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highlighted the importance of providing HBsAg and HBeAg testing and initiating antivirals 4 weeks before giving birth for women who were HBeAg positive. To achieve global hepatitis elimination goal by 2030, a robust programme to integrate the HBsAg and HBeAg screening and tenofovir disoproxil fumarate prophylaxis with antenatal care is essential in LMICs. However, we feel that passive immunisation with HBIg is an option together with hepatitis B vaccine for infants born to women who are HBeAg positive if it is available because it prevents MTCT of HBV.⁸ It is recommended that all infants should receive HepB-BD as soon as possible after birth, preferably within 24 h, followed by two or three doses to complete the primary series to prevent the MTCT of HBV.^{7,9,10}

We declare no competing interests.

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Vaccine pragmatism in the 21st century

One of the many lessons of the past 2 years has been the additional challenges faced by low-income and middle-income countries in accessing and distributing vaccines. Although the major focus has been accessing COVID-19 vaccination,¹ ever-mounting evidence exists to suggest that childhood vaccination programmes generally have been disrupted, for a number of reasons, including restrictions of population movement due to national lockdowns early in the COVID-19 pandemic, and later predominantly due to vaccine stockouts.^{2,3} Novel strategies to circumvent vaccine stockouts might decrease the impact of disrupted vaccination programmes, including using different formulations of homologous vaccines or the use of heterologous vaccine strategies for mixed vaccine schedules. Questions will always be asked however whether these alternative solutions are as effective as vaccination programmes with a single formulation vaccine, the standard method for evaluating vaccine efficacy. In *The Lancet Infectious Diseases*, Suman Kanungo and colleagues' study⁴ examined these questions by

evaluating six different vaccine regimens comparing Rotavac, a monovalent rotavirus vaccine, and Rotasiil, a pentavalent rotavirus vaccine, as single formulation regimens versus mixed formulation regimens. Both Rotavac and Rotasiil are two different commercially available vaccines for rotavirus in infants in India. Establishing whether a mixed formulation vaccination programme is as immunogenic as a single formulation vaccination programme is not the only challenge. Ensuring that such programmes are safe is equally important; given the notoriety of early rotavirus vaccine studies as a cause of increased intussusception,⁵ vaccine safety must also be an important consideration.

Kanungo and colleagues have shown that the commercially available rotavirus vaccines are equally effective non-inferior when given as part of a mix-and-match schedule and when given in a single formulation schedule. Approximately 300 infants were randomly assigned to each group of the trial. Seroresponse rates in the mixed vaccine regimens were



Published Online
May 16, 2022
[https://doi.org/10.1016/S1473-3099\(22\)00181-5](https://doi.org/10.1016/S1473-3099(22)00181-5)
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between 38.2% (ie, group 5 [Rotavac–Rotasiil–Rotasiil]) and 29.3% (ie, group 6 [Rotasiil–Rotavac–Rotavac]) compared favourably with those of the single vaccine regimen Rotavac (ie, group 1; seroresponse rate of 24.1%) and Rotasiil (ie, group 2; seroresponse rate of 35.2%).⁴ Similarly, in the mixed vaccine regimen, 91.1% (95% CI 89.5–92.6) solicited adverse events and 38.7% (36.1–41.4) unsolicited adverse events were reported, which were comparable to the 90.9% (95% CI 88.4–93.0) solicited adverse events and 37.9% (34.2–41.8) unsolicited adverse events observed in the single vaccine regimen.⁴

Increased incidence of childhood diseases and the resultant mortality is a real threat in a pandemic because of disruptions to normal medical services as staff are reassigned or even succumb to the cause. During the Ebola virus disease outbreak in Guinea, a concomitant measles outbreak was reported in 2015, of which 92.6% of cases were reported in children younger than 5 years, due primarily to disrupted vaccination services.⁶ Mix-and-match vaccines are also being explored as options for the prevention of Ebola virus disease outbreaks in health-care workers. An open-label, monocentric, phase 2, randomised trial examining heterologous vaccination of health-care workers is currently underway in the Democratic Republic of the Congo using two different Ebola vaccines (two doses of AD26.ZEBOV followed by an MVA-BN-Filo booster), and results should be available in late 2022.⁷

Rationale exists for mixed vaccine regimen approaches. Ample evidence shows that mixed vaccine regimens can be effective for COVID-19 in preventing severe disease and death, and might contribute to controlling the COVID-19 pandemic. Recent evidence has shown that a heterologous vaccination regimen that includes priming with an adenoviral vector vaccine for COVID-19 followed by an mRNA vaccine booster was non-inferior to two doses of the adenoviral vector vaccine, although the reverse (priming with an mRNA vaccine followed by the adenoviral vector vaccine), could not be shown to be non-inferior to homologous mRNA vaccination,⁸ or boosting with a protein subunit vaccine after priming with an mRNA vaccine,⁹ emphasising the need for formal trials to confirm the value of heterologous and mixed vaccination

programmes. Given the multiple different COVID-19 vaccines for priming and boosting,^{1,8,9} this information is essential to bringing the current COVID-19 pandemic under control.

In light of the high morbidity and mortality, rotavirus was responsible for nearly 130 000 deaths in children younger than 5 years in 2016,¹⁰ and in the absence of adequate vaccination programmes, including insufficient access to a particular vaccine, rotavirus will remain a significant contributor to childhood mortality even as the threat of COVID-19 diminishes. Knowing that in the event of vaccine stockouts or in countries where multiple vaccine preparations for a single disease might be available, pragmatic alternatives to single formulation regimens are reassuring in that they can be offered to bring vaccine-preventable diseases of public health importance under control.

I declare no competing interests.

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