Moving forward with an imperfect vaccine

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Even vaccines used in largely successful disease control programmes (eg, measles, polio, or smallpox) have required high vaccine coverage, often with multiple doses, and do not lead to perfect durable immunity for all people. As vaccines are developed against a wide range of pathogens, including malaria[1] and SARS-COV-2,[2] and many vaccines confer only short-term and modest levels of individual protection, the global community is left to balance limited resources between investments in developing better vaccines and public health efforts to provide imperfect but widespread protection to the masses. Killed whole-cell oral cholera vaccines (OCVs) present one such example.

The current generation of OCVs was prequalified by WHO in 2011.[3] The last published meta-analysis with data from multiple countries illustrated that a two-dose OCV regimen conferred protection (effectiveness: 76%, 95% CI 42–69) over the first years, with young children having roughly half the protection as older children and adults.[4] Before this issue of *The Lancet Infectious Diseases*, only two studies using the modern formulation of OCVs had published cumulative efficacy or effectiveness results over a period of more than 2 years post-vaccination, one from Haiti (4 years)[5] and another from India (5 years).[6] Responding to this limited evidence, Mohammad Ali and colleagues[7] report on estimates of OCV effectiveness from a 2–4-year follow-up of a cluster randomised trial in Bangladesh. They show that overall vaccine effectiveness (a measure of both indirect and direct effects) is sustained for 4 years in people vaccinated when they were 5 years of age or older. However, consistent with previous evidence,[4] their results suggest lower and perhaps less durable protection in young children. In short, they highlight that in this endemic setting, OCV can significantly reduce incidence of severe cholera, but protection is not equally distributed.

OCV use in mass campaigns has substantially increased since the creation of the global stockpile in 2013, from 0·2 million doses deployed to Haiti in the first year[3] to 24 million to multiple countries in 2019.[8] However, this increase is modest compared with the more than one billion at-risk people globally.[9] Only a few countries have started using OCV as part of larger-scale efforts to reduce cholera burden.[3] Highly endemic countries such as Bangladesh and India, where the formative clinical trials were done, have yet to move past piloting stages. The COVID-19 pandemic has further slowed OCV use in 2020 and 2021.

The reasons for this less-than-ideal uptake are complex and linked to both demand and supply. Routine use of the vaccine has been limited due to inconsistencies between the scope of cholera vaccination (targeting all individuals aged ≥1 years in high risk areas, with multiple government sectors) and routine immunisation programmes (typically focused on children nationally and led by a single entity, the Expanded Programme on Immunization), as well as little guidance on how to incorporate OCV into public health systems. Although guidance on who to target with vaccines, how often to revaccinate, and how to balance emergency and non-emergency vaccine use will alleviate some demand bottlenecks, uncertain vaccine supply remains. Although the OCV stockpile was developed to break this cycle of insufficient supply, only a single manufacturer has scaled up production over the past 2 years and countries are left to invest in making future vaccination plans with uncertain prospects of actually receiving vaccines.[10]

OCV is not the ultimate solution to cholera but it gives decision makers time to put in place water, sanitation, and hygiene interventions that are durable, sustainable, and safe.[11] These new data on OCV-derived protection should not be used as an excuse to delay these critical structural interventions. On the contrary, it should motivate progress towards global cholera elimination goals.[11] For OCV to have real public health impact across the globe, there is urgent need for practical guidance on integrating routine use of OCV into national public health systems and developing creative mechanisms to increase vaccine production and availability, while at the same time investing in new and improved vaccine formulations. And, even more importantly, political commitment to end cholera should be fostered at all levels to ensure that sufficient resources (including but not limited to vaccines) are available to countries affected by cholera.

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Lorenzo Pezzoli, Andrew S Azman
lorenzo.pezz@gmail.com

Geneva, Switzerland (LP); Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA (ASA); Médecins Sans Frontières, Geneva, Switzerland (ASA)

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