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Retrospective Cost-Effectiveness Analyses for Polio Vaccination in the United States

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The history of polio vaccination in the United States spans 50 years and includes different phases of the disease, multiple vaccines, and a sustained significant commitment of resources. We estimated cost-effectiveness ratios and assessed the net benefits of polio vaccination applicable at various points in time from the societal perspective and we discounted these back to appropriate points in time. We reconstructed vaccine price data from available sources and used these to retrospectively estimate the total costs of the U.S. historical polio vaccination strategies (all costs reported in year 2002 dollars). We estimate that the United States invested approximately $35 billion (1955 net present value, discount rate of 3%) in polio vaccines between 1955 and 2005 and will invest approximately $1.4 billion (1955 net present value, or $6.3 billion in 2006 net present value) between 2006 and 2015 assuming a policy of continued use of inactivated poliovirus vaccine (IPV) for routine vaccination. The historical and future investments translate into over 1.7 billion vaccinations that prevent approximately 1.1 million cases of paralytic polio and over 160,000 deaths (1955 net present values of approximately 480,000 cases and 73,000 deaths). Due to treatment cost savings, the investment implies net benefits of approximately $180 billion (1955 net present value), even without incorporating the intangible costs of suffering and death and of averted fear. Retrospectively, the U.S. investment in polio vaccination represents a highly valuable, cost-saving public health program. Observed changes in the cost-effectiveness ratio estimates over time suggest the need for living economic models for interventions that appropriately change with time. This article also demonstrates that estimates of cost-effectiveness ratios at any single time point may fail to adequately consider the context of the investment made to date and the importance of population and other dynamics, and shows the importance of dynamic modeling.

KEY WORDS: Cost-benefit analysis; cost-effectiveness analysis; polio; vaccination

1. INTRODUCTION

Few Americans may currently remember the devastating disease burden and fear that poliomyelitis disease (polio) once caused given its elimination from the United States over 25 years ago. However, as shown in Fig. 1 polio paralysis cases numbered in the thousands annually prior to the 1960s. As the world approaches global eradication of polioviruses[1] this represents an important time to look back historically at the evolution of the disease and the vaccines, and to quantify the economic benefits of the U.S. investments in controlling and preventing polio.

The history of polio includes several phases: endemic followed by epidemic disease prior to vaccine availability, epidemic disease with a vaccination

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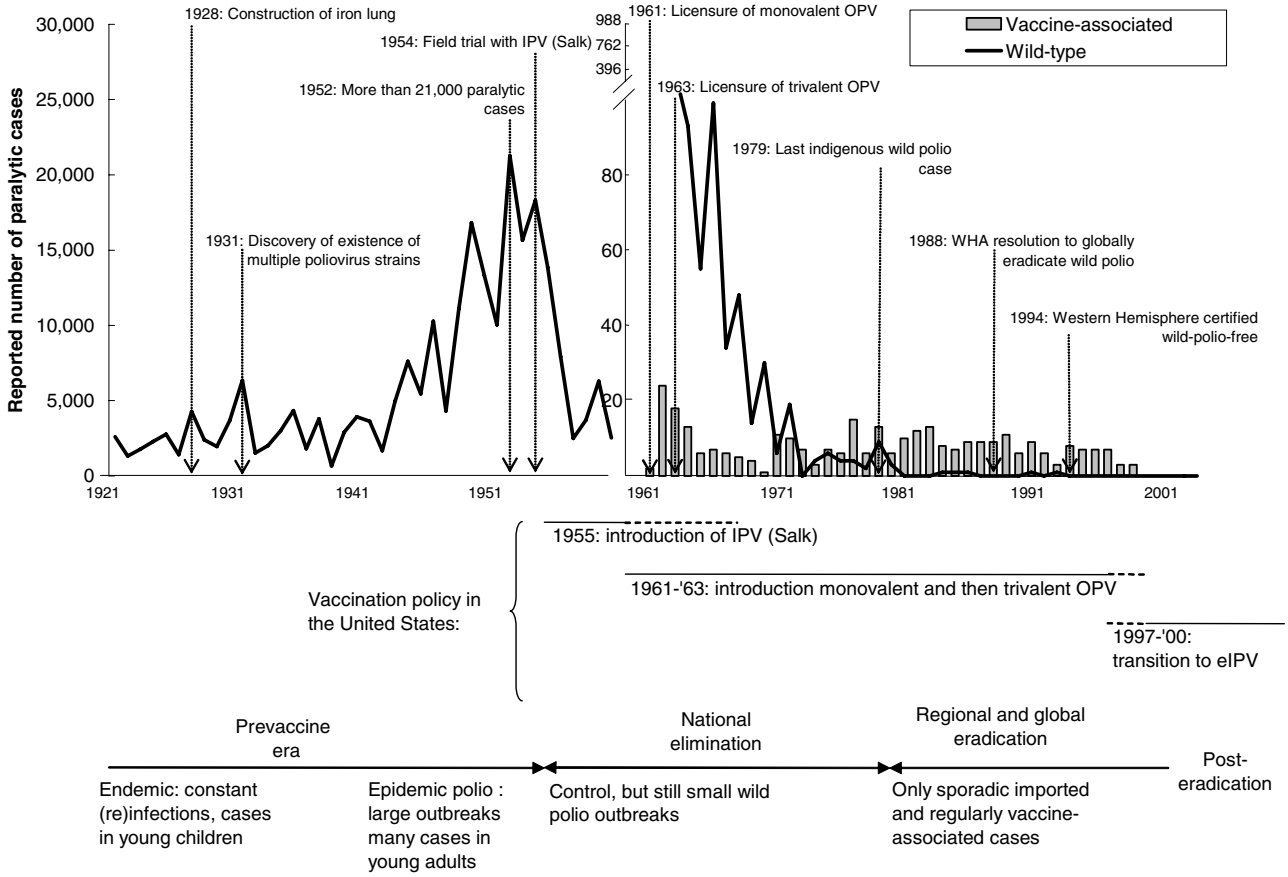
program aimed at control, and eliminated disease with continued vaccination to minimize the impact of potential poliovirus reintroductions. During the prevaccine era (prior to 1955), physicians developed and relied on treatment strategies that included iron lungs and muscular support for paralyzed limbs. No cost-effectiveness estimates of these devices exist, and we could not identify sufficient data to support development of these estimates. Concern about polio led to the creation of the March of Dimes, which invested a reported $25.5 million in research on poliovirus vaccines by 1955.[2] Following the introduction of the (Salk) inactivated poliovirus vaccine (IPV) in 1955, paralytic polio incidence dropped significantly, as shown in Fig. 1. The 1955 Cutter Incident,[3] which involved poorly inactivated vaccine and caused 200 cases of paralysis and 10 deaths, provided an early challenge to mass vaccination efforts and demonstrated that the benefits of polio vaccine came with risks. However, public concern about wild polioviruses and the promise of the vaccines led to widespread support and demand for polio vaccination. In 1961, the United States introduced monovalent oral poliovirus vaccine (OPV) and after 1963 switched to trivalent OPV. Using OPV, the United States successfully eliminated circulating wild polioviruses with the last indigenous case occurring in 1979. However, the transition to OPV soon led to reports of vaccine-associated paralytic poliomyelitis (VAPP) cases. With the near elimination of the wild poliovirus in the United States given the success of the vaccine, the United States began to report more cases of VAPP than paralysis from wild polioviruses starting in 1971. Given this reality, the United States made the costly decision to transition from almost exclusive trivalent OPV use in its routine vaccination



Based on published[41–43,69–71] and unpublished data (Lorraine Alexander; with personal correspondence); paralytic cases before 1951 derived from total reported polio cases divided by 2.5 (see Table I).
eIPV = enhanced-potency inactivated poliovirus vaccine; IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; WHA = World Health Assembly.

Fig. 1. History of polio in the United States since 1921.

program to increasing the use of enhanced-potency IPV (eIPV) (starting in 1997) and the exclusive use of eIPV in 2000.

A number of prior studies provided economic evaluations of polio vaccines and vaccination efforts at different points in time, but none retrospectively. Miller *et al*.[4] estimated a very high incremental cost-effectiveness ratio of approximately $3.5 million (dollar year 2002; corresponds to $3 million in 1995 dollar years) per case of VAPP prevented associated with switching from trivalent OPV to eIPV. This analysis supported a change in policy anticipated by the earlier study by Hinman *et al*.[5] That study found higher costs and more cases for routine vaccination with eIPV than OPV in the context of wild viruses still widely circulating globally, but noted that a decline in exposure to wild virus could "alter the balance significantly" (Reference 5, p. 295). In addition to cost-effectiveness analyses in various other countries,[6,7] other estimates focus on global eradication,[8,9] regional elimination in Latin America,[10] and posteradication policies.[11–13] Although these cost-effectiveness analyses supported decisions made at various points in time, no study to date assessed the costs and effectiveness of different vaccine options for polio or the net benefits in the context of the entire time period.

Disease dynamics play an important role in estimating the benefits of vaccines. Population (or herd) immunity[14–16] arises from the ability of the vaccine to limit the extent of virus transmission (and in the event of a live virus vaccine like OPV to also secondarily immunize contacts of vaccine recipients), and consequently to protect the health of more than just those receiving the vaccine. Although vaccines represent the predominant intervention of focus for pediatric cost-effectiveness and cost-benefit analyses, recognition of the importance of considering the impact of the dynamic nature of the disease remains relatively new[16–34] and the importance of considering the dynamics of interventions is not recognized as essential in cost-effectiveness analysis methodology.[35]

2. METHODS

We estimate the costs and effectiveness of the various historical polio immunization programs in the United States following current recommendations and taking a societal perspective.[35] As shown in Fig. 1, the interventions involved predominantly IPV (Salk) from 1955 to 1961, predominantly trivalent OPV from 1961 to 1997 (with monovalent OPV used on a large scale between 1961 and 1964), and a sequential schedule using eIPV and OPV from 1997 to 2000 before moving to an all eIPV schedule from 2000 onward. Thus, we characterize the costs and effectiveness of IPV indefinitely starting in 1955 versus no program, OPV indefinitely starting in 1961 versus IPV, and IPV versus OPV in 1980 (an intermediate time point we chose because 1979 represented the last year with indigenous wild polio cases) and in 1997. Outcomes for future years incorporate population projections from the U.S. Census Bureau[36] and assume continued use of eIPV through at least 2015, with the number of doses per child and vaccine prices remaining constant at the current levels. We also ran the model through 2099 to explore the long-term impacts of childhood vaccinations since they provide lifetime benefits. In the case of disease elimination, the benefits also extend to future generations so long as eradication is maintained. We note that significant uncertainty surrounds extrapolation of policy into the future, particularly with the approach of global eradication of wild polioviruses. In addition, the recent introduction of IPV in combination vaccines may lead to savings on syringes, storage space, and preparation time and provide benefits associated with less pain and emotional distress experienced by infants from injections that will also impact future estimates of the cost effectiveness of IPV.[37–39]

Consistent with current recommendations,[35] we discount both economic and health outcomes using a discount rate of 3% (range: 0 to 5%). We express the outcomes as the net present value looking prospectively from the first year of a policy (i.e., 1955 for the actual polio immunization programs vs. no program, 1961 for OPV indefinitely vs. IPV indefinitely, etc.). We calculate the total costs for immunization in a given year as a function of the prices and amounts of private and public vaccine doses distributed (corrected for wastage) minus the net treatment costs saved from cases of polio prevented by vaccination (see Appendix).

In estimating the costs and effectiveness of the actual programs, we use reported paralytic cases (corrected for underreporting) and we calculate the cases that we would anticipate for other program options using an adapted existing dynamic disease transmission model.[40] We also used the transmission model to reconstruct the herd immunity effect that occurred after the introduction of massive polio vaccination and to compare this with what an individual-based

(i.e., nondynamic) model would predict. Although the original model aims to simulate polio outbreaks due to virus importations in previously polio-free countries, rather than in situations of endemic circulation of multiple poliovirus strains during many years, we maintained its structure by age groups and partially infectible groups.[40] However, we modified the model to the extent necessary to describe the disease dynamics over a longer period.

We demonstrate the importance of using an appropriate dynamic disease model by also computing the effectiveness results using an individual-based model, which limits the benefits to the vaccinated individuals and does not capture the reduction in the infectious and susceptible proportion of the population. For these calculations, we modify the dynamic model to assume secondary OPV infection rates of zero. We also assume in this case that the force of infection would remain constant over time at the value that follows from the initial values in the dynamic model, R_0, and the average duration of the infectious period.

We present the results using both cost-effectiveness and net benefits frameworks. For the cost-effectiveness metric, we express the health outcomes in terms of paralytic cases prevented. For the net benefit metric, we express the health outcomes in monetary terms using the willingness to pay to prevent one surviving case of paralytic polio (*WTPP*) and the willingness to pay to prevent one death due to paralytic polio (*WTPD*).

2.1. Effectiveness Inputs

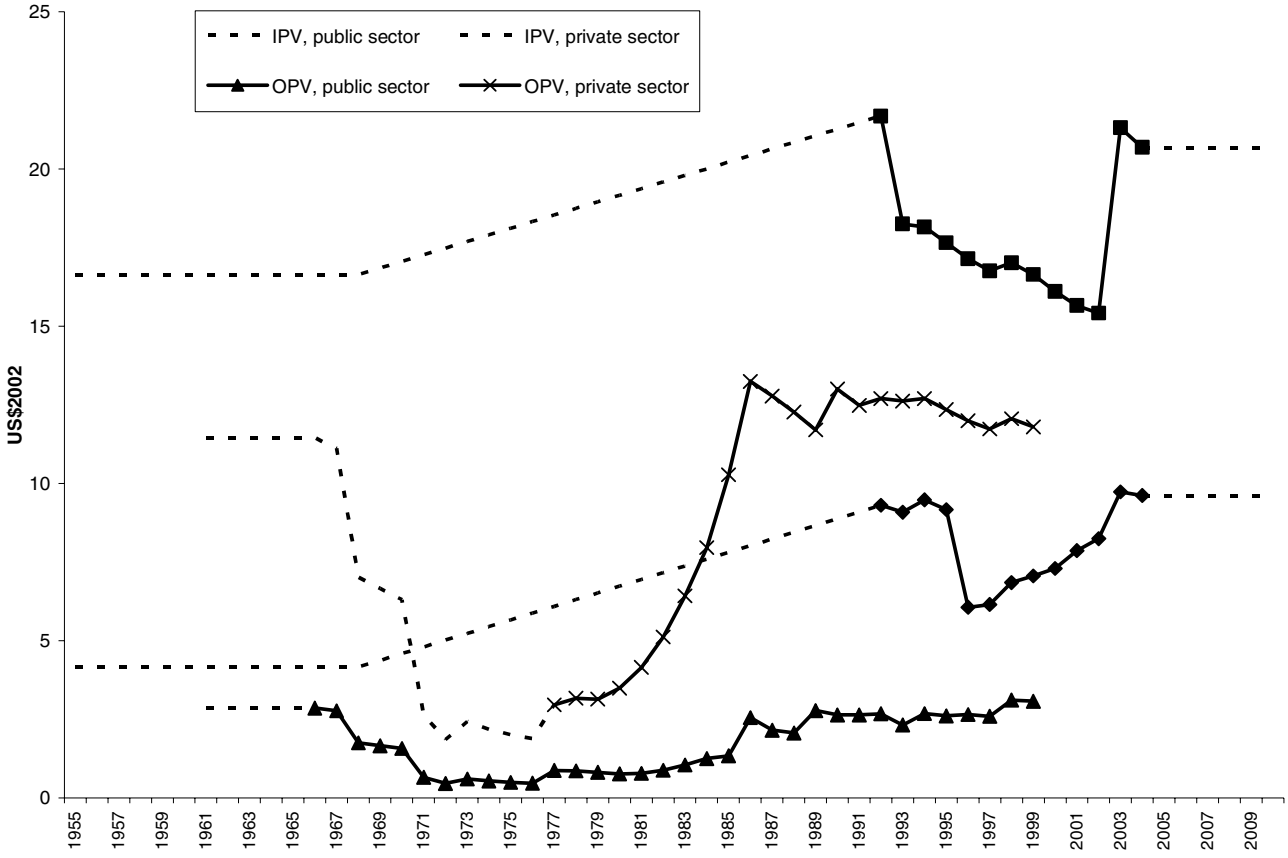
Fig. 1 shows the reported number of paralytic polio cases from 1921 forward based on Alexander *et al.*[41] and unpublished U.S. Centers for Disease Control and Prevention (CDC) data (Lorraine Alexander; with personal correspondence) for 1980–2000, summaries of CDC's *Morbidity and Mortality Weekly Reports* for 1930–1979,[42–44] and approximate extrapolation from the rates per 100,000 people from a figure for 1921–1929 (Reference 45, fig. 7, p. 76). Prior to 1951, polio reporting did not specify paralytic cases separately, and consequently we estimate the number of paralytic cases from the total number of paralytic and nonparalytic polio cases using the average ratio of approximately 2.5 total polio cases per reported paralytic case during the prevaccine years 1951–1954.

In estimating the number of cases prevented, we correct reported numbers for underreporting using the ratio of reported VAPP cases during 1980–1991 as of 2004 (from Alexander *et al.*[41] and Lorraine Alexander; with personal correspondence) to expected number of VAPP cases during 1980–1991 based on a capture-recapture analysis[46] (i.e., $109/114 \approx 96\%$). Although physicians probably exhibited greater alertness to polio disease in the earlier years, we note that current reporting relies on two presumably independent systems,[46] and we assume that reporting efficiency remained constant over time. In 1952, the year of the highest polio incidence, polioviruses caused 21,269 reported paralytic cases, including 3,145 deaths,[47] from which we estimate a case-fatality rate of 15% for paralytic polio.

2.2. Cost Inputs

To ensure meaningful and consistent monetary quantities, we express all costs in 2002 U.S. dollars (noted US$2002) using the general Consumer Price Index available from the Bureau of Labor Statistics.[48] We obtained public and private sector polio vaccine prices from the published literature,[49,50] unpublished data from the CDC (Robert Snyder; with personal correspondence), and the website of CDC's National Immunization Program.[51,52] Fig. 2 shows all of the vaccine price data we obtained (converted to US$2002), along with our extrapolations to years with no available data. For years in which we found only public sector prices available, we assumed private sector prices four times higher than the public sector price based on available data for other years. For years in which we found neither public nor private sector prices, we assumed prices equal to the nearest available quote, with the exception of years without any IPV use (1968–1991; see Fig. 2), for which we linearly interpolate between the 1967 quotes and 1992 estimates (used only for calculations involving the hypothetical *IPV indefinitely* policy). We excluded available private sector price quotes for 1986–1991 given very limited and poorly documented use of IPV. With estimates of the price of monovalent OPV used in the early 1960s lacking, we assumed these prices equaled the price of trivalent OPV in 1966 (i.e., 2.87 US$2002 in the public sector).

We obtained data for the number of doses of polio vaccine distributed annually from the published literature for 1955–1962[53] and from the CDC for 1963–1999 (Robert Snyder; with personal correspondence) (see Fig. 3). For years in which we could not find data on the breakdown by sector we assumed that the public sector distributed 25% of the total doses prior to

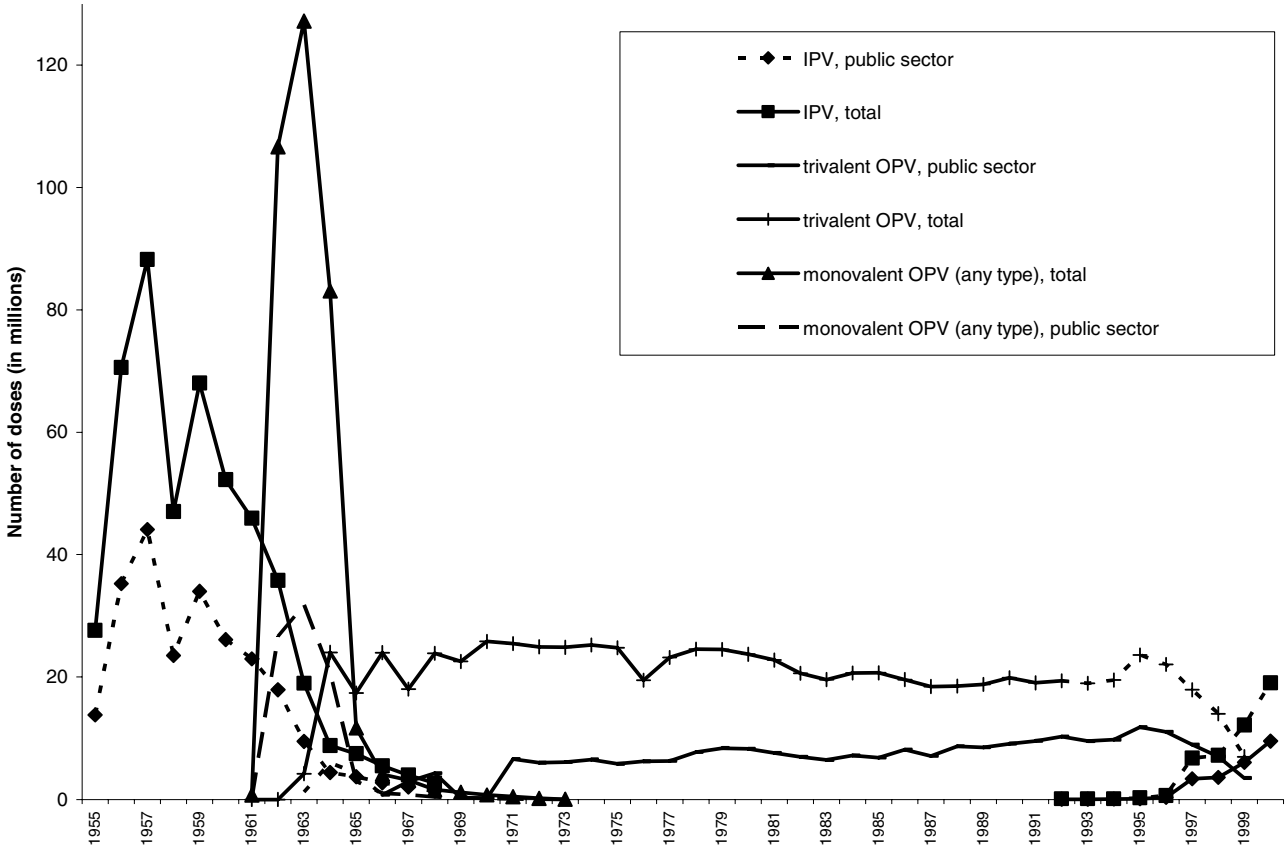


Based on published[50–52] and unpublished data (Robert Snyder; with personal correspondence).
Dotted lines represent extrapolations: if public sector price quotes are available, then we extrapolate assuming that the ratio of the private to public sector price is 4, or if neither public nor private sector prices are available, then we assume prices remain constant at nearest available quote, with the exception of years without any IPV use (1968–1991; see Fig. 3), for which we interpolate linearly between the 1992 quotes and 1967 estimate (used only for calculation of hypothetical *IPV indefinitely* policies). This neglects various available private sector quotes for IPV for 1986–1991.
If different quotes for several vial sizes are available, we use the least expensive vial size.
Prices include excise tax of 0.25 in quoted dollar years since 1987, 0.75 in quoted dollar years since 1997.
IPV = inactivated poliovirus vaccine (Salk IPV until 1968, enhanced-potency IPV since 1992); OPV = oral poliovirus vaccine (all quotes are for the trivalent vaccine).

Fig. 2. Available and extrapolated polio vaccine prices per dose in the United States since 1955.

1973, and 50% from 1994 forward. We assume that the number of doses distributed per newborn after 2000 remains constant (i.e., 4.75 in 2000). Based on a study by Sirken,[54] we estimate the wastage associated with mass IPV immunization at approximately 16%, and we assume the same wastage for mass OPV immunization. Wastage estimates during routine immunization in 1999 indicate much lower rates for OPV (8.4%) and IPV (1.5%),[55] and we adopt these estimates for the routine immunization era.

Table I includes estimates for the administration, travel, and opportunity cost per dose during the mass immunization era (1955–1964) and the routine immunization era (1965 and beyond). Miller *et al.*[4] estimated the administration cost at US$2002 11.10 (assuming the original data[4] represent dollars of the year 1995), the "clinic travel cost" at US$2002 3.54, and the "indirect clinic visit cost" at US$2002 23.49. They attributed one-third of the latter two components to polio vaccination to account for children receiving multiple vaccines during routine immunization clinic visits. Based on these estimates, we assume the travel and opportunity costs equal US$2002 9.01 in the routine immunization era. During the mass immunization campaigns in the 1950s and 1960s, people of all ages went to clinics just to receive polio vaccinations and therefore we assume the travel and opportunity costs then equaled the full clinic visit cost of US$2002 27.03. We obtained an estimate of US$2002 1.91 (US$1955 0.285) for the administration costs during the mass immunization era from a cost study of IPV immunization in Colorado.[56] We assume equal



Based on published[53] and unpublished data (Robert Snyder; with personal correspondence).
Dotted lines represent extrapolations: if the number of public sector doses is unavailable, then we derive it from the total assuming that the public sector distributed 25% and 50% of doses until 1973 and after 1993, respectively (see Table I)
IPV = inactivated poliovirus vaccine (Salk IPV until 1968, enhanced-potency IPV since 1992); OPV = oral poliovirus vaccine.

Fig. 3. Available and extrapolated estimates of the number of publicly and total distributed polio vaccines in the United States since 1955.

nonvaccine costs for IPV and OPV, consistent with the study by Miller *et al.*[4] To estimate net benefits, we used the average estimate of US$2002 1.4 million for the combined treatment costs (*Ctreat*) and the willingness to pay per surviving paralytic case, based on the average of nine compensation awards paid to surviving VAPP patients by the National Vaccine Injury Compensation Program as a proxy for the total direct and indirect treatment costs and the "intangible costs" for suffering.[4] Hatzandrieu *et al.*[57] took the approach of estimating the treatment costs and opportunity costs directly by component and used the human capital approach to estimate the opportunity costs for acute and chronic paralytic polio for surviving patients.[57] Based on the resulting totals (Reference 57, Table 8), we attribute approximately 37% of the total costs per paralytic case to treatment. This results in our base-case estimates of *Ctreat* = US$2002 524,000 and *WTPP* = 892,000 per case. We assume a willingness to pay to prevent one death due to polio of approximately US$2002 4 million, but recognize the important uncertainty and sensitivity of this input, commonly varied between US$2002 1 and 10 million.[58] In sensitivity analyses we vary this input from US$2002 0 to 10 million, where the lower end reflects an analysis that excludes prevented deaths as a consideration.

Finally, based on a study by Lieu *et al.*[38] that found no relationship between the administration cost per clinic visit and the number of injections per clinic visit, we assume equal costs for IPV administered as a single antigen or in a combination vaccine. However, in sensitivity analyses we explore the savings resulting from an IPV combination vaccine compared to a single antigen IPV vaccine from 2005 forward by associating US$2002 10–30 with each injection (i.e., each administered dose) based on parental willingness to pay to forego the discomfort and emotional distress

Table I. Inputs to the Economic Evaluation Model

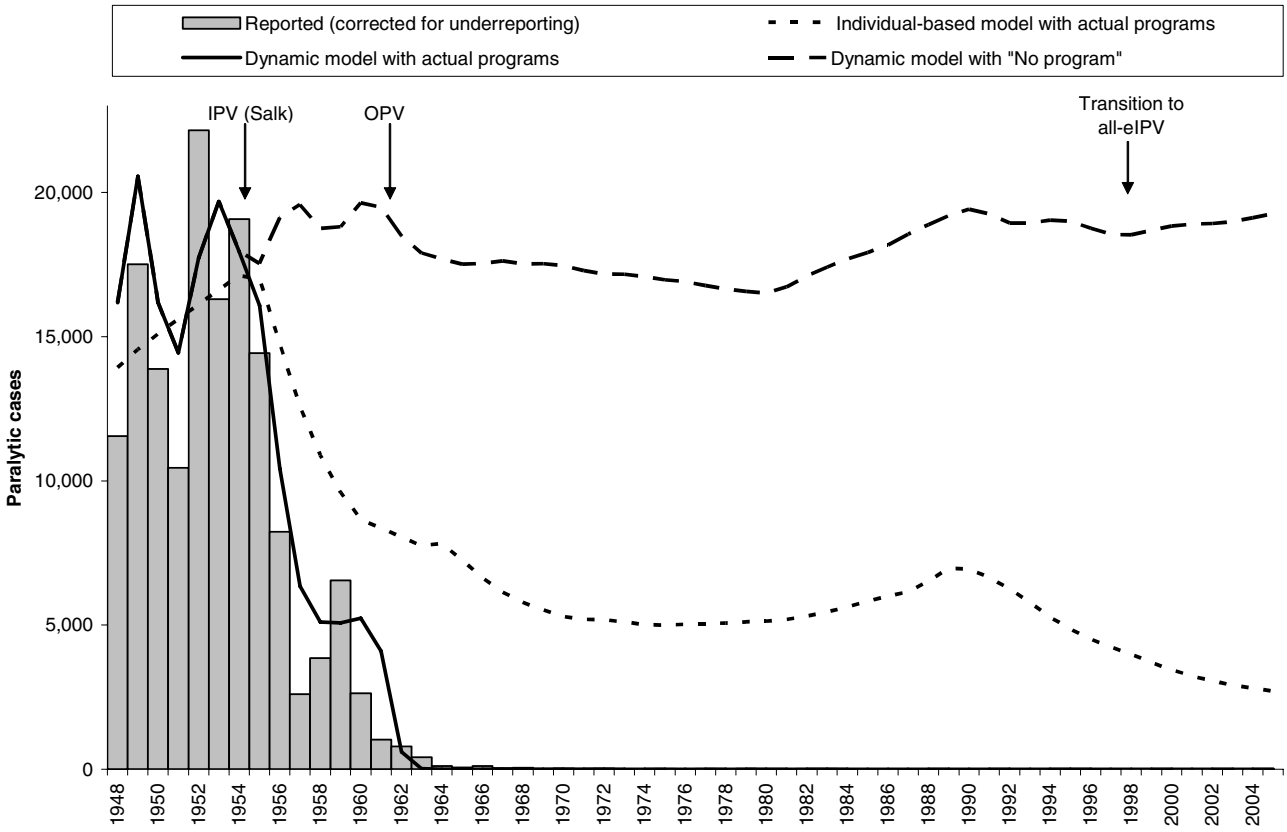
Input [unit]	Lower Bound	Best Estimate	Upper Bound	Source	Notes
Discount rate (%)	0	3	5	(35)	
Administration cost per dose, mass immunization (1955–1964) (US$2002)	1.00	1.91	11.10	(56)	
Travel and opportunity cost per dose, mass immunization (1955–1964) (US$2002)	9.00	27.03	27.03	(4)	Attribute all travel and indirect costs per clinic visit to polio vaccination
Administration cost per dose, routine immunization (>1964) (US$2002)	5.00	11.10	20.00	(4)	
Travel and opportunity cost per dose, routine immunization (>1964) (US$2002)	9.00	9.01	27.03	(4)	Attribute one-third of travel and indirect costs per clinic visit to polio vaccination
IPV wastage, mass immunization (1955–1964) (%)	10	16.13	25	(54)	(Distributed − administered doses)/(100 × distributed doses)
OPV wastage, mass immunization (1955–1964) (%)	10	16.13	25		Assume same wastage as for IPV
IPV wastage, routine immunization (>1964) (%)	0	1.50	16	(55)	
OPV wastage, routine immunization (>1964) (%)	0	8.40	16	(55)	
Publicly/total distributed doses after 1993 (%)	40	50	60		Based on this percentage for years where breakdown is available (see Fig. 3)
Publicly/total distributed doses before 1973* (%)	0	25	50		Based on this percentage for years where breakdown is available (see Fig. 3)
Private/public sector vaccine price before 1977 (proportion)	1	4	4		Based on this ratio in years where both price quotes are available (see Fig. 2)
Completeness of reporting (%)	80	96	100	(46)	See text
Case-fatality rate for paralytic polio† (%)	10	15	25	(47)	Based on case-fatality rate in 1952
Total/paralytic polio cases before 1951 (proportion)	2	2.5	3	(43)	Based on this ratio for 1951–1954
VAPP rate if OPV-only continues after 1997 (cases per million birth cohort)	2	2.2	2.5		Number of VAPP cases 1980–1997 divided by children born in 1980–1997
Average compensation award paid to nine VAPP patients (excluding deaths) (US$2002)	1 million	1.4 million	2 million	(4)	
Percent of average compensation that is attributable to treatment cost (%)	25	37	75	(57)	
Average treatment cost per paralytic polio case (US$2002)	0.25 million	0.52 million	1.5 million		Average VAPP award times proportion attributable to treatment costs
Average willingness to pay to prevent one paralytic polio case (US$2002)	0.25 million	0.89 million	1.5 million		Average VAPP award times one minus proportion attributable to treatment costs
Average willingness to pay to prevent one death due to paralytic polio (US$2002)	0	4 million	10 million	(58)	

*We do not apply this ratio for trivalent OPV doses during 1966–1973 since the actual breakdown was available for those years.
†In reality, the case-fatality ratio depends on many factors, including type of medical treatment (which may improve over time) and whether paralysis affects the respiratory muscles (which becomes increasingly likely with increasing age of onset of paralysis). The estimate here represents an average over these factors.
IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; VAPP = vaccine-associated paralytic polio.

of injections for their children.[30,37,39] We did not include costs related to poliomyelitis research, surveillance, or costs associated with running disease control or eradication programs.

3. RESULTS

Fig. 4 shows the actual paralytic polio cases reported (corrected for underreporting) and the results of the dynamic model (solid curve). The dynamic



Reported numbers based on published[41–43,45,69,71] and unpublished data (Lorraine Alexander; with personal correspondence); corrected for underreporting assuming 96% reporting efficiency (see Table I); paralytic cases before 1951 estimated as total reported polio cases divided by 2.5 (see Table I).
eIPV = enhanced-potency inactivated poliovirus vaccine; IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine (monovalent or trivalent).

Fig. 4. Yearly incidence of paralytic polio (excluding VAPP) in the United States 1948–2004: reported, simulated with the dynamic transmission model[40] (both with and without vaccination programs), and simulated with the individual-based model.

model provides a good approximation of the actual observed experience with polio, and yields an overall estimated 176,000 undiscounted cases between 1948 and 2005 compared to the actual number of 152,000 undiscounted cases during that time period. Fig. 4 also shows the results of an individual-based model (dotted curve) and our modeled projection of the number of cases over time in the absence of a vaccination program for polio (dashed curve). The difference between the top (dashed) curve and the actual cases (vertical bars) represents the estimated benefits (or effectiveness) of vaccination. The use of the traditional individual-based model produces a significant underestimate of benefits (missing over 30% of actual benefits for 1955–2005), while the dynamic model produces a much better approximation of the true benefits. This should serve to motivate future cost-effectiveness modelers to use dynamic models as appropriate.

We estimate that the United States invested approximately US$2002 35 billion (1955 net present value, discount rate of 3%) in polio vaccinations between 1955 and 2005 and will invest approximately US$2002 1.4 billion (1955 present value or US$2002 6.3 billion in 2006 present value) between 2006 and 2015 assuming a policy of continued use of IPV for routine vaccination. These investments translate into over 1.7 billion vaccinations that prevented approximately 900,000 cases of paralytic polio between 1955 and 2005. We estimate that these investments will prevent approximately 200,000 more cases of paralytic polio between 2006 and 2015 (and would prevent 2.3 million more cases between 2016 and 2099 if we extend the time horizon that long). This represents a total of approximately 1.1 million cases prevented, including over 160,000 deaths (1955 net present value of approximately 480,000 cases and 73,000 deaths) (Table II). We found that with a time horizon

Table II. Costs and Effectiveness of Polio Immunization Programs in the United States (Rounded to Two Significant Figures.)

Intervention	Actual Programs	IPV Indefinitely	OPV Indefinitely	IPV Indefinitely	IPV Indefinitely
			IPV	OPV	OPV
Comparator program	No Program	No Program	Indefinitely	Indefinitely	Indefinitely
Year of decision (= year of net present value, using 3% discount rate)	1955	1955	1961	1980	1997
Last year in model	2015	2015	2015	2015	2015
Cumulative discounted costs (or savings) (billions US$2002)*	−180	−110	−76	3.5	1.9
Cumulative discounted paralytic cases (including deaths) prevented†	480,000	340,000	160,000	200	130
Cumulative discounted deaths prevented†	73,000	52,000	23,000	30	20
Cost-effectiveness ratio (US$2002/paralytic case)	NA	NA	NA	17,000,000	14,000,000
Cumulative net benefit (billions US$2002)	840	580	290	−3.2	−1.7

*Numbers represent vaccination costs/savings minus treatment costs/savings. For the price of IPV between 1969–1991, we interpolate linearly between estimates for 1968 and 1993 from Fig. 2. We assume the OPV price will remain constant between 2000–2015 at the 1999 estimates from Fig. 2.

†Underlying assumptions regarding the disease burden: for *actual programs*, we use reported cases (always corrected for underreporting) and assume 0 cases after 2000; for *no program*, we obtain the incidence of paralytic cases from the dynamic transmission model; for *IPV indefinitely* in 1955 and 1961, we obtain the incidence of paralytic cases from the dynamic transmission model assuming all vaccines administered were IPV; for *IPV indefinitely* in 1980 and 1997, we subtract reported VAPP cases from the total number of cases in *actual programs* (i.e., we count only sporadic importations); for *OPV indefinitely*, we use the number of cases from actual programs until 1996 and estimate the VAPP incidence at 2.2 cases per million birth cohort for 1997 and beyond.

IPV = inactivated poliovirus vaccine; NA = not applicable: cost-effectiveness ratio meaningless if either costs or cases are nonpositive; OPV = oral poliovirus vaccine; VAPP = vaccine-associated paralytic polio.

extending to 2015 and a discount rate of 3%, the investment led to cost savings of approximately US$2002 215 billion (1955 net present value) due to treatment costs saved, yielding cumulative net savings of US$2002 178 billion after subtracting the vaccination costs (1955 net present value). If we subtract the estimated March of Dimes research costs of US$2002 $171 million (equivalent to $25.5 million in US$1955), the net benefits remain approximately US$2002 178 billion. We believe that incorporating the intangible costs of suffering, death, and fear would lead to an estimate of the overall net benefit of over US$2002 800 billion (1955 net present value).

Table II shows that the cost-effectiveness ratios varied over time. We provide estimates of the incremental cost-effectiveness ratios and net benefits comparing available interventions to the *status quo* at four major decision points (1955, 1961, 1980, and 1997). The second column in Table II characterizes the overall results for the vaccination programs that occurred (i.e., the estimates of a clairvoyant decision-maker with perfect information in 1955 about the net present value of the vaccine programs that the United States would use over time compared to doing nothing), discounted back to 1955. For the hypothetical program involving continued IPV after 1961, we assumed continued occurrence of wild polio as estimated in the transmission model, while for the programs involving IPV after 1980 we assumed no more wild poliovirus would occur, other than sporadic importations reported to date. Consequently, the decision to switch to OPV in 1961 remains very beneficial due to both vaccination cost savings and prevented disease cases, while the switch back to IPV (hypothetically in 1980 or as occurred in 1997) prevented few polio cases (all VAPP) at a relatively large cost.

For OPV indefinitely, we use the number of cases from actual programs until 1996 and we estimate the VAPP incidence at 2.2 cases per million people in the birth cohort for 1997 and beyond based on this ratio during 1980–1996. We note that our estimate of the cost-effectiveness ratio for 1997 confirms the relatively high estimate by Miller *et al*.[4] Our results also confirm their conclusion that according to strictly applied cost-effectiveness criteria (which ignore changes over time in the interventions, population, and disease), IPV would not represent a comparatively wise investment of resources. We attribute our relatively higher cost-effectiveness ratios than those estimated by Miller *et al*.[4] to the higher actual IPV price that occurred than the prices Miller *et al*. projected.

In the context of cost-effectiveness analysis, elimination raises issues about the potential use of zero cases prevented creating an undefined denominator, and also suggests the need to redefine the base case or *status quo*. For a disease like polio, it also suggests that the larger context of global eradication and the potential for reintroductions resulting in large

outbreaks must factor into policy decisions. Thus, cost-effectiveness ratios may not represent the only consideration because they fail to sufficiently capture the decision dynamics and the path-dependent options.

We explored extending the time horizon of the model and of future IPV use. Extending the last year of the time horizon from 2015 to 2099 increases the net benefits from US$2002 835 billion to almost 1.1 trillion (1955 net present value), again still not accounting for costs associated with death, suffering, and fear. Looking from the perspective of 2006 forward, the cost of vaccinations up to 2099 (assuming continued use of IPV at current costs) would be US$2002 27 billion (2006 net present value), compared to US$2002 6.3 billion if IPV use ceases in 2015. However, given the relatively low vaccination costs compared to the monetary equivalent of paralytic cases prevented, whether or not IPV use continues beyond 2015 has very little impact on our estimates of the net benefits (in 1955 net present value) (see Appendix). Including the parental WTP for reduced injections resulting from use of IPV in a combination vaccine would lead to US$2002 1.9 to 5.8 billion in cost savings compared to IPV as a single antigen vaccine between 2005 and 2015 (2005 net present value), based on assuming savings between US$2002 10 and 30 per administered IPV dose, respectively. Thus, we expect that the costs of IPV may decline with its continued (and increased) use and the trend toward combination vaccines.

Table III shows the results of a simple one-way sensitivity analysis to investigate how the cumulative net benefit of the actual vaccination programs changes with the variations in the economic evaluation model inputs from Table I. We did not vary inputs to the dynamic transmission model,[40] with the exception of assumptions regarding R_0 (see Appendix). Given the analytical time horizon spanning 60 years, by far the most influential input appears to be the discount rate, which reflects a societal time preference rather than a model input uncertainty. The range in cumulative net benefit of US$2002 0.6 to almost 2 trillion (1955 net present value) from variation of the discount rate contains all other ranges. The willingness-to-pay estimates per prevented death or case of paralytic polio (both reflecting societal preferences as well) represent the next two most important inputs, while the average treatment cost per paralytic case emerges as the most influential among the inputs whose ranges represent true uncertainties. The case-fatality rate also substantially impacts the cumulative net benefit estimate since the number of prevented deaths carries such great cost savings. In contrast, changing any of the other inputs changes the cumulative net benefit by less than 2% compared to the base case estimate, in spite of the wide ranges for some inputs. Thus, considering a range of different potential inputs to the model, the robust results suggest that the U.S. polio vaccination program represents a cost-saving historical investment with significant financial net benefits.

4. DISCUSSION

The significant investments made in controlling polio and sustaining its elimination in the United States using vaccines led to net benefits in the range of hundreds of billions to trillions of dollars (1955 net present value). Clearly, this represents one of the best historical investments in health made by the United States, and it demonstrates the potential significant economic impacts of public health interventions. OPV served as a cost- and life-saving vaccine, although its successful use ultimately created the need in the United States to stop OPV use given the few, but measurable cases of VAPP. The switch to IPV did not represent a good investment according to a stringent static cost-effectiveness criterion, as noted by Miller *et al*.[4] However, management of a highly transmissible disease like polio in an increasingly connected world made the switch to IPV an important option given the possibility of imported wild poliovirus introductions. The fact that policymakers ultimately decided to switch to IPV in part also reflects the reality that vaccination policy decisions involve not only costs and effectiveness, but also other ethical considerations, particularly in relation to the acceptability of adverse events.[59]

Uncertainty remains about the capability of IPV to eliminate wild polioviruses and thus the switch from IPV to OPV in the early 1960s represented an important decision with respect to public health. We note that the relatively small risk of VAPP, which only became very apparent in the absence of circulating wild poliovirus cases, demonstrates the reality that individuals within a population may need to accept small risks in order to obtain large collective benefits.[60] The decision made by the United States in the late 1990s to switch from OPV to IPV represents one of the most important questions that most countries in the world will face with the success of global eradication.

Table III. Sensitivity Analysis Results for the Cumulative Net Benefit (NB) of the Actual Vaccination Programs (in 1955 Net Present Value US$2002; Rounded to Three Significant Figures)*

Input*	Lower Bound	Best Estimate	Upper Bound	NB at Upper Bound ($ billions)	NB at Lower Bound ($ billions)	NB at Upper Bound − NB at Lower Bound ($ billions)
Inputs whose ranges represent variations in decisionmaker's or societies' preferences:						
Discount rate (%)	0	3	5	556	1,890	−1,340
Average willingness to pay to prevent one death due to paralytic polio (US$2002)	0	4,000,000	10,000,000	1,270	545	725
Average willingness to pay to prevent one paralytic polio case (US$2002)	250,000	892,417	1,500,000	1,090	571	514
Average compensation award paid to nine VAPP patients (excluding deaths) (US$2002)	1,000,000	1,416,535	2,000,000	1,080	664	411
Inputs whose ranges represent uncertainties:						
Average treatment cost per paralytic polio case (US$2002)	250,000	524,118	1,500,000	1,240	722	514
Case-fatality rate for paralytic polio (%)	10	15	25	960	773	187
Completeness of reporting (%)	80	96	100	838	821	16.8
Private/public sector vaccine price before 1977 (proportion)	1	4	4	835	842	−6.54
Administration cost per dose, routine immunization (>1964) (US$2002)	5	11.1	20	831	838	−6.44
Administration cost per dose, mass immunization (1955–1964) (US$2002)	1	1.91	11.1	830	836	−5.85
Publicly/total distributed doses before 1973* (%)	0	25	50	837	833	3.99
IPV wastage, mass immunization (1955–1964) (%)	10	16	25	836	834	1.81
OPV wastage, routine immunization (>1964) (%)	0	8	16	836	834	1.20
OPV wastage, mass immunization (1955–1964) (%)	10	16	25	836	835	1.19
Publicly/total distributed doses after 1993 (%)	40	50	60	835	835	0.59
IPV wastage, routine immunization (>1964) (%)	0	2	16	835	835	0.29
Inputs whose ranges represent model assumptions:						
Travel and opportunity cost per dose, mass immunization (1955–1964) (US$2002)	9	27.03	27.03	835	846	−10.4
Travel and opportunity cost per dose, routine immunization (>1964) (US$2002)	9	9.01	27.03	827	835	−7.74

*We did not include in our sensitivity analysis the ratio of total to paralytic cases before 1951 and the percent of average compensation that is attributable to treatment cost since both do not factor into the net benefit model.
IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; NB = net benefit of the actual polio vaccination programs 1955–2015; VAPP = vaccine-associated paralytic polio.

However, countries will face different tradeoffs since they vary significantly in their access to resources for disease control and prevention[61] and the world will also face different risks after eradication.[62]

We believe that our retrospective analysis provides an important perspective that current economic analyses frequently lack. Most notably, we see that attempts to estimate the cost-effectiveness

ratio prospectively at any single time point may fail to adequately consider the context of the investment made to date and the importance of population and other dynamics. Failing to account for the population immunity for OPV dramatically underestimates the benefits of the vaccine, and this should serve as a powerful example to cost-effectiveness analysts of the need to incorporate system dynamics concepts.[63] We suspect that contrasting the situation of malaria control and abandoned eradication efforts in Africa (presumably because the initial investments dropped the burden of disease sufficiently to make them no longer a priority) might provide important insights.[64–66] Given the significant investments required to complete eradication, policymakers and analysts must recognize the long-term benefits. Physicians must continue to play a critical role in helping patients appreciate the value of vaccines and disease prevention, particularly in a world in which most people may have little or no memory of the disease.[59]

We believe that the insights from this study remain robust over a range of possible alternative inputs, but we note several limitations. First, all of the issues related to modeling over time apply to this analysis, including preferences related to discounting and the selected rate, adjusting costs over time, and choices for the analytical time horizon. We followed the existing recommendations, but other choices would lead to different numbers. The dynamic disease model we use to predict cases also comes with limitations,[40] including the assumption of a closed system with a well-mixed population. In the case of polio vaccination globally, we also note that the use of OPV, which provides the tool to achieve eradication, causes not only VAPP cases but can also lead to outbreaks of circulating vaccine-derived poliovirus[67] and the eradication of all polio disease requires the cessation of OPV use.[68] We believe that analysts should very carefully evaluate the appropriateness of a cost-effectiveness ratio metric and the implications of zero in the denominator. We faced significant challenges in obtaining data on costs and vaccination rates, particularly further back in time, and we hope that examples like this one will motivate public health agencies and analysts to create and maintain databases that will provide good information for future efforts. Finally, valuation remains a challenge. We relied on willingness to pay estimates, but they may reflect a very limited understanding of the true economic value of vaccines. We did not include an extra cost in our assessments for willingness to accept an injection in our comparisons between IPV and OPV, and we only explored the benefits of reduced injections in the context of switching to a combination vaccine. Moreover, we did not include costs associated with minor adverse events due to injections, although Lieu *et al*.[30] estimated this cost at more than US$2002 7 per vaccination visit.

Although polio no longer ranks highly in the context of its national or global burden of disease, protecting children's health and the national and international investments in polio control and eradication will continue to require some resources. Cost-effectiveness analyses should consider the historical context when making comparisons between disease control programs and recognize that the sunk costs made in prior investments may represent an important consideration in the context of a transmissible disease. Stated differently, path dependence may represent an important and relevant concern in the context of managing diseases in different stages. With respect to vaccines used for eradication, we should expect the cost-effectiveness ratios of the vaccine to change over time, presumably moving from a cost-saving or relatively low cost-effectiveness ratio toward infinity as the denominator approaches zero due to elimination of the disease. This analysis emphasizes the need for a dynamic perspective in the context of economic modeling and demonstrates the impact of failing to adequately account for time.

5. CONCLUSIONS

Retrospectively, the U.S. investment in polio vaccination represents a highly valuable, cost-saving public health program. Observed changes in the cost-effectiveness ratio estimates over time suggest the need for living economic models for interventions that appropriately change with time.

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APPENDIX

We calculate the total costs for immunization in a given year as a function of the prices and amounts of private and public vaccine doses distributed j as

$$C_j = vpr_j \times ndpr_j + vpu_j \times ndpu_j + nvc_j \times (ndpr_j + ndpu_j)(1 - wj) - \left(pp_j^0 - pp_j\right) \times (1 - fr) \times Ctreat, \quad \text{(A1)}$$

where j = years, starting with the starting year of the policy under consideration and ending at the end of the time horizon, vpr_j = the vaccine price in the private sector, vpu_j = the vaccine price in the public sector, $ndpr_j$ = the number of doses distributed in the private sector, $ndpu_j$ = the number of doses distributed in the public sector, nvc_j = the total non-vaccine costs per administered dose (administration, travel, and opportunity costs), w_j = the wastage, i.e., (doses distributed-doses administered)/doses distributed, pp_j^0 = the number of paralytic polio cases with the comparator intervention, pp_j = the number of paralytic polio cases with the immunization intervention, fr = the fatality rate per paralytic case, and $Ctreat$ = the average treatment cost per surviving paralytic polio case.

The number of paralytic cases prevented gives the effectiveness, or $E_j = pp_j^0 - pp_j$. In the cost-effectiveness framework, we express the health outcomes in terms of paralytic cases prevented, using the following formula for the cost-effectiveness ratio CE:

$$CE = \frac{\sum_{j=T_0}^{T_{end}} C_j/(1+d)^{(j-T_0)}}{\sum_{j=T_0}^{T_{end}} E_j/(1+d)^{(j-T_0)}}, \quad \text{(A2)}$$

where d = the discount rate, T_0 = the year of the policy decision, T_{end} = the last year of the analytical time horizon, and $\sum$ denotes summation over years. In the net benefit framework, we express the health outcomes in monetary terms using the willingness to pay to prevent one surviving case of paralytic polio ($WTPP$) and the willingness to pay to prevent one death due to paralytic polio ($WTPD$), such that the formula for the net benefit in net present value for the starting year, T_0, equals

$$NB = \sum_{j=T_0}^{T_{end}} (WTPP \times E_j \times (1 - fr) + WTPD \times E_j \times fr - C_j)/(1+d)^{j-T_0}. \quad \text{(A3)}$$

Table A1. Specific Inputs to the Dynamic Model for Poliovirus Transmission in the United States (for explanation of inputs see Tebbens *et al.*[40])

Inputs to the Transmission Model [unit]	Value	Source
Waning rate* (1/year)	0.5	Judgment
Average ratio of paralytic polio cases per infection for fully susceptibles (proportion)	1/200	(Ref. 40, table 3)
Secondary OPV infection rate for children under age 5, due to mass OPV immunization (1962–1964) (1/year)	0.25	Judgment
Secondary OPV infection rate for last age group, as a proportion of the rate for children under 5 (proportion)	0.3	(Ref. 40, table 1)
Average R_0	6	(Ref. 40, table 3), (high estimate)
Seasonal peak in R_0	7.5	Judgment
Seasonal through in R_0	4.5	Judgment
Peak day of seasonal R_0 (date)	July 31st	Judgment
Take rate for 3 IPV (Salk) doses (%)	82	(Ref. 79)
Take rate for 3 OPV doses (monovalent or trivalent) (%)	95	(Ref. 40, table 3, Ref. 80, table 3)
Take rate for 3 enhanced-potency IPV doses (%)	99	(Ref. 40, table 3)

*This input represents the proportions of "removeds" (recently infected with wild poliovirus) and "partially infectibles group 1" (recently infected with the OPV virus) that get transferred into "partially infectible group 3" (historically OPV or wild poliovirus-infected) per year.
IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; R_0 = basic reproductive number.

We modified the existing dynamic polio outbreak model[40] in several ways. Table A1 summarizes inputs for the transmission model. We also used the generic model inputs of the dynamic model paper (Reference 40, Table 1), with the exception that given our uncertainty about the exact dates of immunization and the negligible effect of the incubation period of 10 days when integrating over long time periods, we excluded these inputs. Substantial uncertainty and variability in the basic reproductive number (R_0) exist.[72,73] Consistent with the high estimate for high-income countries in the original outbreak model (Reference 40, Table 3), we assumed an average R_0 of 6, although the actual input for R_0 to the model captures seasonality and uses a periodic function that peaks each July 31 with a maximum value of 7.5 and a minimum value of 4.5. The much longer time horizon that we consider here motivated us to include the changing population size and include an effect of waning immunity.

Table A2. Demographic Inputs to the Dynamic Model; the Actual Inputs to the Dynamic Model are Linear Interpolating Functions Between Given Years.

Year	U.S. Population (×1,000)*	Birth Rate†	Mortality Rates by Age Group (deaths per 1,000 people per year)‡										
			0	1–4	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75–84	>85
1945	139,928	0.0204	42.50	2.00	0.90	1.90	2.70	4.60	9.60	20.50	42.60	98.40	209.60
1948	146,631	0.0249	35.70	1.60	0.70	1.40	2.00	3.90	9.00	19.70	41.40	95.10	213.20
1950	151,684	0.0241	33.00	1.40	0.60	1.30	1.80	3.60	8.50	19.00	41.00	93.30	202.00
1955	165,275	0.0250	28.50	1.10	0.50	1.10	1.50	3.10	7.50	17.30	37.90	89.00	179.30
1960	180,671	0.0237	27.00	1.10	0.50	1.10	1.50	3.00	7.60	17.40	38.20	87.50	198.60
1965	194,303	0.0194	24.10	0.90	0.40	1.10	1.50	3.10	7.40	16.90	37.90	81.90	202.00
1970	204,879	0.0184	21.40	0.80	0.40	1.30	1.60	3.10	7.30	16.60	35.80	80.00	163.40
1980	227,726	0.0160	12.89	0.64	0.31	1.15	1.35	2.28	5.84	58.20	29.95	66.93	159.79
1990	249,973	0.0166	9.71	0.52	0.29	1.47	2.04	3.10	6.10	15.53	34.92	78.89	180.57
1998	270,299	0.0144	7.55	0.36	0.18	0.46	0.62	1.17	3.09	8.23	19.91	48.83	142.74
2015	312,268	0.0143	8.53	0.36	0.18	0.46	0.62	1.17	3.09	8.23	19.91	48.83	142.74
2050	403,687	0.0140	8.53	0.36	0.18	0.46	0.62	1.17	3.09	8.23	19.91	48.83	142.74
2100	570,954	0.0133	8.53	0.36	0.18	0.46	0.62	1.17	3.09	8.23	19.91	48.83	142.74
Age breakdown in 1948 ($\times 10^6$)§			3.65	11.27	23.09	22.87	23.49	20.79	17.11	12.82	7.95	2.30	1.29

*Population size in thousands on July 1 from the U.S. Bureau of the Census (1975) (Ref. 74, p. 10) for 1948–1970, the U.S. Census Bureau (2000) (Ref. 76, p. 7) for 1980, 1990, and 1998, and the U.S. Census Bureau (2002)[36] for projections.
†Births per year per 1,000 population from the U.S. Bureau of the Census (1975) (Ref. 74, p. 49) for 1948–1970, the U.S. Census Bureau (2000) (Ref. 76, p. 65) for 1980, 1990, and 1998, and the U.S. Census Bureau (2002)[36] for projections.
‡Number of deaths per year per 1,000 population from the U.S. Bureau of the Census (1975) (Ref. 74, p. 60) for 1948–1970, the U.S. Census Bureau (2000) (Ref. 76, p. 86) combined with sex ratios (Ref. 75, p. 15) for 1980, 1990, and 1998. Lacking age-specific mortality rate projections, we assume they remain constant after 1998.
§Data from the U.S. Bureau of the Census (1975) (Ref. 74, p. 10) combined with UN Population Division's 1950 age breakdown[81] for last age groups. Estimate for first age groups equals birth rate times population in 1948, which we subtracted from total population under <5 to obtain the estimate for the second age group. For model age groups that were narrower than the age groups in this table, we divided the estimates by the number of model age groups included in the estimate (e.g., we estimated the number children aged 5–9 at 23.09/2 = 11.54 million).

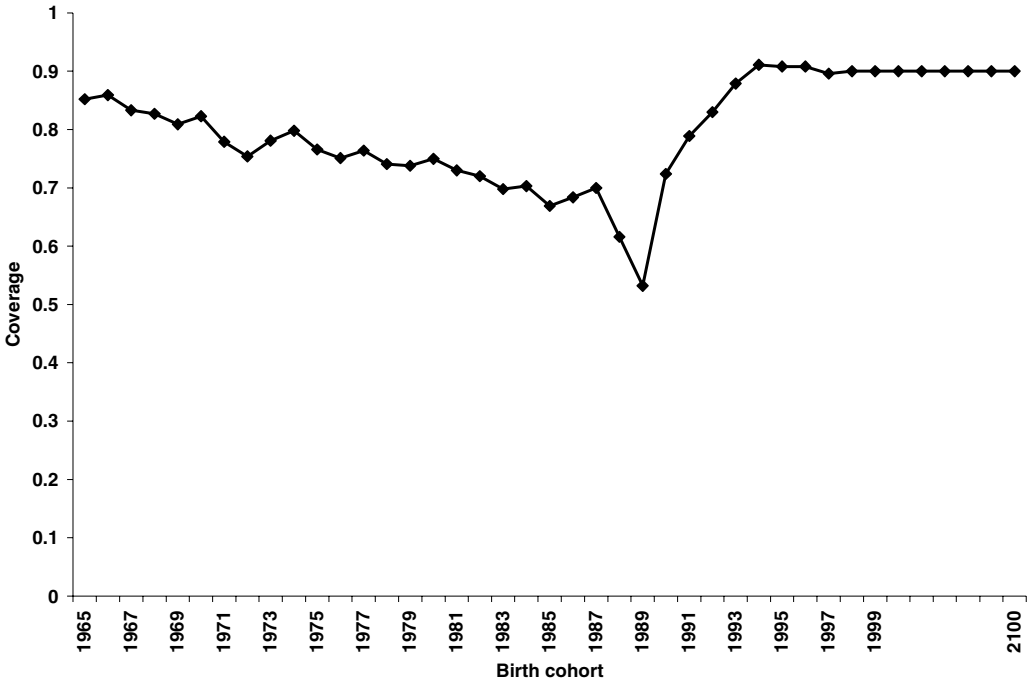
We included waning immunity by assuming that naturally immunes ("removeds") and recent OPV recipients ("partially infectible group 1") transfer into the group of historic OPV/naturally immunes ("partially infectible group 2") at a rate of 0.5 per year (i.e., corresponding to an average duration of stay of 2 years in group 1).

The model also incorporates population data over time (birth rates, age-dependent mortality rates, and total population size) and the breakdown of the population by age groups starting in 1948, the assumed starting year of the transmission model (Table A2).[36,74–76] We derived age-dependent vaccination rates for the mass immunization era from coverage surveys performed at 11 points of time between August 1957 and January 1965 (Table A3).[53,54] Differing from the original model for outbreaks,[40] these rates represent the proportion of an age group receiving a third dose (or more) per year, and consequently we incorporate three-dose take rates in the immunization response functions instead of single-dose take rates. The nature of the mass immunization campaigns stretching over many years also eliminates the need to incorporate a decay in secondary OPV exposure like the outbreak model used in the context of a pulse response.[40] Instead, we modeled a constant rate of 0.25 per year for secondary OPV exposure during mass immunization.

Table A3. Vaccination Rates* per Age Group per Year

Year	Age Group				
	0	1–4	5–14	15–19	20+ years
1955	0.024	0.336	0.406	0.167	0.05
1956	0.024	0.336	0.406	0.167	0.05
1957	0.024	0.392	0.466	0.242	0.05
1958	0.024	0.518	0.475	0.280	0.05
1959	0.093	0.650	0.344	0.163	0.05
1960	0.205	0.670	0.342	0.171	0.05
1961	0.231	0.417	0.227	0.123	0.1
1962	0.25	0.260	0.452	0.319	0.1
1963	0.25	0.351	0.402	0.366	0.1
1964	0.25	0.143	0.163	0.138	0.1

*Vaccination rates represent the proportion of the age group receiving a third dose of Salk IPV per year during 1955–1961, or a third dose of monovalent or trivalent OPV during 1962–1964.
Notes: Based on Sirken (1962)[54] and Morris *et al*. (1967).[53]



Notes: Based on Simpson *et al*. (2001),[77] Zell *et al*. (1994),[78] and unpublished data (Phil Smith; with personal correspondence). The U.S. Immunization Survey estimates (cohorts 1965–1983) adjusted for underestimation (15% added), cohorts 1986 and 1988 estimated using linear interpolation between available estimates.
*Proportion of birth cohort covered with three or more doses of OPV during 1965–1996, three or more doses of either OPV or IPV during 1997–1999, and three or more doses of IPV during 2000 and beyond.
IPV = inactivated poliovirus vaccine (enhanced-potency); OPV = oral poliovirus vaccine (trivalent).

Fig. A1. Routine immunization coverage* in the United States.

The transmission model includes vaccination coverage estimates for the routine immunization era derived from a review by Simpson *et al*.[77] Given the evidence that the U.S. Immunization Surveys probably significantly underestimate the true coverage,[77] we added 15% to each estimate from that survey. For years lacking estimates in the review by Simpson *et al*.,[77] we derived estimates from a published retrospective survey[78] and unpublished CDC data (Phil Smith; with personal correspondence), and linearly interpolated to obtain estimates for remaining missing years according to Fig. A1.

Finally, we derived a smooth initial population immunity profile (i.e., numbers of fully susceptibles, latents, infecteds, removeds, partially infectibles, latent partially infectibles, and reinfected partially infectibles) that corresponds to an equilibrium state with an average R_0 of 6 and a waning rate of 0.5.

In addition to the sensitivity analyses described in the text, we also varied the assumption regarding the future (public and private sector) OPV prices for the 1997 CE ratio of OPV indefinitely versus IPV indefinitely. While the base case assumption that the OPV price remains constant at the 1999 quote yielded a CE ratio of US$2002 15.6 million per case (1997 net present value; Table II), calculating the price based on the latest IPV quotes and the average ratio of OPV price to IPV price during 1997–1999 (i.e., 0.44 for the public sector and 0.71 in the private sector) dropped the CE ratio to US$2002 11.3 million per case (1997 net present value). Furthermore, this outcome proved sensitive to the future VAPP rate, with the lower end rate of two cases per million births resulting in a CE ratio of US$2002 15.3 million per case (1997 net present value) and the upper end of 2.5 cases per million births yielding a CE ratio of US$2002 12.2 million per case (1997 net present value).

Finally, we explored several assumptions regarding the basic reproductive number, R_0, which impact the result of the dynamic submodel used for this analysis.[40] For the base case, we assumed a constant R_0 over the years (seasonal variations notwithstanding) of 6, representing a relatively high estimate among a range of available estimates in the United States before 1955.[72,73] When we instead assumed a constant R_0 of 3, the cumulative net benefit of the

actual programs decreased to US$2002 694 billion (1955 net present value). Given that we also calculated the initial population immunity profile also based on the assumption that R_0 equals 3 (effectively starting the model with more susceptibles), the impact of lowering R_0 remains limited. Alternatively, one may believe that R_0 decreased over the years due to improvement in hygiene and sanitation. When we assumed a linear decrease in R_0 from 6 in 1948 to 3 in 2000, we obtained an even lower net benefit for the actual program (due to fewer prevented cases) of US$2002 625 billion (1955 net present value).

The scenario for R_0 also impacts the results for the hypothetical policy of *IPV indefinitely* in 1955 (as well as 1961). With R_0 constant at 6, we obtained a cumulative net benefit of US$2002 579 billion (1955 net present value) for the policy of *IPV indefinitely* from 1955 forward, with many simulated cases still occurring annually for many years with exclusive IPV use. However, with a constant R_0 of 3, the cumulative net benefit increased to US$2002 625 billion (1955 net present value) due to many fewer simulated cases occurring with continued IPV (despite the fact the model also simulated fewer cases with *no program*). In contrast, the scenario where R_0 decreases from 6 in 1948 to 3 in 2000 yielded a net benefit of only US$2002 527 billion (1955 net present value) since this change reduced the simulated cases under *no program* more significantly than it decreased the number of cases with *IPV indefinitely*.

Table A4 shows the impact of different time horizons and assumptions about the last year IPV use on the net benefit of the actual programs since 1955 versus no program.

Table A4. Impact of Different Time Horizons and Assumptions about the Last Year of Inactivated Poliovirus Vaccine (IPV) Use on the Net Benefit of the Actual Programs Since 1955 Versus No Program

	Net Benefit in Billions US$2002 (1955 net present value)	
Time Horizon End (Year)	IPV Use Stops After 2015	IPV Use Continues to Horizon End
2015	835	835
2025	890	889
2035	935	933
2045	971	968
2055	999	996
2065	1,021	1,018
2075	1,039	1,035
2085	1,053	1,049
2095	1,065	1,060
2099	1,068	1,064

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