

Systematic review of COVID-19 vaccine effectiveness and safety in 930,556 pregnancies

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INTRODUCTION

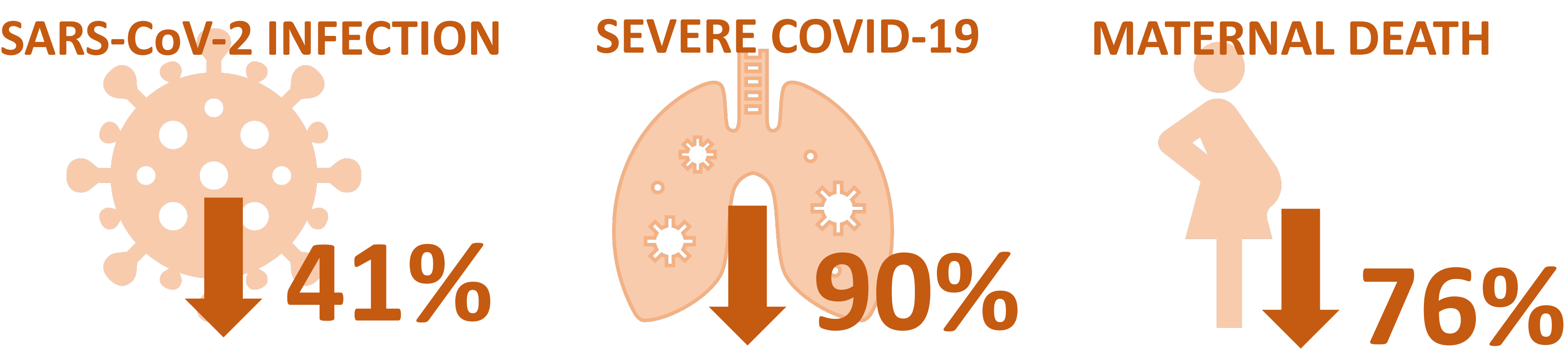
Pregnant and recently pregnant women with SARS-CoV-2 infection are at an increased risk of severe infection with associated mortality and morbidity than non-pregnant women of reproductive age.¹ Vaccines have been the most important intervention in preventing covid-19.²

METHODS

We conducted a living systematic review to identify comparative cohort studies reporting the effects of covid-19 vaccines on maternal infection-related and pregnancy outcomes until 25 October 2022. We also included non-comparative studies reporting on side effects. A random effects meta-analysis was performed and the findings were summarised as odds ratios (OR) and rates with 95% confidence intervals (CI). We undertook subgroup and sensitivity analysis by vaccine type and dose. Heterogeneity was reported as I².

RESULTS

We included **43 comparative cohort studies** (930,556 women) and **16 non-comparative cohort studies** (74,692 women). Pregnant women who received at least one dose of any covid-19 vaccine had a **reduction in the odds of SARS-CoV-2 infection** (OR 0.59, 95% CI 0.48 to 0.73), **severe covid-19 infection** (OR 0.10, 95% CI 0.02 to 0.62) and **all-cause maternal death** (OR 0.24, 95% CI 0.11 to 0.49).



Covid-19 vaccination was also associated with a significant reduction in **preterm birth, miscarriage and admission to the neonatal intensive care unit.**

There were **no differences in the outcomes between the vaccine type**, except for SARS-CoV-2 infection and NICU admission, which were **lower for m-RNA only** vaccine group.

In **fully vaccinated women** (women receiving two doses of a two-dose regimen vaccine or one dose of a one-dose regimen vaccine), the reduction in **SARS-CoV-2 infection, severe covid-19, maternal death, preterm birth and NICU admission** remain similar.

	No of studies	No of events/ No of vaccinated women	No of events/ No of unvaccinated women	Odds Ratio (95% CI)	I ² (%)
Maternal infection-related and all-cause mortality outcomes					
Maternal SARS-CoV-2 infection	3	4509/71822	3429/50177	0.60 (0.37 – 0.99)	91
Severe/critical covid-19	2	4/60679	94/39256	0.04 (0.01 – 0.10)	0
All cause maternal death	3	6/60879	297/41340	0.20 (0.09 – 0.44)	0
Maternal outcomes					
Preterm birth <37 weeks	7	97/1493	330/2931	0.74 (0.56 – 0.98)	11
Offspring outcomes					
Admission to neonatal intensive care unit	5	46/1002	194/1833	0.64 (0.43 – 0.95)	9

Table 1: Sensitivity analysis restricted to fully vaccinated women

The most common side effect after partial and full vaccination was **pain at the injection site.**



CONCLUSIONS

Covid-19 vaccines reduce the odds of SARS-CoV-2 infection, severe covid-19 and maternal death in pregnant and recently pregnant women. There are no safety concerns regarding maternal and perinatal outcomes or systemic side effects. These results should be interpreted with caution as we only included observational and non-randomised studies.

REFERENCES

¹Allotey J, Fernandez S, Bonet M, Stallings E, Yap M, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020 Sep 1;m3320.
²Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis. 2022 Sep;22(9):1293–302.