Trends in the Risk of U.S. Polio Outbreaks and Poliovirus Vaccine Availability for Response

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ABSTRACT

Objectives. The United States eliminated indigenous wild polioviruses (WPVs) in 1979 and switched to inactivated poliovirus vaccine in 2000, which quickly ended all indigenous live poliovirus transmission. Continued WPV circulation and use of oral poliovirus vaccine globally allow for the possibility of reintroduction of these viruses. We evaluated the risk of a U.S. polio outbreak and explored potential vaccine needs for outbreak response.

Methods. We synthesized information available on vaccine coverage, exemptor populations, and population immunity. We used an infection transmission model to explore the potential dynamics of a U.S. polio outbreak and potential vaccine needs for outbreak response, and assessed the impacts of heterogeneity in population immunity for two different subpopulations with potentially low coverage.

Results. Although the risk of poliovirus introduction remains real, widespread transmission of polioviruses appears unlikely in the U.S., given high routine coverage. However, clusters of un- or underimmunized children might create pockets of susceptibility that could potentially lead to one or more paralytic polio cases. We found that the shift toward combination vaccine utilization, with limited age indications for use, and other current trends (e.g., decreasing proportion of the population with immunity induced by live polioviruses and aging of vaccine exemptor populations) might increase the vulnerability to poliovirus reintroduction at the same time that the ability to respond may decrease.

Conclusions. The U.S. poliovirus vaccine stockpile remains an important resource that may potentially be needed in the future to respond to an outbreak if a live poliovirus gets imported into a subpopulation with low vaccination coverage.

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U.S. public health policies generally focus on maintaining high levels of routine coverage with recommended vaccines for 16 vaccine-preventable diseases that remain well-controlled or eliminated.[1] Figure 1 provides a timeline of several key events related to polio vaccine use in the United States.[2–13] Increased reliance on inactivated poliovirus vaccine (IPV)-containing combination vaccines continues to decrease the supply of stand-alone IPV, which dropped from a market share of 100% in 2000–2002 to approximately 60%–65% in 2006–2008 to approximately 30% in 2009 (Unpublished data, Centers for Disease Control and Prevention [CDC],

Figure 1. Timeline of key events related to poliovirus vaccines in the U.S., 1950–2009

1950s	Introduction of IPV in the U.S. in a stand-alone (i.e., vaccines that contained only all three serotypes of poliovirus antigens) formulation
1960s	Introduction of OPV in the 1960s
1979	Elimination of transmission of all three types of indigenous WPV in the U.S.
1994	Certification of elimination of WPV transmission in all of the Americas[a–c]
1997	Switch from a routine OPV schedule to a sequential IPV/OPV schedule to decrease the risk of VAPP[d]
2000	Switch to an all-IPV schedule in 2000[e,f] after observations confirmed no decline in polio vaccination coverage despite the need for additional injections to complete the recommended schedule, leading to the end of indigenous transmission of all live polioviruses and cases of VAPP
2003	Licensure of DTaP-HepB-IPV and beginning of shift toward delivery of IPV in combination (i.e., vaccines that contained all three serotypes of poliovirus antigens and other antigens) vaccine formulations[g]
2005	One case of imported VAPP in the U.S.[h] and evidence of limited transmission of a vaccine-derived poliovirus in Minnesota[i]
2008	Licensure of combination products DTaP-IPV-Hib (recommended at ages 2, 4, 6, and 15–18 months) and DTaP-IPV (recommended for the preschool booster dose at age 4–6 years) continues to increase the proportion of IPV administered in the form of combination vaccines[j,k]
2009	One case of VAPP in an immune-deficient individual in the U.S.[l]

[a]Certification of poliomyelitis eradication—the Americas, 1994. MMWR Morb Mortal Wkly Rep 1994;43(39):720-2.

[b]Follow-up on poliomyelitis—United States, Canada, Netherlands, 1979. MMWR Morb Mortal Wkly Rep 1997;46(50):1195-9.

[c]Thompson KM, Tebbens RJ. Retrospective cost-effectiveness analyses for polio vaccination in the United States. Risk Anal 2006;26:1423-40.

[d]Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP) [published erratum appears in MMWR Morb Mortal Wkly Rep 1997;46(8):183]. MMWR Recomm Rep 1997;46(RR-3):1-25.

[e]Impact of the sequential IPV/OPV schedule on vaccination coverage levels—United States, 1997. MMWR Morb Mortal Wkly Rep 1998;47(47):1017-9.

[f]Prevots DR, Burr RK, Sutter RW, Murphy TV; Advisory Committee on Immunization Practices. Poliomyelitis prevention in the United States. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2000;49(RR-5):1-22.

[g]FDA licensure of diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and poliovirus vaccine combined, (PEDIARIX) for use in infants [published erratum appears in MMWR Morb Mortal Wkly Rep 2003;52(16):379]. MMWR Morb Mortal Wkly Rep 2003;52(10):203-4.

[h]Imported vaccine-associated paralytic poliomyelitis—United States, 2005. MMWR Morb Mortal Wkly Rep 2006;55(4):97-9.

[i]Alexander JP, Ehresmann K, Seward J, Wax G, Harriman K, Fuller S, et al. Transmission of imported vaccine-derived poliovirus in an undervaccinated community in Minnesota. J Infect Dis 2009;199:391-7.

[j]Licensure of a diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, and *haemophilus b* conjugate vaccine and guidance for use in infants and children. MMWR Morb Mortal Wkly Rep 2008;57(39):1079-80.

[k]Licensure of a diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine and guidance for use as a booster dose. MMWR Morb Mortal Wkly Rep 2008;57(39):1078-9.

[l]DeVries AS, Harper J, Murray A, Lexau C, Bahta L, Christensen J, et al. Vaccine-derived poliomyelitis 12 years after infection in Minnesota. N Engl J Med 2011;364:2316-23.

IPV = inactivated poliovirus vaccine

OPV = oral poliovirus vaccine

WPV = wild poliovirus

VAPP = vaccine-associated paralytic polio

DTaP-HepB-IPV = diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and inactivated poliovirus vaccine

DTaP-IPV-Hib = diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, and *Haemophilus influenzae* type b conjugate vaccine

DTaP-IPV = diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine

July 2010). CDC maintains the U.S. Pediatric Vaccine Stockpile to ensure an adequate supply of vaccines to meet unanticipated needs, including use in the event of outbreaks or vaccine shortages.

The target number of doses for the stockpile is based on the amount needed for the U.S. pediatric population for six months of routinely recommended vaccines, as required by the Vaccines for Children (VFC) program legislation. Jenkins and Modlin[14] identified monovalent oral poliovirus vaccine (OPV) as the best theoretical option for outbreak response, if available. A 2004 report recommended that the CDC stockpile eight million doses of IPV for outbreak response and develop access to eight million doses of OPV,[15] although no licensed OPV product has been available in the U.S. since 1999. The CDC stockpile, which relies on stock rotation of products used for routine vaccination to maintain shelf life and minimize wastage, contained 4.5 million doses of stand-alone IPV between 1999 and 2004, which then decreased to 3.7 million doses in 2005 and to <500,000 doses in 2009, mirroring the trend of decreasing market share. The stockpile added 500,000 doses of combination diphtheria-tetanus-acellular pertussis, hepatitis B, and IPV vaccine (DTaP-HepB-IPV) in 2006 and another 135,900 doses in 2010. Changes in the availability of different formulations led us to explore the potential need for IPV-containing vaccines from the stockpile in the unlikely but possible event of a polio outbreak in the U.S.

Although the U.S. stopped indigenous transmission of all live polioviruses in 2000, importations of wild poliovirus (WPV) types 1 and 3 and vaccine-derived polioviruses (VDPVs) of all types provide a potential source for reintroduction, at least until global eradication of all WPVs and global OPV cessation.[9,10] High levels of vaccine coverage generally imply that imported vaccine-preventable diseases do not encounter a sufficient number of susceptible individuals to sustain chains of transmission, although outbreaks can occur in subpopulations with low vaccination coverage. For example, although the U.S. declared measles eliminated in the year 2000, imported cases continue to cause local outbreaks[16] that largely involve unvaccinated or undervaccinated individuals and often lead to large and expensive public health responses.[17–19]

With the current high overall rate for polio vaccination and historically high levels of protection, we do not anticipate sustained transmission of polioviruses in the U.S. population. However, an outbreak (defined as one or more cases of paralytic polio) could potentially occur in susceptible subpopulations. In addition, although poliovirus vaccines offer complete protection from poliomyelitis, they provide incomplete protection from infection, and OPV and IPV differ with respect to their induction of mucosal immunity.[20] Given their ability to excrete virus in feces if infected, we assume that even immune individuals may participate in person-to-person transmission of polioviruses, although to a lesser extent than fully susceptible individuals.[21]

Prior studies provide context related to a global poliovirus vaccine stockpile for managing risks after interruption of WPV circulation globally[22,23] and explore issues related to responding to polio outbreaks globally,[24] but they do not focus on the specific risks or conditions that apply to the U.S. situation. This article explores the changing nature of U.S. population immunity with respect to poliovirus infections and the potential dynamics of polio outbreaks and vaccine needs from a stockpile or other sources for outbreak response.

METHODS

Studies of U.S. vaccine acceptance report relatively greater acceptance of IPV compared with other vaccines,[25,26] but some American children do not receive polio vaccination, according to data reported by vaccine providers to the National Immunization Survey (NIS).[27] We used the NIS data to estimate overall IPV coverage in the U.S. and analyzed 2006 and 2007 NIS data to estimate the means, 95% confidence intervals (CIs), and ranges of the county-level coverage with <2 IPV doses by ages seven months and 13 months to further explore heterogeneity in coverage.[27]

Using the coverage data and other U.S.-specific inputs, we adapted previously developed dynamic poliovirus transmission models for our analysis.[4,21,24] The models simplistically represent the entire U.S. as one homogeneous and instantaneously mixing population, which provides an upper bound of the number of cases that could occur and the speed at which poliovirus could spread if widespread circulation were possible.

Individual immunity depends on vaccination history and exposure to live polioviruses. The aggregation of individual immunity produces population immunity, which determines the extent to which polioviruses transmit in a population. High levels of population immunity inhibit sustained transmission, which protects susceptible individuals from exposure to circulating poliovirus.[28] Even with high coverage, susceptible individuals remain, including those for whom the vaccine may be contraindicated (e.g., children too young to receive the vaccine), those who refuse vaccination, and those missed by the health-care system. We characterized the average population immunity profile using assumptions and data[29,30] to assign members of the U.S.

population in 2010 to one of several different immunity states.[21,24] Specifically, the average population immunity profile describes the proportions of individuals who are (*1*) fully susceptible (i.e., never immunized or infected), (*2*) historically infected with OPV or WPV, or (*3*) IPV-vaccinated only (i.e., vaccinated with IPV, but never infected with OPV or WPV). These three immunity states differ in their relative susceptibility to infection and ability to transmit infections.[21] We assumed that individuals historically infected with OPV or WPV exhibit a substantially greater ability to transmit infections than recently OPV- or WPV-infected individuals (who currently do not exist in large numbers in the U.S.) due to the effect of waning immunity on fecal excretion.[31,32] However, we did not model any effect of waning immunity among IPV-vaccinated individuals, assuming instead that their likelihood of acquiring and transmitting infection remains constant over time after vaccination.

We used 2010 as the starting year and characterized expected changes in the population immunity profile for subsequent years by assuming that current routine coverage rates would apply to each new birth cohort and by aging all other cohorts. We determined the number of fully susceptible people born after 2000 based on the breakdown of coverage by age and dose from our detailed analysis of the combined 2006 and 2007 NIS data. We combined these data with seroconversion rate assumptions (100%, 70%, and 1% of children remain fully susceptible after receiving 0, 1, and ≥2 IPV doses, respectively).[29] We assumed that school laws will remain in place and be enforced, and that personal-beliefs exemptor (PBE) populations (i.e., those who decline vaccine for other than medical reasons) will remain relatively small. We used the NIS data up to 3 years of age, which does not capture any catch-up immunization that might occur subsequently, and we assumed that individuals would retain their immunity status until exposed during an outbreak.

For older age groups, we made several assumptions consistent with the historical use of IPV and OPV. We assumed that vaccinated individuals born prior to 1996 received OPV exclusively. During the years 1996–2000, IPV use gradually increased from 6% of all polio vaccine distributed in 1996 to 100% in 2000, averaging 43% of polio vaccine distributed during the five-year period, with most children receiving a sequential IPV-OPV schedule. Serologic data from inner-city children with below average coverage indicate stable seroprevalence during these transition years, with more than 97%, 99%, and 93% seroprevalence for poliovirus types 1, 2, and 3, respectively, among children vaccinated prior to the recommendation of the sequential schedule.[29] Data from a similar setting, but a decade earlier, showed comparably high seroprevalence.[30] Based on an assumption of frequent exposure to live polioviruses before 1999 (predominantly OPV since 1960 and WPV prior to 1960), we assumed that the seroprevalence observed during 1997–2000[29] represents a lower bound on population immunity for cohorts born prior to 2000. Further, considering the low-coverage setting of the study,[29] we conservatively assumed that 98% of individuals born prior to 2000 experienced live poliovirus infections during the OPV or prevaccine era. We emphasize that the population immunity profile changes over time as the proportion of Americans with only IPV-induced immunity increases.

We characterized the effective susceptible proportion in the population (ESP), which provides a relative measure of the extent to which infections can transmit in the population, with higher values indicating that more transmission will occur upon importation of poliovirus:

$$ESP = p_1 + (s^{rel}_2 \times i^{rel}_2 \times D_2/D) \times p_2 + (s^{rel}_3 \times i^{rel}_3 \times D_3/D) \times p_3$$

where

p_1 = proportion fully susceptible

p_2 = proportion historically infected with live poliovirus

p_3 = proportion IPV-vaccinated (and no live poliovirus infection)

s^{rel}_2 = relative susceptibility for individuals historically infected with live poliovirus = 0.8

s^{rel}_3 = relative susceptibility for IPV-vaccinated individuals = 0.95

i^{rel}_2 = relative infectiousness for individuals historically infected with live poliovirus = 0.5

i^{rel}_3 = relative infectiousness for IPV-vaccinated individuals = 0.75

D = duration of infectiousness for fully susceptibles = 35 days

D_2 = duration of infectiousness for individuals historically infected with live poliovirus = nine days

D_3 = duration of infectiousness for IPV-vaccinated individuals = 20 days

We note that we ignored the small effects of mortality in this model,[21] which would otherwise appear in the equation.

For any disease transmission model, the basic reproductive number, R_0, represents a key input that determines the force of infection and the dynamics of infection transmission, with higher values indicating

relatively greater transmissibility. We assumed a maximum R_0 of 6 for polioviruses in the U.S., and we used this value to explore the upper-bound behavior. Seeing an outbreak in the model requires that the R_0 of the introduced poliovirus (i.e., 6) exceed the theoretical threshold R_0 required to establish transmission and cause an outbreak, which we defined as R_0* (with R_0* = 1/ESP). We note that R_0* decreases as more people become effectively susceptible (i.e., as ESP increases), which occurs in the model either as coverage decreases (i.e., leaving a higher fraction of each new cohort fully susceptible) or as relatively more people benefit from IPV-only induced immunity instead of immunity from exposure to a live poliovirus infection (i.e., WPV or OPV).

Studies measuring rates and amounts of fecal excretion following a challenge with a live poliovirus show higher relative susceptibility (i.e., probability of becoming infected compared with fully susceptible individuals), higher amount of virus excreted (translating into a higher relative infectiousness—i.e., probability of infecting others compared with fully susceptible individuals), and longer duration of infectiousness for IPV-only vaccinated individuals than for those with prior live poliovirus infection.[20,21,33] Thus, the higher potential for fecal-oral transmission for IPV-vaccinated people compared with individuals previously infected with live virus or OPV vaccine leads to a decrease in R_0*, although we emphasize that the model did not factor in any reduction in oropharyngeal transmission that IPV might induce. The U.S. experience following the introduction of IPV in 1955 showed that IPV induced some herd immunity,[34] possibly by reducing the ability of IPV-vaccinated people to participate in oropharyngeal transmission,[35] but that IPV did not prevent familial transmission or completely eliminate WPV transmission in lower-income settings.[36,37] Uncertainty in the model inputs related to infectiousness of reinfected IPV-vaccinated people suggests that while some decreasing trend in the historical R_0* is probably real due to the known difference in fecal excretion between IPV- and OPV-induced immunity, both the current figure and the rate of decrease going forward remain uncertain.

Although we focused on the U.S. population as a whole, we recognize the importance of heterogeneity. For example, some religious communities that generally do not accept vaccination differ from the general population. They may cluster socially and geographically, and may represent important risk groups. Notably, Amish communities experienced the most recent episodes of known community circulation of polioviruses in the U.S.,[3,10,13] and an outbreak occurred in a subpopulation of religious vaccine objectors in the Netherlands in 1992–1993, despite high IPV coverage in the rest of that country.[21,38] Because neither vaccination coverage nor seroprevalence data exist for these communities, we modeled a range of reductions in population immunity using a relative immunity fraction (RIF) for a hypothetical vaccine objector community compared with the average U.S. population. Starting with the proportion of people vaccinated with IPV or historically exposed to live poliovirus in the general population, we defined the RIF as the fraction of that proportion that we treat as fully susceptible in the religious vaccine objector community, applied to all cohorts born since IPV vaccination began in 1955 (i.e., RIF=0 implies that everyone born since 1955 is fully susceptible in the religious vaccine objector community, while RIF=1 implies the same population immunity profile as the general U.S. population). We assumed that an introduction of a live poliovirus with R_0=6 at most could occur in 2010 in a hypothetical religious vaccine objector homogeneously mixed community of 55,000 people, which approximately corresponds to the largest community of Amish people in a U.S. state,[39] using a model that represents this subpopulation in the context of a well-immunized surrounding community similar to our prior model of the outbreak in the Netherlands.[21]

We also explored the impact of heterogeneity in coverage and resulting immunity within a county on the potential for a polio outbreak given virus introduction, building on the insights from Smith et al.,[40] who identified four counties in California (Los Angeles, Orange, San Bernardino, and San Diego counties) with relatively large numbers of unvaccinated children. Recognizing that heterogeneous vaccination coverage and immunity among schoolchildren in large counties currently could potentially manifest as an outbreak, we performed a subcounty analysis using polio vaccine coverage data collected in San Diego County, California, in 2008. Schools within the county showed considerable heterogeneity in rates of PBEs for kindergarten entry, which suggests that an assumption of uniform coverage for polio vaccination for San Diego County (mean = 92.6% ± 2.7%)[41] could miss some potentially high-risk subcounty areas. We combined the San Diego County polio vaccination data with total school enrollment numbers for private, public, and charter schools, and excluded home-schooled children due to lack of data. We focused on potential clustering at the level of individual schools within a district and evaluated whether any individual elementary school within San Diego County might expect to see a case of paralytic polio following a reintroduction of a live poliovirus. Using

Table 1a. U.S. coverage statistics for IPV from the 2008 National Immunization Survey

Child age (number of IPV doses)	*National mean ± 95% CI (percent)*	*Low mean ± 95% CI (percent)*	*Location*	*High mean ± 95% CI (percent)*	*Location*
19–35 months (≥3)	93.6±0.6	88.4±5.6	Oklahoma	99.5±0.6	Connecticut
19–35 months (≥3)[a]	91.8±1.6	84.0±7.6	Texas—Dallas County	97.4±3.6	New York City
3 months (≥1)	87.2±0.9	79.1±5.9	New Jersey	96.5±3.0	Massachusetts
5 months (≥2)	78.1±1.1	64.4±7.1	Oklahoma	91.0±4.0	Massachusetts
7 months (≥2)	90.4±0.8	81.4±5.8	Montana	97.8±1.7	Massachusetts
13 months (≥2)	95.3±0.6	89.5±5.3	Oklahoma	99.2±0.9	Connecticut
19 months (≥3)	89.1±0.8	80.5±8.3	Florida—Miami-Dade County	97.1±2.6	Rhode Island
24 months (≥3)	92.3±0.7	84.9±6.1	Washington State, excluding King County	98.7±1.2	Connecticut

[a]Children in families with incomes below the federal poverty level

IPV = inactivated poliovirus vaccine

CI = confidence interval

the same approach we applied to consider heterogeneity associated with a religious community, we captured a range of immunity reductions in communities with increased PBEs by defining RIF_{PBE} as the fraction of the IPV-vaccinated proportion in the general population treated as fully susceptible.

RESULTS

Nationally, we found high mean levels of polio vaccination coverage for age-appropriate first (87%), second (90%), and third (95%) doses, but the 2008 NIS data showed considerable variation among cities and states (Table 1a). Prior studies show minimal fluctuations in mean coverage, with ≥3 IPV doses among children aged 19–35 months surveyed during 2004–2008, which approximates the cohorts born during 2001–2007 (range 91.8% to 93.6%, with 95% CIs of <1%).[42,43] Analysis of 2006 and 2007 NIS data showed that the national and county-level proportions of children with zero or one dose of IPV by ages seven, 13, and 24 months ranged from 2.0% to 6.1% (Table 1b).

The assumed average U.S. population immunity profile summarized in Table 2 for 2010 indicates an overall low risk for a polio outbreak, with an ESP of 0.16, which implies R_0*=6.1. R_0 values for polioviruses in high-income countries probably range from 3 to 6,[21,44] with 6 representing a plausible estimate in the U.S. for the prevaccine era.[4] Given that R_0*=6.1 exceeds the high estimate of R_0=6, the reintroduction of a live poliovirus currently appears very unlikely to establish sustained transmission, consistent with the lack of observed widespread transmission despite known introductions of transmissible VDPVs.[9,10] Consequently, we did not model any potential outbreak scenarios for the general population in 2010, because our model would yield zero cases for any poliovirus introduced with an R_0 up to 6 and no expected need of vaccine from the stockpile.

The average U.S. population immunity to poliovirus, however, will decline as the proportion of Americans with only IPV-induced immunity increases, because IPV protection does not convey the same level of mucosal immunity as exposure to live polioviruses.

Table 1b. U.S. coverage statistics for IPV showing county-level variability in children with <2 IPV doses from combined 2006 and 2007 National Immunization Survey data

Child age (number of IPV doses)	*National mean (percent)*	*County mean ± 95% CI (percent)*	*County range (percent)*
7 months (0)	3.8	3.8±3.1	0–13.6
7 months (1)	6.1	5.5±4.4	0–21.6
13 months (0)	2.8	2.8±2.5	0–13.6
13 months (1)	2.3	2.2±2.6	0–15.5
24 months (0)	2.0	NA[a]	NA[a]

[a]Data not available at county level due to insufficient sample size

IPV = inactivated poliovirus vaccine

CI = confidence interval

NA = not available

Table 2. U.S. average poliovirus population immunity profile for 2010

Age/age group in 2010 (in years)	*Year(s) of birth*	*Proportion historically infected with live poliovirus (WPV or OPV)*	*Proportion IPV-vaccinated only (i.e., no live poliovirus infection from either WPV or OPV)*	*Proportion fully susceptible (i.e., never immunized or infected)*	*Notes*
0	2010	0	0.910	0.090	[a]
1	2009	0	0.946	0.054	[a]
2	2008	0	0.963	0.037	[a]
3	2007	0	0.966	0.034	[a]
4	2006	0	0.966	0.034	[a]
5–9	2001–2005	0	0.966	0.034	[a]
10–14	1996–2000	0.98	0	0.02	[b]
15–19	1991–1995	0.98	0	0.02	[c]
20–24	1986–1990	0.98	0	0.02	[c]
25–29	1981–1985	0.98	0	0.02	[c]
30–34	1976–1980	0.98	0	0.02	[c]
35–39	1971–1975	0.98	0	0.02	[c]
40–44	1966–1970	0.98	0	0.02	[c]
45–49	1961–1965	0.98	0	0.02	[c]
50–54	1956–1960	0.98	0	0.02	[c]
55–59	1951–1955	0.98	0	0.02	[c]
60–64	1946–1950	0.98	0	0.02	[c]
65–69	1941–1945	0.98	0	0.02	[c]
70–74	1936–1940	0.98	0	0.02	[c]
75–79	1931–1935	0.98	0	0.02	[c]
80–84	1926–1930	0.98	0	0.02	[c]
85–89	1921–1925	0.98	0	0.02	[c]
90–94	1916–1920	0.98	0	0.02	[c]
95–99	1911–1915	0.98	0	0.02	[c]
≥100	1910 or prior	0.98	0	0.02	[c]

[a]Based on proportions with 0 and 1 IPV doses by age and assumed seroconversion rates by dose

[b]Based on the observed seroprevalence during 1997–2000 in a study by Prevots et al. (Prevots DR, Pascual FB, Angellili ML, Brayden R, Irigoyen M, Larussa P, et al. Population immunity to polioviruses among preschool children from four urban underserved low income communities, United States, 1997–2001. Pediatr Infect Dis J 2004;23:1130-6), averaged over serotypes and rounded upwards to correct for low-coverage setting of study.

[c]Based on the assumption that estimates of seroconversion in a study by Prevots et al. (Prevots DR, Pascual FB, Angellili ML, Brayden R, Irigoyen M, Larussa P, et al. Population immunity to polioviruses among preschool children from four urban underserved low income communities, United States, 1997–2001. Pediatr Infect Dis J 2004;23:1130-6) represent a lower bound on immunity level for older individuals.

WPV = wild poliovirus

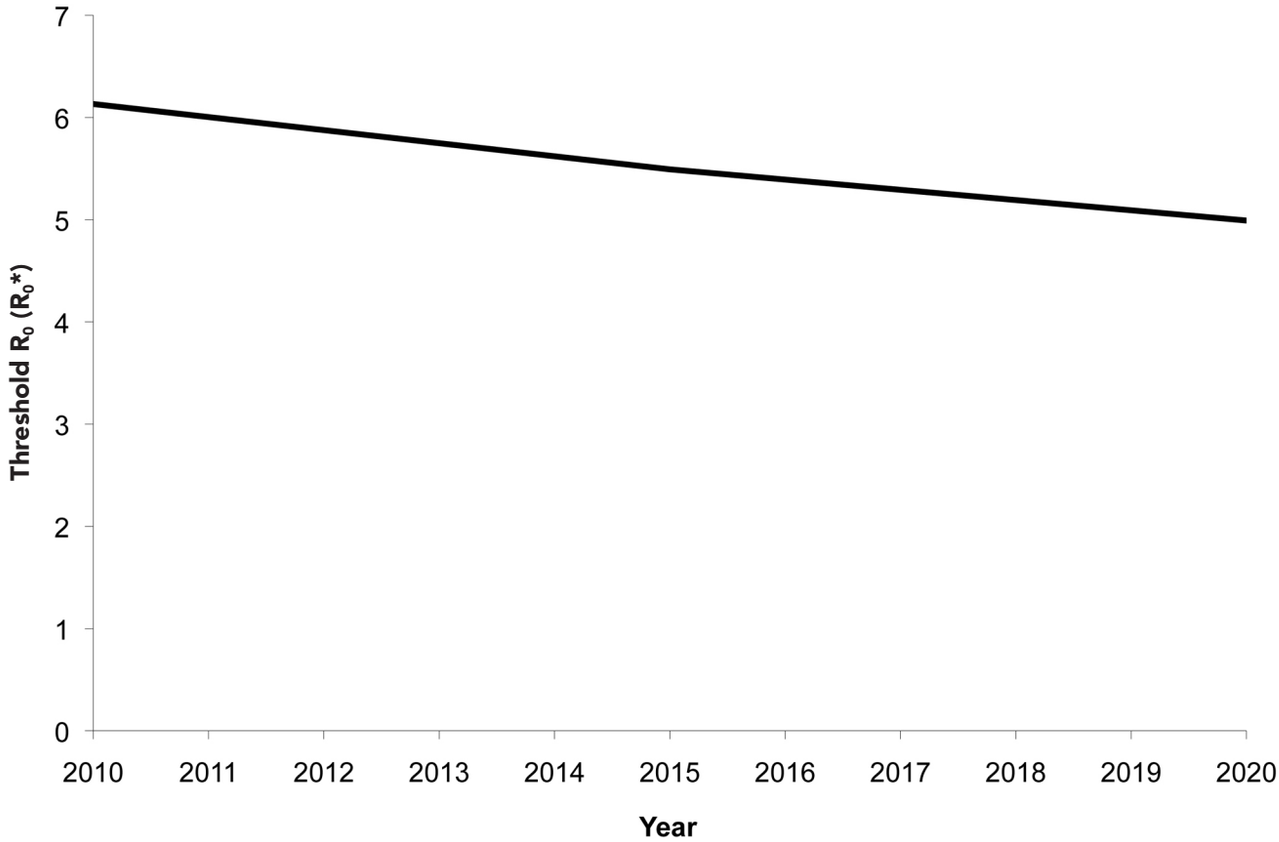
OPV = oral poliovirus vaccine

IPV = inactivated poliovirus vaccine

Thus, the risk for a polio outbreak will increase as the R_0* required to sustain transmission decreases. If we assume constant routine IPV coverage during the next decade at the 2010 levels (Table 2), then the R_0* will decrease to approximately 5.5 by 2015 and to 5.0 by 2020 (Figure 2). This decrease results solely from the shift to a greater proportion of IPV-only vaccinated people in the population and their assumed greater ability to participate in fecal-oral transmission. The absence of boosting due to live poliovirus exposure implies a greater decline in neutralizing antibody levels compared with the time period before the cessation of OPV in 2000.[31,45] Limited data are available regarding the impact of the waning of IPV-induced antibodies on the ability to participate in both fecal-oral or oropharyngeal transmission of poliovirus,[32,46,47] and the model does not include any effect of waning of IPV-induced antibodies. However, even the introduction in 2020 of a poliovirus with an assumed high end R_0 of 6 would spread so slowly that the outbreak, in the absence of any intervention, would not reach its peak until 3.5 years later, due to the small difference between this R_0 and the R_0* of 5.0 in 2020. Overall, the risks to the general U.S. population appear very low, and we do not expect widespread demand for poliovirus vaccines from the stockpile in the near future, although public health officials should periodically (e.g., every five to 10 years) reassess the situation.

The results for the general population do not consider issues related to heterogeneity and the potential

Figure 2. Decrease in R_0* over time for population immunity to poliovirus, using an assumed population immunity profile for 2010 and assumed model inputs related to ability to transmit poliovirus via the fecal-oral route for each immunity state[a]



[a]Duintjer Tebbens RJ, Pallansch MA, Kew OM, Cáceres VM, Sutter RW, Thompson KM. A dynamic model of poliomyelitis outbreaks: learning from the past to help inform the future. Am J Epidemiol 2005;162:358-72.

R_0* = 1/effective susceptible proportion in the population

R_0 = basic reproductive number

for vaccine needs for localized outbreak response activities in high-risk populations. Figure 3a shows the epidemic curves for our model of the introduction of live poliovirus into a hypothetical religious objector community for several RIF values, which reflects a wide range of assumptions about the susceptibility among people born since 1955 in the hypothetical vaccine objector community in the absence of outbreak response vaccination. Assuming everyone born since 1955 is fully susceptible (RIF=0, which implies R_0*=1.3), the model yields 190 cases in five years; assuming a population with more immunity (RIF=0.9, which implies R_0*=4.4) yields an outbreak with 13 cases. Note that if we assume widespread circulation stopped later than the time of introduction of IPV in 1955 due to the occurrence of real outbreaks in some areas into the early 1960s,[35–37,48] then this effectively implies an RIF value slightly higher than 0, which falls within the current range. For all values of the RIF, the epidemic unfolds much faster in the vaccine objector community (Figure 3a) than in the general U.S. population due to the greater difference between R_0=6 and the R_0* implied by the reduced population immunity levels. As shown in Figure 3b, introducing a poliovirus with R_0=5 leads to small and slow outbreaks in the modeled vaccine objector community, even for a relatively high immunity (RIF=0.9).

Figure 4a shows the results of our analysis of the total number of San Diego County kindergarten students in schools in each district as a function of the percentage of students fully vaccinated against polio by kindergarten entry in the district. The vertical line at 95% shows the county average percent vaccinated, weighted by enrollment. Figure 4a shows considerable

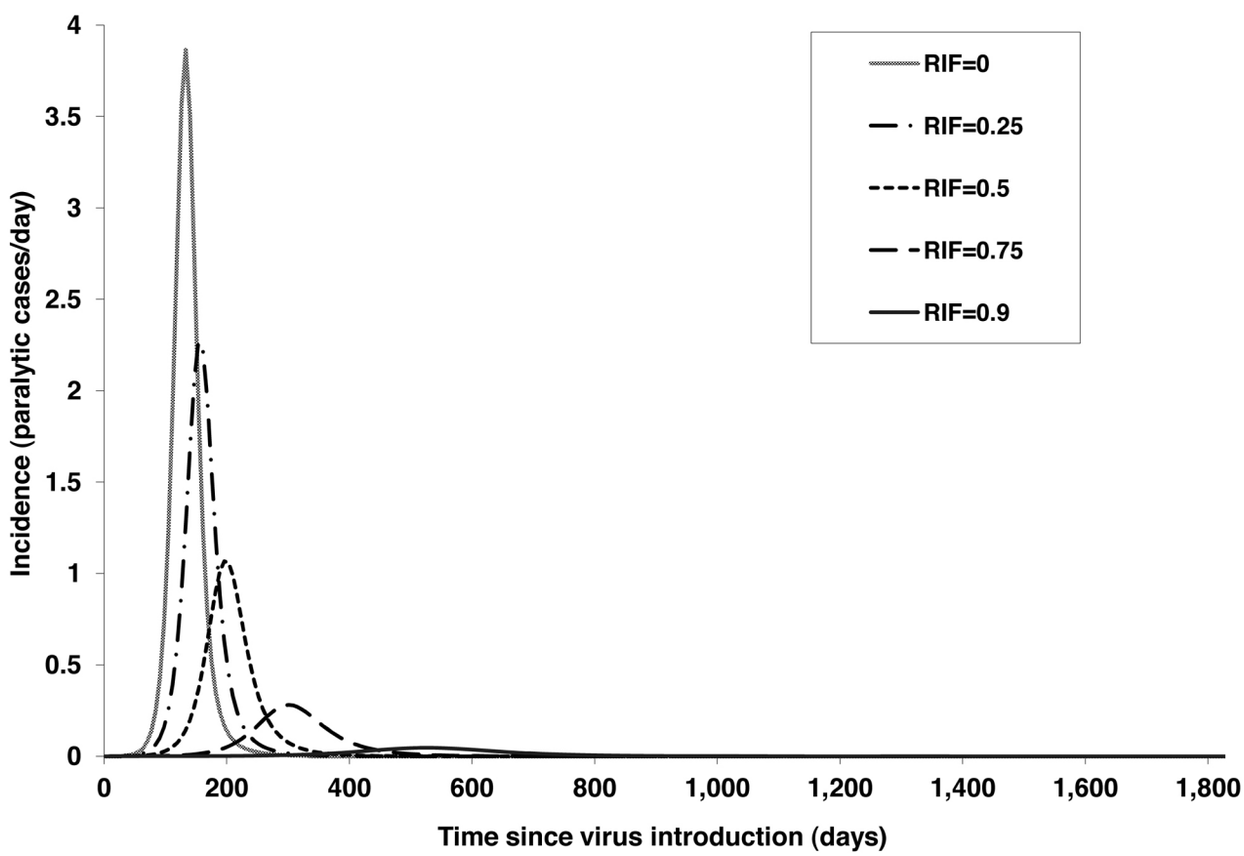
variability in vaccination coverage among districts, consistent with geographical clustering of susceptible children within the county.

Figure 4b shows an estimate of the number of children not fully vaccinated against polio at the level of individual elementary schools, based on extrapolating the percentage of San Diego kindergarten students not fully vaccinated against polio at school entry[40] to each school's total enrollment. Figure 4b focuses on schools with more than 100 expected unvaccinated or undervaccinated students, and shows immunity gaps in all types of schools (public, private, and charter). Assuming that paralysis occurs at a maximum rate of one paralytic case per 100 infections of fully susceptible people,[49] these results suggest that 24 schools in San Diego County might expect to see a case of paralytic polio, although we emphasize that with community transmission, the cases might occur anywhere. Assuming a paralysis-to-infection rate of one case per 200 infections (which we used as an average for the three poliovirus serotypes[21] for the model results presented previously) leads to an expectation that eight individual schools might expect to see a case. Exploring the impact of possible immunity reductions in communities with recently increased PBE rates (RIF_{PBE}) on the R_0* (Table 3), we see a relatively slower decline in R_0* for this type of immunity gap than in the religious vaccine objector community (i.e., immunity reductions in this setting primarily involve young people, with greater than 50% immunity reductions in children younger than 10 years of age required for the R_0* to drop below 5).

DISCUSSION

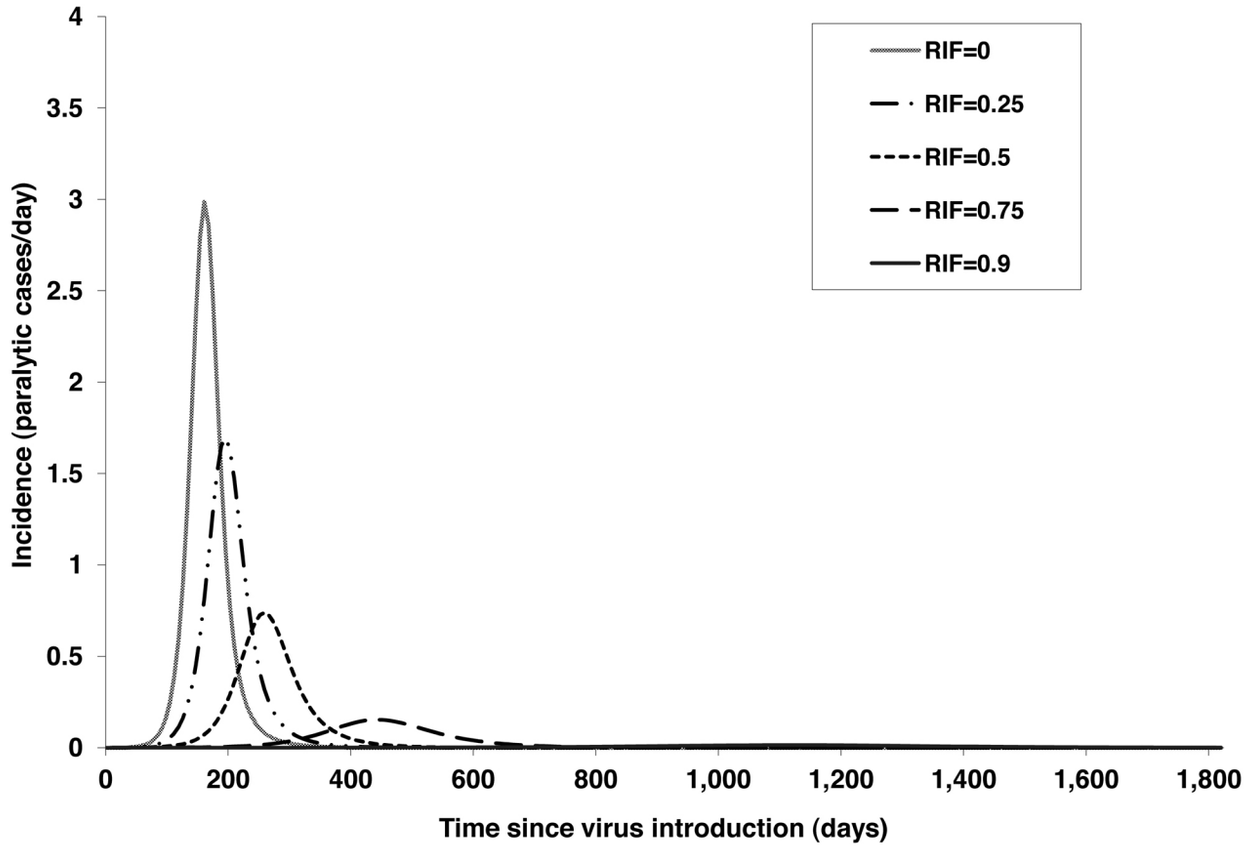
The current and historically high polio vaccination coverage levels suggest that we should not expect to see

Figure 3a. Epidemic curves following an introduction of poliovirus with an R_0 of 6 in 2010, assuming the outbreak stays contained in a religious vaccine objector community as a function of the RIF for people born since 1955



R_0 = basic reproductive number
RIF = relative immunity fraction

Figure 3b. Epidemic curves following an introduction of poliovirus with an R_0 of 5 in 2010, assuming the outbreak stays contained in a religious vaccine objector community as a function of the RIF for people born since 1955



R_0 = basic reproductive number
RIF = relative immunity fraction

sustained transmission of live polioviruses in the U.S. or reestablishment of endemic poliovirus transmission; however, importation of poliovirus could occur and lead to an outbreak in some situations. Fortunately, given the relatively slow expected time course, if circulation occurs, public health authorities could develop an outbreak response strategy at the time of detection of the first few cases without placing large numbers of Americans at significant risk, assuming appropriate diagnosis of cases and maintained high vaccination coverage levels. However, the time characteristics of future outbreaks will change as R_0* decreases, which may imply a need to respond relatively more quickly in the future. Clinicians and public health authorities will need to continue to remain vigilant in their surveillance for poliomyelitis symptoms, particularly as polio becomes an increasingly distant memory. We find that clusters of undervaccinated infants and children in some U.S. counties might face higher risks for a polio outbreak than undervaccinated children living in other counties with higher coverage.

Within an outbreak or threatened community, the public health response could include resource-intensive efforts to document individual immunity, an urgent vaccination response, and/or possibly large-scale contact tracing.[14,50–55] Figure 5 offers some potential characteristics of outbreak response efforts. CDC also maintains recommendations for travelers to endemic areas.[56] We note that the continued decline of standalone IPV means that vaccination efforts potentially indicated for and demanded by a substantial number of people ≥7 years of age in an outbreak situation (e.g., if PBE rates slowly increase[57,58]) may encounter limited supplies of vaccine, and this situation may worsen with time. With IPV-containing combination vaccines not indicated for people older than 6 years of age[59] and evidence suggesting an increase in the number of local reactions and fever with increasing

doses of DTaP,[60] insufficient supplies of stand-alone IPV could pose challenges. While some people who object to vaccination may continue to decline vaccines during an outbreak, the occurrence of paralytic poliomyelitis cases might change the perception of the risk-benefit ratio for vaccination among prior vaccine objectors.

Our exploration of subcounty data from San Diego County suggests that targeting efforts to increase routine vaccination in some school districts might represent an important opportunity for outbreak prevention. We found a strong correlation between the rate of PBEs and lower percentages of kindergarten students fully vaccinated at school entry by district (correlation coefficient = 0.90, $n = 37$ districts), which suggests that these efforts would need to particularly target vaccine exemptors. The implication of asymptomatic infections and the relatively close proximity between people in San Diego County and other California counties with relatively large numbers of unvaccinated children[41] suggest that if a case occurs in one of these counties, then public health authorities should consider outbreak response activities in other communities as well.

Limitations

Numerous limitations and simplifying assumptions may affect the interpretation our results. First, in this analysis we allowed the outbreak model to cover a relatively long period of time (i.e., a decade), and we did not factor in age-dependent mortality or waning of immunity of IPV-vaccinated people or those previously exposed during the outbreak. With these assumptions, the model could underestimate the potential size of outbreaks. Second, the model characterizes routine childhood immunization such that a fraction of the population immediately becomes immune during the newborn period, whereas polio vaccination does not commence until the second month of life. In reality, NIS data show that the fraction of children with <2 doses continues to decrease beyond the first seven months of age, meaning that the inclusion of some immunization among one- and 2-year-olds (or older children) in the model would more adequately capture the impact of routine immunization by age. With this assumption, the model might overestimate the potential consequences of an outbreak.

Figure 4a. Kindergarten enrollment and percentage of kindergarten students fully vaccinated against polio by entry for individual school districts within San Diego County, California, 2008

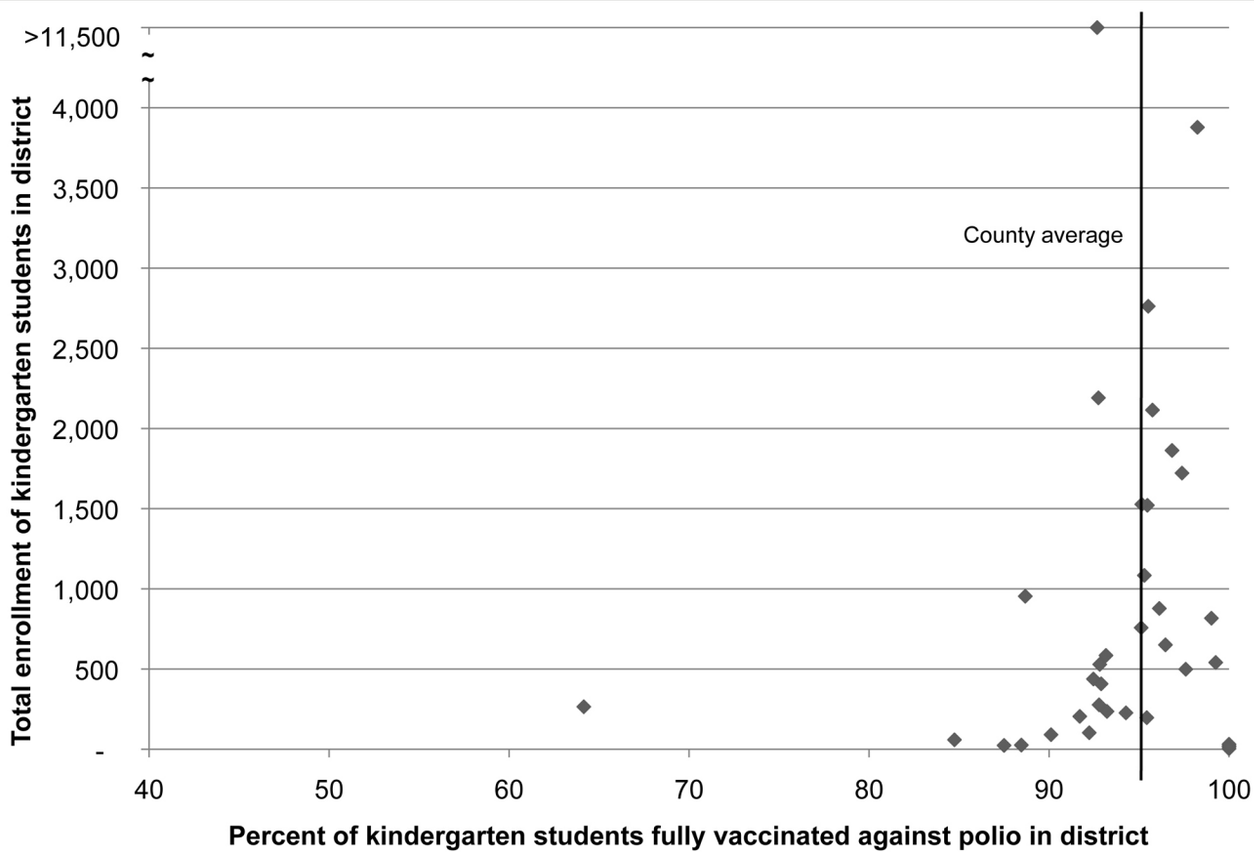


Figure 4b. Estimated total number of children (all grades) not fully vaccinated against polio for individual San Diego County, California, schools with more than 100 such children, as a function of the percentage of kindergarten students fully vaccinated against polio at kindergarten entry, by type of school—2008

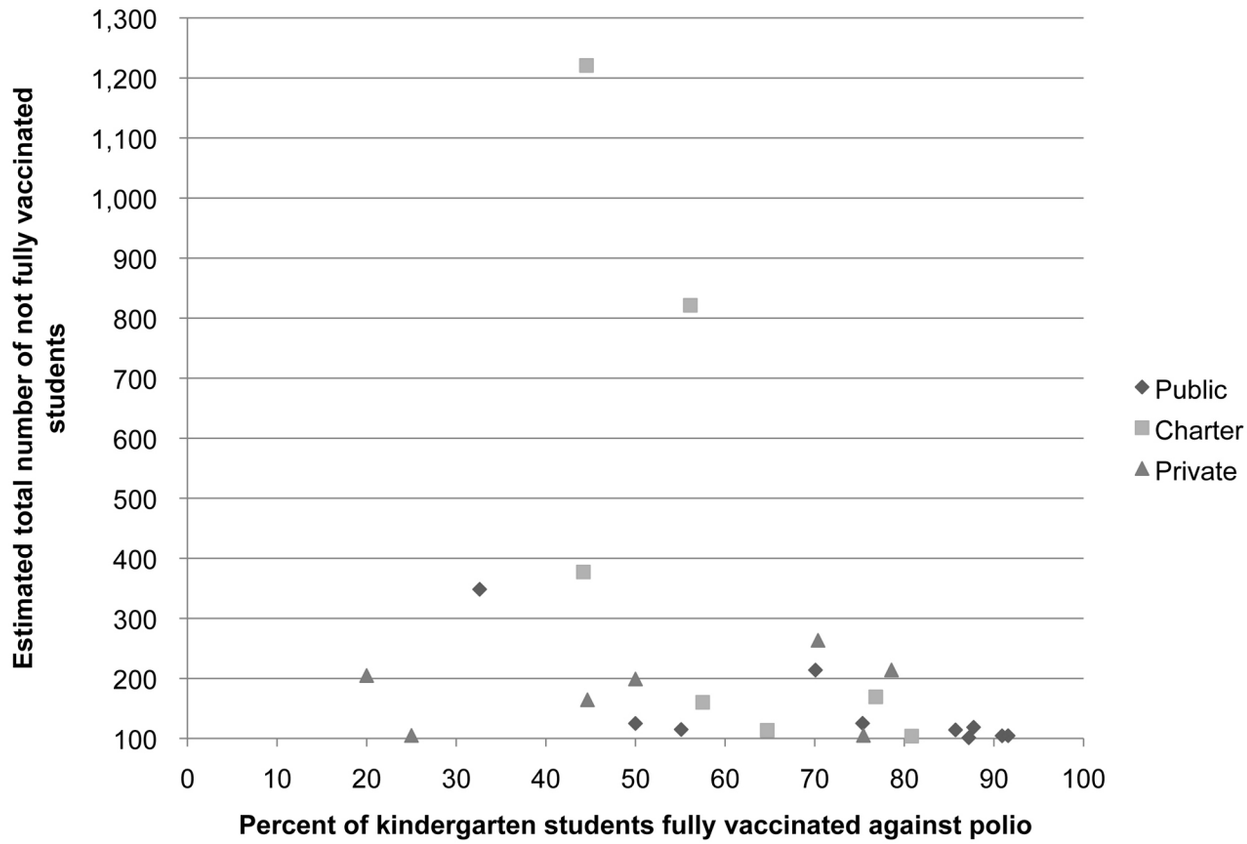


Table 3. The impact of the relative immunity fraction in recent cohorts (RIF_{PBE}) on the R_0* implied by the reduced population immunity in 2010

RIF_{PBE}	*Threshold R_0 (2010)*
1.00	6.1
0.95	6.0
0.90	5.9
0.85	5.7
0.80	5.6
0.75	5.5
0.50	5.0
0.25	4.5
0.00	4.2

RIF_{PBE} = relative immunity fraction, personal-beliefs exemptor population (i.e., the fraction of the inactivated poliovirus-vaccinated proportion in the general population treated as fully susceptible)

R_0* = 1/effective susceptible proportion in the population

R_0 = basic reproductive number

Third, some bias may have occurred in the reported vaccination history of individual children in San Diego County schools. Although the bias of parents reporting their children as vaccinated when they are not may be less likely than reporting their children as not vaccinated when they are vaccinated (e.g., parents obtain a PBE rather than reporting actual vaccination history), we could not ascertain the level of either type of bias in the data we used in our analysis of San Diego County. Fourth, the outbreak model, originally designed primarily to model global conditions, focused mainly on capturing the dynamics in lower-income settings in which fecal-oral transmission represents the dominant mode of spread. If oropharyngeal transmission accounts for a high proportion of transmissions in the U.S., IPV recipients might contribute less to transmission than assumed in the current model because IPV effectively prevents pharyngeal excretion; thus, the model could overestimate the effect of the switch to IPV on population immunity to transmission of infections.

Figure 5. Potential characteristics of outbreak response with IPV[a]

Age group and proximity to outbreak	*Vaccination status before outbreak*	
	<2 doses of IPV	*On schedule or ≥2 doses of IPV*
Children ≤6 years of age for routine or catch-up immunization living in outbreak communities[b]	Administration of a total of two valid doses of IPV-containing vaccine[b] as quickly as possible with a minimum age of six weeks and a minimum interval of four weeks between doses	Completion of a four-dose schedule on time with whatever IPV-containing vaccine formulation is available (i.e., including combination vaccines)[b]
Adults and children >6 years of age for catch-up immunization living in outbreak communities	Administration of a total of two valid doses of stand-alone IPV as quickly as possible with a minimum interval of four weeks between doses	Administration of one booster dose of stand-alone IPV, given sufficient availability of vaccine
Children ≤6 years of age living outside of outbreak communities	Completion of a four-dose schedule on-time with whatever vaccine formulation is available (i.e., including combination vaccines)[b]	Completion of a four-dose schedule on time with whatever vaccine formulation is available (i.e., including combination vaccines)[b]
Adults and children >6 years of age for catch-up immunization living outside of outbreak communities	None	None

[a]Although OPV may offer some advantages in an outbreak (Alexander L, Birkhead G, Guerra F, Helms C, Hinman A, Katz S, et al. Ensuring preparedness for potential poliomyelitis outbreaks: recommendations for the US poliovirus vaccine stockpile from the National Vaccine Advisory Committee [NVAC] and the Advisory Committee on Immunization Practices (ACIP). Arch Pediatr Adolesc Med 2004;158:1106-12), we assume IPV will represent the primary tool for outbreak response given current unavailability of a licensed OPV vaccine in the U.S.

[b]We emphasize the need to reserve any stand-alone preparations of IPV for those with absolute contraindications to other components in IPV-containing combination vaccines and for unvaccinated or undervaccinated people older than 6 years of age. The lack of immediate surge capacity for IPV-containing vaccine production means no excess vaccine availability exists to immunize significantly more people than for those receiving vaccine as routinely recommended.

IPV = inactivated poliovirus vaccine

OPV = oral poliovirus vaccine

Fifth, the assumption of 2010 coverage levels extrapolated into the future could potentially over- or underestimate what will actually occur. Finally, to see an outbreak at all, the R_0 for the introduced poliovirus must exceed the R_0*, which implies a relatively high R_0 (i.e., R_0=6). Conditioning on a high R_0 overestimates the potential for outbreaks to occur and their size, as the R_0 of polioviruses that might get introduced into the population remains uncertain.

Recommendations

Based on our findings, we believe there is a need for additional policy research and modeling related to the U.S. vaccine stockpile,[22,61] including optimization of the types and number of doses of polio vaccines it contains and modeling of outbreak response strategies that explicitly include finite amounts of different formulations of vaccines to support the development of detailed domestic outbreak response plans for different types of susceptible groups. Notably, our analyses do not address the connectivity between communities in which people who are susceptible may cluster, but we expect that connections exist and that outbreak investigations and social network analysis can assist in looking for these connections, which represents an important topic for future research.

Research that would increase the understanding of the nature of poliovirus transmission in the U.S. (and reduce related uncertainties in the modeling) includes studies related to the role of adults in the circulation of polioviruses, the extent to which IPV protects against infection with polioviruses as a function of the number of IPV doses received, and the role of oropharyngeal spread in the context of high vaccine coverage. Studies that provide information about the persistence of neutralizing antibodies, recall of antibodies after challenge, and nature of waning immunity also represent important areas for additional research.

CONCLUSIONS

As the proportion of susceptible people changes over time, and if the global polio eradication program does not interrupt transmission of WPVs and VDPVs during the next decade, then policy makers should not assume that a current lack of demand for stand-alone IPV from the stockpile will provide a good indication of future needs. Further research should focus on the

potential needs and demands for poliovirus vaccine from high-risk subpopulations (e.g., clusters of religious objectors and PBEs).

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