## Vaccination and fertility: A mathematical model raises more questions than it answers

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Dear colleagues,

with some astonishment, we have read the article "Vaccination and fertility: modelling the potential impact of COVID-19 vaccination on total fertility rate in Czechia" by Slaba et al. [1] that was recently published in your journal. The authors observe a significant decrease in the Total Fertility Rate (TFR) of the Czech Republic between 2021–2024 and propose a mechanism that might be responsible for that decline. They hypothesize that Czech women were afraid of adverse effects of COVID-19 vaccines and, consequently, avoided conception in the month of vaccine administration.

The paper does not give any evidence for the hypothesis. On the contrary, the authors cite the work of Paloncyova et al [2] that goes directly against their hypothesis: Paloncyova et al. found that as of April 2021, the desire to have a (or another) child in the near future was primarily influenced by the number of children a family already had and by the values associated with parenthood. She reported that the socioeconomic changes brought about by the pandemic had not yet been reflected in parental plans.

Anyway, we do not question the right of the authors to propose any hypothesis. However, the formulation of their hypothesis ("avoiding conception in the month of the first dose of COVID-19 vaccination") differs from that implemented in their paper. The term "avoiding conception in the month of the first dose" indicates *postponing* conception to some later time after the vaccination. But in their model, they simply "removed" all women vaccinated in each month from the population, and added them back one month later. This means that in their model, vaccinated women did not postpone conception for later, they just completely avoided conception in the respective month without making up for it later.

If vaccinated women simply *postponed* conception, TFR would decrease approximately 9 months after the peak of the vaccination intensity, which would be followed by an increase exceeding the previous baseline (as the children from postponed conceptions would be born) and, finally, TFR would settle on the pre-pandemic levels. However, this does not reflect the observed reality at all. The TFR in the Czech Republic has decreased from 1.83 in 2021 to 1.62 in 2021, and further to 1.45 in 2023 [3]. The current estimate for 2024 runs at 1.30. Thus, the hypothesis of avoiding conception in the month of the vaccine – in the sense of postponing the conception – does not explain the data.

The model actually implemented in the article also fails to reproduce the observed data. The authors avoid comparison of their prediction with the 2023 and 2024 TFR data. In those two years, their model should show almost no decrease in TFR because almost no women of fertile age got vaccinated since the beginning of 2022. However, in reality, the 2023 TFR was 20% lower than in 2021 and decreased further in 2024. Thus, this model also fails to reproduce the observed data, but the authors chose not to report that.

The authors seem to think that "voluntary decision of the woman" is the only permissible causal mechanism that produces association between vaccination status and the probability of conception. However, there are reasons to believe that there may be a direct (i.e. biological) mechanism: Pharmacovigilance Risk Assessment Committee (PRAC, [3]) of the European Medicine Agency analyzed two important safety signals which can cause decrease of

fertility in the vaccinated: (1) heavy menstrual bleeding (heavy periods), and (2) absence of menstruation (amenorrhoea). In 2021, the Czech pharmacovigilance authority SUKL received more than 400 reports on adverse events associated with menstrual disorders [4] and heavy menstrual bleeding was also confirmed by Trogstad et al. [5].

In conclusion, Slaba et al. propose a hypothesis, implement a different one in the model, and fail to report a fundamental discrepancy between the model prediction and observed data. This is rather unfortunate because it distracts from the investigation of the real reasons why TFR in many Western countries began to plummet approximately 9 months after the vaccination of the fertile cohort against COVID-19.

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- [5] Trogstad L, Laake I, Robertson AH, Mjaaland S, Caspersen IH, Juvet LK, et al. Heavy bleeding and other menstrual disturbances in young women after COVID-19 vaccination. Vaccine 2023;41:5271–82. https://doi.org/10.1016/j.vaccine.2023.06.088.