy-related maternal and offspring outcomes (544 314 women).[22–37] We included 16 studies (425 867 women) reporting SARS-CoV-2 infection-related outcomes[6 7 17 19 21 31 33 36 38–45] and 35 (1 362 172 women) reporting pregnancy-related maternal and offspring outcomes in the secondary analysis.[17 18 21–24 29–34 36 38 39 41–60] Twenty-three studies reported reactogenicity outcomes (94 206 women) following vaccination.[38 39 46 61–80]

### Characteristics of the included studies

A third of the included studies were from the Middle East and North Africa (22/67; 193 889 women), followed by North America (28%, 19/67; 397 756 women), Europe and Central Asia (22.5%, 15/67; 1 150 470 women), East Asia and Pacific (10.5%, 7/67; 42 204 women) and Latin America and Caribbean (3%, 2/67; 22 122 women), South Asia (1.5%, 1/67; 247 women) and one was a multicountry study (1.5%, 1/67; 4618 women). Fifty-nine studies were from high-income countries (59/67; 1 782 548 women), six from upper-middle-income countries (6/67; 26 534 women), one from lower-middle-income countries (1/67; 247 women) and one from a mix of high-income, upper-middle-income and lower-middle-income countries (1/67; 4618). Overall, 45 studies

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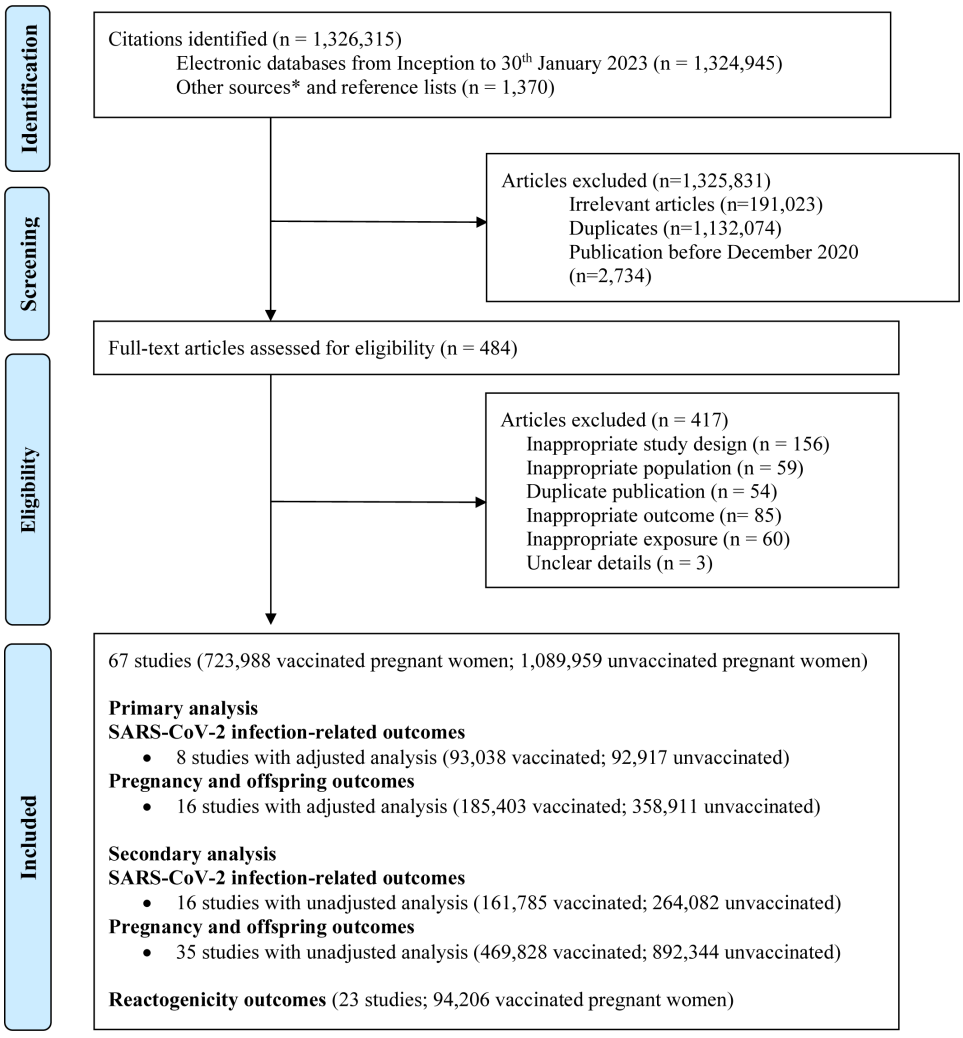


**Figure 1** Study selection process in the systematic review. Created and owned by the authors. *Twitter, national reports, blog Thornton J, ObG Project, COVID-19 and Pregnancy Cases (https://www.obgproject.com/2020/04/07/covid-19-research-watch-with-dr-jim-thornton/); EPPI-Centre, COVID-19: a living systematic map of evidence (http://eppi.ioe.ac.uk/cms/Projects/DepartmentofHealthandSocialCare/Publishedreviews/COVID19Livingsystematicmapoftheevidence/tabid/3765/Default.aspx); Norwegian Institute of Public Health (NIPH), NIPH systematic and living map on COVID-19 evidence (https://www.nornesk.no/forskningskart/NIPH_mainMap.html); John Hopkins University Center for Humanitarian Health; COVID-19, Maternal and Child Health, Nutrition (http://hopkinshumanitarianhealth.org/empower/advocacy/covid-19/covid-19-children-and-nutrition/); ResearchGate, COVID-19 research community (https://www.researchgate.net/community/COVID-19); Living Overview of the Evidence, COVID-19 (https://app.iloveevidence.com/loves/5e6fdb9669c00e4ac072701d?population=5d062d5fc80dd41e58ba8459).

included women vaccinated with mRNA vaccine only (281 030 women), four studies included inactivated virus (3088 women), one study viral vector vaccine (247 women), 14 studies mRNA and/or viral vector vaccines (436 453 women), one mRNA, viral vector and inactivated virus vaccines (2886 women) and two did not report the type of vaccine (284 women). Most of the studies included in the primary analysis were adjusted by maternal age (88%, 21/24), followed by diabetes (42%, 10/24), hypertension (33%, 8/24), BMI (33%, 8/24), gestational age (17%, 4/24) and education (4%, 1/24). Three of the eight studies performing adjusted analysis for SARS-CoV-2 infection-related outcomes were from the Delta and Omicron periods (134 779 women), one study was from the Delta period (464 women), one from the Omicron period (4618 women), one from the Alpha and Beta periods (4534 women), one from the Alpha period and other variants (21 722 women) and one from the Delta period and other variants (19 838 women). Online supplemental appendix 3 describes the characteristics of all included studies.

### Quality of studies included in primary analysis

Figure 2 provides the risk of bias for the included test-negative design and adjusted cohort studies included in the main analysis. For the maternal SARS-CoV-2 infection outcome, 17% of studies (1/6) were considered to be low risk, 66% (4/6) moderate risk and 17% (1/6) as serious risk. Of the two studies reporting severe COVID-19 disease, one was considered to be moderate risk and the



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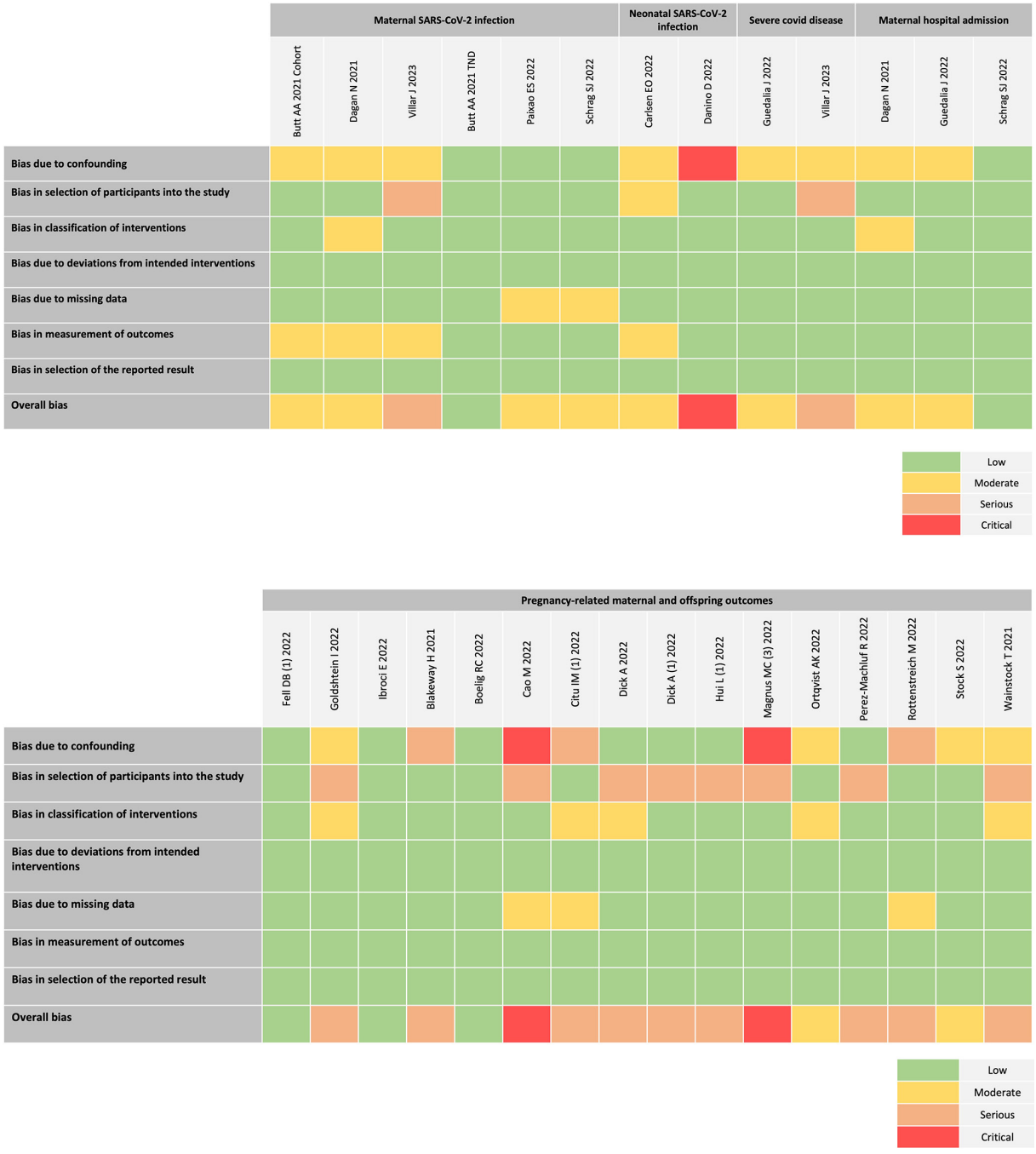


**Figure 2** Quality assessment for risk of bias in studies of primary analysis using Risk of Bias in Non-Randomised Studies of Interventions tool. Created and owned by the authors.

other serious. For maternal hospital admission outcome, two studies were classified as having moderate risk and one as low risk. Of the two studies reporting neonatal SARS-CoV-2 infection, one study was considered to have critical risk of bias rating, as prematurity, a postintervention variable was used as an adjustment factor.[18] More than half of the studies reporting pregnancy-related maternal and offspring outcomes were considered to be serious risk (9/16), 19% (3/16) low risk and 12% (2/16) as moderate or critical risk. Online supplemental appendix 4 describes the consensus judgements used to assign the risk of bias in each domain.

### Effects of COVID-19 vaccines on SARS-CoV-2 infection-related outcomes

In our primary analysis of test-negative design studies, women who were fully vaccinated had a 61% reduction in the odds of SARS-CoV-2 infection during pregnancy (OR 0.39, 95% CI 0.21 to 0.75; 4 studies, 23 927 women; $I^2$=87.2%) and a 94% reduction in the odds of hospital admission (OR 0.06, 95% CI 0.01 to 0.71; 2 studies, 868 women; $I^2$=92%) (figure 3). The effect of the vaccines on infection-related outcomes of the adjusted comparative cohort studies is imprecise and heterogeneous. Although it consistently shows a reduction in the hazard of



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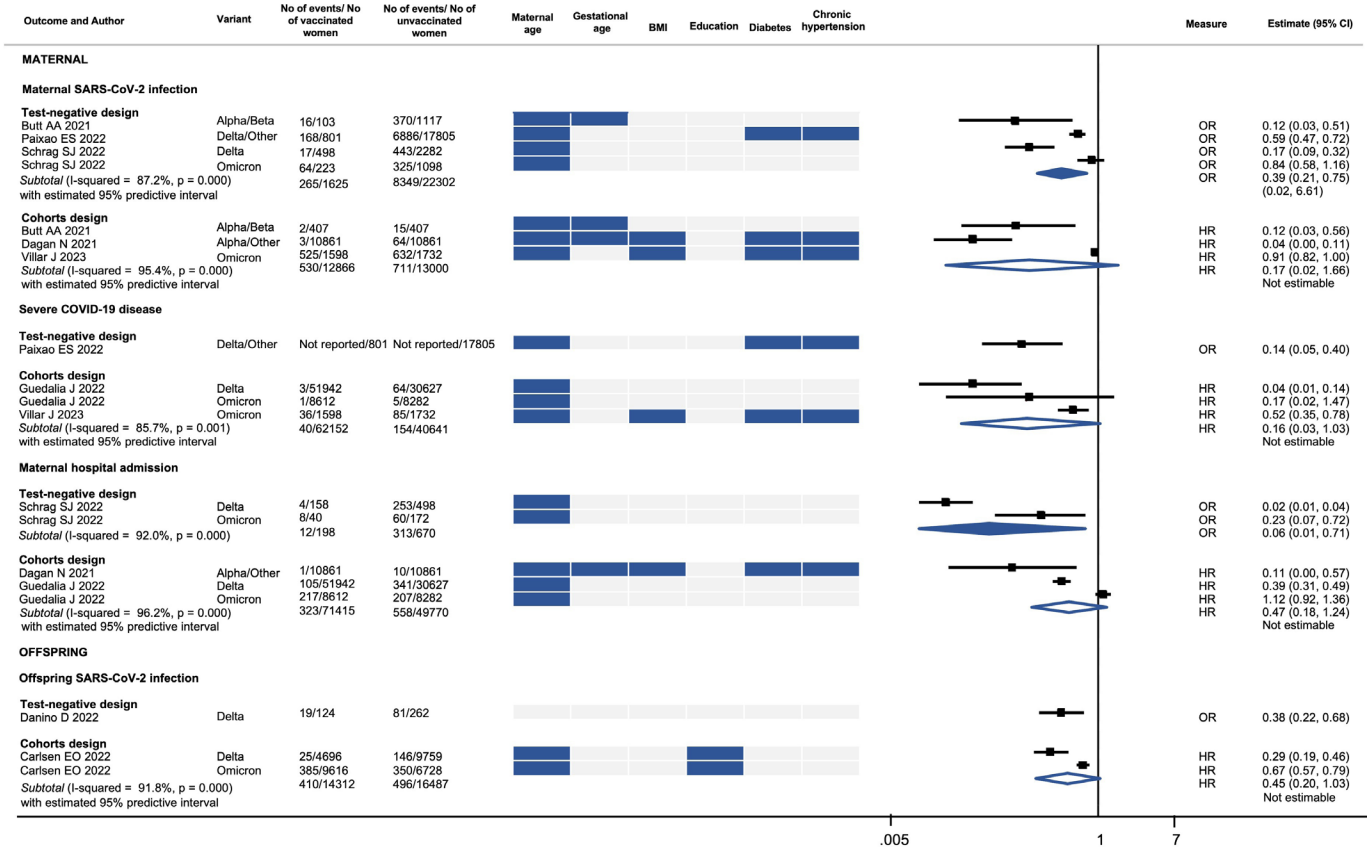


**Figure 3** Vaccine effectiveness for SARS-CoV-2 infection-related outcomes. BMI, body mass index. Created and owned by the authors.

infection-related outcomes, this reduction does not reach statistical significance (figure 3). We did not find any test-negative design study or adjusted comparative cohort study reporting on maternal death. Table 1 provides the summary estimates of the effects of COVID-19 vaccines reported in test-negative design studies (adjusted), comparative cohort (adjusted) and unadjusted cohort studies. Online supplemental appendix 5 provides details of individual unadjusted cohort studies.

### Effects of COVID-19 vaccines on pregnancy-related maternal and offspring outcomes

Meta-analysis of adjusted comparative cohort studies showed a 12% reduction in the risk of hypertensive disorders in pregnancy (RR 0.88, 95% CI 0.82 to 0.92; 2 studies; 115 085 women) in women vaccinated versus not vaccinated in pregnancy. The odds of caesarean section (OR 0.91, 95% CI 0.85 to 0.98; 6 studies; 30 192 women) was reduced in the pooled analysis of adjusted comparative cohorts. We did not find any association between COVID-19 vaccination and other maternal outcomes, except for gestational diabetes (table 1). We observed an 8% reduction in the risk of newborn's admission to the NICU (RR 0.92, 95% CI 0.87 to 0.97; 2 studies; 54 569 women) in babies born to vaccinated versus not vaccinated women. There were no significant differences observed in other offspring outcomes (table 1). The summary findings of data from adjusted and unadjusted cohort studies for pregnancy-related maternal and offspring outcomes are provided in online supplemental appendices 6 and 7. The summary findings from the adjusted individual studies are provided in online supplemental appendices 8 and 9.

### Vaccination in pregnancy and reactogenicity outcomes

The most common side effects reported by pregnant women vaccinated with any number of doses of COVID-19 vaccine were mild pain at the injection site (77%, 95% CI 52% to 94%; 11 studies; 27 195 women), followed by fatigue (29%, 95% CI 15% to 46%; 14 studies; 72 671 women) (table 2). Other side effects, such as headache and myalgia, were reported by 12% of vaccinated pregnant women each, while fever was reported by 5% (95% CI 2% to 8%; 19 studies; 82 972 women) of vaccinated pregnant women (table 2).

## DISCUSSION

COVID-19 vaccination in pregnant women reduces the risks of maternal SARS-CoV-2 infection and admission to the hospital during pregnancy. Vaccination in pregnancy appears to reduce risks of maternal hypertensive disorders during pregnancy, caesarean section and neonatal admission to ICU. Pain at injection site was the most common side effect of COVID-19 vaccination.

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**Table 1** Summary estimates reported in test-negative design (adjusted), comparative cohort (adjusted) and comparative cohort (unadjusted) studies

| Outcome | Test-negative design (adjusted) | | | Comparative cohort (adjusted) | | | Comparative cohort (unadjusted) | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. of studies (women) | HR (95% CI) | $I^2$ (%) | No. of studies (women) | Estimate (95% CI) | $I^2$ (%) | No. of studies (women) | OR (95% CI) | $I^2$ (%) |
| SARS-CoV-2 infection-related outcomes | | | | | | | | | |
| Maternal SARS-CoV-2 infection | 4 (23 927) | 0.39 (0.21 to 0.75) | 87.2 | 3 (25 866) | OR 0.17 (0.02 to 1.66) | 95.4 | 11 (397 679) | 0.63 (0.47 to 0.85) | 98.5 |
| Severe COVID-19 disease | 1 (18 606) | 0.14 (0.05 to 0.40) | | 3 (102 793) | OR 0.16 (0.03 to 1.03) | 85.7 | 11 (132 759) | 0.47 (0.22 to 0.97) | 80.9 |
| Maternal hospital admission | 2 (868) | 0.06 (0.01 to 0.71) | 92 | 3 (121 185) | OR 0.47 (0.18 to 1.24) | 96.2 | 2 (36 782) | 0.41 (0.13 to 1.28) | 92 |
| Offspring SARS-CoV-2 infection | 1 (386) | 0.38 (0.22 to 0.68) | | 2 (30 799) | OR 0.45 (0.20 to 1.03) | 91.8 | 3 (31 848) | 0.52 (0.33 to 0.82) | 87.6 |
| Maternal death | | | | | | | 9 (148 297) | 0.53 (0.12 to 2.47) | 64.4 |
| Pregnancy-related maternal outcomes | | | | | | | | | |
| Miscarriage | | | | 4 (43 465) | OR 0.96 (0.90 to 1.04) | 0 | 3 (1113) | 1.60 (0.70 to 1.91) | 0 |
| Preterm birth <37 weeks | | | | 5 (25 516) | OR 0.79 (0.59 to 1.06) | 68.3 | 21 (1 104 043) | 0.90 (0.83 to 0.97) | 75 |
| | | | | 1 (24 190) | RR 0.95 (0.83 to 1.10) | | | | |
| Caesarean section | | | | 6 (30 192) | OR 0.91 (0.85 to 0.98) | 0 | 15 (188 144) | 1.11 (1.03 to 1.20) | 48.6 |
| | | | | 2 (54 569) | RR 0.94 (0.81 to 1.08) | 34.9 | | | |
| Postpartum haemorrhage | | | | 5 (30 192) | OR 1.49 (0.91 to 2.44) | 86.7 | 6 (104 693) | 0.82 (0.68 to 1.00) | 0 |
| | | | | 1 (52 775) | RR: 0.90 (0.81 to 1.00) | | | | |
| Gestational diabetes | | | | 1 (5618) | OR 1.10 (0.90 to 1.30) | | 11 (263 319) | 1.04 (0.89 to 1.21) | 94.2 |
| | | | | 2 (115 085) | RR 1.17 (1.14 to 1.20) | 0 | | | |
| Hypertensive disorders | | | | 5 (15 739) | OR 1.11 (0.87 to 1.43) | 0 | 10 (217 486) | 1.13 (1.02 to 1.25) | 49 |
| | | | | 2 (115 085) | RR 0.88 (0.85 to 0.92) | 0 | | | |
| Pregnancy-related offspring outcomes | | | | | | | | | |
| Stillbirth | | | | 2 (17 907) | OR 0.38 (0.09 to 1.59) | 89.4 | 11 (1 024 952) | 0.78 (0.65 to 0.92) | 36.5 |
| Admission to neonatal intensive care unit | | | | 4 (173 978) | OR 0.88 (0.71 to 1.08) | 37.9 | 9 (108 534) | 0.82 (0.79 to 0.86) | 0 |
| | | | | 2 (54 569) | RR 0.92 (0.87 to 0.97) | 0 | | | |
| Low 5 min Apgar score <7 | | | | 4 (179 034) | OR 0.89 (0.73 to 1.08) | 29.3 | 9 (113 540) | 0.89 (0.81 to 0.99) | 0 |
| | | | | 1 (51 922) | RR 0.88 (0.77 to 1.01) | | | | |
| Small for gestational age | | | | 6 (172 483) | OR 0.96 (0.90 to 1.02) | 0 | 8 (153 813) | 0.99 (0.95 to 1.03) | 0 |
| | | | | 1 (24 190) | RR 0.97 (0.87 to 1.08) | | | | |
| Neonatal death | | | | 1 (24 190) | RR 0.84 (0.43 to 1.72) | | | | |

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*As reported in the individual studies, adjusted cohort results for pregnancy-related maternal and offspring outcomes are shown as OR or RR.
RR, risk ratio.



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**Table 2** Reactogenicity outcomes in pregnant women vaccinated for COVID-19

| Side effects | Partially vaccinated | | | | Fully vaccinated | | | | Any number of doses | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of studies | No. of events | Proportion (95% CI) | $I^2$ (%) | No. of studies | No. of events | Proportion (95% CI) | $I^2$ (%) | No. of studies | No. of events | Proportion (95% CI) | $I^2$ (%) |
| Fever | 13 | 1683/36 439 | 0.06 (0.03 to 0.10) | 99.2 | 14 | 8158/28 139 | 0.16 (0.07 to 0.26) | 99.7 | 19 | 1766/82 972 | 0.05 (0.02 to 0.08) | 99.5 |
| Headache | 10 | 3987/28 491 | 0.10 (0.05 to 0.17) | 99.4 | 13 | 9207/21 999 | 0.20 (0.09 to 0.34) | 99.7 | 17 | 4885/40 751 | 0.12 (0.06 to 0.18) | 99.7 |
| Myalgia | 8 | 2208/23 392 | 0.09 (0.04 to 0.15) | 98.8 | 11 | 7376/17 345 | 0.28 (0.12 to 0.47) | 99.7 | 13 | 2789/27 920 | 0.12 (0.08 to 0.17) | 98.6 |
| Fatigue | 8 | 6727/22 827 | 0.26 (0.23 to 0.29) | 86.9 | 10 | 12 751/18 746 | 0.52 (0.45 to 0.60) | 98.1 | 14 | 8042/72 671 | 0.29 (0.15 to 0.46) | 99.9 |
| Pain at injection site | 7 | 20540/22 922 | 0.85 (0.76 to 0.93) | 99.3 | 8 | 16 896/18 608 | 0.80 (0.73 to 0.85) | 98.1 | 11 | 21 623/27 195 | 0.77 (0.52 to 0.94) | 99.9 |

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Our comprehensive review on the effects of COVID-19 vaccination in pregnant women provides robust data by focusing on test-negative design studies, which are a rigorous method to reduce the bias, and adjusted comparative cohorts in our main analysis. We used ROBINS-I tool that provides a comprehensive assessment of the risk of bias. We undertook an extensive deduplication process and minimised the risk of including duplicate data. By focusing on both SARS-CoV-2 infection-related and pregnancy-related maternal and offspring outcomes, we addressed questions that are important to women in making decisions regarding vaccination. The large sample size in our review allowed us to assess the magnitude of benefit and risk of harm with high precision, including for less common but important outcomes such as neonatal admission to ICU. We included studies from different regions and income levels, with no language restrictions.

Our review has some limitations. The trimester of exposure to vaccines was poorly reported in primary studies, which did not allow us to see the effect of the timing of vaccination on infection-related, pregnancy-related maternal and offspring or reactogenicity outcomes. We did not find any test-negative design or adjusted comparative cohort study reporting on maternal death. Some of the studies included women vaccinated before or during pregnancy and we were unable to separately give estimates for women vaccinated during pregnancy. We did not evaluate long-term effects of the vaccines and were unable to analyse data on adverse effects such as thrombocytopenia, embolic reactions or myocarditis due to the lack of enough studies reporting these outcomes. Similarly, the sample sizes and event numbers were small for outcomes such as miscarriage and maternal death requiring cautious interpretation. We found an association between vaccination and an increased risk of gestational diabetes, but this is based on two different populations from the same adjusted comparative cohort study.[35] Further data are needed to confirm this. We were unable to assess the effects of vaccines on the different variants due to the few published papers reporting separately for periods of variants of concern. Despite our comprehensive search, most of the studies that met our inclusion criteria are from high-income countries and external validity of our findings may not be accurate for middle-income and low-income settings.

In pregnant women from test-negative design studies, we found a reduction in the odds of SARS-CoV-2 infection and hospital admission after complete vaccination. The findings are similar to those observed in clinical trials and real-world data showing COVID-19 vaccines to be effective in preventing SARS-CoV-2 infections, severe COVID-19 disease and deaths, in the general adult population.[81 82] In general population, the effectiveness of COVID-19 vaccines varied depending on the type of vaccine, the population being vaccinated, the number of doses, the variant and the immunity of individuals.[82] However, we refrained from performing this analysis as

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data were only limited to non-adjusted cohort studies, with high degree of bias. Previous reviews on COVID-19 vaccines in pregnancy often limited their reporting to a few specific regions or countries, or only on SARS-CoV-2 infection.[9 13] In addition, most of these reviews did not include test-negative design studies or did not use data from adjusted comparative cohort studies analysis. Our findings, based on these study designs, are inherently controlled for some sources of bias, such as differences in healthcare-seeking behaviour and access by vaccination status and are less affected by confounding factors.[83]

COVID-19 vaccines are recommended for use in pregnancy by WHO, policymakers and professional bodies globally.[5 84–87] The exclusion of pregnant women from the initial clinical trials limited the acquisition of safety data and the ability to make evidence-based recommendations at the early stages of vaccine implementation. Our study demonstrated that reactogenicity-related side effects of COVID-19 vaccine in pregnant women were generally mild, similar to those reported in the general population. Rare adverse events such as vaccine-associated thrombotic thrombocytopenia (incidence 0.73 cases per 100 000 vaccinated persons receiving adenovirus-based vaccines), myocarditis (12.6 cases per million doses messenger RNA (mRNA) vaccine) and Guillain-Barré syndrome (7.8 cases per million doses adenovirus vaccine) may not be captured, and a very large sample size would be needed to evaluate such rare events during pregnancy.[88]

Pregnant women should be counselled and reassured about the safety and benefits of COVID-19 vaccination during pregnancy, both for their own health and that of their babies. Our findings demonstrate the effectiveness and safety of different COVID-19 vaccines. Although most available data are for the mRNA vaccines Pfizer-BioNTech BNT162b2 and Moderna mRNA-1273, our review also includes data on Sinovac-CoronaVac, Sinopharm BIBP, Janssen Ad26.COV2.S, AZD ChAdOx1-S, Cansino Ad5-nCoV-S and Bharat BBV152 Covaxin. More data on these non-mRNA vaccines would strengthen existing findings. Women should discuss their individual risks and concerns with their healthcare provider, who can help reassure and support them in making the best decision about vaccination.

The response was too slow during the pandemic, and equitable and timely distribution of COVID-19 vaccines to all communities, particularly vulnerable populations, could have saved more lives at the height of the pandemic. Barriers to vaccine access, including transportation, language and technology barriers, should be addressed and ensure that vaccine distribution sites are located in areas that are easily accessible to underserved communities.[89] An investment in providing vaccine education and outreach campaigns to promote acceptance and address hesitancy is critical. Close collaboration is needed between professional colleges and community organisations to provide accurate and appropriate information about vaccine safety and efficacy and continuous monitoring to provide updates to help build trust and confidence.

The virus has shown its ability to mutate, leading to the emergence of new variants. The effectiveness of existing vaccines against these variants is continuously monitored by vaccine manufacturers and health authorities. This has led to the recommendation of supplementary doses to enhance immunity or a single dose in each pregnancy, regardless of previous vaccination status.[90] It is important to continue research on the effectiveness of COVID-19 vaccines against different variants of the virus, the duration of protection they provide and further safety data from non-mRNA vaccines. The Human Reproduction Programme (the United Nations Development Programme/United Nations Population Fund/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction) initiatives can be adapted and generalised to prepare for quicker response in future epidemics.[91] The development of research infrastructure, which includes strengthening laboratories, research facilities and data management systems can be repurposed for epidemic outbreaks. In addition, collaboration with various stakeholders such as governments, non-governmental organisations and research institutions can facilitate faster response times and resource mobilisation. Research should also focus on identifying reasons for vaccine hesitancy, particularly among pregnant women.[92] Effective communication strategies need to be developed to address these concerns.

## CONCLUSION

COVID-19 vaccination in pregnant women is highly effective in reducing the odds of maternal SARS-CoV-2 infection, and hospital admission, and improves pregnancy outcomes, with no serious safety concerns. The interpretation of our findings may be impacted by changes in vaccine recommendations and the changing landscape of SARS-CoV-2 variants.

### Dissemination to participants and related patient and public communities

The PregCOV-19 Living Systematic Review Group will disseminate the findings through a dedicated website (www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/index.aspx) and social media.

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**Contributors** ST, MB and JA conceptualised the study. DS, JS, KL, NO-L, AR, HN, NS, PSu, SMe, PSe, SA, SMa, MM, ZM, HL, MY and TK selected the studies. SF-G, DS, KL, NO-L, AP, CK, ES, JC, SR and WC extracted the data. SF-G, LdC-A and JZ conducted the analyses. All coauthors contributed to the writing of the manuscript and approved the final version. ST, JA and JZ are the guarantors. All members of the PregCOV-19 Living Systematic Review Consortium contributed to study selection and data extraction. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 5 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 6 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 6 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 6 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 6 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 6-7 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 7-8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 7-8 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 7 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 9 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 9 |

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | NA |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 10 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 10-11 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 11 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 12-13 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 12-13 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 15-18 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 16 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 19 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 20 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

**Appendix 2. Details of search strategies used to include studies in the living systematic review on COVID-19 in pregnant and recently pregnant women**

1. Cochrane Gynaecology and Fertility

Pubmed

| Item | Term |
|---|---|
| 1 | pregnancy/ |
| 2 | pregnan*.tw. |
| 3 | neonatal.tw. |
| 4 | perinatal.tw. |
| 5 | mothers/. |
| 6 | mother.tw. |
| 7 | maternal.tw. |
| 8 | obstetric.tw. |
| 9 | infant, newborn/ |
| 10 | infant.tw. |
| 11 | newborn.tw. |
| 12 | child*.tw. |
| 13 | or/1-12 |
| 14 | COVID-19.tw. |
| 15 | COVID-2019.tw. |
| 16 | severe acute respiratory syndrome coronavirus 2.tw. |
| 17 | 2019-nCoV.tw. |
| 18 | SARS-CoV-2.tw. |
| 19 | 2019nCoV.tw |
| 20 | or/14-19 |
| 21 | coronavirus.tw. |
| 22 | 2019/12.pd |
| 23 | 2020.pd. |
| 24 | or/22-23 |
| 25 | 21 and 24 |
| 24 | or/20-25 |
| 25 | 13 and 24 |

Google Scholar and Google
Using the following text words (pregnancy OR neonatal OR perinatal OR maternal OR obstetric OR newborn) AND (COVID-19 or SARS-Cov-2)

2. EPPI Centre

The MEDLINE search strategy is the OVID Expert Search as developed by Wolters Kluwer and available at http://tools.ovid.com/coronavirus/

MEDLINE search strategy

1 exp Coronavirus/
2 exp Coronavirus Infections/
3 (coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4 (or/1-3) and ((20191* or 202*).dp. or 20190101:20301231.(ep).)
5 4 not (SARS or SARS-CoV or MERS or MERS-CoV or Middle East respiratory syndrome or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or influenza virus or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or avian influenza or H1N1 or H5N1 or H5N6 or IBV or murine corona*).mp.
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
7 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
8 COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os.
9 ("32240632" or "32236488" or "32268021" or "32267941" or "32169616" or "32267649" or "32267499" or "32267344" or "32248853" or "32246156" or "32243118" or "32240583" or "32237674" or "32234725" or "32173381" or "32227595" or "32185863" or "32221979" or "32213260" or "32205350" or "32202721" or "32197097" or "32196032" or "32188729" or "32176889" or "32088947" or "32277065" or "32273472" or "32273444" or "32145185" or "31917786" or "32267384" or "32265186" or "32253187" or "32265567" or "32231286" or "32105468" or "32179788" or "32152361" or "32152148" or "32140676" or "32053580" or "32029604" or "32127714" or "32047315" or "32020111" or "32267950" or "32249952" or "32172715").ui.
10 or/6-9
11 5 or 10

The Embase search strategy as at 21st April 2020

1 exp Coronavirus Infections/
2 exp coronavirinae/
3 (coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4 or/1-3
5 4 not (SARS or SARS-CoV or MERS or MERS-CoV or Middle East respiratory syndrome or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or

influenza virus or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or avian influenza or H1N1 or H5N1 or H5N6 or IBV or murine corona*).mp.
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
7 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
8 6 or 7
9 5 or 8

3. WHO COVID-19 database

The WHO COVID-19 database contained articles on the novel coronavirus from the following sources:

- Web of Science
- Oxford Academic Journals
- Pubmed NIH
- Ishiyaku
- J Stage
- Cinii articles
- Ichushi Web – JAMAS
- Science Direct
- Wiley Online Journals
- JAMA Network
- British Medical Journal
- Mary Ann Liebert
- New England Journal of Medicine
- Sage Publications
- Taylor and Francis Online
- Springer Link
- Biomed Central
- MDPI
- ASM
- PLOS
- The Lancet
- Cell Press
- Cell Press Search Interface
- EMBASE
- KoreaMed

- Global Index Medics
- MMWR
- Epidemiology and Health
- American Chemical Society
- Eurosurvellance
- Cambridge Press
- LWW
- Airiti
- JIMR
- Emerging Infectious Diseases
- Osong Public Health & Research Perspectives
- BASE Bielefeld
- LitCOVID

An additional step using the following search terms was added to the WHO search from 12th May 2020

tw:(newborn* OR mother* OR bab* OR wom* OR pregnan* OR postpart* OR neonat* OR fetus OR fetal OR newborn OR mother OR bab*)

Appendix 3. Characteristics of included studies

| **First author, year of publication** | **Study design** | **Study setting: country and hospital**<br><br>**Collection period** | **Adjustement variables** | **Inclusion and exclusion criteria** | **Population exposed to covid-19 vaccine** | **Vaccine platform**<br><br>**Vaccine product**<br><br>**Doses (no. women vaccinated)** | **Time of vaccination (trimester)** | **Reported outcomes of interest** |
|---|---|---|---|---|---|---|---|---|
| Arulappen AL, 2022 | Retrospective cohort | Malaysia<br><br>6 General hospitals in the state of Penang<br><br>March 2021 - | NA | *Inclusion*<br>All pregnant employees who consented to take the mRNA vaccine.<br><br>*Exclusion*<br>Vaccinated pregnant employees who refused to give consent to participate in the study | 121 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (121)<br>Two doses (121) | During pregnancy (1st, 2nd, 3rd) | Headache<br>Myalgia<br>Fatigue |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Bashi TBM, 2021 | Prospective cohort | Israel<br><br>University affiliated tertiary medical center in Tel Aviv<br><br>December 2020 – March 2021 | NA | *Inclusion*<br>All women who received the mRNA COVID-19 vaccine during pregnancy who had not prior COVID-19 infection.<br><br>*Exclusion*<br>Unverified timing of vaccination, prior or active infection with covid-19 and refusal to sign informed consent form. | 58 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (19)<br>Two doses (39) | During pregnancy (3rd) | Pain at injection site<br>Headache<br>Myalgia<br>Fatigue<br>Fever |
| Beharier O, 2021 | Prospective cohort | Israel<br><br>8 medical centres in Israel<br><br>January 2021 – March 2021 | NA | *Inclusion*<br>Pregnant women at an age of 18 years or older and a willingness to participate and provide | 92 | mRNA<br><br>Pfizer-BioNTech<br><br>Non specified | During pregnancy (Non specified) | Preterm birth <37 weeks<br><br>NICU admission |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | informed consent<br><br>*Exclusion*<br>Pregnant women with active maternal COVID-19 disease at delivery | | | | |
| Blakeway H, 2021 | Retrospective cohort | United Kingdom<br><br>St George's University Hospitals<br><br>March 2020 – July 2021 | Non specified | *Inclusion*<br>All pregnant women with known vaccination status and complete maternal and foetal outcome data<br><br>*Exclusion*<br>Women who were vaccinated entirely (i.e., all doses) before pregnancy or after birth or | 140 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>One dose (114)<br>Two doses (26) | During pregnancy (2nd, 3rd) | Maternal covid infection<br>Severe covid disease<br><br>Caesarean section<br>NICU admission<br>Stillbirth<br>Gestational diabetes<br>Postpartum haemorrhage<br>Small for gestational age |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | women who had pregnancies complicated by foetal aneuploidy or genetic syndromes. | | | | |
| Blakeway H, 2022 | Prospective cohort | UK<br><br>April 2021 – September 2021 | NA | *Exclusion*<br>Women who did not return the questionnaire. | 67 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>One dose (67)<br>Two doses (67) | During pregnancy (1st, 2nd, 3rd) | Headache<br>Fever |
| Bleicher I, 2021 | Prospective cohort | Israel<br><br>Online questionnaire<br><br>January 2021 – February 2021 | NA | *Inclusion*<br>All pregnant women that properly filled out the data in questionnaire (valid e-mail address, ID number that | 202 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (68)<br>Two doses (124) | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Miscarriage<br><br>Headache<br>Fever |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | matches the information in both questionnaires and answering all questions until the form is submitted)<br><br>*Exclusion*<br>Registries that were invalid or incompatible with the demands (for example: invalid e-mail address, wrong registration of last menstrual period that could not be correct | | | | |
| Boelig RC, 2022 | Retrospective cohort | USA<br><br>Thomas Jefferson University Hospital | Age<br>BMI<br>Ethnicity<br>Diabetes<br>Chronic hypertension | *Inclusion*<br><br><br>*Exclusion*<br>Pregnant patients with both COVID- | 49 | mRNA<br><br>Non specified<br><br>Non specified | During pregnancy (non specified) | Preterm birth <37 weeks<br>Hypertensive disorder in pregnancy |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | March 2020 – July 2021 | Prior full-term delivery<br>Prior preterm delivery | 19 disease and vaccination | | | | |
| Bookstein-Peretz S, 2021 | Case- control study | Israel<br><br>January 2021-February 2021 | NA | *Inclusion*<br>Pregnant women who were vaccinated<br>By a 2-dose regimen of BNT162b2 vaccine between 2-40weeks of gestation and were recruited via social media publications<br><br>*Exclusion*<br>Pregnant women who gave birth or had an abortion before the second | 390 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (390)<br>Two doses (390) | During pregnancy (1st, 2nd, 3rd) | Pain at injection site<br>Headache<br>Myalgia<br>Fatigue<br>Fever |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | dose of vaccine | | | | |
| Butt AA, 2021 | Cohort | Qatar<br><br>Hamad Medical Corporation<br><br>December 2020 – May 2021 | 10 years age group<br>Nationality<br>Gestational age | *Exclusion*<br>Women with less than 14 days of follow-up after the second dose, those with a single dose, those with prior SARS-CoV-2 infection and those with pregnancy onset after vaccination. | 1053 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (407) | During pregnancy (1st, 2nd) | Maternal covid infection |
| | Test negative case control | | | *Inclusion*<br>All confirmed pregnant women who presented to Hamad Medical Corporation<br><br>*Exclusion*<br>Women who were tested for | | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (103) | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | SARS-CoV-2 by RT-PCR on a nasopharyngeal swab prior to pregnancy and those who had no SARS-CoV-2 testing done between December 20, 2020 and May 30, 2021, as well as those who had at least one dose of vaccination before pregnancy onset. | | | | |
| Cao M, 2022 | Retrospective cohort | China<br><br>Guangzhou Medical University<br><br>March 2021 – September 2021 | Age<br>Infertility duration<br>Number of COS cicles<br>Protocols of COS<br>Endometrial preparation protocol | *Inclusion*<br>Women with confirmed vaccination status from public health surveillance system record of their smartphone | 502 | Inactivated virus<br><br>Sinovac-CoronaVac<br>Sinopharm BIBP<br><br>One dose (30) | Before pregnancy | Miscarriage |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Number of embryos transferred<br>Number of top-quality embryos | app, the first or second cycle of frozen-thawed embryos transferred, women in vaccinated group had embryos frozen prior to the exposure to Covid-19 vaccines, and women aged 20-40 years old<br><br>*Exclusion*<br>Women with three or more cycles of controlled ovarian stimulation, women with repeated spontaneous miscarriage, women with | | Two doses (472) | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | repeated implantation failure, cycles with surgically obtained sperms, cycles with sperm donor, and infertile couples with severe systemic disease which might reduce conception chance | | | | |
| Carlsen EO, 2022 | Retrospective cohort | Norway<br><br>Medical Birth Registry of Norway<br><br>September 2021 – February 2022 | Age<br>Parity<br>Education<br>Country of birth<br>Country of residence | *Inclusion*<br>All live births in Norway between 1 September 2021 and 28 February 2022.<br><br>*Exclusion*<br>Mother and infants with no permanent national | 14312 | mRNA<br><br>Non specified<br><br>Two doses (8915)<br>Three doses (824) | During pregnancy (2nd, 3rd) | Maternal covid infection<br>Preterm birth <37 weeks |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | identification number. | | | | |
| Citu IM, 2022 | Prospective cohort | Romania<br><br>Timisoara Municipality Emergency Hospital<br><br>May 2021 – December 2021 | NA | *Inclusion* | 227 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Janssen<br><br>One dose (58)<br>Two doses (115) | During pregnancy (3rd) | Gestational diabetes<br>Hypertensive disorder in pregnancy<br>Caesarean section<br>Preterm birth <37 weeks<br>Postpartum haemorrhage<br>Abnormal apgar 5<br>Small for gestational age<br><br>Pain at injection site<br>Myalgia<br>Headache<br>Fever<br>Fatigue |
| Citu IM (1) 2022 | Retrospective cohort | Romania<br><br>Obstetrics and gynecology | Age (> 35 years)<br>Overweight status (>25) | *Inclusion*<br>All pregnancies in mothers older | 927 | mRNA<br><br>Pfizer-BioNTech | During pregnancy (1st) | Miscarriage |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | clinic of Timisoara Municipal emergency hospital<br><br>January 2020 – January 2022 | Chronic conditions<br>Previous SARS-CoV-2 infection<br>Smoker<br>Abnormal uterine or cervical anatomy<br>Previous miscarriage<br>Assisted reproductive techniques<br>Vaccine type<br>Number of doses | than 18 years, evaluated from the start of their first trimester during the study period in the clinic.<br>Only pregnant women vaccinated with BNT162b2 or Moderna mRNA-1273.<br><br>*Exclusion*<br>Patients who did not provide consent were excluded | | Moderna<br><br>Two doses (927) | | |
| Collier AY 2021 | Prospective cohort | Israel<br><br>Beth Israel Deaconess Medical center | NA | *Inclusion*<br>Women 18 years or older who had received a covid-19 vaccine<br><br>*Exclusion* | 30 | mRNA<br><br>Pfizer-BioNTech Moderna<br><br>One dose (30) | During pregnancy (1st, 2nd, 3rd) | Fever |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | December 2020 – March 2021 | | | | Two doses (29) | | |
| COVID-NET, 2021 | Retrospective cohort | USA<br><br>Nk<br><br>January 2021 – November 2021 | NA | *Inclusion* | 11 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br><br>Non specified | During pregnancy (non specified) | Severe covid disease<br><br>Miscarriage<br>Caesarean section<br>Maternal death<br>Preterm birth <37 weeks<br>Stillbirth |
| Dagan N, 2021 | Prospective cohort | Israel<br><br>Clalit Health Services (CHS)<br><br>December 2020 – June 2021 | Age<br>Trimester of pregnancy<br>Geostatistical living area<br>Population sector<br>Count of influenza vaccination in the last 5 years<br>Existence of at least one CDC and prevention | *Inclusion*<br>All pregnant women aged 16 years or older, with continuous membership in CHS<br>for 1 complete year, no previous positive SARS-CoV-2 PCR test, no previous SARS-CoV-2 | 10861 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (10861) | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Severe covid disease<br>Maternal hospital admission<br>Maternal death |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | risk factor for severe disease (obesity, diabetes, hypertension) | vaccination, not residing in long-term care facilities, no home confinement due to medical reasons, not being a healthcare worker and no interaction with the healthcare system in the previous 2 d<br><br>*Exclusion*<br>Pregnant women with missing data in CHS | | | | |
| Danino D 2022 | Test negative case-control | Israel<br><br>Soroka Medical center, Schneider medical center, Shamir | Ethnicity<br>Prematurity | *Inclusion*<br>Symptomatic infants suspected of SARS-CoV-2 infection by a physician | 202 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (202) | During pregnancy (2nd, 3rd) | Neonatal covid infection<br>Preterm birth |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | medical center<br><br>March 2021 – November 2021 | | *Exclusion*<br>Infants who were tested during screening or were asymptomatic | | | | |
| DeSilva M, 2022 | Retrospective cohort | USA<br><br>Eigth vaccine safety datalink sites<br><br>December 2020 – July 2021 | NA | *Inclusion*<br>Pregnant women between 16 and 49 years | 45232 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Janssen<br><br>One dose (12438)<br>Two doses (32794) | During pregnancy (1st, 2nd, 3rd) | Fever<br>Fatigue |
| Dick A, 2022 | Retrospective cohort | Israel<br><br>Hadassah-Hebrew University Center<br><br>December 2020 – July 2021 | Age<br>BMI<br>Nulliparity<br>Smoking | *Inclusion*<br>Women with singleton deliveries from December 2020 until July 2021<br><br>*Exclusion* | 2305 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (non specified) | During pregnancy (2nd, 3rd) | Preterm birth <37 weeks<br>Small for gestational age<br>Caesarean section<br>Postpartum haemorrhage<br>Stillbirth |

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| | | | | Women with multiple pregnancy, vaccination prior to pregnancy, COVID-19 infection during or before pregnancy, or unknown timing of vaccination | | Three doses (non specified) | | Hypertensive disorder in pregnancy<br>Gestational diabetes<br>Abnormal apgar 5 |
| Dick A (1), 2022 | Retrospective cohort | Israel<br><br>Nr<br><br>July 2021 – October 2021 | Age<br>BMI<br>Nulliparity<br>Gestational diabetes<br>Smoking | *Inclusion*<br>Women with singleton pregnancies who delivered in the period July-October 2021<br><br>*Exclusion*<br>Women with multiple pregnancy, COVID-19 infection during or | 2845 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (2845)<br>Three doses (294) | During pregnancy (3rd) | Preterm birth <37 weeks<br>Small for gestational age<br>Caesarean section<br>Postpartum haemorrhage<br>Stillbirth<br>Hypertensive disorder in pregnancy<br>Gestational diabetes |

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| | | | | before pregnancy, or unknown timing of vaccination | | | | Abnormal apgar 5 |
| Favre G (2), 2022 | Prospective cohort | Switzerland<br><br>COVI-PREG registry<br><br>March 2021 – December 2021 | NA | *Inclusion*<br>Pregnant women who received at least one injection of a mRNA vaccine against COVID-19 between one week before their last menstrual period and the end of pregnancy were included in the study.<br><br>*Exclusion*<br>Patients under 18 years old who were not able to consent. | 894 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (894) | During pregnancy (1st, 2nd, 3rd) | Pain at injection site<br>Fatigue<br>Headache<br>Myalgia<br>Fever |

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| | | | | Women with no information on the date of injection, the occurrence of early adverse events and their description if any or no information about the type of vaccine used | | | | |
| Fell DB, 2022 | Retrospective cohort | Canada<br><br>Better Outcome Registry and Network Ontario Birth Registry<br><br>May 2021 – December 2021 | NA | *Inclusion*<br>Completed pregnancies between 1 May and 31 December 2021<br><br>*Exclusion*<br>Births to non-Ontario residents and births from pregnancies conceived less | 43099 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>One dose (13416)<br>Two doses (29650)<br>Three doses (33) | During pregnancy (1st, 2nd, 3rd) | Stillbirth<br>Preterm birth < 37 weeks<br>Small for gestational age |

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| | | | | than 42 weeks before the end of the study. Any records with gestational age < 20 weeks and birth weight < 500 gr, or following pregnancy termination | | | | |
| Fell DB (1), 2022 | Retrospective cohort | Canada<br><br>Better Outcome Registry and Network Ontario Birth Registry<br><br>December 2020 – September 2021 | NA | *Inclusion*<br>Pregnancies with a birth date or expected due date on or after December 14, 2020 (when the COVID-19 vaccination program began in Ontario)<br><br>*Exclusion*<br>Ongoing pregnancies as of September | 22660 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>Non specified | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Postpartum haemorrhage<br>Caesarean section<br>NICU admission<br>Abnormal apgar 5 |

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| | | | | 30, 2021, individuals who became pregnant less than 42 weeks before the end of the study period (i.e., those with a last menstrual period after December 9, 2020), records with documented gestational age less than 20 weeks at birth, and pregnancy terminations | | | | |
| Gandhi AP, 2022 | Prospective cohort | India<br><br>July 2021 – October 2021 | NA | *Inclusion*<br>Pregnant women registered with the ANC clinics who went for covid-19 vaccination<br><br>*Exclusion* | 247 | Viral vector<br><br>AZD<br><br>One dose (247) | During pregnancy (non specified) | Fever<br>Pain at injection site |

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| | | | | Women less than 18 years of age and who did not consent to participate in the follow-up | | | | |
| Goldshtein I, 2021 | Retrospective cohort | Israel<br><br>Maccabi Healthcare Services Database<br><br>December 2020 – February 2021 | NA | *Inclusion*<br>All pregnant women in the health fund<br><br>*Exclusion*<br>Pregnant women who joined the fund less than 1 year preconception, with any preconception records indicating SARS- CoV-2 infection, and members who were vaccinated pre-pregnancy with the | 7530 | mRNA<br><br>Pfizer-BioNTech<br><br>Non specified | During pregnancy (non specified) | Maternal covid infection<br>Maternal death<br>Maternal hospital admission<br>Preterm birth <37 weeks<br>Stillbirth<br>Hypertensive disorder in pregnancy |

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| | | | | BNT162b2 mRNA vaccine | | | | |
| Goldshtein I, 2022 | Retrospective cohort | Israel<br><br>Maccabi Healthcare Services Database<br><br>March 2021 – October 2021 | NA | *Inclusion*<br>All singleton live births at any time from March 1, 2021, through September 31, 2021<br><br>*Exclusion*<br>Records with no mother-offspring linkage, multiple births, insufficient prior membership time, or missing covariate data | 16697 | mRNA<br><br>Pfizer-BioNTech<br><br>Non specified | During pregnancy (1st, 2nd, 3rd) | Gestational diabetes<br>Preterm birth <37 weeks<br>Small for gestational age |
| Gray KJ, 2021 | Retrospective cohort | USA<br><br>Questionnaire<br><br>December 2020 – | NA | *Inclusion*<br>Pregnant, lactating and non-pregnant women of reproductive | 83 | mRNA<br><br>Pfizer-BioNTech<br>Moderna | During pregnancy (1st, 2nd, 3rd) | Pain at injection site<br>Headache<br>Myalgia<br>Fatigue<br>Fever |

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| | | February 2021 | | age (18-45), able to provide informed consent and receiving the covid-19 vaccine<br><br>*Exclusion* | | One dose (83)<br>Two doses (77) | | |
| Guedalia J, 2022 | Retrospective cohort | Israel<br><br>MOH Database<br><br>August 2021 – March 2022 | Age<br>Parity<br>Days of follow-up | *Inclusion*<br>Women who had a documented delivery between August 1, 2021, to March 22, 2022<br><br>*Exclusion*<br>Women who received one vaccine or a fourth boosting dose | 60554 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (60554) | During pregnancy (non specified) | Maternal covid infection<br>Severe covid disease<br>Maternal hospital admission<br>Maternal death |
| Halasa NB (1), 2022 | Test negative case-control | USA<br><br>paediatric hospitals in | NA | *Inclusion*<br>Women who received the first dose | 231 | mRNA<br><br>Pfizer-BioNTech | During pregnancy (non specified) | Preterm birth <37 weeks<br>NICU admission |

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| | | the CDC-funded overcoming COVID-19 network July 2021 – March 2022 | | before pregnancy and the second dose during pregnancy<br><br>*Exclusion*<br>Women partially vaccinated during pregnancy (I.e., received one dose during pregnancy and no dose before pregnancy) or who had been fully vaccinated before pregnancy or after delivery, women who had been vaccinated less than 14 days before delivery, and | | Two doses (231) | | |

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| | | | | women who had received a third dose of an mRNA vaccine or had received a non-mRNA vaccine (i.e., Ad26.COV2.S) | | | | |
| Hui L (1), 2022 | Retrospective cohort | Australia<br><br>12 Public Maternity Hospitals in Melbourne<br><br>July 2021 – March 2022 | Age<br>BMI<br>Metropolitan vs regional residence<br>Smoking<br>Region of birth<br>Socioeconomic index for postcodes<br>Diabetes<br>Parity<br>Infant sex<br>Gestation at first antenatal visit<br>Need for interpreter | *Inclusion*<br>Births ≥ 20 weeks from all 12 public maternity hospitals in Melbourne from 1st July 2021 to 1st March 2022<br><br>*Exclusion*<br>Births in exclusively private hospitals and planned home births outside of publicly funded | 17365 | mRNA<br><br>Non specified<br><br>Non specified | Before/during pregnancy | Gestational diabetes<br>Stillbirth<br>Preterm birth <37 weeks<br>NICU admission<br>Abnormal apgar 5<br>Postpartum haemorrhage<br>Caesarean section |

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| | | | | homebirth programs | | | | |
| Ibroci E, 2022 | Prospective cohort | USA<br><br>Mount Sinai Health system<br><br>April 2020-February 2021 | NA | *Inclusion* | 250 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br><br>Non specified | During pregnancy (1st, 2nd, 3rd) | Preterm birth <37 weeks<br>NICU admission<br>Caesarean section<br>Small for gestational age |
| Juttukonda L, 2022 | Prospective cohort | USA<br><br>Boston Medical Center<br><br>July 2020 – November 2021 | NA | *Inclusion*<br>Age minimum of 18 years, singleton pregnancy, full-term (gestational age ≥ 37 weeks) delivery, and English/Spanish speaking | 17 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (17) | During pregnancy (non specified) | Hypertensive disorder in pregnancy<br>Preterm birth <37 weeks<br>Caesarean section<br>Gestational diabetes<br>NICU admission |
| Kachikis AL, 2022 | Prospective cohort | USA<br><br>Questionnaire<br><br>January 2021 – March 2021 | NA | *Inclusion* | 7565 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna | During pregnancy (1st, 2nd, 3rd) | Fever |

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| | | | | | | Janssen<br><br>One dose (7565)<br>Two doses (6232) | | |
| Kadali RAK, 2021 | Cross-sectional study | USA<br><br>Online questionnaire<br><br>Non specified | NA | *Inclusion*<br>Pregnant women admitted for delivery who consented to sample collection for a biorepository | 38 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>One dose (non specified)<br>Two doses (non specified) | During pregnancy (non specified) | Pain at injection site<br>Fatigue<br>Headache<br>Myalgia<br>Fever |
| Kashani-Ligumsky L, 2021 | Retrospective cohort | Israel<br><br>Mayanei Hayeshua medical centre<br><br>February 2021- March 2021 | NA | *Inclusion*<br>Women who delivered singleton livebirths<br><br>*Exclusion*<br>Women who contracted SARS-CoV-2 infection prior | 29 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (29) | During pregnancy (3rd) | Ceasarean section<br>NICU admission<br>Preterm birth <37 weeks |

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| | | | | to vaccination and women with single dose | | | | |
| Kim H, 2022 | Retrospective cohort | South Korea<br><br>Kyungpook National University Chilgok Hospital<br><br>November 2020 – March 2022 | NA | *Inclusion*<br>All pregnant women admitted to the institution for COVID-infection between November 1, 2020, and March 7, 2022 | 39 | mRNA<br><br>Non specified<br><br>Non specified | During pregnancy (Non specified) | Preterm birth <37 weeks |
| Komine-Aizawa S, 2022 | Retrospective cohort | Japan<br><br>Online questionnaire<br><br>October 2021 – November 2021 | NA | *Inclusion*<br>Older than 20 years old or married minors older than 16 years. | 5032 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>One dose (5032)<br>Two doses (4587) | During pregnancy (1st, 2nd, 3rd) | Pain at injection site<br>Fever<br>Fatigue<br>Headache |
| Kugelman N, 2022 | Retrospective cohort | Israel<br><br>Carmel Medical Center | NA | *Inclusion*<br>Women with singleton pregnancy | 930 | mRNA<br><br>Pfizer-BioNTech | During pregnancy (2nd, 3rd) | Caesarean section<br>NICU admission<br>Stillbirth |

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| | | February 2021 – July 2021 | | over 23 weeks of gestation<br><br>*Exclusion*<br>Multiple gestations and those who underwent termination of pregnancy | | One dose (51)<br>Two doses (879) | | Abnormal Apgar 5 |
| Li M, 2022 | Prospective cohort | China<br><br>Beijing Dita Hospital<br><br>March 2021-February 2022 | NA | *Inclusion*<br>Pregnant women who inoculated or never inoculated inactivated covid-19 during the peri-pregnancy period. Pregnant women aged between 10 and 45<br><br>*Exclusion*<br>Family history of hereditary diseases in one | 93 | Inactivated virus<br><br>Sinovac-CoronaVac Sinopharm BIBP<br><br>Non specified | Before/During pregnancy (1st) | Preterm birth <37 weeks Hypertension disorder in pregnancy Postpartum haemorrhage |

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| | | | | or both families of the couple. Women who delivered babies with congenital abnormalities. Three or more spontaneous abortions in the past. Taking drugs that have a definite effect on fetal development during pregnancy. Exposure to toxic substances in early pregnancy. Associated with malignant tumors. Coinfection with hepatitis C, hepatitis D, | | | | |

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| | | | | human immunodeficiency virus, syphilis, toxoplasmosis, rubella or cytomegalovirus. | | | | |
| Lipkind HS, 2022 | Retrospective cohort | USA<br><br>VSD sites in California, Colorado, Minnesota, Oregon, Washington, and Wisconsin (Kaiser Permanente: Colorado, Northern California, Northwest, Southern California, and Washington; Denver Health; | NA | *Inclusion*<br>Singleton live births from eight VSD sites, females aged 16-49 years with estimated pregnancy start during May 17 – October 24, 2020, and expected delivery dates, based on a 40-week gestation, during February 21 – July 31, 2021, and all COVID-19 | 10064 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br><br><br>One dose (2183)<br>Two doses (7881) | During pregnancy (1st, 2nd, 3rd) | Preterm birth <37 weeks<br>Small for gestational age |

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| | | HealthPartners; and Marshfield Clinic).<br><br>December 2020 – July 2021 | | vaccine doses administered from the last menstrual period through 3 days before delivery<br><br>*Exclusion*<br>Vaccines administered within 3 days of delivery | | | | |
| Lis-Kuberka J, 2022 | Cross-sectional | Poland<br><br>Questionnaire<br><br>November 2021 – December 2021 | NA | *Inclusion*<br>Women who were pregnant and/or delivered during pandemic of COVID-19<br><br>*Exclusion*<br>Women who did not fully complete the questionnaire or provided unreliable data | 796 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br>AZD<br><br>Non specified | During pregnancy (1st, 2nd, 3rd) | Caesarean section |

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| Magnus MC (3), 2022 | Retrospective cohort | Sweden/Norway<br><br>Pregnancy Register in Sweden and The Medical Birth Registry of Norway<br><br>January 2021 – January 2022 | Age<br>Gestational age<br>Parity<br>Education<br>Living with a partner<br>Household income<br>Previous positive SARS-CoV-2 test<br>Underlying chronic condition | *Inclusion*<br>All singleton pregnancies ending after 22 completed gestational weeks registered in the Pregnancy Register in Sweden and the Medical Birth Registry of Norway from January 1, 2021, until January 12, 2022 (Sweden), or January 15, 2022 (Norway)<br><br>*Exclusion*<br>Pregnancies ending in multiple births, individuals vaccinated prior to pregnancy, and | 28506 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>One dose (6977)<br>Two doses (21529) | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Abnormal apgar 5<br>Small for gestational age<br>NICU admission<br>Stillbirth<br>Preterm birth <37 weeks |

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| | | | | individuals who received the Johnson & Johnson vaccine | | | | |
| Mascolo A 2022 | Retrospective cohort | Israel<br><br>EV database<br><br>January 2021-December 2021 | NA | *Inclusion*<br><br><br>*Excluded*<br>ICSRs with PTs referred to extraction criteria and without AEFI, uncertain information on the vaccine exposure during pregnancy, and sex or age incoherent or unknown | 3252 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br>AZD<br><br>Non specified | During pregnancy (non specified) | Headache<br>Fatigue<br>Myalgia<br>Pain at injection site |
| Mayo RP, 2021 | Prospective cohort | Israel<br><br>8 medical centres in Israel (Hadassah Mount | NA | *Inclusion*<br>Pregnant women admitted for delivery at 8 medical centres, ≥18 | 125 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (125) | During pregnancy (2nd, 3rd) | Preterm birth <37 weeks<br>NICU admission |

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| | | Scopus, Wolfson, HaEmek, Hillel Yafe, Rabin, Shaare Zedek, Meir, and Sourasky Medical Centers)<br><br>January 2021 – June 2021 | | years old and willing to provide informed consent<br><br>*Exclusion*<br>Pregnant women with active COVID-19 infection | | | | |
| Montalti M, 2022 | Cross-sectional study | Italy<br><br>Online survey<br><br>– January 2021 | NA | *Inclusion*<br>Female members of the Facebook group "Coronavirus, SARS-CoV-2 e COVID-19 gruppo per soli medici" that have been pregnant or breastfeeding for the entire duration of the survey | 31 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (31)<br>Two doses (17) | During pregnancy (non specified) | Fever<br>Fatigue<br>Myalgia<br>Headache |

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| | | | | *Exclusion* | | | | |
| Ortqvist AK. 2022 | Retrospective cohort | Sweden Norway Swedish pregnancy register<br><br>Medical Birth Register in Norway<br><br>May 2021 – May 2022 | Age | *Exclusion:* Vaccinated prior pregnancy | 69512 | mRNA/Viral vector<br><br>Pfizer-BioNTech Moderna AZD<br><br>One dose (9702) Two doses (47699) Booster dose (12111) | Before/during pregnancy (non specified) | Gestational diabetes Hypertensive disorder in pregnancy |
| Paganoti CDF, 2022 | Retrospective cohort | Brazil<br><br>SIVEP-Gripe registry<br><br>May 2021 – November 2021 | NA | *Inclusion:* Pregnant or postpartum of childbearing age (10-55 years), COVID confirmed by PCR, SARS CoV-2 or antigen. Exclusion of influenza infection by | 200 | mRNA/Inactivated virus<br><br>Non specified<br><br>Non specified | During pregnancy (non specified) | Severe covid disease Maternal death |

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| | | | | negative RT-PCR or antigen for influenza. Availability of the outcome (recovery or death) and reliability of vaccination status.<br><br>No exclusion criteria. | | | | |
| Paixao ES 2022 | Test negative case-control | Brazil<br><br>Brazilian Ministry of Health<br><br>January 2021-October 2021 | Age<br>Ethnicity<br>Comorbidities<br>Region of residence<br>IBP<br>Time | *Inclusion:* Pregnant women with symptoms suggesting Covid-19, aged between 18 and 49 years in Brazil with a record of a RT-PCR test between March 15, 2021, and October 03, 2021, | 2033 | Inactivated virus<br><br>Sinovac-CoronaVac<br><br>One dose (995)<br>Two doses (1038) | During pregnancy (non specified) | Maternal covid infection<br>Severe covid disease |

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| | | | | registered in e-SUS Notifica.<br><br>*Exclusion:* Subjects who received any Covid-10 Vaccine: ChAdOx1 nCoV-19 or Ad26.COV2.S (Janssen/Johnson & Johnson) because these are not indicated for pregnant women in Brazil and BNT162b2 numbers of women with complete regimen were too small to allow evaluation given they were included in the | | | | |

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| | | | | Brazilian program. | | | | |
| Peretz - Machluf R 2022 | Retrospective cohort | Israel<br><br>The department of Obstetrics and Gynecology, Chaim Sheba Medical Center<br><br>March 2021 - July 2021 | Age<br>Parity<br>Smoking<br>Gestational age at delivery<br>Background conditions (Obesity, hypertensive disorders, diabetes) | *Inclusion*<br>Vaccinated and non-vaccinated pregnant women with singleton pregnancies.<br><br>*Exclusion*<br>Women with prior COVID-19 infection, multiple gestations, and stillbirth | 3240 | mRNA<br><br>Pfizer-BioNTech<br><br>Non specified | During pregnancy (2nd, 3rd) | Gestational diabetes<br>Hypertensive disorders<br>Small for gestational age<br>Preterm birth <37 weeks<br>Caesarean section<br>Abnormal Apgar 5<br>NICU admission |
| Piekos SN, 2022 | Retrospective cohort | USA<br><br>Providence St Joseph Health Alaska, California, Montana, Oregon, New Mexico, Texas, and Washington | NA | *Inclusion:*<br>18-45 years, with singleton pregnancies<br>Delivery after 20 weeks gestation.<br><br>Positive SARS Cov-2 NAAT test. | 34408 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (26792)<br>Booster dose (7616) | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Maternal death<br>Caesarean section<br>Hypertensive disorders<br>Gestational diabetes |

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| | | Jan 2021- Jul 2022 | | Propensity score matching accounting for demographic, lifestyle, geographical and clinical characteristics for negative maternal-fetal outcomes to generate an unvaccinated matched cohort. | | | | |
| Rottenstreich M, 2022 | Retrospective cohort | Israel<br><br>Shaare Zedek Medical Center (SZMC) and the Bikur Holim Medical Center (BHMC)<br><br>January 2021 – April 2021 | NA | *Inclusion*<br>All pregnant women admitted for delivery aged 18 years or older, with no documented previous positive SARS-CoV-2 | 712 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (712) | During pregnancy (3rd) | Severe covid disease<br>Caesarean section<br>Preterm birth <37 weeks<br>NICU admission<br>Pospartum haemorrhage<br>Abnormal Apgar 5<br>Stillbirth |

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| | | | | | | | | Hypertensive disorders<br>Small for gestational age |
| Rottenstreich M (1), 2022 | Retrospective cohort | Israel<br><br>August 2021 – December 2021 | NA | *Inclusion*<br>All women aged 18 or older, without documented previous positive SARS-CoV-2 PCR test, delivered between August 28 and December 31 2021.<br><br>*Exclusion*<br>Parturients who were previously positive with covid-19 PCR swabs during or before pregnancy. | 1720 | mRNA<br><br>Pfizer-BioNTech<br><br>Two doses (1094)<br>Booster dose (626) | During pregnancy (non specified) | Caesarean section<br>Postpartum haemorrhage<br>Preterm birth <37 weeks<br>Small for gestational age<br>Stillbirth<br>NICU admission<br>Abnormal Apgar 5 |

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| | | | | Women who received only the first dose | | | | |
| Sadarangani M, 2022 | Prospective cohort | Canada<br><br>Seven Canadian provinces and territories<br><br>-November 2021 | NA | *Inclusion*<br>Received first dose of an authorized COVID-19 vaccine within the prior seven days; have active email address and telephone number, can communicate in English or French, reside in one of the seven provinces and territories<br><br>*Exclusion* | 5597 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>One dose (5597)<br>Two doses (3108) | During pregnancy (1st, 2nd, 3rd) | Myalgia<br>Fever<br>Headache |
| Schrag SJ, 2022 | Test negative case-control | USA<br><br>Network of 306 hospitals and 164 | Age<br>Geographic regions<br>Calendar time | *Inclusion:*<br>Aged 18-45 with COVID like illness diagnosis, RT- | 1137 | mRNA<br><br>Pfizer-BioNTech<br>Moderna | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection |

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| | | emergency department and urgent care facilities across 10 US states.<br><br>June 2021 – June 2022 | Local virus circulation | PCR for SARS COV-2 during 14 days before through 72 hours after the medical encounter and pregnant at the time of encounter. Acute respiratory illness – respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza and viral illness otherwise not specified.<br><br>*Exclusion:* Ad.26.COV2.S Janssen vaccine. Single vaccinated or more than 3 | | Two doses (721)<br>Three doses (416) | | Maternal hosital admission |

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| | | | | doses of mRNA vaccine. Those with less than 14 days between second dose and fewer than 7 days since their third dose. | | | | |
| Shanes ED (1), 2021 | Prospective cohort | USA<br><br>January 2021 - April 2021 | NA | *Inclusion* | 84 | Non specified<br><br>Non specified<br><br>Non specified | During pregnancy (Non specified) | Caesarean delivery |
| Shimabukuro TT, 2021 | Retrospective cohort | USA<br><br>V-safe Surveillance System, V-safe pregnancy registry and VAERS system<br><br>December 2020 – | NA | *Inclusion*<br>Received vaccination during pregnancy or in the periconception period and are 18 years of age or older | 16982 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>One dose (16982)<br>Two doses (12273) | During pregnancy (non specified) | Pain at injection site<br>Fatigue<br>Headache<br>Myalgia<br>Fever |

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| | | February 2021 | | | | | | |
| Smithgall MC, 2022 | Prospective cohort | USA<br><br>New York city hospital<br><br>April 2020 – July 2021 | NA | *Exclusion:*<br>Incomplete vaccine administration<br><br>*Inclusion:*<br>Fully vaccinated women, at least 2 doses of a SARs-COV-2 mRNA vaccine at >2 weeks before delivery, included if they did not have positive anti-N antibodies produced in the setting of infection. | 164 | mRNA<br><br>Pfizer-BioNTech<br>Moderna<br><br>Two doses (164) | During pregnancy (non specified) | Caesarena section<br>Preterm birth < 37 week<br>Abnormal Apgar 5<br>Small for gestational age |
| Sourouni M, 2022 | Prospective cohort | Germany | NA | *Inclusion*<br>Women given birth at the hospital who | 70 | mRNA<br><br>Pfizer-BioNTech | During pregnancy (1st, 2nd, 3rd) | Fever<br>Pain at injection site |

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|---|---|---|---|---|---|---|---|---|
| | | University hospital of Münster<br><br>March 2021 – November 2021 | | were vaccinated during pregnancy | | Moderna<br><br>Non specified | | |
| Stock S, 2022 | Retrospective study | UK<br><br>COPS cohort<br><br>September 2021- January 2022 | Age<br>Gestational age at date of vaccination<br>Deprivation<br>Urban/rural status<br>Clinical vulnerability | *Inclusion:*<br>Vaccinated from 6 weeks before conception to 19 weeks and 6 days gestation for miscarriage and 2+6 weeks for ectopic pregnancy.<br><br>*Exclusion:*<br>Completed pregnancies with unknown pregnancy outcome. | 18780 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD<br><br>One dose (non specified)<br>Two doses (Non specified)<br>Booster dose (Non specified) | Before/During pregnancy (1st, 2nd) | Miscarriage |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Theiler RN, 2021 | Retrospective cohort | United States of America<br><br>Hospitals within the Mayo Clinic Health System<br><br>December 2021 – April 2021 | NA | *Inclusion*<br>All women aged 16-55 years old who delivered between December 10, 2020, and April 19, 2021 at a Mayo Clinic hospital.<br><br>*Exclusion*<br>Minnesota patients who delivered in Minnesota and opted out of use of their medical records for research | 140 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br><br>Non specified | During pregnancy (1st, 2nd, 3rd) | Maternal covid infection<br>Severe covid disease<br>Maternal death<br>Caesarean section<br>Preterm birth <37 weeks<br>NICU admission<br>Abnormal Apgar 5<br>Stillbirth<br>Hypertensive disorders<br>Postpartum haemorrhage |
| Toussia-Cohen S (2), 2022 | Prospective cohort | Israel<br><br>Online questionnaire<br><br>January 2021 – November 2021 | NA | *Exclusion:*<br>Chronic hypertension, chronic kidney disease, antiphospholipid syndrome, systemic lupus, | 162 | mRNA<br><br>Pfizer-BioNTech<br><br>Doses 1 and 2 (78) | During pregnancy (2nd, 3rd) | Fever<br>Myalgia<br>Headache<br>Fatigue |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | multiple gestation, and previous preterm birth. Positive PCR SARS COV2 test before or during the study period. | | Booster dose (84) | | |
| UKHSA 27 January 2022 COVID-19 Vaccine Surveillance Report | Retrospective cohort | United Kingdom<br><br>UKHSA<br><br>January 2021 – June 2022 | NA | Not reported | 258639 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>AZD | During pregnancy (non specified) | Preterm birth <37 weeks<br>Stillbirth |
| Villar J, 2023 | Prospective cohort | Argentina, Brazil, Egypt, France, Indonesia, Israel, Italy, Japan, Mexico, Nigeria, North Macedonia, Pakistan, Spain, | Age<br>Overweight or obesity<br>Presence or absence of any pre-existing medical condition<br>Country | *Inclusion*<br>Women with a documented diagnosis of covid-19. Live and stillborn singleton and multiple births, and newborn babies with | 2886 | mRNA/Viral vector/Inactivated virus<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br>AZD<br>SinoVac | During pregnancy (non specified) | Maternal covid infection<br>Severe covid disease<br>Caesarean section<br>Hypertensive disorders<br>Preterm birth <37 weeks |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Switzerland, Türkiye, UK, Uruguay and USA<br><br>Hospitals part of the Oxford Maternal and Perinatal Health institute<br><br>November 2021 – June 2022 | | congenital anomalies. | | Bharat Biotech Sinopharm<br><br>One dose (non specified)<br>Two doses (non specified)<br>Booster dose (non specified) | | |
| Voiniusyte A, 2022 | Retrospective cohort | Lithuania<br><br>Online questionnaire<br><br>-July 2021 | NA | *Inclusion*<br>Pregnant women primarily located in Lithuania who received at least one dose before giving birth.<br>Enrollment was voluntary. | 227 | mRNA/Viral vector<br><br>Pfizer-BioNTech<br>Moderna<br>Janssen<br>AZD<br><br>One dose (227)<br>Two doses (157) | During pregnancy (1st, 2nd, 3rd) | Fever |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Wainstock T, 2021 | Retrospective cohort | Israel<br><br>Soroka University Medical Center<br><br>January 2021 – June 2021 | Non specified | *Inclusion*<br>All women who delivered singletons between January and June 2021 at the Soroka University Medical Center<br><br>*Exclusion* | 913 | mRNA<br><br>Pfizer-BioNTech<br><br>One dose (non specified)<br>Two doses (non specified) | During pregnancy (2nd, 3rd) | Caesarean section<br>Gestational diabetes<br>Hypertensive disorders<br>Abnormal Apgar 5<br>Postpartum haemorrhage<br>Small for gestational age |
| Wang Y (1), 2022 | Retrospective cohort | China<br><br>Peking University Third Hospital<br><br>Non specified | NA | *Inclusion:*<br>Completed gamete retrieval and embryo cryopreservation before getting vaccinated with inactivated COVID-19 vaccine. | 460 | Inactivated virus<br><br>Non specified<br><br>Two doses (460) | Before pregnancy | Miscarriage |
| Zdanowski W, 2022 | Cross-sectional study | Poland | NA | *Exclusions* | 169 | mRNA | During pregnancy | Pain at injection site<br>Headache |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Online questionnaire<br><br>May 2021 – September 2021 | | Moderna and AstraZeneca vaccines. First dose before pregnancy | | Pfizer-BioNTech<br><br>One dose (169)<br>Two doses (121) | (non specified) | Fever<br>Myalgia<br>Fatigue |

Appendix 4. Description of the consensus judgments for assigning a risk of bias in each domain by the ROBINS-I tool

**Table 1. Maternal SARS-CoV-2 infection**

| | Butt AA 2021 Cohort | Dagan N 2021 | Villar J 2023 | Butt AA 2021 TND | Paixao ES 2022 | Schrag SJ 2022 |
|---|---|---|---|---|---|---|
| **Bias due to confounding** | | | | | | |
| Risk of bias judgement | Moderate | Moderate | Moderate | Low | Low | Low |
| Is there potential for confounding of the effect of intervention in this study? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Did the authors use an appropriate analysis method that controlled for all the importantconfounding domains? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | | | | | |
| | N | N | N | N | N | N |
| Did the authors control for any post-intervention variables that could have been affected by theintervention? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | Given that all the included articles are observational in nature, there exists a potential for confounding. While acceptable adjustment techniques were employed across all articles to mitigate this concern, the variables used for such adjustments are limited in number or lack validity and reliability. However, our assessment has led us to assign a "Low" rating to the following articles: Butt AA 2021 TND, Paixao ES 2022, and Schrag SJ 2022. This decision is based on the rationale outlined in the [WHO article], which highlights a significant aspect of the test-negative design—namely, the focus on a population with access to and utilization of medical care. This deliberate restriction serves to minimize unmeasured confounding attributed to healthcare-seeking behaviors. | | | | | |
| **Bias in selection of participants into the study** | | | | | | |
| Risk of bias judgement | Low | Low | Serious | Low | Low | Low |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | | | | | | |
| | N | N | Y | Y | Y | Y |
| Do start of follow-up and start of intervention coincide for most participants? | | | | | | |
| | PY | PY | PN | PN | PN | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | | | | |
| | NA | NA | N | N | N | N |
| Observation: | Through collaborative agreement, we determined that assigning a low risk of bias to this domain would be appropriate when participant selection relied on pre-intervention baseline characteristics and when the initiation of follow-up and the commencement of intervention aligned for most participants. In contrast, the study conducted by Villar J 2023 received a classification of "Serious" risk due to the lack of alignment between the start of follow-up and the initiation of intervention. Furthermore, participant selection was based on post-intervention characteristics. Regarding the TND articles, we deemed the risk of bias to be "Low." This determination stemmed from the fact that while participant selection occurs post-intervention, these designs have undergone extensive validation for assessing vaccine efficacy [WHO reference; Otra referencia]. | | | | | |
| **Bias in classification of interventions** | | | | | | |
| Risk of bias judgement | Low | Moderate | Low | Low | Low | Low |
| Were intervention groups clearly defined? | | | | | | |
| | Y | N | Y | Y | Y | Y |
| Was the information used to define intervention groups recorded at the start of the intervention? | | | | | | |
| | PY | PY | Y | PY | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | | | | | | |
| | PN | PN | PN | PN | PN | PN |
| Observation: | We decided to score this domain as having a low risk of bias if the study described the intervention in terms of the type of vaccine used and the dose administered, which was not the case in the study by Dagan N 2021. | | | | | |
| **Bias due to deviations from intended interventions** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because any deviations from the intended intervention reflected usual practice. | | | | | |
| **Bias due to missing data** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Moderate | Moderate |
| Were outcome data available for all, or nearly all, participants? | | | | | | |
| | Y | Y | Y | Y | N | N |
| Were participants excluded due to missing data on intervention status? | | | | | | |
| | NI | NI | N | N | N | N |
| Were participants excluded due to missing data on other variables needed for the analysis? | | | | | | |
| | NI | PY | N | N | N | N |
| Observation: | We've chosen to assign a "Low" rating to this section due to the adequately comprehensive nature of the data, coupled with the absence of any indications suggesting a notable divergence in the proportion or ratio of missing participant data between the intervention groups. However, for the Paixao ES 2022 and Schrag SJ 2022 items, we've opted for a "Moderate" rating. This decision arises from an insufficiency of information regarding the handling of missing data within the outcome evaluation process. | | | | | |
| **Bias in measurement of outcomes** | | | | | | |
| Risk of bias judgement | Moderate | Moderate | Moderate | Low | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were outcome assessors aware of the intervention received by study participants? | | | | | | |
| | PY | PY | PY | PY | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | Given the observational and retrospective nature of these articles, we acknowledge that clinicians were likely aware of the patients' allocation to specific intervention groups in all instances. Moreover, this awareness might have been influenced by the patients' COVID infection status, potentially introducing bias. Consequently, a "Moderate" rating was deemed appropriate for cohort studies, considering these inherent attributes. However, for test-negative design (TND) studies, which exhibit distinct characteristics pertinent to assessing effectiveness [WHO reference], a "Low" rating was assigned due to the outlined considerations. | | | | | |
| **Bias in selection of the reported result** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases of the result from... multiple outcome measurements within the outcome domain? | | | | | | |
| | N | N | N | N | N | N |
| ... multiple analysis of the intervention-outcome relationship? | | | | | | |
| | N | N | N | N | N | N |
| ... different subgroups? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because we have reported all of the results that we consider to be of interest. | | | | | |
| **Overall bias** | | | | | | |
| Risk of bias judgement | Moderate | Moderate | Serious | Low | Moderate | Moderate |

**Table 2. Neonatal SARS-CoV-2 infection**

| | Carlsen EO 2022 | Danino D 2022 |
|---|---|---|
| **Bias due to confounding** | | |
| Risk of bias judgement | Moderate | Critical |
| Is there potential for confounding of the effect of intervention in this study? | Y | PY |
| Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | Y | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | N | N |
| Did the authors control for any post-intervention variables that could have been affected by the intervention? | N | Y |
| Observation: | Given that all the included articles are observational in nature, there exists a potential for confounding. While acceptable adjustment techniques were employed across all articles to mitigate this concern, the variables used for such adjustments are limited in number or lack validity and reliability. The decision to score Danino D 2022 as "High" risk is based on the use of the variable "Prematurity" as an adjustment variable, this being a post-intervention variable. | |
| **Bias in selection of participants into the study** | | |
| Risk of bias judgement | Serious | Low |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | N | Y |
| Do start of follow-up and start of intervention coincide for most participants? | N | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | N | N |
| Observation: | Through collaborative agreement, we determined that assigning a low risk of bias to this domain would be appropriate when participant selection relied on pre-intervention baseline characteristics and when the initiation of follow-up and the commencement of intervention aligned for most participants. In contrast, the study conducted by Carlsen EO 2022 received a classification of "Serious" risk due to the lack of alignment | |
| **Bias in classification of interventions** | | |
| Risk of bias judgement | Low | Low |
| Were intervention groups clearly defined? | Y | Y |
| Was the information used to define intervention groups recorded at the start of the intervention? | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | PN | PN |
| Observation: | We decided to score this domain as having a low risk of bias if the study described the intervention in terms of the type of vaccine used and the dose administered. | |
| **Bias due to deviations from intended interventions** | | |
| Risk of bias judgement | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because any deviations from the intended intervention reflected usual practice. | |
| **Bias due to missing data** | | |
| Risk of bias judgement | Low | Low |
| Were outcome data available for all, or nearly all, participants? | Y | Y |
| Were participants excluded due to missing data on intervention status? confounding domains? | NI | NI |
| Were participants excluded due to missing data on other variables needed for the analysis? | N | NI |
| Observation: | of the data, coupled with the absence of any indications suggesting a notab | |
| **Bias in measurement of outcomes** | | |
| Risk of bias judgement | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | N | N |
| Were outcome assessors aware of the intervention received by study participants? | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | N | NI |
| Observation: | We decided by consensus | |
| **Bias in selection of the reported result** | | |
| Risk of bias judgement | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases of the result from... multiple outcome measurements within the outcome domain? | N | N |
| ... multiple analysis of the intervention-outcome relationship? | N | N |
| ... different subgroups? | N | N |
| Observation: | We decided by consensus | |
| **Overall bias** | | |
| Risk of bias judgement | Moderate | Critical |

**Table 3. Severe covid disease**

| | Guedalia J 2022 | Villar J 2023 |
|---|---|---|
| **Bias due to confounding** | | |
| Risk of bias judgement | Moderate | Moderate |
| Is there potential for confounding of the effect of intervention in this study? | PY | Y |
| Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | PY | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | N | N |
| Did the authors control for any post-intervention variables that could have been affected by the intervention? | N | N |
| Observation: | We decided by consensus | |
| **Bias in selection of participants into the study** | | |
| Risk of bias judgement | Low | Serious |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | N | Y |
| Do start of follow-up and start of intervention coincide for most participants? | Y | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | NA | N |
| Observation: | We decided by consensus | |
| **Bias in classification of interventions** | | |
| Risk of bias judgement | Low | Low |
| Were intervention groups clearly defined? | Y | Y |
| Was the information used to define intervention groups recorded at the start of the intervention? | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | PN | PN |
| Observation: | We decided by consensus | |
| **Bias due to deviations from intended interventions** | | |
| Risk of bias judgement | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | N | N |
| Observation: | We decided by consensus | |
| **Bias due to missing data** | | |
| Risk of bias judgement | Low | Low |
| Were outcome data available for all, or nearly all, participants? | Y | Y |
| Were participants excluded due to missing data on intervention status? confounding domains? | NI | N |
| Were participants excluded due to missing data on other variables needed for the analysis? | NI | N |
| Observation: | We decided by consensus | |
| **Bias in measurement of outcomes** | | |
| Risk of bias judgement | Low | Moderate |
| Could the outcome measure have been influenced by knowledge of the intervention received? | N | Y |
| Were outcome assessors aware of the intervention received by study participants? | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | N | N |
| Observation: | We decided by consensus | |
| **Bias in selection of the reported result** | | |
| Risk of bias judgement | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases of the result from... multiple outcome measurements within the outcome domain? | N | N |
| ... multiple analysis of the intervention-outcome relationship? | N | N |
| ... different subgroups? | N | N |
| Observation: | We decided by consensus | |
| **Overall bias** | | |
| Risk of bias judgement | Moderate | Serious |

**Table 4. Maternal hospital admission**

| | Dagan N 2021 | Guedalia J 2022 | Schrag SJ 2022 |
|---|---|---|---|
| **Bias due to confounding** | | | |
| Risk of bias judgement | Moderate | Moderate | Moderate |
| Is there potential for confounding of the effect of intervention in this study? | | | |
| | Y | PY | Y |
| Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | | |
| | Y | PY | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | | |
| | N | N | N |
| Did the authors control for any post-intervention variables that could have been affected by theintervention? | | | |
| | N | N | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias in selection of participants into the study** | | | |
| Risk of bias judgement | Low | Low | Serious |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | | | |
| | N | N | Y |
| Do start of follow-up and start of intervention coincide for most participants? | | | |
| | PY | Y | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | |
| | NA | NA | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias in classification of interventions** | | | |
| Risk of bias judgement | Moderate | Low | Low |
| Were intervention groups clearly defined? | | | |
| | N | Y | Y |
| Was the information used to define intervention groups recorded at the start of the intervention? confounding domains? | | | |
| | PY | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | | | |
| | PN | PN | PN |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias due to deviations from intended interventions** | | | |
| Risk of bias judgement | Low | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | | | |
| | N | N | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias due to missing data** | | | |
| Risk of bias judgement | Low | Low | Low |
| Were outcome data available for all, or nearly all, participants? | | | |
| | Y | Y | N |
| Were participants excluded due to missing data on intervention status? | | | |
| | NI | NI | N |
| Were participants excluded due to missing data on other variables needed for the analysis? | | | |
| | PY | NI | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias in measurement of outcomes** | | | |
| Risk of bias judgement | Low | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | | | |
| | N | N | N |
| Were outcome assessors aware of the intervention received by study participants? | | | |
| | PY | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | | | |
| | Y | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | | | |
| | N | N | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Bias in selection of the reported result** | | | |
| Risk of bias judgement | Low | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases of the result from... multiple outcome measurements within the outcome domain? | | | |
| | N | N | N |
| ... multiple analysis of the intervention-outcome relationship? | | | |
| | N | N | N |
| ... different subgroups? | | | |
| | N | N | N |
| Observation: | We decided by consensus | We decided by consensus | |
| **Overall bias** | | | |
| Risk of bias judgement | Low | Moderate | Serious |

**Table 5. Pregnancy-related maternal and offspring outcomes**

| | Fell DB (1) 2022 | Goldshtein I 2022 | Ibroci E 2022 | Blakeway H 2021 | Boelig RC 2022 | Cao M 2022 |
|---|---|---|---|---|---|---|
| **Bias due to confounding** | | | | | | |
| Risk of bias judgement | Low | Moderate | Low | Serious | Low | Critical |
| Is there potential for confounding of the effect of intervention in this study? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Did the authors use an appropriate analysis method that controlled for all the importantconfounding domains? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | | | | | |
| | Y | N | Y | NI | Y | N |
| Did the authors control for any post-intervention variables that could have been affected by the intervention? | | | | | | |
| | N | N | N | NI | N | PY |
| Observation: | Articles demonstrating a strong alignment by employing valid and dependable covariates were categorized as "Low." For those utilizing a limited subset of the crucial adjustment variables or not adhering to sound and reliable construction methods, a "Moderate" classification was assigned. In cases where the model formulation or variable selection lacked accuracy, or when relevant information was absent, an assessment of "Serious" was attributed. The most stringent rating of "Critical" was reserved for instances where post-intervention variables were employed for adjustment purposes. | | | | | |
| **Bias in selection of participants into the study** | | | | | | |
| Risk of bias judgement | Low | Serious | Low | Low | Low | Serious |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | | | | | | |
| | N | N | N | N | N | Y |
| Do start of follow-up and start of intervention coincide for most participants? | | | | | | |
| | PY | PN | PY | PY | PY | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | | | | |
| | NA | N | NA | NA | NA | NI |
| Observation: | By means of a collective consensus, we ascertained that attributing a domain with a low risk of bias is warranted when participant selection hinges on pre-intervention baseline characteristics, and the synchronization between the onset of follow-up and the initiation of intervention is prevalent among the majority of participants. Conversely, a study is designated as "Serious" in cases where the commencement of follow-up and the initiation of intervention do not align, and the authors have not implemented corrective techniques to mitigate this potential bias. | | | | | |
| **Bias in classification of interventions** | | | | | | |
| Risk of bias judgement | Low | Moderate | Low | Low | Low | Low |
| Were intervention groups clearly defined? | | | | | | |
| | Y | N | Y | Y | Y | Y |
| Was the information used to define intervention groups recorded at the start of the intervention? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | | | | | | |
| | PN | PN | PN | PN | PN | PN |
| Observation: | We opted to assign a "Low" risk of bias rating to this domain if the study provided a comprehensive description of the intervention, encompassing details about the specific vaccine type | | | | | |
| **Bias due to deviations from intended interventions** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because any deviations from the intended intervention reflected usual practice. | | | | | |
| **Bias due to missing data** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Moderate |
| Were outcome data available for all, or nearly all, participants? | | | | | | |
| | Y | Y | Y | Y | Y | PN |
| Were participants excluded due to missing data on intervention status? | | | | | | |
| | N | PY | PY | Y | NI | N |
| Were participants excluded due to missing data on other variables needed for the analysis? | | | | | | |
| | N | PY | PY | NI | NI | N |
| Observation: | We've chosen to assign a "Low" rating to this section due to the adequately comprehensive nature of the data, coupled with the absence of any indications suggesting a notable divergence in the proportion or ratio of missing participant data between the intervention groups. We decided a "Moderate" rating if there are inadequate provision of information regarding the outcome missing data. | | | | | |
| **Bias in measurement of outcomes** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | | | | | | |
| | PN | PN | PN | PN | PN | PN |
| Were outcome assessors aware of the intervention received by study participants? | | | | | | |
| | PY | PY | PY | PY | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as "Low" risk of bias because our safety events of interest are well defined and we can considered them as a hard outcomes unlikely to be misinterpreted | | | | | |
| **Bias in selection of the reported result** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases of the result from... multiple outcome measurements within the outcome domain? | | | | | | |
| | N | N | N | N | N | N |
| ... multiple analysis of the intervention-outcome relationship? | | | | | | |
| | N | N | N | N | N | N |
| ... different subgroups? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because we have reported all of the results that we consider to be of interest. | | | | | |
| **Overall bias** | | | | | | |
| Risk of bias judgement | Low | Serious | Low | Serious | Low | Critical |

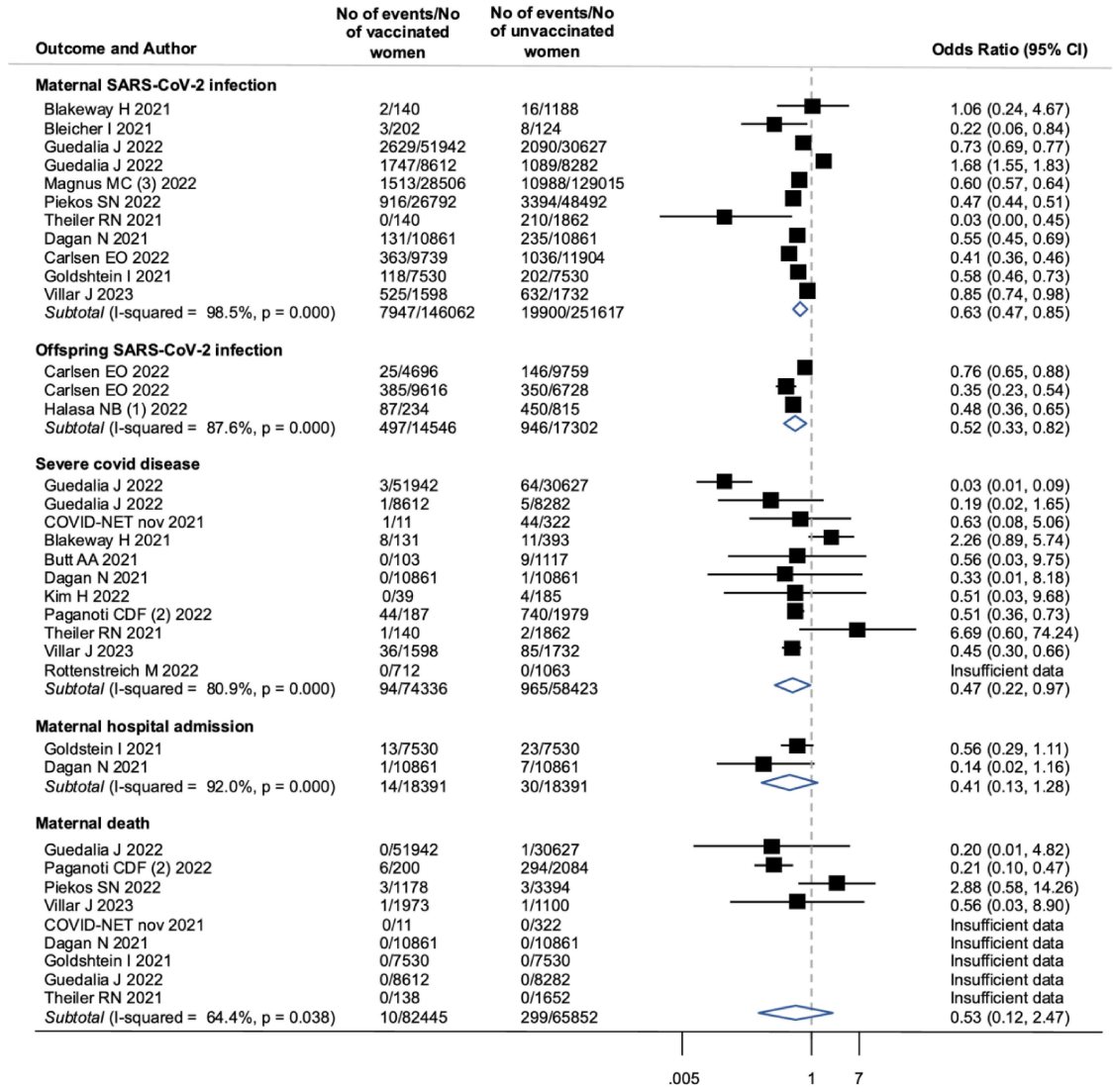
**Table 5. Pregnancy-related maternal and offspring outcomes (continued)**

| | Citu IM (1) 2022 | Dick A 2022 | Dick A (1) 2022 | Hui L (1) 2022 | Magnus MC (3) 2022 | Ortqvist AK 2022 Norway |
|---|---|---|---|---|---|---|
| **Bias due to confounding** | | | | | | |
| Risk of bias judgement | Serious | Low | Low | Low | Critical | Moderate |
| Is there potential for confounding of the effect of intervention in this study? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Did the authors use an appropriate analysis method that controlled for all the importantconfounding domains? | | | | | | |
| | PN | Y | Y | Y | Y | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | | | | | |
| | N | Y | Y | Y | Y | N |
| Did the authors control for any post-intervention variables that could have been affected by the intervention? | | | | | | |
| | N | N | N | N | PY | N |
| Observation: | Articles demonstrating a strong alignment by employing valid and dependable covariates were categorized as "Low." For those utilizing a limited subset of the crucial adjustment variables or not adhering to sound and reliable construction methods, a "Moderate" classification was assigned. In cases where the model formulation or variable selection lacked accuracy, or when relevant information was absent, an assessment of "Serious" was attributed. The most stringent rating of "Critical" was reserved for instances where post-intervention variables were employed for adjustment purposes. | | | | | |
| **Bias in selection of participants into the study** | | | | | | |
| Risk of bias judgement | Low | Serious | Serious | Serious | Serious | Low |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | | | | | | |
| | N | Y | Y | Y | Y | N |
| Do start of follow-up and start of intervention coincide for most participants? | | | | | | |
| | PY | PN | PN | PN | PN | PY |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | | | | |
| | NA | N | N | N | N | NA |
| Observation: | By means of a collective consensus, we ascertained that attributing a domain with a low risk of bias is warranted when participant selection hinges on pre-intervention baseline characteristics, and the synchronization between the onset of follow-up and the initiation of intervention is prevalent among the majority of participants. Conversely, a study is designated as "Serious" in cases where the commencement of follow-up and the initiation of intervention do not align, and the authors have not implemented corrective techniques to mitigate this potential bias. | | | | | |
| **Bias in classification of interventions** | | | | | | |
| Risk of bias judgement | Moderate | Moderate | Low | Low | Low | Moderate |
| Were intervention groups clearly defined? | | | | | | |
| | N | N | Y | Y | Y | N |
| Was the information used to define intervention groups recorded at the start of the intervention? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | | | | | | |
| | PN | PN | PN | PN | PN | PN |
| Observation: | We opted to assign a "Low" risk of bias rating to this domain if the study provided a comprehensive description of the intervention, encompassing details about the specific vaccine type and dosage administered. If such information was lacking, the rating was categorized as "Moderate." | | | | | |
| **Bias due to deviations from intended interventions** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because any deviations from the intended intervention reflected usual | | | | | |
| **Bias due to missing data** | | | | | | |
| Risk of bias judgement | Moderate | Low | Low | Low | Low | Low |
| Were outcome data available for all, or nearly all, participants? | | | | | | |
| | NI | Y | Y | Y | Y | Y |
| Were participants excluded due to missing data on intervention status? | | | | | | |
| | NI | Y | N | N | NI | NI |
| Were participants excluded due to missing data on other variables needed for the analysis? | | | | | | |
| | NI | Y | N | N | N | N |
| Observation: | We've chosen to assign a "Low" rating to this section due to the adequately comprehensive nature of the data, coupled with the absence of any indications suggesting a notable divergence in the proportion or ratio of missing participant data between the intervention groups. We decided a "Moderate" rating if there are inadequate provision of information regarding the outcome missing data. | | | | | |
| **Bias in measurement of outcomes** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | | | | | | |
| | PN | PN | PN | PN | PN | PN |
| Were outcome assessors aware of the intervention received by study participants? | | | | | | |
| | PY | PY | PY | PY | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | | | | | | |
| | Y | Y | Y | Y | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as "Low" risk of bias because our safety events of interest are well defined and we can considered them as a hard outcomes unlikely to be misinterpreted | | | | | |
| **Bias in selection of the reported result** | | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low | Low |
| likely to be selected, on the | | | | | | |
| | N | N | N | N | N | N |
| ... multiple analysis of the intervention-outcome relationship? | | | | | | |
| | N | N | N | N | N | N |
| ... different subgroups? | | | | | | |
| | N | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because we have reported all of the results that we consider to be of | | | | | |
| **Overall bias** | | | | | | |
| Risk of bias judgement | Serious | Serious | Serious | Serious | Critical | Moderate |

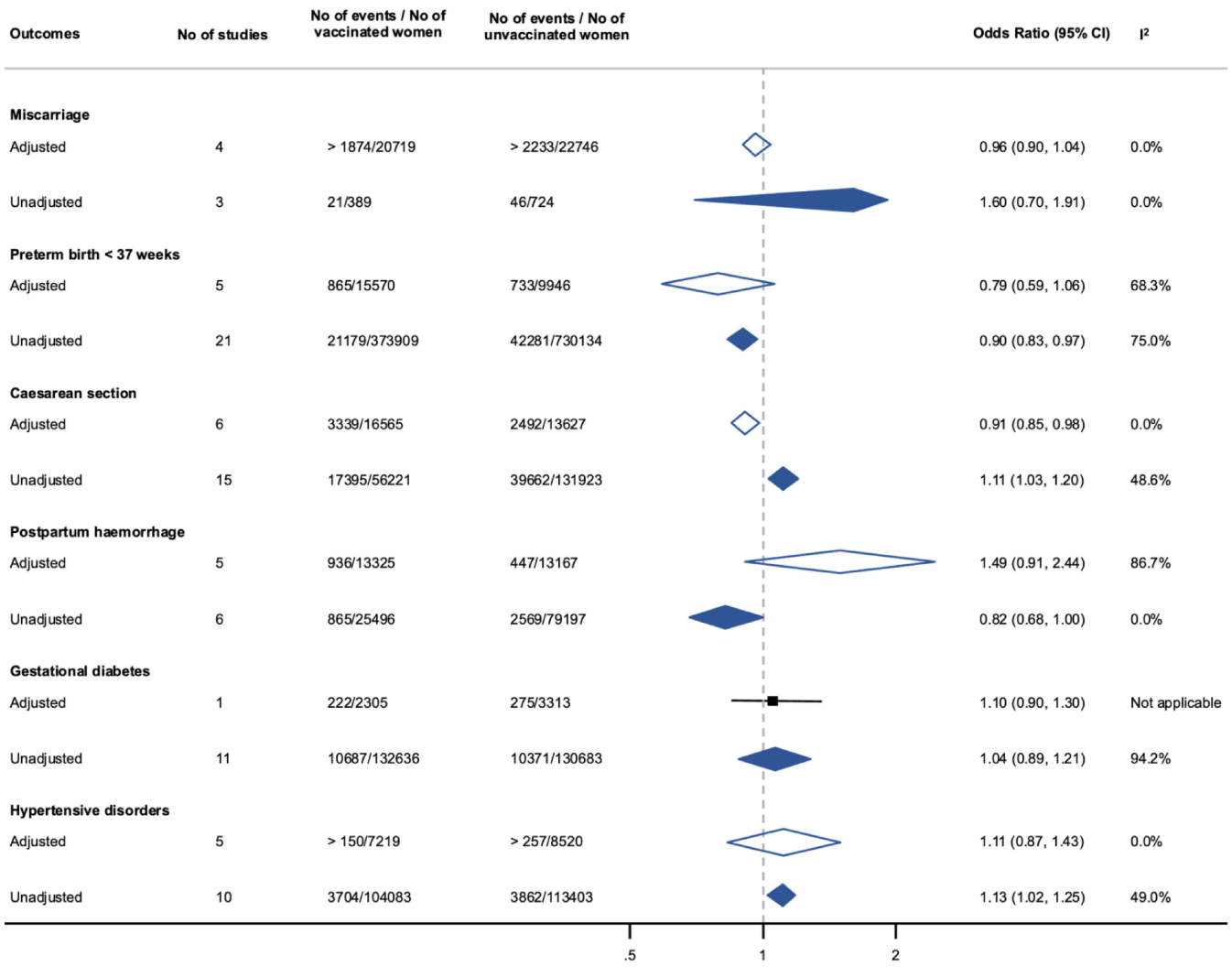
**Table 5. Pregnancy-related maternal and offspring outcomes (continued)**

| | Ortqvist AK 2022 Sweden | Perez-Machluf R 2022 | Rottenstreich M 2022 | Stock S 2022 | Wainstock T 2021 |
|---|---|---|---|---|---|
| **Bias due to confounding** | | | | | |
| Risk of bias judgement | Moderate | Low | Serious | Moderate | Moderate |
| Is there potential for confounding of the effect of intervention in | | | | | |
| | Y | Y | Y | Y | Y |
| Did the authors use an appropriate analysis method that controlled for all the importantconfounding domains? | | | | | |
| | Y | Y | Y | Y | Y |
| Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | | | | |
| | N | Y | NI | N | N |
| Did the authors control for any post-intervention variables that could have been affected by the intervention? | | | | | |
| | N | N | NI | N | N |
| Observation: | Articles demonstrating a strong alignment by employing valid and dependable covariates were categorized as "Low." For those utilizing a limited subset of the crucial adjustment variables or not adhering to sound and reliable construction methods, a "Moderate" classification was assigned. In cases where the model formulation or variable selection lacked accuracy, or when relevant information was absent, an assessment of "Serious" was attributed. The most stringent rating of "Critical" was reserved for instances where post-intervention variables were employed for adjustment purposes. | | | | |
| **Bias in selection of participants into the study** | | | | | |
| Risk of bias judgement | Low | Serious | Low | Low | Serious |
| Was the selection of participants into the study based on participant characteristics observed after the start of the intervention? | | | | | |
| | N | Y | N | Y | Y |
| Do start of follow-up and start of intervention coincide for most participants? | | | | | |
| | PY | PN | PY | PY | PN |
| Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | | | |
| | NA | N | NA | NA | N |
| Observation: | By means of a collective consensus, we ascertained that attributing a domain with a low risk of bias is warranted when participant selection hinges on pre-intervention baseline characteristics, and the synchronization between the onset of follow-up and the initiation of intervention is prevalent among the majority of participants. Conversely, a study is designated as "Serious" in cases where the commencement of follow-up and the initiation of intervention do not align, and the authors have not implemented corrective techniques to mitigate this potential bias. | | | | |
| **Bias in classification of interventions** | | | | | |
| Risk of bias judgement | Moderate | Low | Low | Low | Moderate |
| Were intervention groups clearly defined? | | | | | |
| | N | Y | Y | Y | N |
| Was the information used to define intervention groups recorded at the start of the intervention? | | | | | |
| | Y | Y | Y | Y | Y |
| Could the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | | | | | |
| | PN | PN | PN | PN | PN |
| Observation: | We opted to assign a "Low" risk of bias rating to this domain if the study provided a comprehensive description of the intervention, encompassing details about the specific vaccine type and dosage administered. If such information was lacking, the rating was categorized as "Moderate." | | | | |
| **Bias due to deviations from intended interventions** | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low |
| Were there deviations from the intended intervention beyond what would be expected in usual practice? | | | | | |
| | N | N | N | N | N |
| Observation: | We decided to score this | | | | |
| **Bias due to missing data** | | | | | |
| Risk of bias judgement | Low | Low | Moderate | Low | Low |
| Were outcome data available for all, or nearly all, participants? | | | | | |
| | Y | Y | NI | Y | Y |
| Were participants excluded due to missing data on intervention status? | | | | | |
| | NI | Y | NI | NI | Y |
| Were participants excluded due to missing data on other variables needed for the analysis? | | | | | |
| | N | N | NI | N | NI |
| Observation: | We've chosen to assign a "Low" rating to this section due to the adequately comprehensive nature of the data, coupled with the absence of any indications suggesting a notable divergence in the proportion or ratio of missing participant data between the intervention groups. We decided a "Moderate" rating if there are inadequate provision of information regarding the outcome missing data. | | | | |
| **Bias in measurement of outcomes** | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low |
| Could the outcome measure have been influenced by knowledge of the intervention received? | | | | | |
| | PN | PN | PN | PN | PN |
| Were outcome assessors aware of the intervention received by study participants? | | | | | |
| | PY | PY | PY | PY | PY |
| Were the methods of outcome assessment comparable across intervention groups? | | | | | |
| | Y | Y | Y | Y | Y |
| Were any systematic errors in the measurement of the outcome related to the intervention received? | | | | | |
| | N | N | N | N | N |
| Observation: | We decided to score this domain as "Low" risk of bias because our safety events of interest are well defined and we can considered them as a hard outcomes unlikely to be misinterpreted | | | | |
| **Bias in selection of the reported result** | | | | | |
| Risk of bias judgement | Low | Low | Low | Low | Low |
| Is the reported effect estimate likely to be selected, on the bases | | | | | |
| | N | N | N | N | N |
| ... multiple analysis of the intervention-outcome relationship? | | | | | |
| | N | N | N | N | N |
| ... different subgroups? | | | | | |
| | N | N | N | N | N |
| Observation: | We decided to score this domain as having a low risk of bias because we have reported all of the results that we consider to be of interest. | | | | |
| **Overall bias** | | | | | |
| Risk of bias judgement | Moderate | Serious | Serious | Moderate | Serious |

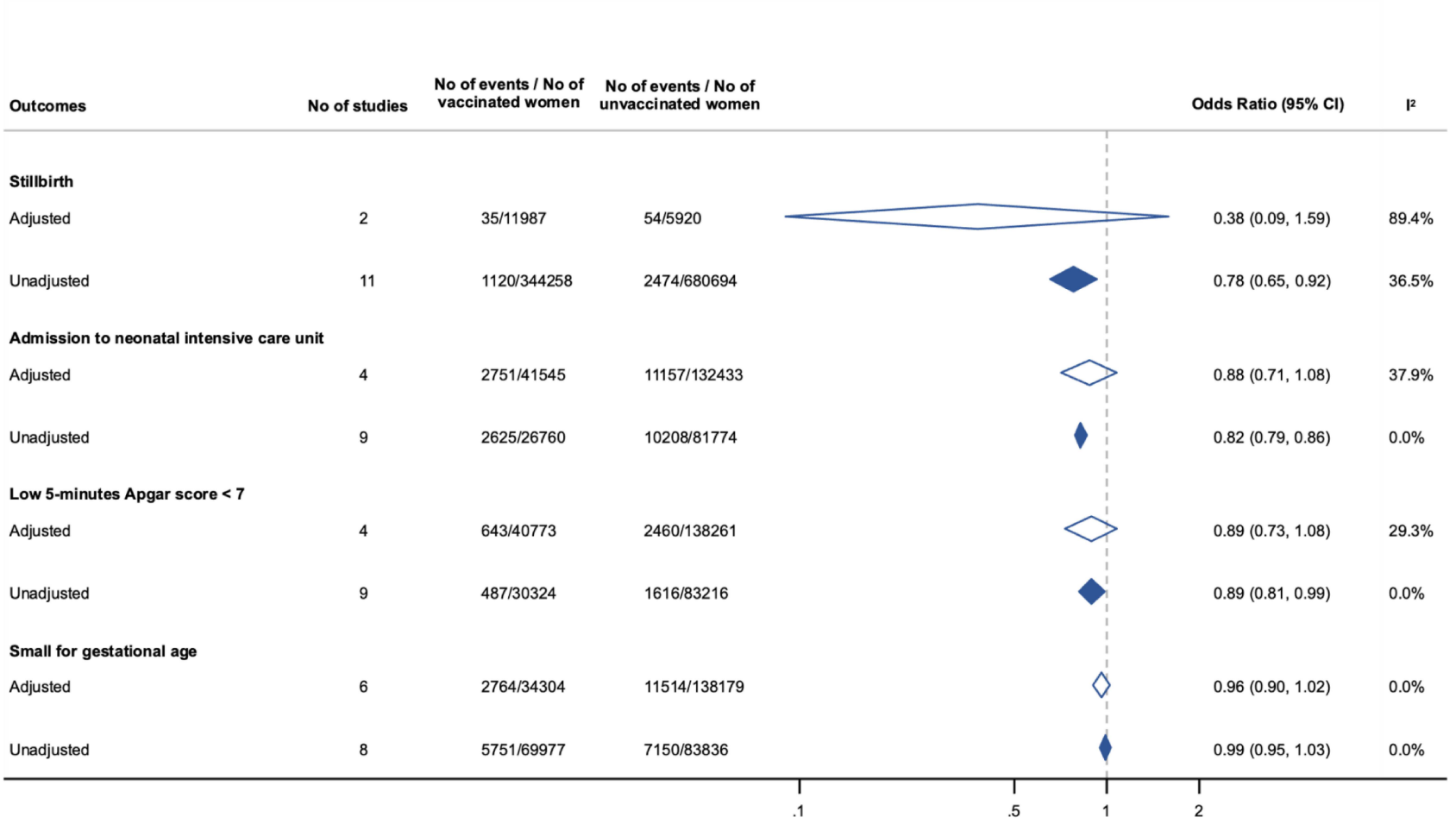
Appendix 5. Vaccine effectiveness for SARS-CoV-2 infection-related outcomes (unadjusted analysis)



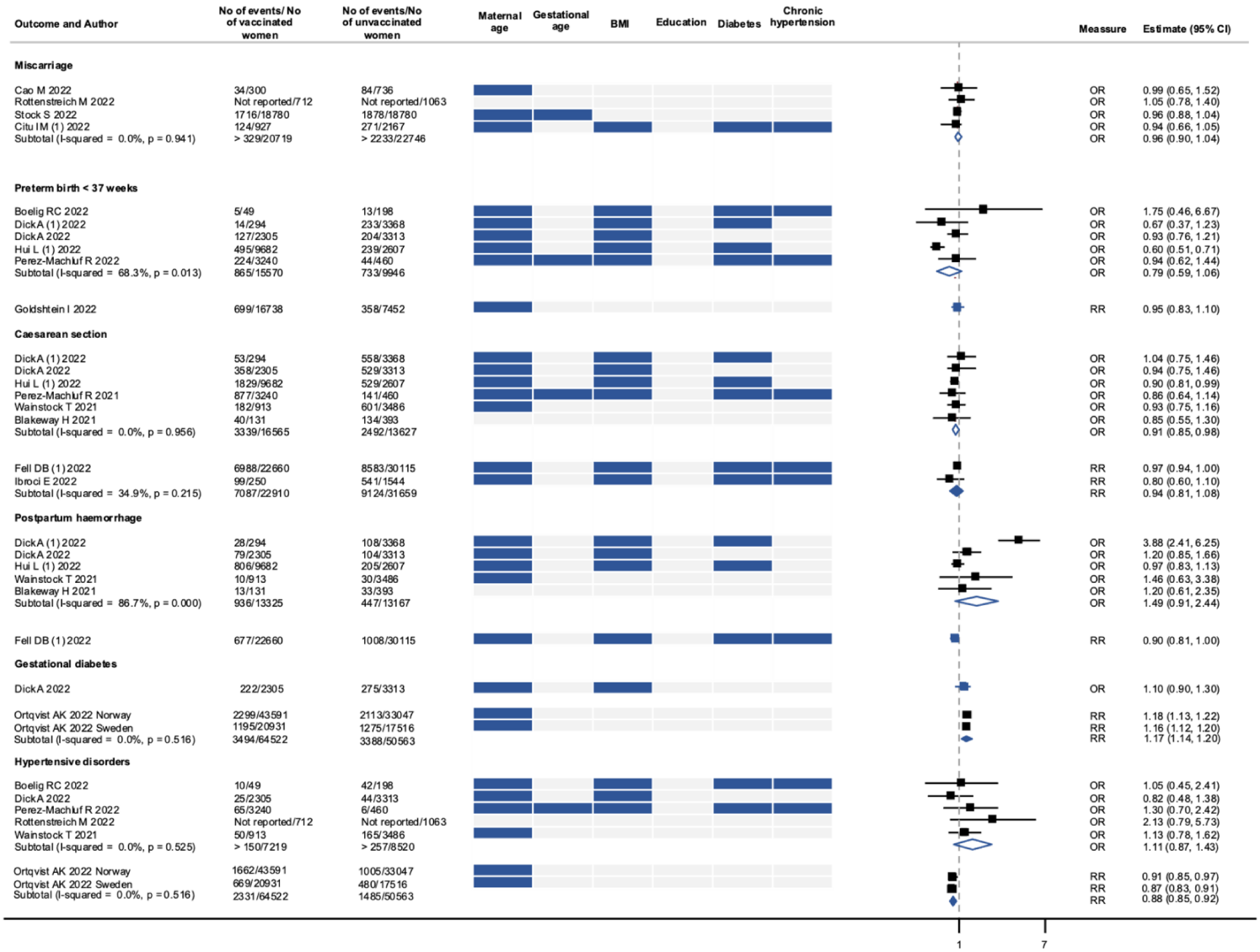
Appendix 6. Effect of vaccine for pregnancy-related maternal outcomes (adjusted and unadjusted analysis)



Appendix 7. Effect of vaccine for pregnancy-related offspring outcomes (adjusted and unadjusted analysis)



Appendix 8. Effect of vaccines on pregnancy-related maternal outcomes (adjusted individual studies)



Appendix 9. Vaccine safety for pregnancy-related offspring outcomes (adjusted individual studies)