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COVID-19 booster doses in pregnancy and global vaccine equity

Immunisation against SARS-CoV-2 with mRNA vaccines remains the most effective way of preventing COVID-19-related morbidity and mortality. Medium-term data show that the efficacy of mRNA vaccination (two doses) is robust for up to 5–6 months, as supported by immunogenicity studies.^{1,2} Thereafter, the effectiveness of mRNA vaccines diminishes, and booster doses have been recommended for various high-risk groups. In 2021, the American College of Obstetricians and Gynecologists recommended booster doses for pregnant and postpartum women on the basis of their increased risk of COVID-19-related

complications.³ However, data on the durability of immune response in pregnant women are scarce.

Barda and colleagues reported the effectiveness of booster mRNA vaccines in a large population study from Israel.⁴ A booster dose administered at least 5 months after the second dose significantly reduced the rate of new COVID-19 infections, hospital admissions, and severe infections in a cohort of 1 158 269 individuals with a median follow-up time of 2 weeks. Based on these results, the number-needed-to-boost (NNB) to prevent one excess case of hospital admission was lower than the NNB to prevent severe COVID-19 (table). However, for each of these outcomes, NNBs were about 20 times higher in those younger than 40 years, and 10–25 times higher in those without comorbidities, reflecting much lower absolute complication rates. Although these NNB estimates to prevent severe COVID-19 might be an overestimate for pregnant women, who have a two to three times increased risk of severe COVID-19 (compared with other women of reproductive age), even halving these NNBs based on age would mean that more than 10 000 booster doses would be required to prevent one case of hospitalisation or severe COVID-19 in pregnancy when administered 5 months after the second dose. The actual NNB to prevent hospitalisation



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	Hospital admissions		Severe COVID-19	
	Excess cases without boosters (per 100 000)	Number-needed-to-boost to prevent one case	Excess cases without boosters (per 100 000)	Number-needed-to-boost to prevent one case
By age, years				
16–39	4.9	20 408	2.5	40 000
40–69	96.7	1034	54.4	1838
By comorbidity				
Without existing comorbidities	11.9	8403	3.1	32 258
One to two comorbidities	101.9	981	78.8	1269

Table: Rate of breakthrough cases without boosters and number-needed-to-boost to prevent one case, by age and comorbidity⁴

or severe COVID-19 will be lower in the long term as the study had a median follow-up time of only 2 weeks. However, only in the presence of comorbidity would the NNBS be comparable to those for initial vaccination in pregnancy.⁵

Given the current low vaccination coverage among pregnant women, efforts have rightly focused on increasing vaccine uptake in unvaccinated individuals. It remains to be seen whether campaigns to address vaccine hesitancy among pregnant women, or ensuring equitable access to vaccination more generally, are more important than the allocation of resources to the administration of booster doses.⁶ Although any individual can decide to maximise their protection via booster doses, regardless of previous risk status, it is important to convey the magnitude of expected absolute effect for informed decision making (table). Algorithms assessing the risk of severe COVID-19 in pregnant women can be useful for triaging the need for boosters,⁷ and for considering women who might be at even higher risk of COVID-19, such as those who might not have developed an adequate immune response to vaccination (eg, organ transplant recipients and those with acquired immune deficiencies), those who might be at increased risk of exposure to SARS-CoV-2 and other breakthrough infections (eg, health-care workers), or those who might be at high baseline risk for severe COVID-19 (eg, those with severe obesity or pregestational diabetes).

The global shortage of vaccines and unequal distribution of the available stock raises an important ethical dilemma for giving booster doses to any group. Unvaccinated pregnant women in low-income and middle-income countries are at much higher risk of dying from COVID-19 but are also less hesitant to receive vaccination.⁸ Furthermore, the absolute reduction in risk following a booster is likely to be small for most

vaccinated pregnant women who do not have a comorbidity. Longitudinal profiling of immunogenicity induced by different types of vaccines in pregnant women is essential for informing booster timing. In the meantime, strategies for more equitable distribution of vaccines and reduction of vaccination hesitancy among the unvaccinated are likely to be more effective in reducing COVID-19 complications than offering boosters to all already-vaccinated pregnant women.

AK is a member of the COVAX working group and principal investigator of the PregCov trial and the Pfizer COVID-19 vaccine trial. PH is the chief investigator of the PregCov trial. All authors are leading and collaborating on COVID-19 vaccine studies.

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Department of Error

Brownlee S, Chalkidou K, Doust J, et al. Evidence for overuse of medical services around the world. *Lancet* 2017; **390**: 156–68—In this Series paper, the references in figure 2 have been corrected. These corrections have been made to the online version as of March 3, 2022.

The Lancet. Managing the opioid crisis in North America and beyond. *Lancet* 2022; **399**: 495—In this Editorial, the statistics on opioid deaths should have read: "opioid overdose deaths have increased in Black (27/100 000 deaths) and Native American and American Indian populations (28/100 000 deaths) such that in 2020, they exceed historically greater white mortality (26/100 000 deaths)". These corrections have been made to the online version as of Feb 16, 2022.

Tatum M. *China's population peak.* *Lancet* 2022; **399**: 509—This World Report should have stated that China's 14th 5-year plan runs from 2021 to 2025. This correction has been made to the online version as of March 3, 2022.



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