Are expensive vaccines the best investment in low-income and middle-income countries?

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In a new study in *The Lancet Global Health*, John Ojal and colleagues[1] project that the use of ten-valent pneumococcal conjugate vaccine (PCV10) will be cost-effective in Kenya after international donor support for vaccine programmes ends in around 2027. Until now, Kenya has relied on funding from Gavi, the international vaccine alliance, to fund its PCV programme. But because Gavi withdraws support from countries as their economies grow, Kenya will have to bear the full $9 per child cost for a three-dose course of PCVs starting in 2027. For Kenya, where annual per capita actual expenditure for health is around $70 (about 5% of GDP), that is not a trivial cost.[2]

Kenya is not alone in having to decide whether expensive vaccines are worth the money, as many other lower-middle-income countries with growing economies will soon lose international support. For these countries, careful evaluation of the cost-effectiveness and affordability of such programmes, and how they hold up against alternative investments in population health, are essential.[3] The current study is a much-appreciated effort to provide important insights to countries around the world as they struggle to decide how best to spend scarce resources.

In their study, Ojal and colleagues used a sophisticated age-structured dynamic disease model to project the costs and benefits of continuing the Kenya PCV10 vaccine programme between 2022 and 2032, compared with letting the programme lapse.[1] The model relied on pneumococcal surveillance, case incidence, and case fatality data for invasive pneumococcal disease (IPD) and severe pneumonia from a large hospital in Kifili. The model accounted for serotype replacement and assessed both direct and indirect vaccine benefits, such as those for older children and seniors. The researchers noted that in 2032, the PCV programme would cost about $150 for every disability-adjusted life-year (DALY) it averts, and have an annual programme cost of about $18 million.

The researchers applied an often-used criterion for cost-effectiveness: is the cost per DALY averted less than the per-capita GDP?[4] Given that Kenya's per-capita GDP in 2016 was $1455, the estimate is easily under the threshold. Ojal and colleagues note that other relatively expensive childhood vaccines such as *Haemophilus influenzae* type b (Hib) vaccine ($85 per DALY averted) and rotavirus vaccine ($200–400 per DALY averted, depending on the vaccine used), are similarly cost effective.[1]

Importantly, in view of the fact that only 2% of the DALYs averted come from prevention of morbidity, the researchers' assessment of cost-effectiveness of PCV in Kenya was based almost entirely on the vaccine's ability to prevent deaths.[1] Their model relies on reasonable assumptions for the incidence of IPD, the ratio of IPD to pneumonia, the case fatality ratios, and other parameters. However, the degree to which PCV use actually reduces pneumococcal mortality in Kenya, or in any setting, is not well studied and far from clear.[5] An often-cited randomised trial in the Gambia reported a 16% reduction in all-cause mortality among vaccinated children,[6] but this was a secondary endpoint with a wide confidence interval. Findings of several studies have convincingly documented a significant reduction in IPD and pneumonia incidence, although serotype replacement can erode PCV benefits over time.[7] However, very few studies have reported on the vaccine's effect on mortality. Results of one recent observational study showed that after PCV10 was introduced in Brazil in 2010, the vaccine caused pneumonia mortality to fall by about 10% nationally by 2014, with larger reductions in strata with lower socioeconomic status.[5]

Another important point is that pneumonia claims far more lives than IPD, and pneumonia mortality in Kenya and other lower-income countries was falling steadily long before the PCV programmes started.[5,8,9] Indeed, teasing vaccine benefits from a background mortality that is rapidly decreasing due to other factors is a difficult modelling challenge. Many factors surely contributed to the decrease, such as better access to health care (especially antibiotics), improved nutrition, better housing, and hygiene.[10] It is worth asking whether the funds needed to keep the PCV programme going would be better spent on non-vaccine programmes that address these factors.

Getting a clear view of mortality benefits of vaccination is not straightforward in any setting, but

it is especially difficult in countries that lack national vital statistics data. Nonetheless, more studies of the mortality benefits of vaccinations in Gavi-transitioning countries are sorely needed, especially when, as in the current study, the perceived cost effectiveness relies almost entirely on the vaccine's mortality benefits.

As lower-income countries continue to grow economically, improvements in pneumococcal mortality will probably continue, whether PCV is part of the solution or not. Against that background, these countries must decide whether they can afford the substantial costs of PCV, as well as other new and expensive vaccines. What is needed is a comprehensive evaluation of the affordability and mortality benefits that takes into consideration the dramatic increase in costs for childhood vaccine programmes, as well as creative thinking about what else that money could buy in lower-income countries. No one should doubt that vaccines are powerful tools, but that does not mean that they are always the tool to reach for first.

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We declare no competing interests.

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