(the standard of care) for the treatment of uncomplicated falciparum malaria. The trial found that the efficacy of arterolane–piperaquine–mefloquine, dosed according to a new weight-based system, was non-inferior to that of artemether–lumefantrine and arterolane–piperaquine. Both arterolane-containing combinations showed a 42-day PCR-corrected efficacy (the primary endpoint) of 100%, and had a longer post-treatment prophylactic effect than did artemether–lumefantrine. Importantly, both combinations were safe and well tolerated, and the only relevant finding was a significantly higher rate of vomiting in the two arterolane groups than in the artemether–lumefantrine group, although no child discontinued the study drugs because of tolerance issues. The thorough electrocardiographic surveillance in place also showed—as expected for any piperaquine-containing combination—that prolongation of the QT interval corrected for heart rate was greater after treatment with the arterolane combinations than after treatment with artemether–lumefantrine, but this result was of no clinical relevance. The study also included a pharmacokinetic component, which did not show any relevant drug interactions, a comforting finding, particularly for the triple combination.

Importantly, in this particular setting, and many years after its introduction as a first-line treatment, the efficacy of artemether–lumefantrine has remained high (96%), and no relevant *Pfkelch13* mutations were observed among the parasites studied. Indeed, widespread artemisinin resistance seen in southeast Asia has yet to reach sub-Saharan Africa, where de novo resistance could also emerge; however, knowing that safe and highly efficacious alternatives are now available, should the situation change, is reassuring. Whether the future treatment of malaria in Africa will require double or triple combinations remains uncertain, but the data presented by this trial are a good starting point and provide solid evidence for future antimalarial policies. Future studies should further explore the safety and efficacy of arterolane combinations (including triple therapies) in younger children (<2 years), assess whether cross-resistance might hamper their efficacy in areas with high background artemisinin resistance phenotypes, and calculate the cost-effectiveness and incremental costs that triple combinations could entail to the already stretched malaria control programmes.

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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

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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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Human papillomavirus vaccinations matter!

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In the 20th century, a range of vaccines enabled major medical breakthroughs that helped to prevent disease, protect public health, and reduce inequities in health care. Crucially, once these vaccines had been proven safe and effective, health gains relied on timely delivery and high uptake. Eric Chow and colleagues report in *The Lancet Infectious Diseases* about the efficacy of male human papillomavirus (HPV) vaccination against the prevalence of high-risk HPV infections in young men who have sex with men (MSM). This cross-sectional study, which took place in an urban Australian setting where the uptake of the HPV vaccine is high, showed a substantial reduction in the prevalence of anal HPV16 infection in those who had been vaccinated compared with those who had not.[1]

Vaccination to prevent anogenital cancers by preventing HPV infection was introduced approximately 15 years ago. The HPV vaccination programme was different from many other previous national vaccination programmes in several ways. First, the HPV vaccine was offered to a new type of target group: preadolescent girls. Second, the HPV vaccine was not targeting an acute infectious disease, like most other vaccines, but cancer, which is a disease that could otherwise occur decades after a persistent infection with a cancer-inducing virus. Third, the HPV vaccination is novel in that it prevents a sexually transmitted infection. Lastly, HPV vaccination was added to many national vaccination programmes in an era in which high vaccine uptake could no longer be taken for granted. All of these factors could have contributed to variable HPV vaccination coverage, and in many countries, HPV vaccination coverage could be much lower than the coverage of other vaccines included in national vaccination programmes.[2]

Persistent infection with high-risk HPV, in particular HPV16, is the main cause of malignancies in the cervix, anus, and, to a lesser extent the vagina, vulva, penis, and oropharynx. Originally, HPV vaccination was mainly intended to prevent cervical premalignancies and malignancies. Potential benefits of the HPV vaccine in the prevention of other genital, anal, and presumably oropharyngeal malignancies have been increasingly recognised.[3]

Australia was one of the first countries to implement the HPV vaccine, and its vigorous programme of vaccinating girls aged 13 years, and a catch-up campaign vaccinating adolescent girls and young women up to age 26 years, has led to a rapid reduction of HPV infections among young women.[4] The herd immunity benefits of the vaccination programme led to a decrease in HPV infections among adolescent heterosexual boys as well,[5] but young gay men might not benefit from this indirect protection. In 2013, Australia was also one of the first countries to widen the vaccination target group to include boys aged 12–13 years; vaccination uptake among this group has been high.[6]

In many low and lower-middle income countries, low uptake of the HPV vaccine, and vaccines in general, is more to do with insufficient access than insufficient acceptance of vaccination. Poor health systems, unstable supply systems, and high vaccine costs hinder vaccine uptake in the most vulnerable populations, which tend to be rural rather than urban, and to have low socioeconomic status. These populations also often have very little access to treatment for HPV-induced malignancies, making prevention through vaccination even more crucial. Furthermore, in a globally interconnected world, infodemics of too much information and so-called alternative facts can rapidly spread and undermine vaccination confidence anywhere in the world, to the detriment of individual and public health.[7] For example, in 2014, the HPV vaccine uptake in Denmark fell from around 90% to below 40% following widespread negative social media coverage,[8] and uptake took several years to recover. Identifying and understanding effective ways to communicate