# Emerging challenges to realizing global polio eradication and their solutions

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#### Abstract

**Background:** The Global Polio Eradication Initiative (GPEI) promised to eradicate polio by 2000, yet the disease remains endemic in 2 countries. The current threat of resurgence in countries with low vaccine coverage and circulating vaccine-derived poliovirus (cVDPV) outbreaks due to oral polio vaccine warrants a strategy review.

**Aims:** To review the performance of the GPEI from a context based in Pakistan, identifying threats to success and suggesting strategy modifications to help achieve eradication.

**Methods:** This was a desk review of the effectiveness of GPEI that was launched in 1988 to eradicate polio by 2000. Subsequent failure to eradicate led to multiple iterations in strategy and planning documents. These documents were reviewed alongside relevant literature to explore the reasons for failure and emergence of cVDPV.

**Results:** GPEI has been effective in reducing the global polio disease burden by > 99%, but it remains endemic in Pakistan and Afghanistan. cVDPV has caused multiple outbreaks since 2000, and caused 7 times more cases than wild poliovirus (WPV) globally in 2020. The Polio Eradication and Endgame Strategic Plan 2013–2018 aimed to eradicate WPV and cVDPV simultaneously. In 2019, Pakistan saw an upsurge in WPV amid an outbreak of cVDPV infection that continued throughout 2020. Wild polio eradication was not realized and the country was unable to transition to inactivated polio vaccine as predicted in the strategic plan.

**Conclusion:** Over 20 countries now report cVDPV outbreaks and many others are at risk. A country-specific modified strategy is required to eradicate WPV and cVDPV simultaneously, more so in endemic countries.

Keywords: poliomyelitis, Pakistan, disease eradication, inactivated poliovirus vaccine, health policy

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### Introduction

Poliomyelitis is caused by poliovirus serotypes 1–3. Most infections remain asymptomatic or cause mild nonspecific symptoms. However, a small proportion of infections (1:200 – varies with serotype) causes paralytic poliomyelitis and permanent disabilities. Involvement of respiratory muscles may result in death in 5–10% of cases.

Humans are the only host; no animal reservoir or vector is involved. Children aged < 5 years are affected more frequently. The most active modes of transmission in low- and middle-income countries with high population density and active transmission are the faecal-oral route and person to person transmission, while saliva and respiratory droplets transmit the disease in high-income countries (1). Understanding these epidemiological factors is critical when planning to break the chain of transmission and ultimately eradicate the disease.

Two effective trivalent vaccines, inactivated polio vaccine (IPV; 1955) and attenuated oral polio vaccine (OPV; 1961), have been used to immunize children for many years. OPV was chosen for inclusion in national programmes of routine immunization and was again

preferred for the Global Polio Eradication Initiative (GPEI) in 1988 to eradicate the disease by 2000. The goal was to immunize every child until there was no virus left to transmit to others. Acute flaccid paralysis surveillance and subsequent environmental sampling were integral components of surveillance and response monitoring (2). Polio vaccination through national programmes of immunization and subsequently through GPEI was effective in reducing the disease burden significantly. In 1988, there were 350 000 cases in 125 endemic countries. By 2012, the Americas, Western Pacific and European regions were certified as polio free and the global disease burden was 650 cases - more than 99% reduction in global cases (2). The last reported case caused by poliovirus serotype 2 was in 1999 and it could not be declared eradicated until 16 years later in 2015; at which time, trivalent OPV (tOPV) was replaced by bivalent (bOPV). Serotype 3 infection was last reported in 2012 and was declared to have been eradicated in 2019. All current cases of wild polio across the globe are caused by serotype 1.

Since the launch of GPEI, the targets set to achieve eradication have been revised on multiple occasions. In 2013, the Polio Eradication and Endgame Strategic Plan introduced a major shift in policy – wild polio

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virus (WPV) and circulating vaccine-derived poliovirus (cVDPV) were to be eradicated simultaneously. A shift from tOPV to bOPV and administering at least one dose of IPV was mandated, among other measures. WP eradication was forecast for 2018, at which stage bOPV would be completely replaced with IPV in national programmes (3).

OPV was included in Pakistan's Expanded Program on Immunization (EPI) in 1978. GPEI has been in place with the highest level of commitment at government level since 1994. In spite of reporting 20 000 cases in 1990, the impetus provided by GPEI led to a 99% reduction in cases, which was a major achievement. Yet, the disease remains endemic in Pakistan. There was a sharp rise of wild polio cases to 147 in 2019 compared to 12 in 2018, 8 in 2017, 20 in 2016, 54 in 2015 and 306 in 2014. Although type 2 vaccine was withdrawn in 2016, an outbreak (22 cases) of cVDPV2 was reported in 2019. One hundred and thirty-five such cases were reported in 2020 in addition to 84 wild polio cases, adding to the challenges of eradication. During this period, environmental samples tested positive for wild polio type 1 and cVDPV from across the country (4, 5). There was a reduction in outbreaks and cases of WPV and cVDPV in 2021. A single case of infection with WPV and 8 with cVDPV had been reported at the time of writing, presenting a window of opportunity to redouble efforts and eradicate the disease from Pakistan.

Given the failure to eradicate polio and a spike in case numbers, a desk review of the literature related to the eradication initiative, changing epidemiology, emerging scientific knowledge and subsequent reorientation of the strategy was relevant. Google Scholar, PubMed, World Health Organization (WHO) publications and the United States Centers for Disease Control website were browsed using search terms poliomyelitis, WHO Global Polio Eradication Initiative, oral polio vaccine, inactivated polio vaccine and circulating vaccine derived polio virus from 1990 to June 2021 where access to free full text was available. Publications related to the objectives of this review were extracted while others were excluded.

# Critical review of polio eradication efforts

Smallpox is the only successful model of global eradication of an infectious disease. A comprehensive strategy of surveillance, isolation, containment and immunization with a heat-stable effective vaccine was adopted in 1967 to eradicate the disease in 10 years' time. The last smallpox case was reported in 1977. The disease was certified to have been eradicated within the stipulated timeframe in 1980. Following success against smallpox, polio was selected for eradication. The disease had several dissimilarities to smallpox, which had only one genetically stable serotype, had obvious clinical diagnosis, no subclinical infection and there was safe, effective and heat-stable vaccine (6). Polio was hardly a fit for the smallpox eradication model. Polio spreads through the faecal-oral route and from person to person. The strategy adopted for its eradication relied heavily on strong immunization and surveillance but ignored a few critical interventions to break the chain of transmission, such as access to clean drinking water, sanitation and hand hygiene (WASH) (7, 8). WASH, one of the components of a comprehensive strategy, would contribute to disease eradication efforts by lowering risk of person-to-person and faecal-oral transmission.

There were multiple extensions to the initial target to eradicate polio by 2000 but the strategy remained largely unchanged, until the launch of the Polio Eradication and Endgame Strategic Plan 2013-2018 in 2013, which introduced a major shift in policy to eradicate both WPV and cVDPV simultaneously. The plan had 4 objectives. Objective 2 dealt with strengthening immunization systems and withdrawal of OPV over a timeline containing key milestones. These included the introduction of at least 1 dose of IPV in national programmes by 2015 and a switch to bOPV by 2016. However, global certification of wild polio eradication in 2018 was not achieved, nor was bOPV stopped to move to an IPV-only schedule by 2019 (3). Hence, the plan was revised again and WHO released the Polio Endgame Strategy 2019-2023. This document focused on reorienting the programme, integrating with other health services and reiterating its goals to interrupt WPV transmission and stop all cVDPV outbreaks (8).

Time and again the deadline for eradication has slipped. Delays in achieving our target within timelines may imply failure to eradicate polio and perhaps a lost opportunity. The latest iteration in play is the Polio Eradication Strategy 2022–2026, Delivering on a Promise. The strategy has the same 2 goals as the earlier documents. Its objectives are to introduce steps to improve governance and efficiency of the programme through integration, accountability and addressing the obstacles to eradication. Many of these recommendations are already in practice and it remains to be seen how they improve programme outcomes. Capacity building for programmes in the 2 endemic countries remains in scope, as do countries at risk of cVDPV outbreaks to hasten outbreak detection and response.

Alongside the above measures, WHO has recommended the introduction of a novel monovalent oral polio vaccine 2 (nOPV2) to interrupt cVDPV2 outbreaks and address low immunity to serotype 2 following the switch to bOPV in 2016 (9). This new vaccine is considered to be more stable genetically. However, it has only undergone phase 1 and phase 2 trials, leading to authorization for emergency use. Since its safety and efficacy have yet to be tested in large randomized clinical trials, we are not sure if the vaccine can live up to its promise. In Pakistan, WPV and cVDPV are in circulation due to factors such as low efficacy of OPV, low vaccine coverage through routine immunization, and growing resistance to all OPVs. Supplementary immunization activities (SIAs) with IPV instead of nOPV2 could provide an opportunity to build immunity against all serotypes, interrupting both WPV and cVDPV transmission simultaneously.

A calculated risk was taken when OPV was chosen for GPEI. OPV may cause vaccine-associated polio – paralysis in 1 out of 2.7 million first doses of vaccine or 2–4 cases per birth cohort of 1 000 000. The choice was made considering the other benefits of OPV over IPV (10), not suspecting the emergence of cVDPV, first reported incidentally in 1999–2000, the target year to have achieved eradication. cVDPV is a genetically divergent vaccine virus strain that can emerge through the use of any of the three Sabin viruses 1–3, causing outbreaks in populations with immunity gaps. Its emergence demands combating WPV transmission and unanticipated cVDPV outbreaks.

Since 2000, 1085 cases of paralysis were caused by cVDPV, of which 932 (~86%) were caused by cVDPV2. A recent study reported that the number of cVDPV outbreaks tripled from 9 to 29 in 15 countries from January 2018 to June 2019. Twenty-five (86%) outbreaks were caused by cVDPV2 outside the monovalent OPV2 response area, mostly in African nonendemic countries around 3 years after the shift from tOPV to bOPV. These made up 124 (77%) of 161 cVDPV cases (11). Burki reported that 2018 also saw 101 cases of cVDPV, which was the second successive year in which cases of cVDPV exceeded those of WPV (12). cVDPV cases were almost double the WPV cases (325 vs 174) in 2019 and about 7 times (992 vs 140) in 2020. Alarmingly, nonendemic countries reported 325 of the 365 global cases of cVDPV in 2019 (2).

OPV has also been found to be less effective in South Asia/India when compared with other regions. A review of studies from India has reported significantly lower tOPV vaccine efficacy. Plotkin has summarized the results of studies on seroconversion after 3 doses of tOPV. Seroconversion was near 100% for all 3 serotypes in the United States of America. Developing countries saw lower seroconversion rates; however, the lowest rates (40-86%; median 63%) were reported in 9 studies from India (13). Efficacy of IPV in India remains comparable with other parts of the world (14,15). Analysis of reported polio cases in Pakistan from 2017 to 2019 suggests low vaccine efficacy (Shafique M, National Institute of Health, Islamabad, unpublished data, 2019). Up to 30% of reported cases had received > 3 doses of vaccine through routine immunization programmes. Accounting for both routine immunization and SIA, > 55% received > 7 doses of OPV, 62% > 4 and 70% > 3.

Not least among concerns has been a growing resistance to OPV that is now more widespread than localized, often resulting in polio health workers being viewed with suspicion and targeted with violence during SIAs (16,17). Combination of cultural, political, religious and other social factors, reluctant parents and weak programme governance contribute to the growing sentiment. However, IPV is nowhere near being hindered, as shown in a study in the conflict zone of Northwest Pakistan (18). Despite insecurity and OPV hesitancy during SIAs, provision of both OPV and IPV through community engagement as a component of other maternal and childhood services significantly improved immunization coverage of both polio and

other vaccines, compared to home delivery of OPV alone during SIAs. This was the first large-scale administration of IPV in the country. Coverage increased to 80% in the study population with no reported refusals.

Polio vaccine coverage in Pakistan varies among provinces but the overall coverage has remained lower than desired for several years (19).

GPEI saw a phased implementation globally in the early 1990s following the adoption of a resolution by the World Health Assembly in 1988. Although GPEI has been effective in reducing the disease burden significantly, its effectiveness has varied across regions. The Americas (1994), Western Pacific (2000) and Europe (2002) saw eradication earlier than Africa, South East Asia and Eastern Mediterranean. In Southeast Asia, India reported its last case of wild polio in 2011 and the region was declared polio free in March 2014 (20). More recently, Africa was certified to be free of wild polio in 2020. However, Pakistan and Afghanistan continue to remain endemic, begging the question: why was a strategy effective in eradication globally less so in the Pakistan– Afghanistan epidemiological unit?

The health system in Pakistan has worked to its capacity and has improved its competence over the years, driven by the high level of commitment to GPEI by successive governments, at times at the expense of other child health programmes. Yet, we have recently noticed an upsurge in wild polio cases alongside a major outbreak of cVDPV, making it pertinent to address both of them simultaneously, as provided in the Polio Eradication and Endgame Strategic Plan 2013–2018. It is time to reconsider the polio eradication strategy for Pakistan and implement these guidelines irrespective of achieving wild polio eradication.

High-income countries initially used OPV to eliminate wild polio and subsequently shifted to IPV to address the issue of vaccine-associated polio (21). However, North European countries have achieved both these phases simultaneously using an IPV only schedule (1, 22).

Stopping circulation of WPV has been a major component of GPEI strategy from the beginning; hence, OPV, which provides mucosal immunity, was preferred to IPV. This objective has yet to be met with the present OPV, which has complicated the eradication process through emergence of cVDPV. Eradication could not be achieved in Pakistan over the last 30 years. Achievement of wild polio virus eradication is a daunting task that cannot be verified reliably. A move towards elimination through introduction of a more effective and safe vaccine, that is, IPV, until we can develop an improved OPV may be the paradigm shift (to eradicate disease instead of the virus) that is needed. Limited transmission may occur for some time but strong population immunity through an effective and safe vaccine would ensure that no one develops disease and eventually, the virus disappears. A shift in strategy to a safer and more effective vaccine (i.e. IPV) should be considered to maintain a high rate of population immunity. Vulnerable populations should be

protected from paralysis through sustainable vaccination programmes with the expectation that WPV circulation will eventually stop (23).

Some recent literature has been critical of the GPEI, calling for a containment strategy to be considered given an insurmountable "final mile" where there are challenges to eradication (24). WHO remains receptive yet concerned. Pivoting from the eradication objective towards a sustained systematic control strategy could lead to polio resurgence- an exponential rise in cases across the next 10 years to as many as 200 000 a year and hundreds of thousands of children living with disability (25). Our gains stacked up against the amount of time, money and resources invested on this initiative - at times to the cost of other cost-effective public health interventions and routine immunization coverage in a resource-poor country - translate into an astronomical cost of failure in the form of polio resurgence. The world cannot afford to lose this battle. If anything, our long-standing strategy needs to be supplemented with measures that help it adapt to current challenges and meet its objectives in the final mile.

# Conclusions

Considering our experience over 30 years of implementing the current polio eradication strategy, changing epidemiology of the disease, as well as scientific evidence that has emerged since then, the following are suggestions for inclusion in a comprehensive strategy for eradication in countries at risk of WPV and cVDPV outbreaks.

- Launch interventions to break the chain of transmission, including an emphasis on hand hygiene, improved access to clean drinking water and sanitation
- Strengthen routine immunization
- Merge GPEI into EPI; assets, equipment, human resource and legacy

- Coverage could be improved by linking the country's national citizenship directory's birth registration with EPI, creating a database so any babies missed out could be tracked and immunized. During the ongoing COVID-19 pandemic and restricted mobility, SIAs are constrained; therefore, it is imperative to focus on routine immunization for high coverage of all available antigens in the programme, including polio.
- Integrate routine immunization with other maternal and child health services
- Shift to a total IPV immunization schedule in routine immunization programmes and withdraw bOPV unconditionally; that is, without waiting for zero WP cases to be reported. mOPV may be used during SIAs.
- Communities must be engaged to build vaccine trust, enhance demand, create public ownership and increase awareness.

Wild polio may be endemic in 2 countries, but the rest of the world remains on guard, continuing with programmes to ensure high vaccination coverage to protect their populations. Unfortunately, more than 20 countries now report cVDPV outbreaks and many others are at risk of resurgence of wild polio,, particularly those with low vaccination coverage. There is now a need to assess the ramifications for several countries and address WPV and cVDPV eradication simultaneously. Our current predicament is a significant global threat in which cVDPV outbreaks compromise the objectives of the GPEI. WHO and its partners must work closer than ever with national governments and professional healthcare societies to arrive at country-specific policies for endemic countries and others at high risk of cVDPV outbreaks because one size rarely fits all.

Addressing our current predicament in Pakistan (cocirculation of WPV and cVDPV, low vaccine coverage, low OPV efficacy and growing resistance to OPV) requires a strategic shift as opposed to reorientation. Our policy must be equipped to handle our challenges.

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**Competing interests:** None declared.

# Nouveaux obstacles à l'éradication mondiale de la poliomyélite et solutions pour y remédier

### Résumé

**Contexte :** L'Initiative mondiale pour l'éradication de la poliomyélite (IMEP) s'est engagée à éradiquer la maladie à l'horizon 2000, mais celle-ci reste endémique dans deux pays. La menace actuelle de résurgence dans les pays ayant une faible couverture vaccinale et des flambées épidémiques de poliovirus circulants dérivés d'une souche vaccinale (PVDVc) imputables au vaccin antipoliomyélitique oral justifie un examen de la stratégie.

**Objectifs :** Examiner les performances de l'IMEP dans le contexte pakistanais, en identifiant les obstacles à la réussite et en suggérant des modifications de la stratégie pour parvenir à l'éradication.

**Méthodes :** Le présent article constitue un examen documentaire de l'efficacité de l'IMEP, qui a été lancée en 1988 pour éradiquer la poliomyélite à l'horizon 2000. Par la suite, l'échec de l'éradication de la maladie a conduit à plusieurs itérations dans la stratégie et la planification. Ces documents de stratégie et de planification ont été examinés parallèlement à la littérature pertinente afin d'explorer les raisons de l'échec et de l'émergence de PVDVc.

**Résultats :** L'IMEP a réussi à réduire la charge mondiale de morbidité due à la poliomyélite de plus de 99 %, mais la maladie reste endémique en Afghanistan et au Pakistan. De multiples flambées de PVDVc ont eu lieu depuis 2000 et

le nombre de cas enregistrés de PVDVc dans le monde en 2020 était sept fois supérieur à celui des cas de poliovirus sauvages (PVS). Le Plan stratégique pour l'éradication de la poliomyélite et la phase finale 2013-2018 visait à éradiquer simultanément le PVS et le PVDVc. En 2019, le Pakistan a connu une recrudescence du poliovirus sauvage dans un contexte de flambée de PVDVc qui s'est poursuivie tout au long de 2020. L'éradication du poliovirus sauvage n'a pas été réalisée et le pays n'a pas été en mesure de mener la transition vers le vaccin antipoliomyélitique inactivé comme le prévoyait le Plan stratégique.

**Conclusion :** Aujourd'hui, plus de 20 pays signalent des flambées épidémiques dues à des PVDVc et de nombreux autres sont à risque. Une stratégie modifiée spécifique au pays est nécessaire pour éradiquer simultanément le PVS et le PVDVc, en particulier dans les pays d'endémie.

التحديات الناشئة أمام تحقيق استئصال شلل الأطفال عالميًّا وحلوها

محمد سلطان

الخلاصة

**الخلفية**: وعدت «المبادرة العالمية لاستئصال شلل الأطفال» باستئصاله بحلول عام 2000، ومع ذلك ما يزال المرض متوطنًا في بلدين. ويستدعي التهديد الحالي بعودة ظهور الفيروس في البلدان ذات التغطية المنخفضة باللقاحات وفاشيات فيروسات شلل الأطفال الدائرة المشتقة من اللقاحات بسبب اللقاح الفموي لشلل الأطفال استعراضًا للمبادرة.

**الأهداف**: هدفت هذه الدراسة اليي استعراض أداء المبادرة العالمية لاستئصال شلل الأطفال في سياق باكستان، وتحديد التهديدات التي تواجه النجاح، واقتراح تعديلات على الاستراتيجية للمساعدة على تحقيق الاستئصال.

**طرق البحث**: كان هذا استعراضًا مكتبيًّا لفعالية «المبادرة العالمية لاستئصال شلل الأطفال» التي أُطلقت في عام 1988، لاستئصاله بحلول عام 2000. وقد أدى الفشل اللاحق في القضاء على المرض إلى تكرارات متعددة في وثائق الاستراتيجية والتخطيط. وكذلك روجعت هذه الوثائق إلى جانب المؤلفات ذات الصلة لاستكشاف أسباب الفشل وظهور فيروسات شلل الأطفال الدائرة المشتقة من اللقاحات.

النتائج: كانت «المبادرة العالمية لاستئصال شلل الأطفال» فعالة في خفض العبء العالمي للمرض بنسبة تزيد على 99٪، لكنه ما يزال متوطنًا في باكستان وأفغانستان. وقد تسببت فيروسات شلل الأطفال الدائرة المشتقة من اللقاحات في فاشيات متعددة منذ عام 2000، وتسببت في حالات إصابة أكثر 7 مرات من الحالات بسبب فيروس شلل الأطفال البري على الصعيد العالمي في عام 2020. واستهدفت «الخطة الاستر شلل الأطفال» والشوط الأخير من استئصاله 2013–2018 استئصال فيروس شلل الأطفال البري على المعيد العالمي في عام 2020. اللقاحات في الوقت نفسه. وفي عام 2019، شهدت باكستان ارتفاعًا مفاجئًا في فيروس شلل الأطفال البري وسط فاشية لعدوى فيروسات شلل الأطفال الدائرة المشتقة من اللقاحات استمرت طوال عام 2020. ولم يتحقق استئصال شلل الأطفال البري، ولم يتمكن البلد من شلل الأطفال الدائرة المشتقة من اللقاحات استمرت طوال عام 2020. ولم يتحقق استئصال شلل الأطفال البري، ولم يتمكن البلد من التحول إلى لقاح

**الاستنتاجات**: أبلغ الآن أكثر من 20 بلدًا عن فاشيات فيروسات شلل الأطفال الدائرة المشتقة من اللقاحات، أيضًا هناك بلدان كثيرة أخرى معرضة للخطر. ويلزم وضع استراتيجية مُعدَّلة خاصة بكل بلد لاستئصال فيروس شلل الأطفال البَرِّي وفيروسات شلل الأطفال الدائرة المشتقة من اللقاحات في الوقت نفسه، وينطبق ذلك أكثر على البلدان التي يتوطن بها هذا المرض.

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