

## CSU

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## 1. No evidence that COVID-19 vaccination is associated with increased risk of miscarriage

Evidence that the Pfizer COVID-19 vaccine is safe during pregnancy has been growing. At the same time, it has become clearer that COVID-19 infection during pregnancy is associated with an increased risk of developing severe disease ([link](#)). This report reviews the data from two studies ([link](#), [link](#)), that evaluate the risk of miscarriage in people who received a COVID-19 vaccine during pregnancy. Both studies show that the rate of miscarriage is similar for vaccinated and unvaccinated pregnant people, and that there is no evidence that the COVID-19 vaccine is associated with an increased risk of miscarriage during pregnancy.

- Shimabukuro *et al*, reported on the safety of receiving the mRNA COVID-19 vaccine for pregnant people ([link](#)). The study included 3,958 pregnant people in the US enrolled in the ‘v-safe’ pregnancy registry. Registry participants had received an mRNA vaccine (Pfizer or Moderna) at some point during their pregnancy. Participants were asked questions relating to pregnancy outcomes, such as pregnancy loss or live birth, and neonatal outcomes such as rate of preterm birth and size for gestational age. Participants were followed for 10-12 weeks post-vaccination.
- The rate for miscarriage, as with most pregnancy outcomes, was evaluated against all completed pregnancies. However, because the Shimabukuro *et al* study reported only 10-12 weeks of follow-up after vaccination, not all the pregnancies evaluated in the study were complete. Therefore, in order to estimate the rate of miscarriage, authors evaluated the outcomes from the completed pregnancies only.
- There were 827 completed pregnancies. Of those, there were 712 births, 104 miscarriages, 1 stillbirth, and 10 other outcomes, e.g., ectopic pregnancy. Therefore, the rate of miscarriage was 104/827 or 12.6%, similar to the background rates for unvaccinated individuals; the background rate for miscarriage for pregnancies in the general population is about 12.5 to 18.7% ([link](#)).
- Most of the individuals were vaccinated in the 3rd trimester (86%), however, and it is reasonable to want to estimate the rate of miscarriage for people vaccinated in the first and second trimester. There were 96 (8.5%) miscarriages reported in the 1st trimester, and the remaining 8 (0.5%) occurred in the 2nd trimester.
- An incorrect method for estimating the rate of miscarriage, but one that has circulated on social media, is to count the number of miscarriages among the 127 individuals who were vaccinated in their 1<sup>st</sup> or 2<sup>nd</sup> trimester and who completed their pregnancies within 3 months of that date (the maximum follow-up time of the study). However, most pregnancies completed within 3 months of the 1<sup>st</sup> or 2<sup>nd</sup> trimesters are not full-term births, by definition. The analysis *should* include all women followed to full-term or the end of their pregnancies, and then determine of those who had miscarriages, rather than selecting only those whose pregnancy ended within the study’s follow-up period (3 months), as this generates a selection bias to include more miscarriages in the analysis.

- In total, there were 2,846 pregnant people who were vaccinated in their 1<sup>st</sup> and 2<sup>nd</sup> trimesters, and the vast majority of the pregnancies (96%) were still ongoing at the end of the follow-up period (3 months). The remaining 127 (4%) pregnancies were completed within 3 months following vaccination in the 1<sup>st</sup> or 2<sup>nd</sup> trimester. This means that almost no completed full-term births are included in the 127 simply because the study does not have sufficient follow-up time. Hence, it is not surprising that of the 127 pregnancies completed within 10-12 weeks of the first and second trimesters, 104 (82%) were recorded as a miscarriage.
- A second study was performed that was able to follow almost all pregnant people from the 1<sup>st</sup> and 2<sup>nd</sup> trimester until completion of the pregnancy, either to full term or other pregnancy outcome. Therefore, this study did not have the bias associated with limited follow-up time. The researchers followed 2,456 pregnant people from vaccination with a COVID-19 vaccine in the first and second trimesters until completion of their pregnancies. All participants in the study received a mRNA COVID-19 vaccine before 20 weeks' gestation ([link](#)). The risk of miscarriage from 6–19 weeks' gestation until the completion of the pregnancy was 14.1% (95% CI: 12.1,16.1%), consistent with background rates. This shows that when pregnant people are vaccinated in the first or second trimesters, and we can follow the individuals until we know the outcomes of all the pregnancies, that the rate of miscarriage is no higher or lower than in unvaccinated pregnant people.

**Comment: There is no evidence that the COVID-19 vaccine is associated with an increased risk of miscarriage during pregnancy.** In general, the benefits of COVID-19 vaccination outweigh the risks from COVID-19.