# Fertility rates and birth outcomes after ChAdOx1 nCoV-19 (AZD1222) vaccination

Fears of adverse effects of COVID-19 vaccination on fertility have affected vaccine uptake in some communities. Despite the absence of supporting evidence for such a risk, low biological plausibility, and preliminary data supporting the safety of mRNA vaccines in pregnancy,[1–3] this claim has become widespread, and it has been challenged by WHO.[4] Vaccine hesitancy during pregnancy, or among women of childbearing age, could have substantial public health consequences because infection with SARS-CoV-2 during pregnancy is a risk factor for severe maternal illness and complications.[5,6]

We have analysed pregnancies that have occurred in four ongoing phase 1, phase 2, and phase 3 clinical trials of ChAdOx1 nCoV-19 (AZD1222)[7] in three countries (NCT04324606 and NCT04400838 in the UK; NCT04536051 in Brazil; and NCT04444674 in South Africa). Participants of childbearing age (defined as 49 years or younger) were randomly assigned to receive ChAdOx1 nCoV-19 or the control vaccine. Pregnancy was an exclusion criterion in all four trials, and all female volunteers tested negative for urine β-hCG before vaccination. Any pregnancies that occurred after vaccination were recorded and followed up until 3 months after birth. Pregnancy outcomes were reviewed by the independent data and safety monitoring board.

121 (1%) of 9755 participants reported a pregnancy during the trials. The fertility outcome analysis set included 93 pregnant women, 50 of whom received ChAdOx1 nCoV-19, and 43 of whom received the control vaccine). The pregnancy outcome analysis set included 107 women (72 of whom received ChAdOx1 nCoV-19, and 35 of whom received the control vaccine; appendix p 1). Miscarriage was defined as pregnancy loss before 23 weeks of gestation. Baseline characteristics were similar between the vaccine and control groups, with the biggest differences being age and current alcohol use (appendix p 2).

We found no evidence of an association between reduced fertility and vaccination with ChAdOx1 nCoV-19 (p=0·53–0·80; table 1; for fertility rates by site, see appendix p 3). Analysis of pregnancy outcomes (table 2) excluded women in the control vaccine groups who had received either ChAdOx1 nCoV-19 or an mRNA vaccine as part of a national vaccine roll-out programme (n=14, including 11 women vaccinated after unmasking and during pregnancy (table 1), plus three additional women who received an mRNA vaccine before pregnancy; appendix p 2). 56 (52%) of 107 pregnancies in the pregnancy outcome analysis set were ongoing at the time of data lock on July 1, 2021.

Notably, the rate of miscarriage was no higher in the ChAdOx1 nCoV-19 group than in the control group, with a risk ratio (RR) of 0·67 (p=0·51). Adjusting the analysis for the effect of possible confounders kept the RR below but closer to unity at 0·84 (appendix p 4). 15 livebirths had taken place by the time of the analysis, and the three preterm births in the ChAdOx1 nCoV-19 group were in the late preterm stage (34–37 weeks of gestation). No stillbirths or neonatal deaths were reported in either group.

No terminations of pregnancy were reported in Brazil. However, termination of pregnancy is illegal in Brazil, and uncertainty remains about whether the reports of early pregnancy losses were all miscarriages. Therefore, a combined analysis of either miscarriage or termination was done for all sites (table 2), with separate subgroup analyses for termination alone and for miscarriage alone, excluding the Brazilian data. This subgroup included 24 participants who received a control vaccine and 43 participants who received ChAdOx1 nCoV-19.

Fertility was unaffected by vaccination with ChAdOx1 nCoV-19. Furthermore, compared with women who received the control vaccine, there was no increased risk of miscarriage and no instances of stillbirth in women vaccinated before pregnancy in global clinical trials of ChAdOx1 nCoV-19.

With increasing availability of misinformation, which continues to affect vaccine uptake, these data, along with published data on mRNA vaccines,[2,3] can provide evidence to support women in making decisions regarding vaccination.

Oxford University has entered into a partnership with AstraZeneca for further development of ChAdOx1 nCoV-19 (AZD1222). AJP is chair of the UK

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See Online for appendix

| | ChAdOx1 nCoV-19 (n=4925) | Control (n=4830)* | Fertility rate ratio (95% CI) | p value |
|---|---|---|---|---|
| Pregnant women (fertility rate)† | 50 (0·0102) | 43 (0·0089) | 1·14 (0·76–1·71) | 0·53 |
| Viable pregnancies (fertility rate)‡ | 32 (0·0065) | 29 (0·0060) | 1·08 (0·66–1·79) | 0·80 |

Data are n (fertility rate) unless otherwise stated. *11 women vaccinated during pregnancy were included in the controls (eight received AZD1222 and three mRNA vaccines). †28 pregnant women (six in the control vaccine group and 22 in the AZD1222 group) were excluded from this fertility analysis because they were unmasked to vaccine allocation before becoming pregnant. ‡Viable pregnancies did not include pregnant women who had a termination or miscarriage.

***Table 1:*** **Fertility rates**

| | ChAdOx1 nCoV-19 (n=72) | Control (n=35) | Risk ratio (95% CI) | p value |
|---|---|---|---|---|
| Miscarriage, excluding Brazilian data | 6/43 (14%) | 5/24 (21%) | 0·67 (0·23–1·97) | 0·51 |
| Termination, excluding Brazilian data | 8/43 (19%) | 6/24 (25%) | 0·74 (0·29–1·89 | 0·55 |
| Miscarriage or termination, all | 23/72 (32%) | 13/35 (37%) | 0·86 (0·50–1·49) | 0·67 |
| Preterm birth | 3/10 (30%) | 0/5 (0%) | Not calculable | 0·51* |
| Full-term birth | 7/72 (10%) | 5/35 (14%) | 0·68 (0·23–1·99) | 0·52 |
| Ongoing pregnancy | 39/72 (54%) | 17/35 (49%) | 1·12 (0·75–1·67) | 0·68 |

Data are n/N (%) unless otherwise stated. *Two-sided p value.

***Table 2:*** **Pregnancy outcomes**

Department of Health and Social Care's Joint Committee on Vaccination and Immunisation but does not participate in its discussions on COVID-19 vaccines, is a member of the WHO Strategic Advisory Group of Experts on Immunization, and a UK National Institute for Health Research senior investigator. All other authors declare no competing interests. The members of the Oxford COVID Vaccine Trial Group are listed in the appendix (pp 5–19).

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