Check for updates

DOI: 10.1111/risa.14159

ORIGINAL ARTICLE

Worst-case scenarios: Modeling uncontrolled type 2 polio transmission

Dominika A. Kalkowska[1] | **Eric Wiesen**[2] | **Steven G. F. Wassilak**[2] | **Cara C. Burns**[3] | **Mark A. Pallansch**[4] | **Kamran Badizadegan**[1] | **Kimberly M. Thompson**[1]

[1]Kid Risk, Inc., Orlando, Florida, USA

[2]Global Immunization Division, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[3]Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[4]National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Correspondence
Kimberly Thompson, Kid Risk, Inc., 7512 Dr. Phillips Blvd. #50-523, Orlando, FL 32819, USA.
Email: kimt@kidrisk.org

Funding information
Centers for Disease Control and Prevention, Grant/Award Number: NU2RGH001915-02-00

Abstract

In May 2016, the Global Polio Eradication Initiative (GPEI) coordinated the cessation of all use of type 2 oral poliovirus vaccine (OPV2), except for emergency outbreak response. Since then, paralytic polio cases caused by type 2 vaccine-derived polioviruses now exceed 3,000 cases reported by 39 countries. In 2022 (as of April 25, 2023), 20 countries reported detection of cases and nine other countries reported environmental surveillance detection, but no reported cases. Recent development of a genetically modified novel type 2 OPV (nOPV2) may help curb the generation of neurovirulent vaccine-derived strains; its use since 2021 under Emergency Use Listing is limited to outbreak response activities. Prior modeling studies showed that the expected trajectory for global type 2 viruses does not appear headed toward eradication, even with the best possible properties of nOPV2 assuming current outbreak response performance. Continued persistence of type 2 poliovirus transmission exposes the world to the risks of potentially high-consequence events such as the importation of virus into high-transmission areas of India or Bangladesh. Building on prior polio endgame modeling and assuming current national and GPEI outbreak response performance, we show no probability of successfully eradicating type 2 polioviruses in the near term regardless of vaccine choice. We also demonstrate the possible worst-case scenarios could result in rapid expansion of paralytic cases and preclude the goal of permanently ending all cases of poliomyelitis in the foreseeable future. Avoiding such catastrophic scenarios will depend on the development of strategies that raise population immunity to type 2 polioviruses.

KEYWORDS
dynamic modeling, eradication, interdependent risks, oral poliovirus vaccine, polio

1 | INTRODUCTION

Although the use of live, attenuated oral poliovirus vaccine (OPV) enabled nearly all countries to stop the transmission of wild polioviruses (WPVs), OPV use comes with risks of vaccine-associated paralytic polio (VAPP) and vaccine-derived polioviruses (VDPVs) (Duintjer Tebbens et al., 2006). Consequently, since the early 2000s, coordinated cessation of all use of OPV after successful WPV eradication has been a key component of strategic planning for the polio endgame (Global Polio Eradication Initiative, 2013, 2019, 2020, 2021; World Health Assembly, 2008; World Health Organization, 2010).

In May 2016, the Global Polio Eradication Initiative (GPEI) coordinated the cessation of all use of type 2 OPV (OPV2), except for emergency outbreak response (Hampton et al., 2016). Prior to OPV2 cessation, the GPEI developed extensive OPV2 cessation risk management plans, which included standard operating procedures (SOPs) for outbreak response and the creation of a stockpile of type 2 monovalent OPV (mOPV2). OPV2 cessation planning assumed an understanding of the risks associated with waning population immunity to type 2 polioviruses and the increasing risk of growth and expansion of vaccine-derived type 2 strains, which motivated the development of SOPs for outbreak response and the introduction of at least one dose of

 © 2023 Society for Risk Analysis.

inactivated poliovirus vaccine (IPV) into all national immunization programs (Global Polio Eradication Initiative, 2016). Prior modeling recognized the possibility of needing to restart OPV2 in routine immunization (RI) for adequate control in the event that outbreak response efforts did not succeed (Duintjer Tebbens et al., 2015; Duintjer Tebbens, Pallansch, et al., 2016).

Despite the planning efforts, since May 2016 over 3000 paralytic polio cases caused by type 2 circulating VDPVs (cVDPV2s) have been reported by 39 countries in different parts of the world (as of April 25, 2023) (Global Polio Eradication Initiative, 2023a; Thompson, 2022b). In 2022 alone, 20 countries reported a total of 673 cases and nine additional countries reported environmental surveillance detections without cases (as of April 25, 2023) (Global Polio Eradication Initiative, 2023a). To curb the emergence of neurovirulent vaccine-derived strains, the GPEI partners supported the accelerated development of novel OPV2 (nOPV2), which is designed to be more genetically stable than Sabin OPV2 (mOPV2). Since 2021, many countries used nOPV2 under World Health Organization (WHO) Emergency Use Listing (Macklin et al., 2023) to respond to cVDPV2 outbreaks. With more than 500 million nOPV2 doses deployed to date (Rachlin et al., 2022), the data on the performance of nOPV2 in the field (e.g., effectiveness, potential to revert) remain preliminary (Martin et al., 2022) and the vaccine is yet to receive a full license. A summary of studies published by June of 2022 (Global Polio Eradication Initiative, 2022) anticipated that nOPV2 clinical results will likely meet expectations as a bioequivalent vaccine compared to Sabin OPV2. However, experience with nOPV2 in the field to date demonstrates its ability to pose risks of VAPP (World Health Organization, 2023) and cVDPVs (Global Polio Eradication Initiative, 2023b), albeit at lower rates than expected with mOPV2. These lower risks are consistent with nOPV2 increased genetic stability and lower observed shedding, which reduce its risk to individuals and the chances of seeding new outbreaks. These benefits, however, come at the cost of reduced secondary spread and population effectiveness (Thompson, 2022a).

Modeling studies performed before the COVID-19 pandemic showed that GPEI efforts to end cVDPV2 transmission were off track, and found that even assuming the best possible properties of nOPV2, with current GPEI and country outbreak response performance, using nOPV2 instead of mOPV2 would not stop cVDPV2 transmission (Kalkowska, Pallansch, Wassilak, et al., 2021; Kalkowska, Pallansch, et al., 2023; Kalkowska, Pallansch, Wilkinson, et al., 2021). Further modeling since COVID-19 explored the consequences of disruptions in RI and polio program activities, and demonstrated the consequences of delaying outbreak response to wait for nOPV2 instead of using mOPV2 (Kalkowska, Pallansch, et al., 2023; Kalkowska, Voorman, et al., 2023; Kalkowska, Wassilak, Pallansch, et al., 2023). Collectively, these modeling studies motivated the exploration of conditions that might lead to uncontrollable cVDPV2 outbreaks and further exploration of the potential benefits of nOPV2 considering the bounds of prior analyses (Kalkowska, Pallansch, et al., 2023; Kalkowska, Voorman, et al., 2023; Kalkowska, Wassilak, Pallansch, et al., 2023). Discussion of the expected trajectories from a recent study (Kalkowska, Wassilak, Wiesen, et al., 2023) also led to questions about variability around the expected values and drivers of the upper bounds.

Integrated modeling provides the opportunity to explore prospective outcomes expected with the application of different strategies or policies with full consideration of stochastic risks that reintroduce live polioviruses into populations from different sources (Thompson & Kalkowska, 2020). For example, reintroductions may follow breaches in containment (Duintjer Tebbens, Kalkowska, et al., 2018), unintentional or intentional reintroductions (Kalkowska, Pallansch, Cochi, et al., 2021; Kalkowska, Pallansch, Wassilak, et al., 2021), introductions due to the excretion of polioviruses from individuals transmitting outbreak viruses or type 2 OPV (OPV2) used for outbreak response, or from immunodeficient individuals with prolonged or chronic infections (iVDPVs) (Kalkowska et al., 2019). These events that occur unpredictably in real life are introduced stochastically in the prospective model to vary the times and places where they occur (Kalkowska, Pallansch, Wassilak, et al., 2021). This leads to different possible futures, although the modeling uses the same set of all other inputs to ensure consistent comparisons across policy or strategy scenarios (Kalkowska, Pallansch, Wassilak, et al., 2021).

Policy analyses generally focus on the expected values of outcomes of different strategies to facilitate overall comparisons (Duintjer Tebbens et al., 2015), in which stochastic results vary for different iterations. Although useful for tracking trends and comparing policies, the expected values do not convey the skewness in the distributions caused by high-consequence events and may miss important associated insights relevant to risk management. For example, prior modeling that explored the specific iterations that led to OPV restart, which the model triggered upon reaching specific cumulative modeled cases, helped to identify specific failure modes (Duintjer Tebbens & Thompson, 2018). Although worst-case scenarios represent low-probability events in the entire simulation space, they can reveal insights about potentially catastrophic consequences and provide opportunities for prospective risk management. Building on recent stochastic polio endgame modeling (Kalkowska, Wassilak, Pallansch, et al., 2023; Thompson et al., 2022), we explore what happens in the worst-case iterations of simulations of the polio endgame using different vaccine choices for outbreak response to identify potential high-consequence events that may lead to large numbers of polio cases.

2 | METHODS

For this analysis, we use an updated global poliovirus transmission model (Kalkowska, Pallansch, Wassilak, et al., 2021; Kalkowska, Pallansch, Wilkinson, et al., 2021; Kalkowska,

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wassilak, Pallansch, et al., 2023) which divides the world according to World Bank Income Level (low-income, LI; lower middle-income, LMI; upper middle-income, UMI; high-income, HI) with current vaccine use in RI (OPV+IPV, IPV/OPV, IPV-only) into 72 blocks of 10 subpopulations of approximately 10.7 million total population and variable age distribution each. The model uses OPV+IPV to refer to the RI schedules of countries that previously relied exclusively on OPV and added one dose of IPV (typically administered at the same time as the third OPV dose) around 2016. This contrasts with sequential IPV/OPV RI schedules, which administer IPV doses at the first individual immunization contacts and then administer OPV at later contacts, that reduce VAPP by giving IPV first. Mixing within blocks occurs homogenously in space and heterogeneously by age. Mixing between blocks occurs according to nine varying preferential mixing areas of different sizes, which in abstract represent larger geographical regions (e.g., continents) (Kalkowska, Pallansch, Wassilak, et al., 2021; Kalkowska, Pallansch, Wilkinson, et al.,2021; Kalkowska, Wassilak, Pallansch, et al., 2023).

Building on recent analyses that explored the consequences of bOPV cessation in 2027 (Kalkowska, Wassilak, Wiesen et al., 2023; Thompson et al., 2022), which optimistically assumed eradication of type 1 WPV (WPV1) in 2023 and realistically assumed current supplementary immunization activity (SIA) performance characteristics (Kalkowska, Badizadegan, et al., 2023; Kalkowska, Pallansch, Wassilak, et al. 2021; Kalkowska, Pallansch, Wilkinson, et al., 2021; Kalkowska, Wassilak, Pallansch, et al., 2023), we used the same realistic SIA performance characteristics for this analysis. The actual performance of SIAs substantially impacts the expected trajectories, as demonstrated elsewhere (Thompson & Kalkowska, 2021; Thompson et al., 2023), which led to emphasis on SIA quality in numerous modeling studies published since 2006 (Thompson et al., 2006) and reviewed elsewhere (Thompson & Kalkowska, 2020). We selected a prospective analytical time horizon of T_0 of January 1, 2022, to T_{end} of December 31, 2035. Recognizing the censoring associated with time horizons, we present the modeling results for both the time horizon of the current GPEI strategic plan of January 1, 2022, to T_{end} of December 31, 2026, and the full modeled time horizon of January 1, 2022, to T_{end} of December 31, 2035. For this analysis, we consider three scenarios based on prior modeling (Kalkowska, Wassilak, Pallansch, et al., 2023) that vary the vaccine of choice use for type 2 outbreak response.

Specifically, we consider the scenarios of (i) *mOPV2*, with its well-established properties from extensive use; (ii) *best nOPV*, which assumes type-specific nOPV use for outbreak response after type-specific OPV cessation, the same effectiveness of nOPV as mOPV, no reversion of nOPV despite transmissibility, and no VAPP; and (iii) *worst nOPV*, which assumes type-specific nOPV use for outbreak response after type-specific OPV cessation, 90% effectiveness of nOPV relative to mOPV, and reduced reversion based on prior modeling (Kalkowska, Pallansch, Wilkinson, et al., 2021) and for which we further reduced VAPP and reversion rates by 10% relative to mOPV2. Recognizing uncertainty in actual performance of nOPV2, we provide bounding analyses (Kalkowska, Pallansch, Wilkinson, et al., 2021) that convey the probable range. We consider the *best nOPV2*, which likely performs better than implied by evidence to date for the actual performance of nOPV2 (e.g., due to some VAPP observed, World Health Organization, 2023, and potentially slightly lower efficacy of nOPV2 relative to mOPV2), and the *worst nOPV2*, which likely performs worse than implied by the evidence from actual nOPV2 use to date. For the extended time horizon, we optimistically assume the potential availability of novel OPV types 1 and 3 at the time of bOPV cessation onward for outbreak response, and we make parallel bounding assumptions for these potential future vaccine products to the ones used for *best nOPV2* and *worst nOPV2* (Kalkowska, Wassilak, Wiesen, et al., 2023; Thompson et al., 2022).

We performed all simulations using JAVA™ programming language in the integrated development environment Eclipse™, and we simulated 100 stochastic iterations starting with the same random number seeds and initial conditions for each scenario. We estimate the probability of die out (POD) for each scenario by counting the number of iterations with no ongoing transmission of type 2 at the end of the time horizon (Kalkowska, Wassilak, Pallansch, et al., 2023). We demonstrate the general variability among 100 stochastic iterations, and we show the 10 worst-performing iterations in terms of cumulative cases of cVDPV2 for each of the model time horizons. We run the model without any restrictions on vaccine supplies to estimate the number of vaccine doses the model would require under this assumption. We summarize both the expected cases for each iteration and the extent of transmission spread through the 720 modeled subpopulations and characterize the possible worst-case scenarios of uncontrolled type 2 transmission for each of the modeled scenarios and time horizons.

Although this analysis focuses on type 2 cases, because cVDPV2 cases currently dominate the global case polio counts, using the extended time horizon the analysis also includes assumptions related to the potential risks associated with bOPV cessation (assuming no bOPV intensification prior to cessation and for which type 1 cVDPV risks after cessation become dominant (Kalkowska, Wassilak, Wiesen, et al., 2023; results not shown). We explore the specific subpopulations that contributed to the incidence that led each of the iterations into the 10 highest case counts. We also explored the characteristics of the 10 iterations with the lowest case counts.

3 | RESULTS

For the time horizon of 2022–2026, the top row of Table 1 (labeled "All blocks") shows the model estimates between 6438 and 22,240 expected cVDPV2 cases in the rightmost columns, depending on the vaccine choice used for outbreak response. Notably, none of the 100 iterations show die out of

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 High R_0 and/or low RI coverage blocks, characteristics, reported, and modeled expected cVDPV2 since OPV2 cessation (as of April 25, 2023) and modeled expected cVDPV2 cases for the 2022–2026 time horizon

Block	IL	Name	R_0	Lowest RI coverage in the block	Reported cVDPV2 cases between May 1, 2016 and December 31, 2022[a]	Modeled expected cVDPV2 cases since OPV2 cessation[b]			Modeled expected cVDPV2 cases 2022–2026		
						mOPV2	best nOPV2	worst nOPV2	mOPV2	best nOPV2	worst nOPV2
All blocks (global)											
1–72					2,973	3,374	3,279	3,393	17,138	6,438	22,240
High R_0 (≥10) and low RI coverage (≤ 0.3) blocks											
1	LI	Central Africa 1	10	0.3	630	310	307	328	2,908	2,116	3,602
2	LI	East Africa 1	11	0.3	61	108	98	108	1,580	423	1,585
3	LI	East Africa 2	10	0.3	90	267	260	261	1,134	155	2,997
5	LI	West Africa 1	11	0.3	450	418	409	420	1,419	191	1,885
32	LI	North Pakistan and Afghanistan 1	11	0.3	461	522	523	523	96	496	181
34	LMI	Rest of Pakistan 1	11	0.3	56	124	125	127	201	149	292
47	LMI	India 1	13	0.3	0	0	0	0	477	86	585
48	LMI	India 2	13	0.3	0	0	0	0	466	66	491
High R_0 ($R_0 \geq 10$) blocks											
49	LMI	India 3	12	0.9	0	0	0	0	367	68	272
50	LMI	India 4	11	0.9	0	3	2	3	276	49	272
51	LMI	India 5	11	0.9	0	0	0	0	227	58	286
52	LMI	India 6	11	0.9	0	0	0	0	223	57	226
53	LMI	India 7	11	0.9	0	0	0	0	330	25	211
54	LMI	India 8	11	0.9	0	0	0	0	299	31	283
55	LMI	India 9	11	0.9	0	0	0	1	273	62	329
56	LMI	India 10	11	0.9	0	5	7	6	314	67	267
57	LMI	India 11	10	0.9	0	0	0	0	321	32	307
58	LMI	India 12	10	0.9	0	0	0	0	201	64	180
68	LMI	South Asia 1	12	0.6	0	0	0	0	124	0	206
69	LMI	South Asia 2	13	0.6	0	2	0	0	118	20	141
Low RI coverage (≤ 0.3) blocks											
7	LMI	Middle-income Africa-Arabia 1	8	0.3	375	729	734	786	746	615	1,107
8	LMI	North Nigeria 1	8	0.1	524	509	509	511	202	249	327
9	LMI	West Africa 2	9	0.3	13	13	13	13	835	276	1,378
13	LMI	South Asia 3	8	0.3	1	1	1	1	18	45	72
36	UMI	Mid-east 2	7	0.05	74	73	73	73	105	83	101
38	LMI	Eurasia 2	7	0.3	2	0	0	0	1	1	1
Other blocks (not High R_0 (≥10) or low RI coverage (≤ 0.3))											
			< 10	> 0.3	236	291	216	231	3,879	953	4,655

Abbreviations: cVDPV2, type 2 circulating vaccine-derived polioviruses; IL, income level; mOPV2, type 2 monovalent OPV; nOPV2, type 2 novel OPV; OPV, type oral poliovirus vaccine; R_0, basic reproduction number; RI, routine immunization.[a]Reported cases after OPV2 cessation (for the period May 1, 2016–December 31, 2022, as of April 25, 2023. [b] Modeled expected cases for the same period as reported.

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

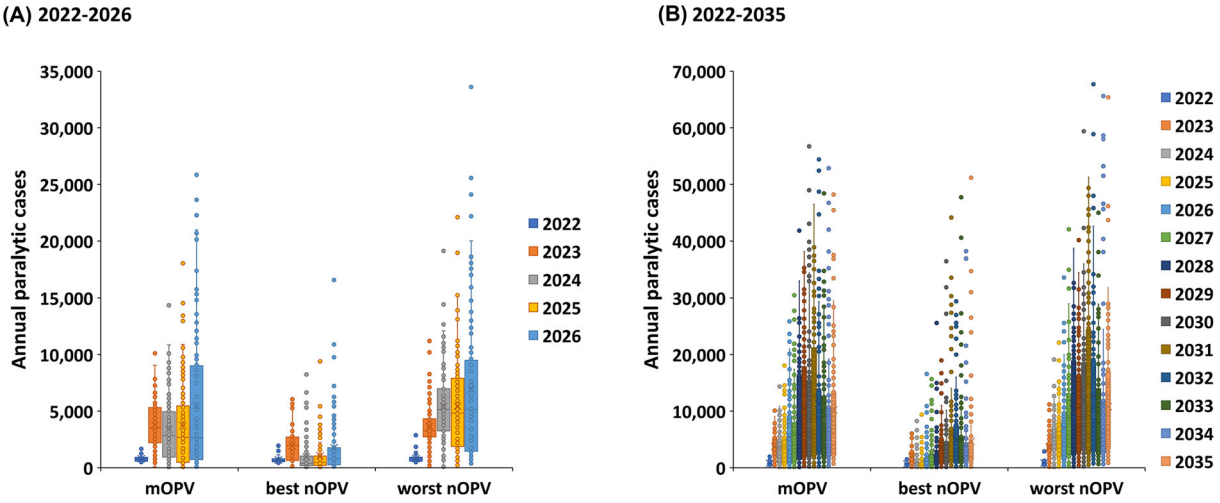

FIGURE 1 Variability among 100 stochastic iterations for RC with outbreak response using mOPV2, best nOPV2, or worst nOPV2 for (A) 2022–2026 and (B) 2022–2035. cVDPV2, type 2 circulating vaccine-derived polioviruses; mOPV2, type 2 monovalent OPV; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine.

transmission at the end of the time horizon, which implies an estimated POD of 0% for cVDPV2 (not shown in Table 1 due to 0 value for all vaccine choice scenarios).

Figure 1A shows the distribution of the cases for the 100 stochastic iterations for each year in the time horizon of 2022–2026 for each of the scenarios using box and whisker plots. The results generally show increasing variability with time with the use of *mOPV2* or *worst nOPV2*, because as transmission continues longer into the time horizon, the specific importation events that restart transmission in new blocks lead to more iterations with high-consequence importations. The *best nOPV2* scenario shows the highest interquartile ranges of cases in 2023. This occurs due to the fact that the *best nOPV2* scenario is not seeding any new outbreaks and ending the transmission that occurs in some, but not all outbreaks. For all vaccine scenarios, the tails of the distributions that correspond to case counts that exceed the interquartile range increase with time.

Since the global model includes subpopulations with properties that abstractly simulate the variability in conditions that influence poliovirus transmission potential in countries (e.g., different vaccine choices, coverage, levels of hygiene and sanitation, etc.), we cannot identify the specific countries that contribute the most to modeled prospective transmission. However, Table 1 lists the 26 abstractly modeled blocks with a high basic reproduction number ($R_0 \geq 10$) and/or blocks with low RI coverage subpopulations (RI coverage ≤ 0.3). Specifically, the top section lists the modeled blocks with both high R_0 and low RI coverage subpopulations, the middle section lists the modeled blocks only with high R_0, and the bottom section lists the modeled blocks with only low RI coverage subpopulations. These blocks and subpopulations represent high-risk areas, in which live polioviruses can transmit most easily and fastest and/or cause the most cases.

The middle columns of Table 1 show the actual reported cVDPV2 cases since OPV2 cessation (from May 2016 through December 31, 2022, using data as of April 25, 2023) and the modeled expected total cVDPV2 cases (without any adjustment for underreporting) for the same time period for comparison. Overall, these results show that 92% of the cVDPV2 cases reported since OPV2 cessation and 91–93% of expected cVDPV2 cases modeled for that period come from 11 out of 26 of these blocks in the model. With actual delays in reporting cases for some countries, Table 1 shows a few blocks for which the model estimates fall notably above or below the reported cases. For example, the ongoing outbreak in the Democratic Republic of the Congo (DRC) accounts for most of the reported cases for the Central Africa 1 block, with 360 confirmed cVDPV2 cases in 2022 reported as of April 25, 2023. With only 64 of the 360 cases reported when we performed the simulations in at the end of July 2022 (and notably only 210 of the 360 cases reported by December 27, 2022, which provides context about the delays in reporting), the model-fitting process reflected our understanding of the data and immunization plans at the time. Specifically, during the model updating process, the smaller epidemiological signal from retrospective data for the DRC led to input assumptions that produced fewer cases in 2022, and which also implied lower transmission in other countries within the same block. For blocks with relative overestimates of modeled cases compared to reported cases, the model assumptions (based on the epidemiological data available at the time) led to increased transmission in the block compared to confirmed cases (to date). Overall, the differences tend to cancel out, which implies small expected overall errors for global trends and totals in the context of our abstract block and subpopulation model structure, which we reiterate does not specifically model or fit data to individual countries.

Table 2 lists the characteristics of the top 10 iterations (out of 100) with very high case counts for each *mOPV2*, *best nOPV2*, and *worst nOPV2* for the time horizon of the current 2022–2026 GPEI Strategic Plan. The specific iteration

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 2 Characteristics of the high case iterations (ordered by the number of cDPV2 cases) for the period of 2022–2026 for mOPV2, best nOPV2, and worst nOPV2

Iteration index	Number of cVDPV2 cases	Number of affected subpopulations	Percentage of cases in high R_0 blocks[a]	Percentage of cases in low RI coverage blocks[b]	Percentage of cases in blocks representing high transmission areas[c]
mOPV2					
23	44,125	197	80	36	54
55	43,054	182	71	49	40
80	41,443	180	75	42	56
5	39,823	173	81	46	56
93	38,616	159	77	43	51
45	38,191	177	75	40	53
87	37,616	124	58	57	16
81	35,092	131	77	43	52
33	34,485	153	87	44	65
57	34,481	124	62	44	46
Best nOPV2					
6	26,209	119	75	32	50
9	25,119	101	95	70	43
100	23,682	103	65	61	35
3	23,222	100	87	52	76
66	17,634	73	76	45	50
5	16,860	74	68	84	0
64	14,947	78	53	67	0
98	14,278	90	26	29	3
94	12,944	52	61	91	4
38	12,585	69	44	64	0
Worst nOPV2					
94	51,270	184	58	46	27
55	50,683	182	67	53	36
6	48,882	179	82	48	52
23	47,918	185	75	39	52
34	46,464	152	60	60	23
66	45,035	160	72	47	48
84	44,178	144	59	54	20
33	43,770	172	76	35	67
100	43,390	132	79	60	43
9	41,759	128	84	55	51

Notes: [a] $R_0 \geq 10$; [b] RI coverage ≤ 0.3, [c] blocks 47–58, 68–69 indicated in Table 1.

Abbreviations: cVDPV2, type 2 circulating vaccine-derived polioviruses; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine; R_0, basic reproduction number; RI, routine immunization.; mOPV2, type 2 monovalent OPV.

numbers that appear in the top 10 differ between scenarios due to the stochastic and dynamic nature of the modeled exportations. However, the top 10 iterations in each scenario share the property of all importations and spread involving the 26 high-risk blocks and subpopulations described in Table 1.

For each of the top 10 iterations listed in Table 2, Figure 2 shows the corresponding modeled total cases by year (solid lines) compared to the expected value of modeled cVDPV2 cases based on all 100 stochastic iterations (dashed lines) for the time horizon of the current 2022–2026 GPEI Strategic Plan. The number of cases in each year reflects the path that the importations take that lead to outbreaks in different subpopulations, with the timing of the importations into the blocks listed in Table 1 accounting for the peaks in Figure 2 due to their higher transmission potential and/or lower coverage. Specifically, once cVDPV2 enters the high R_0 blocks that represent conditions like India and Bangladesh (see last column of Table 2), the transmission spreads extensively

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

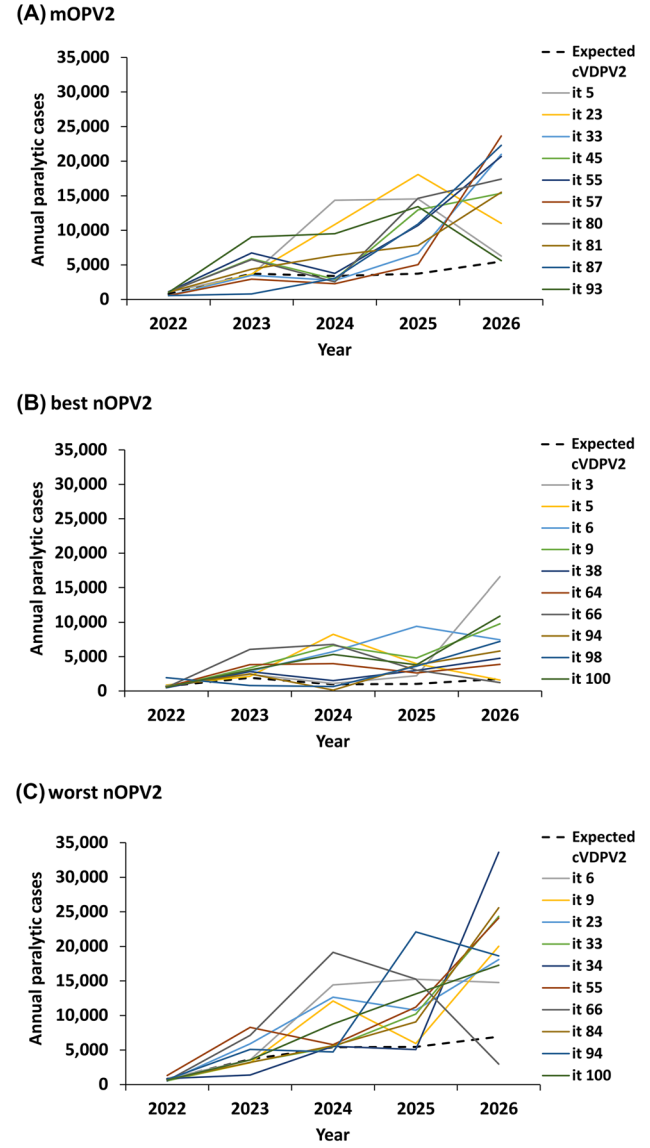

FIGURE 2 Ten (out of 100) worst performing stochastic iterations for RC with outbreak response for the 2022–2026 time horizon using (A) mOPV2, (B) best nOPV2, or (C) worst nOPV2. cVDPV2, type 2 circulating vaccine-derived polioviruses; mOPV2, type 2 monovalent OPV; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine.

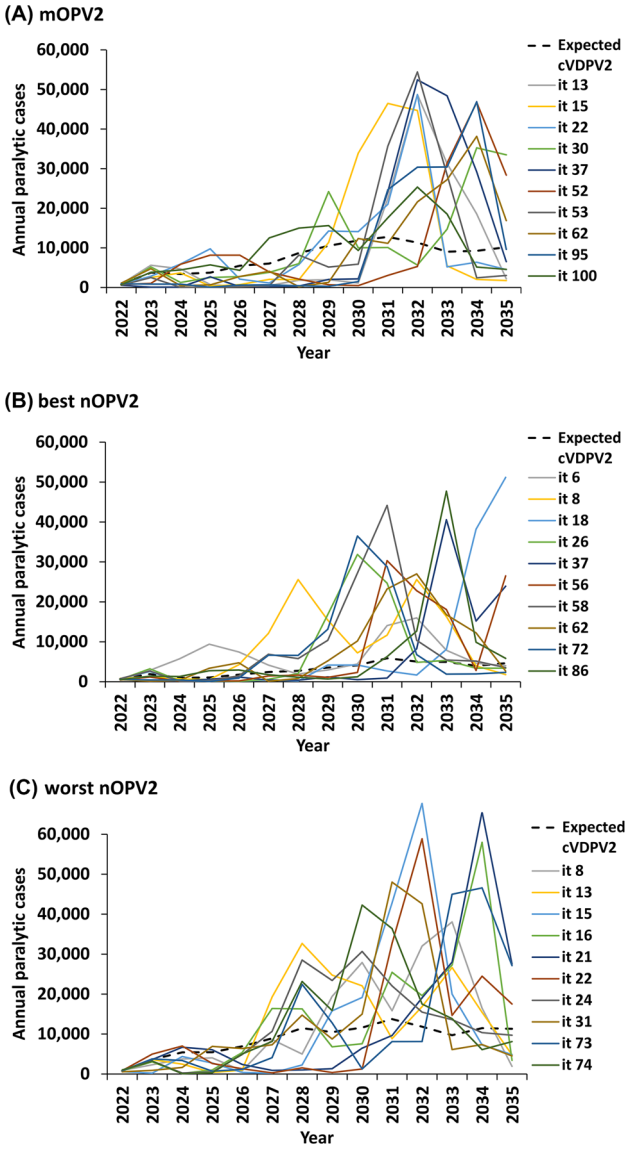

FIGURE 3 Ten (out of 100) worst performing stochastic iterations for RC with outbreak response for 2022–2035 time horizon using (A) mOPV2, (B) best nOPV2, or (C) worst nOPV2. cVDPV2, type 2 circulating vaccine-derived polioviruses; mOPV2, type 2 monovalent OPV; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine.

such that control would require over 1 billion doses of filled OPV in the stockpile plus plans and resources to rapidly conduct outbreak response SIAs (oSIAs) to administer the doses, which is beyond the supply capability of the system in the 2022–2026 time horizon. These iterations show a rapid increase in case count, where the high R_0 blocks account for up to 67% of all estimated cases. Earlier modeling observations of this type of behavior motivated pre-OPV2 cessation modeling to include OPV restart in those studies (Duintjer Tebbens et al., 2015; Kalkowska, Pallansch, Cochi, et al., 2021). We observe this behavior for the *mOPV2* or *worst nOPV2* scenarios within the short time horizon (2022–2026).

For the extended time horizon of 2022–2035, Figure 1B shows the distribution of the cases for the 100 stochastic iterations for each year, and Table 3 and Figure 3 show the comparable results to those reported in Table 2 and Figure 2. As shown by the doubling of the *y*-axis scale for Figure 1B compared to Figure 1A and the results reported in Table 3, the number of overall expected cases increases with the extended time horizon. As expected, the specific iterations in the top 10% of the case counts depend on the timing of when the importations reach the high transmission settings in Table 1. Similar to Figure 2, the model reaches peaks of cases in Figure 3 when the cVDPV2 enters the high transmission settings (i.e., blocks representing conditions like India and Bangladesh summarized in the right column of Table 3). Given the extended time horizon, the peaks become more easily observable for the *best nOPV2* scenario

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 3 Characteristics of the high case iterations (ordered by the number of cDPV2 cases) for the period of 2022–2035 for mOPV2, best nOPV2, and worst nOPV2

Iteration index	Number of cVDPV2 cases	Number of affected subpopulations	Percentage of cases in high R_0 blocks[a]	Percentage of cases in low RI coverage blocks[b]	Percentage of cases in blocks representing high transmission areas[c]
mOPV2					
37	169,097	422	46	40	29
15	157,579	413	49	41	31
30	155,526	388	52	38	37
95	148,077	378	51	35	33
53	147,021	325	58	48	36
52	145,936	310	55	46	34
100	142,682	395	48	41	30
62	142,629	362	56	47	38
22	142,520	398	51	40	29
13	140,721	372	56	40	39
Best nOPV2					
8	127,392	397	51	43	34
58	124,342	355	57	38	42
18	114,699	311	66	25	58
56	109,374	295	58	35	46
62	107,518	352	44	34	34
72	107,213	318	67	47	44
26	97,413	243	57	39	42
86	96,213	263	77	36	64
37	94,151	277	67	39	47
6	86,348	330	49	32	31
Worst nOPV2					
16	191,122	442	53	38	35
15	188,336	457	52	41	34
73	185,292	418	54	40	35
74	181,006	438	49	40	29
13	179,567	454	52	40	33
21	179,088	409	56	41	35
8	177,033	428	51	41	32
24	174,137	443	51	40	32
31	170,745	419	53	36	36
22	168,351	371	54	36	37

Note: [a]$R_0 \geq 10$; [b]RI coverage ≤ 0.3, [c]blocks 47–58, 68–69 indicated in Table 1.

Abbreviations: cVDPV2, type 2 circulating vaccine-derived polioviruses; nOPV2, type 2 novel OPV; OPV, oral poliovirus vaccine; R_0, basic reproduction number; RI, routine immunization.; mOPV2, type 2 monovalent OPV.

compared to short-term use of the *best nOPV2* in Figure 2. The *best nOPV2* scenario requires the extended time horizon to show these effects because the assumptions for nOPV2 for this scenario reduce the number of importations, and therefore it takes longer for imported outbreak viruses to reach the high R_0 blocks representing conditions like India and Bangladesh.

4 | DISCUSSION

The probability of successfully stopping type 2 transmission only with outbreak response campaigns of the current quality continues to decline (Kalkowska, Pallansch, Cochi, et al., 2021; Kalkowska, Pallansch, Wassilak, et al., 2021; Kalkowska, Pallansch, Wilkinson et al., 2021; Kalkowska,

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wassilak, Pallansch, et al., 2023). Despite an estimated 6% chance of needing to restart OPV2 prior to OPV2 cessation (Duintjer Tebbens et al., 2015), the probability of successful OPV2 cessation has continued to drop since 2017 (Kalkowska, Pallansch, Cochi, et al., 2021; Kalkowska, Pallansch, Wassilak, et al., 2021; Kalkowska, Pallansch, Wilkinson, et al., 2021; Kalkowska, Wassilak, Pallansch, et al., 2023).

Eradication represents an unforgiving goal (Thompson & Duintjer Tebbens, 2017), which requires ending all transmission in all areas contemporaneously. Some earlier discussions of the challenges of eradication focused on the weak links (Barrett, 2003, 2009; Barrett & Hoel, 2007), which modeling studies previously referred to as "under-vaccinated subpopulations" (Kalkowska et al., 2014a, 2014b, 2015, 2018), and others currently refer to as populations in "critical" or "consequential" geographies (Independent Monitoring Board of the Global Polio Eradication Initiative, 2022). As time increases since the OPV2 cessation, many countries now include large birth cohorts that have not been exposed to OPV2-related viruses since 2016. The increasing vulnerability of populations to transmission (Duintjer Tebbens et al., 2016a, 2016b; Duintjer Tebbens, Hampton, et al., 2018; Duintjer Tebbens, Hampton, Wassilak, et al., 2016) following the importation of type 2 polioviruses means that responding to outbreaks in these countries will require very large outbreak response activities involving age groups expanded beyond the <5-year-old age range. Our results show that in the absence of a more timely, larger, and better outbreak response, and without a concerted effort to raise the intestinal immunity to type 2 polioviruses in high-risk countries, there is no POD of cVDPV2s and a risk of uncontrolled type 2 outbreaks, regardless of vaccine choice. This may require reintroduction of an OPV2 in RI, followed by recoordination of the cessation of all OPV2 use to achieve cessation of all transmission of type 2 polioviruses.

The results of this analysis come with several limitations. In particular, the model uses conceptual characterization of global variability using block/subpopulation structure and the simplified modeling approach used to simulate effective poliovirus introductions during exportation to new blocks/subpopulations. This simplification allows for faster simulation times but does not allow for direct comparisons of specific blocks with specific countries. Moreover, the results depend on available information/assumptions about the initial conditions as of the end of 2021, expected future policies/actions, the uncertain properties of nOPV2, the uncertain global political climate affecting outbreak response activities, and the implicit assumption of unlimited vaccine supplies.

As type 2 transmission continues, our results suggest that the chances of effectively controlling type 2 poliovirus outbreaks continue to decline. In the model, if any OPV2-related virus reaches high transmission settings, like some areas of India and Bangladesh, very high type 2 case counts would likely follow. Recent importations and transmission of cVDPV2s in high-income countries, including Israel (Zuckerman et al., 2022), the United Kingdom (United Kingdom Department of Health & Social Care, 2022), and the United States (Link-Gelles et al., 2022; Ryerson et al., 2022), confirm that cVDPV transmission can occur even in countries with high overall reported IPV immunization coverage in communities with low coverage (Thompson et al., 2012), with paralytic cases possible in these communities. Countries with relatively lower immunization coverage should expect to fair worse with respect to potential case counts, and they should recognize the need for large and high-quality outbreak responses if they want to keep case counts lower. However, insufficient quantities of vaccine available for responding to type 2 outbreaks may limit the ability of countries to respond, as occurred in the past, and, in this regard, the situation could prove more challenging than what we modeled. These insights may lead to further discussions about the need to improve the quality of cVDPV2 outbreak response, including changes in strategy and tactics that make responses more timely, larger, and higher quality (Kalkowska, Wassilak, Pallansch, et al., 2023). Discussions could also begin to consider the appropriate triggers to preemptively restart OPV2 use in RI and potentially in preventive SIAs in low coverage setting in some OPV-using countries.

ACKNOWLEDGMENTS

The first and last two 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 U.S. Centers for Disease Control and Prevention or the Department of Health and Human Services.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Mark A. Pallansch https://orcid.org/0000-0002-1015-4818
Kamran Badizadegan https://orcid.org/0000-0003-4900-9455
Kimberly M. Thompson https://orcid.org/0000-0002-0849-9147

REFERENCES

Barrett, S. (2003). Global disease eradication. *Journal of the European Economic Association*, *1*(2/3), 591–600.

Barrett, S. (2009). Polio eradication: Strengthening the weakest links. *Health Affairs*, *28*(4), 1079–1090.

Barrett, S., & Hoel, M. (2007). Optimal disease eradication. *Environment and Development Economics*, *12*(5), 627–652.

Duintjer Tebbens, R. J., Hampton, L. M., & Thompson, K. M. (2016a). Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of inadvertent trivalent oral poliovirus vaccine use. *BMC Infectious Diseases*, *16*, 231.

Duintjer Tebbens, R. J., Hampton, L. M., & Thompson, K. M. (2016b). Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of potential non-synchronous cessation. *BMC Infectious Diseases [Electronic Resource]*, *16*, 237.

Duintjer Tebbens, R. J., Hampton, L. M., & Thompson, K. M. (2018). Planning for globally coordinated cessation of bivalent oral poliovirus vaccine: Risks of non-synchronous cessation and unauthorized oral

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

poliovirus vaccine use. *BMC Infectious Diseases [Electronic Resource]*, *18*(1), 165. https://doi.org/10.1186/s12879-018-3074-0

Duintjer Tebbens, R. J., Hampton, L. M., Wassilak, S. G. F., Pallansch, M. A., Cochi, S. L., & Thompson, K. M. (2016). Maintenance and intensification of bivalent oral poliovirus vaccine use prior to its coordinated global cessation. *Journal of Vaccines & Vaccination*, *7*(5), 340. https://doi.org/10.4172/2157-7560.1000340

Duintjer Tebbens, R. J., Kalkowska, D. A., & Thompson, K. M. (2018). Poliovirus containment risks and their management. *Future Virology*, *13*(9), 617–628. https://doi.org/10.2217/fvl-2018-0079

Duintjer Tebbens, R. J., Pallansch, M. A., Kew, O. M., Cáceres, V. M., Jafari, H., Cochi, S. L., Aylward, R. B., & Thompson, K. M. (2006). Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. *Risk Analysis*, *26*(6), 1471–1505.

Duintjer Tebbens, R. J., Pallansch, M. A., Wassalik, S. G. F., Cochi, S. L., & Thompson, K. M. (2015). An economic analysis of poliovirus risk management policy options for 2013–2052. *BMC Infectious Diseases [Electronic Resource]*, *15*(389), https://doi.org/10.1186/s12879-12015-11112-12878

Duintjer Tebbens, R. J., Pallansch, M. A., Wassilak, S. G. F., Cochi, S. L., & Thompson, K. M. (2016). Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. *BMC infectious diseases*, *16*, 137. https://doi.org/10.1186/s12879-016-1465-7

Duintjer Tebbens, R. J., & Thompson, K. M. (2018). Polio endgame risks and the possibility of restarting the use of oral poliovirus vaccine. *Expert Review of Vaccines*, *17*(8), 739–751. https://doi.org/10.1080/14760584.2018.1506333

Global Polio Eradication Initiative. (2013). *Polio eradication and endgame strategic plan (2013–2018)*. World Health Organization. http://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf

Global Polio Eradication Initiative. (2016). *Standard operating procedures: Responding to a poliovirus event or outbreak: Part 1: General SOPs*. World Health Organization. https://s3.amazonaws.com/gpei-tk/reference_links/en/GPEI_SOPs.pdf

Global Polio Eradication Initiative. (2019). *Polio eradication and endgame strategic plan (2019–2023)*. World Health Organization. https://polioeradication.org/wp-content/uploads/2019/06/english-polio-endgame-strategy.pdf

Global Polio Eradication Initiative. (2020). *Strategy for the response to type 2 circulating vaccine-derived poliovirus 2020–2021: Addendum to the polio eradication and endgame strategic plan (2019–2023)*. World Health Organization. http://polioeradication.org/wp-content/uploads/2020/04/Strategy-for-the-response-to-type-2-circulating-Vaccine-Derived-Poliovirus-20200406.pdf

Global Polio Eradication Initiative. (2021). *Polio eradication strategy 2022–2026: Delivering on a promise*. World Health Organization. https://polioeradication.org/wp-content/uploads/2021/06/polio-eradication-strategy-2022-2026-pre-publication-version-20210609.pdf

Global Polio Eradication Initiative. (2022). *nOPV2: Clinical development summary updated June 2022*. World Health Organization. https://polioeradication.org/wp-content/uploads/2022/06/nOPV2-Clinical-Development-Summary_June-2022-Update_Final-EN.pdf

Global Polio Eradication Initiative. (2023a). *Global circulating vaccine-derived poliovirus (cVDPV) as of 25 April 2023*. World Health Organization. https://polioeradication.org/wp-content/uploads/2023/04/weekly-polio-analyses-cVDPV-20230425.pdf

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

Hampton, L. M., Farrell, M., Ramirez-Gonzalez, A., Menning, L., Shendale, S., Lewis, I., Rubin, J., Garon, J., Harris, J., Hyde, T., Wassilak, S. G. F., Patel, M., Nandy, R., & Chang-Blanc, D., & Immunization Systems Management Group of the Global Polio Eradication Initiative. (2016). Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine—Worldwide, 2016. *Morbidity and Mortality Weekly Report*, *65*(35), 934–938. https://doi.org/10.15585/mmwr.mm6535a3

Independent Monitoring Board of the Global Polio Eradication Initiative. (2022). *Highs and lows in the quest for zero, 21st Report, April 2022*. Centers for Disease Control and Prevention. https://polioeradication.org/wp-content/uploads/2022/05/21st-IMB-report-20220430.pdf

Kalkowska, D. A., Badizadegan, K., & Thompson, K. M. (2023). Outbreak management strategies for cocirculation of multiple poliovirus types. *Vaccine*, Advanced online publication. https://doi.org/10.1016/j.vaccine.2023.04.037

Kalkowska, D. A., Duintjer Tebbens, R. J., Grotto, I., Shulman, L. M., Anis, E., Wassilak, S. G. F., Pallansch, M. A., & Thompson, K. M. (2015). Modeling options to manage type 1 wild poliovirus imported into Israel in 2013. *Journal of Infectious Diseases*, *211*(11), 1800–1812.

Kalkowska, D. A., Duintjer Tebbens, R. J., & Thompson, K. M. (2014a). Modeling strategies to increase population immunity and prevent poliovirus transmission in the high-risk area of northwest Nigeria. *Journal of Infectious Diseases*, *210*(Suppl 1), S412–S423.

Kalkowska, D. A., Duintjer Tebbens, R. J., & Thompson, K. M. (2014b). Modeling strategies to increase population immunity and prevent poliovirus transmission in two high-risk areas in northern India. *Journal of Infectious Diseases*, *210*(Suppl 1), S398–S411.

Kalkowska, D. A., Duintjer Tebbens, R. J., & Thompson, K. M. (2018). Another look at silent circulation of poliovirus in small populations. *Infectious Disease Modelling*, *3*, 107–117. https://doi.org/10.1016/j.idm.2018.06.001

Kalkowska, D. A., Pallansch, M. A., Cochi, S. L., Kovacs, S. D., Wassilak, S. G. F., & Thompson, K. M. (2021). Updated characterization of post-OPV cessation risks: Lessons from 2019 serotype 2 outbreaks and implications for the probability of OPV restart. *Risk Analysis*, *41*(2), 320–328. https://doi.org/10.1111/risa.13555

Kalkowska, D. A., Pallansch, M. A., & Thompson, K. M. (2019). Updated modelling of the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus (iVDPV) excreters. *Epidemiology and Infection*, *147*, e295. https://doi.org/10.1017/S095026881900181X

Kalkowska, D. A., Pallansch, M. A., Wassilak, S. G. F., Cochi, S. L., & Thompson, K. M. (2021). Global transmission of live polioviruses: Updated integrated dynamic modeling of the polio endgame. *Risk Analysis*, *41*(2), 248–265. https://doi.org/10.1111/risa.13447

Kalkowska, D. A., Pallansch, M. A., Wassilak, S. G. F., Cochi, S. L., & Thompson, K. M. (2023). Serotype 2 oral poliovirus vaccine (OPV2) choices and the consequences of delaying outbreak response. *Vaccine*, *41*(1)Suppl, A136–A141. https://doi.org/10.1016/j.vaccine.2021.04.061

Kalkowska, D. A., Pallansch, M. A., Wilkinson, A., Bandyopadhyay, A. S., Konopka-Anstadt, J. L., Burns, C. C., Oberste, M. S., Wassilak, S. G. F., Badizadegan, K., & Thompson, K. M. (2021). Updated characterization of poliovirus outbreak response strategies for 2019–2029: Impacts of the use of novel OPV2 strains. *Risk Analysis*, *41*(2), 329–348. https://doi.org/10.1111/risa.13622

Kalkowska, D. A., Voorman, A., Pallansch, M. A., Wassilak, S. G. F., Cochi, S. L., Badizadegan, K., & Thompson, K. M. (2023). The impact of disruptions caused by the COVID-19 pandemic on global polio eradication. *Vaccine*, *41*(1)Suppl, A12–A18. https://doi.org/10.1016/j.vaccine.2021.04.026

Kalkowska, D. A., Wassilak, S. G. F., Pallansch, M. A., Burns, C. C., Wiesen, E., Durry, E., Badizadegan, K., & Thompson, K. M. (2023). Outbreak response strategies with type 2-containing oral poliovirus vaccines. *Vaccine*, *41*(1)Suppl, A142–A152. https://doi.org/10.1016/j.vaccine.2022.10.060

Kalkowska, D. A., Wassilak, S. G. F., Wiesen, E., Burns, C. C., Pallansch, M. A., Badizadegan, K., & Thompson, K. M. (2023). Coordinated global cessation of oral poliovirus vaccine use: Options and potential consequences. *Risk Analysis*. https://doi/10.1111/risa.14158

Link-Gelles, R., Lutterloh, E., Ruppert, S., P, B., P, B., George, S. t., K, R., E, S., Anderson, B. J., Fuschino, M., Popowich, M., Punjabi, C., Souto, M., McKay, K., Rulli, S., Insaf, T., Hill, D., Kumar, J., Gelman, I., … Routh, J. (2022). Public health response to a case of paralytic poliomyelitis in an unvaccinated person and detection of poliovirus in wastewater—New

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

York, June-August 2022. *Morbidity and Mortality Weekly Report*, *71*(33), 1065–1068. https://doi.org/10.15585/mmwr.mm7133e2

Macklin, G. R., Peak, C., Eisenhawer, M., Kurji, F., Mach, O., Konz, J., Gast, C., Bachtiar, N. S., Bandyopadhyay, A. S., & Zipursky, S., & n, O. P. V. W. G.. (2023). Enabling accelerated vaccine roll-out for public health emergencies of international concern (PHEICs): Novel oral polio vaccine type 2 (nOPV2) experience. *Vaccine*, *41*(1)Suppl, A122–A127. https://doi.org/10.1016/j.vaccine.2022.02.050

Martin, J., Burns, C. C., Jorba, J., Shulman, L. M., Macadam, A., Klapsa, D., Majumdar, M., Bullows, J., Frolov, A., Mate, R., Bujaki, E., Castro, C. J., Bullard, K., Konz, J., Hawes, K., Gauld, J., Blake, I. M., Mercer, L. D., Kurji, F., … Zipursky, S. (2022). Genetic characterization of novel oral polio vaccine type 2 viruses during initial use phase under emergency use listing - Worldwide, March-October 2021. *Morbidity and Mortality Weekly Report*, *71*(24), 786–790. https://doi.org/10.15585/mmwr.mm7124a2

Rachlin, A., Patel, J. C., Burns, C. C., Jorba, J., Tallis, G., O'Leary, A., Wassilak, S. G. F., & Vertefeuille, J. F. (2022). Progress toward polio eradication—worldwide, January 2020–April 2022. *Morbidity and Mortality Weekly Report*, *71*(19), 650–655. https://doi.org/10.15585/mmwr.mm7119a2

Ryerson, A. B., Lang, D., Alazawi, M. A., Neyra, M., Hill, D. T., St George, K., Fuschino, M., Lutterloh, E., Backenson, B., Rulli, S., Ruppert, P. S., Lawler, J., McGraw, N., Knecht, A., Gelman, I., Zucker, J. R., Omoregie, E., Kidd, S., Sugerman, D. E., … Rosenberg, E. S. (2022). 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. *Morbidity and Mortality Weekly Report*, *71*(44), 1418–1424. https://doi.org/10.15585/mmwr.mm7144e2

Thompson, K. M. (2022a). Effectiveness of a new vaccine for outbreak response and the increasingly complicated polio endgame. *The Lancet Global Health*, *10*(12), e1697–e1698. https://doi.org/10.1016/S2214-109X(22)00452-1

Thompson, K. M. (2022b). Polio eradication: What kind of world do we want? *The Lancet Infectious Diseases*, *22*(2), 161–163. https://doi.org/10.1016/s1473-3099(21)00458-8

Thompson, K. M., & Duintjer Tebbens, R. J. (2017). Lessons from the polio endgame: Overcoming the failure to vaccinate and the role of subpopulations in maintaining transmission. *Journal of Infectious Diseases*, *216*(suppl_1), S176–s182. https://doi.org/10.1093/infdis/jix108

Thompson, K. M., Duintjer Tebbens, R. J., & Pallansch, M. A. (2006). Evaluation of response scenarios to potential polio outbreaks using mathematical models. *Risk Analysis*, *26*(6), 1541–1556. https://doi.org/10.1111/j.1539-6924.2006.00843.x

Thompson, K. M., & Kalkowska, D. A. (2020). Review of poliovirus modeling performed from 2000–2019 to support global polio eradication. *Expert Review of Vaccines*, *19*(7), 661–686. https://doi.org/10.1080/14760584.2020.1791093

Thompson, K. M., & Kalkowska, D. A. (2021). Reflections on modeling poliovirus transmission and the polio eradication endgame. *Risk Analysis*, *41*(2), 229–247. https://doi.org/10.1111/risa.13484

Thompson, K. M., Kalkowska, D. A., & Badizadegan, K. (2022). Health economic analysis of vaccine options for the polio eradication endgame: 2022–2036. *Expert Review of Vaccines*, *21*(11), 1667–1674. https://doi.org/10.1080/14760584.2022.2128108

Thompson, K. M., Kalkowska, D. A., & Badizadegan, K. (2023). Looking back at prospective modeling of outbreak response strategies for managing global type 2 oral poliovirus vaccine (OPV2) cessation [Original Research.]. *Frontiers in Public Health*, *11*, 1098419. https://doi.org/10.3389/fpubh.2023.1098419

Thompson, K. M., Wallace, G. S., Duintjer Tebbens, R. J., Smith, P. H., Barskey, A. E., Pallansch, M. A., Gallagher, K. M., Alexander, J. P., Armstrong, G. L., Cochi, S. L., & Wassilak, S. G. F. (2012). Trends in the risk of U.S. polio outbreaks and poliovirus vaccine availability for response. *Public Health Reports*, *127*(1), 23–37.

United Kingdom Department of Health & Social Care. (2022). *Joint Committee on Vaccination and Immunisation statement on vaccination strategy for the ongoing polio incident* [Independent report]. https://www.gov.uk/government/publications/vaccination-strategy-for-ongoing-polio-incident-jcvi-statement/joint-committee-on-vaccination-and-immunisation-statement-on-vaccination-strategy-for-the-ongoing-polio-incident

World Health Assembly. (2008). *Poliomyelitis: Mechanism for management of potential risks to eradication (resolution 61.1), WHO, Geneva, 19–24 May 2008*. World Health Organization. http://apps.who.int/gb/ebwha/pdf_files/WHA61-REC1/A61_Rec1-part2-en.pdf

World Health Organization. (2010). *Global Polio Eradication Initiative—strategic plan 2010–2012*. http://www.polioeradication.org/Portals/0/Document/StrategicPlan/StratPlan2010_2012_ENG.pdf

World Health Organization. (2023). Report of the second joint meeting (hybrid) of the WHO Global Advisory Committee on Vaccine Safety and the WHO Advisory Committee on Safety of Medicinal Products, December 14–16, 2022. *Weekly Epidemiological Record*, *98*(9), 83–92. https://apps.who.int/iris/handle/10665/366343

Zuckerman, N. S., Bar-Or, I., Sofer, D., Bucris, E., Morad, H., Shulman, L. M., Levi, N., Weiss, L., Aguvaev, I., Cohen, Z., Kestin, K., Vasserman, R., Elul, M., Fratty, I. S., Geva, M., Wax, M., Erster, O., Yishai, R., Hecht-Sagie, L., … Weil, M. (2022). Emergence of genetically linked vaccine-originated poliovirus type 2 in the absence of oral polio vaccine, Jerusalem, April to July 2022. *Euro Surveillance*, *27*(37), 2200694. https://doi.org/10.2807/1560-7917.Es.2022.27.37.2200694

How to cite this article: Kalkowska, D. A., Wiesen, E., Wassilak, S. G. F., Burns, C. C., Pallansch, M. A., Badizadegan, K., & Thompson, K. M. (2023). Worst-case scenarios: Modeling uncontrolled type 2 polio transmission. *Risk Analysis*, 1–11. https://doi.org/10.1111/risa.14159

15396924, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/risa.14159, Wiley Online Library on [22/06/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License