



POLICY FORUM

ETHICS

Ethics of maternal vaccination

Involvement of women is critical in establishing guidelines

By A. T. Chamberlain,¹ J. V. Lavery,¹
A. White,² S. B. Omer¹

Innovations in vaccine science have given us an incredible opportunity to leverage the maternal immune system to improve maternal, fetal, and infant health outcomes. Maternal vaccination reduces the risk of infant infection primarily through the transfer of protective maternal antibodies to the fetus (1). Although a growing number of countries are adopting maternal vaccine programs against diseases like influenza and pertussis, and there is an increased focus on including pregnant women in trials for new vaccines, there is little discussion of the ethical underpinnings of maternal vaccine programs (2). We see the proposals thus far as being overly paternalistic, founded on a too-limited conception of risk-benefit analyses that has potential to derail the development and use of lifesaving vaccines. By contrast, an ethical approach focused on mothers' primary interests in protecting themselves and their children could serve as the basis of the ethical framework that guides vaccine policies.

Historically, influenza vaccines have been given prenatally to protect expectant mothers from severe influenza-related complications, with more recent research revealing immunologic benefits to the infant (1). Other vaccines, such as those against tetanus and hepatitis B, are primarily pursued in circumstances involving high risk of perinatal

transmission either during birth or after primary or chronic maternal infection (3). Pertussis-containing vaccines, among others, are now being recommended for the primary purpose of conferring immunologic protection to the future infant. Two new vaccines against respiratory syncytial virus (RSV) and group B streptococcus (GBS) are undergoing clinical trials for potential administration during pregnancy and are primarily targeted toward preventing morbidity and mortality in young infants rather than in mothers (3). This proliferation of maternal vaccines for the primary benefit of the infant poses new ethical challenges to national immunization advisory groups looking to establish maternal vaccine programs.

RISKS, BENEFITS, INADEQUACIES

Rationales for large-scale vaccination programs, the quintessential public health intervention, have always recognized the protection of others through herd immunity or indirect protection as a core benefit. But vaccine testing and administration are governed by an ethical and legal paradigm that includes assessment of the acceptability of risk and benefit—and in which the ultimate decisional authority rests in individual informed consent (4, 5). Under this approach, the anticipated protective health benefits are weighed primarily against the risks of injury from vaccination, for the individual receiving the vaccine. And vaccines have historically only achieved recommendation when the benefits (to the individual and the society) outweigh the associated physical risks to the individuals receiving the vaccine.

When considering maternal vaccination

A pregnant woman is vaccinated in Caracas, Venezuela. Research among women from different cultures on the acceptability of maternal vaccination could advance programmatic decisions.

under this risk-benefit paradigm, the ethical calculus is complicated by two unique factors. One is that both the mother and the fetus/infant are involved. In addition, the concept of herd protection to the larger population is less applicable because pregnancy is transient and pregnant women make up just a fraction of the disease-susceptible population. Taking these nuances into account, it is then customary to explore how risks and benefits of a vaccine administered during pregnancy may affect the mother and the infant. But the traditional injury-focused account of risk begins with two substantive flaws: It may, inadvertently, discount a mother's interest in the welfare of her future child; and it may serve as a major barrier to protecting infants in cases where a prenatal vaccine offers little benefit to the mother herself.

A recently published approach to ethical decision-making about maternal vaccine programs (6) serves as an example of the pitfalls associated with applying a conventional risk-benefit paradigm to maternal immunization. The authors conclude that maternal vaccination should only be offered when "concrete, severe risks of disease" are posed to the "mother and child" [emphasis added]. However, if their ultimate conclusion is applied as stated, then even current maternal pertussis vaccination programs could be considered unethical. Although pertussis poses a severe risk to infants, it does not have nearly the same severity for most mothers. The disease risks of pertussis are asymmetrical for the mother and the infant; pertussis does not fit whatever the subjective definition is of a "concrete and severe disease risk" to the mother as it does for the infant. This shortcoming becomes more marked when considering future maternal vaccines such as those against RSV or GBS, which can be deadly to infants but pose very limited threat to mothers (3).

Although it is critical for policy-makers to thoroughly explore and understand the biologic risks a vaccine administered during pregnancy may pose to both the mother and the fetus, approaches thus far (6) fall short by not accounting for a mother's strong interest in having a healthy rather than a sick child. Concluding that a disease risk must be concrete and severe for both the mother and the infant before a maternal vaccine is justifiable unfairly precludes a woman's ability to decide to take preventive action against a threat to her child's life or welfare. This directly violates her

¹Emory University, Atlanta, GA 30322, USA. ²University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA. Email: allison.chamberlain@emory.edu

agency and autonomy in the vaccine decision-making process. Requiring severe and concrete risks to both the pregnant woman and her child constitutes a kind of paternalism that, though seemingly beneficent in its intent to prioritize interventions that also benefit mothers, may ultimately remove a viable means for women to protect their children. It may also stifle extremely promising vaccination campaigns that are poised to reduce some of the greatest threats to neonates worldwide.

Although this approach provides a clear example of how a risk-benefit assessment can go awry, it may not necessarily be representative of all versions of risk-benefit analyses. Other, more holistic approaches might, for instance, explicitly take psychological or social harms into account as well.

INTERESTS-BASED APPROACH

An interests-based approach, rooted in the need to foreground women's agency and to extend considerations of risk beyond the risk-as-physical-injury paradigm, has five distinct advantages over the standard, risk-benefit paradigm.

First, an interests-based approach incorporates the interests of expectant mothers at its core. Under normal circumstances and across most societies, there is no dispute about the legitimacy of a mother's interests in the welfare of her fetus/infant and no question about her unique standing to pursue these interests on behalf of her infant. An interests-based framing keeps a woman's agency front and center, making it less vulnerable to discounting or subversion of the woman's moral standing to make the relevant decisions.

Second, a mother's interest in the welfare of her fetus/infant is at least as concrete and universally understood a consideration as an appeal to the protection of her autonomy. Third, articulating how best to respond to the interests of mothers in the context of decisions about maternal immunization requires substantively and formally including women in developing ethical guidelines. It is not clear whether or how this critical step was reflected in the recent risk-benefit-oriented guidelines; the guidelines' authorship, the primary indicator of substantive, formal contribution to intellectual work, includes no women (6).

Fourth, unlike an approach anchored in the policy goal of minimizing risk, which incorporates any risk to mothers into these threshold determinations (6), an interests-based approach helps clarify the nature of the action being considered by the mother. This approach empowers the mother to consider her interests in the welfare of her fetus/

infant, rather than simply relying on her consent to assume risks for which there are little to no countervailing clinical benefits. Fifth, an interests-based approach would provide robust grounds, anchored in women's interests and corresponding rights in privacy and personal security, to possibly oppose mandatory maternal vaccination. Mandatory immunization could become a plausible scenario if voluntary maternal immunization results in impressive public health outcomes and sufficiently low risk to mothers.

The concept of mandatory maternal interventions and the ethical challenges associated with the asymmetrical risks and benefits for mothers versus infants have arisen in other contexts, perhaps most aptly through folic acid supplementation to prevent neural tube defects. Public health benefits for infants of folic acid were so compelling, with few notable risks to expectant mothers, that many countries required fortification of wheat flour with folic acid (7). Although mandatory vaccination is a well-established

“An interests-based approach would honor a woman’s agency and autonomy... and avoid reducing her to a ‘vaccine delivery system.’”

and ethically justifiable concept in childhood vaccines, especially in societies where vaccination is viewed as a routine parental obligation toward children (8, 9), it should not be a strategy accepted outright for maternal vaccination. An interests-based approach would honor a woman's agency and autonomy in making health-related decisions that affect her and her fetus and avoid reducing her to a “vaccine delivery system.”

To effectively operationalize an interests-based approach, several key steps will be necessary. Rigorous research among women from different cultures on the acceptability of maternal vaccination under a variety of disease scenarios (e.g., for vaccines that only benefit infants) could advance and refine programmatic decisions. This could be accomplished through direct surveys of pregnant women, potentially sponsored by National Immunization Technical Advisory Groups.

Women must be adequately represented in decision-making bodies that influence national- and international-level policy decisions about maternal vaccine programs. Sufficient female representation cannot be assumed, as illustrated by a recent review of gender representation on the boards of 17 global public-private partnerships for health

(10). In this review, on average, women represented only 29% of board members, and only one organization had 50% gender parity of its governing board.

Extending this interests-based approach to developments under way in biomedical and vaccine research is also important. In 2016, the U.S. National Vaccine Advisory Committee (NVAC) issued recommendations aimed at overcoming gaps and barriers in the implementation of maternal vaccine programs, a subset of which focused on ethical issues such as revising the “exclusionary climate” around research in pregnancy (11). This report was followed by a key change to U.S. federal policy for the protection of human subjects (i.e., the Common Rule) removing pregnant women from the list of populations inherently vulnerable to coercion or undue influence (12). These actions, when coupled with rationales for explicitly including women in Zika vaccine trials (2), lend support to a shift toward women-centric, interests-based approaches to maternal vaccine research and decision-making.

The interests-based approach can be used to advance maternal vaccine research; for example, studies assessing women's attitudes toward being offered the option of remaining in a vaccine trial should they become pregnant would help establish a more robust empirical evidence base.

We must not accept an ethical paradigm that does not appropriately account for women's interests in these decisions. Creating strong maternal immunization programs starts with cultivating strong support for the vaccines among the mothers expected to accept them. ■

REFERENCES

1. S. B. Omer, *N. Engl. J. Med.* **376**, 1256 (2017).
2. “Pregnant women & the Zika virus vaccine research agenda: Ethics guidance on priorities, inclusion, and evidence generation,” Ethics Working Group on ZIKV Research & Pregnancy (2017); www.zikapregnancyethics.org/.
3. G. K. Swamy, R. H. Beigi, *Vaccine* **33**, 6436 (2015).
4. A. L. Caplan, J. L. Schwartz, “Ethics,” in *Plotkin’s Vaccines*, P. A. Plotkin, W. A. Orenstein, P. A. Offit, K. M. Edwards, Eds. (Elsevier, ed. 7, 2018), chap. 82, pp. 1631–1637.
5. T. L. Beauchamp, J. F. Childress, *Principles of Biomedical Ethics* (Oxford Univ. Press, New York, ed. 5, 2001).
6. M. Verweij, P. Lambach, J. R. Ortiz, A. Reis, *Lancet Infect. Dis.* **16**, e310 (2016).
7. M. A. Honein, L. J. Paulozzi, T. J. Mathews, J. Erickson, L. C. Wong, *JAMA* **285**, 2981 (2001).
8. P. H. Streefland, A. M. Chowdhury, P. Ramos-Jimenez, *Bull. World Health Org.* **77**, 722 (1999).
9. K. Wilson, M. Barakat, S. Vohra, P. Ritvo, H. Boon, *Public Underst. Sci.* **17**, 231 (2008).
10. S. Hawkes, K. Buse, A. Kapilashrami, *Global Health* **13**, 1 (2017).
11. *Public Health Rep.* **132**, 271 (2017).
12. “Federal policy for the protection of human subjects,” *Fed. Regist.* **82**, 7149 (2017).

10.1126/science.aao4219

Ethics of maternal vaccination

A. T. Chamberlain, J. V. Lavery, A. White and S. B. Omer

Science **358** (6362), 452-453.
DOI: 10.1126/science.aao4219

ARTICLE TOOLS	http://science.sciencemag.org/content/358/6362/452
REFERENCES	This article cites 9 articles, 0 of which you can access for free http://science.sciencemag.org/content/358/6362/452#BIBL
PERMISSIONS	http://www.sciencemag.org/help/reprints-and-permissions

Use of this article is subject to the [Terms of Service](#)

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. 2017 © The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. The title *Science* is a registered trademark of AAAS.