Infectious diseases

https://doi.org/10.1038/s41591-025-04000-2

Ebola vaccine safe for mothers and infants

Beate Kampmann & Alice Hucko

A clinical trial of pregnant women provides critical safety and immunogenicity data in support of a two-dose Ebola vaccine regimen — and reinforces the importance of maternal immunization research, urgently needed for other preventable diseases.

Maternal immunization (that is, vaccinating women during pregnancy) is a promising tool for tackling infant morbidity and mortality worldwide. This approach enhances a 'gift of nature,' whereby antibodies are transferred from mother to fetus — either transplacentally during pregnancy, or postnatally in breast milk — and provide passive, antigen-specific protection against infections during the first few months of life[1]. Any intervention during pregnancy must be not only effective but also safe for both mother and child, before and after birth, in line with the principle of 'first, do no harm'. Yet in public health emergencies, such as those involving Ebola or SARS-CoV-2, safety data in pregnant women were lacking when the respective vaccines were recommended by the World Health Organization (WHO)[2]. Now, a clinical trial by Nyombayire et al.[3], funded by the Coalition for Epidemic Preparedness Innovations and published in this issue of *Nature Medicine*, marks an important contribution to the evidence base for the immunization of pregnant women in the context of public health emergencies.

In this study, healthy pregnant women in Rwanda received a heterologous two-dose Ebola vaccine regimen consisting of Ad26.ZEBOV and MVA-BN-Filo, two non-replicating virus-vectored vaccines administered 56 days apart. The vaccine regimen is currently approved for non-pregnant people over 1 year of age. Prior to the trial, no safety or immunogenicity data existed for this product in pregnant women or infants; this study begins to fill that critical gap.

In the open-label, randomized, controlled trial, 981 women received the two-dose regimen during pregnancy, and 963 women were vaccinated 6–10 weeks postpartum. Those in the postpartum group served as unvaccinated controls for pregnancy safety outcomes. The safety data show no differences between women vaccinated during pregnancy and unvaccinated control participants in the proportion of adverse pregnancy, fetal or infant outcomes. Immunogenicity analyses of a subset of 316 women revealed that >99% developed antibodies targeting the Ebola virus glycoprotein after the second dose, which were sustained in ≥90% of women 1 year later. Cord blood and infant serum samples confirmed the passive transfer of vaccine-induced antibodies and persistence at 14 weeks, with detectable levels in ≥95% of infants. These data support entirely reassuring and comparable safety and immunogenicity outcomes in pregnant and non-pregnant people in the cohort under investigation. Despite limitations of sample size, setting and follow-up, the findings provide valuable support for public health recommendations.

A key question is why crucial safety data are so often generated only after vaccine rollout, as was also seen with SARS-CoV-2. For Ebola, case-fatality rates during pregnancy are estimated at 53% on average, with generally poor fetal outcomes[4]. On the basis of empirical morbidity and mortality data gathered during these health emergencies, vaccines against Ebola and SARS-CoV-2 have proven highly protective in pregnancy, and risk–benefit analyses justified their use. Still, this does not absolve researchers of the responsibility to generate the robust safety data needed to reassure regulators, health systems and, most importantly, women themselves that these vaccines are not causing harm to either women or their offspring.

A major contributing factor to the paucity of data is the long-standing reluctance to include pregnant women in clinical trials, particularly when there is need for rapid approval, as is the case during epidemics[5]. Fortunately, much has changed in recent years, including within regulatory frameworks, since the Ebola and SARS-CoV-2 emergencies. Pregnant women are no longer automatically excluded

CREDIT: IMPRINT NETWORK

from clinical trials; in fact, they are now explicitly included – at least, on paper.

In 2016, the US Congress established the Task Force on Research Specific to Pregnant Women and Lactating Women to identify gaps in the knowledge about safe and effective therapies and vaccines[6]. More recently, the US National Academies of Sciences, Engineering, and Medicine issued nine recommendations to the US Food and Drug Administration, the US Congress and the US National Institutes of Health to improve clarity and predictability, facilitating the inclusion of pregnant and lactating women in research[7]. Alongside regulatory reforms, general protocols have been developed to enable harmonized clinical trials in pregnancy, including in emergency settings[8]. The COVAX Maternal Immunization Working Group and WHO technical advisory boards have published guidelines for the conduct of clinical vaccine trials during pregnancy, to avoid future delays and increase investigator confidence, including by industry[9].

Without question, including pregnant women and their newborns in clinical trials adds complexity, as complications during pregnancy and in the neonatal period are common. These so-called 'adverse events of special interest' must be systematically captured to enable objective risk–benefit assessment and address concerns that an intervention, such as a vaccine, may have caused harm. Further work is needed to ensure consistent follow-up of pregnant women and infants, with post-licensure data collection that goes beyond self-reporting, as was the case for SARS-CoV-2 and the V-Safe initiative[10]. To achieve the robust follow-up required, pregnancy registries and linkages between maternal and child health records must be established to close the widespread gaps that exist even in high-income countries – to ensure continuous safety data collection, including after vaccine rollout. This is the case for overall adverse event reporting by the WHO-supported Global Advisory Committee on Vaccine Safety system, which systematically compiles safety data from routine vaccinations.

While the data published by Nyombayire et al. support the use of Ebola vaccines in pregnancy[3], it is essential to move beyond the current practice of collecting key safety data only after rollout. Much has changed since the Ebola outbreak in West Africa 10 years ago, when some women hid their pregnancies to receive the vaccine, having witnessed pregnant relatives die from the disease while knowing vaccination was not permitted in pregnancy. Since then, international initiatives such as the IMPRINT network (which addresses biological and implementation challenges to vaccines in pregnancy and newborns), SPEAC (Safety Platform for Emergency Vaccines), the Global Advisory Committee on Vaccine Safety, the Safe in Pregnancy portal (which delivers up-to-date evidence-based information on novel vaccines for use in pregnancy) and the Gates Foundation (which has supported clinical and observational studies and advocacy initiatives for vaccination during pregnancy for many years) have contributed to keeping this agenda at the forefront of deliberations about maternal immunization. But many gaps remain. There are still no published data for the safety of mPOX vaccines in pregnant women and very young children, who have high morbidity and mortality from this disease[11], or for vaccines against Lassa fever, for which infection during pregnancy usually results in fetal loss[12].

Science has advanced, but preparedness must also evolve to include pregnant women in clinical trials and to support robust post-licensure studies. These resulting complexities must be acknowledged, funded and integrated to generate safety data proactively. While public health authorities were right to recommend vaccines against Ebola and SARS-CoV-2 during emergencies, safety data should be available beforehand to increase confidence. With new high-risk pathogens likely to emerge, this preparedness is urgent: the time to act is now, with no more excuses.

Beate Kampmann & Alice Hucko
Charité Centre for Global Health, Charité Universitätsmedizin Berlin, Berlin, Germany.
e-mail: beate.kampmann@charite.de

Published online: 09 October 2025

References

1. Saso, A. & Kampmann, B. *Front. Microbiol.* **11**, 1499 (2020).
2. World Health Organization. *Wkly. Epidemiol. Rec.* **99**, 351–362 (2024).
3. Nyombayire, J. et al. *Nat. Med.* https://doi.org/10.1038/s41591-025-03932-z (2025).
4. Kayem, N. D. et al. *Trans. R. Soc. Trop. Med. Hyg.* **116**, 509–522 (2022).
5. Kampmann, B. *Nat. Med.* **27**, 8 (2021).
6. Task Force on Research Specific to Pregnant Women and Lactating Women. *NIH* https://go.nature.com/4nJRe7x (2018).
7. National Academies of Sciences, Engineering, and Medicine. *Advancing Clinical Research with Pregnant and Lactating Populations: Overcoming Real and Perceived Liability Risks* (eds. March, A. et al.) (National Academies Press, 2024).
8. International Council for Harmonisation. *European Medicines Agency* https://go.nature.com/3VRoQol (6 April 2025).
9. Muñoz, F. M. et al. *Vaccine* **62**, 127513 (2025).
10. Centers for Disease Control and Prevention. *CDC* https://go.nature.com/3W6mUIo (31 January 2025).
11. Nachega, J. B. et al. *N. Engl. J. Med.* **391**, 1267–1270 (2024).
12. Chaudhary, M. et al. *Vaccine* **43**, 126479 (2025).