



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Vaccination programmes have also been disrupted by violent conflict. For example, aid agencies have been unable to distribute COVID-19 vaccines, among other vaccines, in Houthi-controlled regions of Yemen.⁹ Similarly, there has been cessation of vaccination in areas of Ukraine targeted by the Russian invasion.¹⁰ Watson and colleagues² estimate that if the WHO targeted coverage of 40% had been achieved, 14 230 additional lives could have been saved in Yemen and 19 300 additional lives could have been saved in Ukraine.

The saving of more than 19 million lives by the unprecedented rapidity of development and roll-out of COVID-19 vaccines is an extraordinary global health feat. Nonetheless, millions of additional lives could have been saved by more equitable distribution of vaccines. The most effective approaches to promote vaccination coverage worldwide are multifaceted, requiring improvements in vaccine supply, cold-chain operations, and public confidence. High coverage in an individual country not only benefits that country but contributes to a worldwide reduction in SARS-CoV-2 transmission and emergence of novel variants. An enduring collective response is both pragmatic and ethically imperative.

We declare no competing interests.

Chad R Wells, *Alison P Galvani
alison.galvani@yale.edu

COVID-19 vaccinations for children

It is widely accepted that vaccination is key to bringing the COVID-19 pandemic under control by preventing severe disease. Due to the global disease distribution and diverse populations affected, multiple vaccine platforms are needed to overcome limitations in manufacture, logistics, and efficacy. Despite the global administration of up to 11.84 billion doses¹ of COVID-19 vaccine to healthy adults and people at increased risk of disease, vaccinations for children are an emerging consideration.

In *The Lancet Infectious Diseases*, Krishna Mohan Vadrevu and colleagues² provide initial safety and immunity data in children in India, who received a whole-virion adjuvanted inactivated SARS-CoV-2 vaccine (BBV152, Bharat Biotech International, Hyderabad, India). In Vadrevu and colleagues' study, participants were

Yale Center for Infectious Disease Modeling and Analysis, Yale School of Public Health, New Haven, CT 06520, USA

- 1 Ritchie H, Mathieu E, Rod s-Guirao L, et al. Coronavirus pandemic (COVID-19). Our World In Data. 2020. <https://ourworldindata.org/coronavirus> (accessed June 14, 2022).
- 2 Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *Lancet Infect Dis* 2022; published online June 23. [https://doi.org/S1473-3099\(22\)00320-6](https://doi.org/S1473-3099(22)00320-6).
- 3 Malpani R, Maitland A. Dose of reality: how rich countries and pharmaceutical corporations are breaking their vaccine promises. *The People's Vaccine*. Oct 21, 2021. <https://app.box.com/s/hk2ezb71vf0sla719jx34v0ehs0l22os> (accessed May 26, 2022).
- 4 Cohen J, Kupferschmidt K. Rich countries cornered the marketplace for COVID-19 vaccines. Here are four strategies to protect the rest of the world. *Science* (Washington, DC), May 26, 2021. <https://www.science.org/content/article/rich-countries-cornered-covid-19-vaccine-doses-four-strategies-right-scandalous> (accessed May 24, 2022).
- 5 Scott D. Congress is cutting corners on COVID-19 funding. We may pay for it later. *Vox*. April 5, 2022. <https://www.vox.com/coronavirus-covid19/23009783/covid-19-relief-funding-bill-senate-vaccines> (accessed May 27, 2022).
- 6 Kakule B, Lubukayi N, Muhindo E, Janoch E, Prather A. At the last mile: COVID-19 vaccines in DRC. *ReliefWeb*. April 27, 2022. <https://reliefweb.int/report/democratic-republic-congo/last-mile-covid-19-vaccines-drc> (accessed May 24, 2022).
- 7 Olu-Abiodun O, Abiodun O, Okafor N. COVID-19 vaccination in Nigeria: a rapid review of vaccine acceptance rate and the associated factors. *PLoS One* 2022; **17**: e0267691.
- 8 Sharfstein JM, Callaghan T, Carpiano RM, et al. Uncoupling vaccination from politics: a call to action. *Lancet* 2021; **398**: 1211-12.
- 9 Page M. Yemen: Houthi risk civilians' health in COVID-19. *Human Rights Watch*. June 1, 2021. <https://www.hrw.org/news/2021/06/01/yemen-houthi-risk-civilians-health-covid-19> (accessed June 6, 2022).
- 10 Chumachenko D, Chumachenko T. Impact of war on the dynamics of COVID-19 in Ukraine. *BMJ Global Health* 2022; **7**: e009173.

enrolled into one of three groups (ages ≥ 2 to 6 years, >6 to 12 years, and >12 to ≤ 18 years), and monitored for solicited and unsolicited adverse events after vaccination. The vaccine is authorised for use in adults by WHO, although not by the US, UK, or EU regulatory authorities.

To grant licensure, regulatory authorities must consider the potential risks and benefits of vaccination. In paediatric populations, both sides of this equation are not yet fully understood. Risks that must be considered include patients at additional risk of severe disease, long COVID, and the potential for children to contribute to disease transmission to other vulnerable groups such as older people, or to teachers and caregivers (which could, in turn, lead to super-spreader events).



Published Online
June 24, 2022
[https://doi.org/10.1016/S1473-3099\(22\)00414-5](https://doi.org/10.1016/S1473-3099(22)00414-5)
See [Articles](#) page 1303

Controlled clinical trials are needed to inform benefits and risks of vaccination. Benefits might lie on a spectrum of reducing severe disease, reducing mild disease, or reducing disease transmission. The efficacy data on BBV152 in children are not yet reported, but neutralising antibody responses were comparable to those previously measured in adult populations.² The initial data indicate no serious adverse events, deaths, or withdrawals due to an adverse event, and no cases of myocarditis; however, ongoing monitoring in larger numbers of vaccine recipients are essential to identify rare occurrences of side-effects. Immediate reactogenicity (eg, pain at the injection site) was low, although limitations of the study include an absence of a placebo group and the small number of participants.

Most countries allow vaccination for children and adolescents aged 16–18 years, and several also approve vaccinations for children younger than 16 years.³ Two other COVID-19 vaccines have been approved for children by the EU and WHO regulators, and both are mRNA based: BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna). BNT162b2 is also approved by the US and UK regulatory authorities for use in children.

Where licenced, mRNA-1273 can be given to children aged 12 years and older at the same dose as adults. The European Medicines Agency has also authorised a half-dose to be given to children aged 6–12 years. BNT162b2 also requires a lower dose to be given to children younger than 12 years. Adults and adolescents older than 12 years receive 30 µg per dose, as opposed to 10 µg per dose for ages 5–11 years.

In this study, the BBV152 vaccine used two doses of 6 µg of whole inactivated virus with toll-like receptor 7/8 agonist molecules absorbed on alum, given in the same dose, volume, and regime as in the adult phase 3 clinical trial.⁴ This strategy offers an easier mode of field implementation, because the same drug product can be formulated and stored to be used for both adults and children. This approach also reduces the potential for misdosing; however, vaccine safety and efficacy must not be compromised for the ease of manufacture or logistics.

Extensive assessment for paediatric clinical trials continues to be a challenge, mainly due to ethical

considerations. Societal and behavioural attitudes towards vaccine acceptance are also important. The few demographic studies that exist show that during the COVID-19 pandemic, parents had increased hesitancy towards COVID-19 vaccination in children, probably associated with increased risk perception.⁵ Knowledge around effectiveness and side-effects are crucial not just for national policy makers, but also for caregivers considering granting consent for their children to be vaccinated.^{6,7}

These trials are crucial to inform the cost-benefit analysis for policy and personal decisions. The risk and benefit of both disease and vaccination should be reported and discussed comprehensively among policy makers, because COVID-19 vaccination in children might assist recovery from the pandemic. But improving global accessibility to vaccines for vulnerable groups of adults, especially in countries with weak health-care systems, remains vital.

KRB is funded by the UK Health Security Agency and UK Vaccine Task Force and the views expressed in this Comment are those of the authors and are not necessarily those of UK Health Security Agency or the Department of Health and Social Care. ARM declares no competing interests.

Crown Copyright © 2022 Published by Elsevier Ltd. All rights reserved.

Abdul Razak Mariatulqabtiyah, *Karen R Buttigieg
karen.buttigieg@ukhsa.gov.uk

Laboratory of Vaccine and Biomolecules, Institute of Bioscience (ARM), and Department of Cell and Molecular Biology, Faculty of Biotechnology and Biomolecular Sciences (ARM), Universiti Putra Malaysia, Serdang, Selangor, Malaysia; UK Health Security Agency, Porton Down, Salisbury SP4 0JG, UK (KRB)

- 1 <https://ourworldindata.org/covid-vaccinations> (accessed June 2, 2022).
- 2 Vadrevu KM, Reddy S, Jogdand H, et al. Immunogenicity and safety of an inactivated SARS-CoV-2 vaccine (BBV152) in children aged 2–18 years: interim data from an open-label, non-randomised, age-de-escalation phase 2/3 study. *Lancet Infect Dis* 2022; published online June 16. [https://doi.org/10.1016/S1473-3099\(22\)00307-3](https://doi.org/10.1016/S1473-3099(22)00307-3).
- 3 Our World in Data. Are children eligible for COVID-19 vaccination?, Dec 8, 2021. <https://ourworldindata.org/grapher/covid-vaccine-age> (accessed June 2, 2022).
- 4 Ella R, Reddy S, Blackwelder W, et al. Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial. *Lancet* 2021; **398**: 2173–84.
- 5 He K, Mack WJ, Neely M, Lewis L, Anand V. Parental perspectives on immunizations: impact of the COVID-19 pandemic on childhood vaccine hesitancy. *J Community Health* 2022; **47**: 39–52.
- 6 Fedele F, Aria M, Esposito V, et al. COVID-19 vaccine hesitancy: a survey in a population highly compliant to common vaccinations. *Hum Vaccin Immunother* 2021; **17**: 3348–54.
- 7 Bell S, Clarke R, Mounier-Jack S, Walker JL, Paterson P. Parents' and guardians' views on the acceptability of a future COVID-19 vaccine: a multi-methods study in England. *Vaccine* 2020; **38**: 7789–98.