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# Safety of mRNA COVID-19 vaccines during pregnancy

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Pregnant people with COVID-19 are at increased risk of severe illness and death compared with non-pregnant females of reproductive age (aged 15–49 years).[1] Additionally, COVID-19 during pregnancy is associated with increased risk for adverse pregnancy outcomes, such as preterm birth and stillbirth.[1] When mRNA COVID-19 vaccines first became available in December, 2020, safety data in pregnancy were limited because pregnant people were excluded from pre-authorisation clinical trials.[2] Lack of data and safety concerns contributed to initially low uptake among pregnant people, which continues to be lower than uptake among non-pregnant females of reproductive age.[3] To address this issue, public health researchers from across the globe have been assessing the safety and effectiveness of COVID-19 vaccines during pregnancy.

In *The Lancet Infectious Diseases*, Manish Sadarangani and colleagues[4] report findings from the Canadian National Vaccine Safety (CANVAS) Network assessing adverse events in the week following mRNA COVID-19 vaccination among pregnant people and compare with both unvaccinated pregnant people and vaccinated non-pregnant females. In this large prospective study, the authors found that 226 (4·0%) of 5597 vaccinated pregnant people reported a significant health event (new or worsening health event sufficient to cause work or school absenteeism, medical consultation, or prevent daily activities) after dose 1 of primary series mRNA COVID-19 (mRNA-1273 [Moderna] or BNT162b2 [Pfizer BioNTech]) vaccination, with similar adverse events for both vaccines. Additionally, 227 (7·3%) of 3108 vaccinated pregnant people reported a significant health event after dose 2 of a primary series, and this did differ by vaccine type, with 147 (12·1%) of 1216 reporting a significant health event after dose 2 of mRNA-1273 and 80 (4·2%) of 1892 after dose 2 of BNT162b2.

The most common significant health events following both doses in pregnant people were malaise or myalgia (66 [3·5%] of 1892 for two doses of BNT162b2 and 139 [11·4%] of 1216 for two doses of mRNA-1273) and headache or migraine (41 [2·1%] of 1892 for two doses of BNT162b2 and 103 [8·5%] of 1216 for two doses of mRNA-1273). Serious health events, defined as any event resulting in emergency department visit or hospital admission in the previous 7 days, were rare (<1·0% in all groups). The most frequently reported adverse pregnancy outcome was a combined outcome of miscarriage and stillbirth and was reported at a similar frequency in vaccinated (81 [1·4%] of 5597) and unvaccinated (seven [2·1%] of 339) pregnant people. In a multivariable analysis among those vaccinated with mRNA-1273 or BNT162b2, pregnancy was associated with reduced odds of significant adverse events reported in the week following receipt of each dose (any mRNA dose 1: aOR 0·63 [95% CI 0·55–0·72]; any mRNA dose 2: aOR 0·62 [0·54–0·71]). Additionally, pregnancy was not associated with increased risk of serious adverse events following immunisation after either dose of BNT162b2 or dose 1 of mRNA-1273, but was associated with increased risk following dose 2 of mRNA-1273 (aOR 2·3 [95% CI 1·2–4·2]). Among 1216 pregnant females who received dose 2 of mRNA-1273, 11 (0·9%) reported a serious adverse event within 7 days.

These findings are consistent with and add to the growing body of evidence that COVID-19 mRNA vaccines are safe during pregnancy. In the USA, data from several vaccine safety monitoring systems, including the Vaccine Adverse Event Report System (VAERS), v-safe, the v-safe COVID-19 Vaccine Pregnancy Registry, and the Vaccine Safety Datalink, have similarly not detected any safety concerns for people who received an mRNA COVID-19 vaccine in pregnancy or for their infants.[5–7] In a large study among people vaccinated early in pregnancy, reactogenicity was similar to current findings reported by Sadarangani and colleagues.[5] In VAERS, a passive vaccine safety monitoring system co-managed by the US Centers for Disease Control and Prevention (CDC), and the US Food and Drug Administration (FDA), no concerning patterns of negative outcomes among pregnant people or their infants were detected following COVID-19 vaccination during pregnancy, but VAERS did not have a control group.[7] Therefore, this finding by Sadarangani and colleagues which includes an unvaccinated pregnant control group is important. As observed by Sadarangani and colleagues, previous studies have found that COVID-19 mRNA vaccination in pregnancy is not associated with an increased risk of miscarriage or stillbirth.[6]

In addition to being safe in pregnancy, other studies have shown that mRNA COVID-19 vaccines are effective

at reducing the risk of severe illness in pregnant people and the risk of COVID-19 hospital admission among their infants younger than 6 months.[6,8] Protection in infants born to people vaccinated during pregnancy is particularly important because while mRNA COVID-19 vaccines were approved by the FDA on June 17, 2022, and recommended by the CDC on June 18, 2022, for children aged between 6 months and 5 years,[9] there are not currently any vaccines available for infants younger than six months.

COVID-19 vaccination among pregnant people continues to be lower than among non-pregnant females of reproductive age.[3] Given the risks of severe illness and adverse pregnancy outcomes, continuing to collect and disseminate data on the safety and effectiveness of COVID-19 vaccination in pregnancy and encouraging health-care providers to promote vaccination during all trimesters of pregnancy is imperative.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. We declare no competing interests.

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1 Allotey J, Stallings E, Bonet M, 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; **370:** m3320.
2 Beigi RH, Krubiner C, Jamieson DJ, et al. The need for inclusion of pregnant women in COVID-19 vaccine trials. *Vaccine* 2021; **39:** 868–70
3 Razzaghi H, Yankey D, Vashist K, et al. COVID-19 vaccination coverage and intent among women aged 18–49 years by pregnancy status, United States, April-November 2021. Vaccine 2022; published online June 13. https://doi.org/10.1016/j.vaccine.2022.06.029.
4 Sadarangani M, Soe P, Shulha HP, et al. Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study. *Lancet Infect Dis* 2022; published online Aug 11. https://doi.org/10.1016/S1473-3099(22)00426-1.
5 Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary indings of mRNA COVID-19 vaccine safety in pregnant persons. *N Engl J Med* 2021; **384:** 2273–82.
6 Prasad S, Kalafat E, Blakeway H, et al. Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy. *Nat Commun* 2022; **13:** 2414.
7 Morro PL, Olson CK, Clark E, et al. Post-authorization surveillance of adverse events following COVID-19 vaccines in pregnant persons in the vaccine adverse event reporting system (VAERS), December 2020–October 2021. *Vaccine* 2022; published online April 12. https://doi.org/10.1016/j.vaccine.2022.04.031.
8 Halasa NB, Olson SM, Staat MA, et al. Maternal vaccination and risk of hospitalization for COVID-19 among infants. *N Engl J Med* 2022; published online June 22. https://doi.org/10.1056/NEJMoa2204399.
9 Fleming-Dutra KE, Wallace M, Moulia DL, et al. Interim recommendations of the advisory committee on immunization practices for use of Moderna and Pfizer-BioNTech COVID-19 vaccines in children aged 6 months–5 years—United States, June 2022. *MMWR Morb Mortal Wkly Rep* 2022; **71:** 859–68.

# Protein-based vaccine as the booster dose for adults: evidence and beyond

Since the pandemic began, there have been more than 500 million COVID-19 cases and 6 million deaths.[1] Despite the large number of previous infections and vaccinations (more than 11 billion doses in total), omicron (B.1.1.529)and its sublineages have caused several waves of infection outbreak globally since the end of 2021.[1] There are many potential reasons that might contribute to the ongoing pandemic, such as the waning of immune protection from vaccine or past infection with time, immune escape of the emerging variants, vaccine hesitancy, and the global inequity of vaccine distribution. Booster dose vaccines have been shown to reinforce the immune reaction and elicit increased protective antibodies.[2,3] The need for one or more booster doses will further increase the demand for vaccines. Given the disparities in economic status, health-care systems, and decision-making processes among different countries or regions, besides vaccines' inherent efficacy and safety profile, global vaccine distribution, accessibility, and uptake as well as vaccine-related policies might be influenced by factors such as costs, manufacturing capacity, and vaccine storage requirements.[4,5] Meanwhile, different vaccine platforms might cater to different settings and have a disparate extent of acceptance in the public. Therefore, it is crucial to explore a diversity of vaccine candidates from different platforms to tackle unpredictable challenges in the pandemic.

Protein-based technology is a traditional vaccine platform, with a promising efficacy and safety profile given the success of many precedent protein-based vaccines (eg, hepatitis B vaccine). NVX-CoV2373 is a protein subunit vaccine containing recombinant ancestral SARS-CoV-2 S protein and an immune-response-enhancing adjuvant. As vaccine-elicited neutralising antibody concentrations decline over time,

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