The role of older children and adults in wild poliovirus transmission

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Edited by Sunetra Gupta, University of Oxford, Oxford, United Kingdom, and accepted by the Editorial Board June 11, 2014 (received for review January 7, 2014)

As polio eradication inches closer, the absence of poliovirus circulation in most of the world and imperfect vaccination coverage are resulting in immunity gaps and polio outbreaks affecting adults. Furthermore, imperfect, waning intestinal immunity among older children and adults permits reinfection and poliovirus shedding, prompting calls to extend the age range of vaccination campaigns even in the absence of cases in these age groups. The success of such a strategy depends on the contribution to poliovirus transmission by older ages, which has not previously been estimated. We fit a mathematical model of poliovirus transmission to time series data from two large outbreaks that affected adults (Tajikistan 2010, Republic of Congo 2010) using maximum-likelihood estimation based on iterated particle-filtering methods. In Tajikistan, the contribution of unvaccinated older children and adults to transmission was minimal despite a significant number of cases in these age groups [reproduction number, $R = 0.46$ (95% confidence interval, 0.42–0.52) for >5-y-olds compared to 2.18 (2.06–2.45) for 0- to 5-y-olds]. In contrast, in the Republic of Congo, the contribution of older children and adults was significant [$R = 1.85$ (1.83–4.00)], perhaps reflecting sanitary and socioeconomic variables favoring efficient virus transmission. In neither setting was there evidence for a significant role of imperfect intestinal immunity in the transmission of poliovirus. Bringing the immunization response to the Tajikistan outbreak forward by 2 wk would have prevented an additional 130 cases (21%), highlighting the importance of early outbreak detection and response.

epidemiology | infectious diseases | mathematical modeling

The Global Polio Eradication Initiative (GPEI) has achieved >99% reduction in the global annual incidence of poliomyelitis since the program began in 1988, and in 2012, just three countries were yet to interrupt wild poliovirus transmission—Afghanistan, Pakistan, and Nigeria—and 223 poliomyelitis cases were reported, the lowest in history (1). However, the absence of wild poliovirus transmission from most of the world, together with long-standing suboptimal vaccination coverage, has created cohorts of susceptible children and adults. As a result, an increased number of polio outbreaks affecting older children and adults have occurred in countries previously free of wild poliovirus (2–6). These outbreaks have significantly raised the cost of the GPEI and are a major challenge to achieving the goal of stopping all transmission by end-2014.

It has also become clear that intestinal immunity to poliovirus wanes over time, allowing individuals vaccinated with oral poliovirus vaccine (OPV) to become reinfected and shed poliovirus (7). Therefore, older children and adults could theoretically contribute to wild poliovirus transmission without developing poliomyelitis. The World Health Organization (WHO) has recommended vaccination of older age groups as a standard for outbreak response (8). In addition, the recent GPEI strategic plan proposes expanding the age range of mass vaccination campaigns that currently target 0- to 4-y-old children in endemic countries as a potential measure to accelerate eradication, even though poliomyelitis is rarely reported at older ages (9, 10).

Poliovirus shedding may not necessarily result in secondary infections, which depends on where the virus is deposited, routes of transmission, contact rates, and population immunity. Older children and adults are considered more hygienic than younger children, and these behavioral factors may limit onward transmission of shed poliovirus (11). Furthermore, the quantity and duration of virus shedding following reinfection of OPV-vaccinated individuals is reduced compared with naïve individuals (7). Where cases of poliomyelitis among older children and adults are rare, consideration of mass vaccination of this age group therefore requires an understanding of their contribution to transmission. This is challenging, however, because traditional methods such as contact tracing are not possible for wild poliovirus, which causes poliomyelitis in only 1 in ~200 primary infections (12).

In 2010, a large outbreak of imported wild poliovirus type 1 of Indian origin in Tajikistan resulted in 518 cases of poliomyelitis (Fig. 1 *A* and *B*) (2). Although this outbreak was associated with poliomyelitis among older children and adults, the initial response with serotype 1 monovalent OPV (mOPV1) targeted children 0–5 y of age, permitting a direct assessment of the contribution of these children and older age groups to transmission. We examined the transmission dynamics during this epidemic and the impact of vaccination by fitting an age-structured mathematical model of transmission using maximum likelihood with a particle-filtering algorithm (13, 14). As a comparison, we also examined the transmission

Significance

The incidence of poliomyelitis has dropped precipitously over the last decade. However, persistent transmission in three countries and outbreaks elsewhere challenge the end-2014 eradication target. The Global Polio Eradication Initiative is considering expanding the age range of vaccination campaigns even in the absence of adult cases, because of concerns about imperfect, waning intestinal immunity. The success of this approach will depend on the contribution to transmission by older ages, which we estimated during two large outbreaks affecting adults. Their contribution was found to depend on the setting, but there was no evidence for imperfect immunity contributing to the transmission of infection. Even small gains in the speed of vaccination response were found to have substantially greater benefit compared with expanded age range campaigns.

Author contributions: I.M.B., R.M., C.W., S.W., R.B.A., and N.C.G. designed research; I.M.B., A.G., N.K., J.E., and N.C.G. performed research; I.M.B. analyzed data; and I.M.B., S.W., R.B.A., and N.C.G. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission. S.G. is a guest editor invited by the Editorial Board.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1323688111/-/DCSupplemental.

www.pnas.org/cgi/doi/10.1073/pnas.1323688111

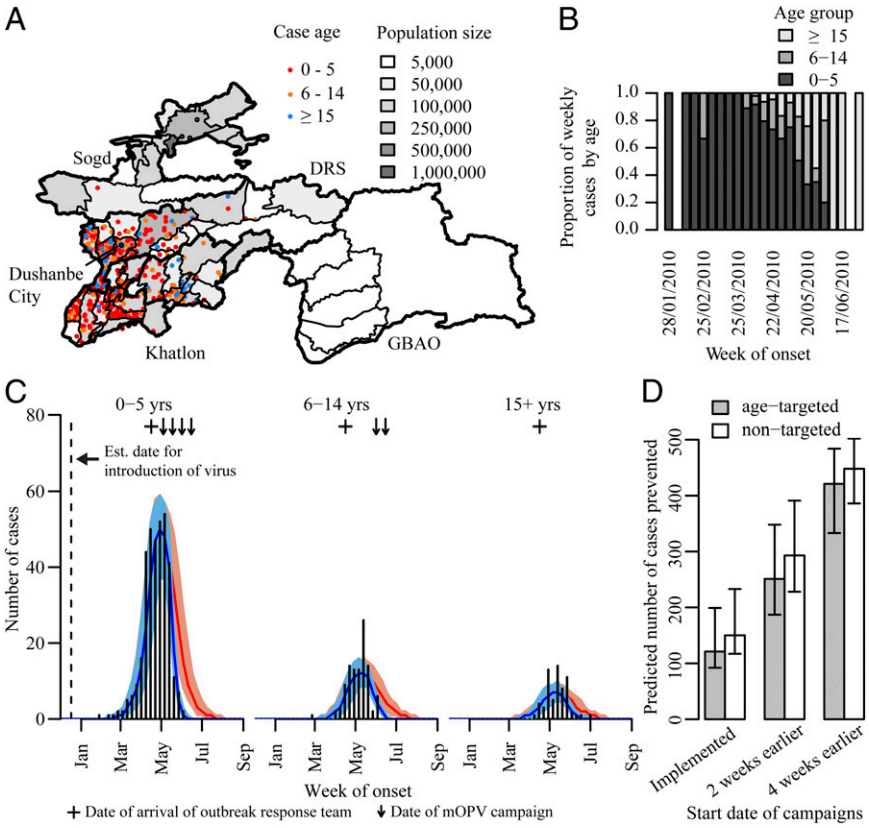

Fig. 1. The 2010 poliomyelitis outbreak in Tajikistan. (*A*) Geographic distribution of poliomyelitis cases plotted by district and colored according to their age group. The total population size for each district is indicated by the shading. Within a district, dots are randomly placed. (*B*) The age distribution of reported poliomyelitis cases by week of onset of paralysis. (*C*) Number of cases of poliomyelitis by week of onset of paralysis by age group (bars) with the median (blue line) and interquartile range (blue shading) of simulations under the best-fit transmission model, conditional on a major epidemic. The median (orange line) and interquartile range (orange shading) for simulations in the absence of a vaccination response are also shown. (*D*) Predicted number of cases prevented by the age-targeted vaccination response and under alternative scenarios (bars, median; error bars, interquartile range).

dynamics during a large type 1 poliovirus outbreak in the Republic of Congo that commenced in late 2010 (442 cases of poliomyelitis) (Fig. 2*A* and *B*) following introduction of virus from Angola (3, 15), as this lower income country, with a poorer level of sanitation, is likely to have had a different transmission pattern.

Results

Tajikistan: Distribution of Poliomyelitis Cases. The outbreak in Tajikistan occurred in the southwest of the country with 32% of individuals affected aged >5 y (Fig. 1*A*). The proportion of weekly cases that arose in the older age groups increased toward the end of the outbreak (Fig. 1*B*). Four national outbreak response vaccination campaigns using mOPV1 occurred on the following dates: May 4–8, 2010, May 18–22, 2010, June 1–5, 2010, and June 15–19, 2010, of which the first two targeted 0- to 5-y-old children only and the latter two extended the age range to 0–14 y. Further vaccination campaigns occurred on October 4–8, 2010, November 8–12, 2010, and April 18–23, 2011, using trivalent OPV.

Tajikistan: Age-Dependent Transmission. We compared the fit of different models of transmission among the three age groups (Table S1). We found that a model with a high transmission rate from infected children 0–5 y of age to susceptible contacts from the same age group, and a single lower rate for transmission from, to, and among older children and adults, gave the best fit [lowest Akaike information criterion (AIC)] (Table S1). Simulations under the best-fitting model compared with the outbreak data by age group are given in Fig. 1*C*. The estimated number of susceptible individuals [based on available seroprevalence data (16) and the model fit] in the age groups 0–5, 6–14, and 15+ y were 110 [95% confidence interval (CI), 91–131], 176 (141–219), and 105 (86–138) thousand, respectively. The estimated reproduction number (expected number of secondary cases) for older children and adults at the start of the epidemic was significantly less than 1 ($P < 0.001$) based on the best-fit model, compared with a relatively high reproduction number for children aged 0–5 y (Table 1). Extending the underlying transmission model to allow for imperfect intestinal immunity of OPV-vaccinated individuals did not provide a significantly better fit to the outbreak data (Table S2). The estimated relative infectiousness of infections among previously vaccinated or infected individuals was 0% (95% CI, 0–37%) compared with unvaccinated individuals (Fig. S1).

Tajikistan: Vaccine Effectiveness. The estimated effectiveness of the mOPV1 campaigns implemented in response to the outbreak (defined as the product of coverage and vaccine efficacy) was 69% on average (Table 1). To examine the impact of the outbreak response using this vaccine, we compared the number of poliomyelitis cases simulated under the best-fit model to the simulated number in the absence of a response. An estimated 121 (interquartile range, 92–199) cases were prevented in the outbreak areas, corresponding to 20% (interquartile range, 16–31%) of the expected number in the absence of a response (Fig. 1*C*). However, the outbreak response campaigns were estimated to commence after there had already been a large depletion of the number of susceptible individuals (Fig. S2*A*). An earlier response would have resulted in a greater number of polio cases prevented [251 prevented cases (interquartile range, 187–348) or 421 prevented cases (interquartile range, 333–484) if campaigns had commenced 2 or 4 wk earlier, respectively (Fig. 1*D*)]. Extending the age range of the four vaccination campaigns with mOPV1 in response to the outbreak would not have prevented many additional cases (29, i.e., 4.8%) (Fig. 1*D*). In addition, later campaigns had a relatively small effect in preventing further cases compared with the first campaign (Fig. S3).

Republic of Congo: Distribution of Poliomyelitis Cases. The majority of cases in the Republic of Congo outbreak were located in

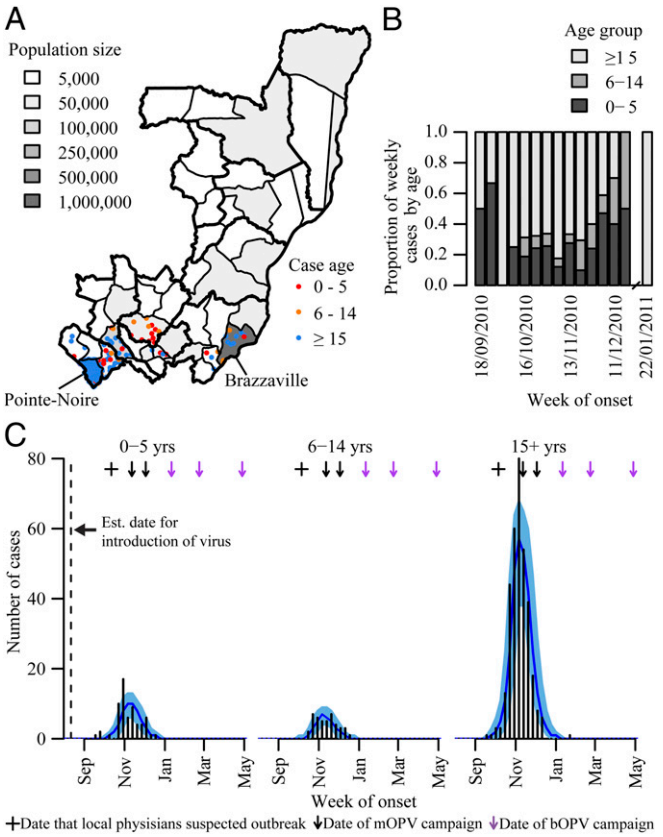

Fig. 2. The 2010–2011 poliomyelitis outbreak in the Republic of Congo. (*A*) Geographic distribution of poliomyelitis cases plotted by district and colored according to their age group. The total population size for each district is indicated by the shading. Within a district, dots are randomly placed. (*B*) The age distribution of reported poliomyelitis cases by week of onset of paralysis. (*C*) Number of cases of poliomyelitis by week of onset of paralysis for each age group (bars) with the median (blue line) and interquartile range (blue shading) of simulations under the best-fit transmission model, conditional on a major epidemic. The expected outbreak dynamics in the absence of a response are not shown (compare with Fig. 1) because of uncertainty in the estimated vaccine efficacy.

Pointe-Noire, the country's second largest city, whereas the remainder occurred in the southern half of the country (Fig. 2*A*). Seventy-six percent of cases were among individuals aged >14 y (Fig. 2 *A* and *B*) and 86% of cases were aged >5 y. Five national outbreak response vaccination rounds occurred on the following dates: November 12–22, 2010; December 3–7, 2010; January 11–15, 2011; February 22–26, 2011; and April 28–30, 2011. All rounds targeted all ages; the first two were carried out using mOPV1 and the latter three using a serotype 1 and 3 bivalent oral poliovirus vaccine (bOPV).

Republic of Congo: Age-Dependent Transmission. We present results from the maximum-likelihood model with the same pattern of transmission by age as that used for Tajikistan to allow direct comparison (this model had a better likelihood but somewhat poorer AIC than a model with homogeneous mixing by age; Table S3). The estimated transmission rate from infected older children and adults to susceptible contacts was significantly higher than that estimated for Tajikistan and also higher than the transmission rate among young children [1.40×10^{-5} (95% CI, 4.7×10^{-6} to 1.69×10^{-5}) compared with 2.56×10^{-7} (1.72×10^{-7} to 4.27×10^{-7}) and 6.46×10^{-8} (0–1.65×10^{-5}), respectively]. The reproduction number was significantly greater than 1 for both age groups (Table 2). The estimated number of susceptible individuals in each group was 19 (14–23), 11 (8–16), and 89 (79–101) thousand in the 0–5, 6–14, and 15+ age groups, respectively. Simulations under this model are compared with the outbreak data in Fig. 2*C*. Extending the underlying transmission model to allow for imperfect intestinal immunity of OPV-vaccinated individuals did not provide a significantly better fit to the outbreak data, but it was not possible to estimate the relative infectiousness of individuals previously vaccinated or infected with poliovirus as was done in Tajikistan (Table S4).

Republic of Congo: Vaccine Effectiveness. The estimated effectiveness of mOPV vaccination campaigns was very low in this setting (95% CI, 0–14%; Table 2). We examined the sensitivity of this result to the assumption of geographically homogeneous mixing, by explicitly modeling two different regions of the outbreak (Kouilou department and the rest of the southern half of country). In this spatially heterogeneous model, vaccine effectiveness in Congo increased to 14.4% (0.0–46.6%) (Table S4). A similar increase in vaccine effectiveness occurred if the last two cases in the outbreak in Congo, which occurred outside Kouilou, were excluded (Table S4). Irrespective of the choice of model, the outbreak response campaigns were estimated to occur after there had been a large depletion of susceptible individuals (Fig. S2*B*). It was not possible to estimate the effectiveness of the bOPV vaccination campaigns as they occurred after the last reported poliomyelitis case.

Discussion

The goal of the GPEI is to stop all wild poliovirus transmission by end-2014 (9). To reach this target, the program is considering expanding the age range of mass immunization campaigns even in the absence of adult cases (9, 10). Such an approach will incur greatly increased vaccine supply and distribution costs, and will only accelerate the interruption of transmission if older ages contribute to transmission.

Table 1. Estimated parameters (95% CI) for the best-fit poliovirus transmission model to the 2010 Tajikistan outbreak

Parameter	Estimate
Reproduction number for children 0–5 y of age at the start of the outbreak*	2.18 (2.06–2.45)
Reproduction number for older children and adults at the start of the outbreak*	0.46 (0.42–0.52)
Duration of infectiousness, d†	4.6 (3.6–7.0)
Date of first infection in Tajikistan	December 17, 2009 (November 21, 2009 to January 6, 2010)
Vaccine effectiveness (per campaign) (efficacy of mOPV1 × campaign coverage)	69% (55–80%)
Reported case: infection ratio before April 16	1/210 (1/278–1/160)
Percentage of people ≥15 y of age susceptible to infection at the start of the outbreak	2.8% (2.3–3.7%)

AIC = 806.

*Overall reproduction number: 1.88, calculated from the dominant eigenvalue of the next generation matrix.

†Represents duration of infectiousness among asymptomatic infections as these determine the transmission dynamics, representing 99.5% of all infections.

Table 2. Estimated parameters (95% CI) for the best-fit poliovirus transmission model to the 2010–2011 Republic of Congo outbreak

Parameter	Estimate
Reproduction number for children 0–5 y of age at the start of the outbreak*	1.57 (1.53–3.39)
Reproduction number for older children and adults at the start of the outbreak*	1.85 (1.83–4.00)
Duration of infectiousness, d[†]	1.0 (1.0–11.5)
Date of first infection in Republic of Congo	August 12, 2010 (July 18, 2010 to August 22, 2010)
Vaccine effectiveness (per campaign) (efficacy of mOPV1 × campaign coverage)	0.4% (0.0–14.0%)
Reported case: infection ratio before October 9	1/108 (1/253–1/48)
Percentage of people 0–5 y of age susceptible to infection at the start of the outbreak[‡]	2.4% (1.8–3.1%)
Percentage of people 6–14 y of age susceptible to infection at the start of the outbreak[‡]	1.5% (1.1–2.0%)
Percentage of people ≥15 y of age susceptible to infection at the start of the outbreak	6.9% (6.1–7.8%)

AIC = 681.

*Overall reproduction number: 1.82 calculated from the dominant eigenvalue of the next-generation matrix.

[†]Represents duration of infectiousness among asymptomatic infections as these determine the transmission dynamics, representing 99.5% of all infections.

[‡]Seroprevalence data were not available and so these were estimated directly by the model (compare with Tajikistan).

Here, we estimated the contribution of unvaccinated individuals to transmission by different age groups during two large poliovirus outbreaks that both commenced in 2010. In Tajikistan, the reproduction number for older children and adults was estimated to be below 1, reflecting limited transmission from these age groups to susceptible contacts. This was despite the estimated number of susceptible individuals [based on available seroprevalence data (16) and the model fit] being somewhat higher at older ages (72% of the total susceptible population at the start of the outbreak were estimated to be older children and adults). The low reproduction number in the older age group is consistent with the strong herd effect observed among older children and adults after vaccination of the younger age groups. In this setting, it is therefore apparent that young children were responsible for the majority of poliovirus circulation and that adult infections were largely a dead end for transmission.

The contribution of older children and adults to poliovirus circulation may depend on the route of transmission. In Tajikistan, a country with relatively good sanitation, the role of fecal–oral transmission may be relatively limited compared with oral–oral transmission (17). In lower income settings with poor sanitation, wild poliovirus transmission by the fecal–oral route is likely to be more efficient. There have been a number of importations of wild poliovirus into lower income countries in the last decade (18). Most of these importations have resulted in limited numbers of poliomyelitis cases, but the serotype 1 wild poliovirus outbreak in the Republic of Congo in 2010–2011 was of similar size to the Tajikistan outbreak. We estimated the contribution to transmission by different age groups in this setting, as a comparison with Tajikistan, but because the outbreak response was not age targeted, the precision of our estimates was more limited.

The relative timing and rapidity of the epidemic among adults in the Republic of Congo was consistent with a high reproduction number in this age group, significantly greater than 1. This was not simply the result of the large number of susceptible adults (an estimated 75% of all susceptible individuals), reflecting past periods of low vaccination coverage (19), but because of a significantly higher estimated transmission rate to susceptible contacts compared with Tajikistan. The greater role of older children and adults in wild poliovirus transmission in the Republic of Congo may be the result of more efficient fecal–oral transmission by person to person and common-source exposures to fecal-contaminated water (17). This is consistent with the observation that the majority of poliomyelitis cases occurred in slum areas of Pointe-Noire and deaths from poliomyelitis were associated with obtaining drinking water from a particular covered well (20). The difference in the estimated duration of infectiousness between the two settings may also be explained by the difference in hygiene behavior, although the CIs in Congo are relatively broad and the difference is not statistically significant.

Waning intestinal immunity among vaccinated individuals that results in a loss of protection against infection and poliovirus shedding, but not against poliomyelitis, may allow older individuals to contribute to transmission (7, 9). In both Tajikistan and the Republic of Congo, we examined the fit of a model that allowed for imperfect intestinal immunity, such that OPV-vaccinated individuals could become infected with wild poliovirus. In neither setting did this model provide a significantly better fit to the data. However, the power to detect a role for imperfect immunity was limited in the Republic of Congo because all age groups were vaccinated during the first outbreak response campaign, unlike Tajikistan where the herd effect observed after vaccinating only young children allowed the contribution of older age groups to poliovirus transmission to be assessed more directly. In addition, there was greater uncertainty in the proportion of the population susceptible to poliomyelitis at the start of the outbreak in the Republic of Congo because of the absence of seroprevalence data, and this also contributed to the limited power to detect imperfect immunity.

The estimated effectiveness (coverage × efficacy) of campaigns with mOPV1 was relatively high in Tajikistan, consistent with immunogenicity studies in former Soviet Union countries and the high coverage achieved (21). However, the impact of these campaigns on the expected size of the outbreak was somewhat limited. This is likely to be due to the late recognition of the outbreak leading to a delayed response and large-scale epidemic, which rapidly depleted the susceptible population, such that incidence began to level off even before the first vaccination campaign. Although the outbreak response occurred just 18 d after the arrival of an outbreak investigation team in Tajikistan on April 16, 2010 (with the outbreak confirmed on April 20), the arrival of this team occurred 17 wk after the date of introduction of wild poliovirus estimated from the model (December 17, 2009) and 11 wk after the date of onset of paralysis of the first confirmed case. We estimated that there had already been a large depletion of susceptible individuals by the time campaigns began. By simulating under the best-fit model but commencing vaccination rounds 1 mo earlier, we have shown that number of poliomyelitis cases prevented would have been much larger [300 additional cases prevented (50% of the expected outbreak size in the absence of vaccination)]. An important caveat here is that further seeding of the virus to other areas of Tajikistan or more widely may have been prevented by the rapid curtailment of the epidemic, and these effects are not captured by our simple model.

The outbreak response vaccination campaigns in Tajikistan were different to previous campaigns in that the campaigns were conducted at short intervals and the third and fourth campaigns

included older children. However, we show that, although cases continued in older age groups for 8 wk after the first vaccination campaign targeting children aged <6 y, extending the age range of the four vaccination campaigns with mOPV1 in response to the outbreak would not have prevented many additional cases because of the limited contribution of older children and adults to transmission and the late response. In addition, in this setting, the large impact of the first campaign on the core transmission group meant that the benefit of the subsequent campaigns was relatively small.

Vaccination campaigns in the Republic of Congo also commenced relatively late, after the susceptible population was already depleted as a result of exposure to the outbreak virus. The effectiveness of campaigns with mOPV1 in this setting was estimated to be very low and this can only partly be explained by low coverage reported in Pointe-Noire from independent monitoring data (62% of surveyed households). The efficacy of oral poliovirus vaccines generally decline with poorer levels of sanitation (22), and as the Republic of Congo has a lower level of sanitation than Tajikistan (17), it is likely the efficacy of the vaccine was lower in this setting as well. Additionally, our analysis was limited in the Republic of Congo because only 64 cases (14%) were confirmed by poliovirus isolation from stool samples (compared to 460, 89%, in Tajikistan). We examined the sensitivity of our results to this limitation by including only laboratory-confirmed cases of poliomyelitis and obtained broadly similar results (Tables S2 and S4). The transmission model was based on the assumption of random mixing with respect to geography across the whole of the population affected by the outbreak. Although this assumption is unlikely to significantly affect our estimates of age-specific transmission rates, it may not fully capture the benefits of vaccination in curtailing the epidemics as noted above and could result in an underestimate of vaccine effectiveness because of cases occurring in regions of low coverage. Examining the sensitivity of our estimates to the assumption of homogeneous mixing in the Republic of Congo did result in an increase in the vaccine effectiveness estimate, as did fitting to the outbreak assuming homogeneous mixing but removing the last two cases in the outbreak reported from outside of Kouilou. A final caveat to our analysis is that we assume the reporting rate of cases to be independent of age. The probability of developing poliomyelitis after infection in older children is somewhat higher than children under 5 y of age (12). We therefore performed a sensitivity analysis by refitting the model to the Republic of Congo outbreak data assuming the reporting rate of cases was twice as high in older children and adults, but found consistent estimates for the reproduction numbers (*SI Methods* and Table S3).

Although it is clear that adults can contribute to wild poliovirus transmission in lower income countries with significant gaps in immunity, there is no evidence from this study that imperfect intestinal immunity can contribute to persistent poliovirus circulation in the absence of older children and adult cases. However, further studies may be warranted, potentially including expanded age group immunization, particularly in endemic areas with poor sanitation where transmission from older children and adults is likely to be more significant, as we found in the Republic of Congo. In countries currently free of wild poliovirus, the clear focus should be maintaining high vaccination coverage and rapid detection of emerging outbreaks such that outbreak response activities can be launched early. The major constraint appears to be the initial detection and investigation of case clusters and reporting to WHO, rather than delays in laboratory confirmation per se, highlighting the need for strong surveillance for acute flaccid paralysis (AFP) even in the absence of recent poliovirus circulation.

Methods

Tajikistan and Republic of Congo Data. Cases of paralytic poliomyelitis were detected through AFP surveillance recommended by the WHO since 1999, whereby the definition of an AFP case is the sudden onset of flaccid paralysis in a child <15 y of age or suspected poliomyelitis in a person of any age (23). Cases of poliomyelitis were identified from the Tajikistan and Republic of Congo AFP databases and were categorized into three age groups (0–5, 6–14, and ≥15 y, corresponding to the age groups targeted by the vaccination campaigns in Tajikistan) for the period October 1, 2009, to September 30, 2010, and May 1, 2010, to May 31, 2011, for Tajikistan and the Republic of Congo, respectively. A laboratory-confirmed case of poliomyelitis was defined as an AFP case with a positive test for wild-type poliovirus from a stool sample, preferably collected within 14 d of the date of onset of paralysis. In Tajikistan, a polio-compatible case was defined as an AFP case who had clinical manifestations compatible with poliomyelitis but from whom stool samples were not available or inadequate and negative on testing. In the Republic of Congo, poliomyelitis was clinically confirmed when stool samples were not available (due to the late investigation of the outbreak) or were negative and collected >14 d after onset and there was a strong likelihood of poliomyelitis based on clinical presentation, location, and expert panel review (3). We used both laboratory, compatible, and clinically confirmed cases in our primary analysis. Information on age was absent for six of the confirmed cases in Republic of Congo, and therefore our analysis was restricted to cases with age information. In both settings, the administrative coverage, based on the quantity of vaccine distributed, was >99% for all mOPV rounds.

Mathematical Model of Poliovirus Transmission. We used an age-structured stochastic mathematical model of poliovirus transmission that was based upon a SEIR framework. In the model, the population progress through a series of four states over time: Susceptible (S) → Latent (E) → Infected (I) → Recovered (R). These states are indexed by the age class (i) and the number of individuals in each class is a function of time (t). We assume only the "infected" class is infectious and individuals in the "recovered" class have developed a fully protective immune response against reinfection. We ignore natural birth and death rates, and aging of the population, due to the relatively short timing of the poliovirus outbreak in comparison with these demographic events. Three age classes are present in the model reflecting the age groups targeted by the Tajikistan supplementary immunization activity (SIA) campaigns (i.e., $i = 1, 2, 3$ representing 0–5, 6–14, and ≥15 y, respectively). The hazard (or "force") of infection for susceptibles in age class i is given as follows: $\lambda_i(t) = \sum_{j=1}^{3} \beta_{i,j} I_j(t)$. The rate of transmission from infectious individuals in age group j to susceptible individuals in age group i is given as $\beta_{i,j}$ (i.e., density-dependent transmission). This parameter captures both biological (viral shedding) and behavioral (e.g., hygiene) components of transmission. Individuals progress from the latent period to the infectious period at a rate ν (1/duration of latency) and recover from infection to be fully immune against reinfection at a rate γ (1/duration of infectiousness). The duration of latency and infectiousness were assumed to be independent of age. The number of individuals in the different model states at a given time can be summarized by the vector $X(t)$ and the transitions follow a Markov process. The stochastic model equations are given in *SI Methods*. The reproduction number for an infected individual in age group i at time t was calculated as follows: $R_i(t) = (1/\gamma)\sum_k \beta_{k,i} S_k$. The overall reproduction number across all ages was calculated from the dominant eigenvalue of the next-generation matrix (24).

The incubation period was assumed to follow an Erlang distribution, with mean 16.5 d and shape parameter $k = 16$ based on independent data from 36 cases of paralytic poliomyelitis with known dates of exposure to an infected individual (25). Only a small number of infected individuals become reported cases, and this number is assumed to follow a binomial distribution with the probability of becoming a reported case given by parameter ρ. We allow this probability to be modified by a factor η before the outbreaks were recognized [date outbreak was declared by WHO in Tajikistan (April 16, 2010) or when formally by local physicians in the Republic of Congo (October 9, 2010)].

Vaccination. At a given time of a vaccination campaign, vaccination is included in the model by moving the number of people with a vaccine-induced protective immune response from S_i to R_i, determined by the product of vaccination coverage at the given campaign and the per-dose vaccine efficacy. For the purpose of the model, all vaccination was assumed to occur on the first day of each SIA, with the exception of the first SIA in the Republic of Congo, where the midpoint was used because of its unusually long duration. We estimate the vaccine effectiveness (coverage × per-dose efficacy) in each setting. Country administrative coverage levels for each campaign, based on the quantity of vaccine distributed, are given in *SI Methods*, but these values were not used to infer vaccine efficacy due to the indirect measure these values provide on the true coverage.

Spatial Transmission. The model was extended to allow for two geographic populations (*A*, *B*) with different patterns of transmission by age within each population and a single rate of transmission between the populations such that the force of infection per susceptible in age class *i* in population *A* was given by the following: $\lambda_{i,A}(t) = \sum_{j=1}^{3} \beta_{i,j} I_{j,A}(t) + \alpha \sum_{j=1}^{3} I_{j,B}$, where $I_{j,A}$ is the number of infectious individuals in population *A* in age group *j*. An analogous term was used for the force of infection in population *B*.

Intestinal Immunity. To assess the contribution of imperfect intestinal immunity to transmission, the SEIR model was extended to allow individuals who had experienced their first infection or who had been immunized with OPV (i.e., individuals in the "R" category) to be reinfected (but not develop disease). These individuals were assumed to be less infectious than individuals infected for the first time. It was possible to estimate their relative infectiousness in Tajikistan, but not for Congo where it was fixed at 10%.

Estimation of Parameters. For each setting, the transmission coefficients $\beta_{i,j}$, the duration of infectiousness $1/\gamma$, average vaccination campaign effectiveness, the date of introduction of the first infection into the country, and the early reporting rate of cases were estimated using maximum likelihood. The daily number of reported poliomyelitis cases in age group *i* can be written as the vector $y_{1:T,i} = (y_{1,i}, \ldots, y_{T,i})$, where *T* corresponds to the number of days of observation. The conditional likelihood for each daily observation is given by $\prod_{i=1}^{3} P(y_{t,i} | y_{1:t-1,i}, \theta, X_i)$, where *i* refers to the age-class index, and θ represents a vector of model parameters, which depends on the transmission model and the (binomial) observation model. The likelihood across the period of observation and across all age groups is therefore given as the product of conditional likelihoods across all observations and age groups: $\prod_{t=1}^{T} \prod_{i=1}^{3} P(y_{t,i} | y_{1:t-1,i}, \theta, X_i)$. For the spatial model with two populations (k = 1, 2), the likelihood is given by $\prod_{t=1}^{T} \prod_{k=1}^{2} \prod_{i=1}^{3} P(y_{t,i,k} | y_{1:t-1,i,k}, \theta, X_{i,k})$, where $y_{t,i,k}$ is the number of cases at time *t* in age group *i* and population *k*.

We used iterated particle filtering to maximize the likelihood for different models of poliovirus transmission, following the approach of Ionides et al. as described in refs. 13, 14, and 26. Further details are given in *SI Methods*. The model was written in C using the math library from R (27), and this was linked to R to perform iterated particle filtering using the package "pomp" (26). We estimated the transmission of poliovirus by age by fitting a series of nested models that ranged in complexity from the simplest model where the transmission coefficients are equal for transmission within and between age groups, to more complex models whereby transmission coefficients differ for transmission within and between different age groups. The AIC provided information on the model that was the most parsimonious yet adequate for each population (28). The duration of latency was assumed to be 4 d (29). The number of poliovirus infections for every reported case was assumed to be 200 for all ages in both settings (i.e., $\rho = 1/200$) following the initial period of possibly poorer sensitivity determined by η (30). Diagnostic plots were performed to check for global convergence from different starting values for the model parameters. Local polynomial regression was used to estimate 95% CIs from profile likelihood plots, under the assumption that the likelihood surfaces were χ^2 distributed (Figs. S4 and S5).

Initial Conditions for Parameter Estimation. For Tajikistan, the proportion of individuals in the recovered class (therefore immune to infection) at the start of the outbreak for the first two age groups, 0–5 and 6–14 y, was set as the proportion with serotype 3 immunity from the seroprevalence survey after the outbreak (16) (*SI Methods*) as a proxy for serotype 1 immunity (the sensitivity to this assumption is examined in Fig. S4). The proportion of individuals in the recovered state ≥15 y was estimated because the seroprevalence survey was limited up to individuals aged 24 y and the third age category in the model accounted for all adults. The proportion susceptible to infection was set as 1 minus the proportion immune. No individuals were assumed to be in the latent class and one infected individual in the youngest age group was assumed at the start of the outbreak. A seroprevalence survey was not conducted in the Republic of Congo, and therefore the proportion susceptible in each class was estimated during the fit of the transmission model. The population numbers for each of the three age groups in each country were taken from WHO population estimates. For further details, see *SI Methods*.

Simulation. Ten thousand stochastic simulations were run under the best-fit model, and the median and interquartile ranges for each time step are presented for all those simulations that resulted in more than one reported case of poliomyelitis. The number of cases averted by the outbreak response, or by hypothetical outbreak responses (such as targeting different age groups or altering the dates of the vaccination campaigns), was evaluated by comparing the simulated number of cases under the best-fit model incorporating these vaccination campaigns with the simulated number of cases assuming no outbreak response.

ACKNOWLEDGMENTS. We acknowledge the assistance of Ben Lopman, Minal Patel, and Kim Porter, and the efforts of all those involved in the epidemiological investigations and laboratory testing of the polio outbreaks in Tajikistan and the Republic of Congo. This work was supported by a grant from the Polio Research Committee of the World Health Organization, the Royal Society, and Centre funding from the Medical Research Council.

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