COVID-19 Vaccination During Pregnancy

To the Editor: In their article, Watanabe and colleagues reported that COVID-19 vaccination during pregnancy was not associated with an increased risk of peripartum outcomes and was associated with a decreased risk of neonatal intensive care unit admission, in utero fetal death, and maternal SARS-CoV-2 infection.

Several issues need to be clarified before a more robust conclusion can be made. Vaccination hesitancy during pregnancy was closely associated with safety and efficacy concern as well as the lack of vaccine knowledge. Active recommendation by health care professionals and accurate cognition promoted the COVID-19 vaccination during pregnancy. In this sense, the pregnant people accepting the COVID-19 vaccination were more likely to be concerned with the impact of the vaccine and health themselves, leading to more frequent follow-up visits and intensive intervention for possible disorders. On the other hand, pregnant people with some comorbidities were more likely to refuse the vaccine due to the health concerns, which indicated that the pregnant people receiving the COVID-19 vaccination may be less likely to be with complications themselves. The participants included in this meta-analysis were largely from high-income countries. The financial status and educational background may also play a role in the efficacy of the COVID-19 vaccination. All these factors may contribute to the good peripartum outcomes of COVID-19 vaccination during pregnancy. Further studies should be performed adjusted for these confounding factors, such as health status, race and ethnicity, income, and educational background.

The timing and doses of COVID-19 vaccination during pregnancy may affect the peripartum outcomes. The study by Watanabe et al showed that COVID-19 vaccination during the second or third trimester was associated with lower risks of preterm birth and small for gestational age vs those who did not receive COVID-19 vaccination during pregnancy. Multiple doses of the COVID-19 vaccine provided better preventive effect of COVID-19 and increased the immunological effect. Maternal antibodies transferred through the placenta from the 17th and 18th week of pregnancy, which indicated that maternal vaccination during the early second trimester of gestation may be helpful for the neonate. Whereas the first 3 months were vital for embryonic development, pregnant women themselves also need the protection of antibodies as soon as possible, and the immunological effect of COVID-19 vaccination may also play a role in the neonate.

Hence, a comprehensive comparison among different timing and doses of COVID-19 vaccination during pregnancy may need to be elucidated the optimal timing and doses for providing a better peripartum outcomes with less complications.

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In Reply: We appreciate the interest and comments on our article by Mao. We have demonstrated the possible benefit of COVID-19 vaccination among pregnant individuals by synthesizing published data and showing better peripartum outcomes in those who received vaccination during pregnancy compared with those who did not.

In the letter, Mao pointed out several issues in our article. First, the concern for the baseline imbalances between vaccinated and unvaccinated individuals was raised. Mao assumed that those with comorbidities could have been more likely to refuse vaccinations, which might have led to better outcomes in vaccinated individuals. However, it should be recognized that Table 1 in our article shows that vaccinated individuals were older in 8 of 9 included studies, potentially leading to a higher risk of pregnancy. Furthermore, since the proportions of previous miscarriage and infertility were consistently higher among vaccinated individuals, this bias would rather favor those unvaccinated. In contrast, economic status and educational background may have played a confounding role. According to a nationwide study included in our article, vaccinated pregnant individuals tended to have higher household incomes and educational levels. A survey conducted in the US also showed that lower income and lower education were associated with COVID-19 vaccine hesitancy and highlighted the importance of clear health communication with patients from various backgrounds. Given the possible associations between financial status and peripartum outcomes, it indeed needs further investigation. Nevertheless, although our study could not adjust these confounding factors, it would.
be very challenging to conduct large-scale randomized trials, given the ample evidence supporting the benefit of COVID-19 vaccination.

Finally, our article could not extensively assess the most effective timing and dose of vaccination since only a few studies reported the difference in the maternal or neonatal protective effects among the first, second, and third trimesters. In our original article,1 vaccination during the second or third trimester was associated with lower incidences of preterm birth and small for gestational age. However, it was compared with unvaccinated individuals instead of those vaccinated during the first trimester. Therefore, it is difficult to determine the best time to receive vaccinations to protect children. Nevertheless, even if it were proven that getting vaccinated later in pregnancy compared with earlier was more effective in reducing neonatal outcomes, that would not necessarily dictate the best timing to be vaccinated because unvaccinated individuals would have to remain having higher risks of SARS-CoV-2 infection while waiting for the second or third trimester. Under current consensus, it can be recommended that pregnant individuals or those of reproductive age be vaccinated against COVID-19.

Overall, we agree that our meta-analysis has several limitations to be acknowledged. However, our findings would promote vaccinating pregnant individuals who have not received one yet due to concerns for the safety and efficacy of COVID-19 vaccines. Future investigations on the optimal dose and timing of COVID-19 vaccination, including the ones for the Omicron variant, for pregnant individuals, are warranted.

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**CORRECTION**

**Coding Error and Errors in Estimates:** The Original Investigation titled “Five-Year Trends in US Children's Health and Well-being, 2016-2020,” published online March 14, 2022, and in the July issue of *JAMA Pediatrics*, there were errors in the estimates for one of the measures of interest. A coding error produced shifts in the single-year estimates for preventive medical visits; however, the interpretation and findings of the study were not affected. This article was corrected online, following a previous correction.1


**Error in Text:** In the Original Investigation titled “Telehealth Treatment of Behavioral Problems in Young Children With Developmental Delay: A Randomized Clinical Trial,” published online January 9, 2023, the Results section of the Abstract and article body incorrectly listed children’s age in years instead of months. This article has been corrected online.


**Errors in the Byline and Text:** In the Viewpoint titled “Is There Enough Choline for Children in Food Aid?,” published online January 23, 2023, the second author’s name was misspelled. The correct spelling is Marie Caudill, PhD. In addition, text was updated to reflect minor clarifications. This article was corrected online.


**Error in Author Affiliations:** In the Research Letter titled “BNT162b2 Vaccine Effectiveness Against the SARS-CoV-2 Omicron Variant in Children Aged 5 to 11 Years,” published online January 9, 2023, the author affiliations were attributed incorrectly. This article was corrected online.