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Repeat Tdap Vaccination and Adverse Birth Outcomes

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In Reply Ms Zhu and colleagues express concerns regarding potential bias and confounding in the study evaluating the safety of repeated tetanus-containing vaccines in pregnancy.

First, they point to the accuracy of methods for identifying gestational age. The pregnancy episode algorithm was used to identify live births in our study but was not the method used for identifying gestational age. The validation data presented were specific to the pregnancy episode algorithm for identifying live births. We stated in the article that we limited the cohort for birth outcomes to "records that contained information on the neonate (ie, weight and gestational age)." In the Vaccine Safety Datalink, gestational age data come from electronic medical record and state birth registry data, which are based on clinician assessment. The clinician uses all available data to determine this estimate, including estimated due date based on ultrasound and last menstrual period data and can adjust this estimate based on the infant's appearance at birth.

Zhu and colleagues also raise concerns about risk factors that were used in the analysis of birth outcomes. Despite the change in direction of the relative risk with adjustment, both the unadjusted and adjusted risk estimates were nonsignificant, and it is inappropriate to overinterpret nonsignificant point estimates on either side of the null. After adjustment for adequacy of prenatal care, comorbidities, and pregnancy complications (which were clinically similar between the groups compared), in addition to gestational age at vaccination, health care site, maternal age, and length of enrollment, we still did not find an association. These adjustments strengthen the overall findings, especially because we had substantial statistical power to detect a difference in birth outcomes. A healthy user effect would not be expected, as all of the women in our study were vaccinated, and women during their prime childbearing years are generally healthy and seek preventive care during pregnancy.

Finally, Zhu and colleagues suggest that because most Tdap vaccinations in our study were given in the third trimester, our results might not apply to vaccinations given earlier in pregnancy. Although it is true that 67.4% of the pregnancies had Tdap in the third trimester, there were 9505 pregnancies in which vaccinations were given in the first or second trimester. The Advisory Committee on Immunization Practices currently recommends Tdap

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at any time during pregnancy with a preference for third trimester administration to "provide the highest concentration of maternal antibodies to be transferred closer to birth."[1] This optimal timing for administration corresponds to the majority of vaccinations given in our study. Therefore, our findings are applicable to pregnant women whose clinicians are following recommendations. However, we agree that additional data for first trimester vaccination will further strengthen the evidence base regarding Tdap safety in early pregnancy.

References

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