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Modeling scenarios for ending poliovirus transmission in Pakistan and Afghanistan

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Abstract

Pakistan and Afghanistan pose risks for international transmission of polioviruses as the last global reservoir for wild poliovirus type 1 (WPV1) and a reservoir for type 2 circulating vaccine-derived polioviruses (cVDPV2s). Widespread transmission of WPV1 and cVDPV2 in 2019-2020 and resumption of intensive supplemental immunization activities (SIAs) in 2020-2021 using oral poliovirus vaccine (OPV) led to decreased transmission of WPV1 and cVDPV2 as of the end of 2021. Using an established dynamic disease transmission model, we explore multiple bounding scenarios with varying intensities of SIAs using bivalent OPV (bOPV) and/or trivalent tOPV (tOPV) to characterize potential die out of transmission. This analysis demonstrates potential sets of actions that may lead to elimination of poliovirus transmission in Pakistan and/or Afghanistan. Some modeled scenarios suggest that Pakistan and Afghanistan could increase population immunity to levels high enough to eliminate transmission, and if maintained, achieve WPV1 and cVDPV2 elimination as early as 2022. This requires intensive and proactive OPV SIAs to prevent transmission, instead of surveillance followed by reactive outbreak response. The reduction of cases observed in 2021 may lead to a false sense of security that polio has already or soon will die out on its own, but relaxation of immunization activities runs the risk of lowering population immunity to, or below, the minimum die-out threshold such that transmission continues. Transmission modeling may play a key role in managing expectations and supporting future modeling about the confidence of no virus circulation in anticipation of global certification decisions.

Social media blurb:

Modeling suggests the need for more intensive immunization to stop the transmission of type 1 wild polioviruses in Pakistan or Afghanistan and prevent the global risks of exportation like the 2022 cases reported in Malawi and Mozambique

Keywords

polio; eradication; dynamic modeling; Pakistan; Afghanistan; oral poliovirus vaccine

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1. Introduction

Prospective integrated modeling studies of poliovirus transmission and economics, as reviewed elsewhere (Thompson & Kalkowska, 2020) helped to inform numerous strategic decisions made by the Global Polio Eradication Initiative (GPEI), but the GPEI also took some actions that differed from those recommended by modeling and modeling groups did not always recommend the same strategies (Thompson & Kalkowska, 2021). Multiple modeling studies by different groups specifically highlighted the importance of responding quickly to outbreaks (Thompson & Kalkowska, 2020, see section 5.1) and the critical role of undervaccinated subpopulations and 'weak links' in sustaining transmission (Thompson & Kalkowska, 2020, see section 5.6), Now over 20 years late on delivering polio eradication, the GPEI seeks to stop the transmission of type 1 wild poliovirus (WPV1) in Pakistan and Afghanistan (Hsu et al., 2020), as well as the vaccine-derived polioviruses (VDPVs) of all three types. Following the globally coordinated cessation of oral poliovirus vaccine (OPV) containing type 2 (OPV2) in early 2016, type 2 circulating VDPVs (cVDPV2s) emerged in some countries, including Pakistan in 2019, which exported it to Afghanistan in 2020 and Tajikistan in 2021 (World Health Organization Global Polio Eradication Initiative, 2022). As the last global reservoir for WPV1, Pakistan and Afghanistan pose risks for international transmission of WPV1 despite international health regulations (Duintjer Tebbens & Thompson, 2017). Notably, in 2022 (as of the end of May), two African countries reported reintroduction of transmission of WPV1 strains genetically linked to Pakistan, with Malawi reporting a case with paralysis onset in November 2021 and Mozambique reporting a case with paralysis onset in March 2022 (World Health Organization, 2022). For the African region to maintain its 2020 certification as free of all WPVs (World Health Organization, 2020), all transmission of WPV1 will need to stop in all outbreak countries with 12 months. Management of WPV reintroduction risks and cVDPV risks requires maintenance of preventive SIAs until homotypic OPV cessation (Duintjer Tebbens, Hampton, Wassilak, et al., 2016; Thompson, Kalkowska, & Duintjer Tebbens, 2015), but investments and actual performance of preventive SIAs using bivalent OPV (bOPV, containing types 1 and 3) have decreased since 2016 (Kalkowska & Thompson, 2021a; Kalkowska, Wassilak, Cochi, Pallansch, & Thompson, 2021).

Numerous prospective modeling studies for Pakistan and Afghanistan emphasized the importance of proactive immunization activities using OPV to maximize population immunity to transmission (Thompson, Pallansch, Duintjer Tebbens, Wassilak, & Cochi, 2013) to prevent poliovirus spread before cases can occur (Duintjer Tebbens et al., 2018; Duintjer Tebbens & Thompson, 2019; Kalkowska, Duintjer Tebbens, Pallansch, & Thompson, 2019; Kalkowska, Duintjer Tebbens, & Thompson, 2019; Kalkowska, Pallansch, Cochi, & Thompson, 2021b; Kalkowska & Thompson, 2021b). These studies encouraged more aggressive immunization activities, similar to prior modeling that demonstrated the need for more intensive immunization to stop transmission in India (Thompson & Duintjer Tebbens, 2007). Notably, prior modeling demonstrated the relationship between the intensity of immunization and the time required to stop transmission (see Figure 1 in (Thompson & Duintjer Tebbens, 2007)). Most significantly, these studies demonstrate an essential concept: immunization coverage levels must exceed the threshold implied for die out and remain

above this minimum level for a sufficient duration of time for die out to occur (Thompson & Duintjer Tebbens, 2007). Thus, a modeling threshold for die out of transmission corresponds to a minimum immunity level that populations must exceed and remain above, not a target to reach. In addition, the seasonal nature of poliovirus transmission implies a time-varying threshold (Duintjer Tebbens et al., 2013).

Modeling of Pakistan and Afghanistan (Thompson & Duintjer Tebbens, 2017b) demonstrated the need to overcome underperforming vaccination campaigns and the substantial role of undervaccinated, repeatedly missed subpopulations in maintaining transmission (Duintjer Tebbens, Kalkowska, & Thompson, 2019; Thompson & Duintjer Tebbens, 2017b). Notably, substantial subnational variability can exist in immunization coverage rates, and while national averaging may suggest immunization coverage that exceeds the threshold for die out, there continues to be low coverage in some sufficiently large subpopulations. This may allow for either sustained transmission (i.e., no die out in those populations) or local die out that restarts transmission upon reintroduction from other subpopulations that mix to some degree (Duintjer Tebbens et al., 2019). The degree of isolation of the undervaccinated subpopulation will impact the extent to which secondary spread from the general population can offset lower coverage in the undervaccinated subpopulation (Duintjer Tebbens et al., 2019). Modeling also demonstrated the need for very high population immunity prior to the cessation of OPV to prevent the emergence and transmission of cVDPV2s (Thompson & Duintjer Tebbens, 2014) and the need for rapid, high coverage, and sufficiently large scope outbreak response using OPV2 to end any cVDPV2 outbreaks that emerged after OPV2 cessation (Duintjer Tebbens, Pallansch, Wassilak, Cochi, & Thompson, 2016).

The source of the emergence of cVDPV2 cases in Pakistan in 2019 (Kalkowska, Pallansch, Cochi, Kovacs, et al., 2021; Macklin et al., 2020) remains unexplained and led us to update the characterization of increased risks related to OPV cessation (Kalkowska, Pallansch, Cochi, Kovacs, et al., 2021). Prior modeling assumed the introduction of partially reverted OPV in the first half of 2019 (Kalkowska, Pallansch, Cochi, Kovacs, et al., 2021; Kalkowska, Pallansch, Cochi, et al., 2021b), and anticipated additional information as investigations occurred that would better inform the modeling inputs. Prior modeling anticipated this risk and characterized the increasing vulnerability of populations to outbreaks from this risk as a function of time since OPV2 cessation (Duintjer Tebbens, Hampton, & Thompson, 2016).

Global polio transmission modeling performed before (Kalkowska, Pallansch, Cochi, Kovacs, et al., 2021; Kalkowska, Wassilak, et al., 2021) and after (Kalkowska, Voorman, et al., 2021) the disruptions of global activities caused by the COVID-19 pandemic estimated that transmission of WPV1 and cVDPV2 would likely continue in Pakistan and Afghanistan. Pre-OPV2 cessation (Duintjer Tebbens, Hampton, & Thompson, 2016; Duintjer Tebbens, Pallansch, et al., 2016) and post-OPV2 cessation modeling (Duintjer Tebbens et al., 2018; Thompson & Duintjer Tebbens, 2017a) identified the important potential role of using trivalent OPV (tOPV, containing all 3 types of OPV) after OPV2 cessation for outbreak response to manage transmission of both WPV1 and cVDPV2, if needed. In late 2020 and early 2021, Pakistan and Afghanistan began using tOPV for some SIAs, which dramatically

decreased reported cases for both WPV1 and cVDPV2 in 2021. The disruptions in national and international travel caused by the COVID-19 pandemic, combined with changes in interpersonal mixing and contacts, slowed the transmission of both WPV1 and cVDPV2 overall (Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska, Voorman, et al., 2021). Pandemic disruptions in immunization activities also decreased immunological protection. As mixing and travel resume, gaps in immunity will pose a risk for resurgence for transmission.

Reflecting the changing epidemiological and geopolitical situations in Pakistan and Afghanistan, and their importance for polio eradication, we updated our poliovirus transmission model for Pakistan and Afghanistan to reflect the available epidemiological and immunization evidence through August 31, 2021, and we use the updated model to explore multiple options for prospective immunization activities that would lead to ending transmission (or not) in these two countries.

2. Methods

We use a previously developed deterministic differential equation-based (DEB) poliovirus transmission and OPV evolution model for Pakistan and Afghanistan that includes 4 subpopulations, with each country divided into a general population and an undervaccinated subpopulation (Duintjer Tebbens et al., 2018; Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b). For technical details about the deterministic DEB model, see the appendix of (Kalkowska, Wassilak, et al., 2021). The undervaccinated population represents a conceptual construct that aggregates all of the historically low immunization coverage communities from different parts of each country (including mobile populations) regardless of geography. Thus, although both countries include 2 distinct known transmission reservoirs and some variable fraction (over time) of the population in Afghanistan inaccessible to vaccinators (Hsu et al., 2020), the transmission model abstractly captures the net effect of the low immunization coverage in these populations as part of the undervaccinated population. As previously estimated, we assume the undervaccinated subpopulation represents a fraction of the total population (5% for Pakistan and 10% for Afghanistan) (Duintjer Tebbens et al., 2018; Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b). The model divides the people in each subpopulation according to eight immunity states representing fully susceptible, maternally immune, and six partially immune states following live poliovirus infections (WPV and/or OPV), and/or successful inactivated poliovirus vaccine (IPV) vaccination (Duintjer Tebbens et al., 2018; Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b). The model describes waning of immunity as a five-stage process, infection as a process with 2 latent and 4 infectious stages for both fecal-oral and oral-oral transmission, and OPV evolution as a 20-stage process (i.e., stage 0 for fully attenuated Sabin strains to stage 19 for fully reverted cVDPV strains that behave with the same transmissibility and neurovirulence as WPVs) (Duintjer Tebbens et al., 2018; Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b). The top of Table 1 summarizes the general inputs for Pakistan and Afghanistan related to the model population structure, poliovirus transmission dynamics, and vaccination assumptions that remain constant for all modeled scenarios. In the absence of better information or a genetic signal that would support our prior assumption

of a partially reverted OPV strain (Kalkowska, Pallansch, Cochi, et al., 2021b) instead of fully attenuated OPV (i.e., unexpected use of OPV containing type 2), we now assume that inadvertent use of OPV2 in either campaigns or routine immunization (Duintjer Tebbens, Hampton, & Thompson, 2016) represented the most likely mechanism for reintroduction of type 2 in Pakistan in 2019.

Prior modeling performed in mid-2020 assumed full recovery to pre-COVID-19 levels of mixing and travel prior to September 1, 2020 (Kalkowska, Pallansch, Cochi, et al., 2021b). Consistent with the observed and continued reduction in travel related to the COVID-19 pandemic, we extended the intensification of isolation and the reduction in average R_0 through August 31, 2021. Although changes in Afghanistan leadership in August 2021 leads to substantial uncertainties with respect to projections, for this exploratory analysis of options, we assume no change in immunization quality or practices for the base case. This assumption implies no substantial improvements in immunization quality or practices during 2021, despite commitments by the governments in both countries to improve quality upon resumption of polio immunization activities in mid-2020. The bottom of Table 1 summarizes the updated model inputs used to characterize the COVID-19 disruptions and changes in Afghanistan leadership, while Table 2 summarizes the mixing matrices assumed for the four subpopulations in Pakistan and Afghanistan over time (Kalkowska, Pallansch, Cochi, et al., 2021b).

In the present model, we updated the COVID-19-related mixing and travel restriction time periods and added intermediate mixing levels during the extended period to better reflect the gradual resumption of activities in both countries (Table 2c and 2e). We also updated the model assumptions for immunization inputs to reflect the actual experience with OPV and IPV through 2021 and GPEI prospective plans (World Health Organization Global Polio Eradication Initiative, 2021). Specifically, we started with the list of SIAs in our last model of Pakistan and Afghanistan (Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b) and we reconstructed the timing, scope, and vaccine choice for the SIAs actually conducted in Pakistan and Afghanistan since the beginning of 2019 through August 2021. Given both uncertainty about actual true coverage of the rounds and the number of children repeatedly missed as well as the “mapping” of actual SIAs that occur on different scales (i.e., national, subnational, outbreak populations) to our abstract subpopulations, we make assumptions for coverage and the probability of repeatedly miss (P_{RM}) of the same children from SIA round to round to reproduce the reported incidence. This process of fitting takes the dates, vaccine choice, target population size, and information about reported coverage, which we then assign to our general population and/or undervaccinated subpopulation, as appropriate. The model uses these to characterize the probability of repeatedly reaching (P_{RR}) the same kids from one SIA to the next, which relates to the reach (i.e., the lower the P_{RM}, the higher the reach). For any given coverage, which factors in the size of the target population, the probability of repeatedly reaching the same kids is constrained such that high overall coverage means fewer children missed overall, therefore the P_{RM} cannot lead to infeasible reach in any subpopulation ($P_{RR}<1$). For the model, we use the P_{RM} that reflects the greatest feasible reach. As occurred in 2021, we include actual use of tOPV in the SIA schedules during 2021 (Figure 1). For the prospective modeling, we assume Pakistan and Afghanistan will continue to perform the equivalent of 4.5 national

immunization days (NIDs) with OPV for 2022-2026. We provide NID equivalents because some of the SIAs will involve more subnational campaigns in some geographies and fewer in other geographies. Reflecting current information about the potential source of unexpected introduction of serotype 2 virus in Pakistan in 2019, we updated previously assumed point introductions of OPV-related virus occurring 10 days apart in the first half of 2019 at the OPV evolution model reversion stage 5 (consistent with partially reverted virus) (Kalkowska, Pallansch, Cochi, et al., 2021b) to introductions at the model reversion stage 0 (consistent with Sabin virus used as point introductions that simulate supplemental immunization activities (SIAs) or as routine immunization (RI)) (Duintjer Tebbens, Hampton, & Thompson, 2016). We also simplified the cross-the-border movement leading to introduction of VDPV2 virus from Pakistan to Afghanistan in February 2020 by introducing 5 individuals (one per each age group older than 3 months and under 5 years of age) at reversion stage 10.

Table 3 shows the different schedules we considered for modeling prospective SIAs in both countries and shows different assumptions for immunization inputs related to coverage. For the base case (BC) or *status quo*, we assume both countries will use bOPV for all SIAs, except for their use of tOPV in some rounds in 2021 and 2022 consistent with current national plans. We assume the same estimates for immunization model inputs (i.e., true coverage and repeatedly missed probabilities (P_{RM} values) (Kalkowska, Wassilak, et al., 2021) from 2022 through the remainder of the time horizon (through December 31, 2026).

Table 4 lists the assumptions for the alternative scenarios we considered with a prospective focus for 2022-2026. We organized the alternative scenarios according to several different themes, which we indicate in Table 4 using small Roman numerals. First, we ask what would need to occur if the coverage, quality, and number of NID equivalent SIAs remains fixed for the time horizon. This theme assumes that quality and total number of SIAs (22.5 NID-equivalent SIAs for 2022-2026) would match the BC. This represents a concept of a financial constraint on the total number of rounds over the 5 years, but no constraints on timing or availability of vaccine. We explored this theme by running: (i) “base, all tOPV, fixed,” which maintains the same schedule as the BC, except it uses tOPV for all SIAs (instead of bOPV), (ii) “compressed, fixed,” which maintains the same cumulative target population over each the year as the BC (equivalent to ~4.5 rounds), but compresses all rounds to occur one month apart at the beginning of each year, (iii) “compressed, all tOPV, fixed,” which maintains the same schedule as the “compressed, fixed” scenario but uses tOPV for all SIAs, (iv) “aggressive, fixed,” which assumes a total of 22.5 NID equivalent SIAs for the 5-year time horizon, but uses monthly NIDs with bOPV from 2022 until elimination of WPV1 followed by conduct of the remaining available equivalent NIDs as rounds evenly distributed in the remaining years of the time horizon, (v) “aggressive, all tOPV, fixed,” which uses the same approach as the “aggressive, fixed” scenario but uses tOPV, and (vi) “aggressive, tOPV then bOPV,” which uses the same approach as the “aggressive, all tOPV, fixed” scenario until elimination of cVDPV2 followed by the “aggressive, fixed” scenario for the remaining years of the time horizon. For the “aggressive, tOPV then bOPV” scenario (v), we recognized the potential to include more than 2 tOPV rounds in 2022 before shifting to bOPV for the remainder of the time horizon. Consequently, we included “aggressive #x, tOPV then bOPV” scenarios (vi), that use # tOPV rounds

followed by bOPV rounds and for which we focused on identifying the minimum reach and coverage required to stop transmission of both WPV1 and cVDPV2 for the # initial tOPV rounds.

Second, we ask what would need to occur if the coverage and quality of the SIAs remains fixed, for which increasing the frequency of rounds starting in 2022 would represent the primary opportunity to increase population immunity. This theme implicitly assumes that quality would neither increase nor decrease with a change in the number of SIAs. We explored this theme by running (vii) “monthly SIAs, fixed” until successful die out, assuming the inclusion of two rounds with tOPV each year (and the rest bOPV) until the disruption of cVDPV2, (viii) “mixed, fixed,” which uses the same approach as the “monthly SIAs, fixed” scenario, except with every other round only targeting the undervaccinated subpopulation, and (ix) “mixed, all tOPV, fixed” which uses the same approach as the “mixed, fixed” scenario but uses only tOPV.

Building on the insights from prior modeling and current programmatic emphasis on improving coverage and identifying and reaching missed children, the third theme maintains the same number, vaccine type, and timing of rounds as the BC, but increases the coverage and/or reach of repeated missed probability to explore the potential for increases in campaign quality. For this theme, we consider multiple scenarios: (x) “increased coverage,” (xi) “increased reach” of repeatedly missed children, and (xii) increased reach and coverage, which we label as “IRC.” As shown in Table 4, for each of these we explore the different ranges of reach and coverage increases starting in 2022, with the coverage assumption in the undervaccinated subpopulation shown after “IRC” in the scenario name. For the “increased coverage” scenarios, we keep the probability of repeated miss (P_{RM}) constant and change the coverage in the undervaccinated population to the level shown, whereas for the “increased reach” scenario, we maintain the coverage of the base case, but use the lowest possible P_{RM} feasible, which corresponds to the highest potential reach of undervaccinated children. For the IRC scenarios, for each level of coverage, we use the lowest possible P_{RM} feasible for the assumed coverage. After resuming polio immunization activities following the disruptions caused by COVID-19, efforts to improve reach and coverage in undervaccinated populations represented programmatic priorities. This led us to explore the potential impacts of earlier quality improvements using the “IRC” scenario but for starting the improvements on (xiii) October 2020 or (xiv) January 2021).

Finally, we further explore combinations of monthly SIAs with increased coverage and/or reach. For this theme, we consider multiple scenarios: (xv) “Monthly SIAs, increased coverage 80,” which increases the coverage up to 80%, (xvi) “Monthly SIAs, increased reach,” which increase the reach of repeatedly missed children, and (xvii) “Monthly SIAs, IRC 80.”

Similar to prior work reviewed elsewhere (Thompson & Kalkowska, 2020), we characterized population immunity to transmission by computing the effective immune proportion adjusted for age and subpopulation mixing (EIPM), with a time-varying effective immunity threshold EIP* calculated as $[1-(1/R_0(t))]$, which represents the minimum level that must be exceeded for an extended period of time for infections to eventually die-out

(Duintjer Tebbens et al., 2018; Duintjer Tebbens et al., 2013) and reflects the time-varying R_0 that occurs with seasonality (Duintjer Tebbens et al., 2013). We also demonstrate the concept of normalization of the EIPM relative to the EIP* over time (Rn), which removes the visual effects of seasonality, and the relevant threshold (Rn*, corresponding to EIP*/EIP*) as a line at 1 (Kalkowska et al., 2015).

3. Results

Figure 2 compares the updated modeled paralytic incidence to reported poliovirus cases for 2016 through 2021 for Pakistan and Afghanistan for (a) type 1 and (b) type 2. The model slightly overestimates the 2020 WPV1 paralytic incidence for Pakistan (i.e., 114 modeled compared to 84 confirmed cases), and underestimates 2020 WPV1 paralytic incidence for Afghanistan (i.e., 45 modeled confirmed to 56 confirmed cases). The model closely estimates 2020 paralytic incidence from cVDPV2 for Pakistan (i.e., 139 modeled compared to 135 confirmed cases), and overestimates the 2020 cVDPV2 paralytic incidence for Afghanistan (i.e., 351 modeled compared to 308 confirmed cases). The results suggest some difference between the expected population immunity based on the model and the reported incidence of paralytic cases between late 2020 to mid-2021.

Table 4 summarizes the prospective scenarios considered (as described above) and the associated outcomes with respect to the timing of elimination of WPV1 and/or cVDPV2 for both countries. Some scenarios suggest that ending WPV1 transmission could occur by 2026, with or without stopping cVDPV2 transmission. With all of the modeled scenarios using bOPV or tOPV and no use of monovalent OPV2 (mOPV2) or novel OPV2 (nOPV2) for outbreak response, all scenarios that use enough tOPV to stop type 2 transmission also stop type 1.

Figure 3 compares the modeled paralytic incidence of the first theme with “base, all tOPV, fixed” (dotted lines), “compressed, fixed” (short dashed lines), “compressed, all tOPV, fixed” (long dashed lines), “aggressive, fixed” (dotted-dashed lines), and “aggressive, all tOPV, fixed” (double dotted-dashed lines), to the BC (solid lines) for 2019 through 2026 for Pakistan and Afghanistan for (a) type 1 and (b) type 2. Figure 3(a) shows that performing the equivalent of 4.5 NIDs per year with the current quality will not eliminate WPV1 transmission regardless of the distribution of the rounds over the year (and the use of bOPV will not stop cVDPV2 transmission). Figure 3(a) also shows small differences in the WPV1 incidence associated with using tOPV instead of bOPV, but Figure 3(b) shows that using tOPV instead of bOPV dramatically reduces cVDPV2 transmission for the 4.5 NID equivalents, although it does not completely interrupt cVDPV2 transmission. Pursuing “aggressive” scenarios leads to the elimination of WPV1 regardless of the vaccine choice, while only the “aggressive, all tOPV, fixed” approach may also interrupt cVDPV2 transmission. However, we observe that continuing to introduce OPV2 into the population with continuing tOPV rounds after the elimination of both WPV1 and cVDPV2 with the current quality leads to seeding new transmission of OPV2-related viruses and to low levels of VDPV2 transmission throughout the time horizon (i.e., endemic VDPV2 transmission). Thus, using tOPV for SIAs in Pakistan and Afghanistan in perpetuity would logically motivate restarting tOPV use in RI (not modeled). This suggests that the best strategy for

achieving elimination of both cVDPV2 and WPV1 would be aggressive tOPV use until elimination of cVDPV2 by the end of 2022, followed by a bOPV maintenance schedule for WPV1 until global OPV cessation of all types, if available vaccine supplies support this approach. With current SIA quality, this scenario requires a minimum of 8 monthly tOPV rounds from January through August of 2022. However, this could be scaled down to as few as 3 monthly tOPV rounds from January through March of 2022 if both countries can achieve higher reach and coverage in the undervaccinated population (see scenarios (vi) in the top of Table 4 for the minimum levels required to achieve cVDPV2 elimination for the indicated number of tOPV rounds and the resulting elimination times). As the number of tOPV SIAs increases from 3 to 8 for these scenarios, the minimum coverage required to stop cVDPV2 transmission decreases, which occurs due to the increased use of the type 2-containing OPV in more rounds (results for permutations other the minimum not shown).

The middle section of Table 4 shows that performing monthly SIAs will eliminate WPV1 transmission (i.e., “mixed, fixed,” “mixed, all tOPV, fixed,” and “monthly SIAs, fixed”), however it will not stop cVDPV2 transmission without the use of more type 2 containing vaccine (i.e., “mixed, all tOPV, fixed”). Figure 4 compares the population immunity (i.e., EIPM) of the BC and “IRC” scenarios to the threshold (EIP*) for 2019 through 2026 for Pakistan and Afghanistan for (a) type 1 and (b) type 2. Figure 4 shows that increasing the reach and coverage in undervaccinated subpopulation will move population immunity over the threshold for long enough to eliminate WPV1 transmission (all scenarios that succeed shown in green), while none of the strategies will stop cVDPV2 transmission due to the lack of use of type 2 containing vaccine (scenarios that fail shown in red). Moreover, increasing coverage (and reach) increases intensity, and this leads to faster elimination (see bottom section of Table 4).

With respect to type 1, as shown in Table 4, increasing reach and coverage from earlier points in time (i.e., October 2020 or January 2021) instead of in January 2022 also leads to earlier elimination dates. Figure 5a shows the modeled incidence over time of WPV1 for 3 scenarios with the same assumed amounts of improvement in reach and coverage, but with 3 different starting times of improvement. As a result, the BC, which does not assume any improvements in coverage or reach and leads to incidence estimates that exceed the results for the other scenarios, may not properly represent the improvements that actually occurred. The scenarios that account for increased reach and coverage lead to dramatically lower modeled expected cases in 2021. As shown in Figures 5b and 5c, the IRC scenarios (shown in green) lead to WPV1 transmission die out, while the BC does not (shown in red). Uncertainty remains about the actual coverage improvements that may have occurred over time, but the scenarios in Figure 5 demonstrate that the abstract model can represent the potential impacts of quality improvements, and reproduce levels of incidence consistent with the encouraging epidemiological and surveillance evidence as of the end of 2021. Challenges with surveillance in some areas and delays in processing samples may lead to future detected events (i.e., reported AFP cases and/or positive environmental surveillance (ES) samples).

In contrast to the situation for type 1, the number of scenarios that achieve type 2 elimination within the time horizon are much more limited. Figure 6 compares the

EIPM of the BC (“solid line”), “aggressive, 8x tOPV then bOPV, fixed” (dotted lines), “aggressive, 3x tOPV then bOPV” (dashed dotted lines), and “monthly SIAs, increased reach and coverage” (dotted-dashed lines) scenarios to the EIP* (solid black line) for 2019 through 2026 for Pakistan and Afghanistan for type 2. While all three alternative scenarios increase population immunity to sufficiently high levels for long enough to eliminate cVDPV2 (shown in green) compared to the BC (shown in red), population immunity of the “aggressive, 8x tOPV then bOPV, fixed” and “aggressive, 3x tOPV then bOPV” scenarios drop to the level provided by routine IPV vaccination after die out of cVDPV2, due to the assumed switch from tOPV to bOPV for these scenarios. In contrast, “monthly SIAs, IRC” periodically brings the population immunity up to hover around the threshold following the continuing annual tOPV SIA rounds in January and February.

4. Discussion

Pakistan and Afghanistan face continued challenges with respect to eliminating transmission of both WPV1 and cVDPV2. Overall, population immunity in Pakistan and Afghanistan tends to hover around the national EIP* threshold, and raising population immunity higher will require more immunization intensity (i.e., better reach and coverage and/or more rounds) in the general population as well as the undervaccinated subpopulations. Our modeling does not address the specific varying challenges, which would likely necessitate different actions for some areas (i.e., specific programmatic shortcomings, accountability for performance, access, and hesitancy differ). Consistent with prior modeling, these results demonstrate that the key to ending transmission of polioviruses in Pakistan and Afghanistan is achieving high quality vaccination with type-specific OPV everywhere at the same time for long enough to ensure that any circulating strains die out. Although we achieve this in the abstract model using NIDs, in practice the geographies that regularly achieve very high coverage (e.g., over 90%) do not need to participate in all SIAs, and thus some SIAs could and would occur as subnational NIDs (as both countries perform now in the base case). The coverage estimated for the general population aggregates over the geospatial and temporal variabilities, and the values we estimate lead us to suggest that more NIDs (and thus more equivalent NIDs) would likely help to increase population immunity to transmission in Pakistan and Afghanistan, particularly in the context of our model that does not include any outbreak response activities. Prior analyses suggested some limitations of reliance on the average overall immunization quality indicators, which may not identify and motivate correction of focal shortcomings within both vaccinated and undervaccinated subpopulations (Kalkowska, Pallansch, Cochi, & Thompson, 2021a).

Population immunity will continue to hover around the threshold if OPV use continues, with WPV1 and/or cVDPV2 transmission dying out if population immunity exceeds the EIP* threshold and stays above it for sufficient time. After successful interruption of cVDPV2 and repeating cessation of type 2 containing OPV (i.e., switch from tOPV to bOPV after die out of cVDPV2), population immunity to transmission (Thompson et al., 2013) will drop to the level provided by IPV, which is not sufficient to prevent or stop transmission following potential future reintroduction (as occurred in 2019 in Pakistan and 2020 in Afghanistan, see Figure 6). Many potential options presented as scenario results in Table 4 (but not limited to these scenarios, which by design do not include outbreak response) suggest that successful

WPV1 and cVDPV2 elimination in Pakistan and Afghanistan may be possible by the end of 2022, provided availability of tOPV and willingness to ensure repeated and/or improved quality of immunization. Uncertainty about the amount of actual improvement in quality that occurred since Pakistan and Afghanistan restarted polio activities after disruptions caused by COVID-19 in late 2020 may imply that the actual current epidemiological situation is better than our modeled base case (as shown in the scenarios with earlier increases in reach and coverage in Table 4 and Figure 5).

Although the reduction of reported WPV1 cases for most of 2021 led some to hope that Pakistan and Afghanistan may have already succeeded in ending WPV1 transmission, continued ES signals, reported cases in both countries in early 2022 (World Health Organization, 2022), and experience from the past warrant caution. In 2017, optimism about low incidence led to speculation about WPV1 elimination, although modeling at the time suggested the need for more intensity of OPV immunization in Pakistan and Afghanistan (Duintjer Tebbens et al., 2018). The low level of poliovirus transmission at this phase of recovery after the COVID-19 pandemic provides an opportunity for Pakistan and Afghanistan to potentially achieve national polio elimination, ideally using tOPV to stop both WPV1 and cVDPV2. Counterintuitively, however, when incidence and the sense of urgency for aggressive action are low due to low disease incidence, countries have the best chance of achieving national elimination if they raise population immunity sufficiently over the threshold for die out to occur. From a modeling perspective using planned SIAs only, tOPV offers the best option for maintaining high population immunity levels for all 3 types. Further analyses should consider the potential use of mOPV2 and nOPV2 vaccines for outbreak response.

Efforts to improve quality should make die out of both types 1 and 2 occur more quickly. Although our BC scenario assumes that quality did not improve over time in the recent past, anecdotal evidence suggests that improvements made since the resumption of polio immunization activities after the post-COVID-19 pandemic pause (spring 2020) may have increased reach and coverage for some previously undervaccinated populations. If this occurred and were sustained, then the model results for scenarios with earlier increased reach and coverage (e.g., scenarios in Figure 5) may better represent current transmission dynamics and future potential trajectories. In August 2021, as the epidemiological reservoir of Pakistan and Afghanistan reached a period of over 6 months with no reported WPV1 cases in either country, some GPEI discussions began to consider the potential for undetected circulation and focus attention on the quality of surveillance information in the context of characterizing the level of confidence of no circulation as a function of time since the last reported WPV1 case. As of May 2022, to date, the longest time between reported WPV1 cases of 9 months corresponded to the time between a reported Pakistan case with onset of paralysis on January 27, 2021 to a reported Afghanistan case with onset of paralysis on October 20, 2021. With 6 reported WPV1 cases in Pakistan and 5 reported cases in Afghanistan between January 2021 and May 2022 (World Health Organization, 2022) and decreasing positive signals in ES in both countries, we updated our prospective modeling of Pakistan and Afghanistan. We separately applied the scenarios with increased reach and coverage in Figure 5 to perform stochastic modeling that may help to inform discussions

about confidence about no circulation of WPV1 in Pakistan and Afghanistan with longer times between reported cases (Kalkowska, Badizadegan, & Thompson, 2022).

This analysis comes with several limitations. First, as with prior prospective models, the results depend on available information, the model structure, and our assumptions, including those related to reconstructing the immunization histories, the 2019 reintroduction of type 2 OPV into Pakistan, and expected future actions (Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska, Wassilak, et al., 2021). Second, this modeling assumes unlimited vaccine supplies for use in Pakistan and Afghanistan, although real constraints exist on global supplies of OPV vaccines. We focused much of our analysis on some scenarios that assume the same total number of OPV doses, and explore the impacts of changes in the OPV formulation and timing of its use, which implicitly holds constant the vaccine administration and purchase costs and demand for doses. Third, the model represents each country using a high level of abstraction and assuming homogeneous mixing within subpopulations, which may imply rapid transmission across relatively large groups of individuals, although we include heterogeneous age mixing and mixing between the subpopulations by applying mixing matrices that limit transmission to some degree. Fourth, we rely on a deterministic DEB transmission and OPV evolution model that reproduces average poliovirus transmission dynamics consistent with the abstract level of the model. Fifth, our model does not seek to capture population micro dynamics that may stochastically impact die-out of transmission and re-introduction of transmission due to imported infectious individuals, and instead it uses deterministic constructs for these. Similarly, the model structure cannot identify critical aspects of the stochastic nature of transmission events in the real populations in Afghanistan or Pakistan. Its representation of one undervaccinated modeled subpopulation in each country abstractly characterizes substantial time-varying heterogeneity in vaccine coverage without regard to the different root causes for undervaccination (e.g., lack of access to populations in disrupted and disputed geographies, nonacceptance of polio vaccines, etc.). Sixth, the geopolitical situation in Afghanistan changed substantially in the summer of 2021, and this may both impact the geopolitical situation in Pakistan relevant to polio transmission areas and necessitate further modeling that uses different assumptions about reach and coverage in both countries. Finally, although we modeled all of 2022 prospectively, as of May 2022, the actual and planned SIAs for both countries appear consistent with the 4.5 SIAs in the BC, with no tOPV rounds in 2022, which implies insufficient population immunity for both types to ensure the disruption of transmission. Due to continued uncertainty about the actual reach and coverage, the model may under-estimate the actual population immunity in one of both countries, and die out of transmission may occur. Notably, the stochastic nature of transmission may lead to die out with different timing than implied by the model. However, the model may also prove correct, if the current trajectory continues, or, both countries may decide to increase their SIAs during 2022 to change their current paths.

As countries and GPEI develop and evaluate future options and strategies, the choices made and policies negotiated at the global and/or regional level may affect the preferences for options at the national level. For example, global policy related to OPV cessation will impact national plans and preferences for OPV use, in addition to impacting the availability of different vaccines. As shown in Figure 6, the choice to complete global

OPV cessation, even with continued IPV use, will likely lead to population immunity levels for which any introductions of live OPVs may restart transmission, as occurred in 2019. OPV cessation, like WPV eradication, represents an all or nothing opportunity, for which global health leaders will need to finish the job by ultimately achieving containment of all live polioviruses. Further modeling studies will need to consider the potential impacts of outbreak response rounds for type 2 (i.e., mOPV2 or nOPV2 during the time horizon), and the potential for using more tOPV instead of bOPV for SIAs or more doses of IPV in RI.

5. Conclusions

As the number of reported polio cases decreases in Pakistan and/or Afghanistan, transmission modeling may play a key role in managing expectations and supporting characterizations about the confidence of no circulation as a function of time since the detection of cases and/or environmental surveillance signals of transmission.

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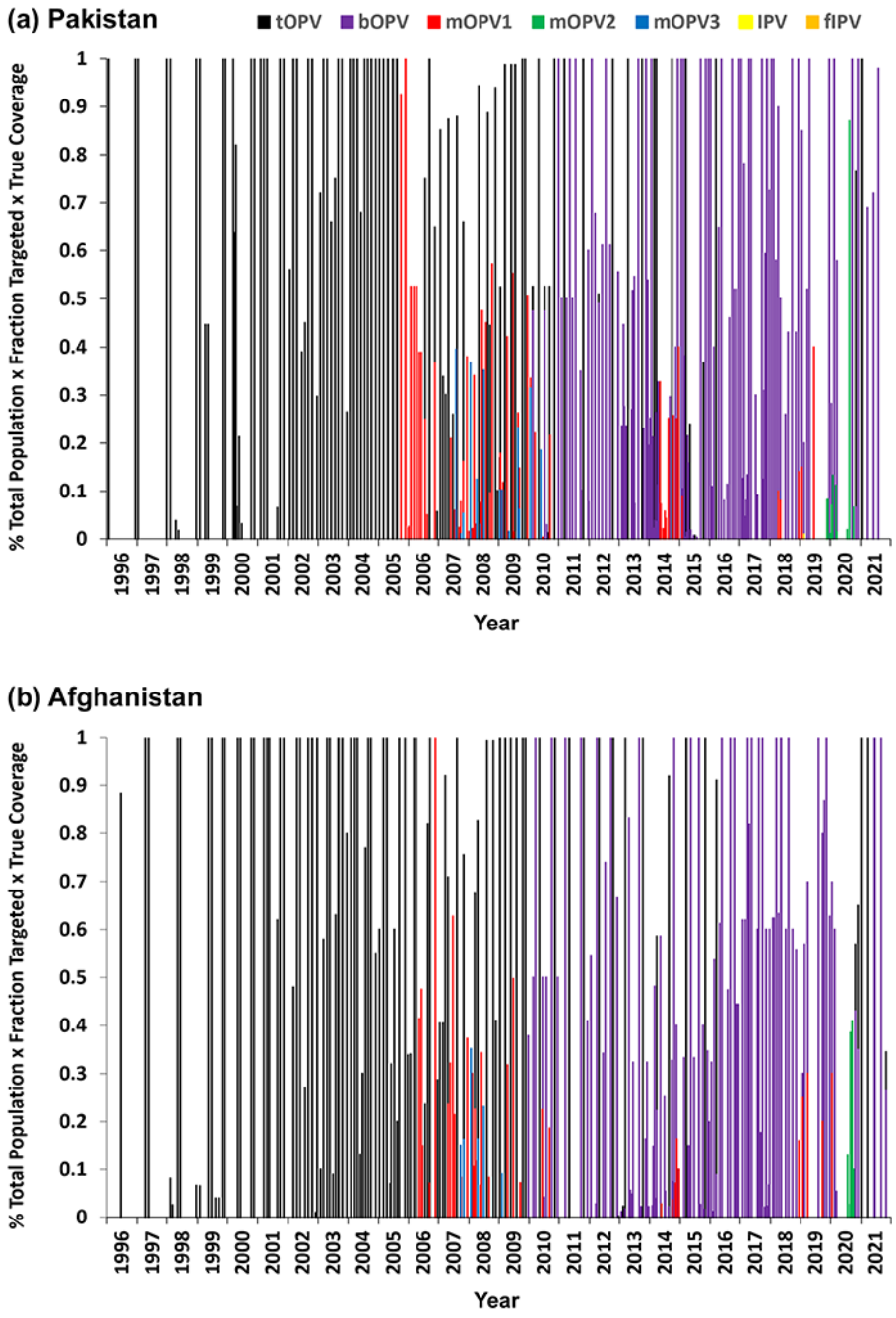

Figure 1.

Historical supplementary immunization activities (SIAs) by type of vaccine used and fraction of the population targeted

Abbreviations: fPV, fractional IPV; IPV, inactivated poliovirus vaccine; bOPV, bivalent OPV; mOPV(1,2,3), monovalent OPV (type 1, 2, 3 containing); OPV, oral poliovirus vaccine; tOPV, trivalent OPV.

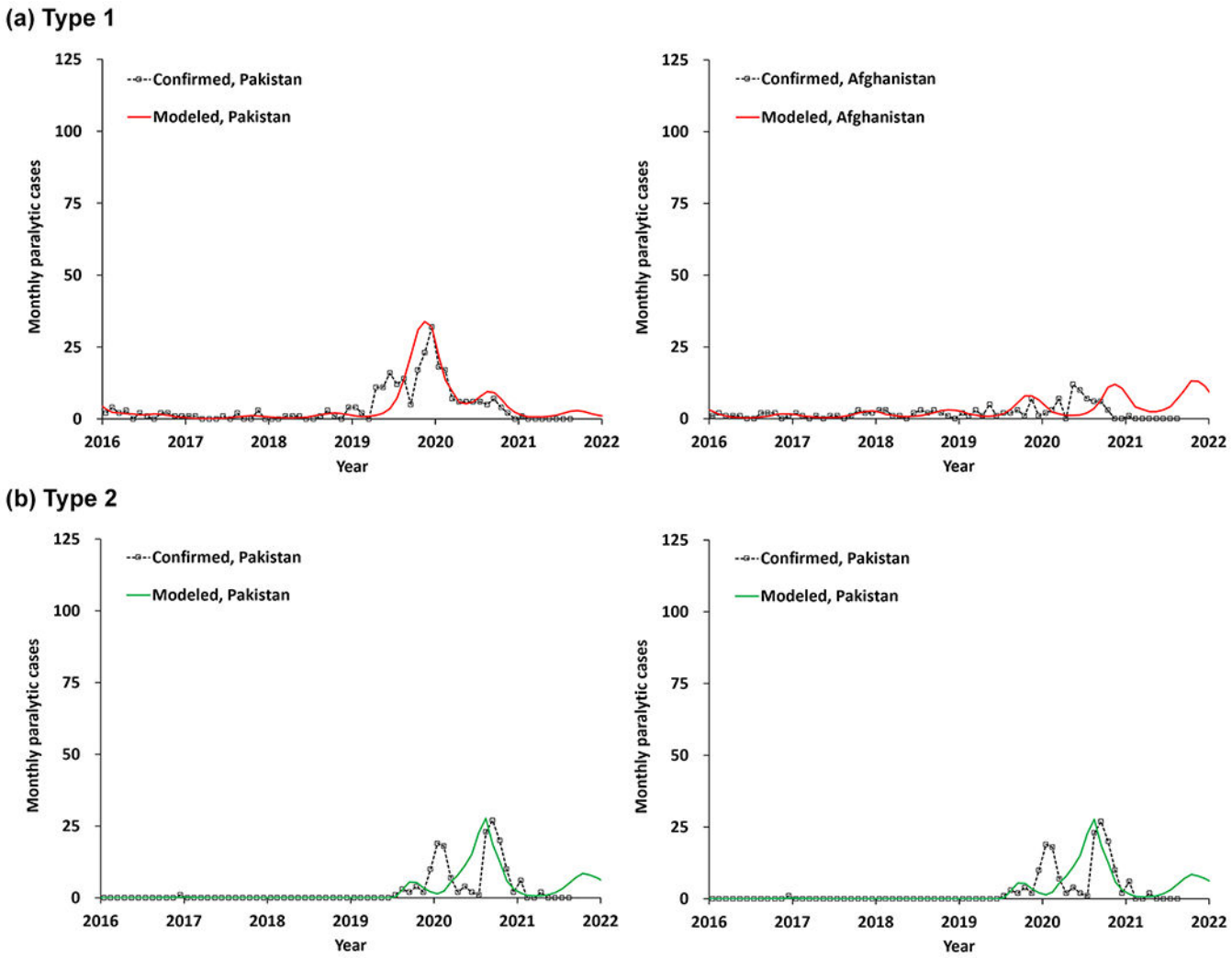

Figure 2.

Updated modeled paralytic incidence for the base case (BC) scenario compared to reported poliovirus cases for 2016-2021 for Pakistan and Afghanistan

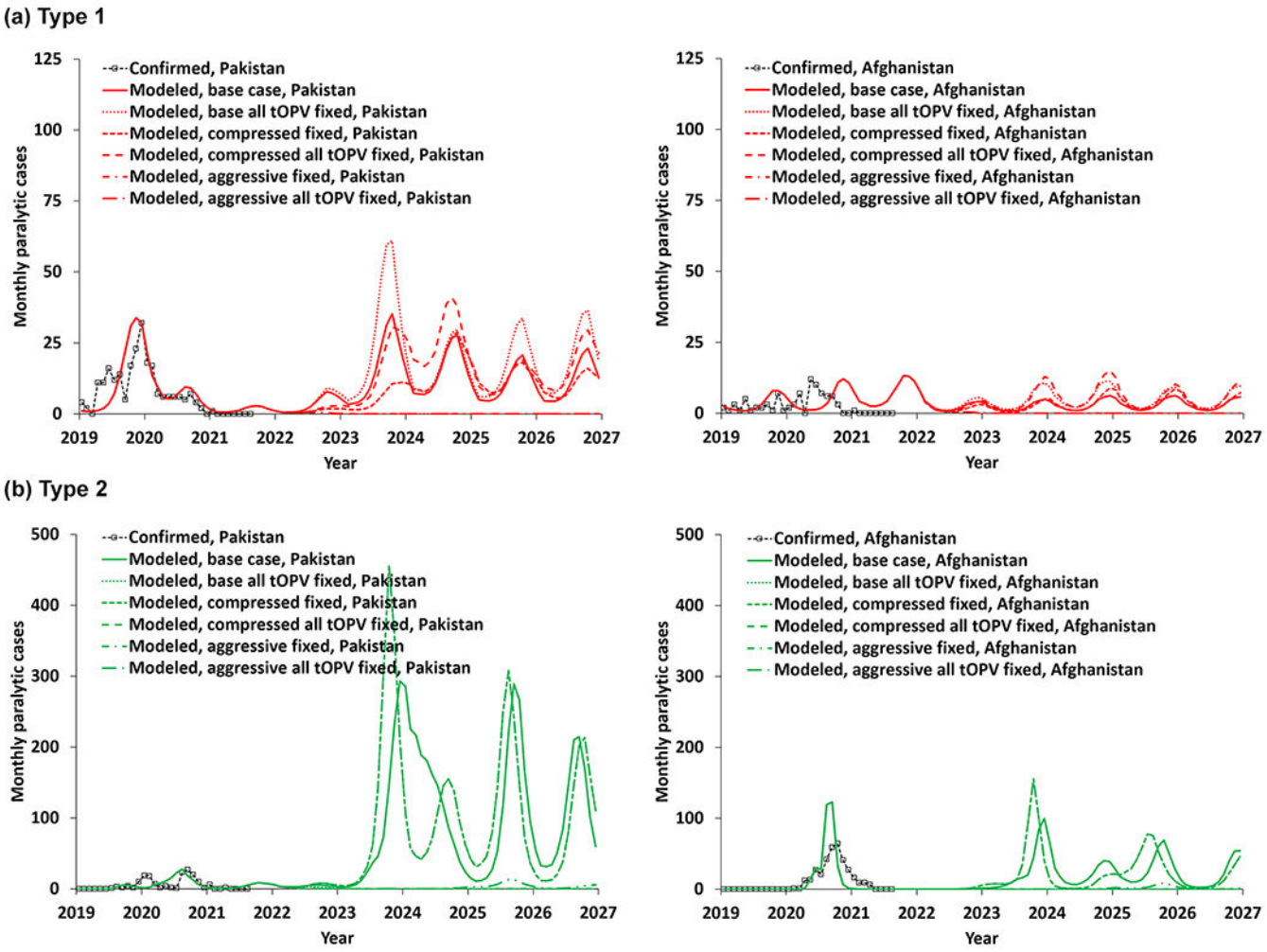

Figure 3.

Modeled paralytic incidence of the vaccination scenarios compared to a base case for 2019-2026 for Pakistan and Afghanistan

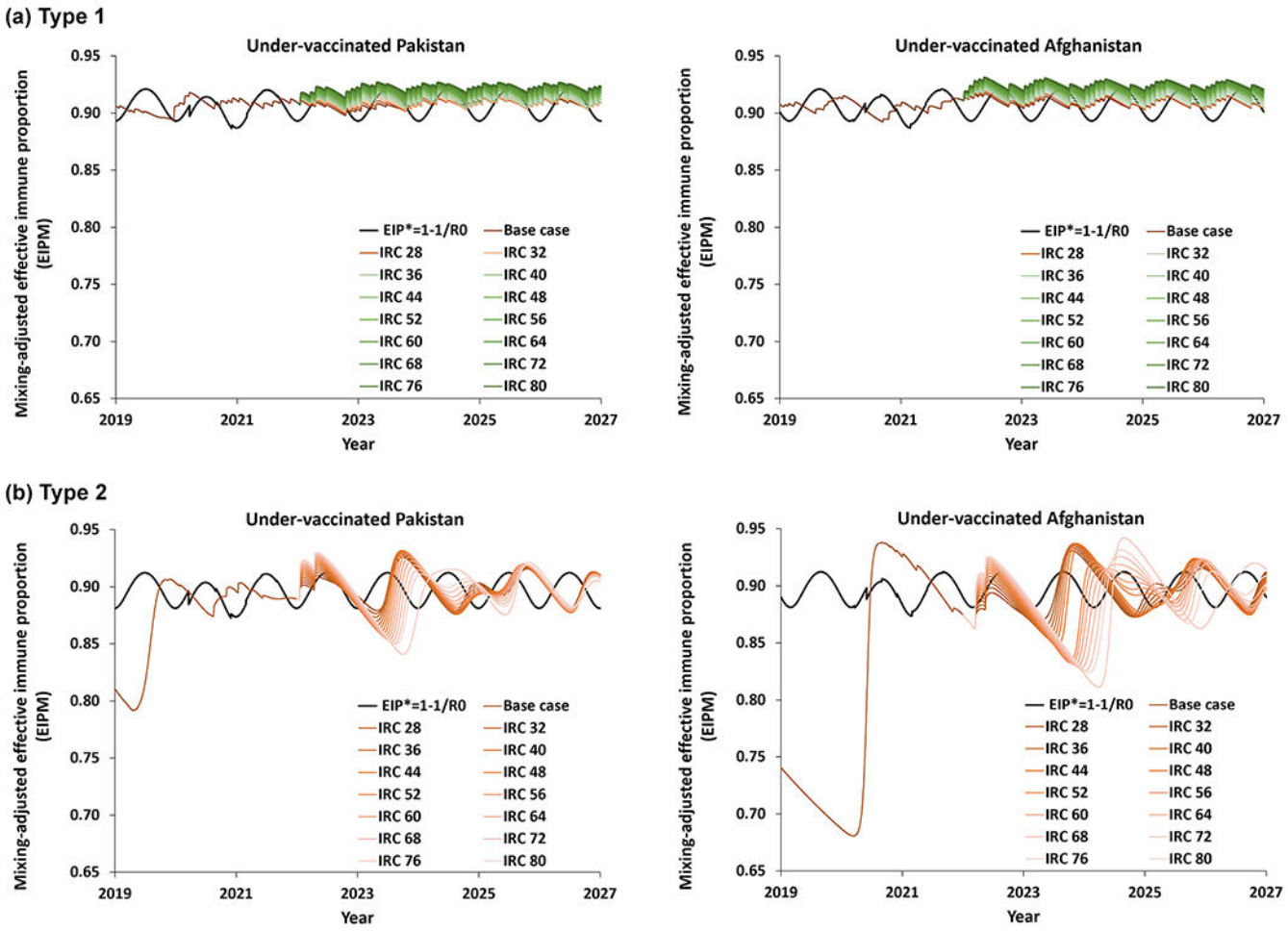

Figure 4.

Modeled mixing-adjusted effective immune proportion (EIPM) of the base case and increased reach and coverage vaccination scenarios compared to the EIP* threshold for 2019-2026 for Pakistan and Afghanistan

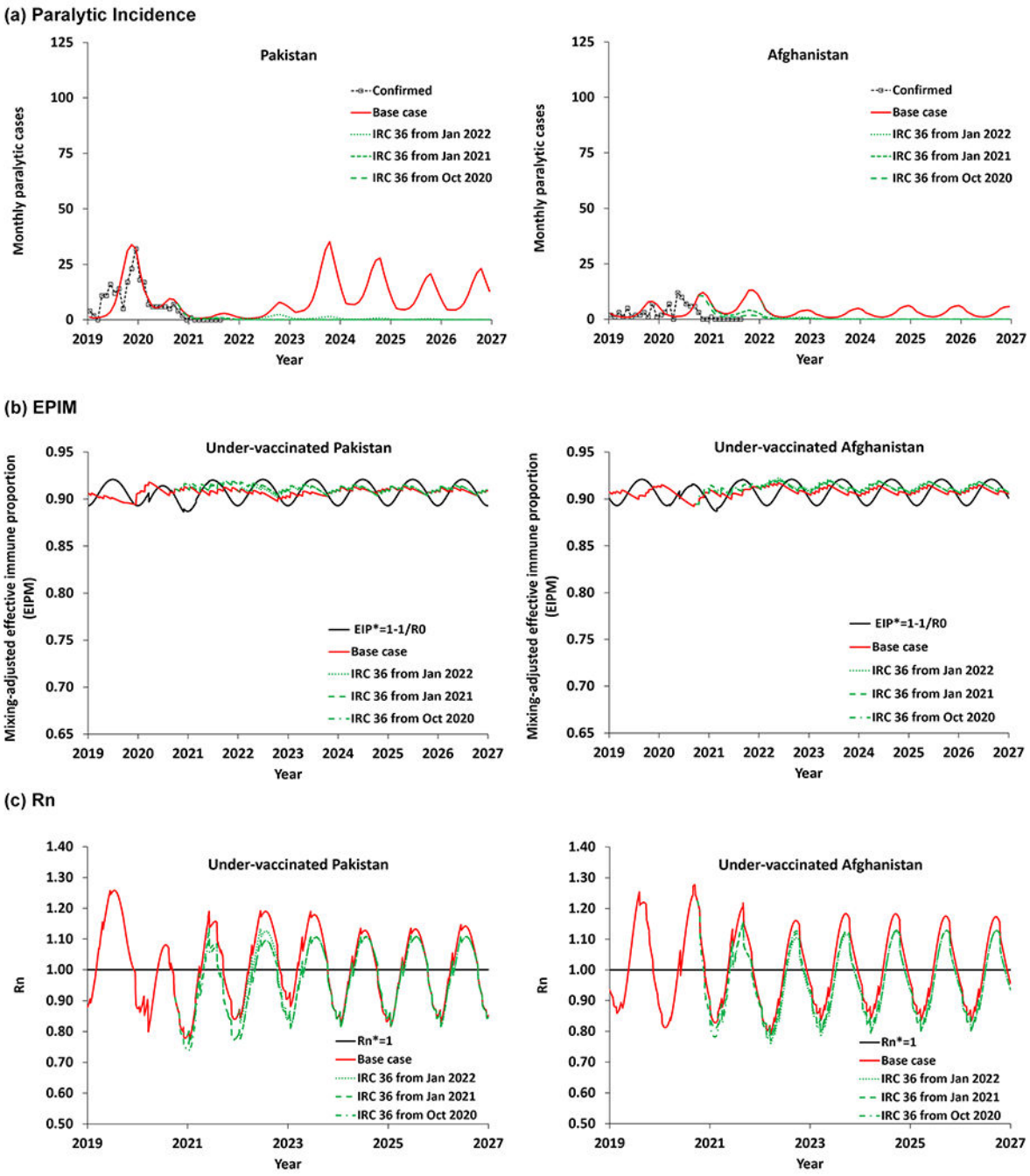

Figure 5.

Modeled (a) paralytic incidence, (b) mixing-adjusted effective immune proportion (EIPM) compared to the EIP* threshold and (c) net reproductive number (Rn) compared to the Rn* threshold of the base case and increased reach and coverage vaccination scenarios with different starting dates for 2019-2026 for Pakistan and Afghanistan for type 1

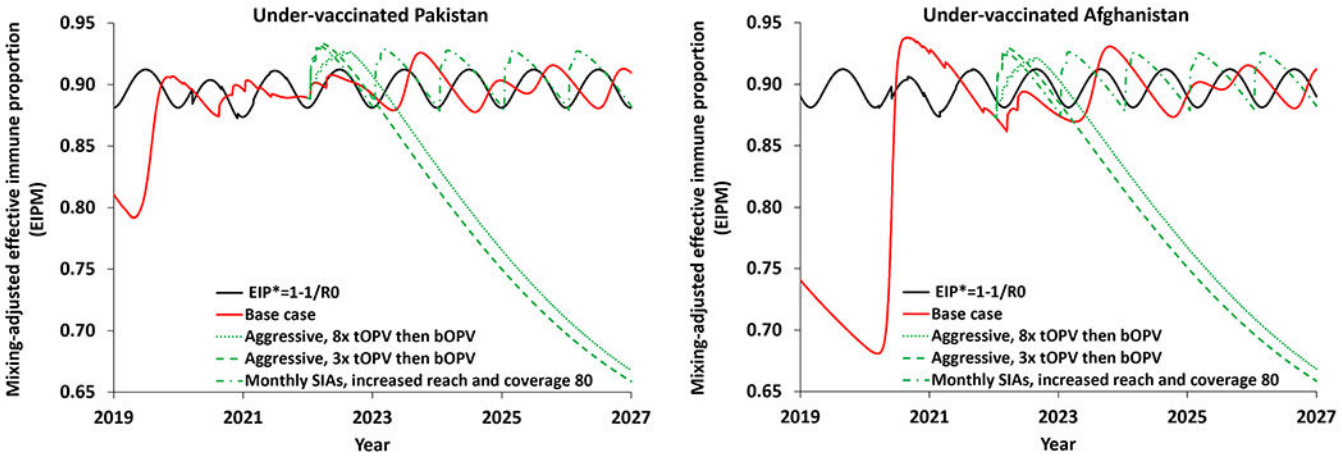

Figure 6.

Modeled mixing-adjusted effective immune proportion (EIPM) of the vaccination scenarios compared to the EIP* threshold for 2019-2026 for Pakistan and Afghanistan for type 2

Table 1.

Pakistan and Afghanistan specific model inputs

Model input	Best estimate	Notes
*General**		
Number of subpopulations	4	
Size of undervaccinated subpopulations relative to total population:		
- Pakistan	0.05	
- Afghanistan	0.10	
Number of age groups	11	0-2, 3-11 months; 1; 2; 3; 4; 5-9; 10-14; 15-24; 25-39*; ≥ 40 years
Number of mixing age groups	3	0–4; 5–14; ≥ 15 years
Proportion of contacts reserved for individuals within the same mixing age group (κ)	0.35	Measure of strength of preferential mixing between age groups; value similar to other high-risk settings
Average basic reproductive number (R_0)		Seasonal variation occurs around the average, ratios by type based on generic model inputs
- type 1	11	
- type 2	9.9	
- type 3	8.25	
Proportional change in R_0 due to seasonality (α)	0.15	Based on judgment and calibration within ranges used for other populations to match incidence pattern
Day of seasonal peak in $R_{0(pd)}$		Broadly consistent with typical precipitation patterns and nonpolio enterovirus isolation rates, calibrated to match incidence patterns
- Pakistan	180 (June 30)	
- Afghanistan	240 (August 29)	
Proportion of transmissions via oropharyngeal route (p^{oro})	0.3	Value used for high R_0 developing country settings
Per-dose take rate (tr) (type 1, 2, 3)		Values based on review of seroconversion studies
- tOPV	0.40, 0.60, 0.52	
- mOPV	0.52, 0.60, 0.52	
- bOPV	0.48, NA, 0.48	
- IPV	0.63, 0.63, 0.63	
Time of IPV introduction in RI		
- Pakistan	August 20, 2015	
- Afghanistan	September 30, 2015	
Time of switch from tOPV to bOPV	April 30, 2016	
Demographics	Time series	Surviving birth rates and age-specific mortality rates over time computed from U.N.-estimated medium variant annual number

Model input	Best estimate	Notes
		of surviving infants and population in each age group and country
Transmission threshold	5/1,000,000	Effective infectious proportion below which we assume 0 force-of-infection
Related to COVID-19		
Mixing restriction start date:		
- Pakistan	March 20, 2020	
- Afghanistan	June 1, 2020	
Mixing restriction end date	August 31, 2021	Updated from prior August 31, 2020 in Kalkowska et al (2021)
Subpopulation-specific absolute R_0 decrease during mixing restriction period:		Updated from prior August 31, 2020 in Kalkowska et al (2021)
- March 20, 2020 - May 31, 2020		
Pakistan		
Afghanistan	−1.00	
- June 1, 2020 - August 31, 2020	−0.125	
	−1.00	
- September 1, 2020 - November 30, 2021	−0.75	
- December 1, 2020 - February 28, 2021	−0.50	
- March 1, 2021 - May 31, 2021	−0.25	
- June 1, 2021 - August 31, 2021	−0.125	
RI reduction start date	March 20, 2020	Kalkowska et al (2021)
RI reduction end date	May 31, 2021	Updated from December 31, 2020 in Kalkowska et al (2021)
Change in average RI coverage during RI reduction period	−0.1	Kalkowska et al (2021)

Abbreviations: bOPV, bivalent oral poliovirus vaccine; COVID-19, coronavirus disease 2019, IPV, inactivated poliovirus vaccine; mOPV, monovalent oral poliovirus vaccine; NA, not applicable; RI, routine immunization; tOPV, trivalent oral poliovirus vaccine; U.N., United Nations.

*All of the General model inputs come directly from prior development and application of the model (Duintjer Tebbens et al., 2018; Duintjer Tebbens & Thompson, 2019; Kalkowska, Duintjer Tebbens, Pallansch, et al., 2019; Kalkowska, Duintjer Tebbens, & Thompson, 2019; Kalkowska, Pallansch, Cochi, et al., 2021b; Kalkowska & Thompson, 2021b). All of the COVID-19 input assumptions reflect available information, including unpublished qualitative descriptions of experiences from individuals shared with us by individuals in the acknowledgments.

Table 2.

Assumed mixing matrices among the four subpopulations in the Pakistan and Afghanistan:

(a) Before intensification of border security (until and including 2016) (Duintjer Tebbens et al., 2018; Duintjer Tebbens & Thompson, 2019; Kalkowska, Duintjer Tebbens, Pallansch, et al., 2019; Kalkowska, Duintjer Tebbens, & Thompson, 2019)				
To\From	**Pakistan undervaccinated**	**Pakistan General**	**Afghanistan undervaccinated**	**Afghanistan general**
Pakistan undervaccinated	0.9970	0.0010	0.0015	0.0005
Pakistan General	0.0006	0.9990	0.0002	0.0002
Afghanistan undervaccinated	0.0010	0.0005	0.9970	0.0015
Afghanistan general	0.0002	0.0002	0.0006	0.9990
(b) After intensification of border security (from January 1, 2017 to March 20, 2020) and once activities disrupted by COVID-19 resume (from September 1, 2021* through the December 31, 2026)				
To\From	**Pakistan undervaccinated**	**Pakistan General**	**Afghanistan undervaccinated**	**Afghanistan general**
Pakistan undervaccinated	0.9982	0.0010	0.0004	0.0004
Pakistan General	0.0006	0.9990	0.0002	0.0002
Afghanistan undervaccinated	0.0004	0.0004	0.9977	0.0015
Afghanistan general	0.0002	0.0002	0.0006	0.9990
(c) During COVID-19 restrictions (from March 20, 2020 to May 31, 2020)				
To\From	**Pakistan undervaccinated**	**Pakistan General**	**Afghanistan undervaccinated**	**Afghanistan general**
Pakistan undervaccinated	0.9996	0.0002	0.0001	0.0001
Pakistan General	0.0002	0.9996	0.0001	0.0001
Afghanistan undervaccinated	0.0001	0.0001	0.9980	0.0018
Afghanistan general	0.0001	0.0001	0.0007	0.9991
(d) During COVID-19 restrictions (from June 1, 2020 to August 31, 2020)				
To\From	**Pakistan undervaccinated**	**Pakistan General**	**Afghanistan undervaccinated**	**Afghanistan general**
Pakistan undervaccinated	0.9996	0.0002	0.0001	0.0001
Pakistan General	0.0002	0.9996	0.0001	0.0001
Afghanistan undervaccinated	0.0001	0.0001	0.9996	0.0002
Afghanistan general	0.0001	0.0001	0.0002	0.9996
(e) During COVID-19 restrictions (from September 1, 2020 to August 31, 2021)				
To\From	**Pakistan undervaccinated**	**Pakistan general**	**Afghanistan undervaccinated**	**Afghanistan general**
Pakistan undervaccinated	0.9990	0.0006	0.0002	0.0002
Pakistan General	0.0004	0.9992	0.0002	0.0002
Afghanistan undervaccinated	0.0002	0.0002	0.9988	0.0008
Afghanistan general	0.0002	0.0002	0.0004	0.9992

Note:

* Updated from August 31, 2020 in (Kalkowska, Pallansch, Cochi, et al., 2021b)

Table 3.

Target population and timing assumptions for supplemental immunization activities (SIAs) using oral poliovirus vaccine (OPV) for modeled annual vaccination schedules for Pakistan and Afghanistan for 2022-2026

Activity start month	Target population, vaccine							
	Pakistan				Afghanistan			
	Base	Compressed	Aggressive	Mixed	Base	Compressed	Aggressive	Mixed
January	100%	100%	100%	100%	60%	100%	100%	100%
February		100%	100%	5%	60%	100%	100%	10%
March	43%	100%	100%	100%	100%	100%	100%	100%
April	100%	100%	100%	5%	60%	100%	100%	10%
May		50%	100%	100%	100%	50%	100%	100%
June	43%		100%	5%			100%	10%
July			100%	100%			100%	100%
August			100%	5%			100%	10%
September			100%	100%			100%	100%
October	60%		100%	5%	70%		100%	10%
November	50%		100%	100%			100%	100%
December	50%		100%	5%			100%	10%

Table 4.

Modeled scenarios for Pakistan and Afghanistan for 2022-2026

Scenario Name	Target (1)	Vaccine type (2)	Coverage (3)		P_{RM} (4)		Elimination date (month/day/year)			
							Pakistan		Afghanistan	
			G	U	G	U	WPV1	cVDPV2	WPV1	cVDPV2
Fixed reach and coverage with 22.5 NID-equivalent SIAs for 2022-2026										
Base case	B	bOPV *	0.80	0.24	0.50	0.80	-	-	-	-
(i) Base case all tOPV, fixed	B	tOPV	0.80	0.24	0.50	0.80	-	-	-	-
(ii) Compressed fixed	C	bOPV *	0.80	0.24	0.50	0.80	-	-	-	-
(iii) Compressed all tOPV fixed	C	tOPV	0.80	0.24	0.50	0.80	-	-	-	-
(iv) Aggressive fixed	A	bOPV *	0.80	0.24	0.50	0.80	1/2/23	-	2/26/23	-
(v) Aggressive all tOPV fixed	A	tOPV	0.80	0.24	0.50	0.80	1/30/23	-	3/28/23	-
Variable reach and coverage with 21 NID-equivalent SIAs for 2022-2026 (vi)										
Aggressive, 3x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.64	0.50	0.57	7/9/22	8/17/22	1/25/23	5/7/22
Aggressive, 4x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.48	0.50	0.65	9/ 14/22	2/3/23	10/25/22	6/18/22
Aggressive, 5x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.40	0.50	0.69	10/21/22	12/30/22	12/5/22	9/ 23/22
Aggressive, 6x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.32	0.50	0.74	11/27/22	1/16/23	1/18/23	11/20/22
Aggressive, 7x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.28	0.50	0.77	12/22/22	1/9/23	2/13/23	12/15/22
Aggressive, 8x tOPV then bOPV	A	tOPV/bOPV **	0.80	0.24	0.50	0.80	1/23/23	1/22/23	3/18/23	1/7/23
Fixed reach and coverage with increased number of SIAs for 2022-2026										
(vii) Monthly SIAs, fixed	A	bOPV +	0.80	0.24	0.50	0.80	1/2/23	-	2/27/23	-
(viii) Mixed, fixed	M	bOPV *	0.80	0.24	0.50	0.80	1/1/23	-	2/26/23	-
(ix) Mixed all tOPV, fixed	M	tOPV	0.80	0.24	0.50	0.80	1/28/23	12/14/22	3/29/23	12/14/22
Increase coverage with 22.5 NID-equivalent SIAs for 2022-2026 (x)										
Increased coverage 28	B	bOPV *	0.80	0.28	0.50	0.80	-	-	-	-
Increased coverage 32	B	bOPV *	0.80	0.32	0.50	0.80	-	-	-	-
Increased coverage 36	B	bOPV *	0.80	0.36	0.50	0.80	-	-	4/29/25	-

Scenario Name	Target (1)	Vaccine type (2)	Coverage (3)		P_{RM} (4)		Elimination date (month/day/year)			
							Pakistan		Afghanistan	
			G	U	G	U	WPV1	cVDPV2	WPV1	cVDPV2
Increased coverage 40	B	bOPV*	0.80	0.40	0.50	0.80	4/4/26	-	4/16/24	-
Increased coverage 44	B	bOPV*	0.80	0.44	0.50	0.80	1/27/25	-	2/20/24	-
Increased coverage 48	B	bOPV*	0.80	0.48	0.50	0.80	2/13/24	-	6/3/23	-
Increased coverage 52	B	bOPV*	0.80	0.52	0.50	0.80	1/1/24	-	5/7/23	-
Increased coverage 56	B	bOPV*	0.80	0.56	0.50	0.80	5/3/23	-	4/18/23	-
Increased coverage 60	B	bOPV*	0.80	0.60	0.50	0.80	3/21/23	-	4/2/23	-
Increased coverage 64	B	bOPV*	0.80	0.64	0.50	0.80	2/28/23	-	3/19/23	-
Increased coverage 68	B	bOPV*	0.80	0.68	0.50	0.80	2/14/23	-	3/6/23	-
Increased coverage 72	B	bOPV*	0.80	0.72	0.50	0.80	2/2/23	-	2/22/23	-
Increased coverage 78	B	bOPV*	0.80	0.76	0.50	0.80	1/23/23	-	2/9/23	-
Increased coverage 80	B	bOPV*	0.80	0.80	0.50	0.80	1/1/23	-	1/29/23	-
Increased reach with 22.5 NID-equivalent SIAs for 2022-2026 (xi)										
Increased reach	B	bOPV*	0.80	0.24	0.50	0.70	-	-	-	-
Increased reach and coverage (IRC) with 22.5 NID-equivalent SIAs for 2022-2026 (xii)										
IRC 28	B	bOPV*	0.80	0.28	0.50	0.77	-	-	-	-
IRC 32	B	bOPV*	0.80	0.32	0.50	0.74	-	-	5/23/26	-
IRC 36	B	bOPV*	0.80	0.36	0.50	0.72	3/18/26	-	4/17/24	-
IRC 40	B	bOPV*	0.80	0.40	0.50	0.69	3/9/24	-	6/24/23	-
IRC 44	B	bOPV*	0.80	0.44	0.50	0.67	1/1/24	-	5/9/23	-
IRC 48	B	bOPV*	0.80	0.48	0.50	0.65	3/27/23	-	4/12/23	-
IRC 52	B	bOPV*	0.80	0.52	0.50	0.63	2/24/23	-	3/22/23	-
IRC 56	B	bOPV*	0.80	0.56	0.50	0.61	2/4/23	-	3/2/23	-
IRC 60	B	bOPV*	0.80	0.60	0.50	0.59	1/19/23	-	2/11/23	-
IRC 64	B	bOPV*	0.80	0.64	0.50	0.57	1/4/23	-	1/24/23	-

Scenario Name	Target (1)	Vaccine type (2)	Coverage (3)		P_{RM} (4)		Elimination date (month/day/year)			
							Pakistan		Afghanistan	
			G	U	G	U	WPV1	cVDPV2	WPV1	cVDPV2
IRC 68	B	bOPV*	0.80	0.68	0.50	0.55	12/21/22	-	1/4/23	-
IRC 72	B	bOPV*	0.80	0.72	0.50	0.53	12/8/22	-	12/16/22	-
IRC 76	B	bOPV*	0.80	0.76	0.50	0.52	11/25/22	-	11/27/22	-
IRC 80	B	bOPV*	0.80	0.80	0.50	0.50	11/28/22	-	11/24/22	-
Increased reach and coverage (IRC) with 22.5 NID-equivalent SIAs for 2022-2026, with increase in reach and coverage from January 2021 (xiii)										
IRC 28	B	bOPV*	0.80	0.28	0.50	0.77	-	-	-	-
IRC 32	B	bOPV*	0.80	0.32	0.50	0.74	-	-	6/23/25	-
IRC 36	B	bOPV*	0.80	0.36	0.50	0.72	2/27/22	-	7/4/23	-
IRC 40	B	bOPV*	0.80	0.40	0.50	0.69	1/27/22	-	4/7/23	-
IRC 44	B	bOPV*	0.80	0.44	0.50	0.67	1/4/22	-	2/6/23	-
IRC 48	B	bOPV*	0.80	0.48	0.50	0.65	12/17/21	-	6/6/22	-
IRC 52	B	bOPV*	0.80	0.52	0.50	0.63	12/2/21	-	5/7/22	-
Increased reach and coverage (IRC) with 22.5 NID-equivalent SIAs for 2022-2026, with increase in reach and coverage from October 2020 (xiv)										
IRC 28	B	bOPV*	0.80	0.28	0.50	0.77	-	-	-	-
IRC 32	B	bOPV*	0.80	0.32	0.50	0.74	3/11/22	-	5/6/26	-
IRC 36	B	bOPV*	0.80	0.36	0.50	0.72	1/18/22	-	5/29/23	-
IRC 40	B	bOPV*	0.80	0.40	0.50	0.69	12/15/21	-	2/28/23	-
IRC 44	B	bOPV*	0.80	0.44	0.50	0.67	11/17/21	-	5/0/22	-
IRC 48	B	bOPV*	0.80	0.48	0.50	0.65	10/20/21	-	4/2/22	-
IRC 52	B	bOPV*	0.80	0.52	0.50	0.63	9/22/21	-	3/3/22	-
Increased reach and/or coverage with increased number of SIAs for 2022-2026										
(xv) Monthly SIAs, increased coverage80	A	bOPV+	0.80	0.80	0.50	0.80	7/15/22	7/15/23	8/17/22	6/23/23
(xvi) Monthly SIAs, increased reach	A	bOPV+	0.80	0.24	0.50	0.70	12/16/22	-	2/10/23	-

Scenario Name	Target (1)	Vaccine type (2)	Coverage (3)		P_{RM} (4)		Elimination date (month/day/year)			
							Pakistan		Afghanistan	
			G	U	G	U	WPV1	cVDPV2	WPV1	cVDPV2
(xvii) Monthly SIAs, IRC 80	A	bOPV $^{+}$	0.80	0.80	0.50	0.50	6/06/22	3/20/23	7/18/22	6/6/22

Abbreviations: bOPV, bivalent OPV; IRC, increased reach and coverage; OPV, oral poliovirus vaccine; tOPV, trivalent OPV

Notes:

1. A=aggressive, B=base, C=compressed, M=mixed (see Table 3)

2. Vaccine type for all rounds (bOPV or tOPV), unless otherwise noted

3. True coverage in the general (G) or undervaccinated (U) subpopulation

4. Assumed probability of repeatedly missing same kids (P_{RM}) in the general (G) or undervaccinated (U) subpopulation, which along with coverage determines the overall probability of repeatedly reaching the same kids and thus the overall reach of previously missed kids in each new SIA round (i.e., the lower the P_{RM}, the higher the reach), see technical appendix elsewhere (Kalkowska, Wassilak, et al., 2021)

*Indicates all bOPV rounds except for first 2 NID rounds in 2022 that use tOPV

**Indicates all tOPV rounds until cVDPV2 elimination, followed by all bOPV rounds

$^{+}$Indicates all bOPV rounds except for first 2 NID rounds each year from 2022 that use tOPV

$^{\#}$Indicates increase in reach and coverage from January 2021

$^{\#\#}$Indicates increase in reach and coverage from October 2020