

## The risk of miscarriage or preterm labor after COVID-19 vaccination before and during pregnancy

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### Background

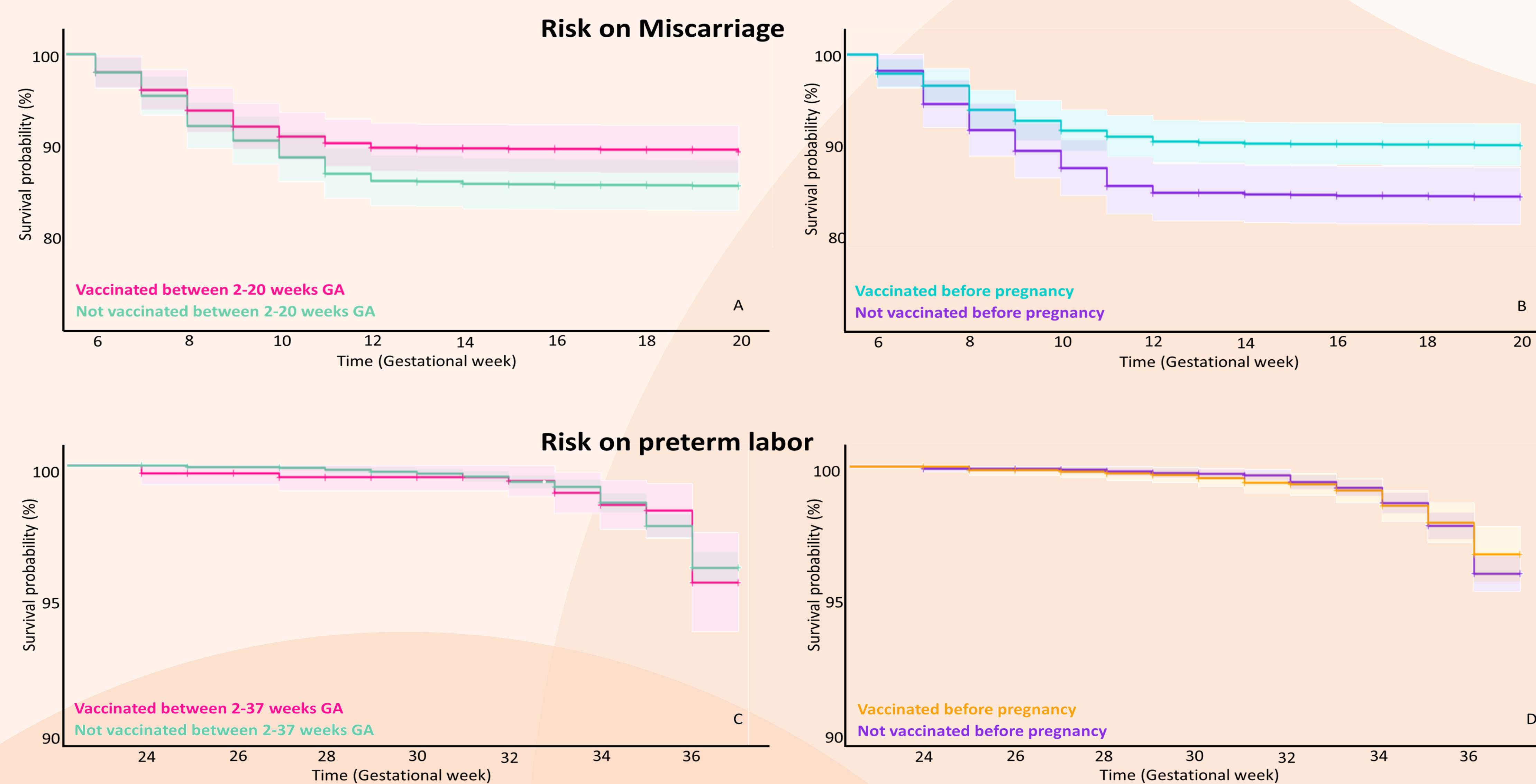
Pregnant women are at higher risk of severe illness and adverse pregnancy outcomes due to a SARS-CoV-2 infection, which can be prevented by COVID-19 vaccination. Observational studies are needed to ascertain safety of COVID-19 vaccination during pregnancy.

### Aim

To assess whether COVID-19 vaccination before or during pregnancy is associated with the risk of miscarriage or preterm labor (PL).

### Conclusion

COVID-19 vaccination prior to or during pregnancy is not associated with an increased risk of miscarriage or PL. These results add to the growing evidence supporting the safety of COVID-19 vaccination prior or during pregnancy.



**Figure:** Kaplan-Meier plot of time by COVID-19 vaccination status. Survival probability for not having a miscarriage, comparing (A) those who received  $\geq 1$  COVID-19 vaccine between 2-20 weeks GA (pink), to those who did not (green) and (B) those who received  $\geq 1$  COVID-19 vaccine before pregnancy (blue), to those who did not (purple). Survival probability for not having preterm labor, comparing (C) those who received  $\geq 1$  COVID-19 vaccine between 2-20 weeks GA (pink), to those who did not (green) and (D) those who received  $\geq 1$  COVID-19 vaccine before pregnancy (orange), to those who did not (purple). Participants start contributing to the plot from the gestational week at the moment of inclusion in the cohort. Vaccination status during pregnancy was time-dependent, meaning that a woman could contribute observation time to the unvaccinated and the vaccinated observation time if she received a COVID-19 vaccination during pregnancy.

### Methods

**Participants** were pregnant women (mean age:  $33.0 \pm 3.7$  years) from the Dutch Pregnancy Drug Register.

**Survival analyses** was used to estimate the adjusted\* hazard ratio (HR) of COVID-19 vaccination before pregnancy and of COVID-19 vaccination during pregnancy.

#### Miscarriage

- defined as spontaneous abortion before 20 weeks gestational age (GA).
- HR was based on a cohort of 4,640 women, comparing those who received  $\geq 1$  COVID-19 vaccine between 2-20 weeks GA, to those who did not.

#### Preterm labor

- defined as livebirth before 37 weeks GA.
- HR was based on a cohort of 5,910 women, comparing those who received  $\geq 1$  COVID-19 vaccine between 2-37 weeks GA, to those who did not.
- HR on PL was also studied for COVID-19 vaccination in trimester 1, 2, or 3 separately.

Vaccination during pregnancy was assessed as a **time-varying** exposure.

### Results

#### Risk of Miscarriage

- 3,202 (69%) women received  $\geq 1$  COVID-19 vaccination between 2-20 weeks GA.
- No association of COVID-19 vaccination during pregnancy with the risk of miscarriage (adjusted\* HR=1.29, 95%CI=0.93;1.74).
- Vaccination before pregnancy was associated with a decreased risk of miscarriage (adjusted\* HR=0.69, 95%CI=0.48;0.99).

#### Risk of preterm labor

- 5,227 (88%) women received  $\geq 1$  COVID-19 vaccination between 2-37 weeks GA.
- No association of COVID-19 vaccination during pregnancy (adjusted\* HR=0.93, 95%CI=0.59; 1.45) or COVID-19 vaccination prior to pregnancy (adjusted\* HR=1.09, 95%CI=0.70;1.71) with the risk of PL.
- No association between the risk of PL and COVID-19 vaccination in any trimester of pregnancy.

\*adjusted for age biological mother, age biological father, educational level of biological parents, level of urbanicity, smoking behavior, alcohol intake, illicit drug use, pre-pregnancy body mass index, history of miscarriage, history of preterm labor, mother belonging to a high priority group for vaccination, and pregnancy start month.

**Acknowledgement:** We are grateful to all participants of the Dutch Pregnancy Drug Register for their contribution. This work was supported by the Ministry of Health, Welfare and Sport, the Netherlands.