

Polio eradication vaccine investment: how do we ensure polio vaccines are available to keep the world polio-free after transmission of wild poliovirus (wPV) has been interrupted?

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POLIO ERADICATION IS IN SIGHT

As of 24 August 2021 there has not been a case of wild poliovirus (wPV) anywhere in the world for more than 7 months. Perhaps this is one of the longest periods, if not the longest, without a case of wPV in the world. We may be much closer to polio eradication than any of us had dared hope. If we are, indeed, entering the final stages of polio eradication, planning for post-eradication is essential to keep the world polio-free.

Since the beginning of 2021, there have been only two reported cases of wPV, compared with 102 cases for the same period in 2020 (January to August). There have been 62 wPV-positive environmental samples reported so far this year till August 2021, compared with 304 for the same period in 2020.¹ There have been no wPV-positive samples from Afghanistan for more than 6 months.² While the polio eradication efforts have made an enormous contribution to COVID-19 control, it may be that the restrictions imposed by the pandemic have brought us this much closer to polio eradication. It is an unexpected synergy. Of course, the reduction in wPV cases in Pakistan may not be sustainable as suggested by Shaikh *et al*,³ noting their belief that the COVID-19 pandemic may have led to under-reporting in 2020. However, the surveillance networks (including environmental sampling) in both Afghanistan and Pakistan continue to function within the parameters set in the Global Polio Eradication Initiative (GPEI) surveillance indicators.

Some have also noted that the global goal should not focus on just zero cases of wPV, but also on circulating vaccine-derived poliovirus

Summary box

- ▶ WHO currently recommends that from 2021 onwards every child should receive at least two doses of inactivated poliovirus vaccine (IPV) to prevent any recurrence of wild poliovirus (wPV) or circulating vaccine-derived poliovirus-induced acute flaccid paralysis cases.
- ▶ Gavi has forecast that by 2024 as many as 146 million doses of IPV and potentially a further 3 million doses of new IPV-containing hexavalent vaccines could be needed to serve the 70 countries benefiting from its support, globally.
- ▶ As of 24 August 2021, there has not been a case of wPV anywhere in the world for more than 7 months and we must start planning for the possibility of eradication much sooner than anticipated.
- ▶ The restrictions imposed by the COVID-19 pandemic may finally have brought us this close to eradication.
- ▶ There is an urgent need for clearer signals from the global health community on the projected demand for IPV and IPV-containing hexavalent vaccines to ensure that investments in production capacity are made by producers and donors in various regions to assure an adequate and timely supply.

(cVDPV) eradication. Chumakov *et al*⁴ wrote in June 2021 that the strategy of the GPEI had always been based on stopping transmission of wPV, but:

As the circulation of wild polioviruses dwindled, the importance of cVDPVs increased, and they now cause the majority of paralytic polio cases in the world. The distinction between cVDPVs and wild polioviruses is purely academic because they both transmit readily in poorly immunised communities, cause outbreaks of paralytic disease, and their presence requires the same programmatic response.

As of 24 August 2021, the cumulative cVDPV cases globally were 209 vs 1105 in the entire 2020, and a total of 179 environmental samples were cVDPV-positive compared with 542 in the year 2020.⁵

As we explain below, cVDPV is linked to today's use of live oral poliovirus vaccines (OPV). Alternative polio vaccines reduce the risk, including a novel OPV vaccine that has been granted WHO Emergency Use Listing and may permit control of outbreaks with a much lower risk of further cVDPV cases⁶ and inactivated poliovirus vaccine (IPV).

Three years after the last case of polio caused by wPV, the world will be declared polio-free. After this, polio immunisation will be needed for many more years, both to prevent possible outbreaks of cVDPV and because polioviruses will persist *in vitro* for many years.⁷ An integral part of the new GPEI Strategy 2022–2026⁸ involves closer coordination with broader public health efforts, both to prevent recurrence of polio cases and to leverage the polio infrastructure to benefit other public health emergencies long after the disease has been eradicated.

PANDEMIC CHALLENGES

The COVID-19 pandemic has not only created a global health crisis, but it has also sparked an economic crisis, slowing the global economy⁹ and disproportionately affecting the economies of low-income and lower-middle-income countries. The global economic contraction will undoubtedly negatively impact health spending in high-income and low-income countries, as seen in past recessions.^{10–12} As donor aid budgets are frequently tied to Gross Domestic Product (GDP), international development funds for health are likely to shrink.¹³ This could affect Gavi counterpart financing and the willingness and capacity of some governments to finance their national immunisation programmes.

THE TRANSITION FROM OPV TO IPV

The WHO polio endgame strategy recommends the cessation of all use of OPV¹⁴ and integrating at least two doses of IPV in routine immunisation (RI) programmes once wPV is finally eradicated. As the GPEI explains, 'OPV is very effective against wild poliovirus, but in very rare cases the vaccine can lead to paralysis...', both from vaccine-associated paralytic poliomyelitis and cVDPV, in which mutated versions of OPV can cause paralysis and spread from person to person.

WHO currently recommends that from 2021 onwards every child should receive at least two doses of IPV to prevent any recurrence of wPV or cVDPV. Gavi and donors have committed to support this introduction in Gavi/GPEI-supported countries.¹⁵ Children in high-income and some middle-income countries receive four doses of IPV, as two doses of IPV provide 90% immunity to all three types of poliovirus, while three or more doses provide at least 99% immunity.¹⁶ It may, therefore,

be that future recommendations are for more than two doses everywhere.

While OPV is inexpensive to produce, it requires a dedicated cold chain (–20°C), making it expensive to distribute, store and deliver. OPV is often delivered through dedicated and repeated campaigns, requiring significant human resources and often delivering more doses of OPV than necessary over time. In contrast, IPV is more expensive but has the potential to be integrated more fully into the RI system. However, the transition from OPV to IPV will create financial challenges as the savings from stopping OPV will only be realised over time while IPV costs will be immediate.

Some have raised concerns that OPV drops are simpler to administer than IPV injections and that coverage with IPV may, as a result, be lower. There may be countries in which this would be true, but UNICEF/WHO data suggest that it is not in large countries such as Nigeria. Coverage for three doses of OPV (POL3) within an RI system there in 2019 was estimated at about 57%, as was coverage for three doses of injectable Diphtheria-Tetanus-Pertussis (DTP) (DTP3). In India, the figures are 90% for POL3 and 91% for DTP3. IPV coverage will depend on the RI programme, and low vaccine coverage rates will need to be addressed through investment in RI.

MEETING POST POLIO ERADICATION DEMAND

GPEI believes 'the backbone of polio eradication and outbreak response remains RI against polio in line with the national childhood immunisation schedule'.¹⁷ Gavi has forecast that by 2024 as many as 146 million doses of IPV and potentially a further 3 million doses of new IPV-containing hexavalent vaccines could be needed to serve the 70 countries benefiting from its support, globally.¹⁸ In fact, demand for IPV and IPV-containing hexavalent vaccines may be much higher as these Gavi forecasts do not include several large middle-income countries not eligible for its support. Alfaro-Murillo *et al*¹⁹ concluded in 2020 that 21.1 million doses of IPV would be required annually in just the Americas for a three-dose schedule, and that globally between 232.6 million (for a two-dose schedule) and 348.7 million (for a three-dose schedule) would be needed.

Many countries may choose to accelerate the introduction of IPV-containing hexavalent vaccines because the introduction of pentavalent vaccines, over the last two decades, increased RI vaccine coverage rates, decreased the demand for cold chain capacity and reduced the time per child required of immunisation staff.²⁰ Countries may try to replicate these as they balance introducing IPV while also strengthening immunisation programmes in the aftermath of lockdowns and administering COVID-19 vaccines. However, the WHO cautions most countries against switching from whole-cell pertussis (wP) vaccines to the acellular pertussis (aP) vaccines used in high-income countries,²¹ so new IPV-containing wP must be

developed and approved for those countries currently using wP combinations.

VACCINE SUPPLY CRITICAL FOR A POLIO-FREE WORLD

Although the production capacity of IPV might be adequate to meet current demand in the short term, an assessment made²² of the different vaccine supply scenarios in the post eradication era suggests there is a significant risk of shortages after wPV transmission is interrupted. Shortages of IPV in 2017 and 2018²³ resulted from the long lead times required to scale up IPV production capacity, as it takes roughly 5–7 years, from start to finish, to bring a new production facility online. IPV production is complex and must comply with regulatory standards, including stringent biosecurity requirements.

Given the coordinated nature of the global polio eradication effort, the IPV market will be largely determined by global policy and funding decisions. To ensure adequate and quality supply of IPV and IPV-containing hexavalent vaccines to meet global demand, new and existing IPV producers as well as pentavalent producers require clear policy and willingness-to-buy signals from the global health community on the projected global demand for these vaccines in the mid and long term. The robustness and believability of these demand projections will determine if and when production investments are made and whether the world has competitive markets and adequate supply in the future.

CONCLUSION

The decisions of policymakers today will determine whether or not there will be an adequate supply of IPV and IPV-containing hexavalent vaccines from multiple suppliers around the world to support polio eradication and then to maintain a polio-free world. Robust demand estimates will shape investment in the development of new IPV-containing hexavalent vaccines²² and in new and existing production of vaccines that will be needed 5–7 years from now.

A recent *BMJ* feature stated²⁴: ‘Since the effort began in 1988 the Global Polio Eradication Initiative has pushed polio to near annihilation, pushing down cases by 99.99%. Perhaps tens of millions of people walking today can thank the GPEI’. We must safeguard this achievement which is at risk from lack of timely and realistic planning.

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