RESEARCH LETTER

Modeling the Health Impact of Discontinuing COVID-19 Vaccination During Pregnancy in the US

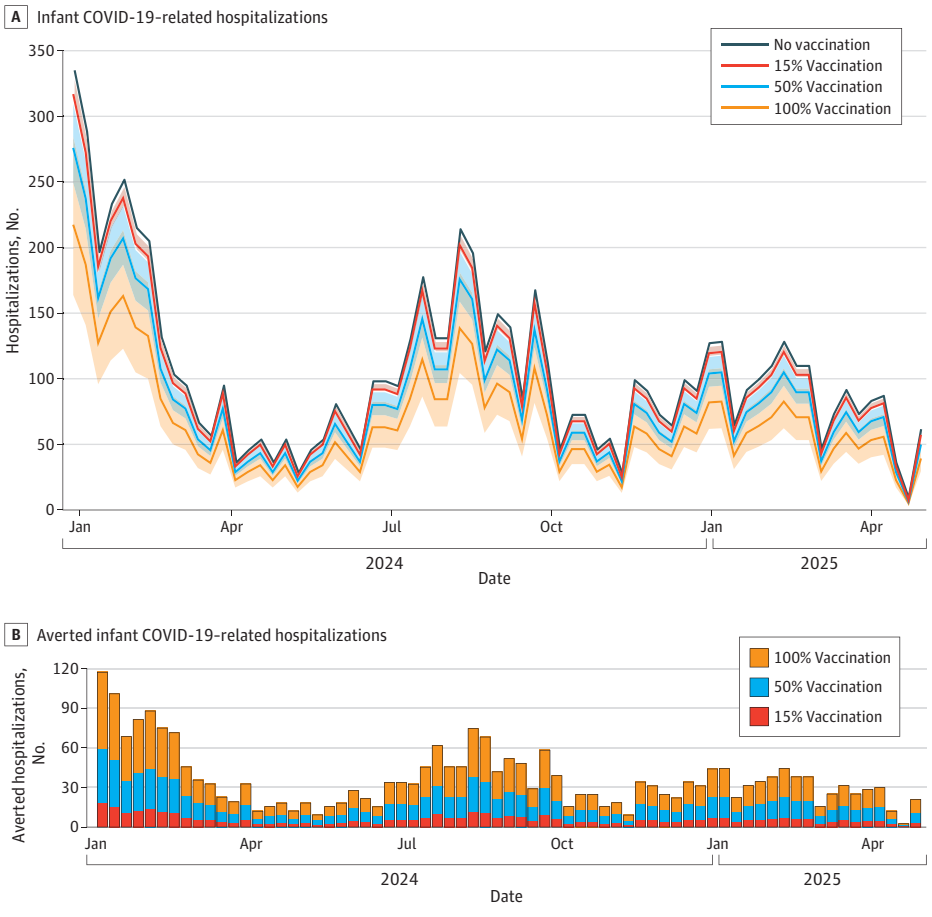
In May 2025, the US Department of Health and Human Services issued guidance to remove pregnancy as an indication for COVID-19 vaccination. Prior guidance recommended COVID-19 vaccination during pregnancy based on evidence that it reduces risk of severe COVID-19 in young infants (aged <6 months) and pregnant persons.[1] Vaccination during pregnancy confers direct protection to newborns through transfer of maternal antibodies, conferring passive immunity to the infant for approximately 6 months, and is associated with significant reductions in infant hospitalizations.[1] Infants younger than 6 months are not eligible for COVID-19 vaccination, and their risk of severe COVID-19 is much higher than other pediatric age groups, often similar to those aged 65 to 74 years in the current epidemiologic era.[2] Pregnancy also doubles the risk of severe COVID-19.[3] In this study, we estimate the number of avertable COVID-19 hospitalizations in young infants and pregnant persons with vaccination during pregnancy.

Supplemental content

Methods | We used publicly available US surveillance data on age-specific incidence of COVID-19 hospitalization (COVID-NET) from January 2024 to May 2025, which directly measures risk in young infants (<6 months).[2] To estimate the risk of COVID-19 hospitalization in pregnant persons, we used the incidence data for those 18 to 49 years, applying a relative risk of 2.65 (95% CI, 2.41-2.88).[3]

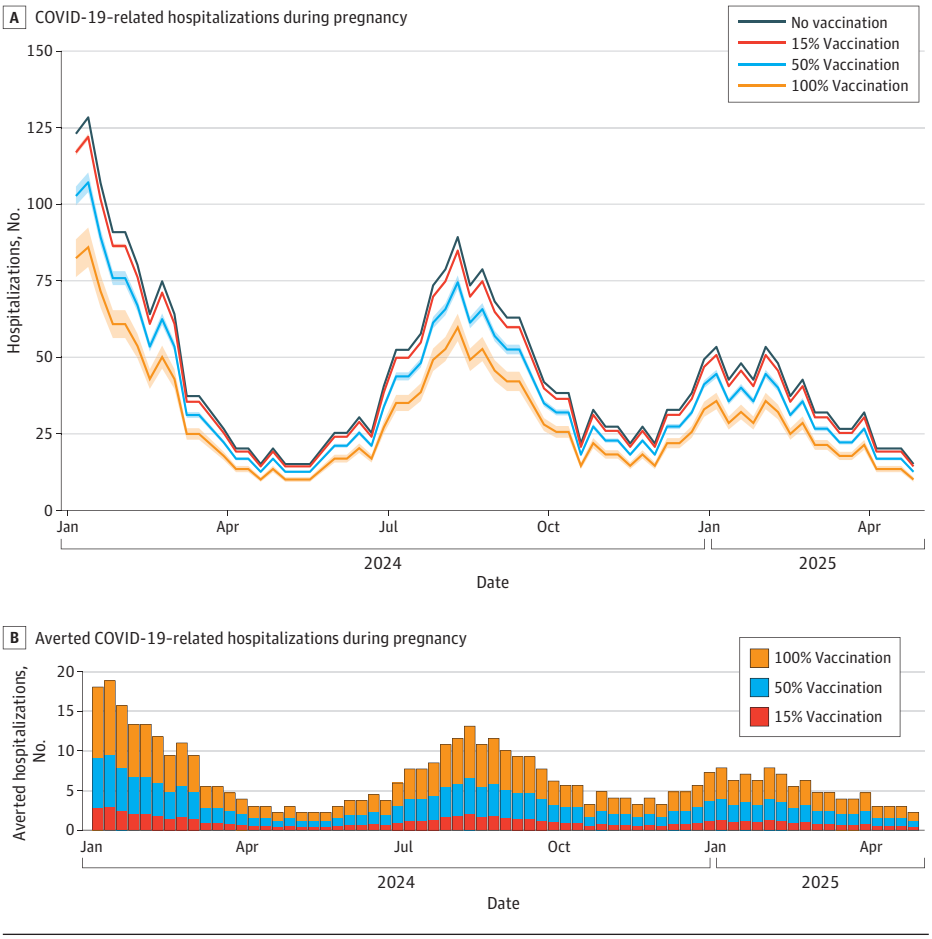
We evaluated the health impact of COVID-19 vaccination during pregnancy (administered predominately during the second or third trimester). We used recent vaccine effectiveness estimates, including 35% (95% CI, 15%-51%) reduction in COVID-19 hospitalization risk among young infants (<6 months), and 33% (95% CI, 28%-38%) vaccine effectiveness for adults over 4 months (eAppendix in Supplement 1).[1,4,5] We estimate $\text{AvertableCases}_t = \text{AR}_{\text{severe\_COVID},t} \times \text{N}_t \times \text{VE} \times \text{V}_{\text{coverage}}$,

Figure 1. COVID-19 Hospitalization Weekly Case Counts in Young Infants (<6 Months) in the US Under Different Vaccination Scenarios



A, We plotted weekly infant COVID-19–related hospitalizations for the US population, with the difference between the dark blue line (no vaccination) and other colored lines (vaccine uptake scenarios) being the projected health impact of COVID-19 vaccination during pregnancy under different coverages. B, Averted cases are plotted in the bar plots.

Figure 2. COVID-19 Hospitalization Weekly Case Counts in Pregnant Persons in the US Under Different Vaccination Scenarios



A, We plotted weekly COVID-19–related hospitalizations during pregnancy for the US population, with the difference between the dark blue line (no vaccination) and other colored lines (vaccine uptake scenarios) being the projected health impact of COVID-19 vaccination during pregnancy under different coverages. B, Averted cases are plotted in the bar plots.

where $AR_{severe\_COVID,t}$ is adjusted time-varying absolute risk of severe COVID-19 in the risk group (young children or pregnant persons), N_t is the number of young infants or pregnant persons, VE is vaccine effectiveness for the risk group, and $V_{coverage}$ is proportion of pregnant persons getting vaccinated. We generated an uncertainty interval based on the 95% confidence intervals of the VE estimates and relative risk for severe COVID-19 during pregnancy. This project was not considered human subjects research. Analytic code (R version 4.4.2 [R Foundation]) is available online, and CHEERS reporting guidelines were followed (eAppendix in Supplement 1).

Results | Under a counterfactual scenario without COVID-19 vaccination during pregnancy, we estimated a total of 7148 COVID-19 hospitalizations of young infants (in a population of 1.83 million within the US population) and 3106 COVID-19 hospitalizations of pregnant persons (in a population of 3 million within the US population) from January 2024 to May 2025 (**Figures 1** and **2**). Under a scenario with 50% or 100% coverage of COVID-19 vaccination during pregnancy, we estimated 1251 (95% CI, 536-1823) and 2502 (95% CI, 1072-3646) averted COVID-19 hospitalizations in young infants, respectively, and 228 (95% CI, 176-285) and 456 (95% CI, 351-570) averted severe COVID-19 cases in pregnant persons, respectively. However, in scenarios of low vaccine coverage (recent vaccination uptake during pregnancy: 15%), we estimated vaccination averted 375 (95% CI, 161-547) COVID-19 hospitalizations in young infants and 68 (95% CI, 53-86) severe cases in pregnant persons. These results are sensitive to COVID-19 incidence, clinical severity, and vaccine effectiveness estimates.

Discussion | This decision analytical model study estimates that COVID-19 vaccination (primarily annual COVID-19 vaccination) during pregnancy will likely continue to yield meaningful public health benefits in the US, especially to reduce COVID-19 hospitalizations in infants. COVID-19 vaccination during pregnancy has been shown to be safe.[6] While there is global variation in policy recommending COVID-19 vaccination during pregnancy, the US has a high risk of severe COVID-19 in newborns, underscoring relevance of maternal COVID-19 vaccination.

This analysis has limitations. We relied on recent COVID-19 incidence data, although this may not capture future epidemiologic patterns. We relied on vaccine effectiveness estimates from recent observational studies, which may be prone

to bias and had some limitations. Historic vaccine uptake is low, which may diminish the impact of maternal vaccination.

This study demonstrates meaningful benefit of COVID-19 vaccination during pregnancy, which has moderately waned over time, but still supports the need to reconsider the decision to remove vaccine eligibility during pregnancy. Continued studies on the COVID-19 risk and vaccine effectiveness in this population are important.

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Correction: This article was corrected on October 27, 2025, to correct the panel label of Figure 2B.

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Author Contributions: Drs Lo and Kiang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Lo, Kiang.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Lo, Kiang.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Lo, Kiang.
Supervision: Lo, Kiang.

Conflict of Interest Disclosures: Dr Lo reported personal fees from the World Health Organization related to guidelines on neglected tropical diseases outside the submitted work. Dr Maldonado reported grants from Pfizer outside the submitted work. Dr Chu reported personal fees from AbbVie, Merck, Roche, and Vir Biotechnology outside the submitted work. Dr Hotez reported being a coinventor on non–revenue-generating patents for neglected tropical diseases, which are owned by Baylor College of Medicine, and a coinventor of a COVID-19 recombinant protein vaccine technology, owned by Baylor College of Medicine, which was licensed by Baylor Ventures nonexclusively and without patent restrictions to several companies committed to advancing vaccine technology for low- and middle-income countries, and receiving royalty income from American Society for Microbiology–Wiley and Johns Hopkins University Press. Dr Kiang reported grants from the US National Institutes of Health outside the submitted work.

Data Sharing Statement: See Supplement 2.

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Clinical Long-Read Sequencing Test for Genetic Disease Diagnosis

Recent work in genome sequencing (GS) shows a 4% to 8% increase in diagnostic yield over exome sequencing (ES) alone, albeit the overall diagnostic gain (<1%) is marginal if GS is compared to combinations of ES with other standard tests.[1]

Supplemental content

Recently, we reported undiagnosed cases following GS could be recovered by long-read sequencing (LRS), due in part to the simultaneous detection of clinically relevant repeat expansions,[2-4] methylation abnormalities,[5] and improved structural variant detection.[6] However, no study has assessed the implementation of LRS as a first-line clinical test. Herein, we report the comparative diagnostic yield and turnaround time and evaluate the ability to consolidate standard-of-care (SOC) approaches using a single clinical LRS test.

Methods | Clinical high-fidelity (HiFi) LRS was performed on 235 patients aged 0 to 18 years compared to an age- and phenotype-matched control cohort of 513 patients. Patients selected for the control group underwent SOC inpatient genetic testing, including expedited ES/GS, karyotype, fluorescence in situ hybridization (FISH), chromosomal microarray (CMA), and targeted panels. The eMethods in Supplement 1 provide further details. The Standards for Reporting of Diagnostic Accuracy (STARD) reporting guidelines were followed.

Results | LRS case results were compared to controls (**Figure 1**), with the true diagnostic rate determined by counting diagnoses explaining the primary signs and symptoms. Variants of uncertain significance, carrier status, incidental findings, or pathogenic changes associated with late-onset or variable phenotypes not directly linked to presenting complaint were excluded.

The LRS cases yielded a significantly higher (P = .004, 2-2 χ^2 test) diagnostic rate compared to the SOC group (**Figure 2**). The mean length of time from test order to diagnostic report (27 days) was significantly (P = .048, t test) shorter among LRS cases (Figure 2) compared to controls (62 days). Similarly, if a negative result was returned, the average time to report was significantly (P < .001, t test) shorter among LRS cases (29 days) compared to controls (91 days).

Factors negatively impacting the time to diagnosis specific to LRS were low sequencing yields requiring reloading and technical limitations of tertiary analysis software. Among the SOC group, the primary cause for delayed diagnosis was mul-