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Serotype 2 oral poliovirus vaccine (OPV2) choices and the consequences of delaying outbreak response

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Abstract

The Global Polio Eradication Initiative (GPEI) faces substantial challenges with managing outbreaks of serotype 2 circulating vaccine-derived polioviruses (cVDPV2s) in 2021. A full five years after the globally coordinated removal of serotype 2 oral poliovirus vaccine (OPV2) from trivalent oral poliovirus vaccine (tOPV) for use in national immunization programs, cVDPV2s did not die out. Since OPV2 cessation, responses to outbreaks caused by cVDPV2s mainly used serotype 2 monovalent OPV (mOPV2) from a stockpile. A novel vaccine developed from a genetically stabilized OPV2 strain (nOPV2) promises to potentially facilitate outbreak response with lower prospective risks, although its availability and properties in the field remain uncertain. Using an established global poliovirus transmission model and building on a related analysis that characterized the impacts of disruptions in GPEI activities caused by the COVID-19 pandemic, we explore the implications of trade-offs associated with delaying outbreak response to avoid using mOPV2 by waiting for nOPV2 availability (or equivalently, delayed responses waiting for national validation of meeting the criteria for nOPV2 initial use). Consistent with prior modeling, responding as quickly as possible with available mOPV2 promises to reduce the expected burden of disease in the outbreak population and to reduce the chances for the outbreak virus to spread to other areas. Delaying cVDPV2 outbreak response (e.g., modeled as no response January-June 2021) to wait for nOPV2 can considerably increase the total expected cases (e.g., by as many as 1,300 cVDPV2 cases in the African region during 2021–2023) and increases the likelihood of

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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.

CRediT authorship contribution statement

Dominika A. Kalkowska: Conceptualization, Methodology, Formal analysis, Visualization, Writing - original draft. **Mark A. Pallansch:** Investigation, Writing - review & editing. **Steven G.F. Wassilak:** Investigation, Writing - review & editing. **Stephen L. Cochi:** Investigation, Writing - review & editing. **Kimberly M. Thompson:** Conceptualization, Visualization, Supervision, Writing - original draft, Funding acquisition.

triggering the need to restart widescale preventive use of an OPV2-containing vaccine in national immunization programs that use OPV. Countries should respond to any cVDPV2 outbreaks quickly with rounds that achieve high coverage using any available OPV2, and plan to use nOPV2, if needed, once it becomes widely available based on evidence that it is as effective but safer in populations than mOPV2.

Keywords

Polio; Eradication; Dynamic modeling; Oral poliovirus vaccine

1. Introduction

In 2016, the Global Polio Eradication Initiative (GPEI) coordinated a switch for national immunization programs that use oral poliovirus vaccine (OPV) from trivalent OPV (tOPV, which contains all 3 serotypes) to bivalent OPV (bOPV, which contains serotypes 1 and 3). This switch led to the cessation of routine use of Sabin strain serotype 2 OPV (OPV2). Since 1999, when the last global case of polio caused by serotype 2 was reported, the only serotype 2 polio cases occurred due to vaccine-associated paralytic polio (VAPP) in recipients and their close contacts, and the development and transmission of serotype 2 circulating vaccine-derived polioviruses (cVDPV2s). Modeling performed prior to the switch explored the dynamics of outbreak response, the dynamics of OPV cessation, and the need for a global OPV stockpile. A 2006 analysis characterized the trade-offs of speed vs. quality for the first round of polio outbreak response activities and demonstrated the primary importance of rapid response [1]. The analysis, by modeling better performance, also emphasized the importance of obtaining high coverage in subsequent outbreak response supplementary immunization activities (oSIAs) [1]. Subsequent modeling papers by multiple groups confirmed the need for high quality (i.e., rapid, high coverage, and sufficient in scope) oSIAs to interrupt the transmission of outbreak viruses [2–5]. Modeling that characterized the dynamics of OPV cessation anticipated the risks of cVDPV2 outbreaks and demonstrated the necessity and effectiveness of increasing population immunity using tOPV prior to its globally coordinated cessation [6]. Additional modeling studies anticipated the decline in population immunity to transmission expected to occur as new birth cohorts that never received OPV2 accumulated, and characterized the likely increasing vulnerability to adverse outcomes following the introduction of OPV2, OPV2-related viruses, or cVDPV2s as a function of time [7,8]. Consistent with these analyses, which suggested the importance of tOPV intensification prior to the switch and the need to fully end all transmission of serotype 2 live polioviruses within 4 to 5 years after OPV2 cessation [7,8], additional modeling supported the critical need for development of a stockpile of mOPV2 and oSIA standard operating procedures (SOPs) to enable rapid outbreak responses [4,9,10].

In preparation for OPV2 cessation, the GPEI procured mOPV2 doses for the stockpile and developed guidance and procedures to manage outbreak response for any cVDPV2 outbreaks that occurred after the switch and procedures for mOPV2 use. At the time of OPV2 cessation, the OPV2 stockpile consisted of bulk mOPV2 produced prior to OPV2 cessation and a small fraction of filled and finished (henceforth simply filled) doses. Filling

mOPV2 requires both time and money and comes with some trade-offs [11]. Too many filled doses in the stockpile leads to excess wastage of the vaccine and depletion of the bulk, because unused filled doses expire, whereas too few filled doses can lead to stock-outs and delays in providing vaccine for outbreak response [11], which can then lead to increased need for vaccine due to the spread of outbreak viruses to geographically larger areas [4].

In 2021, 5 years after the switch, the GPEI and countries continue to face risks associated with the transmission of serotype 2 live polioviruses. Despite the guidance for outbreak response, the actual experience with oSIAs for cVDPV2s since 2016 varied substantially. Many of the outbreak responses worked as planned and effectively interrupted the transmission of the outbreak virus without starting new cVDPV2 outbreaks [12,13], demonstrating the effectiveness of increasing population immunity using tOPV prior to OPV2 cessation and effective outbreak response in these areas [14]. However, in cases in which outbreak response immunization began substantially later than 2 weeks after confirmation of a case (as called for by the SOPs and/or when confirmation was delayed) or when oSIAs achieved low coverage, cVPDV2 transmission continued and often broadened geographically. In addition, some mOPV2 oSIAs seeded the emergence and transmission of new cVDPV2 strains. Notably, in 2019, cVDPV2s also appeared unexpectedly in areas in which no use of OPV2 should have occurred [13,15]. In practical terms, countries faced challenges using the mOPV2 from the stockpile due to concerns about the risks of mOPV2 (i.e., mOPV2 hesitancy after the switch, despite modeling that supported its use), and perceived and real limitations on financial support for conducting oSIAs and/or shortages of filled mOPV2 doses in the stockpile from early 2018 onward. Building on prior work [4,16], modeling specific to Pakistan and Afghanistan in 2018 anticipated the need to manage outbreaks of serotypes 1 and 2, and recognized the potential benefits of using tOPV for outbreak response [17].

Recognizing the risks associated with mOPV2 use, which include VAPP and VDPVs [18], the GPEI partners supported efforts to develop novel OPV (nOPV) strains designed to be much less likely to both lose their attenuating mutations than Sabin strains and to revert toward more neurovirulent and transmissible viruses [19]. In early 2020, recognizing the challenges posed by cVDPV2 outbreaks, the GPEI released an addendum to its 2019–2023 strategic plan, which anticipated broad use of nOPV2 by any country for oSIAs by February 2021 [20]. The GPEI also recognized the risks of relying on a new and untested vaccine in limited supply and procured tOPV for use in Pakistan and Afghanistan and additional mOPV2, both bulk and filled.

Modeling of the polio endgame assumed that a failure to terminate all current VDPV2 transmission in the near future would lead to the restart of OPV2 use in routine immunization in OPV-using countries [11,12,15,21–23]. To implement OPV2 restart, recent modeling studies assumed that 5,000 cumulative cVDPV2 cases since OPV2 cessation (i.e., since early 2016) would trigger the decision to reintroduce OPV2 into routine immunization in OPV-using countries following a time delay sufficient to restart and ramp up production [15,23–27]. One of these analyses showed that nOPV2 is the better option than mOPV2 if its properties are ideal or if mOPV2 use is replaced with inactivated poliovirus vaccine (IPV) in 2024, considering a model time horizon of 2019–2029 [25]. Recognizing uncertainty about

the actual behavior of nOPV2, which we will observe only after widespread use in real populations, prior analyses use ideal (i.e., no reversion, no VAPP) and not ideal (i.e., some reversion, some VAPP) bounds to explore the nOPV2 characteristics [25,27]. Another study provides an updated analysis for the impacts of ideal and not ideal nOPV2 (as characterized in [25]) compared to mOPV2 for oSIAs, which explicitly considers the disruptions caused by COVID-19 and assumed resumption of pre-pandemic GPEI immunization activities on January 1, 2021 [27].

Consistent with the GPEI addendum to its strategic plan [20], many countries expected that they would be able to use nOPV2 for oSIAs as early as mid-2020. However, nOPV2 did not receive an Emergency Use Listing (EUL) until November 13, 2020 [28] and countries remained uncertain about their eligibility. Given the many criteria to meet the EUL requirements for first use of nOPV2 as a new vaccine (e.g., adverse events monitoring, enhanced poliovirus surveillance, no use of mOPV2 for outbreak response 12 weeks prior to using nOPV2) several countries began efforts to ensure their eligibility as they confirmed outbreaks [29]. As of Q1 2021, some countries in the World Health Organization (WHO) African Region (AFR) demonstrated hesitancy to use mOPV2 and delayed oSIAs due to a preference to wait for nOPV2. Given the complexity of the situation and the reality that the risks and benefits of nOPV2 use still remain uncertain [25], this analysis explores the effect of delaying oSIAs. We focus on modeling a hypothetical delay of oSIAs for cVDPV2s in AFR, which is the region most affected by cVDPV2s and by the delay in nOPV2 availability compared to what the GPEI initially planned [20]. Since the wild poliovirus type 1 endemic countries (Pakistan and Afghanistan) began using tOPV to control cVDPV2 outbreaks in 2020, and therefore are not delaying their planned SIAs waiting for nOPV2 [27], we do not consider any delays or issues with vaccine choices in the endemic countries in this analysis. For this analysis we focus on serotype 2, and we assume that preventive SIAs using bOPV occur in the same way as we assumed for a prior analysis [27] to facilitate direct comparison of the modeling results.

2. Methods

We apply an integrated global model for poliovirus transmission updated through the end of 2020 that simulates the current global situation of VDPV2 transmission and poliovirus vaccine use as previously described [27]. The model divides the global population into 72 blocks and organizes them by World Bank income level (low-income, lower middle-income, upper middle-income, and high-income) and the current polio vaccine use according to RI schedules (OPV+IPV with an IPV dose given simultaneously with the third OPV dose, sequential IPV/OPV schedule that gives IPV first followed by OPV, and IPV-only). The model further divides each of the 72 blocks into 10 subpopulations, representing the 2019 global population of approximately 7.2 billion people using 720 subpopulations of approximately 10.7 million each. The model groups the blocks into 9 preferential mixing areas, which represent larger geographical regions (e.g., Africa, Australasia, Europe). The model assumes homogeneous mixing within the subpopulation and heterogeneous mixing by age. To represent heterogeneity in mixing on the global level, the model allows for stochastic long-range exportations of viruses into other subpopulations in the same block or to subpopulations in other blocks based on assumptions about preferential mixing areas.

The model also includes potential stochastic risks of reintroductions from containment failures and other sources. The overall model structure supports a high-level representation of variability in transmission dynamics and values and preferences for investments in health interventions (see [24] and its associated technical appendix).

We begin with a companion analysis [27] that explored the impacts of replacing nOPV2 for mOPV2 in oSIAs assuming a complete switch on July 1, 2021, but not assuming any delays in oSIAs during 2021. Although the complete switch to nOPV2 depends on WHO prequalification of nOPV2 as a licensed vaccine for broad use and substantial ramp up of production (which requires processing time for licensure, prequalification, and production), we focused on the timing communicated by the GPEI in the addendum to the 2019–2023 strategic plan [20] and we used a hypothetical best case for our bounding analysis. Recognizing uncertainty about the actual behavior of nOPV2 that we will observe only after widespread use in real populations, we use the same bounding assumptions made by prior analyses to characterize nOPV2 as ideal (i.e., no reversion, no VAPP) or not ideal (i.e., some reversion, some VAPP) [25,27]. Since that analysis, we have observed the delay and cancellation of some oSIAs in some areas. With respect to outbreak response to cVDPV2s, countries weighed the promise of forthcoming nOPV2 against their perceived risks of using mOPV2, despite uncertainty about their eligibility under EUL criteria and nOPV2 supplies. The deliberation process contributed to many delays in oSIA scheduling as of early 2021. Thus, for this analysis we explore the implications of countries in one preferential mixing area (i.e., the 9 blocks in our model that represent conditions in African countries) delaying the start of oSIAs. We simulate those countries waiting preferentially for nOPV2 availability and approval for use (i.e., cancelling any scheduled mOPV2 oSIAs and not conducting any others in the model during January 1, 2021 to July 1, 2021). We also included an analysis for this effect in all non-endemic countries (e.g., assuming that cVDPV2 outbreak detection in a country like Tajikistan might lead to delayed oSIAs due to its potential preference to use nOPV2 and need to complete multiple sequential steps to become eligible to use nOPV2 under the EUL). In the model, this only affects the countries with outbreaks that scheduled or would have scheduled an oSIA during the first half of 2021. Despite our observation of some delayed and cancelled bOPV SIAs, we assume bOPV SIAs will occur in the same way as the companion analysis [27], and consequently we only focus on serotype 2 for this analysis.

We use the same assumptions used by prior work [25,27] of triggering a restart of OPV2 vaccine broadly once the model accumulates 5,000 cases since OPV2 cessation, and we implicitly assume unconstrained vaccine supplies for outbreak response (i.e., the model uses doses needed without consideration of supply). For all scenarios we characterize the expected number of polio cases and the probability of triggering an OPV2 restart. Table 1 summarizes the different scenarios and assumptions. To facilitate direct comparison with the prior analysis, we include the results for the scenarios COVID+mOPV2, COVID+nOPV2 (ideal), and COVID++nOPV2 (not ideal) from prior work, which start with “COVID” to indicate that the scenarios account for the disruptions that occurred in 2020 due to the COVID-19 pandemic and the challenges that the GPEI faced in 2020 on multiple fronts [27]. We then run the nOPV2 ideal and nOPV2 not ideal scenarios assuming no mOPV2 use between January 1 and July 1, 2021 (i.e., a 6-month delay) in the 9 blocks representing

the WHO African region as above (i.e., COVID+nOPV2 (ideal) AFR6 and COVID+nOPV2 (not ideal) AFR6 with 6 indicating the 6-month delay). We further extended this analysis by considering the impacts of more widespread delay assuming no mOPV2 use between January 1 and July 1, 2021 (i.e., a 6-month delay) in any non-endemic (NE) countries (i.e., COVID+nOPV2 (ideal) NE6 and COVID+nOPV2 (not ideal) NE6 (e.g., for any importations into countries like Tajikistan). We recognize that some countries that warranted oSIAs in 2020 began delaying implementing these oSIAs prior to January 1, 2021 (e.g., Republic of Congo, Chad, Liberia), partly due to the disruptions of the COVID-19 crisis, a desire to use nOPV2, and/or other factors (e.g., Ebola in DRC). In addition, some countries will perform outbreak responses prior to July 1, 2021, which would represent a scenario that would fall between the bounding cases of COVID +mOPV2 and COVID+nOPV2 (ideal) AFR6 (not modeled explicitly). For example, many African countries (i.e., Nigeria, Sudan, South Sudan, Guinea, the Democratic Republic of the Congo (DRC) and Mali already conducted mOPV2 oSIAs in 2021 (by April). Some minimal nOPV2 use also already began associated with field trials conducted to support its licensure in some countries (e.g., The Gambia and Bangladesh). Given uncertainty about what will actually occur prospectively, we focus on characterizing upper and lower bounds of what might occur given what we knew at the end of 2020 using some bounding scenarios and assumptions.

We code the model using the general-purpose programming language JAVA™ in the integrated development environment Eclipse™. We perform 100 stochastic iterations for each scenario using the Amazon Elastic Compute Cloud (Amazon EC2) and we control the stochastic introductions to facilitate comparability of the scenarios.

3. Results

Fig. 1 shows the expected values of the total number of global cVDPV2 cases based on 100 stochastic iterations of each scenario. The three baseline scenarios diverge after 2021 with COVID +nOPV2 (ideal) and COVID+nOPV2 (not ideal) bounding the mOPV2 results [27]. All of the delay scenarios show higher expected cVDPV2 cases in 2021 compared to their respective baseline (Fig. 1), with the extent of the increase depending on geographical scope (i.e., NE6 > AFR6). After an initial increase in expected cases in 2021, all of the delay scenarios show a decrease in cVDPV2 cases due the resumption of outbreak response after the 6-month delay, with the speed of the decrease depending on the properties of the nOPV2 (i.e., faster for ideal and slower for not ideal).

Table 2 summarizes some of the results for the entire time horizon (i.e., 2019–2023) for the 100 iterations of the same scenarios, for which Fig. 1 showed the expected values graphically by year. As shown in the second column, for the baseline scenarios with no delays in outbreak response, the model triggers an OPV2 restart (i.e., 5,000 cumulative cVDPV2 cases since OPV2 cessation) by the end of 2023 for 33, 27, and 38 of the 100 iterations for the COVID +mOPV2, COVID+nOPV2 (ideal) and COVID+nOPV2 (not ideal) scenarios, respectively [27]. (We note that the time horizon used for the model censors the number of restarts triggered, and longer time horizons lead to more restarts triggered until reaching the asymptote of 100%). The number of iterations that trigger an OPV2 restart increases with the 6-month delay in oSIA response and for larger geographical extent of the

delay (i.e., NE6 > AFR6 > no delay). The expected OPV2 restarts triggered associated with 6-month delays for the ideal nOPV2 scenarios increase significantly from 27 to over 45 ($p < 0.05$) and for the not ideal nOPV2 scenarios from 38 to over 50 ($p < 0.05$). The middle columns of Table 2 summarize the expected values, medians, and ranges of cVDPV2 cases in the AFR blocks and globally, the serotype 2 VAPP (VAPP2) cases, and total global cases for the entire time horizon (i.e., 2019–2023) for the 100 iterations. Notably, the number of cases that count toward the OPV2 restart does not vary during 2016–2020, and thus the increased OPV2 restart probabilities reflect differences in the oSIAs that occur during the first 6 months of 2021. The last columns in Table 2 report the expected values, medians, and ranges of doses of mOPV2 and nOPV2 used by the model during the entire time horizon.

Table 3 emphasizes the impact of the modeled strategies by presenting the difference between the expected value of cases for COVID+mOPV2 (used as a reference) and the expected value of cases for each other scenario for the entire time horizon, with the cases broken out by the AFR blocks, the rest of the blocks, and the global totals. The results suggest that nOPV2 is the best option if its properties are ideal (no reversion, no VAPP), but that stopping outbreak response to wait for nOPV2 for a period of 6 months may increase the expected cVDPV2 cases by more than 1,000 in the African region by end of 2023 compared to continuing to use mOPV2 promptly for oSIAs. In addition, uncertainty remains as to whether nOPV2 will exhibit properties more like those characterized by the model as ideal or not ideal. Overall, any delay in outbreak response increases the expected number of cVDPV2 cases, the risk of spread of cVDPV2 to additional subpopulations, the scale of outbreak response required, and the probability of needing to restart OPV2 broadly in preventive immunization.

4. Discussion

Although actual delays in response to cVDPV2 outbreaks and the availability of nOPV2 may vary among countries, our scenarios present upper and lower bounds of the expected impacts of delays in responding to outbreaks. In the worst-case scenario, no outbreak response during January-June 2021 increases the total expected cVDPV2 cases by as many as 1,300 in the African region during 2021–2023 (Table 3). The hesitancy and delay in using mOPV2 for outbreak response and a preference of some countries to wait for nOPV2 instead of responding with mOPV2 could increase the expected number of cVDPV2 cases, increase the spread of cVDPV2 to new geographies, increase the probability of triggering OPV2 restart, and increase the overall global demand for OPV2. We emphasize the nature of this analysis providing bounds as a function of what might occur, and not a representation of what will occur. Consequently, we anticipate that the actual experience would fall somewhere between the upper and lower bounds, and we hope that this analysis serves to emphasize the importance of responding to cVDPV2 outbreaks in 2021 quickly with whatever OPV2-containing vaccine is available.

The model insights come with limitations consistent with the model structure and assumptions (see [24] and its technical appendix for details about the general limitations of the model). Due to computational resource requirements for the model and the desire to expedite the analysis, we run only a limited number of stochastic iterations. We emphasize

that we control the scenarios to ensure their comparability and to limit the impacts of the number of iterations. As with all modeling studies, the time horizon and vaccination policies influence the results, and we refer readers to prior nOPV2 modeling that demonstrated the increased probabilities of OPV restart over a longer time horizon [25]. In the absence of definitive GPEI criteria for OPV2 restart, we assumed 5,000 cumulative cVDPV2 cases as a trigger consistent with prior modeling [15,23–27] (also see analysis in [11]). The actual criteria that would apply remain uncertain, and future work should explore the implications of different options (e.g., yearly incidence and/or geographic criteria in addition to or instead of cumulative cases). Considering the specific results of this analysis, what will actually happen in the future depends on the collection of choices made, and our prospective insights are intended to convey bounding analysis, not to identify the exact trajectory that will occur or the best possible path. No model can predict exactly what will occur prospectively, but some models can provide insights about the expected trade-offs of different choices and different characteristics of interventions (e.g., in this case, different potential characteristics of nOPV2 in the population). Our bounding analyses do not capture the reality that nOPV2 use will gradually replace mOPV2 use during the modeled time horizon, but we suggest that this would lead to results between the bounds. In addition, our results do not consider real constraints on vaccine supply, which might make it impossible for countries to use specific vaccines at the times or in quantities that they would ideally use them. Similarly, the nature of our modeled delay (i.e., allowing oSIAs to resume on July 1) implies some level of synchronization that may impact the dynamics within the region. The results also do not consider the possibility of nOPV2 ultimately failing to receive licensure or extension of the EUL (in the context of modeling a longer time horizon), which could result in the net effect of countries delaying mOPV2 response and then starting it after nOPV2 fails to become a real option. Currently, the GPEI anticipates the availability of sufficient quantities of WHO prequalified licensed nOPV2 for broad use in early 2023, which is much later than implied by the addendum to the 2019–2023 GPEI Strategic Plan [20]. As noted in the methods, we assumed that bOPV pSIAs occur prospectively (i.e., from 2021 on) as modeled previously [27]. However, if these do not occur (e.g., due to lack of resources or they become displaced due to countries conducting OPV2 oSIAs), then we note that this may affect the population immunity to transmission for serotypes 1 and 3 and the increased risks of cVDPV1 and cVDPV3 outbreaks longer term. Finally, due to the short time horizon, these results do not explore the full impacts of OPV2 restart.

The GPEI recently included tOPV in the global OPV stockpile for use in the endemic countries [30]. This raises the possibility of using tOPV more broadly. The results of this study confirm previous modeling that the GPEI is not on track to stop the transmission of cVDPV2 before 2023 with or without nOPV2, even if nOPV2 behaves ideally when used widely, unless there is improvement in outbreak response coverage and operational effectiveness (scope and timing). Future studies will need to model the actual events that occurred and other potential future strategies, including potential strategies for restarting OPV2-containing vaccines in preventive immunization (i.e., OPV2 restart).

5. Data Statement

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

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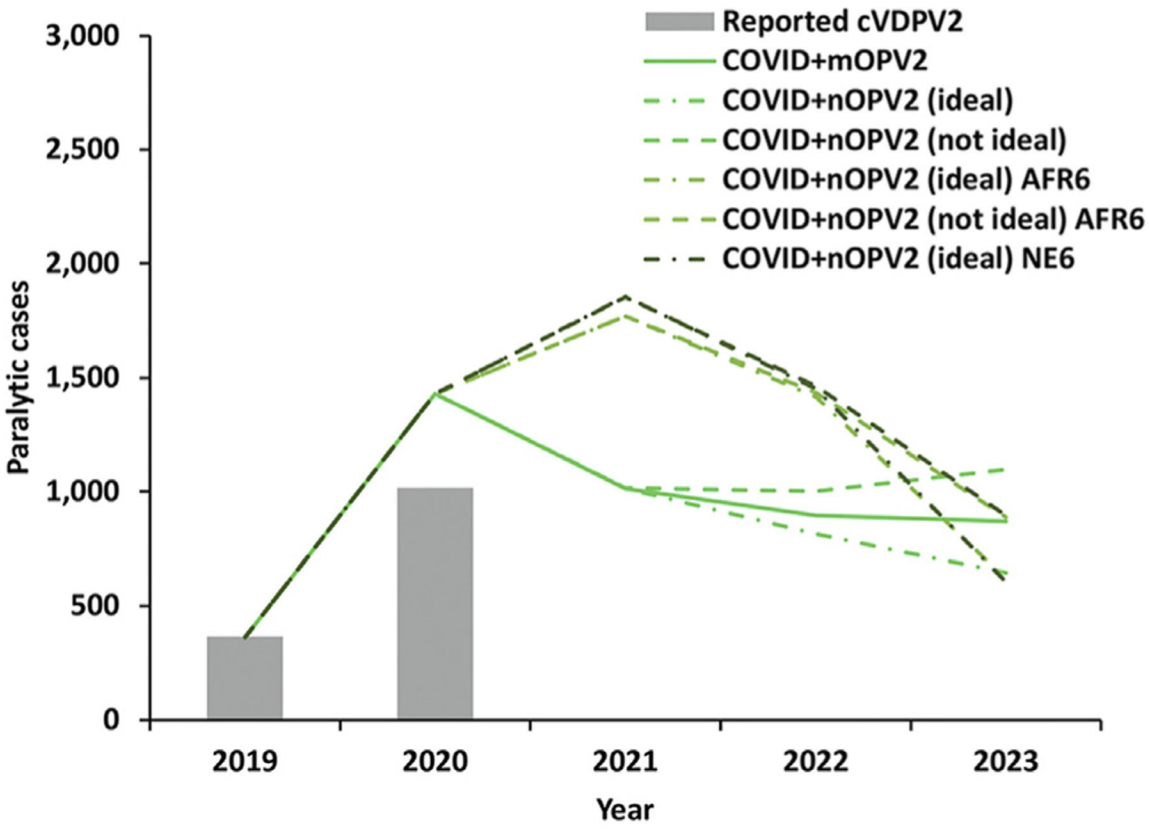

Fig. 1.

Expected global value of cVDPV2 cases by year for 100 stochastic iterations of the modeled scenarios for 2019–2023. Abbreviations: AFR6, 6-month delay in African region blocks; COVID, coronavirus disease 2019; cVDPV2, seroZtype 2 circulating vaccine-derived poliovirus; mOPV2, serotype 2 monovalent oral poliovirus vaccine (Sabin-strain); NE6, 6-month delay in non-endemic countries; nOPV2, serotype 2 novel oral poliovirus vaccine (candidate 1 [19]).

Table 1

Model assumptions used to characterize the impacts of the delays in outbreak response on poliovirus immunization and transmission.

Scenario	Characteristics of oSIA delay		
	Geographical scope	Start date	End date
Baseline			
COVID+mOPV2	NA		
COVID+nOPV2 (ideal)			
COVID+nOPV2 (not ideal)			
Alternative			
COVID+nOPV2 (ideal) AFR6		January 1	July 30
COVID+nOPV2 (not ideal) AFR6	9 blocks representing African region	January 1	July 30
COVID+nOPV2 (ideal) NE6		January 1	July 30
COVID+nOPV2 (not ideal) NE6	Blocks representing all non-endemic countries	January 1	July 30

Abbreviations: AFR, blocks representing countries in the African region; AFR6, 6-month delay in AFR; COVID, coronavirus disease 2019; mOPV2, serotype 2 monovalent oral poliovirus vaccine (Sabin-strain); NE, blocks representing non-endemic countries; NE6, 6-month delay in NE; nOPV2, serotype 2 novel oral poliovirus vaccine (candidate 1 [19]); oSIA, outbreak response supplementary immunization activities

Table 2

Restarts triggered, estimated expected value ((median) and [range]) of cVDPV2 cases and expected value ((median) and [range]) of vaccine use for outbreak response in 100 stochastic iterations for 2019–2023 for the scenarios modeled (see main text for descriptions).

Scenario	OPV2 restarts triggered (%)	Estimated expected AFR cVDPV2 cases (median) [range]	Estimated expected global cVDPV2 cases (median) [range]	Estimated expected global VAPP2 cases (median) [range]	Estimated expected total cases** (median) [range]	Estimated expected millions of oSIA doses used by vaccine type*** (median) [range]	
						mOPV2	nOPV2
COVID+mOPV2	33	3,549 (2,854) [444–10,326]	4,572 (3,807) [1,028–11,549]	16 (15) [10–27]	5,37 (4300) [1,494–12,737]	692 (679) [359–1,219]	NA
COVID+nOPV2 (ideal)	27	3,300 (2,679) [440–9,323]	4,266 (3,501) [897–11,677]	9 (9) [8–13]	4,657 (3,836) [1,070–11,862]	187 (182) [137–274]	358 (328) [175–737]
COVID+nOPV2 (not ideal)	38	3,878 (2,954) [525–10,914]	4,907 (3,885) [1,039–12,114]	16 (15) [10–25]	5,557 (4,364) [1,344–13,731]	187 (182) [137–274]	492 (504) [189–958]
COVID+nOPV2 (ideal) AFR6	46*	4,562 (3,618) [756–12,183]	5,596 (4,727) [1,327–13,774]	8 (8) [7–11]	5,914 (5,093) [1,552–14,078]	155 (153) [119–215]	406 (362) [204–771]
COVID+nOPV2 (not ideal) AFR6	51*	4,871 (3,785) [770–11,200]	5,887 (5,009) [1,257–15,501]	16 (16) [11–28]	6,442 (5,778) [1,861–15,914]	155 (153) [119–215]	520 (536) [204–1,066]
COVID+nOPV2 (ideal) NE6	48*	4,584 (3,705) [756–12,183]	5,705 (4,828) [1,327–13,995]	10 (10) [6–16]	6,031 (5,163) [1,551–14,300]	153 (153) [119–191]	411 (368) [204–787]
COVID+nOPV2 (not ideal) NE6	52*	4,835 (3,780) [770–11,200]	6,005 (5,049) [1,257–15,684]	16 (16) [11–28]	6,582 (5,786) [1,861–16,039]	153 (153) [119–191]	529 (536) [204–1,065]

Abbreviations: AFR6, 6-month delay in blocks representing countries in the African region; COVID, coronavirus disease 2019; cVDPV2, serotype 2 circulating vaccine-derived poliovirus; mOPV2, serotype 2 monovalent oral poliovirus vaccine (Sabin-strain); NE6, 6-month delay in blocks representing non-endemic countries; nOPV2, serotype 2 novel oral poliovirus vaccine (candidate 1[19]), VAPP2, serotype 2 vaccine-associated paralytic polio.

*Restarts triggered differ significantly compared to the same ideal or not ideal scenario with no delay (i.e., 46 and 48 restarts triggered for COVID+nOPV2 (ideal) AFR6 and COVID+nOPV2 (ideal) NE6 statistically significant compared to 27 restarts triggered COVID+nOPV2 (ideal)).

**Includes all type 2 cases (i.e., totals from all infections with live polioviruses, including WPV, VDPVs, and VAPP, which sums to more than the prior two columns due to cases associated with OPV-related viruses and cases associated with rare, but non-zero stochastic risks such as containment breaches)

***Includes doses for the entire time horizon such that all scenarios include mOPV2 use through December 31, 2021.

Table 3

Difference in estimated expected value of cVDPV2 cases relative to COVID+mOPV2 scenario in 100 stochastic iterations for 2019–2023 for the scenarios modeled (see main text for descriptions).

	Estimated expected cVDPV2 cases		
	AFR	**Non-AFR**	**Global**
COVID+mOPV2	0	0	0
COVID+nOPV2 (ideal)	−249	−57	−306
COVID+nOPV2 (not ideal)	329	6	335
COVID+nOPV2 (ideal) AFR6	1,013	12	1,024
COVID+nOPV2 (not ideal) AFR6	1,322	−7	1,315
COVID+nOPV2 (ideal) NE6	1,035	98	1,133
COVID+nOPV2 (not ideal) NE6	1,286	147	1,433

Abbreviations: AFR, blocks representing countries in the African region; AFR6, 6-month delay in AFR; COVID, coronavirus disease 2019; cVDPV2, serotype 2 circulating vaccine-derived poliovirus; mOPV2, serotype 2 monovalent oral poliovirus vaccine (Sabin-strain); NE, blocks representing non-endemic countries; NE6, 6-month delay in NE; nOPV2, serotype 2 novel oral poliovirus vaccine (candidate 1 [19]).