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Trade-offs of different poliovirus vaccine options for outbreak response in the United States and other countries that only use inactivated poliovirus vaccine (IPV) in routine immunization

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ABSTRACT

Delays in achieving polio eradication have led to ongoing risks of poliovirus importations that may cause outbreaks in polio-free countries. Because of the low, but non-zero risk of paralysis with oral poliovirus vaccines (OPVs), countries that achieve and maintain high national routine immunization coverage have increasingly shifted to exclusive use of inactivated poliovirus vaccine (IPV) for all preventive immunizations. However, immunization coverage within countries varies, with under-vaccinated subpopulations potentially able to sustain transmission of imported polioviruses and experience local outbreaks. Due to its cost, ease-of-use, and ability to induce mucosal immunity, using OPV as an outbreak control measure offers a more cost-effective option in countries in which OPV remains in use. However, recent polio outbreaks in IPV-only countries raise questions about whether and when IPV use for outbreak response may fail to stop poliovirus transmission and what consequences may follow from using OPV for outbreak response in these countries. We systematically reviewed the literature to identify modeling studies that explored the use of IPV for outbreak response in IPV-only countries. In addition, applying a model of the 2022 type 2 poliovirus outbreak in New York, we characterized the implications of using different OPV formulations for outbreak response instead of IPV. We also explored the hypothetical scenario of the same outbreak except for type 1 poliovirus instead of type 2. We find that using IPV for outbreak response will likely only stop outbreaks for polioviruses of relatively low transmission potential in countries with very high overall immunization coverage, seasonal transmission dynamics, and only if IPV immunization interventions reach some unvaccinated individuals. Using OPV for outbreak response in IPV-only countries poses substantial risks and challenges that require careful consideration, but may represent an option to consider for some outbreaks in some populations depending on the properties of the available vaccines and coverage attainable.

1. Introduction

In mid-2022, the United States (US) reported a case of paralytic poliomyelitis caused by a circulating vaccine-derived poliovirus type 2 (cVDPV2) that resulted from transmission in New York State (NYS) [1]. The NYS outbreak was genetically and temporally linked to related poliovirus transmission in the United Kingdom (UK) [2] and Israel [3], as well as a limited wastewater signal in Canada [4].

In countries that achieve high overall poliovirus vaccine coverage in routine immunization (RI), the rarity of polio outbreaks (i.e., sustained transmission of imported polioviruses [5]) limits the need for substantial investments in re-evaluating poliovirus outbreak response plans [6]. In addition, the variable characteristics of under-vaccinated communities and imported polioviruses limit the utility of generic outbreak response plans. However, all countries with under-vaccinated communities remain susceptible to sustained poliovirus transmission following importations, including polio-free countries that use only inactivated poliovirus vaccine (IPV) [7–9]. In response to the NYS outbreak, local, state, and national public health authorities appropriately emphasized the need for immunization activities using IPV to boost immunity

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against polio in the under-vaccinated populations [1,10–12]. In addition, NYS public health jurisdictions, in conjunction with the US Centers for Disease Control and Prevention (CDC), took advantage of an existing wastewater surveillance platform for SARS-CoV-2 and began to monitor the scope and extent of poliovirus transmission by testing residual specimens for poliovirus [10–12].

Uncertainty about the origin of the NYS outbreak and genetic linkage of the outbreak virus to detections in UK, Israel, and Canada raised broad questions about the global experience with outbreak response in IPV-only countries and the use of IPV for outbreak response following importations [6,13]. It also led to questions about the potential need to stockpile and use oral poliovirus vaccine (OPV) in the US for outbreak response, which public health authorities debated after the US shifted from Sabin OPV to IPV in 2000 [14]. Reintroduction of any OPV in the US now, for any purpose, would likely face significant regulatory challenges and an uncertain risk–benefit profile [15]. However, recent development [16] and widespread use of novel type 2 OPV for global response to cVDPV2 outbreaks under a World Health Organization emergency use listing increases the complexity of an OPV option [17].

The availability of numerous fundamentally different types and formulations of poliovirus vaccines adds substantial complexity to the polio outbreak response landscape [18,19]. Live, attenuated OPVs (including Sabin and novel OPVs) are delivered easily by mouth, and come with the benefits of lower cost and the ability to spread secondarily to induce and boost both humoral and mucosal immunity in individuals beyond vaccine recipients [20,21]. However, OPV use also comes with the very low, but non-zero, risks of cases from vaccine-associated paralytic polio (VAPP) reported by OPV recipients or their close contacts, as well as cases from vaccine-derived polioviruses (VDPVs) [18,22,23] reported due to ongoing transmission of OPV strains. These risks motivated countries like the US to stop using OPV. In contrast to OPV, IPV requires an injection, only induces humoral immunity, and does not spread beyond the recipient or come with VAPP or VDPV risks [18,20,21]. The development of novel OPVs, combination vaccines that include IPV, and different options for vaccination strategies further complicate decision making about vaccine choices [16,19,24,25].

Poliovirus outbreaks can occur following the importation of a live poliovirus (wild type or a vaccine strain) into populations that previously stopped transmission but failed to maintain sufficient preventive immunization coverage, including IPV-only countries [6,13,26]. Typically, identification of an outbreak follows the detection of at least one clinical case of paralytic poliomyelitis (polio for short) with evidence of local transmission, and more recently, the detection of positive environmental samples with evidence of local transmission [5]. However, detecting poliovirus transmission in polio-free countries that do not maintain routine clinical (i.e., acute flaccid paralysis or acute flaccid myelitis) or environmental (e.g., wastewater) surveillance systems can be challenging and largely depends on the identification of a potential case by an alert clinical provider followed by laboratory confirmation. Identification of sustained poliovirus transmission is further complicated by the fact that only a small fraction of individuals with no prior immunity who become infected will present with polio due to the relatively low paralysis-to-infection ratio for all poliovirus types [27]. Meanwhile, all infected individuals, including those with prior immunity, can potentially transmit the virus [8,28]. Importantly, individuals with immunity induced only by IPV lack significant mucosal immunity and can participate substantially in transmission upon their first exposure to a live poliovirus [20,21]. In addition, the existence of three different stable serotypes of polioviruses (i.e., types 1, 2, and 3) with different epidemiological and clinical behavior necessitates concurrent immunity and management of all the three poliovirus types [28]. Outbreaks of cocirculating poliovirus types represent an increasing global concern [29] and can make public health authorities face the challenges of managing cocirculation of two different polioviruses using two different OPV formulations at the same time [30]. In addition, recent modeling identified increasing risks of type 1 cVDPVs (cVDPV1s) [31], which increasingly affect areas that remained free from cases caused by poliovirus transmission for well over a decade (e.g., Peru [32]) and now account for more reported type 1 cases than those caused by type 1 wild polioviruses.

As countries reduced and ended their transmission of indigenous wild polioviruses (WPVs), they occasionally reported polio cases due to outbreaks and were forced to consider immunization options for outbreak response [26]. In addition, as VAPP risks began to exceed WPV risks in countries that achieved very high RI coverage, many of these countries began to mitigate VAPP risks by using IPV first (i.e., IPV/OPV sequential schedules). For example, the US started with IPV fields trials in 1954 and licensure in 1955, then switched to OPV in the 1960s after its licensure, then shifted to IPV/OPV in 1997, and finally moved to IPV-only in 2000 [7,33]. Other countries have similarly shifted to IPV-only after a period of using OPV and a few countries never used OPV for RI [6]. National and global discussions related to shifting to IPV-only for RI included vaccine preferences for outbreak response and the potential need for vaccines stockpiles [34]. Over time, the Global Polio Eradication Initiative (GPEI) outbreak response standard operating procedures evolved with the changing landscape of polio eradication and the development of new vaccine options [5,35–39].

In the complex global polio eradication landscape, modeling studies are critical in assessing risks, benefits, costs, and outcomes of various policy options. Recent discussions of the mixed epidemiological experience with IPV for outbreak response in both IPV-only and OPV-using countries [6,13], did not include a review of insights from modeling studies that explored the use of IPV for outbreak response. In addition, the recent experience with polio transmission in under-vaccinated populations in high-income countries such as the US and UK that use IPV-only raised questions about the impacts and trade-offs of IPV versus OPV for outbreak response. As such, we sought to characterize outbreak response in such countries through a literature review and application of an established global poliovirus transmission and OPV evolution model tailored for modeling the 2022–2023 NYS outbreak.

2. Methods

2.1. Review of published literature

We identified modeling studies of outbreak response that included IPV use from a prior systematic review of polio modeling literature for studies published between January 1, 2000 and Dec 31, 2019 [40]. We also performed a new search of the biomedical literature published between January 1, 2020, and August 1, 2023, to identify additional relevant papers published since the previous review. We performed the search by executing the following query in PubMed: “polio*”[Title/Abstract] AND “model*”[Title/Abstract] AND “English”[Language] AND 2020/01/01:2023/08/01[Date - Publication]. We reviewed the resulting 257 records to identify modeling studies that met the inclusion criteria for the prior systematic review [40] and had one or more areas of focus on the use of IPV for poliovirus outbreak response.

In our literature review, we included studies that performed transmission modeling and/or health economic analysis that specifically used IPV in outbreak response as an intervention. We categorized these studies by publication years and as specific to an IPV-only setting or global (i.e., IPV and/or OPV use in RI). We extracted overall insights from these analyses related to the use of IPV for outbreak response, with emphasis on capturing comparisons between IPV and OPV use when reported. Based on this review, we explored the factors likely to determine the outcomes from different vaccine options for outbreak response (e.g., characteristics of the outbreak population, poliovirus type, etc.).

2.2. IPV versus OPV for outbreak response in new York State

We applied our model of the 2022–2023 polio outbreak in NYS [9], which distributes the population of the State into outbreak counties (O,

i.e., Rockland, Orange, Sullivan, and Kings) and non-outbreak counties (N, i.e., all others). We further divided each of these into one general (i.e., OG and NG) and one under-vaccinated subpopulation (i.e., OU and NU). The general subpopulations represent the well-vaccinated communities reflective of the high overall reported routine immunization coverage, while the under-vaccinated subpopulations reflect the communities with substantially lower coverage [9]. We modeled the base case assumption for seasonal fluctuation (i.e., amplitude of 35%) and three mixing scenarios related to the level of isolation of the 4 subpopulations. As detailed previously [9], the *no isolation* mixing scenario assumes that all 4 subpopulations mix, with 95% of contacts coming from the two subpopulations of the same vaccination levels, while the remaining 5% of contacts come from both of the other two subpopulations. The *subpopulation isolation* mixing scenario assumes that the under-vaccinated subpopulations remain isolated from the general subpopulations, but mix proportionately between themselves. The *partial isolation* mixing scenario assumes that 95% of contacts come from each under-vaccinated subpopulation with itself, while the remaining 5% come only from the two general subpopulations (see supplemental Table S2 in [9]). These different scenarios reflect various options for exploring the implications of the uncertain actual mixing at the level of abstraction used in our model, for which the *partial isolation* mixing scenario provides the most likely approximation to the actual circumstances in NYS.

In the current analysis, we explore the implications of the hypothetical counterfactual scenario of using type 2 OPV (OPV2) to respond to the cVDPV2 outbreak instead of the actual outbreak response in NYS that used IPV. For consistency with recent prior analyses [30,31], we consider the options of using Sabin monovalent OPV2 (mOPV2) or novel OPV2 (nOPV2) using two nOPV2 bounding case assumptions. Specifically, the *best nOPV2* bounding scenario assumes the same effectiveness as mOPV2, but with no risk of VAPP, and no reversion to neurovirulence, while *worst nOPV2* bounding assumes less effectiveness of nOPV2 than mOPV2, some reversion to neurovirulence, and some potential to create long-term excreters [30,31]. Increasingly available field experience [23,41–43] suggests that the actual nOPV2 performance is bound by these two extremes. For all scenarios, we assume the same number of vaccine doses and same timing of their use as occurred with IPV in 2022 for the incremental outbreak response in NYS [9]. Thus, we hypothetically assume that the response includes only a fixed, very small number of doses. All other model details and inputs are as previously described [9].

Recent global modeling highlighted the potential for increasing risks of type 1 cVDPVs (cVDPV1s) [30,31], which implies future threats of importations of cVDPV1s into the US. Given this risk and the significantly higher transmissibility and neurovirulence of type 1 (see Table S1 in [9], which reports the model inputs for paralysis-to-infection ratios, average basic reproductive numbers (R_0), and relative R_0 values for different types and strains of polioviruses), we also consider the hypothetical importation of a type 1 outbreak poliovirus instead of the actual importation of the vaccine-derived type 2 virus in 2022 in NYS. For this analysis, we use an identical modeling approach as described above, and import a type 1 poliovirus into the population instead of type 2, which implies different properties for the outbreak virus itself and some type-specific differences in the population immunity [28]. For this analysis, we similarly consider outbreak response with IPV as was done in NYS, as well as counterfactual responses with Sabin type 1 monovalent OPV (mOPV1), or theoretical type 1 nOPV (i.e., *best nOPV1* and *worst nOPV1*) for which we assume bounding properties based on prior studies, as described for type 2 above [30,31]. We assume the same timing and number of outbreak response doses to provide direct comparison between types 1 and 2.

3. Results

3.1. Review of published literature

We identified 12 published modeling papers relevant to IPV use in outbreak response. This included 10 studies [14,44–52] out of 476 modeling papers from the prior systematic review [40] and 2 studies [53,54] out of 46 modeling papers published since 2020 that we identified through the current search. Table 1 provides the publication year, category, and brief summary of findings for each of these studies.

We identified only 3 prior studies that modeled IPV use for outbreak response in IPV-only countries [14,46,48]. Jenkins and Modlin presented a decision analysis for outbreak response in the US considering various formulations and schedules for IPV and OPV, and identified type-specific monovalent OPV as the likely preferred vaccine due to its

Table 1
Summary of modeling literature with at least one area of focus on the use of IPV for poliovirus outbreak response.

Year [Ref]	Category	Description
2006 [14]	IPV-only country (US)	US decision analysis for outbreak response considering both OPV and IPV, recommended OPV use if available
2008 [44]	Global	Global pulse of IPV to stop cVDPVs identified as a potential strategy to deal with global cVDPV outbreaks and achieve eradication
2015 [45]	Global	IPV response to any outbreaks that occur 5 or more years after globally-coordinated homotypic OPV cessation assuming OPV use no longer available and risks of OPV cessation failure necessitating OPV restart
2015 [46]	IPV-only country (Israel)	IPV use in 2013 Israel outbreak response baseline and demonstration of faster stop of transmission with earlier bOPV use
2016 [47]	Global	IPV response in IPV/OPV ring strategy with mixed results and 5 or more years after homotypic OPV cessation
2017 [48]	IPV-only country (hypothetical)	IPV immunization of immigrants coming from OPV-using countries to stop transmission, success depends on IPV coverage in the receiving country
2017 [49]	Global	Adding IPV use to OPV response compared to OPV alone only marginally effective and not cost-effective
2017 [50]	Global	IPV response with OPV may help to increase immunity during outbreaks in some settings
2017 [51]	Global	Shift from OPV to IPV for outbreak responses that occur starting at different numbers of years after globally-coordinated homotypic OPV cessation show larger risks of OPV restart with earlier shift to IPV
2018 [52]	Global	IPV use for outbreak response 5 or more years after globally-coordinated homotypic OPV cessation
2021 [53]	Global	IPV response 8 or more years after the tOPV-bOPV switch and 5 or more years after planned bOPV cessation showing increased risks of OPV2 restart
2021 [54]	Global (hypothetical)	IPV use to respond to hypothetical emergence of new pandemic-like poliovirus

Abbreviations: *IPV, inactivated poliovirus vaccine; OPV, oral poliovirus vaccine; OPV2, type 2 OPV; cVDPV, circulating vaccine-derived poliovirus.*

ability to induce more robust immunity, if available for use [14]. Kalkowska *et al.* simulated the 2013 wild poliovirus type 1 outbreak in Israel, which included an initial IPV response and then bivalent OPV (bOPV, containing types 1 and 3), demonstrating the ability of earlier bOPV use to shut down the outbreak more quickly [46]. Dénes and Székely showed that the ability of IPV to stop transmission, when used to respond to re-emergence of polio due to immigration from OPV-using regions of the world into IPV-only European countries, depends on sufficiently high IPV coverage in the outbreak country [48].

Three other studies addressed the use of IPV for outbreak response globally. Recognizing the need to end cVDPV transmission globally for a successful polio endgame, Wagner and Earn modeled a global pulse of

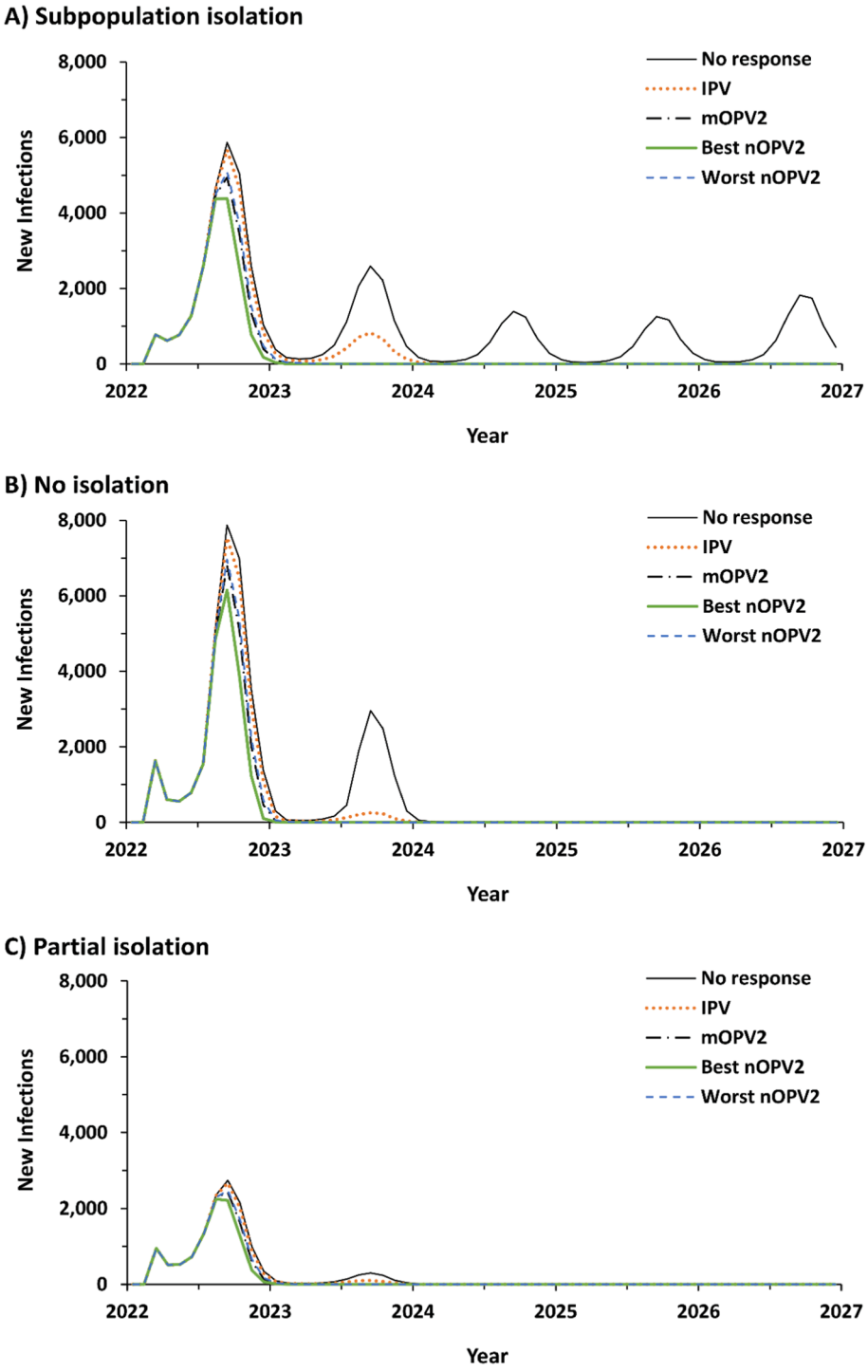

Fig. 1. Monthly expected new infections for the 2022 New York State type 2 polio outbreak assuming the same number of doses of different polio vaccine options for outbreak response (or no response) for different mixing scenarios. A: Subpopulation isolation assumes that the under-vaccinated subpopulations remain isolated from the general subpopulations, but mix proportionately between themselves. B: No isolation assumes that all 4 subpopulations mix, with 95% of contacts coming from the two subpopulations of the same vaccination levels, while the remaining 5% of contacts come from both of the other two subpopulations. C: Partial isolation assumes that 95% of contacts come from each under-vaccinated subpopulation with itself, while the remaining 5% come only from the two general subpopulations. The results show that the use of any OPV2 formulation reduces the expected numbers of new infections and ends the outbreak transmission more quickly (curves shifted down and to the left), with best nOPV2 providing the most effective outbreak response.

IPV to stop cVDPVs as a potential strategy to manage all cVDPV outbreaks simultaneously [44]. McCarthy *et al.* focused on the role of IPV in RI and suggested that using IPV in outbreak response campaigns could help to increase immunity during outbreaks in some settings [50]. Following the early global experience with COVID-19 response, Thompson *et al.* compared the different properties of IPV and different formulations of OPV (Sabin and novel) to respond to the hypothetical emergence of new pandemic-like polioviruses [54].

Several other studies modeled the use of IPV for outbreak response after globally-coordinated cessation of homotypic OPV use (a stated goal of the GPEI), with the explicit assumption that OPV use for outbreak response from global stockpiles would end after a period of 5 or 8 years [45,47,49,51–53]. Of note, Duintjer Tebbens and Thompson suggested that the poor cost-effectiveness and potentially limited vaccine supply in the global market make IPV economically unattractive for high-risk settings, in which IPV does not significantly affect transmission [49]. More recently, however, the development of nOPV2 and its preferential use for outbreak response in the foreseeable future in OPV-using countries led integrated global modeling studies to no longer include IPV for outbreak response in those countries [30,31,55,56]. Overall, the limited number of published modeling studies found marginal effectiveness of IPV use for outbreak response and identified OPV use as more cost-effective, if available [14,45,47,49,51–53].

3.2. IPV versus OPV for outbreak response in New York State

Recent modeling of IPV use for outbreak response in NYS [9] facilitates modeling other vaccine options in this setting, including comparisons between IPV and OPV presented here. Fig. 1 shows the expected new infections over time for the cVDPV2 outbreak with different mixing assumptions and types of vaccine. The no response curves provide a bounding scenario for what to expect in the absence of any outbreak response, and the IPV curves represent the actual response to the NYS outbreak as detailed previously [9]. For all vaccine options modeled, transmission of the outbreak virus ended during the modeled time horizon. Modeling found that the use of OPV2 for the NYS outbreak would likely have ended the transmission of the outbreak viruses several months earlier than IPV. However, the introduction of OPV2 would have come with substantial regulatory obstacles and identifiable risks to individual vaccine recipients and the population (i.e., VAPP, immunodeficiency-associated VDPVs), as well as potential reputational risks for public health authorities. Notably for this outbreak, only the subpopulation mixing scenario and the assumption of no response shows sustained transmission over the model time horizon. Despite the risks associated with OPV, including the potential for VAPP and seeding of new VDPVs, we do not expect either of these two potential negative consequences with the low number of OPV model doses delivered. Both the transmission of the outbreak virus and any OPV used would present some risk of chronically infecting an individual with a primary immunodeficiency, and for the duration of the outbreak, any circulating polioviruses could introduce transmission in other areas. Table 2 shows the low expected burden of polio cases, which reflects the high level of routine IPV coverage and relatively low transmissibility and neurovirulence of the type 2 outbreak virus.

In contrast to the type 2 outbreak, if the NYS introduction in 2022 had involved a type 1 poliovirus (instead of type 2), then the outbreak would have led to substantially more expected new infections (note much higher y-axis values for Fig. 2 than Fig. 1 and higher expected cases for type 1 than type 2 in Table 1). This reflects the relatively greater transmissibility and neurovirulence of type 1 than type 2. For this hypothetical modeled outbreak, with the small number of outbreak response doses used, only availability and use of a theoretical vaccine with the characteristics of *best nOPV1* would stop all transmission of the outbreak virus with the small number of doses used. However, for this analysis, we did not increase the size of the outbreak response or number of doses or explore other interventions, despite the likelihood that the greater extent of transmission and larger number of expected cases could potentially lead to a larger response if it increased demand for vaccination from un(der)vaccinated individuals. The introduction of a type 1 poliovirus poses a substantially greater risk of sustained transmission and paralysis than the cVDPV2 virus introduced in 2022. Since we simulated the possibility of a type 1 outbreak instead of the type 2 outbreak that occurred, this differs from simulation of the introduction of a type 1 poliovirus into the same population now.

4. Discussion

The use of IPV with high coverage in RI successfully prevents most imported polioviruses from restarting transmission, and IPV use in outbreak response successfully stops some poliovirus outbreaks in IPV-only countries. Although the actual immunization thresholds required to stop poliovirus transmission depend on the poliovirus type as well as the outbreak population size, density, hygiene, mixing, and other characteristics, this analysis provides some insights. IPV will likely only stop outbreaks in IPV-only using countries with high overall immunization coverage (i.e., no or relatively small un(der)vaccinated outbreak subpopulations), for polioviruses with relatively low transmission potential, favorable seasonal transmission dynamics, and immunization interventions that reach some of the un(der)vaccinated individuals. Existing literature and the new results presented here suggest that for some outbreaks in IPV-only countries, public health authorities could consider OPV, while recognizing that any OPV (including nOPV) would come with real, albeit potentially statistically small risks of polio cases.

Considering the recent epidemiological experience with outbreaks of genetically linked poliovirus transmission in the US, UK, and Israel in 2022–2023, we see different situations and outcomes. The UK did not report any paralytic polio cases, but it responded with IPV and the transmission likely died out, since there have been no wastewater detections since November 2022 as of May 2023 [57]. The US identified the transmission after the detection of a case, and it responded with IPV [9]. It appears the cVDPV2 transmission in NYS may have died out based on no wastewater detections since February 2023 as of December 2023 [58]. Israel responded with IPV and it continues to offer supplemental immunization to reach under-vaccinated populations as well as to monitor the outbreak with its longstanding wastewater poliovirus surveillance system [59]. Israel reported a polio case from this outbreak and its last positive detection in February 2023 [29].

In Israel, the recent experience with cVDPV2s contrasts with prior

Table 2
Expected paralytic cases under different model mixing scenarios for an outbreak like the New York State 2022–2023 type 2 circulating vaccine-derived poliovirus (cVDPV2) (or hypothetical type 1) using different formulations of poliovirus vaccines for outbreak response.

	Modeled cVDPV2 cases					Modeled cVPDV1 cases				
Vaccine used for outbreak response	IPV	None	mOPV2	nOPV2 best	nOPV2 worst	IPV	None	mOPV1	nOPV1 best	nOPV1 worst
Subpopulation isolation	0.88	1.89	0.64	0.55	0.67	56	163	45	22	47
No isolation	0.64	0.39	0.51	0.44	0.53	130	179	91	26	97
Partial isolation	0.35	0.86	0.30	0.27	0.31	36	45	23	11	25

Abbreviations: *IPV, inactivated poliovirus vaccine; OPV, oral poliovirus vaccine; mOPV, monovalent OPV (specific for each type), nOPV, novel OPV (specific for each type, see text for characteristics of nOPV best and nOPV worst).*

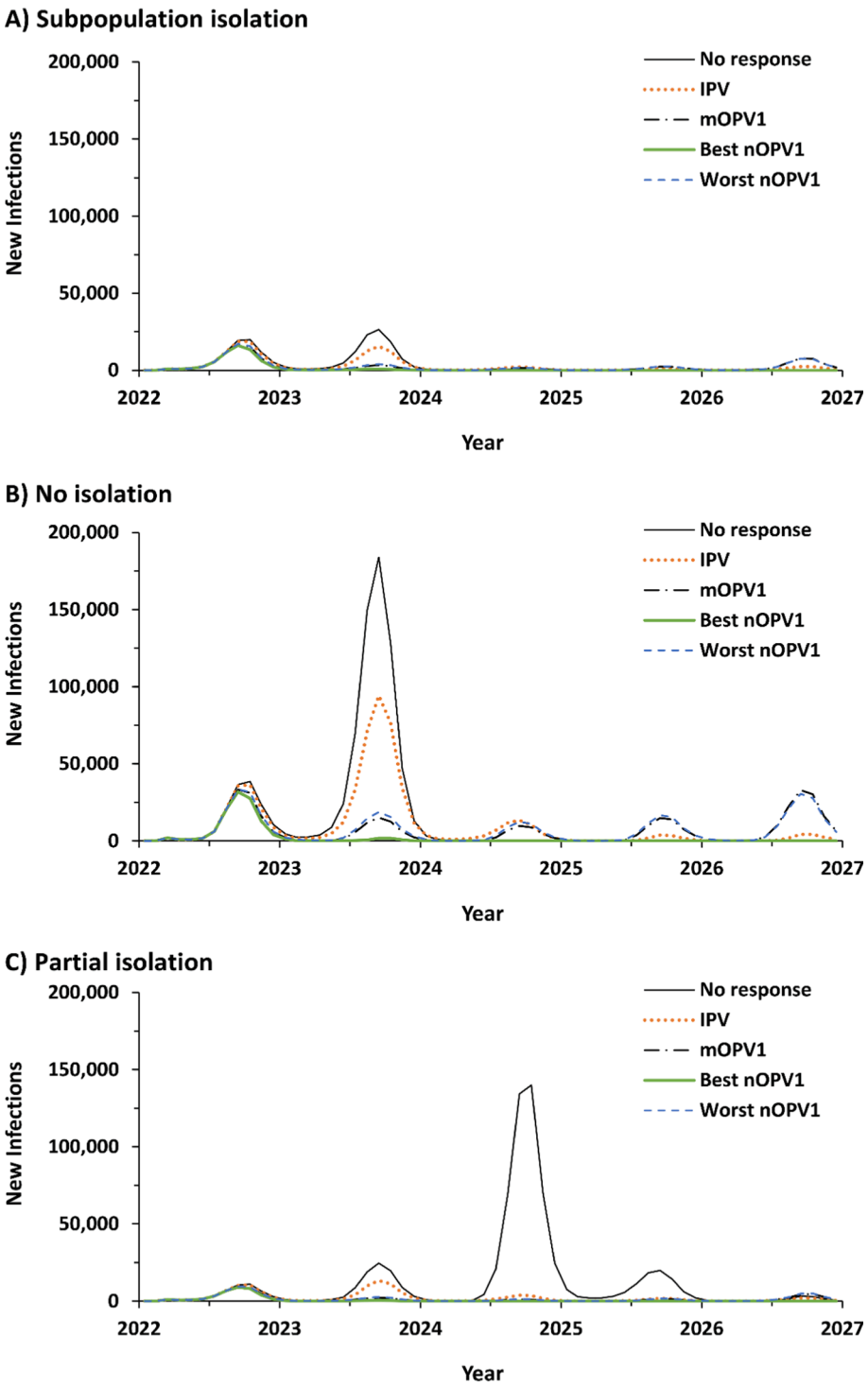

Fig. 2. Monthly expected new infections for a modeled hypothetical type 1 poliovirus outbreak resulting from importation identical to the 2022 New York State polio outbreak (except type 1 instead of type 2) and assuming the same number of doses of different polio vaccine options for outbreak response (or no response) for different mixing scenarios. A: Subpopulation isolation assumes that the under-vaccinated subpopulations remain isolated from the general subpopulations, but mix proportionately between themselves. B: No isolation assumes that all 4 subpopulations mix, with 95% of contacts coming from the two subpopulations of the same vaccination levels, while the remaining 5% of contacts come from both of the other two subpopulations. C: Partial isolation assumes that 95% of contacts come from each under-vaccinated subpopulation with itself, while the remaining 5% come only from the two general subpopulations. The results show that the use of any OPV1 formulation reduces the expected numbers of new infections, with hypothetical best nOPV1 providing the only option that ends transmission during the modeled time horizon.

experience of a WPV1 outbreak in 2013, which led to use of OPV for outbreak response when IPV did not appear sufficient to stop the WPV1 transmission [46,60–62]. Notably, following that outbreak, Israel reintroduced bOPV into its RI as part of a sequential IPV/OPV schedule [63], a practice that continues to date [64]. Restart of bOPV in Israel occurred after significant legal and ethical questions were raised and these eventually escalated to its Supreme Court [65,66]. Core issues in the discussions included the ethics of asking IPV-vaccinated children to

receive bOPV to help end the transmission of WPV1 in Israel with full awareness that this offered relatively little benefit to them since their receipt of IPV already protected them from paralysis. Importantly, Israel only recommended bOPV restart in the setting of a sequential IPV-OPV regimen, and Israel did not give OPV to individuals until and after they received IPV.

Although the US, UK, and Israel all maintain high coverage with IPV in RI, they differ with respect to their population sizes, heterogeneity in immunization coverage, mixing, seasonality, and other factors, including social and medicolegal structures. Our systematic review combined with epidemiological experience [6,13] demonstrates that multiple factors lead to different risks with respect to the potential for sustained transmission following an introduction of a poliovirus into IPV-only countries. Key characteristics include the transmission potential of the imported poliovirus into the specific population (e.g., type, strain, transmission dynamics, and other factors), and the level and nature of immunity prior to the importation.

The results of this analysis come with limitations related to our modeling choices. Most notably, we did not explore all possible undervaccinated communities in the US or other IPV-only countries, and we limited this analysis to assuming the same conditions and scale of intervention associated with the recent NYS outbreak, which included relatively low uptake of vaccines by unvaccinated individuals. We used an existing deterministic model for which this analysis includes the same limitations as previously discussed in detail [9]. Moreover, this analysis assumes bounding scenarios for effectiveness of nOPV in place of yet unknown potential future characteristics of nOPV1 and confirmed effects of nOPV2 when used on a large scale. In addition, we did not consider all possible conditions of a potential outbreak in NYS. We rely on modeling to demonstrate concepts and to inform decisions, but conditions in specific outbreaks will determine outcomes.

While IPV-only countries to date demonstrated that they will likely respond to polio outbreaks (and potentially to sufficient environmental signals of poliovirus transmission) with IPV, this analysis and some prior experience suggests that some countries may prefer using OPV for some outbreaks. For example, the outbreak community could view OPV as more acceptable due to its ease of delivery, and/or OPV could represents the only option for achieving sufficiently high coverage rapidly in the context of a circulating more virulent outbreak virus. However, compounding the risks of OPV use, we foresee substantial challenges that require careful consideration prior to OPV use in IPV-only countries, particularly since countries like the US ended all licensed use of OPV due to its risks [67]. Historically, VAPP risks from OPV use contributed substantial motivation for the development of the US Vaccine Injury Compensation Program [68]. In addition to licensed vaccine availability, concerns about the potential risks and uncertainties about the potential benefits may reduce the level of coverage and therefore outbreak response effectiveness. The acceptability of receiving OPV by the at-risk population will determine its ability to stop transmission, and low uptake could prove ineffective at stopping the outbreak virus. In spite of the current research use of OPV in the US for clinical trials related to the development of novel OPVs (e.g., ClinicalTrials.gov identifiers NCT04529538 and NCT04544787), uncertainty remains about whether these novel vaccines would gain public acceptance and receive licensure for outbreak response in the US. Achieving sufficiently high coverage to stop transmission of an outbreak poliovirus with any polio vaccine will ultimately depend on the acceptability of the vaccine to recipients and perceptions about the risk–benefit trade-offs for the specific outbreak. Recognizing that increasing population immunity prior to importations of polioviruses remains an opportunity for risk management, the US updated its vaccine recommendations in June 2023 to include a primary polio vaccination series with IPV for all U.S. adults aged $\geq$ 18 years who are known or suspected to be unvaccinated or incompletely vaccinated against polio [69].

Disclaimer

The views expressed are solely those of the authors and do not necessarily represent the official views of the US Centers for Disease Control and Prevention, Department of Health and Human Services.

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CRediT authorship contribution statement

Kimberly M. Thompson: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Dominika A. Kalkowska:** Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Sarah E. Kidd:** Investigation, Resources, Writing – review & editing. **Cara C. Burns:** Investigation, Resources, Writing – review & editing. **Kamran Badizadegan:** Conceptualization, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Kid Risk authors (KMT, DAK, KB) reports financial support was provided by Centers for Disease Control and Prevention. Kid Risk authors (KMT, DAK, KB) reports a relationship with Centers for Disease Control and Prevention that includes: funding grants.

Data availability

No new data were used for the research described in the article.

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References

[1] Link-Gelles R, Lutterloh E, Schnabel Ruppert P, et al. Public health response to a case of paralytic poliomyelitis in an unvaccinated person and detection of poliovirus in wastewater - New York, June-August 2022. MMWR Morb Mortal Wkly Rep 2022; 71(33):1065-1068 DOI: 10.15585/mmwr.mm7133e2.

[2] Klapsa D, Wilton T, Zealand A, et al. Sustained detection of type 2 poliovirus in London sewage between February and July, 2022, by enhanced environmental surveillance. Lancet 2022;400(10362):1531–8. https://doi.org/10.1016/S0140-6736(22)01804-9.

[3] Zuckerman NS, Bar-Or I, Sofer D, et al. Emergence of genetically linked vaccine-originated poliovirus type 2 in the absence of oral polio vaccine, Jerusalem, April to July 2022. Euro Surveill 2022;27(37):2200694. https://doi.org/10.2807/1560-7917.ES.2022.27.37.2200694.

[4] Pan American Health Organization. 2022. *Epidemiological Update Detection of poliovirus in wastewater: Considerations for the Region of the Americas 30 December 2022.* Regional Office for the Americas of the World Health Organization. (Accessed Jan 10, 2023). Available from: https://www.paho.org/en/documents/epidemiological-update-detection-poliovirus-wastewater.

[5] Global Polio Eradication Initiative. 2022. *Standard operating procedures: Responding to a poliovirus event or outbreak, Version 4.1.* World Health Organization. (Accessed Aug 2, 2023). Available from: https://polioeradication.org/wp-content/uploads/2022/09/Standard-Operating-Procedures-For-Responding-to-a-Poliovirus-Event-Or-Outbreak-20220905-V4-EN.pdf.

[6] Bandyopadhyay AS, Cavestany RL, Blake IM, et al. Use of inactivated poliovirus vaccine for poliovirus outbreak response. Lancet Infect Dis 2023. https://doi.org/10.1016/S1473-3099(23)00505-4.

[7] Thompson KM, Wallace GS, Tebbens RJ, et al. Trends in the risk of U.S. polio outbreaks and poliovirus vaccine availability for response. Public Health Rep 2012; 127(1):23–37. https://doi.org/10.1177/003335491212700104.

[8] Thompson KM, Pallansch MA, Duintjer Tebbens RJ, et al. Modeling population immunity to support efforts to end the transmission of live polioviruses. Risk Anal 2013;33(4):647–63. https://doi.org/10.1111/j.1539-6924.2012.01891.x.

[9] Thompson KM, Kalkowska DA, Routh JA, et al. Modeling poliovirus transmission and responses in New York State. J Infect Dis 2023:doi: 10.1093/infdis/jiad355 DOI: 10.1093/infdis/jiad355.

[10] New York City Department of Health and Mental Hygiene. 2022. *Polio.* New York City Department of Health and Mental Hygiene. (Accessed Jan 3, 2023). Available from: https://www.nyc.gov/site/doh/health/health-topics/poliomyelitis.page.

[11] New York State Department of Health. *Polio*. 2022. (Accessed 3 Jan). Available from: https://www.health.ny.gov/diseases/communicable/polio/.

[12] Ryerson AB, Lang D, Alazawi MA, et al. Wastewater testing and detection of poliovirus type 2 genetically linked to virus isolated from a paralytic polio case - New York, March 9-October 11, 2022. MMWR Morb Mortal Wkly Rep 2022;71 (44):1418–24. https://doi.org/10.15585/mmwr.mm7144e2.

[13] Estivariz CF, Kovacs SD, Mach O. Review of use of inactivated poliovirus vaccine in campaigns to control type 2 circulating vaccine derived poliovirus (cVDPV) outbreaks. Vaccine 2023;41(Suppl 1):A113–21. https://doi.org/10.1016/j.vaccine.2022.03.027.

[14] Jenkins PC, Modlin JF. Decision analysis in planning for a polio outbreak in the United States. Pediatrics 2006;118(2):611–8. https://doi.org/10.1542/peds.2005-2358.

[15] Thompson KM, Kalkowska DA, Badizadegan K. A health economic analysis for oral poliovirus vaccine to prevent COVID-19 in the United States. Risk Anal 2021;41(2): 376–86. https://doi.org/10.1111/risa.13614.

[16] Macklin GR, Peak C, Eisenhawer M, et al. Enabling accelerated vaccine roll-out for Public Health Emergencies of International Concern (PHEICs): Novel Oral Polio Vaccine type 2 (nOPV2) experience. Vaccine 2023;41 Suppl 1(Suppl 1):A122–7. https://doi.org/10.1016/j.vaccine.2022.02.050.

[17] Hill M, Bandyopadhyay AS, Pollard AJ. Emergence of vaccine-derived poliovirus in high-income settings in the absence of oral polio vaccine use. Lancet 2022;400 (10354):713–5. https://doi.org/10.1016/s0140-6736(22)01582-3.

[18] Duintjer Tebbens RJ, Pallansch MA, Kew OM, et al. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. Risk Anal 2006;26(6): 1471–505. https://doi.org/10.1111/j.1539-6924.2006.00827.x.

[19] World Health Organization. Polio vaccines: WHO position paper - June 2022. Wkly Epidemiol Rec 2022;97(25):277–300.

[20] Duintjer Tebbens RJ, Pallansch MA, Chumakov KM, et al. Expert review on poliovirus immunity and transmission. Risk Anal 2013;33(4):544–605. https://doi.org/10.1111/j.1539-6924.2012.01864.x.

[21] Duintjer Tebbens RJ, Pallansch MA, Chumakov KM, et al. Review and assessment of poliovirus immunity and transmission: synthesis of knowledge gaps and identification of research needs. Risk Anal 2013;33(4):606–46. https://doi.org/10.1111/risa.12031.

[22] Duintjer Tebbens RJ, Pallansch MA, Kim JH, et al. Oral poliovirus vaccine evolution and insights relevant to modeling the risks of circulating vaccine-derived polioviruses (cVDPVs). Risk Anal 2013;33(4):680–702. https://doi.org/10.1111/risa.12022.

[23] Global Polio Eradication Initiative. 2023. *GPEI Statement on cVDPV2 detections in Burundi and Democratic Republic of the Congo.* World Health Organization. (Accessed June 27, 2023). Available from: https://polioeradication.org/news-post/gpei-statement-on-cvdpv2-detections-in-burundi-and-democratic-republic-of-the-congo/.

[24] Yeh MT, Smith M, Carlyle S, et al. Genetic stabilization of attenuated oral vaccines against poliovirus types 1 and 3. Nature 2023. https://doi.org/10.1038/s41586-023-06212-3.

[25] Kalkowska DA, Wassilak SGF, Wiesen E, et al. Complexity of options related to restarting oral poliovirus vaccine (OPV) in national immunization programs after OPV cessation [version 1; peer review: 1 approved]. Gates Open Res 2023;7:55.

[26] Patriarca PA, Sutter RW, Oostvogel PM. Outbreaks of paralytic poliomyelitis, 1976–1995. J Infect Dis 1997;175(Suppl 1):S165–72. https://doi.org/10.1093/infdis/175.supplement_1.s165.

[27] Nathanson N, Kew OM. From emergence to eradication: the epidemiology of poliomyelitis deconstructed. Am J Epi 2010;172(11):1213–29.

[28] Duintjer Tebbens RJ, Pallansch MA, Kalkowska DA, et al. Characterizing poliovirus transmission and evolution: insights from modeling experiences with wild and vaccine-related polioviruses. Risk Anal 2013;33(4):703–49. https://doi.org/10.1111/risa.12044.

[29] Global Polio Eradication Initiative. 2023. *Circulating vaccine-derived poliovirus (as of 8 Aug 2023).* World Health Organization - Global Polio Eradication Initiative. (Accessed August 15, 2023). Available from: https://polioeradication.org/polio-today/polio-now/this-week/circulating-vaccine-derived-poliovirus/.

[30] Kalkowska DA, Badizadegan K, Thompson KM. Outbreak management strategies for cocirculation of multiple poliovirus types. Vaccine 2023. https://doi.org/10.1016/j.vaccine.2023.04.037.

[31] Kalkowska DA, Wassilak SGF, Wiesen E, et al. Coordinated global cessation of oral poliovirus vaccine use: Options and potential consequences. Risk Anal 2023. https://doi.org/10.1111/risa.14158.

[32] Al-Kassab-Cordova A, Napanga-Saldana O, Pena-Sanchez R, et al. Vaccine-derived polio in Peru after 32 years of elimination: reflections on the routine childhood immunisation coverages. Lancet Reg Health Am 2023;23:100532. https://doi.org/10.1016/j.lana.2023.100532.

[33] Thompson KM, Duintjer Tebbens RJ. Retrospective cost-effectiveness analyses for polio vaccination in the United States. Risk Anal 2006;26(6):1423–40. https://doi.org/10.1111/j.1539-6924.2006.00831.x.

[34] Thompson KM, Kalkowska DA, Badizadegan K. Oral polio vaccine stockpile modeling: insights from recent experience. Expert Rev Vaccines 2023;22(1): 813–25. https://doi.org/10.1080/14760584.2023.2263096.

[35] Global Polio Eradication Initiative. 2017. *Standard operating procedures: Responding to a poliovirus event or outbreak, Version 2.4 Part 1: General SOPs.* World Health Organization. (Accessed Aug 2, 2023). Available from: https://www.medbox.org/document/responding-to-a-poliovirus-event-or-outbreak-part-1-general-sops#GO.

[36] Global Polio Eradication Initiative. 2017. *Standard operating procedures: Responding to a poliovirus event or outbreak, Version 2.4 Part 2: Protocol for poliovirus type 2.* World Health Organization. (Accessed Aug 2, 2023). Available from: http://polioeradication.org/wp-content/uploads/2018/01/pol-sop-responding-polio-event-outbreak-part2-20180117.pdf.

[37] Global Polio Eradication Initiative. 2020. *Standard operating procedures: Responding to a poliovirus event or outbreak, Version 3.1.* World Health Organization. (Accessed Aug 2, 2023). Available from: https://apps.who.int/iris/handle/10665/331895.

[38] Global Polio Eradication Initiative. 2015. *Responding to a poliovirus outbreak: Standard operating procedures for a new polio outbreak in a polio-free country.* World Health Organization. (Accessed 15 March 2015). Available from: http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/1a.PolioOutbreakGuideline20150220.pdf.

[39] Global Polio Eradication Initiative. 2015. *Protocol for notification, risk assessment, and response following detection of poliovirus type 2 following globallycoordinated cessation of serotype 2-containing oral polio vaccine.* World Health Organization. (Accessed Aug 2, 2023). Available from: https://www3.paho.org/hq/dmdocuments/2015/Poliovirus-type2-response-protocol-eng.pdf.

[40] Thompson KM, Kalkowska DA, Review of poliovirus modeling performed from,. to 2019 to support global polio eradication. Expert Rev Vaccines 2000;2020:1–25. https://doi.org/10.1080/14760584.2020.1791093.

[41] Global Polio Eradication Initiative. 2023. *nOPV2: Clinical Development and Evidence Summary.* World Health Organization - Global Polio Eradication Initiative. (Accessed 4 July 2023). Available from: https://polioeradication.org/wp-content/uploads/2023/05/EN_nOPV2-Clinical-Development-Summary_Apr-2023.pdf.

[42] Wilkinson AL, Zaman K, Hoque M, et al. Immunogenicity of novel oral poliovirus vaccine type 2 administered concomitantly with bivalent oral poliovirus vaccine: an open-label, non-inferiority, randomised, controlled trial. Lancet Infect Dis 2023; 23(9):1062–71. https://doi.org/10.1016/S1473-3099(23)00139-1.

[43] Thompson KM. Polio endgame complexity: updating expectations for nOPV2. Lancet Infect Dis 2023;23(9):992–4. https://doi.org/10.1016/S1473-3099(23)00133-0.

[44] Wagner BG, Earn DJ. Circulating vaccine derived polio viruses and their impact on global polio eradication. Bull Math Biol 2008;70(1):253–80. https://doi.org/10.1007/s11538-007-9255-4.

[45] Duintjer Tebbens RJ, Pallansch MA, Cochi SL, et al. An economic analysis of poliovirus risk management policy options for 2013–2052. BMC Infect Dis 2015; 15:389. https://doi.org/10.1186/s12879-015-1112-8.

[46] Kalkowska DA, Duintjer Tebbens RJ, Grotto I, et al. Modeling options to manage type 1 wild poliovirus imported into Israel in 2013. J Infect Dis 2015;211(11): 1800–12. https://doi.org/10.1093/infdis/jiu674.

[47] Duintjer Tebbens RJ, Pallansch MA, Wassilak SG, et al. Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. BMC Infect Dis 2016:16:137. https://doi.org/10.1186/s12879-016-1465-7.

[48] Denes A, Szekely L. Global dynamics of a mathematical model for the possible re-emergence of polio. Math Biosci 2017;293:64–74. https://doi.org/10.1016/j.mbs.2017.08.010.

[49] Duintjer Tebbens RJ, Thompson KM. Costs and benefits of including inactivated in addition to oral poliovirus vaccine in outbreak response after cessation of oral poliovirus vaccine use. MDM Policy Pract, 2017. 2, 2381468317697002 DOI: 10.1177/2381468317697002.

[50] McCarthy KA, Chabot-Couture G, Famulare M, et al. The risk of type 2 oral polio vaccine use in post-cessation outbreak response. BMC Med 2017;15(1):175. https://doi.org/10.1186/s12916-017-0937-y.

[51] Thompson KM, Duintjer Tebbens RJ. Lessons from globally coordinated cessation of serotype 2 oral poliovirus vaccine for the remaining serotypes. J Infect Dis 2017; 216(suppl_1):S168–S175. https://doi.org/10.1093/infdis/jix128.

[52] Duintjer Tebbens RJ, Thompson KM. Polio endgame risks and the possibility of restarting the use of oral poliovirus vaccine. Expert Rev Vaccines 2018;17(8): 739–51. https://doi.org/10.1080/14760584.2018.1506333.

[53] Kalkowska DA, Pallansch MA, Wilkinson A, et al. Updated characterization of outbreak response strategies for 2019–2029: Impacts of using a novel type 2 oral poliovirus vaccine strain. Risk Anal 2021;41(2):329–48. https://doi.org/10.1111/risa.13622.

[54] Thompson KM, Kalkowska DA, Badizadegan K. Hypothetical emergence of poliovirus in 2020: part 2. exploration of the potential role of vaccines in control and eradication. Expert Rev Vaccines 2021;20(4):449–60. https://doi.org/10.1080/14760584.2021.1891889.

[55] Thompson KM, Kalkowska DA, Badizadegan K. Health economic analysis of vaccine options for the polio eradication endgame: 2022–2036. Expert Rev Vaccines 2022;21(11):1667–74. https://doi.org/10.1080/14760584.2022.2128108.

[56] Kalkowska DA, Wiesen E, Wassilak SGF, et al. Worst-case scenarios: Modeling uncontrolled type 2 polio transmission. Risk Anal 2023. https://doi.org/10.1111/risa.14159.

[57] UK Health Security Agency. 2023. *Polio immunisation response in London 2022 to 2023: information for healthcare practitioners.* GOV.UK. (Accessed Aug 11, 2023). Available from: https://www.gov.uk/government/publications/inactivated-polio-vaccine-ipv-booster-information-for-healthcare-practitioners/polio-immunisation-response-in-london-2022-to-2023-information-for-healthcare-practitioners.

[58] Kalkowska DA, Badizadegan K, Routh JA, et al. Modeling undetected poliovirus circulation following the 2022 outbreak in the United States. Expert Rev Vaccines 2024;23(1):186–95. https://doi.org/10.1080/14760584.2023.2299401.

[59] Shulman LM, Manor Y, Hindiyeh M, et al. Molecular characterization of polio from environmental samples: ISSP, the Israeli sewage surveillance protocol. Methods Mol Biol 2016;1387:55–107. https://doi.org/10.1007/978-1-4939-3292-4_5.
[60] Pan American Health Organization. 2013. *WHO sends mission to Israel following detection of wild poliovirus in sewage.* Regional Office for the Americas of the World Health Organization. (Accessed Aug 11, 2023). Available from: https://www3.paho.org/hq/index.php?option=com_content&view=article&id=8857:2013-who-sends-mission-israel-following-detection-wild-poliovirus-sewage&Itemid=0&lang=en#gsc.tab=0.
[61] Yaari R, Kaliner E, Grotto I, et al. Modeling the spread of polio in an IPV-vaccinated population: lessons learned from the 2013 silent outbreak in southern Israel. BMC Med 2016;14(1):95. https://doi.org/10.1186/s12916-016-0637-z.
[62] Anis E, Kopel E, Singer SR, et al., *Insidious reintroduction of wild poliovirus into Israel, 2013.* Euro Surveill 2013; 18(38) DOI: 10.2807/1560-7917.es2013.18.38.20586.
[63] Kopel E, Kaliner E, Grotto I. Lessons from a public health emergency - importation of wild poliovirus to Israel. N Engl J Med 2014;371(11):981–3. https://doi.org/10.1056/NEJMp1406250.
[64] Chorin O, Markovich MP, Avramovich E, et al. Oral and fecal polio vaccine excretion following bOPV vaccination among Israeli infants. Vaccine 2023;41(28):4144–50. https://doi.org/10.1016/j.vaccine.2023.05.036.
[65] Eyal NK. The right for autonomy, the duty of disclosure and public health considerations – The 2013 polio crisis in Israel as a case study. Pace Law Rev 2016;36(3):908–69. https://doi.org/10.58948/2331-3528.1930.
[66] Kamin-Friedman S. Would it be legally justified to impose vaccination in Israel? Examining the issue in light of the 2013 detection of polio in Israeli sewage. Isr J Health Policy Res 2017;6(1):58. https://doi.org/10.1186/s13584-017-0182-z.
[67] Prevots DR, Burr RK, Sutter RW, et al. Poliomyelitis prevention in the United States. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2000;49(RR-5):1–22.
[68] Thompson KM, Orenstein WA, Hinman AR. Performance of the United States Vaccine Injury Compensation Program (VICP): 1988–2019. Vaccine 2020;38(9):2136–43. https://doi.org/10.1016/j.vaccine.2020.01.042.
[69] Kidd S, Clark T, Routh J, et al., *Use of inactivated polio vaccine among U.S. adults: updated recommendations of the advisory committee on immunization practices - United States, 2023.* MMWR Morb Mortal Wkly Rep 2023; 72(49):1327-1330 DOI: 10.15585/mmwr.mm7249a3.