

Pregnant People's Paradox—Excluded From Vaccine Trials Despite Having a Higher Risk of COVID-19 Complications

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Kristina Adams Waldorf, MD, recently coauthored a [study](#) that found a higher risk of hospitalization and death among people with coronavirus disease 2019 (COVID-19) who were pregnant than among those who weren't pregnant.

Still, 1 of her patients, a pregnant health care worker, "is kind of unsure" about whether she should get vaccinated, Adams

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Waldorf, an obstetrician-gynecologist at the University of Washington, said in an interview. The patient

worries that a COVID-19 vaccine could harm her fetus.

No wonder she is concerned.

All the COVID-19 vaccine trials, [like virtually all clinical trials](#), have excluded pregnant and lactating individuals from participating; however, developmental and reproductive toxicity [studies](#) with the Moderna vaccine in rats haven't uncovered any worrisome signals.

But while pregnant patients puzzle over whether they should get vaccinated, evidence is mounting that they have a higher risk of COVID-19 complications and death than people who aren't pregnant. Some [studies](#) also suggest that among pregnant patients with COVID-19, disease severity may increase the risk of preterm delivery.

"We are pretty confident that maternal deaths [from COVID-19] are being undercounted nationally," Adams Waldorf said. "We have terrible national data on this."

Behind the Headlines

Growing evidence that pregnant individuals are more likely to experience COVID-19 complications than nonpregnant individuals includes these 3 studies reported in late January:

- Adams Waldorf's retrospective cohort study, published online on January 19, focused on 240 pregnant Washington State patients with severe acute respiratory syn-



drome coronavirus 2 (SARS-CoV-2) infection confirmed by polymerase chain reaction (PCR) testing between March 1 and June 30, 2020. Of the 240, 24 were hospitalized due to COVID-19 and 3 died. The pregnant patients' risk of dying from COVID-19 was 13.6 times higher than that of nonpregnant individuals the same age.

- Another retrospective cohort [study](#), of 262 women of childbearing age diagnosed with symptomatic COVID-19, found that the 22 who were pregnant were at a significantly increased risk of severe disease.
- A [study](#) presented at the recent annual meeting of the Society for Maternal-Fetal Medicine found that rates of gestational hypertension and preeclampsia without severe features were significantly higher in pregnant patients with positive PCR test results for COVID-19 than in those who tested negative for COVID-19.

Mixed Messages?

Also during January, medical and public health groups released a series of statements about whether pregnant individuals should be vaccinated against COVID-19.

- January 7: The US Centers for Disease Control and Prevention (CDC) [updated](#) its

COVID-19 vaccination guidelines for pregnant people. "Based on how [messenger] RNA [Pfizer-BioNTech and Moderna] vaccines work, experts believe they are unlikely to pose a specific risk for people who are pregnant," the update's authors wrote. However, the actual risks to pregnant individuals and their fetuses are unknown because the vaccines haven't been studied in this population. The bottom line, the CDC said, is that vaccination "is a personal choice for people who are pregnant."

- January 8: In a [recommendation](#) about the Pfizer-BioNTech vaccine, the World Health Organization (WHO) recommended withholding vaccine from pregnant women unless the benefit of vaccination outweighs the potential risk, as in the case of health care workers or those who have comorbidities linked with severe COVID-19.
- January 25: The WHO issued an [interim recommendation](#) for use of Moderna's vaccine, repeating the advice it gave for pregnant women in its recommendation about the Pfizer-BioNTech vaccine.

- January 27: Responding to the WHO recommendations to withhold vaccines from pregnant people unless they are at high risk of exposure or severe COVID-19, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) issued a [joint statement](#) reaffirming that all pregnant individuals should be able to decide whether they want to be vaccinated against a potentially life-threatening virus.
- January 29: In a [statement](#), the WHO noted that its recommendations for immunizing pregnant women with COVID-19 vaccine are "very similar" to those of the CDC. The main difference, WHO officials said, is that its recommendations place more emphasis on guiding immunization program decisions, while the CDC's recommendations emphasize guiding individual decision-making.

"The conflicting information being provided to pregnant individuals stems from long-standing obstacles to the inclusion of pregnant and lactating people in clinical research," Diana Bianchi, MD, director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and 2 coauthors noted February 10 in a [JAMA Viewpoint](#)

about the need for involving pregnant people in COVID-19 vaccine research.

Seeking Answers

Despite some confusion and hesitancy, pregnant individuals are getting vaccinated.

As many as 300 000 health care workers, members of the highest-priority group for vaccination, are pregnant, a recent [opinion piece](#) noted. In addition, a few dozen phase 3 vaccine trial participants [didn't know they were pregnant](#) when they received their injections. So multiple efforts are underway to collect information about pregnant individuals who receive COVID-19 vaccines. Among them:

- BioNTech and Pfizer [plan to enroll](#) approximately 4000 pregnant women at 21 US sites in a phase 2/3 placebo-controlled COVID-19 trial of their vaccine.
- Johnson & Johnson subsidiary Janssen Vaccines will enroll 824 pregnant participants in a phase 2 placebo-controlled trial of its COVID-19 vaccine.
- The CDC's [V-safe After Vaccination Health Checker](#), a smartphone-based tool that uses text messaging and web surveys asks participants whether they are pregnant.
- [Moderna has created a registry](#) to monitor pregnancy outcomes in people who received the company's COVID-19 vaccine.

- The University of Washington Department of Obstetrics and Gynecology, where Adams Waldorf is on the faculty, has [established a registry](#) involving individuals who are pregnant, postpartum, lactating, or contemplating pregnancy in the next 1 or 2 years.

- [Pregistry](#), a startup company focused on improving maternal and fetal health, is collaborating with the Harvard School of Public Health on a [registry](#) that aims to enroll 5000 people to evaluate obstetric, neonatal, and infant outcomes after COVID-19 vaccination during pregnancy.

The Upshot

Already, the [CDC recommends](#) receiving the influenza and the tetanus, diphtheria, and pertussis vaccines during each pregnancy.

"Pregnant women are very, very susceptible to influenza," noted Adams Waldorf, who is studying a nonhuman primate model to learn about differences between the immune response in pregnant vs non-pregnant people.

As for the COVID-19 vaccine, "pregnant women who are at high risk should be given the choice" to get it, Adams Waldorf said, "and if it were me, I would take it in a heartbeat." ■

Note: Source references are available through embedded hyperlinks in the article text online.