

POLICY FORUM

INFECTIOUS DISEASE

Global withdrawal of Sabin oral poliovirus type 2 vaccine in 2016

Evaluation guides strategy for the polio eradication endgame

By **Natalia A. Molodecky¹, Roland W. Sutter², the Switch Evaluation Sounding Board (SESB)**

Live Sabin oral poliovirus vaccine (OPV), a live-attenuated vaccine, is genetically unstable and can revert back to neurovirulence and transmissibility, causing vaccine-associated paralytic poliomyelitis (VAPP) and circulating vaccine-derived poliovirus (cVDPV). Following a resolution of the World Health Assembly (WHA) in 2015, the Global Polio Eradication Initiative (GPEI) set the target for global withdrawal of the type 2 component of OPV (OPV2) for April 2016 (i.e., the switch). Within 12 to 18 months after the switch, it became apparent that the GPEI struggled to close out (stop and confirm absence of transmission) cVDPV2 outbreaks from undetected transmission and new emergences from OPV2 use in outbreak control. In 2023, the GPEI began discussing the global cessation of all Sabin polioviruses, necessitating the discontinuation of bivalent (type 1 and 3) OPV (i.e., bOPV). We attempt to identify and highlight the causes for the post-switch epidemiologic situation and offer some suggestions on how to avert such a development in the future.

In 1988, the WHA, the oversight body of the World Health Organization (WHO), resolved to eradicate poliomyelitis by the year 2000 (1). The goal was partly achieved with the eradication of wild poliovirus type 2 (WPV2) globally in 1999, with the last detection in Northern India, and eventual certification of eradication in 2015. In addition, wild poliovirus type 3 was last detected in Nigeria (2012) and Pakistan (2012) and certified as eradicated in 2019. However, as of late 2024, wild poliovirus type 1 (WPV1) continues to circulate in Afghanistan and Pakistan (2).

Concomitantly to the efforts to eradicate polio, the GPEI established a road map toward the eventual withdrawal of all OPV, including the three serotypes used in the trivalent OPV (tOPV), starting with OPV2. Although OPV has played a key role in po-

lio eradication and reduced the global polio case burden by >99.9%, its continued use is not compatible with eradication. The continued VAPP burden [around 200 to 400 cases each year (3)] was becoming more unacceptable following WPV2 eradication, and cVDPVs (typically emerging and spreading in populations of low immunity, with cVDPV2 most common) posed a threat to reestablishing poliovirus transmission.

The major elements of OPV2 withdrawal were outlined in the 2013–2018 Strategic Plan of Action (4). The plan called for certification of WPV2 eradication by the Global Commission for the Certification of Polio Eradication (achieved in late 2015) and specified several prerequisites (readiness criteria) that needed to be met before OPV2 withdrawal could be implemented. Routine immunization (RI) would switch from tOPV to bOPV, and subsequent campaigns would only use bOPV. Inactivated poliovirus vaccine (IPV) would be introduced into RI to mitigate against risk of paralysis from cVDPV2 infection.

Following substantial progress of GPEI toward meeting the readiness criteria, the initial logistical phase of the OPV2 withdrawal was evaluated and deemed successful (5). But there followed subsequent struggles to close out outbreaks particularly in countries with suboptimal infrastructures for delivering vaccines, especially the eastern part of the Democratic Republic of the Congo (DRC) and Northern Nigeria (6). In the context of the 2023 GPEI discussions toward global cessation of types 1 and 3 vaccines, a review and evaluation of the 2016 switch from tOPV to bOPV was conducted (7) to compile the lessons learned and provide input into the bOPV cessation plan.

EVALUATION APPROACH

The Strategy Committee (SC) of GPEI, the managing body for polio eradication, issued a mandate to conduct an external evaluation of the basis and outcome of the switch from tOPV to bOPV in 2016. The evaluation commenced in August 2023 after constitu-

tion of the evaluation team by the authors of this report (N.A.M., R.W.S.) and process of the peer panel review for the observations and recommendations.

The evaluation was necessary because the GPEI had started to discuss the withdrawal of Sabin types 1 and 3 contained in bOPV. Even though WPV1 remained in endemic transmission, the initial planning for bOPV withdrawal was underway. The focus of the evaluation was to identify and compile the lessons learned from the 2016 switch. A three-pronged approach was pursued: (i) qualitative evaluation (following the guidelines of the American Evaluation Society) using the 2013–2018 Strategic Plan (3) as the template for the evaluation; (ii) quantitative evaluation (conducting additional analyses) using data from the polio information system (POLIS) maintained by the WHO; and (iii) interviews with stakeholders and an extensive peer-review process (including calls for and review of public comments).

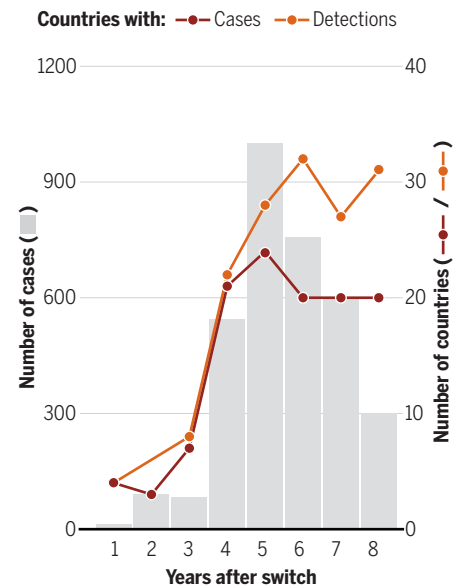
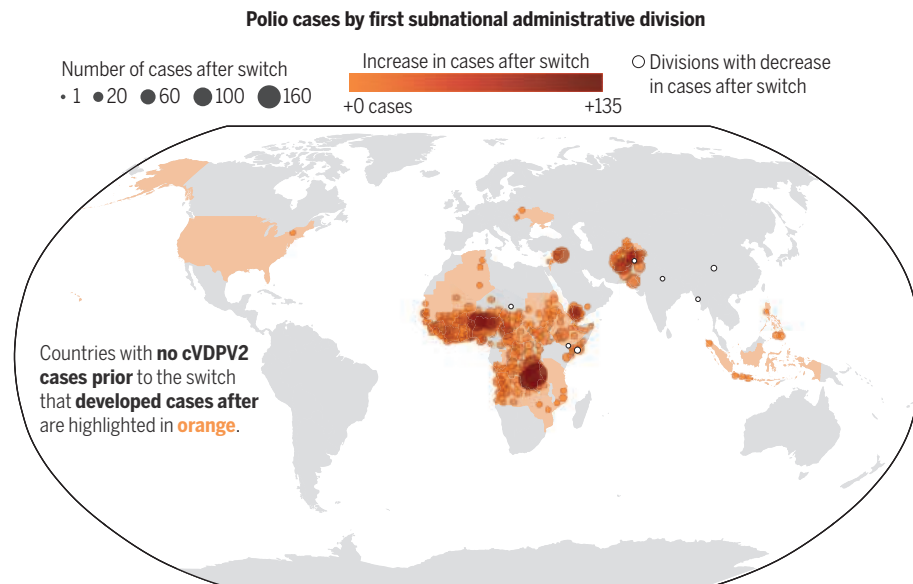
The qualitative evaluation followed a process that started with specification of elements for evaluation, determined the standard for each element, evaluated the standard versus achievement, assessed the implication of a “failing” standard, weighed the relevance for the planned bOPV cessation, drew lessons learned, and finally highlighted policy implications. To assist the evaluation team, a seven-member “sounding board” was established, which reviewed progress reports and helped to create standards for elements that were not specified in the 2013–2018 Strategic Plan (4) or recommendations of the Strategic Advisory Group of Experts on Immunization (SAGE) (8).

The quantitative evaluation focused on specific elements that were identified in the qualitative evaluation and conducting specific analyses to derive or underline the conclusions. A major focus was the in-depth review of outbreak control efforts, focusing on quality, scope, and timeliness (7). In addition, the 10 key factors that emerged during our review as contributing to or exacerbating the switch failure were assessed in detail (7). The final evaluation element was the extensive peer-review process, starting and ending with a public comment opportunity, using the “sounding board” to guide the evaluation and critically review it, and giving all stakeholders a chance to provide comments and suggestions.

¹The Task Force for Global Health, Atlanta, GA, USA. ²Tamayo Federal Solutions LLC, Virginia Beach, VA, USA. SESB members and their affiliations are listed at the end of this article. Email: rolandsutter@gmail.com; nmolodecky@gmail.com

Evolving epidemiology post switch

Global withdrawal of the type 2 component of oral poliovirus vaccine (OPV2) occurred in April 2016 (i.e., the switch). Both graphics show the change in circulating vaccine-derived poliovirus type 2 (cVDPV2) cases. The map reflects changes from pre-switch (1 January 2010 to 30 April 2016) to post-switch (1 May 2016 to 30 April 2024) time periods. Data are aggregated at the first subnational administrative division within the country (i.e., state or province, but which can also be called governorates or prefectures). The chart reflects the post-switch period. See (7) and supplementary materials for details on data and methods.



POST-SWITCH INCREASE

In the 8 years after the switch (from 1 May 2016 to 30 April 2024), a total of 53 countries were infected with cVDPV2, >3300 children were paralyzed by cVDPV2 (across 43 countries), and >\$1.8 billion was spent on outbreak control. The scale of the withdrawal effort was staggering: stopping the use of tOPV in 155 countries; replacing it with bOPV, all in a narrow 2-week window in April 2016; and ensuring introduction of at least one dose of IPV into RI in advance of the switch. See (7) for the findings of the qualitative evaluation, including which prerequisites were achieved or not met.

The goal of the switch was to stop the use of Sabin poliovirus type 2 vaccine in order to prevent cVDPV2 (and VAPP). However, since the switch, there has been an approximate 10-fold increase in cVDPV2 case burden. As seen from the pre- and post-switch cVDPV2 cases (see the figure), in the approximately 6½ years pre-switch, 319 cVDPV2 cases were reported across 15 countries. By contrast, over a similar period of time post-switch (by end of 2022), 2967 cVDPV2 cases had already been reported across 38 countries, with widespread transmission continuing to result in high case burden. By 15 May 2024 (end of the evaluation period), a total of 3393 cases had been reported. Data prior to January 2010 are not available. As shown by the number of cVDPV2 cases by year since the switch (see the figure), the initial success was followed by rapid expansion of

cVDPV2 outbreaks starting in year 3 (May 2018 to April 2019) after the switch. Figure S1 shows the number of new cVDPV2 emergences by year and demonstrates the continued seeding of cVDPV2 (moment of evolution from OPV2 to cVDPV2) since the switch, including from novel OPV2 (nOPV2) use (highlighting that despite best efforts to create a more genetically stable vaccine, strong preventive and outbreak control measures will still be required for any future OPV withdrawal efforts).

The overriding reason for this failure was the inability of GPEI to close out outbreaks shortly after the switch and in the ensuing 8 years. The contributing factors were suboptimal quality of the outbreak control efforts, inadequate geographic scope, and long delays in timing (7), resulting in massively expanding outbreaks in year 4 after the switch and slow progress toward control in subsequent years (see the figure). The failure was aggravated by the inability of GPEI leadership to recognize the seriousness of the evolving problem and take effective corrective action (7).

In addition, 10 factors that exacerbated the negative outcomes included (i) IPV supply constraints affecting introduction in RI and use in outbreak control, contributing to the high case burden; (ii) gaps in pre-switch poliovirus type 2 immunity in critical geographies (Nigeria, DRC, and Pakistan), resulting in early seeding events; (iii) continued and undetected cVDPV2 transmission at the time of the switch

(Somalia, Syria, and the Philippines); (iv) limited progress in RI and lack of alternative strategies to increase coverage, leaving a weak foundation of type 2 immunity and contributing to the high case burden; (v) limited stockpile of monovalent type 2 OPV (mOPV2), resulting in highly focused and insufficient outbreak response scope; (vi) revisions of outbreak response Standard Operating Protocols (SOPs), reducing the number of rounds and target population, and eliminating IPV from outbreak response; (vii) delays in nOPV2 development and introduction and perceived and communicated risk of mOPV2, resulting in substantial delays in outbreak response; (viii) leftover tOPV vials in storage sites, likely seeding at least one cVDPV2 outbreak; (ix) inadequate or late detection of cVDPV2 (both new emergences and ongoing transmission) delaying implementation of outbreak control measures; and (x) delays in processing and notifying cVDPV2 acute flaccid paralysis cases and environmental surveillance samples, exacerbating delayed responses. Additional details are provided in (7).

LESSONS LEARNED

The 2016 Sabin poliovirus type 2 cessation (i.e., switch) was a failure, causing >3300 paralytic poliomyelitis cases, primarily on the African continent, the vast majority of which were entirely preventable. The switch also offers an opportunity to learn and prevent such a failure from ever hap-

pening again, especially with the anticipated bOPV withdrawal.

The GPEI was aware of the risks, starting with warnings in 1997 (9) and discussion of “a dangerous endgame” (10). The end game or exit strategy (4) required the removal of the vaccine—the OPV—that had allowed the program to get to the brink of eradication with the certification of eradication of two of the three wild poliovirus serotypes (type 2 and 3) (11).

The issue of “fighting fire with fire” (12), controlling cVDPV outbreaks with mOPV2 (the same virus that caused the outbreak in the first place), was discussed extensively in the lead-up to the OPV2 cessation in 2016. It was thought at that time that high vaccination coverage would negate this potential problem. However, the series of preventive supplementary immunization activities with tOPV did not achieve sufficiently high coverage to stop or prevent the emergence of cVDPV2 in selected critical geographies (Nigeria, DRC, Pakistan, Syria, Somalia, and the Philippines). Furthermore, high coverage was unlikely in many areas with suboptimal health systems in sub-Saharan Africa. It was essential to rapidly control and interrupt all cVDPV2 chains of transmission before population immunity had decreased sufficiently to allow widespread transmission by years 3 to 4 after the switch. This was further exacerbated by underestimating the reversion potential of OPV2 (emerging into cVDPV2) and the delays in waiting for a nOPV2 vaccine that was expected to be more genetically stable.

Polio eradication requires the removal of all polioviruses from populations (13). Without accomplishing this feat, eradication is not possible and only leads to a high level of control that is fragile at best. However, even if polio eradication is not achieved and the program discontinued, we must recognize that more than 20 million children can walk today because of the eradication efforts.

The lessons learned from this evaluation should be considered by policy-makers, program managers, and oversight committees to strengthen the planning and execution of the anticipated withdrawal of bOPV. They are contained in the complete switch evaluation report (7) and include proposed triggers and possible prerequisites (to initiate the process and lay the foundation) for a successful bOPV withdrawal.

While focusing on the failure, we must also acknowledge the many countries and WHO regions that successfully implemented the switch and have prevented a substantial number of Sabin type 2-related VAPP cases, the major adverse effect

of OPV use. Many of these countries and WHO regions have a stronger health infrastructure and better immunization delivery systems. Eight years after the switch, the vast majority of cVDPV2 outbreaks are ongoing on the African continent and southwestern part of the Arabian Peninsula, and implementing the necessary control measures remains difficult, especially in areas of conflict.

However, given that bOPV vaccine will be used until its withdrawal, GPEI must assume and plan for undetected transmission of poliovirus types 1 and 3. GPEI must operate under the assumption that there will be cVDPV2 outbreaks in the immediate aftermath of the bOPV withdrawal. To eliminate the risk of continued emergence and transmission of cVDPV2, it is critical to take steps to prevent such emergences, and terminate chains of transmission, if any arise, and avoid the problems that occurred with the tOPV-to-bOPV switch. However, the requirements this time around for bOPV cessation must be more stringent than in 2016. See (7) for our suggestions, both in terms of triggers and prerequisites.

Therefore, whether the anticipated bOPV withdrawal, even under greatly enhanced and more stringent requirements, is feasible remains uncertain. A newly developed OPV (i.e., nOPV2), was designed to be genetically more stable and decrease the emergence of cVDPV2. However, since its introduction in March 2021, a total of 18 cVDPV2 outbreaks can be attributable to nOPV2 (an incidence that appears to be lower than one observed after mOPV2 use yet continues to pose a substantial risk) (14).

The only poliovirus vaccine that does not seed new emergences of cVDPV2 is IPV. Expanded use of this vaccine in new strategies (such as fractional IPV using house-to-house modality), especially associated with greatly increased RI coverage, and the introduction of the combination hexavalent vaccine (that includes IPV) could be game changers for RI and polio eradication. But as with every vaccine, to harvest the full potential of hexavalent vaccine, high vaccination coverage will be critical, including in the most difficult parts of the world.

Moreover, the evaluation of the switch has stimulated discussions on current GPEI strategy, including action for strengthening outbreak response [e.g., improving the flow of technical and financial resources to outbreak countries, broadening scope of outbreak responses, and enhancing support to countries for planning and implementing campaigns (15)] and work to improve IPV coverage in RI through closer coordination between RI and polio programs.

Polio eradication is a very difficult ambition to achieve, even with the >99.9% decrease in poliomyelitis cases. The next decade will seal the fate of polio eradication—either succeed or fail. Failure will lead to a massive resurgence and will paralyze tens of thousands of children, mostly residing in the poorest countries of the world. ■

REFERENCES AND NOTES

1. World Health Assembly. *Global eradication of poliomyelitis by the year 2000: Resolution 41.28* (World Health Organization, 1988).
2. K. Geiger et al., *MMWR Morb. Mortal. Wkly. Rep.* **73**, 441 (2024).
3. L. R. Platt, C. F. Estivariz, R. W. Sutter, *J. Infect. Dis.* **210** (suppl. 1), S380 (2014).
4. Global Polio Eradication Initiative, *Polio Eradication & Endgame Strategic Plan 2013–2018* (World Health Organization (2013)).
5. M. Patel, S. Cochi, *J. Infect. Dis.* **216** (suppl. 1), S1 (2017).
6. J. P. Bigouette et al., *MMWR Morb. Mortal. Wkly. Rep.* **72**, 366 (2023).
7. N. Molodecky, R. Sutter, “Evaluation of Switch from tOPV to bOPV. Lessons learned and implications for an anticipated bOPV cessation” (2024); <https://polioeradication.org/wp-content/uploads/2024/11/Switch-Report-20240930.pdf>.
8. World Health Organization, Meeting of the Strategic Advisory Group of Experts on Immunization, October 2014 – conclusions and recommendations [Wkly. *Epidemiol. Rec.* **89**, 561–576 (2014)].
9. A. W. Dove, V. R. Racaniello, *Science* **277**, 779 (1997).
10. N. Nathanson, P. Fine, *Science* **296**, 269 (2002).
11. R. W. Sutter, O. M. Kew, S. L. Cochi, R. B. Aylward, “Poliovirus Vaccine-Live” in *Plotkin’s Vaccines*, S. A. Plotkin et al., Eds. (Elsevier, 2018), chap. 49, pp. 866–917.
12. P. E. Fine, R. W. Sutter, W. A. Orenstein, *Dev. Biol.* **105**, 129, discussion 149–50 (2001).
13. W. R. Dowdle, S. L. Cochi, *Vaccine* **29** (suppl. 4), D70 (2011).
14. C. M. Peak et al., *Vaccines* **12**, 1308 (2024).
15. GPEI Statement on Independent Switch Evaluation Report, <https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/opv-cessation/>.

ACKNOWLEDGMENTS

The authors acknowledge the contributions of many interested parties that freely answered questions and helped to focus this report, and appreciate suggestions of the public in responding to calls for comments. The authors thank S. Wassilak, Centers for Disease Control and Prevention (CDC), for helping to focus and to guide along the evaluation path. The Switch review (7) was promoted and funded by the CDC, Atlanta, GA, USA. The Switch Evaluation Sounding Board was composed of senior polio eradication experts covering epidemiology, virology, clinical medicine, policy, and program implementation: Walter Orenstein³, Rana Muhammad Safdar⁴, Hiroyuki Shimizu⁵, J. Peter Figueroa⁶, Rose Gana Fomban Leke⁷, and Sunil Kumar Bahl⁸. John Sever, formerly of Children’s National Medical Center, Washington, DC, USA, was also a member of the SESB but sadly passed away in March 2024 before the Switch Report was finalized. W.O. is a consultant for Sanofi Vaccines and for the Bill & Melinda Gates Foundation. ³Emory Vaccine Center, Emory University, Atlanta, GA USA. ⁴Ministry of National Health Services, Regulation and Coordination, Islamabad, Pakistan. ⁵Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan. ⁶Department of Community Health and Psychiatry, University of the West Indies, Kingston, Jamaica. ⁷Department of Microbiology, Hematology and Immunology, University of Yaounde I, Yaounde, Cameroon. ⁸WHO South-East Asia Regional Office, New Delhi, India.

SUPPLEMENTARY MATERIALS

[science.org/doi/10.1126/science.adu6580](https://doi.org/10.1126/science.adu6580)

10.1126/science.adu6580