Vaccine xxx (xxxx) xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Outbreak management strategies for cocirculation of multiple poliovirus types

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ARTICLE INFO

Article history:
Available online xxxx

Keywords:
Polio
Eradication
Dynamic modeling
Oral poliovirus vaccine
Outbreak response

ABSTRACT

Prior modeling studies showed that current outbreak management strategies are unlikely to stop outbreaks caused by type 1 wild polioviruses (WPV1) or circulating vaccine-derived polioviruses (cVDPVs) in many areas, and suggested increased risks of outbreaks with cocirculation of more than one type of poliovirus. The surge of type 2 poliovirus transmission that began in 2019 and continues to date, in conjunction with decreases in preventive supplemental immunization activities (SIAs) for poliovirus types 1 and 3, has led to the emergence of several countries with cocirculation of more than one type of poliovirus. Response to these emerging cocirculation events is theoretically straightforward, but the different formulations, types, and inventories of oral poliovirus vaccines (OPVs) available for outbreak response present challenging practical questions. In order to demonstrate the implications of using different vaccine options and outbreak campaign strategies, we applied a transmission model to a hypothetical population with conditions similar to populations currently experiencing outbreaks of cVDPVs of both types 1 and 2. Our results suggest prevention of the largest number of paralytic cases occurs when using (1) trivalent OPV (tOPV) (or coadministering OPV formulations for all three types) until one poliovirus outbreak type dies out, followed by (2) using a type-specific OPV until the remaining poliovirus outbreak type also dies out. Using tOPV first offers a lower overall expected cost, but this option may be limited by the willingness to expose populations to type 2 Sabin OPV strains. For strategies that use type 2 novel OPV (nOPV2) concurrently administered with bivalent OPV (bOPV, containing types 1 and 3 OPV) emerges as a leading option, but questions remain about feasibility, logistics, type-specific take rates, and coadministration costs.

1. Introduction

Paralytic poliomyelitis (polio for short) is a clinical manifestation of neurological involvement by one of the three known poliovirus types. Cocirculation of more than one poliovirus type represented the norm prior to the introduction of polio vaccines, but global success in polio eradication efforts led to substantial decreases in cases and less cocirculation as high immunization coverage led to die out of indigenous strains of wild polioviruses for types 2 and 3 [1]. Nonetheless, in populations with low polio immunization coverage, cocirculation still can occur, with the identification of more than one poliovirus type in a community raising challenging questions about vaccine choices and vaccination strategies. Immunological protection for polio requires the induction of immunity for each of the three types of polioviruses (types 1, 2, and 3). Historically, routine immunization (RI) programs relied on delivering multiple doses of trivalent formulations of the oral poliovirus vaccine (OPV) and/or the inactivated poliovirus vaccine (IPV) to ensure adequate "take" (i.e., successful induction of immunity) for each of the three poliovirus types [2,3]. IPV is supplied only in trivalent formulations that contain all three poliovirus types, and take rates for each of the three poliovirus types are roughly similar and increase in a dose-dependent fashion with high immunity to all poliovirus types after 2 doses [4]. However, as an injected vaccine, IPV use generally remains limited to the coverage levels achieved in RI.

OPV formulations and use, in contrast, are much more complicated. Trivalent OPV (tOPV, containing types 1, 2, and 3) shows different effectiveness for each dose given in RI, with type 2 historically more likely to take first in immunologically naïve individuals for Sabin tOPV, but relatively high take rates for all three types observed after 3 tOPV doses in most settings [2,3]. With the addition of supplemental immunization activities (SIAs) to global polio eradication efforts, some countries delivered OPV to

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https://doi.org/10.1016/j.vaccine.2023.04.037
0264-410X/

under-vaccinated populations either in preventive SIAs (pSIAs) or in outbreak response SIAs (oSIAs). In contrast to the inactivated virus in IPV, which induces humoral immunity in the absence of viral replication, OPV is a live attenuated virus vaccine given orally with multiple distinct characteristics. OPV viruses replicate in the oropharynx and gastrointestinal tract to induce mucosal and humoral immunity in recipients [5]. Fecal excretion and secondary spread of the replicating viruses can induce or boost immunity secondarily in contacts of OPV recipients, resulting in population immunity benefits that extend beyond the vaccinated individual. In spite of these benefits, OPV comes with small risks of vaccine-associated paralytic polio (VAPP) and the development of vaccine-derived polioviruses (VDPVs) [6,7]. VDPVs pose a particular threat when OPV use occurs in populations with low immunization coverage, because the OPV-related viruses can evolve, recombine, lose their attenuating mutations (“revert”), and become circulating VDPVs (cVDPVs) that essentially behave like wild polioviruses (WPVs) [6,8]. IPV, which costs more to produce and to administer via injection, does not cause VAPP, does not replicate to produce VDPVs, and does not induce measurable mucosal immunity or result in secondary spread or associated-population immunity benefits [5,9].

Until recently, national immunization programs only used trivalent polio vaccines (IPV and tOPV). However, following the global certification of eradication of indigenous transmission of type 2 wild polioviruses (WPV2) in 2015 [10], the Global Polio Eradication Initiative (GPEI) coordinated the end of all use of type 2 OPV (OPV2) in RI and pSIAs by May 2016 (“OPV2 cessation”). OPV2 cessation meant that all tOPV-using countries switched from tOPV to bivalent OPV (bOPV, containing types 1 and 3) [11]. The GPEI also developed a stockpile of type 2 monovalent OPV (mOPV2) to support emergency response use in oSIAs in the event of detections of type 2 outbreaks after OPV2 cessation, and supported the introduction of at least one dose of IPV in RI in all countries [11]. Since 2016, numerous outbreaks of type 2 cVDPVs (cVDPV2s) occurred and led to increasing mOPV2 use for outbreak response. This motivated the accelerated development of a genetically modified novel OPV2 (nOPV2) designed to reduce the probability of reversion to neurovirulence phenotype [12], and its widespread use [13] under an Emergency Use Listing (EUL) [14].

Over the last 2 decades, numerous prior modeling studies provided insights into different aspects of the global polio eradication successes and setbacks, including various risk, decision and economic analyses (see [15] for a review of modeling studies published between 2000 and 2019). Our work has historically occupied a unique position among the modeling groups because our studies include transmission dynamics of all poliovirus types (including asymptomatic transmission) in all age groups and all immunity states in the entire population [16]. In addition, we routinely integrate financial and health outcome analyses with our modeling polio transmission dynamics and risk management strategies [17,18].

As polio eradication efforts changed over time with the introduction of various mOPV and bOPV regimens, our modeling studies explored cocirculation of poliovirus types 1 and 3 and showed that multivalent vaccines generally outperform separate monovalent vaccines in oSIAs [19–22]. This conclusion reflected our focus on population immunity to transmission as the key public health metric in polio eradication [23], instead of outcomes for individual vaccine recipients. Specifically, using Sabin tOPV leads to a small reduction in vaccine effectiveness for types 1 and 3 for a single SIA in individuals seeing a specific type of OPV for the first time. However, this type-specific reduction in immune response in immunologically naïve individuals is completely offset at the population level, because of the increased opportunity for boosting of immunity in those with some prior OPV-exposure throughout the population [16,19–22]. For example, while using tOPV may mean that individuals seeing OPV for the first time will primarily take to type 2, those with pre-existing immunity to type 2 will take to types 1 and/or 3, and so on. In contrast, the use of a monovalent type 1 OPV (mOPV1) only allows for immunity induction or boosting to type 1, without any opportunity for that SIA round to increase population immunity for other poliovirus types. Numerous modeling studies emphasized that the key to achieving global eradication is to achieve high immunization coverage with vaccine for all three types of polioviruses and to recognize that under-vaccinated populations remain at risk for all types such that the use of type-selective OPVs (i.e., mOPVs or bOPV) opens immunity gaps for the OPV types not used [15,16,19–29].

Similar to the pre-OPV2 cessation modeling, studies performed after OPV2 cessation suggested that tOPV would always outperform monovalent OPV2 (mOPV2) or IPV for oSIAs [15,16,24–29]. Studies showed essentially no difference for type 2 oSIA outcomes when using tOPV vs. mOPV2 (all else equal), but large differences for poliovirus types 1 or 3, which represents a major deficiency in the context of existing cocirculation [15,16,24–29]. The development of nOPV2 focused on reducing the risk of reversion to neurovirulence [12], which necessarily resulted in a vaccine with reduced replicative fitness [30] and reduced fecal shedding relative to Sabin OPV2 [31]. Outbreak response modeling with nOPV2 showed a potentially larger difference for type 2 oSIA outcomes when considering Sabin OPV2 vs. nOPV2, with tOPV or mOPV2 slightly better than nOPV2 due to reduced secondary transmission of nOPV2 (because of its reduced shedding and/or replicative fitness relative to Sabin) [28,29].

Since 2019, some countries (e.g., Pakistan and Afghanistan [32]) managed cocirculation of WPV1 and cVDPV2 viruses using tOPV in oSIAs. However, the GPEI plans now emphasize the use of nOPV2 for type 2 oSIAs as the vaccine of choice [33]. In the context of this recommendation, hesitancy to use vaccines that contain Sabin OPV2 (i.e., tOPV and mOPV2) for oSIAs leads to questions about vaccine choices and immunization strategies, even for outbreaks with cocirculating types of polioviruses.

Some prior modeling that explored the differences between immunization strategies and policies for modeled hypothetical populations [16,23,34–39] supported discussions related to the development of standard operating procedures (SOPs) for outbreak response and overall strategies [40–43]. In this study, we apply our poliovirus transmission model to a hypothetical population with conditions similar to populations currently experiencing outbreaks of both types 1 and 2 circulating vaccine-derived polioviruses (cVDPVs) (e.g., the Democratic Republic of the Congo and Mozambique). By highlighting what is required to achieve success in a modeled hypothetical population, these analyses could inform policy deliberations and decisions by demonstrating the implications of using different vaccine formulations and vaccination strategies.

2. Methods

We use an existing deterministic, differential equation-based (DEB) poliovirus transmission and OPV evolution model [3,8,27,44–48] and apply generic inputs typical for lower income, developing countries, similar to prior modeling of hypothetical populations [16,23,34–39]. The model divides the population into eight immunity states (i.e., fully susceptible, maternally immune, and six partially immune states resulting from different numbers of live poliovirus infections and/or successful IPV vaccination) [3,44,45]. We model waning of immunity as a five-stage process, infection as a six-stage process (i.e., two latent and four infectious stages) for both fecal–oral and oropharyngeal transmission, and OPV evolution as a 20-stage process, starting with stage 0 for fully

attenuated Sabin strains and progressing to stage 19 for fully reverted strains that behave like homotypic WPV [3,8,44,45]. We assume that only fully susceptible individuals (including infants born with maternal immunity losing protective maternal antibody levels) can develop paralytic polio following live poliovirus infection, but any individuals (from all immunity states) can get re-infected and participate in poliovirus transmission (asymptomatically and to varying degrees).

We use hypothetical population of 10 million people, which we divide into general and under-vaccinated subpopulations of 9 and 1 million people, respectively. The general population represents the fraction of the total population with high vaccination, while the under-vaccinated subpopulation represents communities with low immunization coverage (see Table 1). We further subdivide each subpopulation into four age groups (i.e., 0–2 months, 3–59 months, 5–14 years, and $\geq$ 15 years). We use preferential mixing between subpopulations and broad mixing age groups (i.e., 0–59 months, 5–14 years, and $\geq$ 15 years), and the death rate equal to birth rate to maintain constant population size for this hypothetical population. We assume WPV1 R_0 = 10, which provides the basis for characterization of all of the transmission dynamics for all 3 types due to fixed assumptions for relative R_0 values for all other live polioviruses for this hypothetical population in our model structure (e.g., R_0 for cVDPV2 = 9) [16,23,34–39]. We also assume moderate seasonal variations and low contribution of oropharyngeal transmission to overall poliovirus transmission in both subpopulations, consistent with our assumptions for lower-income hypothetical populations [16,23,34–39]. The model simulates poliovirus elimination in a subpopulation as soon as the effective (i.e., infectiousness-weighted) prevalence of given poliovirus type infection decreases below a threshold of 5 per million people, at which point the model sets the force of infection for that poliovirus type to 0. The top of Table 1 shows population- and transmission-related model input assumptions.

We use per-dose tOPV, bOPV, mOPV, and IPV take rate values previously assumed for developing country settings [2,46]. Given limited published data about nOPV2 performance when used in oSIAs [49], we explore the bounds of the potential nOPV2 trajectories [27–29,48,50–53]. Specifically, we consider the two scenarios: "best nOPV2," which assumes the same effectiveness as mOPV2, no reversion to neurovirulence despite transmissibility, and no VAPP; and "worst nOPV2," which assumes the 90% of the effectiveness of mOPV2, prior assumptions for reduced reversion to neurovirulence [27], further reduced by 10%, and VAPP occurring at a rate 10% lower than the VAPP rate of mOPV2 [51–53]. For potential concurrent use of bOPV and nOPV2 (i.e., bOPV + nOPV2), based on our limited understanding of preliminary field trial results considering coadministration of bOPV + nOPV2 (ClinicalTrials.gov Identifier: NCT04579510), we assumed a lower take rate for the type 2 component (i.e., nOPV2 take rate equal to 68% of the Sabin OPV2 take rate), but no effect for types 1 or 3 (see Table 1).

To model outbreak management strategies for cocirculation of multiple poliovirus types, we build an immunity profile consistent with the populations in which cVDPV1 and cVDPV2 transmission has recently emerged and continued. Specifically, we simulate the concept that our hypothetical population historically began with three tOPV doses in RI, then we introduce a birth dose in the general population, and we add one IPV dose shortly before a switch from tOPV in RI to bOPV to simulate OPV2 cessation (see middle of Table 1 and supplemental Figure A1 and for details). We also introduce between two and five SIAs per year (see middle of Table 1 and supplemental Figure A2 and for details).

We define a reference case (RC), in which the model eliminates WPV1 and WPV2 transmission using OPV, and then allows the population immunity to evolve as a function of the RI and SIAs. The modeled cessation of Sabin OPV2 following the shift from tOPV to bOPV, which occurs with insufficient population immunity in the modeled population, leads to OPV evolution and emergence of cVDPV2 transmission. In addition, due to the decline in the number of bOPV SIAs, a cVDPV1 also emerges.

Table 2 summarizes the modeled outbreak response strategies. Given potential delays in detection and longer response times in countries with cocirculation in 2022 (e.g., Democratic Republic of the Congo, Mozambique [54]), we assume outbreak response begins 135 days after the first cVDPV1 case occurs in the model. For any oSIA that uses nOPV2, given uncertainty about its field properties, we separately consider either "best nOPV2" or "worst nOPV2" for the nOPV2 oSIA rounds. We focus on four major strategies: (1) "*all at once*," (2) "*sequential elimination*," (3) "*concurrent administration*," and (4) "*alternate administration*." First, the "*all at once*" strategy assumes monthly tOPV oSIA rounds until elimination of cVDPV2, followed by monthly bOPV oSIA rounds until elimination of cVDPV1 transmission. Second, the "*sequential elimination*" focuses on elimination of one type at a time, and therefore follows two possible sub-strategies: (2a) "cVDPV1 first," which assumes monthly bOPV oSIA rounds until elimination of cVDPV1 transmission, followed by monthly mOPV2 or nOPV2 oSIA rounds until elimination of cVDPV2 transmission; or (2b) "cVDPV2 first," which assumes monthly mOPV2 or nOPV2 oSIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV oSIA rounds until elimination of cVDPV1 transmission. Third, the "*concurrent administration*" assumes simultaneous monthly administration of bOPV and nOPV2 (i.e., bOPV + nOPV2) oSIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV oSIA rounds until elimination of cVDPV1 transmission. Finally, the "*alternate administration*" strategy assumes the vaccine type used for each oSIA round alternates monthly until elimination of cVDPV2 transmission, followed by monthly bOPV oSIA rounds until elimination of cVDPV1 transmission. Here, we also consider two sub-strategies by choosing which vaccine use occurs first (i.e., (4a) "bOPV first" or (4b) "OPV2 first").

We use a three-year analytical time horizon for the model and we perform all simulations using JAVA™ programming language in the integrated development environment Eclipse™. Recognizing that different attributes of oSIAs may represent important considerations for immunization program leaders, we report the numbers of rounds of each type of vaccine for each strategy. Given our focus on identifying the minimum number of rounds for each scenario required to stop transmission of both types of cocirculating polioviruses and our assumed fixed timing between oSIA rounds, we recognize that the time required to complete the outbreak responses, and thus the time to achieve elimination of both cVDPV1 and cVDPV2, varies by strategy. We report the total elimination time since the beginning of analytical time horizon (T0) as a way to facilitate comparisons for this attribute. In addition, we recognize that the costs of the different strategies will vary due to the different numbers of rounds and doses of vaccines required. We use previously developed cost input assumptions [55] to estimate the costs of the oSIAs for each scenario, with the cost input assumptions required for this analysis shown in the bottom of Table 1. Consistent with our focus on outbreak response, we use a model time horizon of 3 years.

3. Results

As shown in Fig. 1, the prospective model time horizon begins at T0 (year 0) with already established cocirculation of cVDPV1 and cVDPV2 representing the current global situation with cocirculating polioviruses in some countries. Detection of the first modeled paralytic case of cVDPV1 occurs in the under-vaccinated subpopulation within the third month of transmission (indicated

Table 1
Model inputs.

Model input	Estimate	Notes
Transmission model inputs		
Number of subpopulations	2	Under-vaccinated and general
Population size	10,000,000	
- under-vaccinated subpopulation	1,000,000	
- general population	9,000,000	
Initial age distribution		Mixing age groups of 0–4, 5–14, and $\geq$ 15 years
- 0–2 months	0.01	
- 3–59 months	0.15	
- 5–14 years	0.25	
- $\geq$ 15 years	0.59	
Proportion of contacts reserved for individuals within		Extent of preferential mixing
- the same subpopulation (p_{within})	0.90	
- the same mixing age group (κ)	0.35	
Birth rate (b) and death rate (μ)	0.02	
Average basic reproductive number (R_0) (PV1; PV2; PV3)	10; 9; 7.5	
Proportional change in R_0 due to seasonality (α)	0.15	
Day of seasonal peak in $R_{0(pd)}$	0 (January 1)	
Proportion of transmissions via oropharyngeal route (p^{oro})	0.3	High R_0 developing country value
Transmission threshold	5/1,000,000	
Paralysis-to-infection ratio for fully susceptible individuals		Upper and lower bounds of PV evolution process by poliovirus type
- infected with FRPV (PV1; PV2; PV3)	0.005; 0.0005; 0.001	
- infected with OPV (PV1; PV2; PV3)	7.4×0^{-8}; 6.2×0^{-7}; 1.3×10^{-6}	
Time inputs		
- run-up start	T0 – 72.00	
- R_0 seasonality start	T0 – 47.00	
- die out first allowed	T0 – 47.00	
- OPV RI start	T0 – 42.00	
- birth dose start	T0 – 32.00	
- SIA start	T0 – 26.00	
- IPV RI start	T0 – 6.00	
- tOPV-bOPV switch	T0 – 5.75	
- RI coverage increase stop	T0 – 2.00	
- end of analytical tie horizon	T0 + 3.00	
Vaccination related inputs		
Per-dose take rate (tr) (PV1; PV2; PV3)		Developing country values
- tOPV	0.45; 0.70; 0.35	
- bOPV	0.54; 0.00; 0.54	
- mOPV	0.60; 0.70; 0.60	
- nOPV	NA; 0.70; NA	
- bOPV + nOPV2	0.54; 0.48; 0.54	
- IPV	0.63; 0.63; 0.63	
Relative nOPV2 take rate (reltr)		
- best	1.00	
- worst	0.90	
Routine immunization coverage (subpopulation; general)		
- birth dose	0.00; 0.40	
- 3 dose	0.25; 0.80	
SIA intensity (under-vaccinated; general)		
- true coverage (TC)	0.25; 0.80	
- repeated missed probability (P_{RM})	0.84; 0.70	
Cost inputs		
Vaccine cost per dose	0.150	US$2019
Waste factor	1.333	
Non-vaccine cost per dose	0.948	US$2019
Coadministration factor	1.5	

Abbreviations: PV(1,2,3), poliovirus(type); bOPV, bivalent OPV; FRPV, fully-reverted poliovirus (stage 19 of PV evolution process, including both wild PV and circulating vaccine-derived PV); IPV, inactivated poliovirus vaccine; mOPV, monovalent OPV; nOPV, novel OPV; OPV, oral poliovirus vaccine (stage 0 of PV evolution process); RI, routine immunization; SIA, supplementary immunization activity; tOPV, trivalent OPV; US$2019, 2019 United States dollars

by a black diamond tick mark in Fig. 1). This is an important landmark, because we assume outbreak response begins 135 days after the first cVDPV1 case (see Methods).

For context, the RC explores the transmission dynamics assuming no outbreak response. Fig. 1 shows the daily incidence of paralytic cases (left) and cumulative number of cases (right) by type of cVDPV and for each subpopulation as a function of time since T0. Note that in this model the daily "incidence" can be a fraction because it simply represents virus transmission rate multiplied by the infection to paralysis ratio for the respective virus, unlike the actual observations of any cases that occur stochastically.

Without any outbreak response, the modeled paralytic incidence reaches 624 expected cases during the prospective 3-year model time horizon (482 cVDPV1 cases and 142 cVDPV2 cases,

Table 2
Outbreak management strategies.

Option	Vaccines	Description
1. All at once	tOPV then bOPV	Monthly tOPV SIA rounds until elimination of cVDPV2, followed by monthly bOPV SIA rounds until elimination of cVDPV1 transmission
2. Sequential elimination		
a) cVDPV1 first	i) bOPV then mOPV2 ii) bOPV then best nOPV2 iii) bOPV then worst nOPV2	Monthly bOPV SIA rounds until elimination of cVDPV1 transmission, followed by monthly mOPV2 or best nOPV2 or worst nOPV2 SIA rounds until elimination of cVDPV2 transmission
b) cVDPV2 first	i) mOPV2 then bOPV ii) best nOPV2 then bOPV iii) worst nOPV2 then bOPV	Monthly mOPV2 or best nOPV2 or worst nOPV2 SIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV SIA rounds until elimination of cVDPV1 transmission
3. Concurrent administration	i) bOPV + best nOPV2 ii) bOPV + worst nOPV2	Simultaneous monthly administration of bOPV and best nOPV2 or worst nOPV2 SIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV SIA rounds until elimination of cVDPV1 transmission, using low or high effectiveness assumptions
4. Alternate administration		
a) bOPV first	i) bOPV then mOPV2 ii) bOPV then best nOPV2 iii) bOPV then worst nOPV2	Alternate monthly bOPV and mOPV2 or best nOPV2 or worst nOPV2 SIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV SIA rounds until elimination of cVDPV1 transmission
b) OPV2 first	i) mOPV2 the bOPV ii) best nOPV2 then bOPV iii) worst nOPV2 then bOPV	Alternate monthly mOPV2 or best nOPV2 or worst nOPV2 and bOPV SIA rounds until elimination of cVDPV2 transmission, followed by monthly bOPV SIA rounds until elimination of cVDPV1 transmission

Abbreviations: bOPV, bivalent OPV; cVDPV(1,2), circulating vaccine-derived poliovirus (type 1 or 2); mOPV2, type 2 monovalent OPV; nOPV, type 2 novel OPV; OPV, oral poliovirus vaccine; SIA, supplementary immunization activity; tOPV, trivalent OPV.

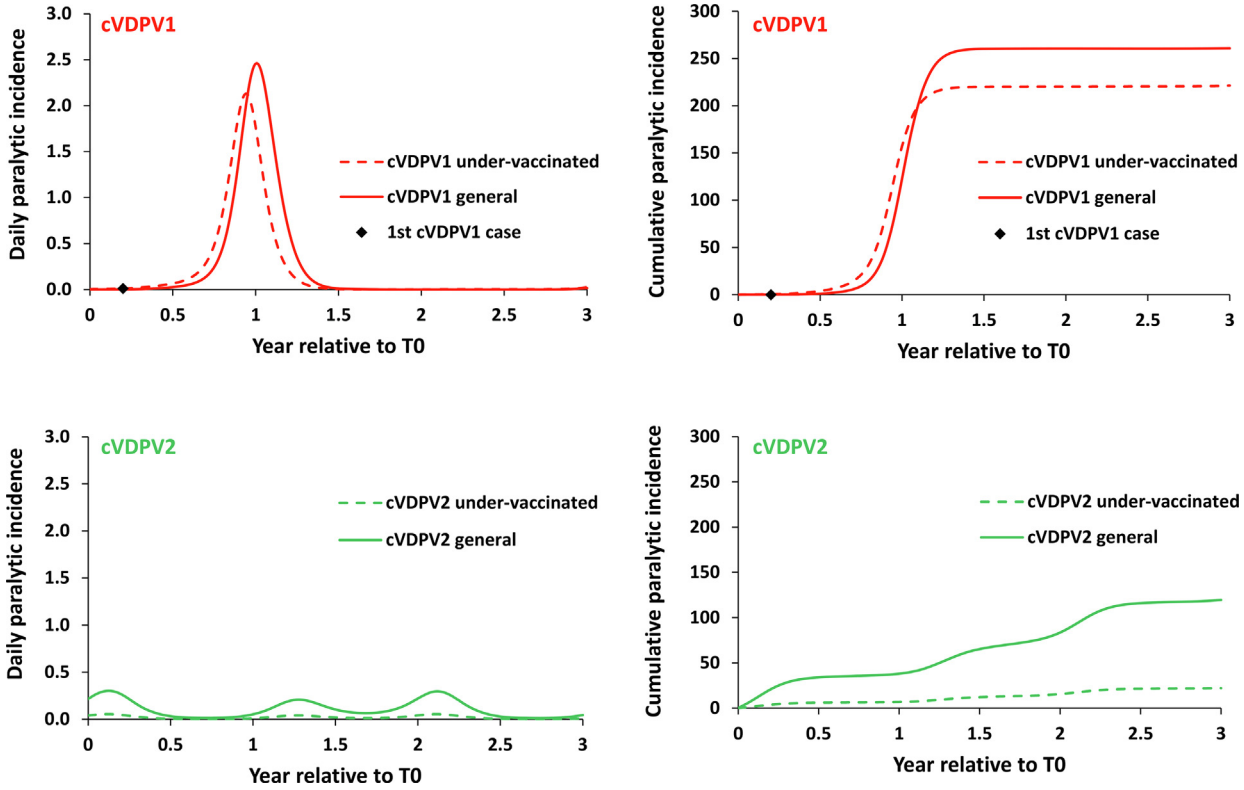

Fig. 1. Reference case (RC) paralytic incidence in the absence of outbreak response SIAs. For this hypothetical model, we use time in years since T0 instead of actual calendar dates on the x-axis.

see also the first row of results in Table 3). In the RC, the transmission of both viruses continues throughout the time horizon. Thus, although the curves shown in Fig. 1 suggest a substantial drop in the cVDPV1 transmission, without oSIAs to increase population immunity to type 1, after the cVDPV1 burns through the accumulated susceptible population, the transmission does not die out. Given enough time, the low level of transmission will periodically increase to cause outbreaks due to the accumulation of new susceptible individuals in the population, and the cVDPV1 re-establishes endemic transmission (as already occurred for cVDPV2 prior to T0). The shapes of the curves for the two types in Fig. 1 demonstrate the different nature of endemic transmission and an

Table 3
Performance of SIA schedules for outbreak management strategies.

Option	Vaccines	Number of monthly rounds	Minimum number of rounds to achieve elimination		Number of cases by cVDPV type and total			Elimination time (days after T0)		Total cases prevented	Intervention costs (US$2019, millions)
			bOPV	OPV2	1	2	Total	cVDPV1	cVDPV2		
Reference case	No OPV	NA	NA	NA	482	142	624	–	–	0	0
1. All at once	tOPV then bOPV	12	9	3	167	41	208	994	578	416	9.37
2. Sequential elimination											
a) cVDPV1 first	i) bOPV then mOPV2	18	14	4	152	88	240	881	960	384	14.05
	ii) bOPV then best nOPV2	17	14	3	152	87	239	881	887	385	13.27
	iii) bOPV then worst nOPV2	19	14	5	152	88	240	881	961	384	14.84
b) cVDPV2 first	i) mOPV2 then bOPV	7	4	3	301	41	342	710	578	282	5.47
	ii) best nOPV2 then bOPV	7	4	3	301	41	342	710	400	282	5.47
	iii) worst nOPV2 then bOPV	8	4	4	361	41	402	631	537	222	6.25
3. Concurrent administration	i) bOPV + best nOPV2	14	14	3	152	41	193	881	486	431	12.31
	ii) bOPV + worst nOPV2	14	14	5	152	42	194	881	605	431	13.22
4. Alternate administration											
a) bOPV first	i) bOPV then mOPV2	11	8	3	221	42	263	901	550	361	8.59
	ii) bOPV then best nOPV2	11	9	2	208	42	250	728	491	374	8.59
	iii) bOPV then worst nOPV2	12	8	4	225	42	267	944	567	357	9.37
b) OPV2 first	i) mOPV2 then bOPV	10	7	3	247	41	288	680	550	335	7.81
	ii) best nOPV2 then bOPV	10	8	2	226	41	267	685	474	356	7.81
	iii) worst nOPV2 then bOPV	10	6	4	254	42	296	737	547	329	7.81

Abbreviations: bOPV, bivalent OPV; cVDPV(1,2), circulating vaccine-derived poliovirus (type 1 or 2); mOPV2, type 2 monovalent OPV; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine; SIA, supplementary immunization activity; tOPV, trivalent OPV; US$2019, 2019 United States Dollars;

epidemic or outbreak following (re)introduction into a population that previously stopped transmission.

For the different outbreak response strategies listed in Table 2, Table 3 shows the minimum number of rounds needed to achieve die out of both types of cVDPVs in the outbreak population as well as the cases by type and total expected for each strategy. Depending on the strategy and the OPV2 vaccine used, the model can eliminate the transmission of both viruses while preventing between 222 and 431 paralytic cases. The most successful strategies aim to target both viruses at the same time (i.e., "*all at once*" with tOPV or "*concurrent administration*" with bOPV and nOPV2 used for as long as both viruses are in cocirculation). The "*concurrent administration*" strategies prevent 431 expected cases, requiring vaccine doses to perform the equivalent of 17 SIA rounds, when using bOPV and best nOPV2, or 19 SIA rounds when using bOPV and worst nOPV2.

The more efficient strategy uses doses of tOPV and then switches to bOPV after eliminating cVDPV2, which requires 12 SIA rounds and prevents the total of 416 paralytic cases. However, if countries prefer not to use tOPV due to the Sabin OPV2 component, then, if they can concurrently administer bOPV and nOPV2 and achieve the same coverage with both vaccines, then they can prevent the same number of cases with the same number of rounds at a higher cost, if nOPV2 behaves like the assumed best nOPV2. If nOPV2 behaves like the assumed worst nOPV2, then this strategy implies fewer cases prevented, more rounds, and higher costs (see Table 3).

Notably, the results for concurrent administration implicitly ignore any logistical challenges that could lead to delays and/or additional costs or impact coverage achieved for either type (i.e., the results implicitly assume that all children vaccinated in the oSIAs receive both doses). In addition, we highlight uncertainty about the cost implications of concurrent administration, for which we assumed that delivering two doses of OPV containing vaccines at the same oSIA contact would cost less than two separate contacts due to cost-savings for some oSIAs activities (e.g., social mobilization), but more than delivering only one vaccine. In addition, concurrent administration of bOPV and nOPV2 falls outside of GPEI policies for nOPV2 use [56].

Although for this analysis we focused on comparison of strategies assuming no limitations on the availability of vaccine supplies, the "*sequential elimination*" strategy may prove useful when facing shortages of a specific vaccine type. However, focusing on elimination of only one virus at a time comes with a burden of paralytic cases caused by the virus that was left unmanaged and may change the number of oSIA rounds required in the long run due to the transmission dynamics. For example, in our hypothetical situation, focusing on "*cVDPV2 first*" and delaying bOPV response allows for cVDPV1 transmission to burn through the majority of the low-immunity population. In contrast, focusing on "*cVDPV1 first*" prevents more cases, but requires more effort to stop the outbreak due to the higher level of transmission, and ultimately leads to the highest number of minimum rounds required to stop transmission of both types.

Finally, if the simultaneous administration of bOPV and nOPV2 is not possible, those immunization programs that want to make progress on both cVDPV types without using tOPV might prefer the "*alternate administration*" strategy. Table 3 shows the relative expected increase in costs, time, and cases associated with such national preferences.

4. Discussion

The polio endgame strategy continues to increase in complexity due to ongoing transmission of type 2 polioviruses, new emergences of type 1 polioviruses, and the development of novel vaccines, including nOPV2 currently in use under emergency use listing by the World Health Organization. As such, the cocirculation of poliovirus types 1 and 2 in several areas in the context of different national and regional preferences for specific vaccines and limitations in the availability of vaccines represent substantial management challenges. The current dynamics of transmission of multiple types of polioviruses globally demonstrates the limited ability of IPV use in RI to substantially contribute to preventing poliovirus transmission in most countries. Thus, despite substantial investments by all countries to introduce IPV into their RI programs, poliovirus transmission continues in many countries and globally 23 years after the original global target of achieving polio eradication by the year 2000. In addition, as the complexity increases, so do the cumulative costs of polio eradication [17].

The logistical challenges of responding to cocirculation include multiple issues. We highlighted issues related to the management of vaccine supplies for outbreaks. The development of global stockpiles of OPV2-containing vaccines (i.e., mOPV2, tOPV, and nOPV2) continues to face challenges due to mismatches between global forecasting, vaccine production and filling decisions, and demand from countries for oSIAs. In addition, the relatively poor performance and low coverage achieved by oSIAs in some countries [27,28,46,47], may imply higher vaccine demands for oSIAs globally due to longer, larger, and more-widely spread transmission.

The most important management insight gained from this modeling exercise comes from recognizing that saving the largest number of children from paralytic polio in the context of cocirculating viruses requires responding with immunization activities that include coverage for all three virus types at the onset (Table 3). This may include tOPV or concurrent administration of nOPV2 and bOPV. In order to operationalize this approach, however, national preferences and/or administrative obstacles must be first removed. Reluctance to use Sabin OPV2s presents a substantial obstacle that is rooted in the perceived notion that the risk of seeding new outbreaks is higher than the risk of continued circulating viruses, which runs counter to both modeling experience and global policy recommendations [57,58]. Although coadministration of nOPV2 with other vaccines is not contraindicated under EUL [14], the GPEI operational guidelines prohibit delivery of nOPV2 with bOPV [56,59] presents another substantial obstacle. In addition, data on the immunogenicity and take rate of nOPV2 when coadministered with bOPV are not currently available. Anecdotally, preliminary results from a clinical trial conducted in 2021 (ClinicalTrials.gov Identifier: NCT04579510) suggest that bOPV interferes with immunogenicity of nOPV2 when administered at the same time (A. Wilkinson, personal communication), but the final results of this trial are not available publicly.

From a logistical perspective, maximizing the number of lives saved may not always be achievable. Specifically, the monetary or personnel costs of such interventions may exceed the available resources, or the interventions may be not feasible from a healthcare delivery perspective. In our modeling exercise, the sequential elimination strategy of cVDPV2 first, followed by cVDPV1 second, required the least number of total oSIA rounds and lowest cost of all modeled interventions (Table 3). However, this strategy resulted in nearly twice as many paralytic cases compared to the *all at once* or *concurrent* elimination strategies discussed above.

In order to visualize some of these tradeoffs, we present Fig. 2, in which we compare cases prevented and intervention costs for all modeled scenarios. Fig. 2 clearly demonstrates that sequential elimination with bOPV first followed by any monovalent OPV2 (red circles) are neither cost preferred nor lead to the largest number of cases prevented. As such, these strategies appear the least favorable. In contrast, sequential elimination with mOPV2 or best nOPV2 first (blue circles) represent the lowest cost strategies that

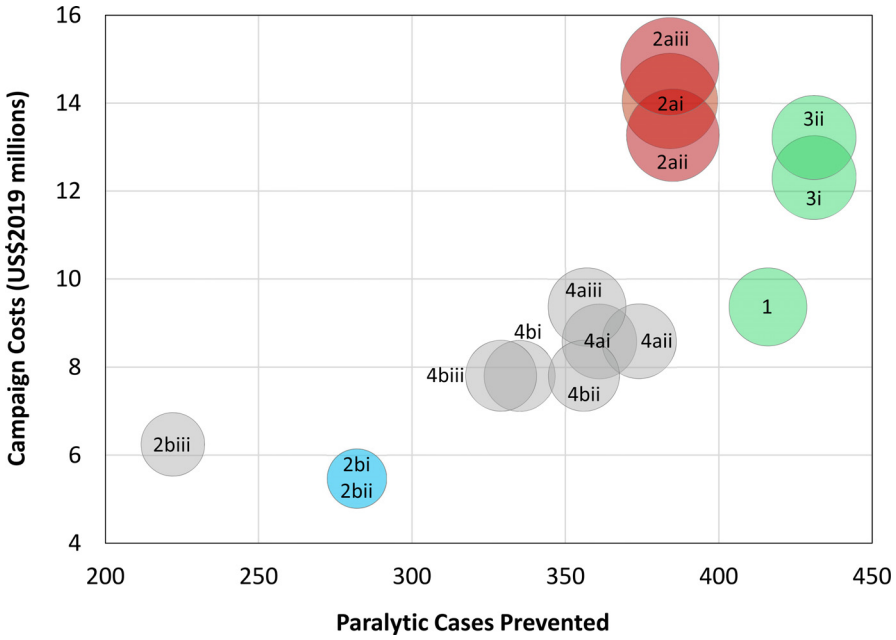

Fig. 2. Demonstration of tradeoff between various outbreak management strategies (see Table 2 for descriptions of the scenarios that correspond to the circle labels and Table 3 for cases and numbers of rounds) based on the number of paralytic cases prevented (x-axis), immunization campaign costs (y-axis) and the number of monthly campaign rounds needed (area of circles) to control the outbreak of cocirculating types 1 and 2. Strategies highlighted in green save the most patients from paralytic disease, those in blue are the most cost-effective in terms of paralytic cases prevented per dollars spent and the number of rounds needed to control the outbreak, and the strategies highlighted in red are the least cost-effective both in terms of money spent and campaign rounds conducted per paralytic case prevented. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

result in elimination of circulating viruses with the least number of campaign rounds, albeit at the cost of increased paralytic cases. The largest numbers of paralytic cases are prevented when campaigns target eliminating both types of cVDPVs at the same time (green circles). The lowest cost strategy that targets both cVDPV types at once is to use tOPV, but other scenarios with concurrent administration of nOPV2 with bOPV achieve the similar clinical objective, albeit at higher cost.

We use modeling to gain policy insight, and fully acknowledge the limitations of our poliovirus modeling with limitations discussed in detail elsewhere [46,47]. In addition, any hypothetical modeling also comes with the limitations associated with the simplifying assumptions made that affect its behavior [16,23,34–39]. For this analysis, we use a hypothetical population to systematically explore vaccination strategies using scenarios that only vary the oSIA vaccine strategy. As a hypothetical population model, the outcomes of the scenarios may differ from the real-life situations in countries with reported cocirculation, because population immunity profiles are specific to national vaccination and poliovirus transmission histories. In addition, we use a simplified, deterministic approach to characterize the poliovirus transmission die out, although in reality the die out of a poliovirus in small populations can occur by chance, even with low vaccination coverage [60]. Due to uncertainty about the actual costs, clinical feasibility, and effectiveness of campaigns with coadministration of nOPV2 and other polio vaccines, future policy analyses will need to use any available improved data. Finally, with our focus on a hypothetical population for this analysis, we implicitly leave efforts to explore the implications of different oSIA vaccine choices and strategies for specific countries or other geographic regions with cocirculating viruses and the collective impacts of strategies at the global level to future modeling studies.

In spite of its limitations, our hypothetical model provides insights about the management of current outbreaks of types 1 and 2 polioviruses. Despite their risks, in the context of cocirculating outbreaks, Sabin OPVs are a favorable choice. In contrast, sequential approaches that prioritize type 1 appear unfavorable, while sequential strategies targeting cVDPV2 first are highly cost effective and result in most rapid elimination of circulating viruses for a situation similar to the hypothetical population we modeled. Coadministration of nOPV2 with bOPV is also a favorable strategy based on our modeling studies, but better estimates of the costs, feasibility, and effectiveness of such campaign depend on additional field and clinical data.

Funding

The authors acknowledge support for this publication under Cooperative Agreement Number NU2RGH001915-02-00 funded by the Centers for Disease Control and Prevention. The views expressed are solely those of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or Department of Health and Human Services.

CRediT authorship contribution statement

Dominika A. Kalkowska: Conceptualization, Methodology, Formal analysis, Visualization, Writing – original draft. **Kamran Badizadegan:** Conceptualization, Methodology, Formal analysis, Visualization, Writing – original draft. **Kimberly M. Thompson:** Conceptualization, Visualization, Supervision, Writing – original draft, Funding acquisition.

Data availability

All of the data that the authors can share is available in the public domain and appropriate citations are provided.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors thank John Paul Bigouette, Omotayo Bolu, Frank Mahoney, Steven Wassilak, and Eric Wiesen for helpful discussions.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2023.04.037.

References

[1] Badizadegan K, Kalkowska DA, Thompson KM. Polio by the numbers-A global perspective. J Infect Dis 2022;226:1309–18.
[2] Thompson KM, Pallansch MA, Duintjer Tebbens RJ, Wassilak SG, Kim JH, Cochi SL. Preeradication vaccine policy options for poliovirus infection and disease control. Risk Anal 2013;33:516–43.
[3] Duintjer Tebbens RJ, Pallansch MA, Chumakov KM, et al. Expert review on poliovirus immunity and transmission. Risk Anal 2013;33:544–605.
[4] Grassly NC. Immunogenicity and effectiveness of routine immunization with 1 or 2 doses of inactivated poliovirus vaccine: systematic review and meta-analysis. J Infect Dis 2014;210(Suppl 1):S439–46.
[5] Connor RI, Brickley EB, Wieland-Alter WF, et al. Mucosal immunity to poliovirus. Mucosal Immunol 2022;15:1–9.
[6] 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;26:1471–505.
[7] Kew OM, Morris-Glasgow V, Landaverde M, et al. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus. Science 2002;296:356–9.
[8] 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;33:680–702.
[9] Thompson KM, Duintjer Tebbens RJ. Current polio global eradication and control policy options: perspectives from modeling and prerequisites for oral poliovirus vaccine cessation. Expert Rev Vaccines 2012;11:449–59.
[10] World Health Organization. 14th Meeting of the Global Commission for Certification of Poliomyelitis Eradication (GCC), Bali, Indonesia, 20-21 September, 2015 Summary of findings, decisions and recommendations. Available at: http://polioeradication.org/wp-content/uploads/2016/07/1Report.pdf. Accessed Jul 22 2021.
[11] Hampton LM, Farrell M, Ramirez-Gonzalez A, et al. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - Worldwide, 2016. MMWR 2016;65:934–8.
[12] Macklin G, 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 Vaccine 2023 Apr 6;41 Suppl 1:A122-A127. doi: 10.1016/j.vaccine.2022.02.050. Epub 2022 Mar 17.
[13] Harutyunyan V, Quddus A, Pallansch M, et al. Global oral poliovirus vaccine stockpile management as an essential preparedness and response mechanism for type 2 poliovirus outbreaks following global oral poliovirus vaccine type 2 withdrawal. Vaccine 2023;41(Suppl 1):A70–8. https://doi.org/10.1016/j.vaccine.2022.02.058.
[14] World Health Organization. Recommendation for an emergency use listing (EUL) of novel oral polio vaccien type 2 (nOPV2 Submitted by PT Biofarma (Persero) Available at: https://extranet.who.int/pqweb/sites/default/files/documents/nOPV2_EUL_recommendation.pdf. Accessed Jan 24 2023.
[15] Thompson KM, Kalkowska DA. Review of poliovirus modeling performed from 2000–2019 to support global polio eradication. Expert Rev Vaccines 2020;19:661–86.
[16] Thompson KM, Duintjer Tebbens RJ. Lessons from the polio endgame: Overcoming the failure to vaccinate and the role of subpopulations in maintaining transmission. J Infect Dis 2017;216:S176–82.
[17] Thompson KM, Kalkowska DA. An updated economic analysis of the Global Polio Eradication Initiative. Risk Anal 2021;41:393–406.
[18] Thompson KM, Kalkowska DA, Badizadegan K. Polio health economics: assessing the benefits and costs of polio, non-polio, and integrated activities of the Global Polio Eradication Initiative. Gates Open Res 2022;6:5.
[19] Duintjer Tebbens RJ, Kalkowska DA, Wassilak SG, Pallansch MA, Cochi SL, Thompson KM. The potential impact of expanding target age groups for polio immunization campaigns. BMC Infect Dis 2014;14:45.
[20] Kalkowska DA, Duintjer Tebbens RJ, Thompson KM. Modeling strategies to increase population immunity and prevent poliovirus transmission in 2 high-risk areas in northern India. J Infect Dis 2014;210(Suppl 1):S398–411.
[21] Kalkowska DA, Duintjer Tebbens RJ, Thompson KM. Modeling strategies to increase population immunity and prevent poliovirus transmission in the high-risk area of northwest Nigeria. J Infect Dis 2014;210(Suppl 1):S412–23.
[22] Thompson KM, Duintjer Tebbens RJ. The differential impact of oral poliovirus vaccine formulation choices on serotype-specific population immunity to poliovirus transmission. BMC Infect Dis 2015;15:376.
[23] Thompson KM, Pallansch MA, Tebbens RJ, Wassilak SG, Cochi SL. Modeling population immunity to support efforts to end the transmission of live polioviruses. Risk Anal 2013;33:647–63.
[24] Duintjer Tebbens RJ, Pallansch MA, Wassilak SGF, Cochi SL, Thompson KM. Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. BMC Infecti Dis 2016;16:137.
[25] Duintjer Tebbens RJ, Thompson KM. Poliovirus vaccination during the endgame: Insights from integrated modeling. Expert Rev Vaccines 2017;16:577–86.
[26] Kalkowska DA, Pallansch MA, Cochi SL, Thompson KM. Updated characterization of poliovirus transmission in Pakistan and Afghanistan and the impacts of different outbreak response options. J Infect Dis 2021;224:1529–38.
[27] Kalkowska DA, Pallansch MA, Wilkinson A, et al. Updated characterization of poliovirus outbreak response strategies for 2019–2029: Impacts of the use of novel OPV2 strains. Risk Anal 2021;41:329–48.
[28] Kalkowska DA, Pallansch MA, Wassilak SGF, Cochi SL, Thompson KM. Serotype 2 oral poliovirus vaccine (OPV2) choices and the consequences of delaying outbreak response. Vaccine. 2023;41(Suppl 1):A136–41. https://doi.org/10.1016/j.vaccine.2021.04.061.
[29] Kalkowska DA, Wassilak SGF, Pallansch MA, et al. Outbreak response strategies with type 2-containing oral poliovirus vaccines. Vaccine 2023;41(Suppl 1):A142–52. https://doi.org/10.1016/j.vaccine.2022.10.060.
[30] Konopka-Anstadt JL, Campagnoli R, Vincent A, et al. Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization. npj Vaccines 2020;5:26.
[31] Gast C, Bandyopadhyay AS, Sáez-Llorens X, et al. Fecal Shedding of 2 Novel Live Attenuated Oral Poliovirus Type 2 Vaccine Candidates by Healthy Infants Administered Bivalent Oral Poliovirus Vaccine/Inactivated Poliovirus Vaccine: 2 Randomized Clinical Trials. J Infect Dis 2022;226:852–61.
[32] Kalkowska DA, Badizadegan K, Thompson KM. Modeling scenarios for ending poliovirus transmission in Pakistan and Afghanistan. Risk Anal 2023 Apr;43 (4):660-676. doi: 10.1111/risa.13983. Epub 2022 Jun 23.
[33] WHO. Standard Operating Procedures - Responding to a Poliovirus Event or Outbreak - Version 4. Geneva, Switzerland: World Health Organization; 2022.
[34] Duintjer Tebbens RJ, Pallansch MA, Kew OM, Cáceres VM, Sutter RW, Thompson KM. A dynamic model of poliomyelitis outbreaks: learning from the past to help inform the future. Am J Epidemiol 2005;162:358–72.
[35] Thompson KM, Duintjer Tebbens RJ, Pallansch MA. Evaluation of response scenarios to potential polio outbreaks using mathematical models. Risk Anal 2006;26:1541–56.
[36] Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SGF, Thompson KM. Modeling undetected live poliovirus circulation after apparent interruption of transmission: Implications for surveillance and vaccination. BMC Infect Dis 2015;15:66.
[37] Thompson KM, Duintjer Tebbens RJ. Modeling the dynamics of oral poliovirus vaccine cessation. J Infect Dis 2014;210(Suppl 1):S475–84.
[38] Duintjer Tebbens RJ, Thompson KM. Modeling the potential role of inactivated poliovirus vaccine to manage the risks of oral poliovirus vaccine cessation. J Infect Dis 2014;210(Suppl 1):S485–97.
[39] Kalkowska DA, Duintjer Tebbens RJ, Thompson KM. Another look at silent circulation of poliovirus in small populations. Infect Dis Model 2018;3:107–17.
[40] World Health Organization Global Polio Eradication Initiative. Standard operating procedures: Responding to a poliovirus event or outbreak: Part 1: General SOPs. Available at: https://s3.amazonaws.com/gpei-tk/reference_links/en/GPEI_SOPs.pdf. Accessed April 20 2016.
[41] World Health Organization Global Polio Eradication Initiative. Standard operating procedures: Responding to a poliovirus event or outbreak: Part 2: Protocol for poliovirus type 2. Available at: http://polioeradication.org/wp-content/uploads/2018/01/pol-sop-responding-polio-event-outbreak-part2-20180117.pdf. Accessed August 20 2020.
[42] World Health Organization Global Polio Eradication Initiative. Standard operating procedures: Responding to a poliovirus event or outbreak: Version 3, January 2019. Available at: http://polioeradication.org/wp-content/uploads/2016/07/sop-polio-outbreak-response-version-20193101.pdf. Accessed August 20 2020.
[43] World Health Organization Global Polio Eradication Initiative. Standard operating procedures: Responding to a poliovirus event or outbreak: Version 3.1, March 2020. Available at: http://polioeradication.org/wp-content/uploads/2020/04/POL-SOP-V3.1-20200424.pdf. Accessed August 20 2020.
[44] 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;33:606–46.
[45] Duintjer Tebbens RJ, Pallansch MA, Kalkowska DA, Wassilak SGF, Cochi SL, Thompson KM. Characterizing poliovirus transmission and evolution: insights

from modeling experiences with wild and vaccine-related polioviruses. Risk Anal 2013;33:703–49.
[46] Kalkowska DA, Wassilak SGF, Cochi SL, Pallansch MA, Thompson KM. Global transmission of live polioviruses: Updated integrated dynamic modeling of the polio endgame. Risk Anal 2021;41:248–65.
[47] Kalkowska DA, Pallansch MA, Cochi SL, Kovacs SD, Wassilak SGF, Thompson KM. Updated characterization of post-OPV cessation risks: Lessons from 2019 serotype 2 outbreaks and implications for the probability of OPV restart. Risk Anal 2021;41:320–8.
[48] Kalkowska DA, Voorman A, Pallansch MA, et al. The impact of disruptions caused by the COVID-19 pandemic on global polio eradication. Vaccine. 2023;41(Suppl 1):A12–8. https://doi.org/10.1016/j.vaccine.2021.04.026.
[49] Mirzoev A, Macklin GR, Zhang Y, et al. Assessment of serological responses following vaccination campaigns with type 2 novel oral polio vaccine: a population-based study in Tajikistan in 2021. Lancet Glob Health 2022;10:e1807–14.
[50] Thompson KM, Kalkowska DA, Badizadegan K. No role for reintroducing OPV into the United States with respect to controlling COVID-19 [Response to the letter to the editor by Chumakov et al]. Risk Anal 2021;41:389–92.
[51] Thompson KM, Kalkowsa DA, Badizadegan K. Looking back at prospective modeling of outbreak response strategies for managing global type 2 oral poliovirus vaccine (OPV2) cessation. Front Public Health 2023;11:1098419. https://doi.org/10.3389/fpubh.2023.
[52] Kalkowska DA, Wassilak SGF, Wiesen E, et al. Coordinated global cessation of oral poliovirus vaccine use: Options and potential consequences. Risk Anal 2023. In press.
[53] Kalkowska DA, Wassilak SGF, Wiesen E, et al. Worst-case scenarios: Modeling uncontrolled type 2 polio transmission. In review.
[54] Global Polio Eradication Initiative. Polio Now - This Week. Available at: https://polioeradication.org/polio-today/polio-now/this-week/. Accessed 19 Jan 2023.
[55] Thompson KM, Kalkowska DA. Potential future use, costs, and value of poliovirus vaccines. Risk Anal 2021;41:349–63.
[56] World Health Organization Global Polio Eradication Initiative. Interim guidance on the use of novel oral polio vaccine type 2 (nOPV2) for the response to type 2 circulating vaccine-derived poliovirus (cVDPV2) during the initial use period (Addendum to the standard operating procedures for response to a poliovirus event or outbreak, version 3.1). Available at: https://polioeradication.org/wp-content/uploads/2020/11/EN-interim-Guidance-on-the-use-of-nOPV2-during-the-initial-use-period-Oct2020.pdf. Accessed Nov 7 2022.
[57] World Health Organization. Meeting of the Strategic Advisory Group of Experts on immunization, 22–24 March 2021: conclusions and recommendations. Wkly Epidemiol Rec 2021;96:197–216.
[58] World Health Organization. Meeting of the Strategic Advisory Group of Experts on immunization, October 2021: conclusions and recommendations. Wkly Epidemiol Rec 2021;96:613–32.
[59] World Health Organization Global Polio Eradication Initiative. Novel oral polio vaccine (nOPV2) management, monitoring, removal and disposal (in 50-dose vials with VVM type 2), Technical guidance. Available at: https://polioeradication.org/wp-content/uploads/2022/10/nOPV2-vaccine-handling.pdf. Accessed Nov 7 2022.
[60] Duintjer Tebbens RJ, Kalkowska DA, Thompson KM. Global certification of wild poliovirus eradication: insights from modelling hard-to-reach subpopulations and confidence about the absence of transmission. BMJ Open 2019;9:e023938.