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Economic analysis of the global polio eradication initiative

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ABSTRACT

The global polio eradication initiative (GPEI), which started in 1988, represents the single largest, internationally coordinated public health project to date. Completion remains within reach, with type 2 wild polioviruses apparently eradicated since 1999 and fewer than 2000 annual paralytic poliomyelitis cases of wild types 1 and 3 reported since then. This economic analysis of the GPEI reflects the status of the program as of February 2010, including full consideration of post-eradication policies. For the GPEI intervention, we consider the actual pre-eradication experience to date followed by two distinct potential future post-eradication vaccination policies. We estimate GPEI costs based on actual and projected expenditures and poliomyelitis incidence using reported numbers corrected for underreporting and model projections. For the comparator, which assumes only routine vaccination for polio historically and into the future (i.e., no GPEI), we estimate poliomyelitis incidence using a dynamic infection transmission model and costs based on numbers of vaccinated children. Cost-effectiveness ratios for the GPEI vs. only routine vaccination qualify as highly cost-effective based on standard criteria. We estimate incremental net benefits of the GPEI between 1988 and 2035 of approximately 40–50 billion dollars (2008 US dollars; 1988 net present values). Despite the high costs of achieving eradication in low-income countries, low-income countries account for approximately 85% of the total net benefits generated by the GPEI in the base case analysis. The total economic costs saved per prevented paralytic poliomyelitis case drive the incremental net benefits, which become positive even if we estimate the loss in productivity as a result of disability as below the recommended value of one year in average per-capita gross national income per disability-adjusted life year saved. Sensitivity analysis suggests that the finding of positive net benefits of the GPEI remains robust over a wide range of assumptions, and that consideration of the additional net benefits of externalities that occurred during polio campaigns to date, such as the mortality reduction associated with delivery of Vitamin A supplements, significantly increases the net benefits. This study finds a strong economic justification for the GPEI despite the rising costs of the initiative.

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1. Introduction

Following the achievement of smallpox eradication in 1980 [1], and heavily influenced by the substantial progress towards regional polio elimination in the Americas [2], the 41st World Health Assembly (WHA) in 1988 committed to "global eradication of poliomyelitis by the year 2000," [3] which led to the launch of the Global Polio Eradication Initiative (GPEI) – the single largest, internationally coordinated public health project to date. The WHA resolution focused on "elimination of the indigenous transmission of wild poliomyelitis viruses in ways which strengthen and sustain ... national immunization programmes." The WHA resolution recognized "that achievement of the goal will depend on the political will of countries and on the investment of adequate human and financial resources," [3] although "some delegates to the assembly in 1988 might not have made a truly informed decision on the launching of the initiative, since there had been no clear statement on resource requirements or strategies" [4, p. 913].

Consistent with the 1988 WHA resolution, we use the term "eradication" to mean contemporaneous interruption of the circulation of wild polioviruses (WPV) everywhere [5]. However we recognize that ending all poliomyelitis disease will ulti-

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mately depend on the subsequent successful containment of all live polioviruses, including attenuated OPV viruses, given the potential for vaccine-associated paralysis and the risk of outbreaks of circulating vaccine-derived polioviruses (cVDPVs) [6]. A 2008 WHA resolution recognized this formally by asking the WHO Director-General "to set, if and when appropriate, a date for the eventual cessation of use of oral poliomyelitis vaccine [. . .] in routine immunization programmes." [7]

With the eradication of type 2 WPV and interruption of types 1 and 3 WPV approaching, this study aims to evaluate the costs and benefits of the GPEI from a societal perspective between 1988 (T_{WHA}) and 2035 (T_{end}). The analysis includes prospective considerations because (1) efforts to interrupt the transmission of WPV continue, (2) post-eradication risk management policies will require resources into the future [6,8–10], and (3) the achievement of polio eradication will prevent future poliomyelitis cases from WPV and thus accrue long-term benefits.

Although several prior studies provide important economic support for polio eradication efforts [4,10–14], none of the existing studies specifically assessed the economics of the GPEI. One evaluation of the US historical and projected polio vaccination programs since 1955 reported $220 billion (2008 US dollars) in net benefits from the US polio vaccination efforts over time due to the prevented treatment costs alone [15], but no comparable analysis of global historical and projected polio vaccination programs exists. This study focuses on quantifying the costs and benefits of the GPEI, reflecting the most up-to-date status of the program and consideration of post-eradication risk management policies [6,16]. Although this study focuses only on the GPEI and does not quantify the global costs or benefits from all global historical investments in polio control and eradication, it provides important insights about the economics of the GPEI that may inform discussion and debate about future eradication initiatives.

2. Methods

Our analysis assumes feasibility of WPV types 1 and 3 eradication given sufficient global commitment, with interruption of WPV transmission by 2012 (T_{WPV}), and consideration of the impact of delays in eradication of WPVs out to 2015 [17]. We assume a 3-year period of continued OPV vaccination with periodic SIAs after T_{WPV}, with intense surveillance, containment, and preparation for the post-eradication era [18,19], followed by assumed globally coordinated cessation of OPV [7,20] (to reduce the risks associated with continued OPV use [21]) after certification of WPV eradication from all populations in 2016 ($T_{post} = T_{WPV} + 4$). We assume that SIAs during the 3 years after T_{WPV} will keep population immunity high, which will help to prevent cVDPV outbreaks prior to and after OPV cessation, but we also consider the impacts of cessation of SIAs prior to OPV cessation. Given continuing development of post-eradication vaccination policies, we examine the *comparator* (i.e., *Routine vaccination*) against the *intervention* (i.e., the *GPEI*) with two distinct potential future post-eradication vaccination policies representing the spectrum of expected costs and cases [6]: (1) *GPEI then universal IPV* and (2) *GPEI then no routine vaccination*. Universal IPV means that all countries considered in the model (and currently using OPV for routine vaccination) will switch to a policy of routine IPV vaccination, while no routine vaccination means that the countries in the model would stop using OPV and not begin using IPV. For both post-eradication policies, the model includes the risk of cVDPVs and other outbreaks, and assumes that mOPVs from a stockpile successfully control any outbreaks. Table 1

summarizes the model inputs and the technical appendix provides details about the model (see Appendix A1).

2.1. Scope

We identified the countries impacted by the GPEI and stratified these countries by income levels (see Appendix A2). We started with all 194 countries for which we found detailed demographic data [22] and 2002 World Bank income level classifications [23]. We excluded all 32 countries in the WHO Region of the Americas, because we assumed that the GPEI did not play a major role in the elimination of WPVs from the Western Hemisphere (i.e., the Pan-American Health Organization committed to polio eradication prior to and independent of the GPEI). We also excluded all 44 remaining high-income countries and 13 upper middle-income countries that never received funds from the GPEI [24], because we assumed that domestic efforts to eliminate polio in these countries did not change in response to the WHA decision in 1988 to globally eradicate polio. We further excluded the Occupied Palestinian Territory due to missing WHO/UNICEF immunization coverage estimates [25]. Thus, we assume that the GPEI directly impacted 104 countries that represented approximately 3.6 billion people in 1988 (70% of the global population) [22] and collectively reported approximately 34,000 paralytic poliomyelitis cases (i.e., 99% of the 1988 reported global burden) [26]. We assigned income level-specific inputs using the 2002 World Bank classification [23] consistent with prior work [6,9,16,20,27], which yielded 64 low-, 35 lower middle-, and 5 upper middle-income countries. To estimate economic outcomes (i.e., costs, cases, incremental cost-effectiveness ratios, incremental net benefits) for each income group (i.e., the aggregation over all countries within an income level), we estimate these for each country and then sum. To do so, we use a combination of information for individual countries (e.g., demographic data, coverage, external contributions to the GPEI, per-capita incomes, reported cases, surveillance indicators), income level-specific model inputs (infection transmission model inputs, routine vaccination unit costs), and economic outcomes (expected costs and cases after eradication over time) by income group from prior models [6,16]. Similar to our prior work, we stratified our analysis by World Bank income level because this level of stratification provided important insights relevant to interpretation of the global analysis. We emphasize that given our focus on characterizing the global economics of the GPEI, we did not find a need for further stratification, although countries differ within an income group and variability exists within an individual country.

2.2. Incidence estimation

Economic analysis requires characterization of the disease burden over time for the *Routine vaccination* comparator and the *GPEI then universal IPV* and *GPEI then no routine vaccination* intervention scenarios. While the GPEI may have contributed to changes in routine vaccination coverage in some of the 104 countries, we assume that the estimated polio routine vaccination coverage represents a good proxy for the comparator coverage. We estimate incidence for the comparator using WHO/UNICEF-estimated national coverage with 3 doses of OPV by age 1 year (POL3) for 1980–2008 [25,28] and a simplified dynamic infection transmission model for each country based on published poliovirus transmission models [10,27,29] to capture secondary OPV transmission and herd immunity (see Appendix A3).

For both intervention scenarios we rely on reported incidence figures [26,30] to estimate incidence between 1988 and 2009. However, we correct these estimates to account for the historical discrepancies between reported and estimated incidence and the improvement in surveillance sensitivity over time [31]. Assuming that our infection transmission model provides accurate incidence estimates, we use the ratio for total model-estimated cases to total reported cases in 1987 [26] of approximately 7:1 as a crude under-

Table 1
List of model inputs excluding those used in the infection transmission model (listed in Tables A5 and A6 of the appendix). All monetary amounts reported in 2008 US dollars ($).

Model input	Base case value [unit]	Interpretation	Source(s)
Analytical framework			
T_{WHA}	1988	Beginning of analytical time horizon	Framing assumption
T_{WPV}	2012	Year wild poliovirus interruption achieved	Framing assumption
T_{post}	T_{WPV} + 4 = 2016	Year of OPV cessation and implementation of globally synchronized post-eradication policies	Framing assumption
T_{end}	T_{post} + 19 = 2035	Last year of analytical time horizon	Framing assumption
Discount rate	3 [%]	Input reflecting preference about future financial and health costs from a 1988 perspective	WHO and Gold et al. [34,35]
Population, 1980 to T_{end}	Time series [people]	Number of people included in the model, by country	UN (medium variants) [22]
Disease burden			
Incidence, routine vaccination, 1980 to T_{end}	Time series [cases/year]	Estimated annual paralytic poliomyelitis cases (incl. VAPP), by income group	Infection transmission model (see Appendix A3)
Reported incidence, GPEI, 1980–2009	Time series [cases/year]	Confirmed annual paralytic poliomyelitis cases, by country	WHO incidence series for 1980–1995 [26], AFP data for 1996–2008 [30]
Non-polio AFP rates, 1996–2009 (NP_{AFP})	Time series [cases/100,000 children]	Reported annual AFP cases per 100,000 children younger than 15 years of age, by country	AFP data [30]
Specimen collection rates 1996–2009 (SC_{AFP})	Time series [%]	Percentage of AFP cases with adequate specimens collected, by country	AFP data [30]
Underreporting factor, 1980–1995	7 [dmnl]	Model-estimated divided by reported paralytic poliomyelitis cases in 1987[a]	Calibration of reported data to model
AFP indicator-based underreporting factor, 1996–2009		Post-1996 correction factor (assume pre-1996 factors if $NP_{AFP} \leq 1$, or $SC_{AFP} \leq 60$, or data unavailable)	Judgment
- Medium performance	2 [dmnl]	Apply if $1 < NP_{AFP} < 2$ *or* $60 < SC_{AFP} < 80$	
- High performance	1.11 [dmnl]	Apply if $NP_{AFP} \geq 2$ *and* $SC_{AFP} \geq 80$	
Incidence, 2010 to T_{WPV}		Estimated annual paralytic poliomyelitis cases (excl. VAPP) until interruption of WPV (all cases assumed to occur in low-income countries)	Judgment
- 2010	1500 [cases/year]		
- 2011	1000 [cases/year]		
- 2012	500 [cases/year]		
Incidence, T_{WPV} + 1 to $T_{post} - 1$	Time series [cases/(person × year)]	Estimated annual paralytic poliomyelitis cases (incl. VAPP) per person from post-eradication model with continued OPV, by income level[b]	Thompson et al. [6] and Duintjer Tebbens et al. [16]
Incidence, T_{post} to T_{end}	Time series [cases/(person × year)]	Estimated annual paralytic poliomyelitis cases (incl. VAPP) per person from post-eradication model, by policy permutation and income level[c]	Thompson et al. [6] and Duintjer Tebbens et al. [16]
VAPP rate, GPEI		Average number of VAPP cases per birth assuming routine vaccination and regular SIAs	Duintjer Tebbens et al. [20]
- LOW	$2.6/10^6$ [cases/person]		
- LMI and UMI	$2.2/10^6$ [cases/person]		
Costs			
External funds of GPEI, 1988–2008	Time series [$/year]	External financial expenditures of the GPEI	GPEI external funds database [24]
Estimated external funds of GPEI, 2009 to T_{WPV}	Time series [$/year]	Projected external financial resource requirements of the GPEI for 2009-2012	WHO data [37,38]
Fully OPV-vaccinated infants, 1980 to T_{end}	Time series [people]	Number of newborns receiving 3 doses of OPV, by income group and scenario	Infection transmission model (see Appendix A3)

Table 1 (*Continued*)

Model input	Base case value [unit]	Interpretation	Source(s)
Ratio internal to external funds, T_{WHA} to T_{WPV}	1 [dmnl]	Factor to include national contributions from countries receiving external GPEI funds	Assumption based on Aylward et al. [4]
Costs, $T_{WPV}+1$ to $T_{post}-1$	Time series [$/(person × year)]	Estimated annual costs per person from post-eradication model with continued OPV, by income level[b]	Thompson et al. [6] and Duintjer Tebbens et al. [16]
Post-eradication costs, T_{post} to T_{end}	Time series [$/(person × year)]	Estimated annual costs per person from post-eradication model (excl. treatment costs), by policy permutation and income level[c]	Thompson et al. [6] and Duintjer Tebbens et al. [16]
OPV price, T_{WHA} to T_{WPV}		Average price of OPV per dose	Duintjer Tebbens et al. [9]
- LOW and LMI	0.11 [$/dose]		
- UMI	0.12 [$/dose]		
IPV price, T_{post} to T_{end}		Notation indicates (mode, lower bound, upper bound) of triangular distribution for price in $ per dose	Duintjer Tebbens et al. [9]
- LOW	(1.2, 0.60, 2.4)		
- LMI	(2.09, 0.60, 3.59)		
- UMI	(3.0, 1.2, 6.0)		
OPV doses administered (all income groups)	3 [doses/infant]	Average number of OPV doses received per fully vaccinated infant	Duintjer Tebbens et al. [9]
Non-vaccine costs, T_{WHA} to T_{WPV}		Average non-vaccine costs per fully OPV-vaccinated child, including for personnel, training, transportation and cold chain, building and equipment	Duintjer Tebbens et al. [9]
- LOW&LMI	2.40 [$/infant]		
- UMI	6.34 [$/infant]		
Wastage		Percent of distributed doses not administered	Duintjer Tebbens et al. [9]
- LOW&LMI	20 [%]		
- UMI	15 [%]		
Assumed treatment costs per case		Best-estimate average direct treatment costs associated with one paralytic poliomyelitis case (average assumed to account for fatal cases or cases receiving no treatment)	Thompson et al. [6] and Duintjer Tebbens et al. [16]
- LOW	600 [$/case]		
- LMI	6000 [$/case]		
- UMI	60,000 [$/case]		
DALYs per case		Average disability-adjusted life-years associated with one paralytic poliomyelitis case, with no age-weighting	Same approach as prior work [6,16,48] with most recent available life-expectancy data (2005, 2006, or 2007) [71] for 104 modeled countries, by income group
- LOW	13 [DALY/case]		
- LMI	14 [DALY/case]		
- UMI	14 [DALY/case]		
Assumed societal willingness-to-pay per case prevented		Best-estimate societal willingness-to-pay associated with one paralytic poliomyelitis case based on average per-capita GNI per DALY averted	Same approach as prior work [6,16] with most recent available (2005, 2006, or 2007) GNI data [71] for 104 modeled countries
- LOW	12,000 [$/case]		
- LMI	44,000 [$/case]		
- UMI	110,000 [$/case]		

Acronyms: AFP = acute flaccid paralysis; DALY = disability-adjusted life-year; GNI = gross national income; GPEI = global polio eradication initiative; IPV = inactivated poliovirus vaccine; LOW = low-income; LMI = lower middle-income; OPV = oral poliovirus vaccine; SIA = supplemental immunization activity; VAPP = vaccine-associated paralytic polio; WHO = World Health Organization; UMI = upper middle-income; UN = United Nations.

[a] However, we assumed 90% completeness of reporting (i.e., underreporting factor of 1.1) for the reported incidence in China during 1989–1992 and Oman during 1988 given large, actively investigated outbreaks.

[b] Based on post-eradication model results during first 3 years after "T_0," (=T_{post} in the article) assuming continued OPV with periodic SIAs, AFP surveillance, a 70-day delay from outbreak detection to first response round, maximum population immunity at T_0, and containment maintained [6,16].

[c] Policy permutations assume either IPV or no routine, passive surveillance, a 70-day delay from outbreak detection to first response round, maximum population immunity at T_0, and containment maintained [6,16].

reporting correction factor applied through 1995 (see Appendix A3). The approximately 14% completeness of reporting implied by this factor remains somewhat higher than estimates of approximately 10% completeness of reporting derived from surveys of lameness performed in developing countries in the 1980s [32], which leads the model to give conservative estimates for the number of cases prevented by the GPEI (i.e., the intervention scenarios) due to an assumed relatively low incidence at the outset of the program in 1988. Moreover, we conservatively assume that no improvements in underreporting occurred in the GPEI through 1995. The acute flaccid paralysis (AFP) surveillance system provides disaggregated (national) data since 1996 on the numbers of clinically confirmed and WPV/virologically confirmed poliomyelitis cases and indicators of surveillance quality (i.e., non-polio AFP rates, percent of AFP cases with adequate specimens) [30]. We used its data from 1996 to 2009 to estimate incidences of WPV-associated poliomyelitis cases for the interventions using underreporting factors that depend on national surveillance indicators (Table 1).

We assume a gradual decline in annual incidence for the intervention between 2010 and 2012 (i.e., T_{WPV}) (Table 1). For the 3 years before implementation of long-term post-eradication policies (2013–2015), we use estimated numbers of cases (mostly due to VDPV outbreaks) using our post-eradication model results [6,16], adjusted for differences in geographical and temporal scope (see Appendix A4). To estimate the incidence of vaccine-associated paralytic poliomyelitis (VAPP) for the comparator, we multiply the numbers of OPV infections estimated by the infection transmission model by the average VAPP rates per recipient and contact OPV infection based on prior work (see Appendix A3) [20]. For

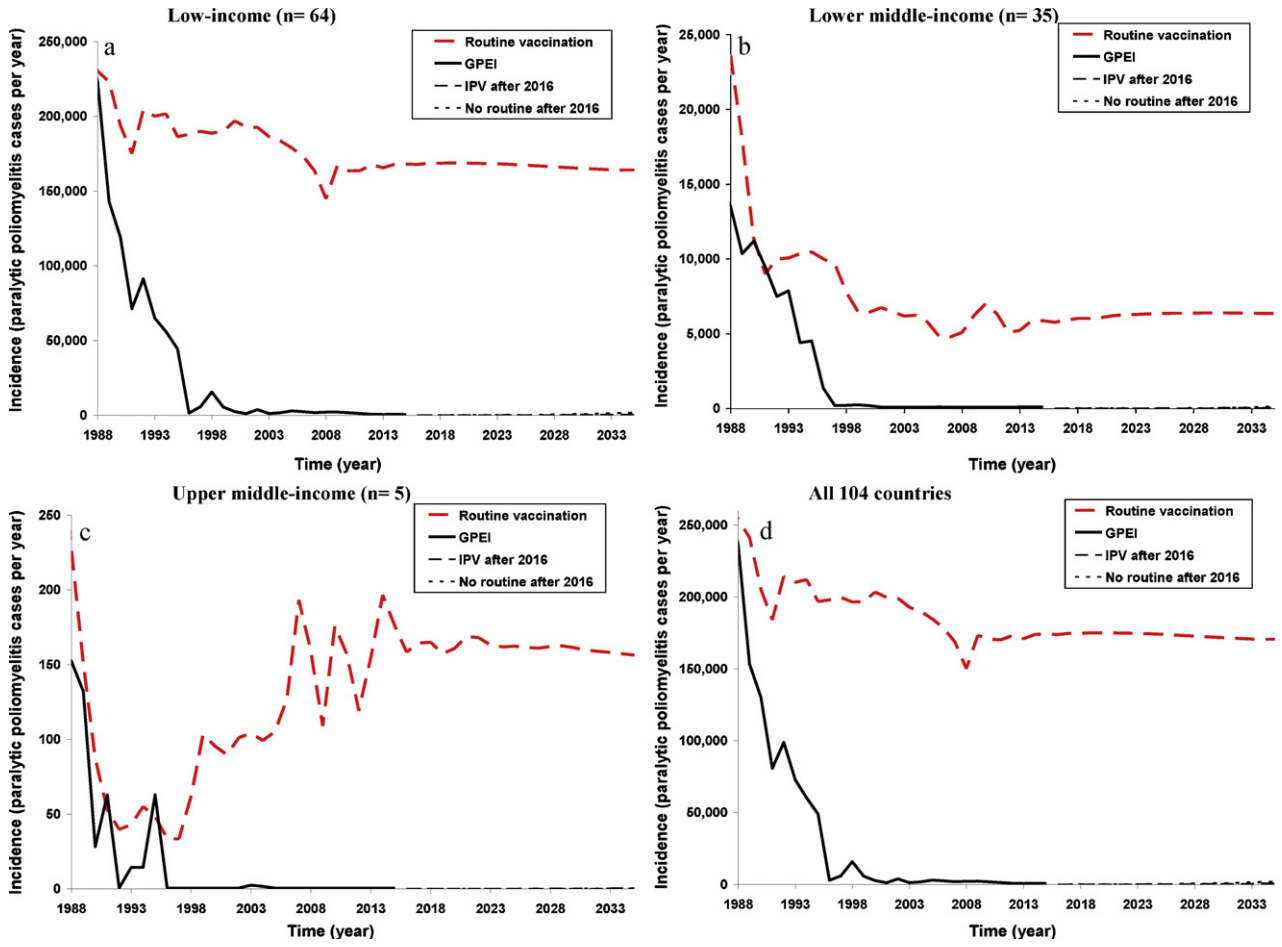

Fig. 1. Estimated annual incidence (not discounted) for the different scenarios in the model, broken down by income groups (panels a–c) and aggregated over all income groups (panel d) (NOTE: the scales on the *y*-axes differ across panels and the curves for *IPV after 2016* and *No routine after 2016* are very close to the x-axes given the low number of expected cases compared to the *Routine vaccination* curve; GPEI = global polio eradication initiative; IPV = inactivated poliovirus vaccine).

the intervention, we do not use a transmission model to estimate OPV infections, and consequently we estimate VAPP cases based on births and the rate of VAPP per birth for routine vaccination and supplemental immunization activities (SIAs) from prior work (Table 1) [20]. We assume that any VDPVs for the comparator would either replace or be displaced by WPV, implying that the incidence from the infection transmission model includes all cases due to VDPVs. For the interventions, we include 392 reported cases associated with VDPVs during 2000–2009 in the 104 modeled countries [33], and we correct for underreporting of VDPVs using the same assumptions as for WPV, assuming that this captures all immunodeficient and ambiguous VDPVs as well. For the intervention scenarios, the incidence estimates after OPV cessation T_{post} also include paralytic poliomyelitis cases from all forms of live polioviruses (i.e., WPV, VDPVs, and VAPP) [6,16].

2.3. Cost estimation

Following guidelines for cost-effectiveness analyses [34,35], we discount costs and cases back to 1988 net present values using a 3% discount rate for the base case. We express all monetary amounts in year 2008 US dollars (US dollars ($)), converted using the US Consumer Price Index [36] and publicly available market exchange rates for non-US currencies. For the comparator, we estimate costs using the number of covered children and inputs from a prior cost study [9] (see Table 1 and Appendix A5). For the intervention, we estimate actual costs through the end of 2008 by extracting these from the GPEI external funds database [24]. The estimated costs totaled approximately $6.5 billion (converted to 2008 US dollars) between 1988 and 2008 for the 104 modeled countries. We allocated multi-country funds to each of the three income groups in the model on the basis of relative numbers of children in each income group (see Appendix A5). We used the GPEI's Financial Resource Requirements as of June 2009 [37] for 2009 and as of January 2010 [38] to estimate 2010–2012 costs and we allocated all global programmatic costs to income groups following the same approach used to allocate the multi-country historic costs. Given that recipient countries also contributed substantial volunteer time, in-kind contributions and financial resources, we attempted to obtain cost data from individual countries by contacting Health Ministries, but we learned that data to support better estimates of national costs do not exist. Consequently, we assumed an average ratio of 1:1 for internal to external contributions for all income levels and that this ratio captures the costs of any external in-kind contributions made to the GPEI. This implies total costs of the GPEI equal to approximately twice the amount of external contributions, and given the uncertainty about this assumption we ran sensitivity analyses to explore a wide range [4,9].

We assume that countries incurred the costs associated with routine vaccination programs independent from the GPEI, and consequently the costs of the GPEI are incremental to the comparator. Consistent with the incidence assumptions, we estimate the costs during the 3 years before T_{post} from annual expected income-level dependent costs from our post-eradication model, including AFP surveillance costs per child and global costs for the global polio lab-

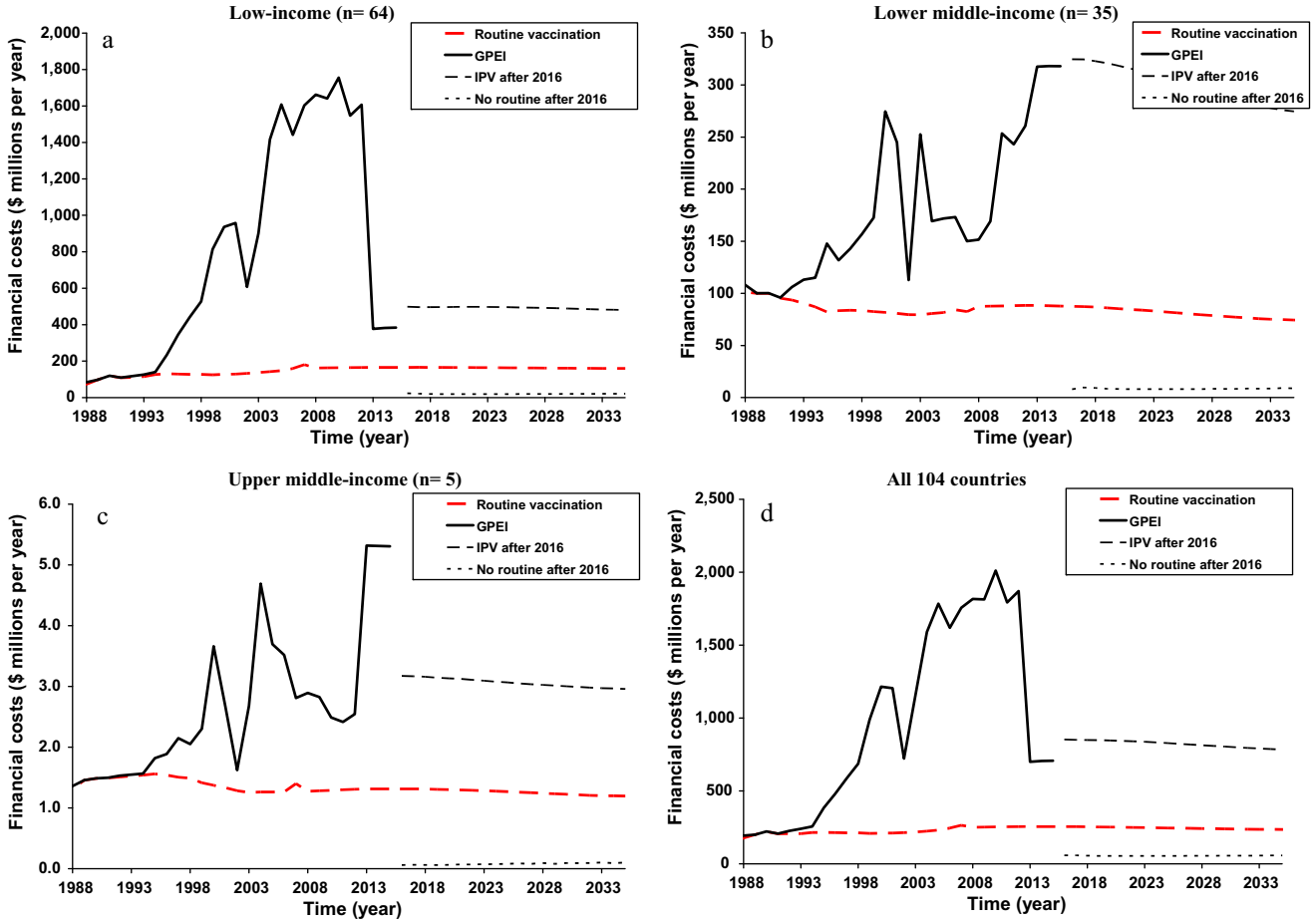

Fig. 2. Annual financial cost estimates (not discounted; reported in 2008 US dollars ($))) excluding treatment costs for the different scenarios in the model by income group (panels a–c) and aggregated (panel d) (*note*: the scales on the *y*-axes differ across panels; in the lower middle-income group, costs increase in the transition period from 2013 to 2016 because of the assumption of periodic SIAs and use of different methodologies (GPEI expenditures vs. extrapolated post-eradication model results [6,16]) before and after 2013) GPEI = global polio eradication initiative; IPV = inactivated poliovirus vaccine).

oratory network and containment [6,9,16]. From T_{post} forward, we use adjusted cost estimates from our post-eradication model [6,16], (see Appendix A4) including global programmatic costs associated with maintaining the global polio laboratory network and high levels of containment for laboratories and vaccine production sites [9,39,40], allocated to income groups as multi-country funds. We assume that external GPEI resources up to T_{WPV} include the costs of establishing a post-eradication era vaccine stockpile [17], although we note that challenges remain with respect to optimizing the stockpile [41].

The incremental cost-effectiveness ratios include the savings of treatment costs from prevented paralytic poliomyelitis cases. We used our prior estimates for income-level dependent treatment costs [6,16], consistent with the range of other estimates from the literature (see Appendix A5) [11,12,14,42–45], although we emphasize that to our knowledge no comprehensive study quantifies the costs of paralytic polio treatment in developing countries. To compute incremental net benefits, we must also include the societal willingness-to-pay to prevent economic loss due to lost productivity and suffering from permanent paralysis (i.e., the total amount of money that a given society or country would pay to prevent one case of paralytic polio and all of the associated societal impacts). Current limited data for valuation suggest important differences between countries and large uncertainty in the true values [6,11,12,14,16,42–45]. WHO recommends that "in the absence of data, analysts might use estimates of the gross national income (GNI) or GDP per capita to value lost time," [35, p. 25]. Consequently, we value each DALY saved as equal to one year of per capita income (see Table 1 and Appendix A5 for details and data used). Economists typically assume that this method conservatively estimates the real human capital costs associated with disability, with values up to three times the per capita income per DALY saved sometimes used to estimate the full economic benefits, including prevented suffering [35,46,47]. We used a range to capture our uncertainty about the valuation inputs with a lower bound, which assumed only the best-estimate treatment costs and half the best-estimate willingness-to-pay value for prevented cases, and an upper bound, which assumed the best-estimate treatment costs and doubled the best-estimate willingness-to-pay values.

2.4. Outcomes

We report incremental cost-effectiveness ratios in both $ per paralytic poliomyelitis case prevented and $ per DALY saved [6,16,48] and provide incremental cost-effectiveness ratios only by income group given the potential for misleading ratios when aggregated over different income groups [6]. We report the incremental net benefits in dollars and provide the incremental net benefits by income group and summed over all income groups to obtain the overall aggregate incremental net benefits for all countries in the model.

Table 2
Economic outcomes (in 2008 US dollars ($)) of main policy scenarios, aggregated over full time horizon 1988–2035 (using a 3% discount rate).

Intervention vs. comparator by income group(s)	GNI per capita [71][a] [$]	Incremental cost-effectiveness ratio		Incremental net benefits best estimate (range)[b] [$ billions]	Threshold[c]	
		[$ per paralytic case prevented]	[$ per DALY saved]		[$ per paralytic case prevented]	[$ per DALY saved]
GPEI then universal IPV vs. Routine vaccination						
Low-income	930	2700	210	37 (13–85)	3300	250
Lower middle-income	3200	14,000	1000	4.5 (1.2–11)	21,000	1500
Upper middle-income	8000	Cost and life saving	Cost and life saving	0.41 (0.27–0.70)	12,000	910
All 104 countries[d]				42 (15–96)		
GPEI then no routine vaccination vs. Routine vaccination						
Low-income	930	1900	140	40 (16–88)	2500	190
Lower middle-income	3200	1100	79	6.5 (3.1–13)	7700	560
Upper middle-income	8000	Cost and life saving	Cost and life saving	0.43 (0.29–0.72)	4800	350
All 104 countries[d]				47 (20–100)		

Acronyms: DALY = disability-adjusted life-year; GNI = gross national income; GPEI = global polio eradication initiative; IPV = inactivated poliovirus vaccine.

[a] GNI per capita averaged over the countries in each age group in the model based on the most recent available estimates (from 2005, 2006, or 2007, using the Atlas method [71]) exclude 3 of 64 low-income and 2 of 35 lower middle-income countries due to missing recent GNI estimates.

[b] Best estimates assume countries in each income group value a $ per DALY saved equal to the average GNI per capita, range reflects a lower bound that assumes the best-estimate treatment costs and half the best-estimate societal willingness-to-pay value for prevented cases and an upper bound that assumes the best-estimate treatment costs and doubled the best-estimate societal willingness-to-pay values (Table 1).

[c] Threshold total economic costs per case prevented (i.e., treatment cost and societal willingness-to-pay) and total economic cost per DALY saved for which the overall net benefits of the *GPEI* become positive compared to *Routine vaccination*.

[d] Incremental cost-effectiveness ratios not meaningful when aggregated over income groups [6].

Finally, although the base case characterizes the economics for the primary objective of eradication of WPV, the GPEI supported other interventions as part of some OPV campaigns (e.g., delivery of Vitamin A supplements or distribution of bed nets during NIDs) [49,50] and its laboratory network contributed to surveillance and laboratory capacity for other infectious diseases, especially measles and other vaccine-preventable diseases [4]. To demonstrate the potential economic importance of these types of positive externalities, we estimated the net benefits associated with reduced childhood mortality due to delivery of Vitamin A supplements during OPV campaigns to date [51] in a sensitivity analysis (see Appendix A6.1 for the methods used to estimate mortality reduction due to Vitamin A). We did not include sensitivity analyses for any effect (positive or negative) of the GPEI on overall routine vaccination coverage, because these remain poorly characterized [4,52–56]. We performed additional sensitivity analyses on the discount rate, ratio of internal to external contributions, assumptions about incidence in 1988, delay in achieving eradication, IPV prices, and assumed coverage levels for the *Routine vaccination* comparator (see Appendix A6.2 for details).

3. Results

Fig. 1 shows the estimated annual incidence of paralytic poliomyelitis cases from 1988 forward based on the reported numbers [26,30] corrected for underreporting. It also shows the model estimates for the comparator and for the future. For the comparator, our estimate of approximately 270,000 cases during 1987 is consistent with case number estimates from the late 1980s [31,57–61]. Over time, our model suggests a substantial decrease in global polio incidence as a result of routine vaccination alone, with the GPEI activities accounting for the additional reduction in incidence to the current low level. Overall, the GPEI prevents approximately 8 million total (undiscounted) paralytic poliomyelitis cases over the time horizon (4 million discounted cases, 1988 net present value). Most of the incidence occurs in the low-income group and very few cases occur in the upper middle-income group with its relatively small population and high coverage. Reconstructing polio incidence at the outset of the GPEI remains challenging due to poor surveillance and coverage data at the country level, and this leads to some notable differences between estimated and reported cases when we explore the numbers by income group (see Appendix A3). However, we tried many different approaches to calibrate the model and compare with reported numbers, and in the process we found that the assumption about the initial total incidence in 1987 for all 104 countries before the GPEI started dominates the results. Consequently, the sensitivity analysis shows the impact of a wide range values for this assumption.

Fig. 2 shows the estimated costs over time from 1988 forward for the comparator and the intervention, excluding costs of poliomyelitis cases. The prevention of paralytic cases in Fig. 1 comes at a large cost, particularly during the last phases of eradication. Countries that switch to IPV after T_{post} will incur higher annual costs than under the comparator, which assumes continued routine vaccination with OPV for the modeled countries in perpetuity. Discontinuing polio vaccinations altogether after global OPV cessation (T_{post}) leads to much lower costs than universal IPV with only marginally more expected cases despite a low probability of larger outbreaks long after cessation, although we emphasize the need to continue vaccination currently to achieve eradication [16]. Overall, the results in Fig. 2 suggest that the intervention will cost between $17 billion (i.e., *GPEI then no routine vaccination*) and $31 billion (i.e., *GPEI then universal IPV*) more than the comparator in undiscounted vaccination and program costs over the model time horizon ($11–$16 billion, 1988 net present value). As with incidence, low-income countries account for the bulk of the costs, mainly due to the sizeable external contributions, which we assume match the internal contributions at the same rate in each income group (Table 1). For the comparator, the lower middle-income countries account for a much larger proportion of the total routine

Table 3
Sensitivity analyses showing impact of selected assumptions on the aggregate net benefits (in billions of 2008 US dollars ($)) in all 104 modeled countries, with the best-estimate willingness-to-pay values of Table 1.

Modified assumption(s)	GPEI then universal IPV vs. R routine vaccination	GPEI then no routine vaccination vs. R routine vaccination
Base case	42	47
Benefits of Vitamin A included (conservative)[a]	59	64
Benefits of Vitamin A included (maximum)[b]	130	140
Discount rate at 0%	80	95
Discount rate at 7%	23	24
Ratio internal to external funds equal to 0	48	53
Ratio internal to external funds equal to 2	36	41
Incidence calibrated to 350,000 cases per year in 1987[c]	59	65
Eradication delayed by 3 years (T_{WPV} = 2015 instead of 2012) with continued high cases and costs until eradication	40	44
No SIAs during transition period	42	47
IPV price at upper end of triangular range (Table 1)	40	No change
IPV price at lower end of triangular range (Table 1)	44	No change
Vaccination coverage remains at 1987 levels in perpetuity for Routine vaccination	91	96

Acronyms: GPEI = global polio eradication initiative; IPV = inactivated poliovirus vaccine; SIAs = supplemental immunization activities.

[a] The 'conservative' scenario assumes a per-dose reduction of 5.75% in mortality between ages 1 and 4 years, calculates disability-adjusted life-years per death averted based on the estimated life expectancy at birth in a country during the first year of Vitamin A administration with polio campaigns in that country, assumes 0 children reached for campaigns with number of children reached unavailable, and includes costs of $0.13 for each administered dose of Vitamin A (see Appendix A6.1 for details).

[b] The 'maximum' scenario assumes a per-dose reduction of 11.5% in mortality between ages 0 and 4, calculates disability-adjusted life-years per death averted based on the estimated life expectancy at birth in a country during the actual year of Vitamin A administration with polio campaigns, assumes that number of children reached equals number of children targeted for campaigns with number of children reached unavailable, and includes no costs for Vitamin A doses administered (see Appendix A6.1 for details).

[c] This assumption applies an underreporting correction factor of approximately 9 (11% completeness of reporting) in the context of poor or no acute flaccid paralysis surveillance.

vaccination costs than for the intervention given the absence of a concerted push to finish eradication in the low-income countries in this scenario.

Table 2 summarizes the results of the incremental economic analyses. We note that "WHO classifies interventions as 'highly cost-effective' for a given country if results show that they avert a DALY for less than the per capita national GNI or GDP" [35, p. 65] and consequently the first column in Table 2 provides the average GNI per capita for each income group as a reference. In the upper middle-income groups, on average the interventions save money in addition to preventing disease (i.e., they are *cost and life saving*). This reflects the fact that the expected prevented treatment costs exceed the difference in program costs between the interventions and the comparator. In the low-income group, the program costs remain higher relative to the comparator (Fig. 2) and the treatment costs are much lower than in the other income groups (Table 1), which implies the need to pay some costs to obtain effectiveness (i.e., incremental cost-effectiveness ratios greater than 0). Nevertheless, the costs per DALY saved remain low in each income group compared to national averages of GNI per capita.

Given the uncertainty about the societal willingness-to-pay per paralytic case in different countries, Table 2 gives ranges of net benefit estimates based on a half and twice the societal willingness-to-pay estimates in addition to the treatment costs (Table 1). The best estimates suggest incremental net benefits for the intervention (i.e., for the GPEI summed over the full set of 104 countries) of between approximately $40 and $50 billion when compared to *Routine vaccination*, assuming reasonable economic values for the prevention or treatment of paralysis. Table 2 provides the thresholds for the total economic costs per case (i.e., treatment cost and societal willingness-to-pay) and total economic cost per paralytic case or DALY saved for which the overall net benefits of the *GPEI* intervention becomes positive compared to *Routine vaccination*. The GPEI prevented relatively many paralytic cases (Fig. 1c) at relatively small extra costs (Fig. 2c) in the 5 modeled upper middle-income countries, which led to a lower threshold value for the upper middle-income group compared to the lower middle-income group.

Table 3 shows the results of sensitivity analyses. Although the benefits of the GPEI extend beyond polio, the base case results only assess the economics for the primary goal of polio eradication. Table 3 includes a sensitivity analysis that captures the benefits of one of the major positive externalities of the GPEI, which administered a minimum of 1.3 billion Vitamin A supplements in conjunction with 352 polio SIAs [51], preventing between 1.1 ('conservative') and 5.4 ('maximum') million deaths. This mortality reduction translates into discounted net benefits of between $17 and $90 billion, even without including reductions in morbidity associated with Vitamin A supplementation, such as prevention of blindness and Bitot spots [49].

Table 3 also shows, not surprisingly [34,35], that choices about how much we discount future costs and cases (i.e., value them relative to current costs and cases) impact the overall outcomes, as seen by the impact of the discount rate. Given that the net benefits come out positive in each year, the cumulative net benefits over the full time horizon (i.e., the net present value) decreases as we decrease the relative value of future costs and cases (i.e., as we increase the discount rate). In contrast, we found a relatively moderate impact associated with varying the assumed ratio of internal to external funds between 0 and 2, because the cost savings associated with prevented cases dominate the vaccination and program costs.

As noted above, we reconstructed global estimates of the historical paralytic polio cases. We estimated the completeness of reporting as 14% for the base case based on dividing the number of cases we obtained using the infection transmission model in 1987 (i.e., 270,000) by the number of actual reported cases. If we instead use 350,000 as the true number of cases prior to 1988, which represents a prevailing assumption based on lameness studies [20,62–66], then this implies 11% completeness of reporting. Adjusting the infection transmission model so that we obtain 350,000 cases in 1987 for the comparator increases the net benefits of the GPEI by approximately $17 billion. This difference in net benefits covers the wide range of differences in net benefits that we could obtain by using different plausible strategies for fine-tuning the infection transmission model and/or correcting the reported numbers for underreporting.

We found a relatively small decrease in expected net benefits associated with a delay of eradication of 3 years, with high financial costs and cases through 2015. Although achieving eradication faster is better [10], because delays in eradication substantially increase the total costs of the GPEI, during the delay we would continue to prevent paralytic cases and receive benefits, which limits the impact of delays on the overall net benefits of the program. Similarly, while countries might find the option of stopping SIAs during the transition period between T_{WPV} and OPV cessation attractive, the continuation of SIAs represents the best approach to limit the occurrence and magnitude of cVDPV outbreaks, and relaxing to a policy of no SIAs does not noticeably impact the overall net benefits of the GPEI. Eliminating SIAs during the transition period will lead to slightly lower annual costs for the GPEI between T_{WPV} and OPV cessation, but higher cases associated with cVDPVs during those years and beyond. The recent outbreak in Tajikistan [67] provides an indication that population immunity requires active management so long as OPV use continues, and that continued SIAs will represent an important activity during the transition period. We also found that changes in IPV costs show a relatively small impact, but that assuming 1987 levels of coverage for the comparator over the time horizon (instead of the actual estimated routine vaccination) would significantly increase the net benefits.

4. Discussion

The GPEI achieved enormous success by globally eradicating wild poliovirus type 2, eliminating type 1 and 3 transmission in all but a few remaining endemic areas, and reducing the overall incidence of paralytic poliomyelitis by over 99%. Nevertheless, the program encountered significant hurdles since 2000, and accumulated financial costs at an increasing rate associated with delays and increased intensity of efforts. Our analysis indicates that the incremental cost-effectiveness ratios for the GPEI remain positive, with values typically considered "highly cost-effective," [35] even with relatively conservative assumptions and our focus on only the 104 countries directly impacted by the GPEI. Further, if we value each DALY saved at the "typical" value of 1 per capita GNI [35,46,47], then the aggregated net benefits exceed tens of billions of dollars. While critics of the eradication program emphasize the high financial burden imposed on the poorest countries [52], our analysis suggests these countries benefit the most due to the huge incremental number of paralytic poliomyelitis cases prevented that account for approximately 85% of the estimated total net benefits generated by the GPEI in the base case analysis.

Our analysis provides an opportunity to review prior studies and their assumptions [68]. For example, prior studies (not specifically focused on the GPEI) assumed that all polio vaccination would stop by 2005 [12] or 2010 [14] and estimated lower costs consistent with achieving eradication earlier and with less intense efforts than the GPEI is currently undertaking. Although our analysis indicates higher costs and longer delays in achieving eradication, the same economic justification of eradication based solely on prevented treatment costs [11,12,14] holds if the true direct treatment costs remain above the thresholds in Table 2. We also note that including the costs associated with lost productivity at values equivalent to one half or more per-capita GNI per DALY saved implies that eradication pays for itself much faster than suggested by prior studies, which did not consider lost productivity [11,12,14].

While the decision to continue an eradication program represents a prospective choice, our analyses suggest that policy makers should appreciate the enormous value of disease prevention, and especially eradication, and consider the dynamics and trade-offs of the alternatives available at the time. We previously showed that finishing polio eradication remains economically justified given that the alternative (i.e., 'control') would lead to a very substantial increase in disease burden, unless expenditures remain extremely high in perpetuity [10]. That analysis (like this one) assumes technical feasibility of global eradication of WPV types 1 and 3 [10]. The challenge to contemporaneously interrupt WPV transmission across northern India [69] has led some to question the technical feasibility of eradication, but the biological principles remain sound [70]. The GPEI has already demonstrated the ability to successfully eradicate wild poliovirus type 2 and to interrupt wild poliovirus transmission of all types in many of the most difficult places in the world. While further mathematical modeling and economic analyses can help guide and inform eradication and post-eradication policy, it appears increasingly evident that the best economic outcomes occur if the world does not waver in its commitment and it completes polio eradication as soon as possible.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.vaccine.2010.10.026.

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