The Risks, Costs, and Benefits of Possible Future Global Policies for Managing Polioviruses

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Objectives. We assessed the costs, risks, and benefits of possible future major policy decisions on vaccination, surveillance, response plans, and containment following global eradication of wild polioviruses.

Methods. We developed a decision analytic model to estimate the incremental cost-effectiveness ratios and net benefits of risk management options for polio for the 20-year period and stratified the world according to income level to capture important variability between nations.

Results. For low-, lower-middle-, and upper-middle-income groups currently using oral poliovirus vaccine (OPV), we found that after successful eradication of wild polioviruses, OPV cessation would save both costs and lives when compared with continued use of OPV without supplemental immunization activities. We found cost-effectiveness ratios for switching from OPV to inactivated poliovirus vaccine to be higher (i.e., less desirable) than other health investment opportunities, depending on the actual inactivated poliovirus vaccine costs and assumptions about whether supplemental immunization activities with OPV would continue.

Conclusions. Eradication promises billions of dollars of net benefits, although global health policy leaders face difficult choices about future policies. Until successful eradication and coordination of posteradication policies, health authorities should continue routine polio vaccination and supplemental immunization activities. (*Am J Public Health.* 2008;98:1322–1330. doi:10.2105/AJPH.2007.122192)

Before the World Health Assembly committed to eradicating wild polioviruses (types 1, 2, and 3) in 1988,[1] these viruses had been paralyzing an estimated 350 000 children per year globally.[2] Policymakers anticipated that vaccination would stop following global eradication of wild polioviruses, similar to the cessation of vaccination that occurred after the eradication of smallpox.[3] Anticipation of large economic savings and demonstrated successful use of the inexpensive and effective trivalent oral poliovirus vaccine (OPV) to eradicate wild polioviruses in the Americas[4,5] supported this international commitment. The Global Polio Eradication Initiative to date has reduced the annual burden of disease by more than 99% to less than 2000 cases of paralysis annually[6] and has achieved eradication of wild poliovirus type 2.[7] Currently, wild poliovirus types 1 and 3 remain endemic in only 4 countries (Nigeria, India, Pakistan, and Afghanistan). Recent importations of wild poliovirus into previously polio-free areas[8,9] demonstrate the importance of finishing the job of eradication, maintaining high levels of vaccination coverage—at least until successful eradication—and carefully considering the risks, costs, and benefits of alternatives.[10]

The Global Polio Eradication Initiative relies on an eradication strategy that disrupts transmission of wild poliovirus by giving susceptible individuals (mainly children) multiple doses of OPV to ensure high levels of immunity. The Global Polio Eradication Initiative uses the live OPV instead of the inactivated poliovirus vaccine (IPV) as its vaccine of choice because of OPV's substantially lower cost and ease of administration,[11] superior enteric mucosal immunity,[12] and ability to enhance population immunity through spread to nonimmunized individuals.[13–15] In addition to routine childhood immunization with OPV, the Global Polio Eradication Initiative conducts supplementary immunization activities (SIAs) in the form of mass vaccination campaigns.

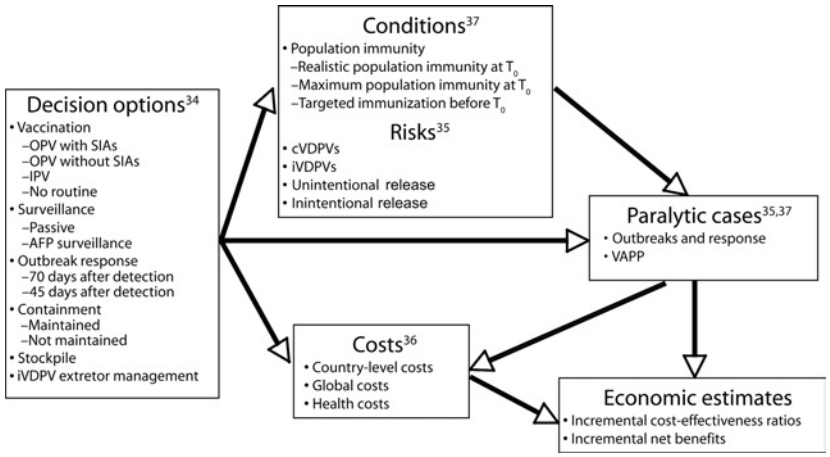
Despite its benefits, OPV comes with the relatively rare side effect of vaccine-associated paralytic polio, which does not occur with the more costly IPV.[16] Although relatively small in the context of circulating wild poliovirus, the current estimated global burden of 250 to 500 cases of vaccine-associated paralytic polio annually that would result from extended use of OPV appears large in comparison to no naturally occurring polio cases in a world free of wild poliovirus.[17] Indeed, with the increasing success of eradication and lower risks of importations, despite its relatively higher cost[18] IPV gradually has become the vaccine of choice for routine immunization in many high-income countries that seek to eliminate cases of vaccine-associated paralytic polio while remaining protected from polio.

Within the past decade, polio outbreaks also occurred from circulating vaccine-derived poliovirus—outbreaks in which OPV viruses regained neurovirulence and greater transmissibility as they circulated in susceptible populations.[2,19] These events provided an even stronger case for coordinated OPV cessation[20–24] while raising the question of whether such outbreaks might persist after OPV cessation.[25]

Previous studies presented cost-effectiveness analyses for the US domestic polio vaccination program at various points in time[18,26] and retrospectively[27] for various other countries[28–30] and for global[31,32] and regional eradication.[33] However, no studies provide comprehensive estimates of the cost-effectiveness of the numerous posteradication risk management policy options.[34]

METHODS

We developed a decision analytic model to estimate the incremental cost-effectiveness



Note. cVDPVs = circulating vaccine-derived polioviruses; IPV = inactivated poliovirus vaccine; iVDPVs = immunodeficiency-associated vaccine-derived polioviruses; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities; VAPP = vaccine-associated paralytic polio.

FIGURE 1—Model components leading to health and economic estimates of possible global policies for managing polioviruses.

ratios and net benefits of risk management options for polio for the 20-year period following the expected end of routine vaccination with OPV (T_0). Figure 1 describes the model components, and Table 1 summarizes the key inputs. We previously identified 7 major categories of decisions: routine immunization, SIAs, outbreak response, stockpile, surveillance, containment, and management of chronic excretors.[34] We then evaluated the risks and costs associated with the options and conditions[35,36] and used the results of an outbreak model[37] to estimate the potential number of future cases.

The overall probabilistic model focuses on policy at the global level but stratifies the world into 4 income groups on the basis of the 2002 World Bank classification.[41] This captures previously identified important policy, cost, risk, and epidemiological differences between low-, lower-middle-, upper-middle-, and high-income countries.[34–37] We estimated the incremental cost-effectiveness ratios and incremental net benefits of different options and characterized uncertainty about these estimates. (Full details are available from the authors on request.)

Policymakers face several important choices (summarized in the left box in Figure 1), including several vaccination options. The reference case assumes continued IPV routine vaccination in high-income countries and continued OPV use in the rest of the world. We considered continued use of OPV both with SIAs, which would be required to maintain high levels of coverage[50] and is currently recommended,[51] and without SIAs, which reflects the fact that many countries have reduced or eliminated their use of SIAs following interruption of wild poliovirus transmission. For the IPV option, we assumed that high-income groups would use a 3-dose schedule delivered in a combination vaccine, whereas all other income groups would use 2 doses in a single (trivalent) antigen vaccine formulation.[52–54] We modeled the option of continued acute flaccid paralysis surveillance to detect the circulation of polioviruses in the human population (assuming this detects an outbreak at the onset of the first paralytic case)[2,55–57] versus passive surveillance (assumed to detect the outbreak at onset of the fifth paralytic case).[37]

With actual outbreak response plans still under formulation, we modeled multiple response strategies that use monovalent OPV given current recommendations[58] and assuming access to sufficient quantities of vaccine (e.g., in the global stockpile).[2,48] For the base case, we assumed response with 3 rounds of monovalent OPV starting 70 days after outbreak detection, independent of the outbreak origin (wild or vaccine derived), occurring 30-days apart, lasting 3 days, achieving 90% coverage in each round, and targeting all people born since the past year of IPV or OPV vaccination (rounded to the next multiple of 5).

Given progress toward a global monovalent OPV stockpile with estimated costs of approximately $360 million,[59] we modeled only this stockpile option (although some countries may build national ones[60]). Similarly, given progress toward containment, we assumed for the base case that actively enforcing containment will lead to global discounted costs of approximately $6.7 million (90% confidence interval [CI]=1.9, 12 million).[2,36,61–63] We modeled the risks associated with potential reintroductions of polioviruses from the few individuals with certain primary B-cell–related immunodeficiency syndromes who may continue to excrete vaccine-derived polioviruses,[35,64] because the possibility of transmission exists.[65] We did not include any related policy options (although future development of antivirals might someday prove helpful in treating immunodeficient individuals who continue to excrete vaccine-derived polioviruses).[66]

With respect to conditions at T_0, policy choices associated with immunization activities just before T_0 will influence global population immunity conditions. The base case assumes realistic population immunity,[37] which implies no SIAs in low-income countries for 3 years before T_0 or in lower-middle- or upper-middle-income countries for 5 years before T_0. For high-income countries, IPV routine immunization coverage applies for all years since 1998, the approximate year that most high-income countries switched.[54] We explored the implications of spending an estimated cost of $1.1 billion (90% CI=0.86, 1.3 billion) to conduct one large round of immunization in low- and middle-income groups immediately before T_0 that would yield maximum population immunity. Given insufficient current resources despite continued circulation of wild poliovirus, we also considered the impact of conducting targeted immunization activities in high-risk areas (i.e., modeled specifically as targeting the children younger than 5 years within a population of 600 million

TABLE 1—Base Case Values or Distributions of Inputs and Alternatives Considered in the Model Exploring Global Policies for Managing Polioviruses

Model Input	Base Case	Notes
Model framework inputs		
Analytic time horizon	20 years	
Population projections[a] [38]		Assume 2010–2029 projections reasonably represent this time period
Discount rate[39]	3%	0%, 7% also considered, all costs in 2002 US dollars, adjusted as needed using the Consumer Price Index[40]
	Policy-related inputs	
Vaccination schedule		
OPV, low- and middle-income groups[b]	Three doses	
IPV, low- and middle-income groups[c]	Two doses, single antigen vaccine	Three doses, combination vaccine also considered
IPV, high-income group[d]	Three doses, combination vaccine	
Number of rounds per year if policy involves SIAs[36] (distribution)	Triangular with base 0.67 and range 0.4–2.0	The distribution implies a mean value of approximately one round per year
Population immunity profile at T_0 [35,37]		
OPV with SIAs	Maximum population immunity	
OPV without SIAs, IPV, or no routine	Realistic population immunity	Maximum population immunity, TIAs also considered
	Economic inputs	
Costs for establishing a global monovalent OPV stockpile (distribution)	Triangular with base $325 million and range $250–$500 million	Estimate does not include costs to maintain the stockpile; implied mean global costs of $360 million (90% CI $280–$450 million) before T_0 are not included in the income group totals
Annual costs of the global polio laboratory network[36] (distribution)	Triangular with base $22 million and range $15–$30 million	Implied mean global costs of $340 million (90% CI = $270, $420 million) over 20 years are not included in the income group totals
Annual costs of maintaining high-level containment[36] (distribution)	Triangular with base $300 000 and range $0–$1 million	Implied mean global costs of $6.7 million (90% CI = $1.9, $12 million) over 20 years are not included in the income group totals
Costs to achieve population immunity at T_0 (if no OPV with SIAs)[36]	0	$1.1 billion (90% CI of $0.86–$1.3 billion) for maximum population immunity and $81 million (90% CI = $61, $100 million) for TIAs also considered
DALYs averted per prevented paralytic polio case[41–43]		
Low-income group	13.3	Base case estimates assume 3% discount rate with no age-weighing; adjusted estimates for discount rate alternatives also considered
Lower-middle-income group	13.7	
Upper-middle-income group	13.9	
High-income group	14.1	
Willingness to pay to prevent a paralytic polio case[41,44]		
Low-income group	$5 300	On the basis of minimal willingness to pay equal to average per capita gross national income per DALY averted[45]; higher estimates also considered
Lower-middle-income group	$17 000	
Upper-middle-income group	$63 000	
High-income group	$340 000	
Treatment cost per paralytic polio case[18,31,33,36,46,47]		
Low-income group	$500	
Lower-middle-income group	$5 000	
Upper-middle-income group	$50 000	
High-income group	$500 000	

Continued

TABLE 1—*Continued*

Outbreak-related inputs		
Probability of circulating VDPV outbreak risk on the basis of observed frequency of[35] (distribution)		
Confirmed VDPV outbreaks only	0.5	
Confirmed and ambiguous VPDVs	0.5	
Time of outbreak detection[37]	Onset of fifth paralytic case (passive surveillance)	Onset of first paralytic case (acute flaccid paralysis surveillance) also considered
Outbreak response characteristics[37,48]		
Delay from outbreak detection to first response round	70 days	45 days also considered
Response vaccine	Monovalent OPV	Serotype matched to outbreak virus
Number of rounds	3	
Coverage of each round	90%	
Duration of each round	3 days	
Interval between rounds	30 days	
Target age groups	Cohorts born since cessation of routine vaccination	Rounded to the next multiple of 5 years (e.g., 7 years after cessation, target children younger than 10 years); if continued routine vaccination, target children younger than 5 years
Outbreak-specific R_0[37] (distribution)		
Low-income group	10, 13	Low, high point estimates shown (base case assumes equal probabilities of each; different probability distributions were also considered)
Lower-middle-income group	8, 11	
Upper-middle-income group	6, 9	
High-income group	4, 6	
Outbreak-specific routine immunization coverage since last SIAs[49] (distribution)		
Low-income group	68%, 40%, 25%	Expected, low, and lowest point estimates shown (base case assumes probabilities of, respectively, 0.8, 0.1, and 0.1 for these; different probability distributions were also considered)
Lower-middle-income group	90%, 70%, 50%	
Upper-middle-income group	92%, 70%, 60%	
High-income group	94%, 85%, 80%	
Heterogeneity in population immunity if continued SIAs		
Low-income group	Medium	Represents probabilities of 0.75, 0.20, and 0.05 of, respectively, 0%, 10%, and 25% reduction in partially infectibles
Middle-income groups	Low	Represents probabilities of 0.9, 0.1, and 0 of, respectively, 0%, 10%, and 25% reduction in partially infectibles

Note. OPV = oral poliovirus vaccine; IPV = inactivated poliovirus vaccine; SIAs = supplemental immunization activities; TIAs = targeted immunization activities; T_0 = period following the expected end of routine vaccination with OPV; CI = confidence interval; DALY = disability-adjusted life year; VDPV = vaccine-derived poliovirus.

[a]Data available from authors upon request.

[b]We used best estimates of the OPV price of $0.09, $0.09, and $0.10 per dose in the low-, lower-middle-, and upper-middle-income groups, respectively, and modeled the uncertainty in both antigen price and administration costs using triangular distribution.[36]

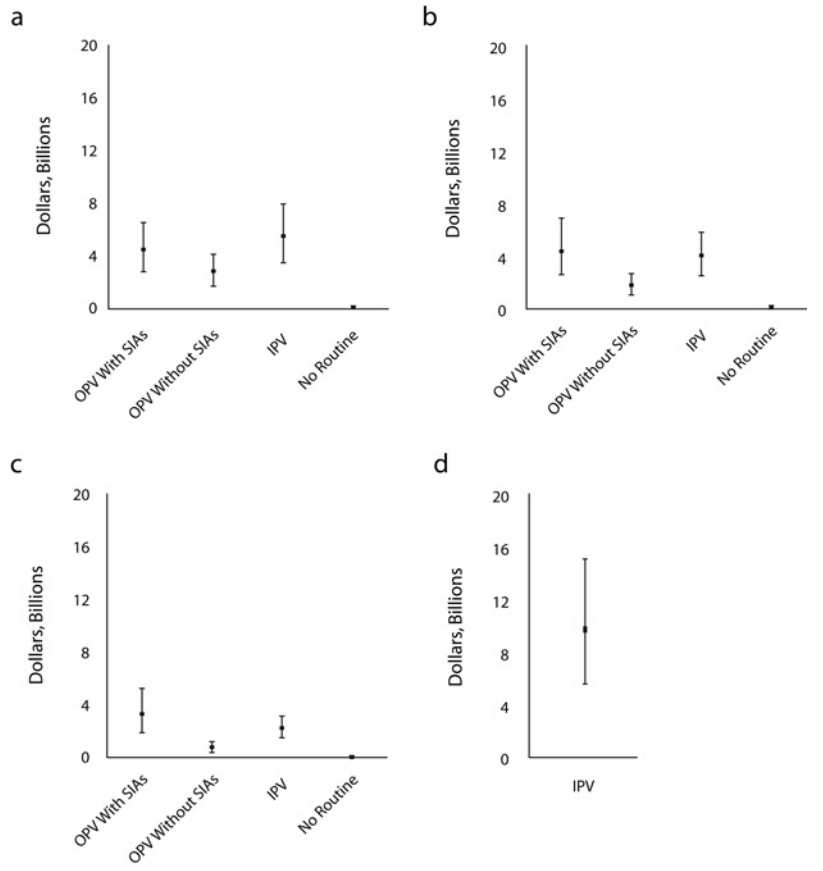
[c]We used best estimates of the IPV price of $1.00, $1.75, and $2.50 per dose in the low-, lower-middle-, and upper-middle-income groups, respectively, and modeled the uncertainty in both antigen price and administration costs using triangular distribution.[36]

[d]We used a best estimate of the IPV price of $10.00 per dose and modeled the uncertainty in both antigen price and administration costs using triangular distribution.[36]

people in low-income countries and 100 million in lower-middle-income countries), for which we estimated global costs of $81 million (90% CI = 61, 100 million).

To model the risks of outbreaks, we assumed annual Poisson rates per 100 million people and independence of the rates between geographical areas and for different outbreak types (i.e., circulating vaccine-derived polioviruses, immunodeficiency-associated vaccine-derived polioviruses, unintentional releases, or intentional acts).[35] We used the distribution of population sizes in the relevant year and income group to determine the outbreak population size[38,67] and included uncertainty in our characterization of these risks. For example, we modeled different rates for the risk of circulating vaccine-derived polioviruses assuming an equal chance that the observed frequency of confirmed circulating vaccine-derived poliovirus outbreaks represents the true risk and that the sum of the confirmed circulating vaccine-derived polioviruses and ambiguous vaccine-derived poliovirus events represents the true risk.[35]

We performed 10 000 iterations to obtain distributions for the uncertain number of total cases (including vaccine-associated paralytic polio) and total costs for each



Note. IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities.

FIGURE 2—Expected costs (mean and 95% confidence interval) for the vaccination options considered for managing polioviruses for the 20-year time horizon, by low income (a), lower-middle income (b), upper-middle income (c), and high income (d).

permutation of policies by inputting the risks and conditions into the dynamic disease transmission submodel.[37] We then estimated the economic outcomes as a function of disability-adjusted life-years (DALYs) averted assuming no age-weighing,[41–43,68] societal willingness to pay on the basis of per capita gross national incomes,[44] and treatment cost estimates on the basis of the very limited data that vary significantly across studies,[18,31,33,36,46,47] (Table 1) with the relatively small global-level costs omitted from the income-level incremental cost-effectiveness ratios.

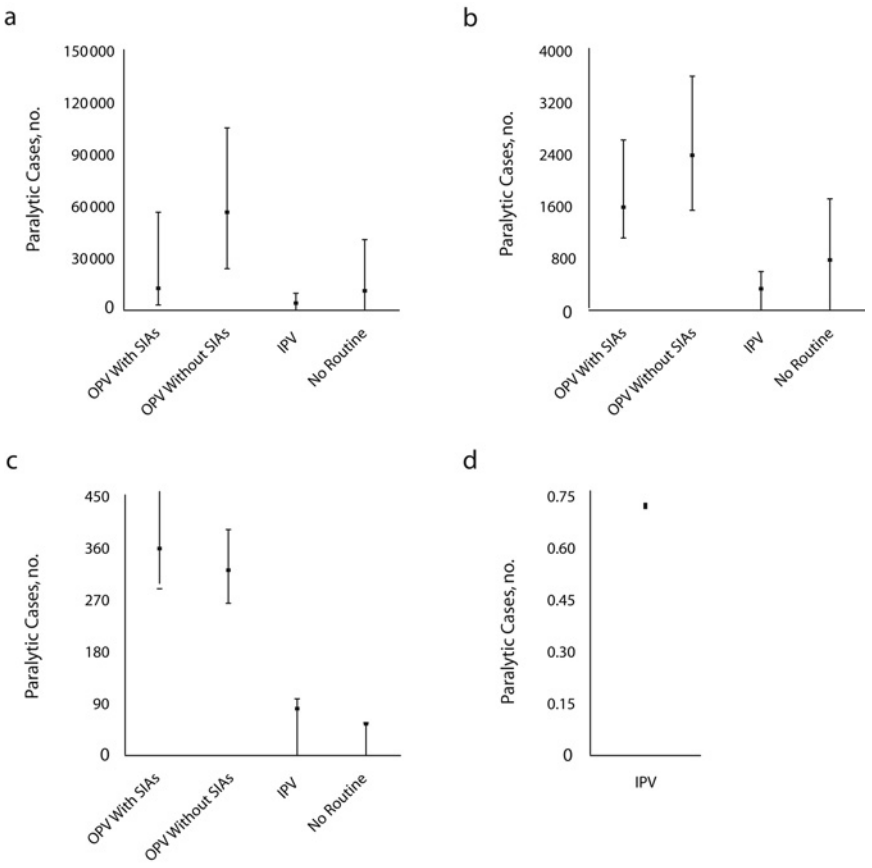
RESULTS

Figure 2 shows the expected costs (and 5th and 95th percentiles), including the outbreak response costs and treatment costs of paralytic cases, for the different routine vaccination options aggregated by income group over the 20 years. The results suggest costs of billions of dollars for continued vaccination with OPV or IPV in the 20-year period. For countries in the high-income group, we modeled only the option of continued IPV because we did not expect their routine vaccination preference to change. Depending on the income group, either IPV or OPV with SIAs represents the highest-cost option, and no routine consistently offers the lowest cost. Figure 3 shows the aggregate estimates of paralytic cases.

The numbers of expected future outbreaks differ significantly, with decreasing outbreaks expected with increasing income levels and hence fewer cases expected in higher-income level countries. Most outbreaks associated with OPV cessation result from circulating vaccine-derived polioviruses that occur during the first few years after cessation. However, continued use of OPV for routine vaccination, particularly without SIAs, leads to a relatively large number of expected outbreaks over the 20-year period. IPV and no routine tend to yield the lowest expected number of cases, although in the low-income group OPV with SIAs yields a comparable estimate to these options. The greater expected burden of OPV with SIAs compared with OPV without SIAs in the upper-middle-income group results mainly from a difference in vaccine-associated paralytic polio incidence.

As shown in Table 2, the no routine vaccination option is both cost and life saving compared with OPV (with or without SIAs), and it yields very high net benefits. Despite the generally lower number of expected paralytic cases with SIAs than without SIAs, the additional costs of the SIAs result in much greater net benefits for no routine compared with OPV with SIAs than without SIAs. The net benefit estimates probably provide policymakers with more useful information than do the cost-effectiveness ratios, and we expect that after global eradication most countries would tend toward OPV without SIAs. Table 2 also shows that the cost-effectiveness ratios represent very large numbers for the policy of switching from OPV without SIAs to IPV compared with typical values of accepted societal health interventions; and they increase with income group. Comparing IPV to OPV with SIAs, lower-middle- and upper-middle-income countries achieve both cost and life savings with 2 doses of IPV as a single antigen, depending on the actual IPV costs incurred and SIA costs saved. For low-income countries, OPV with SIAs yields fewer costs than IPV, although other IPV formulations could reduce the costs of IPV in these countries.

Because these results assume routine coverage with IPV at the level currently achieved with routine OPV (and no SIAs with IPV), if policymakers move toward a strategy with greater use of IPV, they will need to consider the impact of different actual levels of coverage. The results in Table 2 also show that the economic estimates do not favor a policy of initiating IPV given a comparator of no



Note. IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities.

FIGURE 3—Expected paralytic cases (mean and 95% confidence interval) for the vaccination options considered for managing polioviruses for the 20-year time horizon, by low income (a), lower-middle income (b), upper-middle income (c), and high income (d).

routine (i.e., after OPV cessation), and restarting SIAs if OPV continues may represent an unfavorable option after SIAs stop—except, possibly, for the low-income group, in which SIAs would prevent the most cases.

We found that opportunities to enhance population immunity before T_0 may reduce the expected burden of paralytic cases by up to 50% (i.e., by achieving maximum population immunity in the low-income group before OPV cessation). However, given that these relatively small health savings in absolute numbers come at a substantial cost, we did not find favorable economic estimates for these activities. Targeted immunization activities appear somewhat more cost-effective with cost-effectiveness ratios of approximately $19 000 and $42 000 per case of paralytic polio prevented in the low-income group for future vaccination policies of no routine and routine IPV immunization, respectively. Similarly, maintaining acute flaccid paralysis surveillance yields substantial health savings (i.e., up to 75% reduction in expected paralytic cases, depending on the income group and immunization policy), but because of its additional costs, it yielded cost-effectiveness ratios of between $27 000 and over $1 million per case of paralytic polio prevented.

We performed numerous sensitivity analyses. We found that responding to an outbreak at day 45 instead of day 70 after detection provided up to 75% reduction in expected cases. We also found that poor maintenance of containment guidelines led to substantial increases in expected cases, particularly in scenarios with wide use of IPV, given the risk associated with handling large amounts of wild poliovirus for IPV production. In the upper-middle-income group, for which we assumed a much greater likelihood of domestic IPV production than for the 2 lower-income groups, we observed a 375% increase in expected cases associated with a failure to vigilantly maintain long-term containment and, consequently, a higher risk of a virus release from an IPV manufacturing site.[35] By contrast, if we assume containment is maintained and the same low risk of IPV production site releases in the upper-middle-income groups as in the 2 lower-income groups, the expected burden with IPV remains lower than with no routine, changing the comparison of IPV versus no routine from "dominated" (Table 2) to merely cost-ineffective (i.e., a ratio exceeding $85 million per case of paralytic polio prevented).

DISCUSSION

Policymakers will face a number of difficult choices and trade-offs in managing the risks of polio following eradication of wild polioviruses[50,69]; models like this will provide constructive insights. Given the different risks and conditions, policymakers may rationally prefer and pursue different policies. For example, the no-routine option remains cost and life saving compared with OPV without SIAs in each of the lowest 3 income groups, but countries with relatively higher income and abilities to pay may prefer to switch to (or continue to use) IPV (as we assumed for the high-income group). Successful eradication must be a starting point, and before eradication, clinicians and public health leaders must keep coverage and population immunity high via routine vaccination and campaigns.

Whether the appropriate basis for comparison at T_0 is OPV with SIAs or OPV without SIAs is important in the consideration of a switch to IPV for middle-income countries. The tendency of countries to stop or substantially reduce the use of OPV with SIAs following interruption of the transmission of wild polioviruses within their borders suggests that the starting point at T_0 is more likely OPV without SIAs. This becomes clearer the more global pressure increases to reduce expenditures on polio and the longer it takes to achieve eradication. Because continued use of

TABLE 2—Expected Values of Economic Outcomes of Routine Immunization Policies (in 2002 US Dollars) by Income Group for the 20-Year Time Horizon Described in a Model Exploring Global Policies for Managing Polioviruses

Policy Comparison	Incremental Cost Effectiveness Ratio		Incremental Net Benefit, $ (Billions)
	$/Prevented Paralytic Case	$/DALY Averted	
No routine vs OPV (without SIAs)			
Low-income group	Cost and life saving	Cost and life saving	3.0
Lower-middle-income group	Cost and life saving	Cost and life saving	1.7
Upper-middle-income group	Cost and life saving	Cost and life saving	0.8
No routine vs OPV (with SIAs)			
Low-income group	Cost and life saving	Cost and life saving	4.4
Lower-middle-income group	Cost and life saving	Cost and life saving	4.3
Upper-middle-income group	Cost and life saving	Cost and life saving	3.3
IPV vs OPV (without SIAs)			
Low-income group	51 000	3 800	−2.4
Lower-middle-income group	1 100 000	80 000	−2.2
Upper-middle-income group	6 000 000	440 000	−1.4
IPV vs OPV (with SIAs)			
Low-income group	120 000	9 000	−1.0
Lower-middle-income group	Cost and life saving	Cost and life saving	0.3
Upper-middle-income group	Cost and life saving	Cost and life saving	1.1
IPV vs no routine			
Low-income group	760 000	58 000	−5.4
Lower-middle-income group	8 900 000	650 000	−4.0
Upper-middle-income group	Dominated	Dominated	−2.2
OPV with SIA vs OPV without SIAs			
Low-income group	37 000	2 800	−1.4
Lower-middle-income group	3 200 000	230 000	−2.6
Upper-middle-income group	Dominated	Dominated	−2.5

Note. DALY = disability-adjusted life-year; OPV = oral poliovirus vaccine; SIAs = supplemental immunization activities; IPV = inactivated poliovirus vaccine.

OPV with low levels of coverage creates optimal conditions for circulating vaccine-derived polioviruses, modeling the use of OPV with and without SIAs demonstrates that continued use of OPV would necessitate a sustained commitment to SIAs or to very significant improvements in routine coverage for much of the global population. Absent this, these results provide strong economic support for pursuing a policy of global OPV cessation. Along with evidence from recent outbreaks, these results provide a strong warning that countries should not stop vaccination efforts until a global agreement coordinates OPV cessation.

Although important uncertainties exist in the estimates from this study, our results remain remarkably robust.[70] Nonetheless, we note a few important limitations. First, our model assumes no undetected circulation of wild polioviruses at T_0, because any circulation would not be consistent with eradication and high-quality surveillance remains an essential prerequisite for OPV cessation. Second, we assume that chronic excretors of immunodeficiency-associated vaccine-derived polioviruses will pose a small risk of reintroduction within the time frame, although they represent an important and currently at best partially managed source of potential reintroduction of live polioviruses. Third, our model assumes that the global stockpile contains sufficient vaccine to cover all needs of outbreak response. Failure of the stockpile to do so would result in long response delays and high costs associated with restarting OPV production and much larger expected outbreaks.[48]

Fourth, the outbreak submodel[37] assumes containment of outbreaks within the population of origin and does not incorporate the risk of OPV viruses used during outbreak response, resulting in new outbreaks. Given the likelihood of outbreaks in the post-OPV environment, the development of effective response plans for the post-OPV era that address these factors represents an important challenge.[48] Future research using more stochastic and heterogeneous transmission models may help us better understand the risk of circulating vaccine-derived poliovirus emerging because of an outbreak response with OPV and may help us quantify the probability of continued undetected wild poliovirus after apparent eradication.[71]

Fifth, large uncertainty exists about future prices, and manufacturers' forecasts of IPV prices for high-income countries proved optimistic upon validation.[27] However, the attractiveness of IPV as an option depends significantly on its cost, and it offers the lowest number of expected cases. Given the importance of assumptions about cost, we explored the range of the incremental cost-effectiveness estimates for IPV versus OPV without SIAs as a function of the uncertain IPV price in upper-middle-income countries (see the figure available as a supplement the online version of this article at http://www.ajph.org). Research on IPV fractional doses, alternative administration strategies (intradermal), and attractive combination vaccines may provide a basis for altering the assumptions about IPV in the future, and policymakers can most likely best evaluate the cost-effectiveness of switching to IPV formulations in countries as the actual future IPV vaccine products and prices materialize.

Finally, the model does not address any current or future externalities associated with polio immunization services that were not previously captured in estimating costs (i.e., current cost sharing for epidemiological, laboratory transport, cold chain, surveillance, vaccinators, and other resources that are currently not exclusively maintained for polio eradication). The interaction between vaccine-related services may require that policymakers consider additional potential costs and

savings because of externalities and network effects. Although some of these limitations can be addressed through further modeling efforts, they all provide additional motivation for continued research and planning.

We estimate that the highest risks of outbreaks after OPV cessation will occur immediately after cessation, when circulating vaccine-derived poliovirus risk is highest, and policymakers should plan for at least 1 outbreak to occur somewhere in the world and prepare to respond. In addition, although we expect the probability of virus introductions to decline over time, the increasing buildup of susceptible persons means that any outbreaks that occur in the future will lead to much larger numbers of expected cases. Thus, the quality of ongoing surveillance will affect our ability to rapidly detect and respond to any outbreaks and will significantly influence the size of outbreaks that may occur in the future. Efforts to sustain surveillance should address the difficult reality of maintaining recognition for a disease that we hope will no longer harm people following success of the Global Polio Eradication Initiative and implementation of coordinated and well-informed policies. Given the great economic benefits to pursuing a policy of global OPV cessation after successful eradication of wild polioviruses, global policy discussions will need to coordinate and effectively implement posteradication risk management activities. However, countries should not stop vaccination efforts until such a global agreement exists. ■

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Note. *The contents of this article 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 World Health Organization.*

Contributors

K.M. Thompson and R.J. Duintjer Tebbens developed the model, conducted all the modeling and analysis, wrote the first draft of the article, and edited the article. M.A. Pallansch, R.W. Sutter, R.B. Aylward, and S.L. Cochi contributed sections of writing to the article, participated in discussions related to framing the analysis and conceptualization of this effort from its inception, obtained and synthesized existing data for use in the analysis, and edited the article. O.M. Kew, M. Watkins, H.E. Gary, J. Alexander, and H. Jafari provided comments on the article and contributed to the discussion of the presentation of the results.

Human Participant Protection

No protocol approval was needed for this study.

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