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Influenza immunisation in pregnancy is efficacious and safe, but questions remain

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- 6 Institute for Health Metrics and Evaluation. GBD Compare—Viz Hub. <https://vizhub.healthdata.org/gbd-compare/> (accessed March 12, 2020).
- 7 Stanaway JD, Afshin A, Gakidou E, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1923–94.
- 8 Wang M, Luo X, Xu S, et al. Trends in smoking prevalence and implication for chronic diseases in China: serial national cross-sectional surveys from 2003 to 2013. *Lancet Respir Med* 2019; **7**: 35–45.
- 9 Martinez CH, Mannino DM, Jaimes FA, et al. Undiagnosed obstructive lung disease in the United States: associated factors and long-term mortality. *Ann Am Thorac Soc* 2015; **12**: 1788–95.
- 10 Labaki WW, Han MK. Improving detection of early chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2018; **15** (suppl 4): S243–48.
- 11 National Institutes of Health. Estimates of funding for various research, condition, and disease categories (RCDC). Feb 24, 2020. https://report.nih.gov/categorical_spending.aspx (accessed March 11, 2020).
- 12 Reyfman PA, Washko GR, Dransfield MT, Spira A, Han MK, Kalhan R. Defining impaired respiratory health. A paradigm shift for pulmonary medicine. *Am J Respir Crit Care Med* 2018; **198**: 440–46.

Influenza immunisation in pregnancy is efficacious and safe, but questions remain



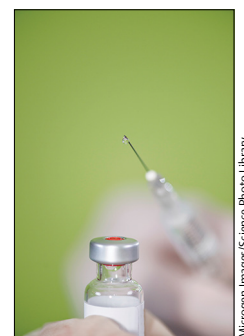
Pregnant women and infants are at high risk of severe influenza.^{1,2} Since 2012, WHO has recommended influenza immunisation during pregnancy in any trimester and targets pregnant women as a high priority in annual influenza vaccination programmes. Although trivalent seasonal inactivated influenza vaccine (IIV) has shown efficacy against influenza infections in both pregnant women and infants,^{3,4} the optimal timing of vaccination and effect on infant outcomes and safety remain controversial. The Bill & Melinda Gates Foundation funded three large randomised controlled trials in South Africa, Mali, and Nepal, which were done between 2011 and 2014, to increase the evidence base for the effects of maternal influenza immunisation.^{5–7} The three trials showed that IIV was effective in preventing laboratory-confirmed influenza in pregnant women and in infants younger than 6 months. In the trial done in Nepal, maternal immunisation reduced the frequency of low birthweight infants by 15%.

In *The Lancet Respiratory Medicine*, Saad B Omer and colleagues⁸ report the pooled analysis of these three trials, which included 10 002 pregnant women (5017 assigned to IIV and 4985 assigned to control) and 9800 liveborn infants (4910 livebirths from women who received IIV, and 4890 livebirths from women who received control) representing the largest dataset on women and newborns concerning influenza immunisation during pregnancy.

Several lessons can be learned from the results of Omer and colleagues' study. First, trivalent IIV administered at any time during pregnancy is effective in protecting pregnant women against PCR-confirmed influenza with a vaccine efficacy of 42% (95% CI 12–61) during

pregnancy and 60% (36–75) in the postpartum period. Efficacy lasted until 6 months after vaccination (49%, 95% CI 29–63), which has implications for countries with year-round influenza virus circulation.

Second, although maternal immunisation appears to be effective in protecting infants up to 6 months of age (vaccine efficacy 35% [95% CI 19 to 47] on cumulative episodes of PCR-confirmed influenza), this protection is significant only up to 4 months of age (56% [28 to 73] before 2 months and 39% [11 to 58] between 2 and 4 months) but not between 4 and 6 months of age (19%, 95% CI –9 to 40) underscoring the progressive decline in maternal antibody titre. This finding has two implications. First, it supports the immunisation strategy based on the passive transplacental transfer of anti-influenza antibodies, which allows for effective protection of children who cannot be vaccinated against influenza, because influenza vaccines are not approved in children 0–6 months old. Second, it shows that there is a period between the ages of 4 months (disappearance of maternal antibodies) and 6 months (possible start of vaccination) when children are no longer protected, which should be considered in immunisation strategies based on recombinant or high dose or adjuvanted influenza vaccines during pregnancy. Moreover, in this pooled analysis, the vaccine was not effective against influenza B in infants (vaccine efficacy 13%, 95% CI –21 to 37). This finding could be explained by the frequent mismatch between vaccine and circulating influenza B strains in trivalent IIV. Research on the use of the quadrivalent IIV in pregnant women, which would probably improve the overall vaccine efficacy and the



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efficacy against influenza B, especially in children, is therefore warranted.

Third, the optimal timing of immunisation during pregnancy remains unclear. Whether the gestational stage of pregnancy affects responses to vaccines has not yet been extensively studied and conflicting results on seroconversion after seasonal influenza immunisation exist. In this study, there was no difference in efficacy against PCR-confirmed influenza in infants when the mothers were vaccinated before or after 29 weeks of gestation. Concerning the mothers, there was no efficacy against PCR-confirmed influenza when they were vaccinated before 29 weeks gestational age (vaccine efficacy 30%, 95% CI -2 to 52). As explained by the authors, this absence of efficacy in mothers vaccinated before 29 weeks gestational age is probably due to statistical considerations (lack of power), rather than a real difference in efficacy, as this would be inconsistent with studies that have shown a waning serological response to influenza immunisation as pregnancy progresses.⁹

Fourth, these results confirm that seasonal influenza vaccination during pregnancy is safe. In addition to studies that did not show an increased incidence of adverse events in mothers,³ safety in fetuses and newborns was also shown when considering low birthweight, stillbirth, preterm birth, and small for gestational age. However, contrary to what was suggested in the trials in Bangladesh⁴ and Nepal,⁷ the pooled data show no positive association between maternal immunisation and low birthweight. These findings would be a strong argument for recommending generalised maternal influenza immunisation in resource-limited countries and suggest that further research considering the heterogeneity of the findings across countries is needed.

In conclusion, these pooled data confirm that influenza immunisation during pregnancy is safe and

effective for protecting both women and infants. Further research is warranted to consider more immunogenic vaccines to fill the protection gap in infants between 4 and 6 months of age and improve understanding of the association between maternal immunisation and child weight and length at birth at 6 months of age.

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- 1 Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998; **148**: 1094–102.
- 2 Neuzil KM, Mellen BG, Wright PF, Mitchel EF, Griffin MR. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *N Engl J Med* 2000; **342**: 225–31.
- 3 Loubet P, Kerneis S, Anselem O, Tsatsaris V, Goffinet F, Launay O. Should expectant mothers be vaccinated against flu? A safety review. *Expert Opin Drug Saf* 2014; **13**: 1709–20.
- 4 Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 2008; **359**: 1555–64.
- 5 Madhi SA, Cutland CL, Kuwanda L, et al. influenza vaccination of pregnant women and protection of their infants. *N Engl J Med* 2014; **371**: 918–31.
- 6 Tapia MD, Sow SO, Tamboura B, et al. Maternal immunisation with trivalent inactivated influenza vaccine for prevention of influenza in infants in Mali: a prospective, active-controlled, observer-blind, randomised phase 4 trial. *Lancet Infect Dis* 2016; **16**: 1026–35.
- 7 Steinhoff MC, Katz J, Englund JA, et al. Year-round influenza immunisation during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial. *Lancet Infect Dis* 2017; **17**: 981–89.
- 8 Omer SB, Clark DR, Madhi SA, et al. Efficacy, duration of protection, birth outcomes, and infant growth associated with influenza vaccination in pregnancy: a pooled analysis of three randomised controlled trials. *Lancet Respir Med* 2020; **8**: 597–608.
- 9 Schlaudecker EP, Ambroggio L, McNeal MM, Finkelman FD, Way SS. Declining responsiveness to influenza vaccination with progression of human pregnancy. *Vaccine* 2018; **36**: 4734–41.



Challenges in the interpretation and application of typical imaging features of COVID-19

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The detailed report by Timothy Harkin and colleagues¹ of an unusual case of respiratory illness eventually diagnosed as COVID-19 raises issues about the role of imaging in the

management of the disease. The causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can result in lethal pneumonia, so might chest imaging