Published in final edited form as:

Future Virol. 2018 August 10; 13(9): 617–628. doi:10.2217/fvl-2018-0079.

Poliovirus containment risks and their management

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Abstract

Aim: Assess risks related to breaches of poliovirus containment

Method: Using a dynamic transmission model, we explore the variability among different populations in the vulnerability to poliovirus containment breaches as population immunity to transmission declines after oral poliovirus vaccine (OPV) cessation.

Results: Although using OPV instead of wild poliovirus (WPV) seed strains for inactivated poliovirus vaccine (IPV) production offers some expected risk reintroduction of live polioviruses from IPV manufacturing facilities, OPV seed strain releases may become a significant threat within 5-10 years of OPV cessation in areas most conducive to fecal-oral poliovirus transmission, regardless of IPV use.

Conclusions: Efforts to quantify the risks demonstrate the challenges associated with understanding and managing relatively low-probability and high-consequence containment failure events.

Executive summary

• Breaches in containment of polioviruses pose a risk for the polio endgame that requires ongoing management

• IPV manufacturing facilities differ with respect to the types of poliovirus strains that they might release and the settings into which the releases occur

• Within 5-10 years after OPV cessation, even attenuated OPV vaccine used as IPV seed strains may be able to establish population-wide transmission in settings conducive to high fecal-oral transmission despite high IPV-only coverage

• The costs and benefits of poliovirus containment activities require further characterization

• Quantifying the uncertain risks of breaches in poliovirus containment will remain important for the polio endgame

Keywords

polio; eradication; containment

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Conflicts of interest

None.

Introduction

Following the eradication of a vaccine-preventable disease, containment of any and all remaining stocks of potentially infectious materials emerges as an essential activity for maintaining eradication [1]. Notably, a laboratory release of variola virus in the United Kingdom led to the last reported case of smallpox [2], and motivated the destruction of nearly all stocks of variola virus [3, 4]. In the context of this experience, numerous studies explored issues related to poliovirus containment (e.g.,[1, 5-9]).

The Global Polio Eradication Initiative (GPEI) developed and maintains a Global Action Plan to minimize poliovirus facility-associated risk in the post-eradication/post-oral poliovirus vaccine (OPV) era (GAPIII) [10]. Strategies to achieve and certify poliovirus containment continue to develop and evolve, with current efforts focused on providing guidance and policies for certification. GAPIII identifies different types of facilities, including poliovirus vaccine manufacturers, poliovirus-essential facilities (PEFs) [10], and the development of new guidance is underway to support risk assessment and management in facilities that hold potentially infectious materials [11]. Annexes 2 and 3 of GAPIII include requirements for facilities that hold live poliovirus (LPV) materials similar to Biosafety Level 3 with some additional conditions. With the requirements for serotype 2 LPV materials now going into effect (due to the global eradication of serotype 2 wild poliovirus (WPV2) eradication [12] and subsequent global cessation of serotype 2-containing OPV (OPV2) in 2016 [13]), further evaluation of their costs and benefits appears warranted to support appropriate adjustments.

Prior efforts attempted to quantify the risks associated with breaches in containment (i.e., containment risks) and considered the benefits of risk management. Specifically, two analyses explored the risks of poliovirus reintroduction from all sources for the polio endgame and provided the only available quantitative estimates used for modeling containment risks in the polio endgame [14, 15].

Table 1 summarizes the known events of poliovirus releases [16-20] some of which served as the evidence base that supported the development of prior risk estimates [14, 15]. Observed events to date include occurrences both of the release of virus through an infected laboratory worker and direct transmission from a poliovirus vaccine manufacturing site to the environment. High levels of population immunity for all 3 serotypes most likely masked historical releases of poliovirus from laboratories involving small numbers of asymptomatically infected individuals. Thus, the limited evidence in Table 1 exists in the context of significant challenges associated with assessing the historic frequency of potential reintroduction events. The ability of reintroduced viruses to spread will depend on the hygienic, sanitary, and crowding conditions in the population, which influence inherent transmissibility of polioviruses in a population (i.e., the basic reproduction number R_0 that reflects the average number of new infections caused by a single infection in a fully susceptible population) and the contribution of the fecal-oral and oropharyngeal routes to transmission. The events in Table 1 highlight vaccine manufacturing facilities and activities as high-risk, with no known releases from other types of laboratories that handle

polioviruses in the last 30 years or more (i.e., during the time of active poliovirus vaccination that limited the motivation and ability to detect events).

Of the six episodes of known poliovirus releases from poliovirus vaccine manufacturers, five originated from inactivated poliovirus vaccine (IPV) manufacturing sites. While IPV represents a highly effective vaccine at inducing individual immunity to poliomyelitis disease and preventing oropharyngeal excretion in all settings, it does not provide much protection from potential asymptomatic participation in fecal-oral transmission [21-23]. Therefore, populations with conditions conducive to fecal-oral poliovirus transmission may experience extensive poliovirus transmission despite high IPV coverage [24, 25]. This implies that in some populations, IPV production after OPV cessation may result in a risk of population-wide transmission and polio outbreaks. Recognizing the high inherent transmissibility of WPV seed strains for IPV production, the GPEI stimulated successful efforts to produce IPV using the attenuated strains in OPV (i.e., Sabin IPV) [26-28]. However, long enough after OPV cessation, even attenuated seed strains may be able to establish population-wide transmission in settings conducive to high fecal-oral transmission despite high IPV-only coverage. The experience with OPV viruses suggests that if they establish transmission in a population with low immunity, they may evolve to a circulating vaccine-derived poliovirus (cVDPV) capable of causing outbreaks similar to WPVs [29-32]. Similarly, releases of WPV and OPV strains handled in PEFs and facilities that hold potentially poliovirus-infectious materials could trigger WPV outbreaks or population-wide transmission of OPV-related viruses that could lead to cVDPV outbreaks. Despite these risks, no prior analyses specifically focused on characterizing the vulnerability of different types of populations to poliovirus containment breaches as a function of time after OPV cessation for different OPV serotypes or characterized the impact of IPV use on this vulnerability. This analysis characterizes vulnerability as the extent to which populations can sustain transmission in the event of a LPV reintroduction and explores the changes in vulnerability as a function of time since OPV cessation.

Methods

This study aims to elucidate the vulnerability of different types of populations to poliovirus containment breaches as a function of time after OPV cessation by performing one analysis based on using an existing model [15] and one analysis that presents new modeling. For the first analysis, we use results derived from the existing model [15] to show the vulnerability of realistic but abstract populations to serotype 2 poliovirus reintroduction following OPV2 cessation. The second analysis focuses on the differences between serotypes and the impact of IPV use on vulnerability.

We first examine the vulnerability to potential poliovirus release from manufacturing sites or laboratories of different types of populations using a previously developed global model for long-term poliovirus risk management [15]. Specifically, we consider populations of the global model with characteristics representative of realistic populations that we expect may continue to produce IPV or maintain PEFs after OPV cessation. Table 2 highlights some selected properties of the populations we considered as likely to potentially represent locations for IPV production (see complete properties available in the appendix of Duintjer

Tebbens et al. [15]). Notably, Table 2 does not include any low-income countries, because we do not consider it likely that IPV production would occur in any low-income countries. To characterize vulnerability as a function of time since OPV cessation, we focus on the mixing-adjusted net reproduction number (R_n), which represents the average number of secondary infections generated by a single infection in a population. The R_n accounts for population immunity to poliovirus transmission, which considers the aggregated ability of all individuals to participate in transmission based on their immunity state [33, 34] and the transmissibility of the released poliovirus (with lower relative transmissibility for attenuated strains (OPV/Sabin) compared with WPV or cVDPV strains). The model focuses on tracking infections, not on paralytic cases, which occur in the model as a function of first infections in fully-susceptible individuals. The model recognizes that while prior infection with a LPV (including OPV) or effective immunization with IPV provides protection from poliomyelitis disease, potential reinfection with a LPV remains a possibility, with reinfected individuals able to excrete virus and participate in transmission. If $R_n>1$, then population-wide transmission could occur following the release of virus due to a containment breach, with higher values implying that the virus would spread more rapidly and become more difficult to control. We characterize the R_n for both wild strains and attenuated vaccine strains with consideration of the seasonality in transmission. The vulnerability to wild strains pertains to the risk of a release from the seed strains used in conventional IPV production and also any samples containing wild strains or fully reverted VDPV strains, which we assume remain as transmissible as wild strains. The vulnerability to vaccine strains pertains to the risk of a release from the seed strains used in Sabin IPV production or any samples from individuals infected with OPV. However, in the event of an OPV infection, the virus will evolve to some extent toward higher transmissibility as it replicates in the host and any infected contacts. Therefore, the vulnerability to OPV in some ways represents a lower bound of the true vulnerability to a reintroduction of the OPV. In addition to vulnerability, whether the OPV establishes transmission depends on the number of initial infections [35], local heterogeneity, and chance, which remain beyond the scope of this study.

The global model reflects idealized implementation of risk management policies and the state of the world as of 2015, which means before OPV2 cessation [15]. Unfortunately, the existing model does not reflect the current reality of delayed WPV eradication, insufficient IPV supplies, insufficient trivalent OPV intensification and resulting serotype 2 cVDPV outbreaks, and other differences with actual experience. However, it exhibits the key behaviors of interest for this abstract exploration, because this analysis focuses on characterizing vulnerability as a function of time after OPV cessation, and not the specific timing of the OPV cessation. Although the probability of reintroducing LPVs into a population depends on the presence of sources for those viruses, we focused on characterizing vulnerability for all populations because polioviruses do not respect borders. For this analysis, we model vulnerability as a function of the time (in years) since homotypic OPV cessation, whenever it occurs, without linking homotypic OPV cessation to any particular calendar year(s). For lower middle-income countries, we assumed a single dose of IPV in routine immunization (RI) for 5 years after the cessation of serotypes 1 and 3 OPV. We further assumed that some upper middle-income and all high-income countries already

introduced IPV before 2015 and that all of them will continue a full IPV schedule after cessation of OPV containing serotypes 1 and 3.

For the second analysis, we prospectively explore the effect of different risk factors and IPV use on the vulnerability to containment releases in a differential equation-based model of poliovirus transmission and OPV evolution (see appendix for model details) [33]. We considered the time until the R_n exceeds 1 for different hypothetical populations characterized by overall poliovirus transmissibility (R_0) and the contribution of oropharyngeal transmission (p^{oro}). Table 3 provides the assumptions for the second analyses. For all of the populations, we explored the vulnerability to containment breaches if these populations use 0, 1, 2, or 3 IPV doses in RI after OPV cessation with coverage with the full schedule (i.e., RI coverage) equal to 0.3, 0.6, 0.98 (both before and after OPV cessation). We ignored seasonality in R_0 for these analyses so that the R_n values increase monotonically after OPV cessation (to make the trends easier to see). Exceeding and increasing R_n values of 1 implies increasing vulnerability. For all populations in Table 3, we adopted the general characteristics of lower middle-income populations in the global model [15], including demographics and a compressed run-up from pre-vaccine era to introduction of IPV prior to OPV cessation. We also assume that high quality SIAs with OPV (i.e., 5 per year if RI coverage of 0.3 or RI coverage of 0.6 and R_0 of 13, and 3 per year in all other cases) provide high population immunity to transmission at the time of OPV cessation of each serotype.

Results

Figure 1 shows the vulnerability to OPV2 (panel a) and WPV2 strains (panel b) for realistic populations from the global model [15]. Consistent with prior work [36, 37], Figure 1a suggests that populations with high fecal-oral transmission (e.g., northern India) become vulnerable to the establishment of transmission following an introduction of OPV2 virus within a few years of OPV2 cessation. The periodic nature of the results in Figure 1a reflects the impact of seasonality. We note that with R_n values near 1, a release may or may not establish transmission depending on chance (i.e., which and how many people get infected initially and who they contact). [35] Moreover, seasonality may lead any initial transmission to die out in the low season and therefore, the timing of the actual introduction within the year influences the risk of transmission becoming established. Looking beyond seasonal fluctuations, Figure 1 shows that populations conducive to fecal-oral transmission continue to become more vulnerable with time since OPV2 cessation and the model suggests that most tropical settings can support transmission of attenuated OPV2 strains within approximately 10 years of OPV2 cessation. More temperate settings and relatively higher-income settings, including China and Japan, may remain protected from the establishment of transmission and evolution of OPV2 strains for longer. Figure 1b shows the same patterns for wild strains as shown in Figure 1a for vaccine strains, but with much higher R_n values. Although a WPV2 release in a high-income setting may not result in any transmission (as apparently occurred in The Netherlands in 2017, see Table 1) or may result only in transient transmission (i.e., during the high season), Figure 1b suggests that middle-income settings could experience widespread transmission in the event of a WPV2 release at any future time.

Figure 2 shows the effect of different amounts of IPV use for varying risk factors on the vulnerability to a release of wild or vaccine strains of each serotype as a function of fecal-oral transmission settings defined in Table 3. The figure indicates the time at which the introduction of the specific virus strain leads to an R_n of 1 as a function of RI coverage with IPV. This effectively conveys vulnerability, or alternatively shows a lack of vulnerability over the entire time horizon considered (i.e., 35 years following OPV2 cessation) as a horizontal line placed at 40 years for the corresponding assumptions under which this occurs (with all lines that overlap with the blue line indicated by an asterisk (*) in the panels of Figure 2). In settings with very high fecal-oral transmission potential (Figure 2a), releases involving serotype 3 OPV strains would not result in established transmission because of the presumed low transmissibility of serotype 3 OPV. This result reflects the relatively high level of baseline population immunity to transmission for serotype 3 that exists at the time of coordinated cessation of serotype 3 OPV, which leads to enough residual population immunity to transmission to prevent the serotype 3 OPV virus from establishing transmission. However, populations with very high fecal-oral transmission potential become vulnerable to attenuated serotype 1 or 2 OPV strains regardless of the extent of IPV use (Figure 2a). For serotype 2, even with RI coverage of 0.98 and 3 IPV doses, a reintroduced OPV strain could establish transmission 8 or more years after OPV2 cessation, while lower coverage or fewer IPV doses would result in earlier vulnerability. For reintroduced serotype 1 OPV strains, the time until R_n exceeds 1 ranges from less than 5 (no IPV use) to 17 years (3 IPV doses with RI coverage of 0.98). In contrast, as shown in Figure 2b, for wild strains of any serotype, vulnerability begins much sooner and within 3 years for any serotype independent of the extent of IPV use. Figures 2c and 2d show that populations with high fecal-oral transmission (Table 3) also remain protected for longer, but still all eventually become vulnerable to releases of serotype 1 or 2 OPV strains and all serotypes of wild strains. In populations with medium fecal-oral transmission (Figures 2e and 2f), the use of at least 2 IPV doses or high coverage with 1 IPV dose may prevent serotype 1 OPV strains from establishing transmission. However, only very high coverage with 3 IPV doses would permanently protect medium fecal-oral transmission populations from OPV2 transmission in the context of no seasonality. In these types of populations, no extent of IPV use can prevent eventual vulnerability to wild strains of any serotype. Finally, Figure 2g suggests that populations with low fecal-oral transmission potential may remain protected from OPV strains over the time horizon, even with no or minimal IPV use, because of the low inherent transmissibility of OPV in such settings, although vulnerability to serotype 2 occurs at 35 years in the absence of IPV use. Consistent with the lack of WPV outbreaks in high-income countries that already stopped OPV use many years ago (or never used OPV), Figure 2h shows that IPV use in settings with low fecal-oral transmission potential can also substantially delay the time until they become vulnerable to wild strains. High coverage with and/or more doses of IPV can permanently protect populations with low fecal-oral transmission from widespread WPV transmission in the event of WPV reintroduction or protect them longer from becoming vulnerable.

Discussion

IPV production after OPV cessation in settings with a high risk of fecal-oral transmission implies significant risks of outbreaks in the event of a failure to contain the seed strains used to manufacture IPV. While the use of Sabin instead of WPV seed strains delays the point in time when such populations become vulnerable, it does not eliminate the risk of viral transmission. The extent of IPV use affects the time until populations become vulnerable to transmission of different types of LPVs. However, due to the ability of IPV vaccine recipients to contribute asymptomatically to poliovirus transmission, even very high coverage with a full IPV schedule cannot prevent released LPV strains from establishing viral transmission, eventually finding and paralyzing unvaccinated individuals, and leading to uncontrolled outbreaks that would trigger a need to restart OPV use in most countries. Prior use of the global model found a low probability (<1%) of outbreaks or OPV restarts associated with releases from an IPV manufacturer or other containment breaches if IPV production and use in low- and lower middle-income continues for 7 years after globally-coordinated cessation of bivalent OPV.[38] Future models should consider the delays in interrupting WPV transmission, which will mean later cessation of serotype 1 OPV (i.e., 2021 or later) and thus a longer time since OPV2 cessation until IPV production and use would stop. Moreover, current recommendations aim for IPV use for at least 10 years after cessation of the last OPV serotype, which would imply IPV use for 15 years after OPV2 cessation. This study suggests that any IPV production in medium- or high-risk settings for this long after OPV2 cessation could imply risks of outbreaks in the event of a release. Given the past frequency of publicly-reported IPV site releases (Table 1), our analysis highlights the importance of 1) ensuring strict compliance to containment guidelines by IPV manufacturers, even if they use Sabin seed strains, 2) developing non-replicating or non-reverting (rather than merely attenuated) IPV seed strains, and 3) considering carefully the costs and benefits of IPV production in settings conducive to fecal-oral transmission.

Currently, the GPEI efforts related to containment suggest the imposition of significant costs for compliance with requirements, although the quantification of the costs and the benefits of investing in risk management warrants further study. One critical issue for the GPEI stakeholders remains the inherent conflict between managing vaccine resources to support the polio endgame and eliminating all sources of potential reintroduction of LPVs. Currently, the GPEI assumes that manufacturers will continue poliovirus vaccine production (i.e., IPV or perhaps some other poliovirus vaccine in the long-term), but as containment requirements increase, so will the costs of production. The GPEI, external funders, and national governments remains highly sensitive to IPV price, and they do not appear to recognize that GPEI efforts to make the retention of LPVs costly influences the manufacturers in a way that will feedback to national governments and any stakeholders responsible for poliovirus vaccine management for the endgame (e.g., stockpile managers, financial supporters, and users). As the costs of containment increase, so will the cost for the vaccine, since any increased costs of production will flow through to the vaccine purchasers. This means that during the polio endgame, vaccine supplies will require active management, and those interested in ensuring their availability will need to expect to pay higher prices.

This study relied on previously calibrated models of poliovirus immunity and OPV evolution [31, 33, 39, 40] and previously developed characterizations of global variability in conditions [15]. These models comes with limitations and uncertainties related to model input assumptions, whose impact we discussed and analyzed for sensitivity elsewhere [33, 36, 38, 41-43]. As mentioned, the global model emphasized idealized assumptions about the implementation of risk management strategies and assumed achievement of WPV eradication in 2016, neither of which occurred. Therefore, the analysis shown in this study primarily serves to explore trends, illustrate dynamic behavior, and highlight the importance of the global variability in the context of developing appropriate poliovirus containment strategies.

Conclusion

Ongoing IPV production and storage and use of LPVs in facilities will imply ongoing risks of potential future poliovirus infections and spread in populations. Managing containment risks represents a critical component of the polio endgame and risk management efforts will increase prices for IPV production.

Future perspective

Over the next 5-10 years, we should observe the complete cessation of OPV use and full transition to the polio endgame, or sadly, the failure of complete polio eradication (i.e., the failure to permanently prevent all cases of poliomyelitis). We anticipate that during the next several years the full costs of containment will become apparent, along with the IPV vaccine supply, use, and costs. Time will tell whether any reintroductions of live polioviruses released from containment breaches will lead to any outbreaks during the next 10 years. The actual vulnerability of countries to reintroductions of live polioviruses will depend on the actions that they take between now and the time of the introduction. The extent to which ongoing immunization achieves and maintains high population immunity to poliovirus transmission will impact the starting point for the vulnerability analysis that will need to occur at the time of OPV cessation to update the analysis.

Summary:

Following the certification of global wild poliovirus (WPV) eradication and cessation of oral poliovirus vaccine (OPV) use, the potential reintroduction of live polioviruses will represent an important risk. Continued inactivated poliovirus vaccine (IPV) production will require the use of WPV or OPV seed strains, and any laboratories that (un)knowingly harbor live polioviruses could potentially reintroduce transmission. We explored the variability among different populations in the vulnerability to poliovirus containment breaches as population immunity to transmission declines. Using OPV instead of WPV seed strains for IPV production offers some expected reduction in the risks of reintroduction from IPV manufacturing facilities, but not enough to stop transmission in areas most conducive to fecal-oral poliovirus transmission, regardless of the extent of IPV use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the Centers for Disease Control and Prevention for supporting for this work. The contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

Funding

This publication was supported by Cooperative Agreement Number 5NU2RGH001913-02-00 funded by the Centers for Disease Control and Prevention.

Abbreviations:

AFP	acute flaccid paralysis
cVDPV	circulating VDPV
GAPIII	global action plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use
GPEI	Global Polio Eradication Initiative
IPV	inactivated poliovirus vaccine
OPV(2)	(serotype 2-containing) oral poliovirus vaccine
PEF	polio-essential facility
R_0	basic reproduction number
R_n	net reproduction number
RI	routine immunization
VDPV	vaccine-derived poliovirus
WPV(1,2,3)	wild poliovirus (of serotype 1, 2, 3, respectively)

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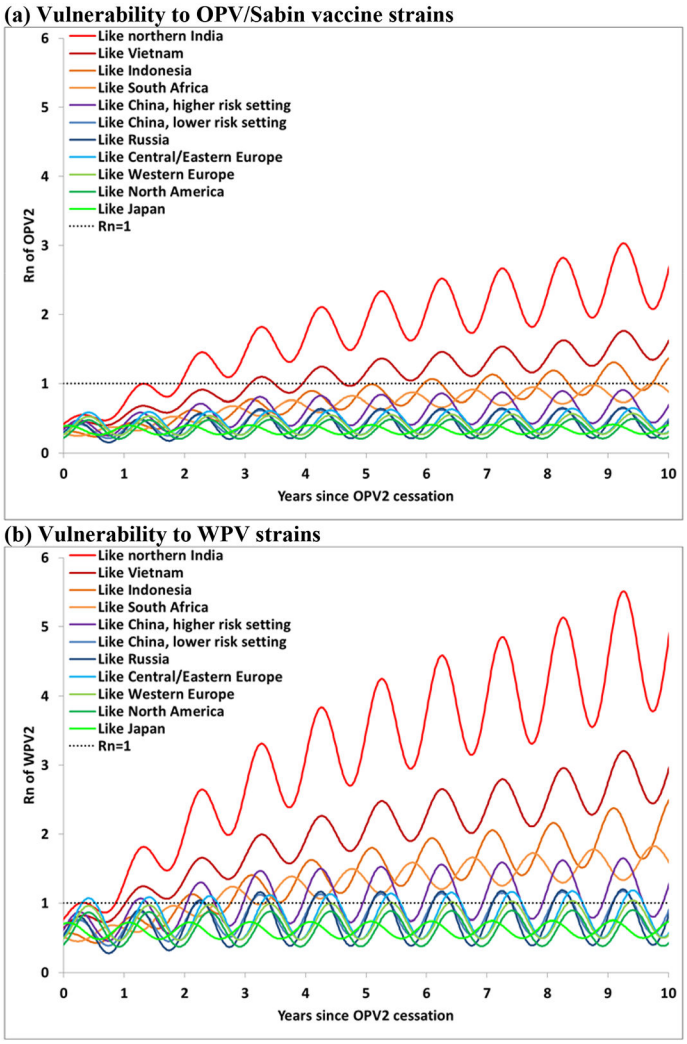

Figure 1:

Examples of vulnerability to releases of serotype 2 poliovirus strains in realistic populations in the global model [15] representative of settings that may produce IPV or maintain PEFs (see Table 2) and including seasonality

Abbreviations: IPV, inactivated poliovirus vaccine; OPV2, serotype 2-containing oral poliovirus vaccine; PEF, poliovirus essential facility; R_n= mixing-adjusted net reproduction number; WPV2, serotype 2 wild poliovirus

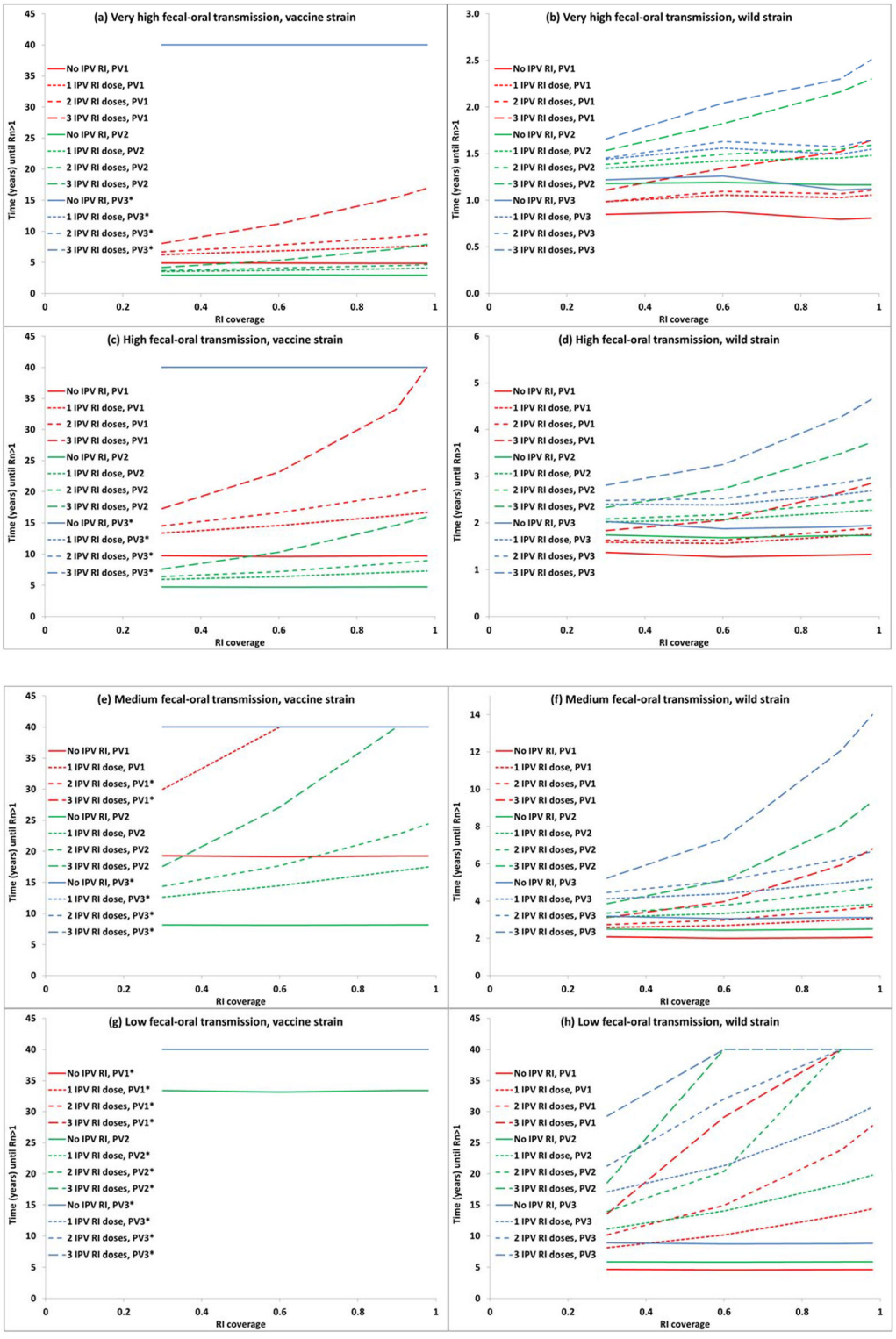

Figure 2:

Vulnerability of live polioviruses introduced into hypothetical populations as a function of RI coverage, serotype, strain, IPV schedule, and setting, and ignoring seasonality. If the $R_n < 1$ for the entire time horizon tested, the figure represents the time as 40 years. An asterisk

indicates that $R_n < 1$ for the entire time horizon for all RI coverage levels, which causes curves to overlap with each other. Note y-axis scales change for panels in the right column for wild strains (b, d, f, h).

* Indicates overlapping curves, **Abbreviations:** IPV, inactivated poliovirus vaccine; RI, routine immunization; PV(1,2,3), poliovirus (serotype 1, 2, or 3, respectively); R_n = mixing-adjusted net reproduction number

Table 1:

Historical publicly-reported releases

Location, Timing	Virus strain	Nature of release	Ref
France, 1991	WPV3	Isolation from an IPV-Saukett prototype strain from an Algerian woman (unknown source)	[16]
The Netherlands, 1992	WPV1	Isolation from the son of a worker in an IPV manufacturing facility accidentally exposed to a prototype IPV-Mahoney virus strain	[16]
The Netherlands, 1993	WPV3	Isolation from a child exposed to an IPV-Saukett strain used for IPV production and as a reference strain in some countries but not in the Netherlands (unknown source)	[16]
India, 2000 (3 cases), 2002 (5 cases), 2003 (2 cases)	WPV2	Isolated viruses closely related to a laboratory reference strain of serotype 2 wild poliovirus (i.e., MEF-1) (releases occurred in years that followed the global elimination of serotype 2 wild polioviruses)	[17]
Belgium, 2014	WPV3	Accidental release of 45 liters of concentrated live polio virus solution into a sewage system and discharged directly to a wastewater treatment plant and subsequently into rivers that flowed to the Western Scheldt and the North Sea, which led to no isolations from individuals or the environment	[18, 19]
The Netherlands, 2017	WPV2	Isolation of serotype 2 (MEF-1) wild poliovirus from one of two fully-vaccinated workers exposed to a spill of partly aerosolized high titer monovalent WPV2 in a Dutch vaccine manufacturing plant detected in stool 4 days after exposure and later in sewage samples (both exposed workers advised on stringent personal hygiene and monitored for virus shedding, and infected worker isolated at home and followed up until shedding stopped 29 days after exposure)	[20]

Table 2:

Assumed properties of populations global model [15] representative of settings that may produce IPV or maintain PEFs (used in Figure 1) (complete properties available in the appendix of Duintjer Tebbens et al. 2015[15])

Population like	Income level	Polio RI policy[a]				R_0 (amplitude)	p^{oro}	Take rate level[b]	RI coverage
		Before 2015	2015-2019	2019-2024	After 2024				
Northern India	LMI	OPV(4)	OPV(3)+OPV/IPV	IPV(1)	None	13 (0.2)	0.3	2	0.60
Vietnam	LMI	OPV(4)	OPV(3)+OPV/IPV	IPV(1)	None	8 (0.15)	0.3	5	0.98
Indonesia	LMI	OPV(4)	OPV(3)+OPV/IPV	IPV(1)	None	6 (0.2)	0.6	6	0.60
South Africa	UMI	IPV(2)+OPV(2)	IPV(2)+OPV(2)	IPV(3)	IPV(3)	7 (0.15)	0.6	6	0.60
China, higher risk	UMI	OPV(3)	IPV(2)+OPV(2)	IPV(3)	IPV(3)	7 (0.35)	0.6	7	0.98
China, lower risk	UMI	OPV(3)	IPV(2)+OPV(2)	IPV(3)	IPV(3)	6 (0.35)	0.8	8	0.98
Russia	HIGH	IPV(2)+OPV(2)	IPV(2)+OPV(2)	IPV(3)	IPV(3)	6 (0.50)	0.8	7	0.98
Central/Eastern Europe	HIGH	IPV(3)	IPV(3)	IPV(3)	IPV(3)	5 (0.40)	0.8	8	0.90
Western Europe	HIGH	IPV(3)	IPV(3)	IPV(3)	IPV(3)	5 (0.35)	0.9	8	0.90
North America	HIGH	IPV(3)	IPV(3)	IPV(3)	IPV(3)	4 (0.40)	0.9	8	0.98
Japan	HIGH	IPV(3)	IPV(3)	IPV(3)	IPV(3)	4 (0.20)	0.9	9	0.98

[a] Schedule notation reflects order of vaccines given (and number of vaccine doses in the schedule), with OPV/IPV indicating coadministration

[b] Higher take rate level implies higher average per-dose take rates for all OPV formulations, with the assumed values for each level depending on serotype and vaccine formulation, as listed in the appendix of Duintjer Tebbens et al. 2015[15]. For IPV, we assumed average per-dose take rates of 0.63, 0.70, and 0.75 in LMI, UMI, and HIGH, respectively.

Abbreviations: HIGH, high-income; IPV, inactivated poliovirus vaccine; LMI, Lower middle-incomeOPV, oral poliovirus vaccine; p^{oro}, proportion of transmissions via the oropharyngeal route; RI, routine immunization; R_0, basic reproduction number; UMI, upper middle-income

Table 3:

Assumed properties of fecal-oral transmission settings (used in Figure 2)

Setting	R_0 [a]	p^{oro}	Trivalent OPV take rate			Bivalent OPV take rate (same for serotypes 1 and 3)
			Serotype 1	Serotype 2	Serotype 3	
Very high	13	0.3	0.35	0.60	0.27	0.42
High	10	0.3	0.40	0.65	0.32	0.50
Medium	8	0.5	0.55	0.73	0.45	0.70
Low	5	0.9	0.65	0.75	0.55	0.80

Abbreviations: OPV, oral poliovirus vaccine; p^{oro}, proportion of transmissions via the oropharyngeal route; R_0, basic reproduction number

[a] R_0 for serotype 1 wild poliovirus shown, with other serotypes and strains directly dependent on the population specific R_0 for serotype 1 wild poliovirus[40]