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COVID-19 vaccines on maternal

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

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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 metaanalysis and reported findings as HRs, risk ratios (RRs), ORs or rates with 95% Cls.

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% Cl 0.21 to 0.75; 4 studies, 23 927 women; l^2 =87.2%) and 94% reduced odds of hospital admission (OR 0.06, 95% Cl 0.01 to 0.71; 2 studies, 868 women; l^2 =92%). In adjusted cohort studies, the risk of hypertensive disorders in pregnancy was reduced by 12% (RR 0.88, 95% Cl 0.82 to 0.92; 2 studies; 115 085 women), while caesarean section was reduced by 9% (OR 0.91, 95% Cl 0.85 to 0.98; 6 studies; 30 192 women). We observed an 8% reduction in the risk of

WHAT IS ALREADY KNOWN ON THIS TOPIC

- $\Rightarrow\,$ 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.
- \Rightarrow Existing reviews of observational studies do not account for confounding effects when combining studies, resulting in biased estimates and decreased confidence in findings.

neonatal intensive care unit admission (RR 0.92, 95% Cl 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% Cl 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.

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 healthcareseeking 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

- \Rightarrow 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.⁴⁵

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.⁹¹³

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-19like 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 casecontrol studies with a minimum of 10 participants if they reported on reactogenicity outcomes of COVID-19

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 testnegative 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; infectionrelated 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 infectionrelated, 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 infectionrelated 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 I². 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 (1813947 women) from 1326315 identified articles (figure 1). Twenty-four were included in the primary analysis, with eight performing adjusted analysis (185955 women) for SARS-CoV-2 infectionrelated 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 (544314 women).²²⁻³⁷ We included 16 studies (425867 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 analvsis.^{17 18 21–24 29–34 36 38 39 41–60} Twenty-three studies reported reactogenicity outcomes (94206 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; 193889 women), followed by North America (28%, 19/67; 397756 women), Europe and Central Asia (22.5%, 15/67; 1 150 470 women), East Asia and Pacific (10.5%, 7/67; 42204 women) and Latin America and Caribbean (3%, 2/67; 22122 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; 26534 women), one from lower-middle-income countries (1/67; 247 women) and one from a mix of high-income, upper-middle-income and lower-middleincome 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-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 (281030 women), four studies included inactivated virus (3088 women), one study viral vector vaccine (247 women), 14 studies mRNA and/or viral vector vaccines (436453 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 (134779 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 (21722 women) and one from the Delta period and other variants (19838 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 testnegative 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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		M	aternal SARS	-CoV-2 infect	ion		Neonatal S infe	ARS-CoV-2	Severe cov	vid disease	Materna	I hospital a	Imission
	Butt AA 2021 Cohort	Dagan N 2021	Villar J 2023	Butt AA 2021 TND	Paixao ES 2022	Schrag SJ 2022	Carlsen EO 2022	Danino D 2022	Guedalia J 2022	Villar J 2023	Dagan N 2021	Guedalia J 2022	Schrag SJ 2022
Bias due to confounding													
Bias in selection of participants into the study													
Bias in classification of interventions													
Bias due to deviations from intended interventions													
Bias due to missing data													
Bias in measurement of outcomes													
Bias in selection of the reported result													
Overall bias													
													low
													Moderate
													Serious
													Critical



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 infectionrelated 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, 23927 women; I²=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; I²=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

Measure	Estimate (95% CI)
OR OR OR OR	0.12 (0.03, 0.51) 0.59 (0.47, 0.72) 0.17 (0.09, 0.32) 0.84 (0.58, 1.16) 0.39 (0.21, 0.75) (0.02, 6.61)
HR HR HR HR	0.12 (0.03, 0.56) 0.04 (0.00, 0.11) 0.91 (0.82, 1.00) 0.17 (0.02, 1.66) Not estimable
OR	0.14 (0.05, 0.40)
HR HR HR HR	0.04 (0.01, 0.14) 0.17 (0.02, 1.47) 0.52 (0.35, 0.78) 0.16 (0.03, 1.03) Not estimable
OR OR OR	0.02 (0.01, 0.04) 0.23 (0.07, 0.72) 0.06 (0.01, 0.71)
HR HR HR HR	0.11 (0.00, 0.57) 0.39 (0.31, 0.49) 1.12 (0.92, 1.36) 0.47 (0.18, 1.24) Not estimable
OR	0.38 (0.22, 0.68)
HR HR HR	0.29 (0.19, 0.46) 0.67 (0.57, 0.79) 0.45 (0.20, 1.03) Not estimable
ted and ow	ned by
offspring l appendic adjusted i emental ap	outcome ces 6 an ndividua opendice

Outcome and Autho

Maternal SARS-CoV-2 infection Test-negative design Butt AA 2021

MATERNAL

					.005	1	7	
Subtotal (I-squared = 91.8%, p = 0.0 with estimated 95% predictive interva	000) al	410/14312	496/16487				HR	0.45 (0.20 Not estima
Cohorts design Carlsen EO 2022 Carlsen EO 2022	Delta Omicron	25/4696 385/9616	146/9759 350/6728			-	HR HR	0.29 (0.19 0.67 (0.57
Test-negative design Danino D 2022	Delta	19/124	81/262				OR	0.38 (0.22
Offspring SARS-CoV-2 infection								
OFFSPRING								
Cohorts design Dagan N 2021 Guedalia J 2022 Guedalia J 2022 Subtotal (I-squared = 96.2%, p = 0.0 With estimated 95% predictive interva	Alpha/Other Delta Omicron 000) al	1/10861 105/51942 217/8612 323/71415	10/10861 341/30627 207/8282 558/49770				HR HR HR HR	0.11 (0.00 0.39 (0.31 1.12 (0.92 0.47 (0.18 Not estim:
Test-negative design Schrag SJ 2022 Schrag SJ 2022 Subtotal (I-squared = 92.0%, p = 0.0	Delta Omicron 100)	4/158 8/40 12/198	253/498 60/172 313/670				OR OR OR	0.02 (0.01 0.23 (0.07 0.06 (0.01
Maternal hospital admission								
Cohorts design Guedalia J 2022 Guedalia J 2022 Villar J 2023 Subtotal (I-squared = 85.7%, p = 0.0 with estimated 95% predictive interva	Delta Omicron Omicron 101) al	3/51942 1/8612 36/1598 40/62152	64/30627 5/8282 85/1732 154/40641	_		-	HR HR HR HR	0.04 (0.01 0.17 (0.02 0.52 (0.35 0.16 (0.03 Not estima
Test-negative design Paixao ES 2022	Delta/Other	Not reported/801	Not reported/17805		_	- -	OR	0.14 (0.05
Severe COVID-19 disease								
Cohorts design Butt AA 2021 Dagan N 2021 Villar J 2023 Subtotal (I-squared = 95.4%, p = 0.0 with estimated 95% predictive interval	Alpha/Beta Alpha/Other Omicron 000) al	2/407 3/10861 525/1598 530/12866	15/407 64/10861 632/1732 711/13000		-		HR HR HR HR	0.12 (0.03 0.04 (0.00 0.91 (0.82 0.17 (0.02 Not estima
Test-negative design Butt AA 2021 Paixao ES 2022 Schrag SJ 2022 Subtotal (I-squared = 87.2%, p = 0.0 with estimated 95% predictive interva	Alpha/Beta Delta/Other Delta Omicron 000) al	16/103 168/801 17/498 64/223 265/1625	370/1117 6886/17805 443/2282 325/1098 8349/22302				OR OR OR OR	0.12 (0.03 0.59 (0.47 0.17 (0.09 0.84 (0.58 0.39 (0.21 (0.02, 6.6

Chroni

Education Diabotor

Figure 3 Vaccine effectiveness for SARS-CoV-2 infection-related outcomes. BMI, body mass index. Creat the authors.

infection-related outcomes, this reduction does not reach statistical significance (figure 3). We did not find any testnegative 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; 115085 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; 30192 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; 54569 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 o nes are provided in online supplemental nd 7. The summary findings from the ual studies are provided in online supple ices 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; 27195 women), followed by fatigue (29%, 95% CI 15% to 46%; 14 studies; 72671 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; 82972 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.

Table 1 Summary estimates reported in	n test-negativ	e design (adjusted)	, compa	rative cohort	(adjusted) and compara	tive coho	ort (unadjusted) s	studies	
	Test-negat	iive design (adjuste	d)	Comparativ	e cohort (adjusted)		Comparative c	ohort (unadjusted)	
Outcome	No. of studies (women)	HR (95% CI)	l² (%)	No. of studies (women)	Estimate (95% Cl)	l² (%)	No. of studies (women)	OR (95% CI)	1 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 5min 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)				
Created and owned by the authors. *As reported in the individual studies, adjuste RR, risk ratio.	ed cohort resu	lts for pregnancy-rel	ated mate	ernal and offsp	ring outcomes are shown	as OR or	RR.		

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Table 2 R	sactogeni	city outcomes i	in pregnant women v	accinat	ed for CO	VID-19						
	Partially	vaccinated			Fully vac	cinated			Any num	oer of doses		
Side effects	No. of studies	No. of events	Proportion (95% CI)	l ² (%)	No. of studies	No. of events	Proportion (95% CI)	l² (%)	No. of studies	No. of events	Proportion (95% CI)	l² (%)
-ever	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
leadache	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	80	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
-atigue	80	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
Dain at njection site	2	20540/22 922	0.85 (0.76 to 0.93)	99.3	ω	16 896/18 608	0.80 (0.73 to 0.85)	98.1	1	21 623/27 195	0.77 (0.52 to 0.94)	99.9
Created and o	wned by th	le authors.										

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.⁸¹⁸² 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

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 100000 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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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.	
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

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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.

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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

- 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 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 "3217786" 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 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 $12^{\rm th}$ 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 Collection period	Adjustement variables	Inclusion and exclusion criteria	Population exposed to covid-19 vaccine	Vaccine platform Vaccine product Doses (no. women vaccinated)	Time of vaccination (trimester)	Reported outcomes of interest
Arulappen AL, 2022	Retrospective cohort	Malaysia 6 General hospitals in the state of Penang March 2021 -	NA	Inclusion All pregnant employees who consented to take the mRNA vaccine. Exclusion Vaccinated pregnant employees who refused to give consent to participate in the study	121	mRNA Pfizer- BioNTech One dose (121) Two doses (121)	During pregnancy (1st, 2nd, 3rd)	Headache Myalgia Fatigue

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

				informed				
				consent				
				Exclusion				
				Pregnant				
				women with				
				active maternal				
				COVID-19				
				disease at				
				delivery				
Blakeway H	Retrospective	United	Non specified	Inclusion	140	mRNA/Viral	During	Maternal
2021	cohort	Kingdom	rion speemea	All pregnant	110	vector	nregnancy	covid
2021	conore	Ringdom		women with		veetor	(2nd 3rd)	infection
		St George's		known		Pfizer-	(2110, 510)	Severe covid
		University		vaccination		BioNTech		disease
		Hospitals		status and		Moderna		uisease
		Tiospitais		status allu				Cassaraan
		March 2020		complete matamal and		ALD		Caesarean
		$\frac{1}{1}$		finaternal and		One data		NICL
		July 2021		lotal outcome		One dose		NICU
				data		(114)		admission
						Two doses		Stillbirth
				Exclusion		(26)		Gestational
				Women who				diabetes
				were				Postpartum
				vaccinated				haemorrhage
				entirely (i.e.,				Small for
				all doses)				gestational
				before				age
				pregnancy or				
				after birth or				

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

				matches the information in both questionnaires and answering all questions until the form is submitted) <i>Exclusion</i> 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				
Boelig RC, 2022	Retrospective cohort	USA Thomas Jefferson University Hospital	Age BMI Ethnicity Diabetes Chronic hypertension	<i>Exclusion</i> <i>Exclusion</i> Pregnant patients with both COVID-	49	mRNA Non specified Non specified	During pregnancy (non specified)	Preterm birth <37 weeks Hypertensive disorder in pregnancy

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

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

				SARS-CoV-2				
				by RT-PCR on				
				a				
				nasopharyngea				
				1 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	China	Age	Inclusion	502	Inactivated	Before	Miscarriage
	cohort		Infertility	Women with		virus	pregnancy	
		Guangzhou	duration	confirmed				
		Medical	Number of	vaccination		Sinovac-		
		University	COS cicles	status from		CoronaVac		
			Protocols of	public health		Sinopharm		
		March 2021 –	COS	surveillance		BIBP		
		September	Endometrial	system record				
		2021	preparation	of their		One dose		
			protocol	smartphone		(30)		

	Number of	app, the first or	Two doses	
	embryos	second cycle	(472)	
	transferred	of frozen-	(1/2)	
	Number of	thawed		
	top_quality	embryos		
	ombruos	transforrad		
	chibiyos	women in		
		women m		
		vaccillated		
		group nad		
		embryos factor anion to		
		frozen prior to		
		the exposure to		
		Covid-19		
		vaccines, and		
		women aged		
		20-40 years		
		old		
		Exclusion		
		Women with		
		three or more		
		cycles of		
		controlled		
		ovarian		
		stimulation,		
		women with		
		repeated		
		spontaneous		
		miscarriage,		
		women with		

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

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

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

		December 2020 – March 2021				Two doses (29)		
COVID- NET, 2021	Retrospective cohort	USA Nk	NA	Inclusion	11	mRNA/Viral vector	During pregnancy (non	Severe covid disease
		January 2021 – November				Pfizer- BioNTech Moderna	specified)	Miscarriage Caesarean section
		2021				Janssen		Maternal death
						Non specified		Preterm birth <37 weeks Stillbirth
Dagan N, 2021	Prospective cohort	Israel	Age Trimester of	Inclusion All pregnant	10861	mRNA	During pregnancy	Maternal covid
		Clalit Health	pregnancy	women aged		Pfizer- BioNTach	(1st, 2nd, 3rd)	infection Sovere covid
		(CHS)	living area	older, with		DIOINTCCII	510)	disease
			Population	continuous		Two doses		Maternal
		December 2020 – June	sector Count of	CHS		(10861)		admission
		2021	influenza	for 1 complete				Maternal
			vaccination in	year, no				death
			the last 5	previous				
			Existence of	SARS-CoV-2				
			at least one	PCR test. no				
			CDC and	previous				
			prevention	SARS-CoV-2				

			risk factor for	vaccination.				
			severe disease	not residing in				
			(obesity	long-term care				
			diabetes	facilities no				
			hypertension)	home				
			nypertension)	confinement				
				due to medical				
				reasons not				
				hoing a				
				beilig a				
				worker and no				
				interaction				
				with the				
				haalthaara				
				inearthcare				
				system in the				
				previous 2 d				
				Evolution				
				Exclusion				
				Pregnant				
				women with				
				missing data in				
Denine D	Testassi	Terre el	Etherica i da a	CHS Inclusion	202		Dearing	N. e. m. et al.
Danino D	Test negative	Israel	Elinnicity	Inclusion	202	MKNA	During	Neonatai
2022	case-control	0 1	Prematurity	Symptomatic		DC	pregnancy	covid
		Soroka		infants		Pfizer-	(2nd, 3rd)	infection
		Medical		suspected of		BIONTech		Preterm birth
		center,		SARS-CoV-2				
		Schneider		intection by a		Two doses		
		medical		physician		(202)		
		center, Shamir						

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

				Women with		Three doses		Hypertensive
				multiple		(non		disorder in
				pregnancy,		specified)		pregnancy
				vaccination				Gestational
				prior to				diabetes
				pregnancy,				Abnormal
				COVID-19				apgar 5
				infection				
				during or				
				before				
				pregnancy, or				
				unknown				
				timing of				
$\mathbf{D}^{\prime} 1 \mathbf{A} 1$	Detrement	T	A	vaccination	29.45		Data	Destance 1 ref
Dick A(1),	Retrospective	Israel	Age	Inclusion	2845	MKNA	During	Preterm birth
2022	conort	N	DIVII Naulia anita	women with		Dfine	pregnancy (2 nd)	N37 Weeks
		INF	Nulliparity	singleton		Plizer-	(3rd)	Small for
		1 1 2021	Gestational	pregnancies		BION LECH		gestational
		July $2021 -$	diabetes Smalsing	who delivered		Moderna		age
		October 2021	Smoking	In the period		True deses		Caesarean
				July-October		Two doses		Section De stra articula
				2021		(2843) Three deser		Postpartum
				T 1 ·		(204)		naemormage
				Exclusion		(294)		Suiidirtu
				women with				Hypertensive
				multiple				disorder in
				COVID-19				Gestational
								Ocstational
				intection				diabetes
				infection				diabetes

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

				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,	Retrospective	Canada	NA	Inclusion	43099	mRNA/Viral	During	Stillbirth
2022	cohort			Completed		vector	pregnancy	Preterm birth
		Better		pregnancies			(1st, 2nd,	< 37 weeks
		Outcome		between 1 May		Pfizer-	3rd)	Small for
		Registry and		and 31		BioNTech		gestational
		Network		December		Moderna		age
		Ontario Birth		2021		AZD		
		Registry						
						One dose		
				Exclusion		(13416)		
		May 2021 –		Births to non-		Two doses		
		December		Ontario		(29650)		
		2021		residents and		Three doses		
				births from		(33)		
				pregnancies				
				conceived less				
				than 42 weeks				
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				before the end				
				of the study.				
				Any records				
				with				
				gestational age				
				< 20 weeks				
				and birth				
				weight ≤ 500				
				gr or				
				following				
				nregnancy				
				termination				
Fell DB (1)	Retrospective	Canada	NΔ	Inclusion	22660	mRNA/Viral	During	Maternal
2022	cohort	Callada	1 1 1 1	Pregnancies	22000	vector	pregnancy	covid
2022	conort	Better		with a birth		vector	(1st 2nd	infection
		Outcome		date or		Dfizor	(1st, 2hd, 3rd)	Postpartum
		Degistry and		avported due		PioNTach	510)	hoomorrhogo
		Notwork		data on or after		Moderna		Cassoroon
		Ontonio Dinth		December 14				Caesalean
		Diliario Dilui		December 14,		ALD		NICU
		Registry		the COVID 10		Non encoified		NICU
		Describer				Non specified		
		December		vaccination				Abnormai
		2020 -		program began				apgar 5
		September		in Ontario)				
		2021						
				Exclusion				
				Ongoing				
				pregnancies as				
				of September				

				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				
				documented gestational age less than 20 weeks at birth, and pregnancy terminations				
Gandhi AP, 2022	Prospective cohort	India July 2021 – October 2021	NA	Inclusion Pregnant women registered with the ANC clinics who went for covid- 19 vaccination <i>Exclusion</i>	247	Viral vector AZD One dose (247)	During pregnancy (non specified)	Fever Pain at injection site

				Women less than 18 years of age and who did not consent to participate in the follow- up				
Goldshtein I, 2021	Retrospective cohort	Israel Maccabi Healthcare Services Database December 2020 – February 2021	NA	Inclusion All pregnant women in the health fund <i>Exclusion</i> 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 Pfizer- BioNTech Non specified	During pregnancy (non specified)	Maternal covid infection Maternal death Maternal hospital admission Preterm birth <37 weeks Stillbirth Hypertensive disorder in pregnancy

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

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

the CDC-	before		
funded	pregnancy and	Two doses	
overcoming	the second	(231)	
COVID-19	dose during		
network	pregnancy		
July 2021 –			
March 2022	Exclusion		
	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		

				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 12 Public Maternity Hospitals in Melbourne July 2021 – March 2022	Age BMI Metropolitan vs regional residence Smoking Region of birth Socioeconomi c index for postcodes Diabetes Parity Infant sex Gestation at first antenatal visit Need for interpreter	<i>Inclusion</i> Births ≥ 20 weeks from all 12 public maternity hospitals in Melbourne from 1 st July 2021 to 1 st March 2022 <i>Exclusion</i> Births in exclusively private hospitals and planned home births outside of publicly funded	17365	mRNA Non specified Non specified	Before/durin g pregnancy	Gestational diabetes Stillbirth Preterm birth <37 weeks NICU admission Abnormal apgar 5 Postpartum haemorrhage Caesarean section

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

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

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

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

		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,		

				human immunodeficie ncy virus, syphilis, toxoplasmosis,				
				cytomegalovir				
				us.				
Lipkind HS,	Retrospective	USA	NA	Inclusion	10064	mRNA/Viral	During	Preterm birth
2022	cohort			Singleton live		vector	pregnancy	<37 weeks
		VSD sites in		births from			(1st, 2nd,	Small for
		California,		eight VSD		Pfizer-	3rd)	gestational
		Colorado,		sites, females		BioNTech		age
		Minnesota,		aged 16-49		Moderna		
		Oregon,		years with		Janssen		
		Washington,		estimated				
		and		pregnancy start				
		Wisconsin		during May 17		One dose		
		(Kaiser		– October 24,		(2183)		
		Permanente:		2020, and		Two doses		
		Colorado,		expected		(7881)		
		Northern		delivery dates,				
		California,		based on a 40-				
		Northwest,		week				
		Southern		gestation,				
		California,		Labrary 21				
		allu Washington:		$\frac{1}{100} \frac{1}{100} \frac{1}{21} \frac{1}{2000} \frac{1}{100} \frac{1}$				
		Vi asiiiigioii, Danvar		$\begin{bmatrix} July & J1, & 2021, \\ and all \end{bmatrix}$				
		Health;		COVID-19				

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

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

				individuals				
				who received				
				the Johnson &				
				Johnson				
				vaccine				
Mascolo A 2022	Retrospective cohort	Israel EV database January 2021- December 2021	NA	<i>Inclusion</i> <i>Excluded</i> ICSRs with PTs referred to extraction criteria and without AEFI, uncertain information on the vaccine exposure during pregnancy, and sex or age incoherent or	3252	mRNA/Viral vector Pfizer- BioNTech Moderna Janssen AZD Non specified	During pregnancy (non specified)	Headache Fatigue Myalgia Pain at injection site
		T 1		unknown	105	DNIA		
Mayo RP,	Prospective	Israel	NA	Inclusion	125	mRNA	During	Preterm birth
2021	conort	0		Pregnant		DC	pregnancy (2 d 2 d)	NICU
		8 medical		women		Prizer-	(2nd, 3rd)	NICU
		centres in		admitted for		BIOIN LECU		admission
		Israel		delivery at 8				
		(Hadassah		medical		Two doses		
		Mount		∣ centres, ≥18		(125)		

		Scopus, Wolfson, HaEmek, Hillel Yafe, Rabin, Shaare Zedek, Meir, and Sourasky Medical Centers) January 2021 – June 2021		years old and willing to provide informed consent <i>Exclusion</i> Pregnant women with active COVID- 19 infection				
Montalti M, 2022	Cross- sectional study	Italy Online survey – January 2021	NA	Inclusion 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 Pfizer- BioNTech One dose (31) Two doses (17)	During pregnancy (non specified)	Fever Fatigue Myalgia Headache

				Exclusion				
Ortqvist AK. 2022	Retrospective cohort	Sweden Norway Swedish pregnancy register Medical Birth Register in Norway May 2021 – May 2022	Age	<i>Exclusion:</i> Vaccinated prior pregnancy	69512	mRNA/Viral vector Pfizer- BioNTech Moderna AZD One dose (9702) Two doses (47699) Booster dose (12111)	Before/durin g pregnancy (non specified)	Gestational diabetes Hypertensive disorder in pregnancy
Paganoti CDF, 2022	Retrospective cohort	Brazil SIVEP-Gripe registry May 2021 – November 2021	NA	<i>Inclusion:</i> 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/Inacti vated virus Non specified Non specified	During pregnancy (non specified)	Severe covid disease Maternal death

				negative RT-				
				PCR or antigen				
				for influenza.				
				Availability of				
				the outcome				
				(recovery or				
				death) and				
				reliability of				
				vaccination				
				status.				
				No exclusion				
				criteria				
Paixao ES	Test negative	Brazil	Age	Inclusion.	2033	Inactivated	During	Maternal
2022	case-control	Diali	Ethnicity	Pregnant	2000	virus	pregnancy	covid
		Brazilian	Comorbidities	women with			(non	infection
		Ministry of	Region of	symptoms		Sinovac-	specified)	Severe covid
		Health	residence	suggesting		CoronaVac	1 /	disease
			IBP	Covid-19,				
			Time	aged between		One dose		
		January 2021-		18 and 49		(995)		
		October 2021		years in Brazil		Two doses		
				with a record		(1038)		
				of a RT-PCR				
				test between				
				March 15,				
				2021, and				
				October 03,				
				2021,				

		registered in e-		
		SUS Notifica.		
		Exclusion:		
		Subjects who		
		received any		
		Covid-10		
		Vaccine:		
		ChAdOx1		
		nCoV-19 or		
		Ad26.COV2.S		
		(Janssen/Johns		
		on & 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		

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

		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 Shaare Zedek Medical Center (SZMC) and the Bikur Holim Medical Center (BHMC) January 2021 – April 2021	NA	Inclusion All pregnant women admitted for delivery aged 18 years or older, with no documented previous positive SARS-CoV-2	712	mRNA Pfizer- BioNTech Two doses (712)	During pregnancy (3rd)	Severe covid disease Caesarean section Preterm birth <37 weeks NICU admission Pospartum haemorrhage Abnormal Apgar 5 Stillbirth

								Hypertensive
								disorders
								Small for
								gestational
D	D	T 1			1500	DILA		age
Rottenstreich	Retrospective	Israel	NA	Inclusion	1720	mRNA	During	Caesarean
M (1), 2022	cohort			All women		DC	pregnancy	section
				aged 18 or		Pfizer-	(non	Postpartum
		4		older, without		BioNTech	specified)	haemorrhage
		August 2021		documented		T 1		Preterm birth
		– December		previous		Two doses		<3/ weeks
		2021		positive		(1094) Deceter dece		Small for
				SARS-COV-2		Booster dose		gestational
				rCK test,		(020)		age Stillbirth
				between				NICU
				August 28 and				admission
				December 31				Abnormal
				2021				Abnorman Angar 5
				2021.				Apgai 5
				Exclusion				
				Parturients				
				who were				
				previously				
				positive with				
				covid-19 PCR				
				swabs during				
				or before				
				pregnancy.				

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

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

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

		February 2021						
Smithgall	Prospective	USA	NA	Exclusion:	164	mRNA	During	Caesarena
MC, 2022	cohort			Incomplete			pregnancy	section
		New York		vaccine		Pfizer-	(non	Preterm birth
		city hospital		administration		BioNTech Moderna	specified)	< 37 week Abnormal
		April 2020 –		Inclusion:				Apgar 5
		July 2021		Fully		Two doses		Small for
		5		vaccinated		(164)		gestational
				women, at				age
				least 2 doses of				e
				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.				
Sourouni M,	Prospective	Germany	NA	Inclusion	70	mRNA	During	Fever
2022	cohort			Women given			pregnancy	Pain at
				birth at the		Pfizer-	(1st, 2nd,	injection site
				hospital who		BioNTech	3rd)	

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

Theiler RN, 2021	Retrospective cohort	United States of America Hospitals within the Mayo Clinic Health System December 2021 – April 2021	NA	Inclusion All women aged 16-55 years old who delivered between December 10, 2020, and April 19, 2021 at a Mayo Clinic hospital. <i>Exclusion</i> Minnesota patients who delivered in Minnesota and opted out of use of their medical records for	140	mRNA/Viral vector Pfizer- BioNTech Moderna Janssen Non specified	During pregnancy (1st, 2nd, 3rd)	Maternal covid infection Severe covid disease Maternal death Caesarean section Preterm birth <37 weeks NICU admission Abnormal Apgar 5 Stillbirth Hypertensive disorders Postpartum haemorrhage
				research				
Toussia- Cohen S (2), 2022	Prospective cohort	Israel Online questionnaire January 2021 – November 2021	NA	<i>Exclusion:</i> Chronic hypertension, chronic kidney disease, antiphospholip id syndrome, systemic lupus,	162	mRNA Pfizer- BioNTech Doses 1 and 2 (78)	During pregnancy (2nd, 3rd)	Fever Myalgia Headache 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 UKHSA January 2021 – June 2022	NA	Not reported	258639	mRNA/Viral vector Pfizer- BioNTech Moderna AZD	During pregnancy (non specified)	Preterm birth <37 weeks Stillbirth
Villar J, 2023	Prospective cohort	Argentina, Brazil, Egypt, France, Indonesia, Israel, Italy, Japan, Mexico, Nigeria, North Macedonia, Pakistan, Spain,	Age Overweight or obesity Presence or absence of any pre-existing medical condition Country	<i>Inclusion</i> Women with a documented diagnosis of covid-19. Live and stillborn singleton and multiple births, and newborn babies with	2886	mRNA/Viral vector/Inactiv ated virus Pfizer- BioNTech Moderna Janssen AZD SinoVac	During pregnancy (non specified)	Maternal covid infection Severe covid disease Caesarean section Hypertensive disorders Preterm birth <37 weeks

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

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

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

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

Initial Adv 2021 Cohort Data No. 2022 Ville / 2023 Initial Adv 2021 TRD Palese DS 2022 S 5 Bits of base posterial or controlling of the effects of intervention in facts table representation of the effects of the pale of the effects of the effects of the pale of the pale of the pale of the effects of the pale of the pale of the pale of the pale of the effects of the pale	Schrag SJ 2022 Low Y Y N	aixao ES 2022		Butt AA 2021 TND	Villar J 2023 Moderate	Dagan N 2021 Moderate	Butt AA 2021 Cohort Moderate ding of the effect of interven	as due to confounding sk of bias judgement
Add that substantial Moderate Moderate Moderate Low is there participated in a substantial of an endershift of attraversion in this subs? Y Y Y Y with a authors use an appropriate analysis method that controlled for all the important ordnaming domaina? Y Y Y Y with a authors use an appropriate analysis method that controlled for all the important ordnaming domaina? Y Y Y Y with exactions: use an appropriate analysis method that could have been affected by theinservention? N N N N Add the authors: control for any post-intervention variables that could have been affected by theinservention? N N N Add the authors: control for any post-intervention variables used for sub-adjustments are limited in numer or tack valiant with ordinal bits control, the valiant with an author with the valiant the included articles are discarding articles. But AR 2017 TWP, Proise S 2022, pub Schng S 2022, TWB	Y Y N	Low Y	Ì	Low	Moderate	Moderate tion in this study?	Moderate ding of the effect of interven	sk of bias judgement
there potential for confuseding of the effect of intervention in this study? V	Y Y N	Y				tion in this study?	ding of the effect of interven	these notential for conform
the authors use an appropriate analysis method that controlled for all the important confounding domains? Y <t< td=""><td>Y N</td><td></td><td></td><td>Y</td><td>Y</td><td>Ŷ</td><td>Y</td><td>there potential for conroun</td></t<>	Y N			Y	Y	Ŷ	Y	there potential for conroun
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ere confounding domains that were controlled for measured validity and reliably by the variables available in this study? It is a confounding domains that were controlled for measured validity and reliably by their envention? N	N	Y [Y	contounding domains? Y	ontrolled for all the important Y	v Y	the authors use an approp
the calculation of participants in the calculation of participant characteristics observed after the start of the intervention? If we authors control for any post-intervention variables that could have been affected by theintervention? N Given that all be included articles are observational in nature, there exists a pointial for conforming. While acceptable adjunctment techniques areas en referented to minimize this concern, the variables and for cut adjunctments are finited in number or take wildings and takes and the start adjunctment techniques areas en referented to minimize the included articles are observational in nature, there exists a pointial for conforming. While acceptable adjunctment techniques servation: If a different is the included articles are observational in nature, there exists a pointial for conforming will be acceptable adjunctment techniques servation: If a different is the included articles are observational in nature, there exists a soft of the intervention? If a different is the included articles are observed after the start of the intervention? If a different is the included articles are observed after the start of the intervention? If a different is the included articles are observed after the start of the intervention? If a different is the included articles are observed after the start of the intervention? If a different is the included articles are observed after the start of the intervention? If a different is conside for nost participant characteristics observed after the start of the intervention? If a different is the intervention characteristics observed after the start of the intervention? If a different is the intervention characteristics observed after the start of the intervention? If a different is the intervention characteristics observed after the start of the intervention? If a different is the intervention characteristics observed after the start of the intervention? If a different is the intervention characteristics observed after the start of	N			+.2	a variables available in this s	ured validly and caliably by the	hat were controlled for meas	asa confounding domains t
the authors control for any post-intervention variables that could have been affected by theintervention? N <t< td=""><td></td><td>N</td><td><u> </u></td><td>N</td><td>N</td><td>N</td><td>N</td><td>ere contouriung domains o</td></t<>		N	<u> </u>	N	N	N	N	ere contouriung domains o
N N N N N N N Given that all the included articles are observational in nature, there exists a potential for confounding. While acceptable adjustment techniques were en articles to mitigate this concern, the variables used for such adjustments are limited in number or lade validity and eliability. However, or unsassment his life to be savige a "Gw" tarting to the following articles tot. Adjustments are limited in number or lade validity and the following structured to harthcare-seeking behaviors. Set Abs indicement Low					by theintervention?	that could have been affected	v post-intervention variables	d the authors control for an
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sk of blas judgement. Low Low Seriou Low	ere employed across decision is based or ccess to and utilizat	ljustment techniques w y. on Schrag SJ 2022. This on a population with a viors.	acceptable and reliabi ao ES 2022, iely, the foc seeking be	or confounding. While act number or lack validity ar utt AA 2021 TND, Paixao negative design—namely rributed to healthcare-se	ture, there exists a potential ch adjustments are limited i ting to the following articles: significant aspect of the tes ze unmeasured confounding	rticles are observational in na tern, the variables used for su is led us to assign a "Low" rat HO article], which highlights a e restriction serves to minimia	Given that all the included a articles to mitigate this con However, our assessment h rationale outlined in the [W medical care. This deliberat ts into the study	bservation: as in selection of participar
as the selection of participants into the study based on participant characteristics observed after the start of the intervention? N Y Y Y Y istart of follow-up and start of intervention coincide for most participants? PN PN<	Low	Low		Low	Serious	Low	Low	sk of bias judgement
N N Y Y Y start of follow-up and start of intervention coincide for most participants? PY PN PD				rvention?	erved after the start of the ir	articipant characteristics obs	ants into the study based on p	as the selection of participa
Start of Norw op Norw PK PK PN PN PN are adjustment techniques used that are likely to correct for the presence of selection biases? NA NA N N N Trough collaborative agreement, we determined that assigning allow risk of bias to this domain would be appropriate when participants in contrast, the study is 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 selection was lased on post-intervention, these designs have undergone extensive validation for assessing vaccine efficacy (WHO reference in the start of the intervention and the start of the intervention? in classification of intervention groups recorded at the start of the intervention? PY PY Y Y Y as the information used to define intervention groups recorded at the start of the intervention? PY PY Y Y Y We decided to score this domain as having a low risk of bias if the study described the intervention in tervention in tervention status have been affected by knowledge of the outcome or risk of the outcome? PN PN PN PN PN PN Image: PN PN	<u>Y</u>	Y		Y	Y	N N	N t of intervention coincide for	start of follow-up and star
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rere intervention groups clearly defined? Y N Y Y Y as the information used to define intervention groups recorded at the start of the intervention? PY PY Y Y Y as the information used to define intervention groups recorded at the start of the intervention? PY PY Y PY Y Y uld the classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? PN Edwards and the dose adm	Low	Low		Low	Low	Moderate	Low	k of bias judgement
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re participants excluded due to missing data on intervention status?	Moderate	Moderate		Low	Low	Low	Low	k of bias judgement
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No real 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 handling of missing data within the outcome evaluation process. I measurement of outcomes	N lications suggesting	N In the absence of any in	coupled w	N ive nature of the data	N to the adequately comprehe	PY ow" ratios to this section due	NI We've chosen to assign a "I	
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re any systematic errors in the measurement of the outcome related to the intervention receivedr	N	N		N	tion received? N	N	N	re any systematic errors in
Given the observational and retrospective nature of these articles, we acknowledge that clinicians were likely aware of the patients' allocation to specific 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 (pecific intervention esign (TND) studies,	patients' allocation to s tially introducing bias. ver, for test-negative d	aware of th status, pot ributes. Hov	clinicians were likely aw ients' COVID infection st ing these inherent attribu	articles, we acknowledge th ave been influenced by the p ate for cohort studies, consid	retrospective nature of these cover, this awareness might h rating was deemed appropria	Given the observational and groups in all instances. More Consequently, a "Moderate"	
s in selection of the reported result	crations.	. to the outlined consid	a assigned (ej, a cow raung was a	5 criectiveness (WHO refere	tensues pertinent to assessin	ed result	is in selection of the report
		Low		Low	Low	Low	Low	k of bias judgement
ik of blas judgement Low Low Low Low Low Low	Low		domain?	s within the outcome dor	ultiple outcome measureme	bases of the result from m	e likely to be selected, on the	he reported effect estimat
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ik of bias judgement Low	Low N	N [N	N	ip? N	ervention-outcome relations N	multiple analysis of the int different subgroups?
sk of bias judgement Low	Low N N	N I	we consider	N N all of the results that we	N N ias because we have reporte	ip? N N main as having a low risk of b	ervention-outcome relations N N We decided to score this do	multiple analysis of the int different subgroups? sservation:

Table 2. Neonatal SARS-CoV-2 infection

Table 3. Severe covid disease

	Carlsen EO 2022	Danino D 2022	Guedalia 2022 Villar 2023
Bias due to confounding	Canacia de Loca	Contro o zocc	Bias due to confounding
Risk of bias judgement	Moderate	Critical	Risk of bias judgement Moderate Moderate
Is there potential for confounding of	the effect of intervention in this stud	y? I pv	Is there potential for confounding of the effect of intervention in this study?
		F1	Did the authors use an appropriate analysis method that controlled for all the
Did the authors use an appropriate a	nalysis method that controlled for all	the important confounding domains	important confounding domains?
Were confounding domains that we	Y Y controlled for measured validly and	Y Freliably by the variables available in	PY Y Were confounding domains that were controlled for measured validly and reliably b
this study?	e controlled for measured fundity and		the variables available in this study?
	N	N	N N
Did the authors control for any post-	ntemention variables that could have	been affected by the intervention?	Did the authors control for any post-intervention variables that could have been affected by the intervention?
bid the additions condition on any post-	N	Y	N N
	Given that all the included articles a	re observational in nature, there	
	exists a potential for confounding. V	Vhile acceptable adjustment	
	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 base	i i
19	on the use of the variable "Prematu	rity" as an adjustment variable, this	22 5 25 25 25 1
Observation: Bias in selection of participants into	being a post-intervention variable.		Observation: We decided by consensus Blas in selection of participants into the study
Risk of bias judgement	Serious	Low	Risk of bias judgement Low Serious
Was the selection of participants int	o the study based on participant char	acteristics observed after the start of	Was the selection of participants into the study based on participant characteristics
the intervention?	N	v	observed after the start of the intervention?
Do start of follow-up and start of int	ervention coincide for most participal	i	Do start of follow-up and start of intervention coincide for most participants?
	N	PN	Y PN
Ware adjustment to halo and the	at are likely to correct for the correct	se of selection biar3	Were adjustment techniques used that are likely to correct for the presence of relection biogen?
were adjustment techniques used th	N	N	NA N
	Through collaborative agreement, w	e determined that assigning a low	
	risk of bias to this domain would be selection relied on pre-intervention	appropriate when participant baseline characteristics and when the	
	initiation of follow-up and the comm	nencement of intervention aligned for	
	most participants. In contrast, the st	tudy conducted by Carlsen EO 2022	
Observation:	received a classification of "Serious"	' risk due to the lack of alignment	Observation: We decided by consensus
Bias in classification of interventions Risk of bias judgement	Low	low	Bias in classification of interventions
Were intervention groups clearly def	ined?	1 100	Were intervention groups clearly defined?
	Y	Y	<u> </u>
			Was the information used to define intervention groups recorded at the start of the
Was the information used to define	Intervention groups recorded at the s	v	v v
Could the classification of intervention	on status have been affected by know	ledge of the outcome or risk of the	Could the classification of intervention status have been affected by knowledge of the
outcome?	*****		outcome or risk of the outcome?
	PN We decided to score this domain as	PN having a low risk of bias if the study	PN PN
	described the intervention in terms	of the type of vaccine used and the	
Observation:	dose administered		
	dose doministered.		Observation: We decided by consensus
Bias due to deviations from intended	l interventions	1	Observation: We decided by consensus Blas due to deviations from intended interventions Blab due to deviations from intended interventions Blab due to deviations Blab due to deviation
Blas due to deviations from intended Risk of bias judgement	l interventions Low	Low	Observation: We decided by consensus Blas due to deviations from Intended interventions Risk of bias judgement Low Low Were there deviations from the intended intervention beyond what would be
Blas due to deviations from intender Risk of blas judgement Were there deviations from the inter	interventions Low nded intervention beyond what would	Low	Observation: We decided by consensus Blas due to deviations from intended interventions Risk of blas judgement Low Low Low Were there deviations from the intended intervention beyond what would be expected in usual practice?
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Bias due to confounding	Dagan N 2021	Guedalia J 2022	Schrag SJ 2022			
Blas due to confounding Risk of bias judgement	Moderate	Moderate	Moderate			
Is there potential for confou	unding of the effect of inte	rvention in this study?	i moderate			
	Y	PY	Y			
Did the authors use an ap	opropriate analysis method	I that controlled for all the imp	portant confounding domains			
	Y Y	PY	Ý			
Were confounding domains study?	that were controlled for n	neasured validly and reliably b	y the variables available in th			
510071	N	N	N			
Did the authors control for a	any post-intervention varial	bles that could have been affe	cted by theintervention?			
Observation: Bias in selection of particip	We decided by consensu	us We decided by consensu	s			
Risk of bias judgement	Low	Low	Serious			
Was the selection of partici	pants into the study based	on participant characteristics	observed after			
the start of the intervention	N	N	Y			
Do start of follow-up and st	art of intervention coincide	e for most participants?				
	PY	Υ	PN			
Were adjustment technique	es used that are likely to co	prect for the presence of select	tion biases?			
	NA	<u> NA</u>	N			
Observation:	We decided by consense	us We decided by consensu	S			
Risk of bias judgement	Moderate	Low	Low			
Were intervention groups cl	learly defined?					
	N	Y	<u> </u>			
Was the information used t	o define intervention group	ps recorded at the start of the	intervention?			
	I PY	N. N.	V V			
Could the classification of in outcome?	ntervention status have bee	en affected by knowledge of t	he outcome or risk of the PN			
Could the classification of ir outcome?	ntervention status have bee	en affected by knowledge of t	ne outcome or risk of the PN			
Could the classification of in outcome? Observation: Blas due to deviations from	PN We decided by consensu	en affected by knowledge of t PN us We decided by consensu	ne outcome or risk of the PN			
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	Fell DB (1) 2022	Goldshtein I 2022	Ibroci E 2022	Blakeway H 2021	Boelig RC 2022	Cao M 2022
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Bias due to confounding	<u>.</u>					-
Risk of bias judgement	LOW	Moderate	Low	Serious	Low	Critical
is there potential for confoundi	v	v	v	v	v	v
Did the authors use an appropri	ate analysis method that contro	lled for all the important confou	inding domains?		L	
	Y	Y	Υ	Y	Ŷ	Y
Were confounding domains tha	t were controlled for measured	validly and reliably by the variab	les available in this study?			
	ΥΥ	N	Υ	NI	Υ	<u>N</u>
Did the authors control for any	post-intervention variables that	could have been affected by the	intervention?			
	j N Articlas domonstration extran	N N	j N	NI NI	N N	PY
	variables or not adhering to so	und and reliable construction m	ethods, a "Moderate" classificat	ion was assigned. In cases where	the model formulation or vari	able selection lacked
	accuracy, or when relevant info	ormation was absent, an assessm	nent of "Serious" was attributed.	The most stringent rating of "Cr	itical" was reserved for instance	es where post-intervention
Observation:	variables were employed for ac	ljustment purposes.				
Bias in selection of participants	into the study		1			
Risk of bias judgement	Low	Serious	Low	Low	Low	Serious
Was the selection of participant	is into the study based on partici	pant characteristics observed af	ter the start of the intervention	2		
	i N	j N	<u>i</u> N	<u>N</u>	<u>N</u>	Ŷ
Do start of follow-up and start o	py	participants?	PV	py	py	PN
Were adjustment techniques us	ed that are likely to correct for t	he presence of selection biases?		·		
	NA	N	NA	NA	NA	NI
	By means of a collective conser	nsus, we ascertained that attribu	iting a domain with a low risk of	bias is warranted when particip	ant selection hinges on pre-inte	ervention baseline
	characteristics, and the synchr	onization between the onset of	follow-up and the initiation of i	ntervention is prevalent among	he majority of participants. Co	nversely, a study is
	designated as "Serious" in case	s where the commencement of f	ollow-up and the initiation of in	tervention do not align, and the	authors have not implemented	d corrective techniques to
Observation:	mitigate this potential bias.					9/
Bias in classification of interven	titions 1 million	Moderate	l com	Terre	Law	1.000
Were intervention groups clear	LOW	Moderate	LOW	i Low	LOW	LOW
were intervention groups crean	Y	N	γ	Υ	Ŷ	γ
Was the information used to de	fine intervention groups recorde	ed at the start of the intervention	n?			
	Y	Y	Y	Y Y	Y	Υ
Could the classification of inter-	vention status have been affecte	by knowledge of the outcome	or risk of the outcome?		·	
	PN	PN PN	PN	PN	PN	PN
	We opted to assign a "Low" ris	of bias rating to this domain if t	the study provided a compreher	sive description of the intervent	tion, encompassing details abo	ut the specific vaccine type
Observation:			;			
Bias due to deviations from into	anded Interventions	Leve	Level 1		Low	1 Louis
Were there deviations from the	intended intervention beyond w	what would be expected in usual	practice?	i LOW	LOW	LOW
	N	N	N	N	N	N
Observation:	We decided to score this doma	in as having a low risk of bias be	cause any deviations from the in	tended intervention reflected u	sual practice.	
Bias due to missing data	-					:
Risk of bias judgement	Low	Low	Low	Low	Low	Moderate
Were outcome data available fo	r all, or nearly all, participants?		·,····			
	<u> </u>	Y	<u> </u>	Y	Y	PN
Were participants excluded due	to missing data on intervention	status?	nv.		NI	
Were narticinants excluded due	i n a to missing data on other variah	les needed for the analysis?	PT		i	N
Were participants excluded due	N	PY	PΥ	NI	NI	N
	We've chosen to assign a "Low"	rating to this section due to the	adequately comprehensive nat	ure of the data, coupled with th	e absence of any indications su	ggesting a notable
	divergence in the proportion o	r ratio of missing participant da	ta between the intervention gro	ups. We decided a "Moderate" r	ating if there are inadequate pr	ovision of information
Observation:	regarding the outcome missing	g data.				
Bias in measurement of outcon	nes					
KISK OF DIAS JUDgement	Low	Low	Lów	Lów	LOW	Low
couru che outcome measure ha	PN	PN	PN	PN	PN	PN
Were outcome assessors aware	of the intervention received by s	tudy participants?				
	PY	PY	РҮ	РҮ	PY	РҮ
Were the methods of outcome a	assessment comparable across in	tervention groups?		r		
	Υ	Y	Υ	Y	γ	Y
Were any systematic errors in th	ne measurement of the outcome	related to the intervention rece	ived?			
<u> </u>	N N	i N in at "Low" tick of bias because	i N	i N voll defined and we can consider	N N	i N likely to be ministerented
	we decided to score this doma	ITT 05 LOW TISK OF DIAS DECAUSE C	our salecy events of interest are v	ven Genned and We can consider	eu ciem as a naro outcomes ur	inkely to be misinterpreted
Observation:	d contraine					*
Risk of hiss judgement	low	low	lew	Low	Low	Low
Is the reported offect with the P	kolute herelected an the torus	of the coult fromitic'	teeme measureer setundation at	,	LOW	LUW
is the reported effect estimate li	kely to be selected, on the bases	or the result from multiple ou M	N N	e outcome domain r	N	N
multiple analysis of the interv	rention-outcome relationshin?	<u>, n</u>]	19	18	<u>1</u>
	N	N	N	N	N	N
different subgroups?		****				
	N	N	N	N	N	N
Observation:	We decided to score this doma	in as having a low risk of bias be	cause we have reported all of the	results that we consider to be c	finterest.	
Overall bias						
KISK OF DIAS JUDgement	LOW	aerious	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					Contract of the second	
Is there potential for confoundir	ng of the effect of inte	ervention in this study?	LOW	LOW	Critical	i woderate
	Ŷ	Ŷ	Ŷ	Y	Ŷ	Y
Did the authors use an appropria	ate analysis method t	hat controlled for all th	neimportantconfou	ding domains?		
Ware confounding domains that	PN	Y measured validuard s	Y aliably by the yariabl	Y or available in this st	Y Verbu	<u> Y</u>
were comounding domains that	N N	Y	Y	Y	Y Y	N
Did the authors control for any p	post-intervention var	iables that could have l	been affected by the	ntervention?		
	N	N	N	N	PY	N
	Articles demonstrat	ing a strong alignment	by employing valid a	nd dependable cova	iates were categorized a	is "Low." For those
	"Moderate" classific	ubset of the crucial adju	istment variables or rases where the mode	not adhering to soun	d and reliable construct able selection lacked ar	ion methods, a
	information was ab	sent, an assessment of "	Serious" was attribu	ed. The most stringe	nt rating of "Critical" wa	as reserved for instances
Observation:	where post-interver	ntion variables were em	ployed for adjustme	nt purposes.		
Bias in selection of participants	into the study					
Was the selection of participant	LOW s into the study base	on participant charac	teristics observed aft	er the start of the int	ervention?	LOW
	N	Ŷ	Ŷ	Y	Ŷ	N
Do start of follow-up and start o	fintervention coinci	de for most participant	s?	•		
	PY	PN	PN	PN	PN	PY
Were adjustment techniques us	ed that are likely to c	orrect for the presence N	of selection biases?	N	N	NA
	By means of a collec	tive consensus, we asce	ertained that attribu	ting a domain with a	low risk of bias is warrar	ted when participant
	selection hinges on	pre-intervention baseli	ne characteristics, a	nd the synchronizatio	on between the onset of	follow-up and the
	initiation of interve	ntion is prevalent amo	ng the majority of pa	rticipants. Conversel	y, a study is designated a	as "Serious" in cases where
-	the commencement	t of follow-up and the in ate this potential bias	nitiation of intervent	ion do not align, and	the authors have not in	npiemented corrective
Observation: Bias in classification of interests	tions	are this potential plas.		-		
Risk of bias judgement	Moderate	Moderate	Low	Low	Low	Moderate
Were intervention groups clearly	y defined?					
	N	N	Y	<u>ү</u>	Y	N
Was the information used to def	ine intervention gro	ups recorded at the star	t of the intervention	?	v	
Could the classification of interv	vention status have b	een affected by knowle	dge of the outcome o	r risk of the outcome	?	J
	PN	PN	PN	PN	PN	PN
	We opted to assign	a "Low" risk of bias ratir	ng to this domain if t	he study provided a c	omprehensive descripti	on of the intervention,
	encompassing detai	Is about the specific va	ccine type and dosag	e administered. If su	h information was lack	ing, the rating was
Observation:	categorized as "Moo	lerate."				
Bias due to deviations from inte	nded interventions					
Risk of bias judgement	Low	Low	Low	Low	Low	Low
were there deviations nom the	N	N	N N	N	N	N
Observation:	We decided to score	e this domain as having	a low risk of bias bec	ause any deviations f	rom the intended interv	vention reflected usual
Bias due to missing data						
Risk of bias judgement	Moderate	Low	Low	Low	Low	Low
Were outcome data available for	r all, or nearly all, par	ticipants?			, v	
Were narticinants excluded due	to missing data on ir	tervention status?	Y	i	<u>т</u>	jY
	NI	Y	N	N	NI	ŇI
Were participants excluded due	to missing data on o	ther variables needed fo	or the analysis?	•		
	NI	Υ	N	<u>N</u>	N	j <u>N</u>
	We've chosen to ass	ign a "Low" rating to th	is section due to the	adequately compreh	ensive nature of the dat	a, coupled with the
	intervention group	s. We decided a "Moder	ate" rating if there ar	e inadequate provisi-	on of information regard	ding the outcome missing
Observation:	data.					
Bias in measurement of outcom	les			:		
Risk of bias judgement	Low	Low	Low	Low	Low	Low
Could the outcome measure hav	PN PN	knowledge of the inter	vention received?	DN	DN	ры
Were outcome assessors aware o	of the intervention re	ceived by study partici	pants?	<u> N</u>	<u>, rn</u>	<u>r n</u>
	PY	PY	PY	PY	РҮ	PY
Were the methods of outcome a	ssessment comparab	le across intervention	groups?			Y
	Y	Y	Y	Y J	Y Y	<u>ү</u>
were any systematic errors in th	N N	N	N N	N	N	N
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	We decided to score	e this domain as "Low"	risk of bias because o	ur safety events of ini	erest are well defined a	nd we can considered
Observation:	them as a hard outc	omes unlikely to be mi	sinterpreted			
Bias in selection of the reported	d result					
Risk of bias judgement	Low	Low	Low	Low	Low	Low
likely to be selected, on the						·····
multiple apply is of the inter-	N aption outcome	N tionthin?	N	N	N	<u>i N</u>
multiple analysis of the interv	N	N N	N	N	N	N
different subgroups?						
	N	N	N	N	N	N
Observation:	We decided to score	e this domain as having	a low risk of bias bec	ause we have reporte	d all of the results that	we consider to be of
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			E	2	
Risk of bias judgement	Moderate	Low	Serious	Moderate	Moderate
Is there potential for confoundin	g of the effect of intervention in				
	γ	Υ	<u>γ</u>	Y Y	Y
Did the authors use an appropria	te analysis method that control	led for all the important confou	nding domains?	· · · · · · · · · · · · · · · · · · ·	······
	Y	Υ	Y	Υ	Y
Were confounding domains that	were controlled for measured v	alidly and reliably by the variab	les available in this study?		······
Bilde the second second	N	Y	i Ni	j N	<u> N</u>
Did the authors control for any p	ost-intervention variables that	could have been affected by the	intervention?	•	
	N Articles demonstrating a strong	N alianment hy amploying valid	j nd dependable covariator were	N Contenerized or "Low " For there	j N utilizion a limitad cubrat of the
	crucial adjustment variables or	not adhering to sound and relia	and dependable covariates were	Anderate" classification was assis	and in cases where the model
	formulation or variable selectic	in lacked accuracy, or when rela	want information was absent a	n assessment of "Serious" was at	tributed The most stringent
Observation	rating of "Critical" was reserved	for instances where nost-interv	ention variables were employed	for adjustment purposes	chouted. me most scringent
Rise in selection of participants	nto the study	tor instances where post interv	ention vondores were employe	a for sujustiment purposes.	
Bick of bice judgement	low	Seriour	Low	Low	Cortinue
Was the selection of participants	into the study based on partici	pant characteristics observed af	ter the start of the intervention	2	
and the selection of participants	N	Y	N N	y v	Y
Do start of follow-up and start of	intervention coincide for most	participants?	1		·
	PY	PN	PY	Рү	PN
Were adjustment techniques use	d that are likely to correct for th	e presence of selection biases?			ł
kkkkkk	NA	N	NA	NA	N
	By means of a collective consen	sus, we ascertained that attribu	ting a domain with a low risk of	bias is warranted when particip	ant selection hinges on pre-
	intervention baseline character	istics, and the synchronization	between the onset of follow-up	and the initiation of interventio	in is prevalent among the
	majority of participants. Conve	rsely, a study is designated as "S	erious" in cases where the comr	nencement of follow-up and the	initiation of intervention do
Observation:	not align, and the authors have	not implemented corrective te	chniques to mitigate this poten	tial bias.	
Bias in classification of intervent	lons				
Risk of bias judgement	Moderate	Low	Low	Low	Moderate
Were intervention groups clearly	defined?		***************************************		
	N	Ŷ	Υ	Y Y	N
Was the information used to defi	ne intervention groups recorde	d at the start of the intervention	, 1?		
	Ŷ	Y	Y Y	Y	Y
Could the classification of interve	ention status have been affected	by knowledge of the outcome	or risk of the outcome?		
	PN	PN	PN	PN	PN
	We opted to assign a "Low" risk	of bias rating to this domain if t	he study provided a compreher	sive description of the intervent	tion, encompassing details
Observation:	about the specific vaccine type	and dosage administered. If suc	h information was lacking, the r	rating was categorized as "Moder	ate."
Bias due to deviations from inter	nded interventions			-	
Risk of bias judgement	Low	Low	Low	Low	Low
Were there deviations from the in	ntended intervention beyond w	hat 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	Ŷ	NI	Υ	Y
Were participants excluded due	to missing data on intervention	status?			
	NI	Ŷ	NI	NI	Y
Were participants excluded due	to missing data on other variabl	es needed for the analysis?			
	N	<u>N</u>	NI	N	NI
	We've chosen to assign a "Low"	rating to this section due to the	adequately comprehensive nat	ure of the data, coupled with th	e absence of any indications
	suggesting a notable divergence	in the proportion or ratio of m	issing participant data between	the intervention groups. We de	cided a "Moderate" rating if
Observation:	there are inadequate provision	of information regarding the ou	itcome missing data.		
Bias in measurement of outcom	05			4	
Risk of bias judgement	Low	Low	Low	Low	j Low
Could the outcome measure have	e been influenced by knowledge	of the intervention received?			
1	PN	PN	<u>I PN</u>	j PN	1PN
Were outcome assessors aware o	the intervention received by st	udy participants?	[
	PY	PY	<u> </u>	<u> PY</u>	<u> </u>
Were the methods of outcome as	ssessment comparable across in	ervention groups?		······	1
	· · · · · · · · · · · · · · · · · · ·	Y	i ř	1	i
were any systematic errors in the	e measurement of the outcome i	related to the intervention rece	ived r		N N
<u></u>	N We desided to see this descel	N as "I ave" sizk of kins because a	j IN	i N well defined and we can appeid a	i N j
	unlikely to be ministerented	in as LOW TISK OF DIAS DECAUSE C	an safety events of interest are v	wen denned and we can consider	eu chem as a nard outcomes
Observation:	annikely to be misinterpreted				
Bias in selection of the reported	result				
Risk of bias judgement	Low	Low	Low	Low	Low
Is the reported effect estimate lik	ely to be selected, on the bases				
	N	N	N	N	N
multiple analysis of the interve	ention-outcome relationship?				·
	N	N	<u>N</u>	<u>j N</u>	i N
different subgroups?			,		,
	N	N	j N	1 N	j N
Observation:	we decided to score this domai	n as naving a low risk of bias be	cause we have reported all of th	e results that we consider to be c	or interest.
overall blas	Med				
nisk of blas judgement	wooerate	aenous	Serious	Moderate	SUGEDUS

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

	No of events/No of vaccinated	No of events/No of unvaccinated		
Outcome and Author	women	women		Odds Ratio (95% CI)
Maternal SARS-CoV-2 infection				
Blakeway H 2021	2/140	16/1188		1.06 (0.24, 4.67)
Bleicher I 2021	3/202	8/124		0.22 (0.06, 0.84)
Guedalia J 2022	2629/51942	2090/30627	_	0.73 (0.69, 0.77)
Guedalia J 2022	1747/8612	1089/8282		1.68 (1.55, 1.83)
Magnus MC (3) 2022	1513/28506	10988/129015	∎ a ti	0.60 (0.57, 0.64)
Plekos SN 2022 Theiler BN 2021	916/26/92	3394/48492		0.47(0.44, 0.51)
Dagan N 2021	131/10861	235/10861		0.55 (0.45, 0.43)
Carlsen FO 2022	363/9739	1036/11904		0.41 (0.36, 0.46)
Goldshtein I 2021	118/7530	202/7530		0.58 (0.46, 0.73)
Villar J 2023	525/1598	632/1732		0.85 (0.74, 0.98)
Subtotal (I-squared = 98.5%, p = 0.000) 7947/146062	19900/251617		0.63 (0.47, 0.85)
Offspring SARS-CoV-2 infection				
Carlsen EO 2022	25/4696	146/9759	_	0.76 (0.65, 0.88)
Carlsen EO 2022	385/9616	350/6728	;	0.35 (0.23, 0.54)
Halasa NB (1) 2022	87/234	450/815		0.48 (0.36, 0.65)
Subtotal (I-squared = 87.6%, p = 0.000) 497/14546	946/17302		0.52 (0.33, 0.82)
Severe covid disease			_	
Guedalia J 2022	3/51942	64/30627		0.03 (0.01, 0.09)
Guedalia J 2022	1/8612	5/8282		0.19 (0.02, 1.65)
COVID-NET nov 2021	1/11	44/322		0.63(0.08, 5.06)
Blakeway H 2021	8/131	0/11/393		2.26 (0.89, 5.74)
Dagan N 2021	0/103	1/10961		0.33 (0.01, 9.75)
Kim H 2022	0/39	4/185		0.53 (0.01, 0.18)
Paganoti CDF (2) 2022	44/187	740/1979	. !	0.51 (0.36, 0.73)
Theiler RN 2021	1/140	2/1862		- 6.69 (0.60, 74.24)
Villar J 2023	36/1598	85/1732	- H i	0.45 (0.30, 0.66)
Rottenstreich M 2022	0/712	0/1063		Insufficient data
Subtotal (I-squared = 80.9%, p = 0.000) 94/74336	965/58423	\diamond	0.47 (0.22, 0.97)
Maternal hospital admission				
Goldstein I 2021	13/7530	23/7530	_ - - i	0.56 (0.29, 1.11)
Dagan N 2021	1/10861	7/10861		0.14 (0.02, 1.16)
<i>Subtotal</i> (I-squared = 92.0%, p = 0.000) 14/18391	30/18391		0.41 (0.13, 1.28)
Maternal death			_	
Guedalia J 2022	0/51942	1/30627		0.20 (0.01, 4.82)
Paganoti CDF (2) 2022	6/200	294/2084		0.21 (0.10, 0.47)
Piekos SN 2022	3/1178	3/3394		2.88 (0.58, 14.26)
Villar J 2023	1/1973	1/1100	-	0.56 (0.03, 8.90)
Degen N 2021	0/11	0/322		Insufficient data
Goldshtein I 2021	0/7530	0/7530	1	Insufficient data
Guedalia J 2022	0/8612	0/8282	1	Insufficient data
Theiler RN 2021	0/138	0/1652		Insufficient data
Subtotal (I-squared = 64.4%, p = 0.038) 10/82445	299/65852		0.53 (0.12, 2.47)
* ***				
			005 4 7	
			.005 1 7	

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

Outcomes	No of studies	No of events / No of vaccinated women	No of events / No of unvaccinated women		Odds Ratio (95% CI)	1 2	
Miscarriage							
Adjusted	4	> 1874/20719	> 2233/22746	\diamond	0.96 (0.90, 1.04)	0.0%	
Unadjusted	3	21/389	46/724		1.60 (0.70, 1.91)	0.0%	
Preterm birth < 37 wee	ks						
Adjusted	5	865/15570	733/9946		0.79 (0.59, 1.06)	68.3%	
Unadjusted	21	21179/373909	42281/730134	•	0.90 (0.83, 0.97)	75.0%	
Caesarean section							
Adjusted	6	3339/16565	2492/13627	\diamond	0.91 (0.85, 0.98)	0.0%	
Unadjusted	15	17395/56221	39662/131923	•	1.11 (1.03, 1.20)	48.6%	
Postpartum hæmorrha	age						
Adjusted	5	936/13325	447/13167		1.49 (0.91, 2.44)	86.7%	
Unadjusted	6	865/25496	2569/79197		0.82 (0.68, 1.00)	0.0%	
Gestational diabetes							
Adjusted	1	222/2305	275/3313		1.10 (0.90, 1.30)	Not applicable	
Unadjusted	11	10687/132636	10371/130683		1.04 (0.89, 1.21)	94.2%	
Hypertensive disorders	5						
Adjusted	5	> 150/7219	> 257/8520		1.11 (0.87, 1.43)	0.0%	
Unadjusted	10	3704/104083	3862/113403	•	1.13 (1.02, 1.25)	49.0%	
			l .5	1 I 1 2			

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

Outcomes	No of studies	No of events / No of vaccinated women	No of events / No of unvaccinated women		Odds Ratio (95% CI)	 2
Stillbirth						
Adjusted	2	35/11987	54/5920		0.38 (0.09, 1.59)	89.4%
Unadjusted	11	1120/344258	2474/680694	•	0.78 (0.65, 0.92)	36.5%
Admission to neonatal intensive care	unit				1	
Adjusted	4	2751/41545	11157/132433	<	0.88 (0.71, 1.08)	37.9%
Unadjusted	9	2625/26760	10208/81774	•	0.82 (0.79, 0.86)	0.0%
Low 5-minutes Apgar score < 7					1	
Adjusted	4	643/40773	2460/138261	<	0.89 (0.73, 1.08)	29.3%
Unadjusted	9	487/30324	1616/83216		0.89 (0.81, 0.99)	0.0%
Small for gestational age					1	
Adjusted	6	2764/34304	11514/138179	(0.96 (0.90, 1.02)	0.0%
Unadjusted	8	5751/69977	7150/83836		0.99 (0.95, 1.03)	0.0%
				G. 1	1 2	

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

Outcome and Author	No of events/ No of vaccinated women	No of events/No of unvaccinated wome n	Materna I age	Gestational age	BMI	Education	Diabetes	Chronic hypertension		Meassure	Estimate (95% CI)
Miscarriage											
Cao M 2022 Rottenstreich M 2022 Stock S 2022 Citu IM (1) 2022 Subtotal (I-squared = 0.0%, p = 0.941)	34/300 Not reported/7 12 17 16/18780 124/927 > 329/207 19	84/736 Not reported/1063 1878/18780 271/2167 > 2233/22746							-	OR OR OR OR	0.99 (0.65, 1.52) 1.05 (0.78, 1.40) 0.96 (0.88, 1.04) 0.94 (0.66, 1.05) 0.96 (0.90, 1.04)
Preterm birth < 37 weeks											
Boelig RC 2022 DickA (1) 2022 DickA 2022 Hui L (1) 2022 Perez-Machuf R 2022 Subtotal (I-squared = 68.3%, p = 0.013)	5/49 14/294 127/2305 495/9682 224/3240 865/15570	13/198 233/3368 204/3313 239/2607 44/460 733/9946								- OR OR OR OR OR OR	$\begin{array}{c} 1.75 & (0.46, 6.67) \\ 0.67 & (0.37, 1.23) \\ 0.93 & (0.76, 1.21) \\ 0.60 & (0.51, 0.71) \\ 0.94 & (0.62, 1.44) \\ 0.79 & (0.59, 1.06) \end{array}$
Goldshtein I 2022	699/16738	358/7452							+	RR	0.95 (0.83, 1.10)
Caesarean section											
DiokA (1) 2022 DiokA 2022 Hui L (1) 2022 Perez-Machuf R 2021 Wahstock T 2021 Blakeway H 2021 Subtotal (I-squared = 0.0%, p = 0.956)	53/294 358/2305 1829/9682 877/3240 182/913 40/131 3339/16565	558/3368 529/3313 529/2607 141/460 601/3486 134/393 2492/13627								OR OR OR OR OR OR	$\begin{array}{c} 1.04 \ (0.75, 1.46) \\ 0.94 \ (0.75, 1.46) \\ 0.90 \ (0.81, 0.99) \\ 0.86 \ (0.64, 1.14) \\ 0.93 \ (0.75, 1.16) \\ 0.85 \ (0.55, 1.30) \\ 0.91 \ (0.85, 0.98) \end{array}$
Fell DB (1)2022 Ibroci E 2022 Subtotal (I-squared = 34.9%, p = 0.215)	6988/22660 99/250 7087/22910	8583/30115 541/1544 9124/31659							-	RR RR RR	0.97 (0.94, 1.00) 0.80 (0.60, 1.10) 0.94 (0.81, 1.08)
Postpartum haemorrhage											
DickA (1) 2022 DickA 2022 Hui L (1) 2022 Wainstock T 2021 Blakeway H 2021 Subtotal (I-squared = 86.7%, p = 0.000)	28/294 79/2305 806/9682 10/913 13/131 936/13325	108/3368 104/3313 205/2607 30/3486 33/393 447/13167								- OR OR OR OR OR OR	3.88 (2.41, 6.25) 1.20 (0.85, 1.66) 0.97 (0.83, 1.13) 1.46 (0.63, 3.38) 1.20 (0.61, 2.35) 1.49 (0.91, 2.44)
Fell DB (1)2022	677/22660	10 08/30 115								RR	0.90 (0.81, 1.00)
Gestational diabetes											
DickA 2022 Ortqvist AK 2022 Norway Ortqvist AK 2022 Sweden Subtotal (I-squared = 0.0%, p = 0.516)	222/2305 2299/43591 1195/20931 3494/64522	275/3313 2113/33047 1275/17516 3388/50563								OR RR RR RR	1.10 (0.90, 1.30) 1.18 (1.13, 1.22) 1.16 (1.12, 1.20) 1.17 (1.14, 1.20)
Hypertensive disorders											
Boelig RC 2022 Dick A 2022 Perez-Machulf R 2022 Rottenstreich M 2022 Wahstock T 2021 Subtotal (I-squared = 0.0%, p = 0.525)	10/49 25/2305 65/3240 Not reported/712 50/913 > 150/7219	42/198 44/3313 6/460 Not reported/1063 165/3486 > 257/8520								OR OR OR OR OR	1.05 (0.45, 2.41) 0.82 (0.48, 1.38) 1.30 (0.70, 2.42) 2.13 (0.79, 5.73) 1.13 (0.78, 1.62) 1.11 (0.87, 1.43)
Ortqvist AK 2022 Norway Ortqvist AK 2022 Sweden Subtotal (I-squared = 0.0%, p =0.516)	1662/43591 669/20931 2331/64522	1005/33047 480/17516 1485/50563								RR RR RR	0.91 (0.85, 0.97) 0.87 (0.83, 0.91) 0.88 (0.85, 0.92)
									1	7	

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

Outcome and Author	No of events/No of vaccinated women	No of events/No of unvacinated women	Maternal age	Gestational age	BMI	Chronic Education Diabetes hypertensio	'n	Meassure	Estimate (95% CI)
Stillbirth									
Dick A 2022 Hui L (1) 2022 <i>Subtotal</i> (I-squared = 89.4%, p = 0.002)	20/2305 15/9682 35/11987	33/3313 21/2607 54/5920				_		OR OR OR	0.78 (0.42, 1.44) 0.18 (0.09, 0.37) 0.38 (0.09, 1.59)
Admission to neonatal intensive care uni	it								
Hui L (1) 2022 Magnus MC (3) 2022 Perez-Machluf R 2022 Blakeway H 2021 <i>Subtotal</i> (I-squared = 37.9%, p = 0.185)	236/9682 2419/28492 89/3240 7/131 2751/41545	106/2607 11011/128973 16/460 24/393 11157/132433						OR OR OR OR OR	0.70 (0.53, 0.91) 0.97 (0.86, 1.10) 1.06 (0.54, 2.10) 0.86 (0.36, 2.06) 0.88 (0.71, 1.08)
Fell DB (1) 2022 Ibroci E 2022 <i>Subtotal</i> (I-squared = 0.0%, p = 0.944)	2508/22660 25/250 2533/22910	3852/30115 152/1544 4004/31659						RR RR RR	0.92 (0.87, 0.97) 0.90 (0.50, 1.70) 0.92 (0.87, 0.97)
Low 5 -minutes Apgar score < 7									
Dick A (1) 2022 Dick A 2022 Hui L (1) 2022 Magnus MC (3) 2022 <i>Subtotal</i> (I-squared = 29.3%, p = 0.236)	2/294 42/2305 170/9682 429/28492 643/40773	257/3368 63/3313 80/2607 2060/128973 2460/138261				_		OR OR OR OR	0.27 (0.04, 1.98) 0.92 (0.60, 1.43) 0.72 (0.51, 1.01) 0.97 (0.87, 1.08) 0.89 (0.73, 1.08)
Fell DB (1) 2022	403/22334	508/29588					-	RR	0.88 (0.77, 1.01)
Small for gestational age									
Dick A (1) 2022 Dick A 2022 Magnus MC (3) 2022 Perez-Machluf R 2022 Wainslock T 2021 Blakeway H 2021 <i>Subtotal</i> (I-squared = 0.0%, p = 0.692)	20/294 142/2305 2143/27421 417/3240 26/913 16/131 2764/34304	235/3368 233/3313 10821/127159 49/460 131/3486 45/393 11514/138179		-				OR OR OR OR OR OR	1.10 (0.68, 1.82) 0.81 (0.65, 1.05) 0.97 (0.90, 1.04) 1.01 (0.66, 1.55) 0.79 (0.48, 1.31) 1.07 (0.58, 1.97) 0.96 (0.90, 1.02)
Goldshtein I 2022	1053/16738	473/7452					÷	RR	0.97 (0.87, 1.08)
Ne onatal de ath									
Goldshtein I 2022	24/16738	13/7452						RR	0.84 (0.43, 1.72)
							1 2		