Use of inactivated poliovirus vaccine for poliovirus outbreak response

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With continued wild poliovirus transmission in Afghanistan and Pakistan and circulating vaccine-derived poliovirus in certain countries, there exists an ongoing risk of importation of polioviruses into other countries, including those that have been polio-free for decades. Diversifying the poliovirus outbreak response toolkit is essential to account for different public health and epidemiological contexts. In this Personal View, we discuss data on intestinal and pharyngeal mucosal immunity induced by inactivated poliovirus vaccine (IPV), previous programmatic experience of poliovirus outbreak response with IPV, and outbreak response guidelines in countries that exclusively use IPV. With recent reports of poliovirus detection in polio-free countries such as the USA and the UK, it is important to assess the interplay of virus transmission dynamics, vaccine impact on preventing paralysis and virus spread, and regulatory complexities of using oral poliovirus vaccine (OPV) and IPV options for outbreak response. As the global eradication programme navigates through cessation of routine OPV use with replacement by IPV and stockpiling of novel OPVs, clarity on the impact of IPV use will be important for informed decision making by global, regional, and national policy makers.

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Introduction

Since the Global Polio Eradication Initiative (GPEI) was established in 1988, global incidence of polio has decreased by 99·9%.[1] In 2022, there were 22 paralytic cases due to wild poliovirus type 1 in Afghanistan and Pakistan, the last remaining endemic countries, and eight cases in Mozambique.[2] On rare occasions, live-attenuated viruses in oral poliovirus vaccines (OPVs) can circulate in populations with inadequate immunisation levels for an extended period and revert into circulating vaccine-derived polioviruses (cVDPVs) capable of inducing paralysis.[3] This makes outbreak response challenging in these populations since OPV is the vaccine of choice to interrupt person-to-person transmission. Despite the removal of type 2 poliovirus from trivalent OPV (tOPV), replaced by bivalent types 1 and 3 OPV (bOPV) for routine immunisation in 2016,[4] cases of cVDPV have increased. In 2022, there were 676 type 2 cVDPV cases, 187 type 1 cVDPV cases, and one type 3 cVDPV case, primarily in the Democratic Republic of the Congo, Yemen, and Nigeria.[5]

As they become certified polio-free, some countries and regions have switched their routine immunisation schedules from OPV to inactivated poliovirus vaccine (IPV). IPV-only countries are mainly from the WHO European region, the WHO region of the Americas, and the WHO Western Pacific region. However, with the global cessation of type 2-containing OPV in routine immunisation in 2016,[4] all countries can be considered IPV-only for protection against type 2 polioviruses.

Recent type 2 cVDPV outbreaks and persisting wild poliovirus type 1 transmission in endemic countries increase the ongoing risk of poliovirus importation into all countries, including those exclusively using IPV. Within the WHO European region, there were type 2 cVDPV outbreaks in Tajikistan and Ukraine in 2021; increased population movements due to the war from Ukraine into neighbouring IPV-only European countries heightened the risk of virus spread.[5] In 2022, type 2 cVDPV was detected in several IPV-only countries certified polio-free: the UK, the USA, and Canada.[6–8]

WHO's *Standard Operating Procedures: Responding to a Poliovirus Event or Outbreak, Version 4* defines an outbreak as detection of wild poliovirus or cVDPV with community-level transmission, as demonstrated by: (1) detection in a human, unless there is a travel history to an infected area within 35 days before onset of paralysis or a confirmed type-specific virus exposure in a laboratory or vaccine production facility; (2) two separate detections from the environment, where separate means the samples were collected from two different sites with no overlapping catchment areas or from the same site but at least 2 months apart; or (3) any newly detected cVDPV, whether in a human or environmental sample—ie, when a VDPV isolated either in human stool or the environment can immediately be genetically linked to another VDPV, thereby confirming circulation in the areas of detection.[9]

For outbreak response, OPV is the vaccine of choice to rapidly interrupt disease transmission. This is because of its capacity to induce intestinal mucosal immunity that limits viral replication and excretion on subsequent exposure and secondary spread of vaccine virus into close contacts, contributing to herd immunity. In October, 2021, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) emphasised the importance of a timely response to type 2 cVDPV outbreaks using any available type 2 OPV, whether it be Sabin type 2 monovalent OPV (mOPV) or type 2 novel OPV (nOPV).[10] However, countries exclusively using IPV for routine immunisation schedules are often reluctant to use OPV following poliovirus detections due to anticipated regulatory hurdles for OPV import and use and the perceived risks of vaccine-associated paralytic

poliomyelitis and seeding of new cVDPVs.[11] Moreover, as these countries typically have higher sanitation and hygiene standards than countries that continue to use OPV in routine immunisation, the relative impacts of oral–oral transmission and faecal–oral transmission on transmission dynamics need further exploration, especially in the context of using IPV vaccination to prevent spread. It has not been clearly established that higher standards of hygiene decrease the average infectious faecal dose, but it is possible that IPV-induced immunity can protect against lower levels of poliovirus circulation.

	Location	Vaccination schedule	Age at time of administration	OPV challenge vaccine	Minimum titre of challenge poliovirus (log_{10} $TCID_{50}$)	Detection method	Proportion shedding % (n/N)		Mean duration of shedding (days)*	Mean amount of virus shed on day 7 (log_{10} $TCID_{50}$/g stool, unless otherwise indicated)
							After 7 days	After 21 days		
Enders-Ruckle and Siegert (1961)[14]	Germany	Unvaccinated or two doses of IPV	NA	tOPV	NA	Culture	Unvaccinated: 39% (7/18) type 1, 0% (0/18) type 2, 89% (16/18) type 3 Vaccinated: 63% (12/19) type 1, 0% (0/19) type 2, 58% (11/19) type 3	Unvaccinated: 56% (10/18) type 1, 6% (1/18) type 2, 33% (6/18) type 3 Vaccinated: 47% (9/19) type 1, 0% (0/19) type 2, 42% (8/19) type 3	Unvaccinated: NA (type 1), NA (type 2), 36 days (type 3) Vaccinated: 48 days (type 1), NA (type 2), 39 days (type 3)	Unvaccinated: median 3·5 irrespective of type Vaccinated: median 2·5 irrespective of type
Cuba IPV Study Collaborative Group (2007)[15]	Cuba	Unvaccinated or two or three doses of IPV	Ages 6, 10, and 14 weeks for the three-dose group and 8 weeks and 16 weeks for the two-dose group	tOPV	6 of type 1, 5 of type 2, and 5·8 of type 3	Culture	Three-dose IPV group: 19% (10/52) type 1, 87% (45/52) type 2, 10% (5/52) type 3 Two-dose IPV group: 18% (13/72) type 1, 93% (67/72) type 2, 14% (10/72) type 3 Unvaccinated: 17% (9/54) type 1, 89% (48/54) type 2, 6% (3/54) type 3	NA	NA	Three-dose IPV group: 3·46 irrespective of type Two-dose IPV group: 3·37 irrespective of type Unvaccinated: 3·89 irrespective of type
Ghendon and Sanakoyeva (1961)[16]	Russia	Unvaccinated (seronegative) or two doses of IPV (seropositive) or OPV (seropositive)	Children	Type 1 mOPV	6	Culture	Unvaccinated: 80% (24/30) Two-dose IPV group: 68% (21/31) Two-dose OPV group: 36% (12/33)	NA	Unvaccinated: 20 days Two-dose IPV group: 12 days Two-dose OPV group: 5 days	Unvaccinated: 5·15 Two-dose IPV group: 4·11 Two-dose OPV group: 2·18
Henry et al (1966)[17]	UK	Unvaccinated, three or four doses of IPV, or three doses of tOPV	Unvaccinated group: type 1 mOPV challenge at age 6 months Three-dose IPV group: IPV at ages 2, 3, and 4 months and type 1 mOPV challenge at age 6 months Four-dose IPV group: IPV at ages 2, 3, 4, and 15 months and type 1 mOPV challenge at age 16 months tOPV group: tOPV at ages 7, 8, and 9 months and type 1 mOPV challenge at age 16 months	Type 1 mOPV	1·7–5·7	Culture	Unvaccinated: 83% (40/48) Three-dose IPV group: 86% (42/49) Four-dose IPV group: 65% (28/43) tOPV group: 32% (16/50)	NA	Unvaccinated: >18 days Three-dose IPV group: >18 days Four-dose IPV group: >18 days tOPV group: 10–18 days	Unvaccinated: median 4·1–5·0 Three-dose IPV group: median 4·1–5·0 Four-dose IPV group: median 4·1–5·0 tOPV group: median <3·0
Kok et al (1992)[18]	Kenya	Three doses of tOPV or IPV	Both groups received primary immunisations at ages 2, 4, and 6 months; challenge with type 1 mOPV was given at age 8 months	Type 1 mOPV	3·7	Culture	tOPV group: 3% (2/60) IPV group: 7% (6/84)	NA	NA	NA

(Table 1 continues on next page)

In 2022, following a request from the European Technical Advisory Group of Experts on Immunization (ETAGE) for a literature and data review to inform recommendations on poliovirus outbreak response options in countries using only IPV in routine immunisation, SAGE recommended a structured discussion focusing on three issues: (1) intestinal and pharyngeal mucosal immunity induced by IPV-only vaccination, (2) programmatic experience with response to poliovirus outbreaks in countries using only IPV, and (3) guidelines of the National Immunization Technical Advisory Groups from IPV-only countries. In this Personal View, we discuss these three areas to explain the evidence about IPV, from immunological and programmatic perspectives, on poliovirus outbreak response options, which has informed new SAGE

	Location	Vaccination schedule	Age at time of administration	OPV challenge vaccine	Minimum titre of challenge poliovirus (log_{10} $TCID_{50}$)	Detection method	Proportion shedding % (n/N)		Mean duration of shedding (days)*	Mean amount of virus shed on day 7 (log_{10} $TCID_{50}$/g stool, unless otherwise indicated)
							After 7 days	After 21 days		
(Continued from previous page)										
Laassri et al (2005)[19]	USA	Unvaccinated or two doses of tOPV or IPV	Both vaccine groups received primary immunisations at ages 2 months and 4 months; challenge with tOPV was given at age 6 months	tOPV	5·4 of type 1, 4·5 of type 2, and 5·2 of type 3	PCR	Unvaccinated: 42% (20/48) type 1, 88% (42/48) type 2, 58% (28/48) type 3 tOPV group: 7% (3/41) type 1, 10% (4/41) type 2, 17% (7/41) type 3 IPV group: 55% (23/42) type 1, 76% (32/42) type 2, 50% (21/42) type 3	Unvaccinated: 40% (19/48) type 1, 58% (28/48) type 2, 48% (23/48) type 3 tOPV group: 2% (1/42) type 1, 0% (0/42) type 2, 5% (2/42) type 3 IPV group: 26% (10/38) type 1, 26% (10/38) type 2, 21% (8/38) type 3	Unvaccinated: NA (type 1), 41 days (type 2), 71 days (type 3) tOPV group: 14 days (type 1), 4 days (type 2), 11 days (type 3) IPV group: 19 days (type 1), 19 days (type 2), 16 days (type 3)	
Modlin et al (1997)[20]†	USA	Three doses of IPV or tOPV	Both groups received primary immunisations at ages 2, 6, and 15 months; challenge with tOPV was given at age 18 months	tOPV	6·5 of type 1, 5·4 of type 2, and 6·3 of type 3	Culture	IPV group: 18% (13/74) type 1, 39% (29/74) type 2, 78% (58/74) type 3 tOPV group: 4% (3/73) type 1, 3% (2/73) type 2, 10% (7/73) type 3	NA	NA	NA
Onorato et al (1991)[21]	USA	Three doses of tOPV or IPV	Both groups received primary immunisations at ages 2, 4, and 18 months; challenge with type 1 mOPV was given on average at age 23–27 months	Type 1 mOPV	2·7–5·7	Culture	tOPV group: 11% (9/79) IPV group: 52% (48/93)	tOPV group: 1% (1/79) IPV group: 12% (11/93)	tOPV group: 6 days IPV group: 16 days	tOPV group: 2·54 log_{10} pfu/g IPV group: 3·24 log_{10} pfu/g
Public Health Laboratory Service (1965)[22]	UK	Unvaccinated or three doses of IPV or tOPV	NA	Type 1 mOPV	4·7	Culture	Unvaccinated: 83% (19/23) IPV group: 80% (55/69) tOPV group: 34% (18/53)	NA	NA	NA
WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines (1996)[23]	The Gambia	Three doses of IPV (IPV-only group), four doses of tOPV plus three doses of IPV (tOPV plus IPV group), or four doses of tOPV (tOPV-only group)	IPV-only group: IPV at ages 6, 10, and 14 weeks and type 1 mOPV challenge at age 24 weeks tOPV plus IPV group: tOPV at birth; tOPV and IPV at ages 6, 10, and 14 weeks; and type 1 mOPV challenge at age 24 weeks tOPV-only group: tOPV at birth and ages 6, 10, and 14 weeks, and type 1 mOPV challenge at age 24 weeks	Type 1 mOPV	6	Culture	IPV-only group: 16% (18/112) tOPV plus IPV group: 9% (10/111) tOPV-only group: 4% (4/111)	NA	NA	NA

(Table 1 continues on next page)

	Location	Vaccination schedule	Age at time of administration	OPV challenge vaccine	Minimum titre of challenge poliovirus (log_{10} $TCID_{50}$)	Detection method	Proportion shedding % (n/N)		Mean duration of shedding (days)*	Mean amount of virus shed on day 7 (log_{10} $TCID_{50}$/g stool, unless otherwise indicated)
							After 7 days	After 21 days		
(Continued from previous page)										
WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines (1996)[23]	Oman	Three doses of IPV (IPV-only group), four doses of tOPV plus three doses of IPV (tOPV plus IPV group), or four doses of tOPV (tOPV-only group)	IPV-only group: IPV at ages 6, 10, and 14 weeks and type 1 mOPV challenge at age 24 weeks tOPV plus IPV group: tOPV at birth; tOPV and IPV at ages 6, 10, and 14 weeks; and type 1 mOPV challenge at age 24 weeks tOPV-only group: tOPV at birth and ages 6, 10, and 14 weeks, and type 1 mOPV challenge at age 24 weeks	Type 1 mOPV	6	Culture	IPV-only group: 10% (18/177) tOPV plus IPV group: 11% (19/177) tOPV-only group: 13% (23/177)	NA	NA	NA
WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines (1996)[23]	Thailand	Three doses of IPV (IPV-only group), four doses of tOPV plus three doses of IPV (tOPV plus IPV group), or four doses of tOPV (tOPV-only group)	IPV-only group: IPV at ages 6, 10, and 14 weeks and type 1 mOPV challenge at age 24 weeks tOPV plus IPV group: tOPV at birth; tOPV and IPV at ages 6, 10, and 14 weeks; and type 1 mOPV challenge at age 24 weeks tOPV-only group: tOPV at birth and ages 6, 10, and 14 weeks, and type 1 mOPV challenge at age 24 weeks	Type 1 mOPV	6	Culture	IPV-only group: 57% (75/132) tOPV plus IPV group: 14% (19/133) tOPV-only group: 14% (19/133)	NA	NA	NA

IPV=inactivated poliovirus vaccine. mOPV=monovalent oral poliovirus vaccine. NA=not available. OPV=oral poliovirus vaccine. pfu=plaque-forming units. $TCID_{50}$=tissue-culture infectious dose. tOPV=trivalent oral poliovirus vaccine. *Mean duration of shedding was estimated from the fit of an exponential curve to the prevalence of shedding over time unless given directly in the paper. †In this study, the stool sample was taken 3–21 days after the challenge dose.

Table 1: **Studies included in the meta-analysis by Hird and Grassly[13] that examined poliovirus shedding in stool samples taken after administration of a challenge dose of OPV, comparing IPV-only and OPV-vaccinated or OPV-unvaccinated study groups**

vaccination policies and identified gaps requiring further research.

Mucosal immunity

Vaccine-induced protection against poliomyelitis has two key features: humoral and mucosal immunity. Although poliovirus-specific neutralising antibody titres, predominantly IgG, in the blood provide a measure of humoral protection against infection, the two primary sites of poliovirus replication are in the nasopharyngeal and intestinal mucosae, where immunity through local IgA or transudation of serum antibodies prevents viral replication and shedding. Therefore, vaccine-induced mucosal immunity provides evidence of a vaccine's capacity to interrupt transmission.

Shedding positivity after OPV challenge

Published reports of enhanced intestinal mucosal immunity following IPV in individuals previously vaccinated with OPV suggest that induction of intestinal mucosal immunity by IPV is dependent on previous exposure to wild or live-attenuated polioviruses.[12,13] A 2012 meta-analysis by Hird and Grassly assessed the impact of IPV vaccination alone, without past exposure to OPV, on intestinal mucosal immunity.[13] 16 studies included IPV-only vaccination groups, including 12 that directly compared faecal shedding between OPV-vaccinated and unvaccinated individuals (table 1). No significant difference in the overall odds ratio (OR) for viral shedding was found after an OPV challenge dose between IPV-immunised and unvaccinated individuals (OR 0·81 [95% CI 0·59–1·11]). In contrast, the odds of shedding were significantly lower in OPV-immunised than IPV-immunised children (0·15 [0·08–0·27]) or unvaccinated children (0·13 [0·08–0·24]). Two studies[15,19] reporting stool shedding of Sabin type 2 poliovirus after tOPV challenge found no significant difference in proportions of children shedding between IPV-vaccinated and unvaccinated groups. In the USA, Laassri and colleagues[19] found that 7 days after administration of one tOPV dose, Sabin type 2 virus was shed by 88% (95% CI 75–95) of unvaccinated children, 76% (61–88) of children after two IPV doses, and only 10% (2·7–23·1) of children after two tOPV doses. The Cuba IPV Study Collaborative

	Location	Vaccination schedule	Age at challenge dose	OPV challenge	Detection method	Proportion shedding, % (n/N)	Time of sample collection after challenge, days
Bauer (1968)[29]*	Austria	Unvaccinated or up to three doses of IPV	NA	tOPV	Culture	9% (6/65) for type 1, 2% (1/50) for type 2, and 2% (1/56) for type 3	7
Glezen et al (1966)[30]*	USA	Unvaccinated or up to six doses of IPV	6–9 years	Type 1 mOPV	Culture	10% (9/92)	3–7
Kok et al (1992)[18]	Kenya	Three doses of tOPV or IPV	8–9 months	Type 1 mOPV	Culture	tOPV group: 0% (0/60) IPV group: 0% (0/84)	7
Onorato et al (1991)[21]	USA	Three doses of tOPV or IPV	>18 months	Type 1 mOPV	Culture	tOPV group: 3% (2/78) IPV group: 1% (1/91)	7

IPV=inactivated poliovirus vaccine. mOPV=monovalent oral poliovirus vaccine. NA=not available. OPV=oral poliovirus vaccine. tOPV=trivalent oral poliovirus vaccine. *Shedding data were not disaggregated by number of doses in these two studies.

Table 2: **Studies included in the meta-analysis by Hird and Grassly[13] that measured the presence of poliovirus in nasopharyngeal samples after challenge with OPV**

Group[15] found no significant difference in the proportions of children shedding Sabin type 2 virus 7 days after tOPV challenge after receiving either no IPV dose, two IPV doses (at ages 8 and 14 weeks), or three IPV doses (at ages 6, 10, and 14 weeks): 89% (95% CI 77–96), 93% (85–98), and 87% (74–94), respectively.

Several studies measured poliovirus shedding in children who received bOPV alone or alongside IPV, with differing results. In a meta-analysis of routine immunisation schedules, Macklin and colleagues[24] found the average proportion of individuals who did not shed type 2 virus 7 days after type 2 OPV challenge was 30% (95% CI 17–48) following three bOPV doses, 25% (22–29) following three bOPV doses plus one IPV dose, and 28% (22–29) following three bOPV doses plus two IPV doses, compared with 89% (58–98) following three tOPV doses. From this study we can conclude that adding IPV to the bOPV series has no significant effect on post-challenge viral shedding compared with bOPV alone. A Latin American study[25] that assessed differences in a shedding index endpoint—a composite of proportion shedding and viral concentration over time—between bOPV schedules with zero, one, or two IPV doses found that one or two IPV doses significantly reduced the median shedding index endpoint compared with bOPV-only schedules. A Swedish study analysing the intestinal antibody response to type 1 mOPV challenge in adults immunised only with IPV found modest poliovirus type 1-specific neutralisation activity and no detectable IgA response in stool samples.[26] Some studies have shown that IPV-vaccinated children mount a modest type-specific intestinal response 2 weeks after OPV challenge.[27,28]

Duration of shedding and virus titre

As well as proportions of participants shedding virus after OPV challenge, several studies assessed the impact of IPV on the duration or titre of faecal viral shedding. In the meta-analysis by Hird and Grassly, five studies examined duration of shedding; Laassri and colleagues and Ghendon and Sanakoyeva found a shorter period of shedding in IPV-vaccinated children than in unvaccinated children.[14,16,17,19,21] One study[19] assessed duration of shedding for type 2 virus specifically. In the study by Laassri and colleagues,[19] 30 days after tOPV challenge, proportions shedding Sabin type 2 virus had decreased to 58% (95% CI 43–72) of unvaccinated children, 26% (13–43) of children vaccinated with two IPV doses, and 0% (0–8) of children vaccinated with two tOPV doses. The mean duration of Sabin type 2 shedding was 41 days in unvaccinated children, 19 days in IPV-vaccinated children, and 4 days in tOPV-vaccinated children.

In five studies, three with tOPV challenge[14,15,19] and two with type 1 mOPV challenge,[16,17] IPV vaccination reduced the mean quantity of shed poliovirus of any type in stool samples by 63–91% compared with unvaccinated children.

Nasopharyngeal mucosal immunity

Four studies in the meta-analysis by Hird and Grassly assessed nasopharyngeal secretion following OPV challenge (table 2).[13] Two studies comparing groups with different vaccination histories found no significant difference in post-challenge nasopharyngeal shedding.[18,21] In Kenya, Kok and colleagues[18] observed that no individual shed type 1 poliovirus 7 days after type 1 mOPV challenge, including those vaccinated with three tOPV doses (n=60) or two or three doses of IPV (n=84). In the USA, Onorato and colleagues[21] observed that 7 days after type 1 mOPV challenge, 3% (two of 78) and 1% (one of 91) of children vaccinated with three doses of tOPV or three doses of IPV, respectively, had positive nasopharyngeal samples. Type 1 poliovirus-specific IgA antibody was detected in two of 15 IPV and four of 21 OPV vaccinees.[21] However, assessment of the impact of IPV vaccination on mucosal immunity was limited in both studies, with few individuals having detectable virus in nasopharyngeal washings. Kok and colleagues concluded that the type 1 mOPV challenge dose (3000–7000 $TCID_{50}$) was not sufficiently infectious to determine mucosal immunity from shedding due to the high carrier rate of non-polio enteroviruses.[18] Of 144 children, only 12 excreted challenge viruses in stool after 7 days; only two (8·3%) of a separate group of 24 non-immunised infants aged 2–4-months

	Vaccine schedule	Age at time of administration	Proportion with detectable antibody, %		Geometric mean antibody titre	
			Neutralising antibody	IgA antibody	Neutralising antibody	IgA antibody
Faden et al (1990)[31]	Three doses of tOPV or IPV	Both groups received primary immunisations at ages 2, 4, and 12 months	tOPV group: 70% for type 1, 85% for type 2, 75% for type 3 IPV group: 43% for type 1, 60% for type 2, 66% for type 3	tOPV group: 100% for all three types IPV group: 89% for type 1, 91% for type 2, 89% for type 3	tOPV group: 5·66 for type 1, 17·15 for type 2, 6·50 for type 3 IPV group: 2·74 for type 1, 4·93 for type 2, 5·26 for type 3	tOPV group: 68·59 for type 1, 97·01 for type 2, 128·00 for type 3 IPV group: 23·69 for type 1, 24·64 for type 2, 31·17 for type 3
Zhaori et al (1989)[32]	Three doses of OPV or IPV	Both groups received primary immunisations at ages 2, 4, and 12 months	OPV group: 82·4% for type 3 IPV group: 56·5% for type 3	OPV group: 76% for type 3 IPV group: 13% for type 3	OPV group: 3·2 (2·2) for type 3* IPV group: 2·0 (2·1) for type 3*	OPV group: 7·2 (1·7) for type 3* IPV group: 4·5 (2·6) for type 3*
Faden and Duffy (1992)[33]†	Three doses of OPV or IPV	Both groups received primary immunisations at ages 2, 4, and 12 months	NA	NA	OPV group: 3·8 (2·3) irrespective of type* IPV group: 2·3 (2·0) irrespective of type*	OPV group: 6·0 (1·8) irrespective of type* IPV group: 5·2 (1·4) irrespective of type*

All studies were done in the USA. IPV=inactivated poliovirus vaccine. NA=not available. OPV=oral poliovirus vaccine. *Geometric mean titre (SD) in $\log_2$ scale. †Data from healthy controls were used.

Table 3: **Studies that measured poliovirus secretory antibodies in nasopharyngeal samples 30 days after completion of different primary immunisation schedules**

excreted virus in stool after a challenge dose. In Kenya, there could also be interference with natural exposure to poliovirus; six wild polioviruses were isolated (five from the IPV study group). Onorato and colleagues found that after type 1 mOPV challenge, type 1 poliovirus was isolated in stools of 63% (59 of 93) of IPV vaccinees and 13% (ten of 79) of tOPV vaccinees after 7 days (p<0·0001).[21]

Three studies compared levels of poliovirus-specific antibodies in nasopharyngeal secretions by vaccination history (table 3). Faden and colleagues found that after two doses, proportions of individuals with detectable neutralising and IgA-specific antibodies against poliovirus type 2 in nasopharyngeal secretions were 66·7% and 100%, respectively, after tOPV and 11·5% and 90·4%, respectively, after IPV.[31] 1 month after the full immunisation series with three doses (at 3, 4, and 12 months) proportions with neutralising and IgA-specific antibodies were 85·0% and 100%, respectively, after tOPV and 60·4% and 90·6%, respectively, after IPV. Antibody titres of both type 2 neutralising and IgA antibodies were significantly higher after OPV than IPV (p<0·05 for both).

Zhaori and colleagues measured secretory IgA against virion proteins (VP1, VP2, and VP3) in nasopharyngeal samples after one, two, or three doses of OPV or IPV.[32] Secretory IgA responses to VP1 (65–94%) and VP2 (43–65%) were not significantly different between vaccine groups after one, two, or three doses. However, IgA responses to VP3 were significantly higher after three doses of OPV (76%) than IPV (13%, p<0·01). In nasopharyngeal samples, frequencies of neutralising antibody responses to intact poliovirus type 3 were not significantly different between OPV-vaccinated and IPV-vaccinated individuals; however, after three doses, mean titres were significantly higher after OPV (3·2 [SD 2·2]) than IPV (2·0 [2·1]).

In addition to interventional studies on IPV immunogenicity and nasopharyngeal shedding after OPV challenge, an observational study during a wild poliovirus type 1 outbreak in 1960 in the USA documented the influence of IPV vaccination on virus excretion in stool and nasopharyngeal samples.[34] The study found a significant impact of baseline serum antibody levels on nasopharyngeal shedding in 15 index poliomyelitis cases and their families, 29 contact families, and 11 non-contact families. 33% (13 of 40) of poliovirus-infected children in index families and contact families with detectable levels (≥8) of antibody during the first 8 days after presumed onset had virus detected in nasopharyngeal samples compared with 75% (21 of 28) of children without detectable antibodies (<8). By comparison, poliovirus-infected children with and without detectable antibody levels had similarly high frequencies of virus in stool samples. However, after 3 weeks, there was a significant reduction in the frequency of isolation from stool in the subgroup with antibody titres of 128 and higher (χ^2=5·58, p<0·02). The study had limitations as the correlation between baseline antibody titres and IPV history was not exact: 12 of 28 children with antibody titres of less than 8 reported having received one or more IPV doses, while eight of 40 children with antibody titres of 8 or higher had not received any IPV. The study concluded that when vaccine failures (ie, titre <8) were accounted for, IPV vaccination had a marked influence on pharyngeal virus excretion.

Exclusive use of IPV for outbreak response

To discuss the literature on the historical role of IPV in stopping poliovirus transmission in populations immunised exclusively with IPV we used: (1) previously published reviews of IPV use in the context of indigenous wild poliovirus transmission and outbreaks of poliovirus from 1960 onwards,[35–38] and (2) records of more recent poliovirus outbreaks and their associated responses

	Year of last wild poliovirus case	Immunisation strategy*	Reference
Sweden	1962	High routine immunisation coverage	35
Finland	1964	Low routine immunisation coverage and three mass IPV campaigns	35,40
Netherlands	1971	High routine immunisation coverage	35
Iceland	1960	High routine immunisation coverage	35
Canada (Ontario, Nova Scotia)	1970s	High routine immunisation coverage	41

IPV=inactivated poliovirus vaccine. *Exact coverage levels are not given and are reported qualitatively.

Table 4: **Countries and two Canadian provinces that achieved wild poliovirus elimination through exclusive use of IPV**

stored in the Polio Information System alongside country immunisation schedules.[39]

First, we briefly discuss the only four countries that eliminated indigenous wild poliovirus transmission with exclusive use of IPV: Sweden, Iceland, the Netherlands, and Finland (table 4). Sweden, Iceland, and the Netherlands were all reported to have high routine immunisation coverage with IPV (although exact coverage was not documented) and eliminated circulation between 1962 and 1971.[35] Finland had very low routine immunisation coverage (18%) in the early 1960s; three mass vaccination campaigns with IPV during 1960–61 successfully stopped transmission.[40] It is unclear whether these mass IPV campaigns boosted intestinal immunity, but it has been shown that additional IPV doses substantially boost intestinal immunity in OPV-vaccinated or previously infected individuals.[42,43] In addition, two Canadian provinces exclusively used IPV in routine immunisation with high coverage and stopped wild poliovirus circulation in the 1970s.[41]

In the USA, poliovirus transmission was not stopped with exclusive IPV use between 1955 and 1961, but the number of cases decreased more rapidly than expected based on estimated direct effects of vaccination.[44] This decrease was attributed to IPV providing herd protection; simultaneous improvements in sanitation might have also reduced transmission.[45] Investigations into local poliovirus transmission in 1959 across multiple cities in the USA found no poliovirus in sewage of high-income areas and no cases reported in unvaccinated individuals. In contrast, multiple poliovirus detections in sewage were documented from low-income areas, alongside large numbers of cases reported in unvaccinated individuals.[46–48]

Summary of poliovirus outbreaks and responses in exclusive IPV-using countries

Outbreaks have not spread outside of isolated communities with poor vaccination coverage in countries exclusively using IPV except for a type 3 wild poliovirus outbreak in Finland (1984–85), a type 1 wild poliovirus outbreak in Israel (2013), and concurrently circulating type 1 and type 2 VDPV outbreaks in Malaysia (2019–20; table 5).

In countries where outbreaks were stopped without OPV (ie, Canada and Sweden), relatively high (≥87%) routine immunisation coverage was reported. Some single introductions might not have spread simply due to chance, but poliovirus transmission stopped nonetheless, and sewage surveillance in Sweden only detected poliovirus for a short period (<1 month) following importation from Finland.[48] In these countries, the response strategy was to offer IPV or OPV immunisation to unvaccinated children, rather than mass vaccination campaigns. The success of IPV administered through routine immunisation in stopping circulation has been attributed to high standards of sanitation, which is believed to limit faecal–oral transmission.[59]

Later outbreaks in Finland (1984–85), Israel (2013), and Malaysia (2019–20) led to implementation of OPV campaigns to stop transmission. Finland had low routine immunisation coverage (15% of children had not received any IPV) of low-potency IPV and the circulating type 3 wild poliovirus strain was antigenically distant from the IPV product. The outbreak response included mass OPV campaigns to stop transmission.[39] No cases of paralytic poliomyelitis were reported during the 2013 type 1 wild poliovirus outbreak in Israel and routine immunisation coverage with IPV was very high (97%); widescale environmental surveillance was important in documenting extensive silent transmission in the country.[53] Increasing viral load in environmental surveillance indicated that transmission persisted despite an initial local IPV catch-up campaign; OPV was deemed necessary to stop poliovirus spread.[53,60] Poliovirus circulation in this population was attributed to lower levels of sanitation in the impoverished Bedouin population in the south of the country, making the widespread nature of transmission in the country difficult to explain.[60] VDPV outbreaks in Sabah state, Malaysia, occurred where an estimated 30% of residents lacked regular access to health care and immunisation.[54] Some districts had routine immunisation coverage below 80%, and some areas had poor sanitation facilitating faecal–oral transmission. Multiple detections in environmental surveillance provided evidence of persistent viral circulation and an OPV response (bOPV and type 2 mOPV) was implemented.[54] The outbreaks in Israel and Malaysia highlight how crucial it is to rapidly scale up environmental surveillance when poliovirus circulation is detected.

Recently, type 2 cVDPV has appeared in countries exclusively using IPV due to population movements from countries experiencing poliovirus transmission or

For the **Polio Information System** see https://extranet.who.int/polis/public/CaseCount.aspx

	Year of outbreak	Type of poliovirus in circulation	Number of AFP cases	Further details of the outbreak	National IPV routine immunisation coverage at outbreak onset	Immunisation strategy	Reference
Sweden	1977	Type 2 WPV	1	..	High*	IPV routine immunisation with high coverage (no outbreak response)	49
Netherlands	1978	Type 1 WPV	110	AFP cases in unvaccinated communities	96% except for zero-dose religious communities	High routine immunisation outside religious groups prevented onward spread; unvaccinated individuals outside the affected communities protected by herd immunity	50
Canada	1978–79	WPV	9	AFP cases in unvaccinated religious communities	High*	High routine immunisation (no spread outside of unvaccinated communities)	37
Sweden	1984	Type 3 WPV (exposure from Finland)	0	Positive environmental surveillance detections	98%	IPV routine immunisation with high coverage (no outbreak response)	51
Finland	1984–85	Type 3 WPV	9	..	84% and low-potency IPV	OPV mass campaign	51
Canada	1988	WPV	1	..	87%	High routine immunisation coverage	37
Netherlands	1992	Type 3 WPV	71	AFP cases in unvaccinated communities	97% except for zero-dose religious communities	High routine immunisation outside religious groups prevented onward spread; one tOPV dose to unvaccinated individuals, one IPV dose to undervaccinated individuals	35,52
Canada	1993	Type 3 WPV	0	21/45 positive stool samples in religious communities	90%	High routine immunisation coverage	37
Canada	1996	Type 1 WPV	0	Asymptomatic importation	89%	High routine immunisation coverage	37
Israel	2013	Type 1 WPV	0	Multiple environmental surveillance sites with positive detections across the country	97%	IPV catch-up to unvaccinated children and booster for adults; two bOPV campaigns	53
Malaysia	2019–20	Types 1 and 2 VDPV	4 (all caused by type 1 VDPV)	Multiple environmental surveillance sites positive in Sabah state of both serotypes	97% (but 30% under-vaccinated in affected sub-populations)	Two bOPV rounds and two type 2 mOPV rounds	54
Spain	2021	Type 2 VDPV	1	AFP case was a traveller from Senegal; paralysis onset occurred in Senegal, but poliovirus was isolated from stool in Murcia, Spain	92%	IPV to close contacts	55
UK	2022	Type 2 VDPV	0	Positive environmental surveillance detections	93% (lower in London)	One IPV booster dose to 900 000 children aged 1–9 years	56
USA	2022	Type 2 VDPV	1	AFP case in an unvaccinated individual; positive environmental surveillance detections	93%	Routine immunisation catch-up; one IPV booster dose to fully immunised individuals	57
Canada	2022	Type 2 VDPV	0	Positive environmental surveillance detections	92%	Routine immunisation catch-up	58

AFP=acute flaccid paralysis. bOPV=bivalent oral poliovirus vaccine. IPV=inactivated poliovirus vaccine. mOPV=monovalent oral poliovirus vaccine. Ref=reference. tOPV=trivalent oral poliovirus vaccine. VDPV=vaccine-derived poliovirus. WPV=wild poliovirus. *Routine immunisation coverage is not reported, just referred to as high.

Table 5: **Outbreaks or poliovirus exposure in countries exclusively using IPV, in chronological order**

where OPV is used. In 2021, an imported type 2 cVDPV case in Spain resulted in one case of acute flaccid paralysis.[55] In 2022, there were genetically linked type 2 cVDPV isolations in London, New York, Quebec, and Jerusalem.[61] These detections likely arose from shedding and subsequent circulation of Sabin-like type 2 virus by individuals vaccinated overseas with type 2 Sabin OPV; pockets of undervaccinated communities create a permissible environment for ongoing type 2 VDPV transmission.[62] London had repeated detections of Sabin-like type 2 virus, and subsequently type 2 cVDPV, in sewage samples from February, 2022, to the latest detection in November, 2022,[7] leading to expansion of environmental sampling to multiple sites across the UK.[63] The Joint Committee of Vaccination and Immunisation (JCVI) planned for immunisation catch-ups in undervaccinated children, as well as an IPV booster campaign targeting children aged 1–9 years in London.[56] If the risk status changes, JCVI plans for a type 2 nOPV campaign, with regulatory preparations underway with discussions between the Medicines and Healthcare products Regulatory Agency and WHO to acquire the vaccine in-country.[56]

In July, 2022, an unvaccinated person living in a community with low vaccination coverage in Rockland County, NY, USA, had acute flaccid paralysis caused by

type 2 VDPV. The most recent detection from New York was from environmental sampling in February, 2023.[64] In response to the case of acute flaccid paralysis, the Rockland County Department of Health launched a county-wide catch-up vaccination effort with IPV; routine immunisation coverage was 60·3% in August, 2022, with zip code-specific coverage as low as 37·3%.[65] Shortly after, the New York State Health Department called for all state residents to catch up on missed immunisations immediately and for those with increased risk of exposure to receive one booster of IPV.[57] In August, 2022, two wastewater samples collected in Quebec, Canada, tested positive for type 2 cVDPV. Genetic sequencing found these to be linked to the isolates in New York.[58] Government officials urged citizens to catch up on their vaccinations but did not plan for a targeted vaccination campaign.

Two IPV-using countries that also use OPV (China and Ukraine) responded to type 2 cVDPV outbreaks solely with IPV campaigns after type 2 OPV had been withdrawn from routine immunisation. During the 2019 type 2 cVDPV outbreak in China, two campaigns with Sabin IPV were conducted in the affected prefecture and the neighbouring population targeting children aged 2 months to 5 years; 58% of the children were born before 2016, so had been eligible to receive tOPV during routine immunisation, meaning intestinal immunity might have been boosted by administration of IPV.[66] A type 2 cVDPV outbreak in Tajikistan originating from an emergence cluster in Pakistan resulted in 35 cases of acute flaccid paralysis in 2021, the first historic instance of type 2 cVDPV transmission in the WHO European region; successful outbreak response in Tajikistan included several vaccination campaigns with type 2 nOPV.[67] In late 2021, in Ukraine, a country with an OPV-based routine immunisation schedule, there were two cases of acute flaccid paralysis and several contact and environmental detections, with isolates linked to the Tajikistan outbreak. The outbreak response included a nationwide accelerated catch-up campaign with IPV for underimmunised children aged 6 months to 6 years, but full implementation was delayed until September, 2022, due to the active conflict in the country. No new type 2 cVDPV detections followed the response, and Ukraine has been removed from the list of countries with polio.[68]

National recommendations for poliovirus outbreak response in countries only using IPV

Having considered countries exclusively using IPV and their recently reported routine immunisation coverage to understand the current context of IPV use compared with that achieved historically when poliovirus was circulating in such countries, we review current country-level guidelines and compare them in terms of poliovirus outbreak readiness and vaccination response strategy.

Most countries exclusively using IPV have very high coverage of three doses of IPV in routine immunisation (appendix). Notable exceptions are Austria, Argentina, Mexico, and Finland, who reported less than 90% coverage in 2021.[69] These countries have a substantial immunity gap, leaving large numbers of children susceptible to paralysis if an outbreak were to occur. What is not apparent from these data is the concerning scale of subnational heterogeneity in vaccination coverage across different countries.

See Online for appendix

Guidelines from the National Immunization Technical Advisory Groups of various IPV-only countries from each WHO region are summarised in table 6; seven countries (Australia, Belgium, Canada, Denmark, Mexico, the UK, and the USA) were directly contacted via National Immunization Technical Advisory Group representatives to define current polio vaccination recommendations if there was an outbreak. Otherwise, we reviewed publicly available national outbreak response plans found on respective government websites. Outbreak response plans are either absent or significantly varied across countries exclusively using IPV. Some countries, including Argentina, Chile, Mexico, and the USA, follow the current WHO guidelines,[10] indicating OPV for outbreak response. Other countries, including Spain, Portugal, the UK, Belgium, Ireland, and Australia, outline using IPV as an initial response while assessing the extent of the outbreak for an OPV campaign. Finally, some countries, including South Korea, Germany, Canada, and Norway, have guidelines to only use IPV.

In the WHO European region, the WHO Regional Certification Commission for Poliomyelitis Eradication (RCC) obliges all member states to have outbreak preparedness plans, including access to vaccines. The RCC reviews these plans annually; country-level risk assessments and recommendations are formulated accordingly.[74] However, several countries have consistently not met RCC obligations with outdated or no national outbreak response plans, including Romania, Croatia, Armenia, Hungary, Estonia, France, Malta, and Cyprus.

Some countries exclusively using IPV have not experienced poliovirus transmission in decades and have no hands-on experience with outbreak response and a diminished perceived imperative for preparedness. OPV reintroduction could face resistance by the population, as previously demonstrated in a study mapping global vaccine hesitancy.[83] Furthermore, regulatory hurdles to obtain and use OPV in-country could delay a timely outbreak response. For instance, the USA last updated its poliovirus outbreak response guidelines in 2000, stating that OPV should be used.[73] However, OPV licensure has not been maintained for use in the country, compromising the outlined response strategy. Following the recent type 2 cVDPV detections in the UK and the USA, it has been possible to observe how these countries responded. In the UK, the vaccination response with IPV

	Population	Vaccine response	Details and comments	Year of latest guidelines	Source
WHO region of the Americas					
Argentina	Children <5 years	OPV	Two rounds of type 2 mOPV	2019	Ref 70
Canada	All (including infants)	IPV	IPV routine immunisation catch-up for children and single lifetime IPV booster for adults; no authorised OPV product in Canada	2021	Ref 71 and NITAG representative
Chile	Children <5 years (if no evidence of circulation in individuals >5 years) in directly affected area, then an assessment for a wider-area campaign	OPV	Two rounds of type 2 mOPV (if type 2 cVDPV); IPV if type 1 or 3 wild poliovirus or cVDPV	2020	Ref 72
Mexico	Undefined	OPV	In case mOPV is not available, hexavalent vaccine (contains IPV, used in routine immunisation) would be used	2022	NITAG representative
USA	Undefined	OPV	Response plan outdated since OPV is unlicensed for use in the USA; there has been no formal publication from the US Centers for Disease Control and Prevention or vote by the Advisory Committee on Immunization Practices on OPV for outbreak response since the statement in 2000; IPV was used after type 2 cVDPV detections in New York, NY, in 2022	2000	Ref 73 and NITAG representative
WHO European region					
Armenia	NA	NA	Expired outbreak response plan	2023	Ref 74
Belgium	Begin with close index contacts who are underimmunised or non-immunised	IPV or OPV after consultation with WHO and Global Polio Eradication Initiative	Geographical scale of response dependent on extent of transmission; no defined NITAG policies but have a national action plan	2018	NITAG representative
Croatia	NA	NA	Expired outbreak response plan	2023	Ref 74
Cyprus	NA	NA	No national outbreak response plan	2023	Ref 74
Denmark	Close contacts	IPV	In case of a wider outbreak, supplemental immunisation activities (with IPV) can be considered depending on risk assessments	2023	National polio preparedness specialist
Estonia	NA	NA	No national outbreak response plan	2023	Ref 74
France	NA	NA	No national outbreak response plan	2023	Ref 74
Germany	Contacts of index case (regardless of their vaccination status); a secondary case is a cause for ring vaccinations	IPV only	IPV for immediate post-exposure; ring vaccinations with IPV and further measures by health authorities in the occurrence of a secondary case	2015	Ref 75
Hungary	NA	NA	Outbreak response plan needing significant revision	2023	Ref 74
Ireland	Contacts of index case, including health-care workers, who are underimmunised or non-immunised	Initial IPV response, consider OPV if needed	Vaccinated contacts could receive IPV booster; country would work closely with WHO for discussions and preparation of novel OPV if needed	2023	Ref 76
Malta	NA	NA	No national outbreak response plan	2023	Ref 74
Norway	Close contacts (regardless of vaccination status)	IPV	Depending on the epidemiological circumstances, supplementary immunisation activity on municipality, regional, or other sub-national levels or in specific age groups or socioeconomically defined groups will be considered	2018	Ref 77
Portugal	Depending on level of alert (1–5)	Initial IPV response, consider OPV if needed	IPV for alert levels 1–4; for alert level 5, OPV in three rounds to children <18 years, regardless of vaccination history	2014	Ref 78
Romania	NA	NA	Expired outbreak response plan	2023	Ref 74
Spain	Children <5 years; areas with vaccination coverage <90%	Initial IPV response, consider OPV if needed	First round with IPV, then depending on the scale of the outbreak, second round with mOPV; Ministry of Health indicated an updated plan will be available at the end of 2023	2016	Ref 79 and NITAG representative
UK	Close family contacts, regardless of vaccination history; extended depending on assessment	Initial IPV response, consider OPV if needed	IPV initially; if needed, request OPV stock to WHO (not licensed in the UK, permission needed from Medicines and Healthcare products Regulatory Agency for importation)	2019	Ref 80
WHO Western Pacific region					
Australia	Case contacts	Initial IPV response, consider OPV if needed	Booster dose of IPV, or if unvaccinated or vaccination history is unknown, a full series of three IPV doses; if there is a larger outbreak, will request type-specific mOPV from WHO global stockpiles	2019	Ref 81
South Korea	Case contacts	IPV only	IPV booster for vaccinated people and three IPV doses when unvaccinated or vaccination history is unknown	2013	Ref 82

cVDPV=circulating vaccine-derived poliovirus. IPV=inactivated poliovirus vaccine. mOPV=monovalent oral poliovirus vaccine. NITAG=National Immunization Technical Advisory Group. OPV=oral poliovirus vaccine. Ref=reference.

Table 6: **Current national recommendations for outbreak response after confirmation of poliovirus transmission**

followed the Public Health England National Polio Guidelines last published in 2019,[80] but in the USA the response with IPV did not follow the published guidelines.

In 2016, the European Centre for Disease Prevention and Control performed a qualitative polio outbreak readiness assessment in Poland and Cyprus,[84] two countries classified as at intermediate risk of poliovirus transmission following importation. The case study provides a framework to enhance intersectoral preparedness status against cross-border health threats, with inclusion of key items like clear response frameworks, sensitive environmental surveillance, high routine immunisation coverage, and addressing vaccine hesitancy. Outbreak protocols can be tested through simulation exercises to strengthen capacity and identify gaps.[85]

Although WHO has developed Standard Operating Procedures, and the RCC obliges EU member states to have polio mitigation plans, the wide variability, and in some cases absence, of polio outbreak response plans in countries exclusively using IPV warrant addressing this gap and developing outbreak response strategies that cater to each country's public health status and epidemiological context. This is especially relevant following the recent detections of type 2 cVDPV in IPV-only countries such as the USA and the UK.

Current policy recommendations for vaccine choice and transitions

The two main aims of poliovirus outbreak response are stopping community transmission and individual protection against paralysis. Although IPV provides excellent humoral protection against paralysis, mucosal immunity is needed to stop poliovirus transmission. IPV might induce limited transmission-blocking immunity, but there is significant uncertainty about how much it impacts transmission in IPV-only high-income settings.

Based on the evidence discussed in this Personal View, SAGE made new policy recommendations for IPV use in poliovirus outbreak response, departing from the long-standing WHO Standard Operating Procedures mandating only OPV use.[9] In October, 2022, SAGE recommended that "countries with exclusive IPV vaccination and a high level of sanitation and hygiene may opt to conduct a timely initial outbreak response with IPV…if poliovirus transmission is confined to a well-defined population group or geographical area. If transmission persists, an OPV response should be considered."[86] As such, spread and scale of the poliovirus outbreak are central for the design of the response, including vaccine choice and transition from an IPV-only to an OPV response. Some key considerations for this transition are community vaccine acceptance, vaccine coverage in the affected sub-population, population migration dynamics, trend of spread over time, age and demographic characteristics of the affected population, paralytic case burden relative to burden of infection, genetic diversity of the outbreak virus over time, and regulatory criteria for vaccine importation and use. IPV-only using countries, such as Ireland and Canada, have begun to adopt this SAGE policy, writing it into their national poliovirus outbreak response guidelines.[87,88]

In March, 2023, SAGE recommended an additional vaccination response with IPV (full or fractional dose) in areas with persistent poliovirus circulation where repeated OPV campaigns have not stopped virus transmission.[89] In the past, GPEI has successfully implemented IPV campaigns in such areas—eg, in Pakistan, Kenya, and India. The rationale is that a dose of IPV in those previously vaccinated with multiple OPV doses or exposed to poliovirus will provide a more effective boost to humoral and mucosal immunity than an additional OPV dose.[42,43,90,91]

Discussion

With the initiation of sequential, global withdrawal of OPVs from routine use, there is an increasing reliance on IPV during the interim phase of the eradication endgame. In this Personal View, we have discussed data on intestinal and pharyngeal mucosal immunity induced by exclusive IPV vaccination, previous programmatic experience of poliovirus outbreak response with IPV, current response guidelines in IPV-only countries, and the latest SAGE policies, including adding IPV to the outbreak response toolkit. Although IPV vaccination alone seems to have little impact on viral shedding without past exposure to live poliovirus, there is some evidence that suggests it shortens duration and lowers viral loads of faecal and nasopharyngeal shedding, but scarce evidence for its role in nasopharyngeal immunity warrants additional studies. In assessing programmatic use and outbreak control strategies with IPV across different contexts, three of four countries that stopped indigenous wild poliovirus transmission with IPV exclusively reported high (exact values were not documented) routine immunisation coverage. IPV boosting of intestinal immunity might have played an important role in interrupting poliovirus transmission due to natural exposure to poliovirus in the past. The UK is the first example of a rolling IPV vaccination being implemented as an outbreak response strategy in a country that exclusively uses IPV, although the response was restricted to London where the detections were made.

Countries that stopped poliovirus outbreaks during exclusive IPV use without OPV campaigns reported high (≥87%) routine immunisation coverage. In these settings, outbreak response strategies focused on prioritising vaccination efforts to previously unvaccinated individuals. High standards of sanitation in these countries suggest a larger role of the oral–oral compared with faecal–oral transmission route, and thus the impact of IPV on duration and titre of nasopharyngeal shedding might be

relevant to explore further. In countries exclusively using IPV where OPV campaigns were required to stop poliovirus outbreaks, factors such as low routine immunisation coverage, lower standards of sanitation in vulnerable populations, and use of lower potency IPV in routine immunisation contributed to sustaining transmission.

Outbreak response plans in countries exclusively using IPV vary substantially; some countries have not published final mitigation plans despite formal RCC obligations and WHO Standard Operating Procedures. The lack of current, context-relevant response planning needs to be addressed as the absence of poliovirus transmission for extended periods has the potential to reduce the perception of risk and the urgency of preparedness. Regulatory challenges and perceptions around OPV might also delay or hinder appropriate outbreak responses.[11,92]

Following certified wild poliovirus eradication, it will be important that IPV can fulfil the role of OPV to provide sufficient immune protection to the global community against risk of paralysis in case poliovirus is reintroduced to the population, especially reintroductions arising from people who are immunodeficient who might excrete the virus for long periods of time or from accidental release from facilities handling live polioviruses. Many policy makers already see IPV as meeting that need, but some gaps in our knowledge remain, particularly in the capacity of IPV to induce or enhance mucosal immunity, which is vital to interrupt poliovirus outbreaks. Further studies to investigate this aspect of the immune response are necessary to inform future outbreak response strategies. Most importantly, adequate global supply of affordable IPV and high routine immunisation coverage will be crucial to ensure complete protection against risk of paralysis from all forms of polioviruses. Adequate stockpiles of novel OPVs will also strengthen the likelihood of success in interrupting community spread of poliovirus outbreaks following eradication in an IPV-only era. In summarising the evidence on IPV use and its impact, we provide valuable insights that have informed recent SAGE outbreak response recommendations. IPV can be useful as an initial timely response for IPV-only countries and as an additional tool in areas with persistent poliovirus transmission following repeated OPV campaigns.

Contributors

GM, IMB, and RLC did the literature search, made contact with the National Immunization Technical Advisory Group (NITAG) representatives, and with ASB wrote the first draft of the manuscript. LC, NG, OM, and ALMdSN reviewed, advised upon, and edited the manuscript, and all authors approved the submission of the final draft.

Declaration of interests

We declare no competing interests.

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