

## APPENDIX

**Title:** Economic analysis of the Global Polio Eradication Initiative

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**Reference:** Vaccine 2011;29(2):334-343

This appendix provides details about the: (1) equations used for the economic analyses, (2) scope of the analysis, (3) infection transmission model and underreporting correction factors used to estimate incidence, (4) assumptions related to use of the prior post-eradication model, (5) cost data and assumptions used to allocate costs to income groups, (6) sensitivities analyses. We use the same acronyms as in the main paper a separate list of references. Figure, table, and equation numbers not preceded by “A” refer to the main paper.

## A1. Equation used for the economic analyses

For this paper, we model the incremental cost-effectiveness ratio in \$ per paralytic poliomyelitis case of the intervention (*IP*) compared to the comparator (*CP*) in income group *i*, which equals:

$$ICER(IP, CP, i) = \frac{\sum_{j=T_{WHA}}^{T_{end}} \left[ (C_{i,j,IP} - C_{i,j,CP} - (PP_{i,j,CP} - PP_{i,j,IP})T_{pp,i}) / (1 + \delta)^{j-T_{WHA}} \right]}{\sum_{j=T_{WHA}}^{T_{end}} \left[ (PP_{i,j,CP} - PP_{i,j,IP}) / (1 + \delta)^{j-T_{WHA}} \right]}$$

where  $C_{i,j,p}$  = programmatic costs in income group *i* and year *j* for policy scenario *p*,  
 $PP_{i,j,p}$  = incidence of paralytic poliomyelitis cases in income group *i* and year *j* for policy scenario *p*,  
 $T_{pp,i}$  = direct treatment costs per paralytic poliomyelitis case in income group *i*, and  
 $\delta$  = discount rate.

We provide incremental cost-effectiveness ratios only by income group given the potential for misleading ratios when aggregated over vastly different ratios in each income group.[1] We multiply the denominator by the average number of DALYs saved per prevented paralytic poliomyelitis case[1-3] to express incremental cost-effectiveness in \$ per DALY saved. Cost-effectiveness ratios require inclusion of the average treatment cost per case ( $T_{pp,i}$ ), but not the total economic costs per case ( $E_{pp,i}$ ), which include the societal willingness-to-pay per case, assuming that the decision maker will factor this in when considering the health outcomes estimated in the denominator. In contrast, the incremental net benefits of the intervention (*IP*) compared to the comparator (*CP*) in income group *i* equal:

$$INB(IP, CP, i) = \sum_{j=T_{WHA}}^{T_{end}} \left[ ((PP_{i,j,CP} - PP_{i,j,IP})E_{pp,i} - (C_{i,j,IP} - C_{i,j,CP})) / (1 + \delta)^{j-T_{WHA}} \right]$$

where  $C_{i,j,p}$  = programmatic costs in income group *i* and year *j* for policy scenario *p*,  
 $PP_{i,j,p}$  = incidence of paralytic poliomyelitis cases in income group *i* and year *j* for policy scenario *p*,  
 $E_{pp,i}$  = total economic costs per paralytic poliomyelitis case (i.e., treatment costs plus societal willingness-to-pay) in income group *i*, and  
 $\delta$  = discount rate.

Unlike the cost-effectiveness ratios, which must be considered independently for each income group, we can sum the incremental net benefits over all income groups to obtain the overall aggregate incremental net benefits for all countries in the model.

## A.2 Scope

We summarize the findings of several prior studies that evaluated the economics of global or regional polio eradication (reporting all monetary values in 2008 US dollars). Although none of these analyses focused only on the countries that benefitted from the GPEI, they provide useful context. In 1988, Musgrove found sufficient economic justification of the elimination of wild polioviruses from the Americas “solely in terms of the reduced treatment costs and irrespective of reduced pain, suffering, or incapacitation.”[4, p. 16] Assuming successful eradication and discontinuation of polio vaccination by 2005, Bart et al. (1996) estimated that the net benefits of global polio eradication would become positive by 2007 and reach approximately \$20 billion by the year 2040.[5] Aylward et al. (2003) found that polio eradication would avert over 50 million disability-adjusted life years (DALYs) between 2001 and 2040 compared to routine vaccination only. Aylward et al. (2003) also reported cost savings in all income groups, except for low-income countries for the scenario of universal routine inactivated polio vaccine (IPV) immunization after eradication, for which they reported a relatively low cost-effectiveness ratio of about \$61 per DALY averted.[6, 7] Kahn and Ehreth (2003) considered the global costs and benefits of polio vaccination between 1970 and 2050 and estimated that if polio vaccination could safely cease in 2010, the total program cost of \$84 billion would lead to more than \$160 billion in medical care cost savings and prevent 855,000 deaths, 4 million paralytic cases, and 40 million DALYs.[8] Finally, Thompson and Duintjer Tebbens (2007) compared the costs and benefits of finishing eradication in low-income countries, without including the prior investments and benefits accrued.[9] They estimated a minimum economically justifiable budget of \$3.5 billion for low-income countries alone to finish eradication based on a 20-year time horizon and no vaccination after eradication. The minimum budget increases to over \$10 billion after inclusion of a societal willingness-to-pay of approximately \$6,300 per paralytic poliomyelitis case prevented. Although an evaluation of the US historical and projected polio vaccination programs since 1955 reported \$220 billion in net benefits from the US polio vaccination efforts over time due to the prevented treatment costs alone,[10] the comparable analysis of global historical and projected polio vaccination programs remains an important gap in the literature (and is not addressed in this paper).

For this analysis, we applied the process described in the main text to identify the countries impacted by the GPEI (i.e., those countries that we assume would not have sought to eliminate WPVs in the absence of the GPEI). Tables A1 and A2 lists all 194 countries for which we found detailed demographic data[11] and 2002 World Bank income level classifications.[12] Table A1 lists the 104 countries and the first year that non-zero WHO/UNICEF coverage estimates with 3 doses of polio vaccine became available for the countries included in the base case.[13] Table A2 lists the 91 countries that we excluded from the analysis, with the reason for exclusion. Table A3 shows that the majority of children under 5 years of age in the 104 modeled countries live in low-income countries and very few live in upper middle-income countries.

We note that due to its scope, our analysis does not consider the intangible, but real and indirect benefits experienced by the excluded countries related to polio eradication. Notably, reductions in global poliovirus prevalence reduce the risk of importation outbreaks in the excluded countries, and thus the costs and cases associated with those outbreaks, even if they would only affect small subpopulations due to otherwise high routine vaccination coverage.[14] In addition, the reduced

importation outbreak risk allowed many industrialized countries to switch from OPV to IPV and avoid VAPP cases, albeit at a high financial cost.[15-17] Finally, while we expect most industrialized countries to continue routine polio vaccination indefinitely due to a perception of an unacceptable bioterrorism risk if they stop vaccinating, the absence of poliovirus outbreaks for a prolonged period of time provides the option of potentially safely stopping polio vaccination and saving the associated financial costs.

### A3. Description of the infection transmission model and correction factors

Figure A1 shows a schematic of the dynamic infection transmission model we used to estimate incidence for the comparator scenarios. The infection transmission model does not capture the same level of detail related to age groups and characterization of vaccination activities provided in our prior model, [18] but it includes the basic transmission dynamics at a population level as well as secondary OPV transmission to better capture the impact of vaccination on herd immunity over time. We apply the model to each of the 104 countries in the analysis using country-specific coverage and population data and income level dependent  $R_0$ s and vaccine take rates. Table A4 shows the list of model inputs and symbols. While most input values follow directly from prior work,[18] we highlight the inputs related to secondary OPV transmission. We assume that on average the  $R_0$  of OPV viruses equals 0.4 times that of wild polioviruses,[19, 20] which ignores the reversion of OPV strains towards the wild type strains. Further, we assume that the duration of infection for an OPV virus remains 0.5 times that of wild poliovirus.[18, 20] For the former Soviet Republics, Yugoslav Republics, Timor-Leste, and Eritrea, we did not include separate incidence estimates in income group totals until reporting started, but for the purpose of initializing the model we assumed coverage estimates equal to those of the Russian Federation, Serbia, Indonesia, and Ethiopia, respectively. For all other countries with missing coverage estimates, we assumed coverage equal to the first year with an available coverage estimate in that country. We used historic and projected population data series from the UN[11] and income-level specific model inputs (provided in Table A4). Without attempting to customize model inputs for each country, we varied the take rates and  $R_0$  values for the four most populous countries (China, India, Indonesia, and the Russian Federation/Soviet Union) in order to maintain plausible model inputs and outputs (Table A5 shows specific values for these countries). For example, for India and Indonesia, the two largest countries in the low-income group, we assumed values of  $R_0$  and vaccine take rate at the lowest and highest end of the ranges determined in prior work,[18] respectively.

Model input  $\mu$  serves to ensure net population growth consistent with the births and population data. We use  $N_i$  to represent the population in a given country and year  $i$  and  $b_i$  as the corresponding number of live births, which makes the population in the following year approximately equal to:

$$N_{i+1} = N_i + b_i - \mu_i N_i$$

Thus,  $\mu_i = (N_i + b_i - N_{i+1}) / N_i$ . We note that for some countries and years,  $\mu_i$  became negative, indicating substantial immigration or other reasons for increases in population size estimates not explained by births (e.g., differences in registration systems). However, the total population

sizes calculated in the model remained consistent with the time series data for total population.[11]

We assume that the model starts at equilibrium in each country, which we obtain by running the model at initial coverage and population values (with  $\mu$  set equal to  $b/N$ ) sufficiently long to reach the equilibrium corresponding to the initial coverage level (30 years proved long enough). At that point, we began using the time series data starting from 1980 (Table A4).

The paralytic incidence follows from the flow of *WPV infection* and the *paralysis to WPV infection ratio* (Figure A1). Thus, the *WPV associated paralytic incidence* equals (using symbols from Table A4 and  $foi$  for force of infection):

$$foi^{wpv}(t)S(t)p_{wpv} = (\mu(t) + 1/D)(R_0 / N(t))\{I(t) + i^{rl}RL^{wpv}(t) + i^{hl}HL^{wpv}(t)\}S(t) \times p_{wpv}$$

The VAPP incidence follows from the sum of the flows of *vaccinated newborns* and *OPV infections* multiplied by the *VAPP to primary infection ratio* and *VAPP to secondary infection ratio*, respectively. Thus, the VAPP incidence equals (using symbols from Table A4):

$$b(t) \times vc(t) \times tr \times p_{opv1} + (\mu(t) + 1/(D \times D^{opv}))(R_0 R_0^{opv} / N(t))\{I^{opv}(t) + i^{rl}RL^{opv}(t) + i^{hl}HL^{opv}(t)\}S(t) \times p_{opv2}$$

The underreporting correction factor through 1995, with exception of two outbreaks in China and Oman for which we assumed 90% completeness of reporting, equals the model-estimated divided by reported paralytic poliomyelitis cases in 1987 (Table 1). The assumed underreporting correction factors after 1996 are based on approximately 14% completeness of reporting (i.e., the pre-1996 correction factor of 7) for countries and years with: (1) a non-polio AFP rate  $\leq 1$  per 100,000 children younger than 15 years of age, (2) a proportion of AFP cases with adequate specimens  $\leq 60\%$ , or (3) missing data on either indicator. We assumed 50% completeness of reporting (i.e., correction factor of 2) for countries and years with: (1) a non-polio AFP rate between 1 and 2 per 100,000 children younger than 15 years of age or (2) a proportion of AFP cases with adequate specimens between 60% and 80%. Finally, we assumed 90% completeness of reporting (i.e., correction factor of 1.1) for countries and years with: (1) a non-polio AFP rate  $> 2$  per 100,000 children younger than 15 years of age and (2) a proportion of AFP cases with adequate specimens  $> 80\%$ .

The top of Figure A2 shows the average of the correction factors used over time for underreporting for the base case and three alternative assumptions, including a higher pre-1996 factor, and a lower (1.1) or higher (7) factor for intermediate surveillance quality (compared to the base case factor of 2). The bottom of Figure A2 shows how the correction factor assumptions impact the overall estimates of paralytic cases. Changing the assumed correction factor for intermediate quality surveillance shows relatively little impact on the incidence estimates.

Changing the correction factor for the outbreaks that occurred during 1988-1992 in China and Oman from 0.90 to 0.80 or 1 changed the incremental net benefit in lower and upper middle-

income countries by less than 2%, and the overall incremental net benefits in the 104 countries by less than 0.3%.

We note that some of our assumptions could lead to potential errors. For example, while the underreporting factor calibrated to the model ensures that the global totals match in 1987, we assumed that the incidence in each country started at the equilibrium corresponding to the estimated coverage in 1980. This assumption led to a slower decline in modeled incidence than in the reported numbers during the 1980s and to some differences between the modeled and actual starting points in 1988, particularly in the middle-income groups, which were furthest away from equilibrium during that time period (Figure 1). The model for the lower middle-income countries yields slightly higher totals than the estimated actual numbers around 1988, which we attribute to the two largest countries in that income group (i.e., China and the Russian Federation) and their heterogeneous populations. These countries did not experience WPV transmission in large parts of the country, and mainly incurred sporadic local epidemics. However, given the size of the populations and the assumption of homogeneous mixing in the model for each country, we either obtain 0 cases (if coverage exceeds a certain threshold) or many cases (if coverage remains below that threshold). For these two countries, we calibrated  $R_0$  and the vaccine take rate such that the incidence remained minimal but still allowed low-level endemic transmission. In the five upper middle-income countries we included, the model incidence for *Routine vaccination* starts somewhat higher than the reported numbers (corrected for underreporting), continues towards near-elimination, but then returns to a new equilibrium. Further inspection revealed that the model-estimated increase in cases after 1990 trace almost exclusively to 2 of the 5 countries upper middle-income countries (Gabon, Lebanon), which experienced decreasing and relatively low routine vaccination coverage after 1990. This observation supports the notion that vaccination campaigns and GPEI activities in addition to routine vaccination helped these countries achieve and maintain polio-free status.

#### **A4. Assumptions related to use of the prior post-eradication model[1, 2]**

For the interventions between  $T_{WPV}$  and  $T_{post}$ , we used the results of the post-eradication model for 3 years assuming continued OPV with periodic SIAs, AFP surveillance, a 70-day delay from outbreak detection to first response round, maximum population immunity at  $T_{post}$  (referred to as  $T_0$  in the post-eradication model), and maintained containment of poliovirus stocks in laboratory and IPV production sites. For the interventions after  $T_{post}$ , we used policy permutations for universal IPV or no routine vaccination, passive surveillance, a 70-day delay from outbreak detection to first response round, maximum population immunity at  $T_{post}$ , and maintained containment of poliovirus stocks in laboratory and IPV production sites.[1, 2] Although we assumed that all countries would maintain maximum population immunity until  $T_{WPV}$  (i.e., the outset of this three-year period), the absence of SIAs during this time period would decrease the population immunity to the realistic population immunity level by the year  $T_{post}$ . Given that our original model analyzed a somewhat different time period (i.e., 2010-2029) and set of countries (i.e., all low-, lower middle-, and upper middle-income countries), we adjusted for differences by computing the expected costs and cases per capita for each year and income group in the post-eradication model, and then multiplying these per-capita estimates by the number of people in each year and income group in this analysis.

## A5. Cost data and allocation to income groups

We estimated costs for the comparator by using the infection transmission model to determine the annual number of fully-vaccinated infants ( $fvi$ ) for each income group based on the different coverage assumptions. We then used the price of OPV per dose ( $c_{opv}$ ), administration and other costs associated with routine vaccine delivery ( $nv$ ) per fully OPV-vaccinated infant, and the percent wastage ( $w$ ) (Table 1) and assumed an average number of 3 OPV doses per  $fvi$  (i.e.,  $nd=3$ ), to obtain the total annual costs equal to:  $fvi \times (c_{opv} \times nd / (1-w) + nv)$ . In reality, covered children may receive more than 3 OPV doses on average and some not covered children may receive some doses as well, but does not significantly impact the overall results because the routine vaccination costs cancel out in the incremental analysis (i.e., the same costs occur both in the interventions and the comparator).

Between 1988 and 2008 the GPEI spent approximately \$6.5 billion US\$2008 in external funds on eradication activities in the 104 modeled countries. Figure A3 shows the breakdown by recipient. Overall 4.5 billion US\$2008 (70%) went to specific countries, including 4.4 billion US\$2008 (97%) to low-income, 140 million US\$2008 (3%) to lower middle-income and 3 million US\$2008 (<1%) to upper middle-income countries included in the analysis. Of the 1.9 billion US\$2002 not designated as linked to specific countries, we could identify the recipient region for roughly half, while the other half listed no region but reflected a global or programmatic activity (i.e., global, HQ, Emergency response, ICP, or UNICEF).

To perform the cost-effectiveness analysis, we must specify the full costs and benefits for all countries included in the model. While it might seem logical to consider the incremental cost-effectiveness ratios (ICERs) for all countries combined (i.e., to construct an average global ICER), countries differ substantially in their interpretation of ICERs. Typically, countries of a higher income tend to spend resources on interventions with relatively higher ICERs (i.e., higher costs per prevented loss of health) than countries of lower income, because they can afford to do so. Reporting ICERs for each income group requires that we allocate multi-country funds (i.e., global or regional funds not awarded to individual countries) to each income group. We considered two approaches. The first approach assumes that the GPEI distributed all multi-country funds on the basis of the size of the population less than five years of age. This approach allocates funds according to the distribution of children less than five years of age by income groups in the year and group of countries (i.e., region or world) of the award. For example, we would allocate a global fund awarded in 1988 according to the ratios in the first column of Table A3. The second approach assumes that the GPEI distributed multi-country funds across income groups at the same ratios as single-country funds. Given that some regions or income groups did not receive any single-country funds in some years, we applied the overall ratios of single-funds of 0.97, 0.031, and 0.00066 for low-, lower middle-, and upper middle-income countries, respectively. Table A6 shows the allocation of the multi-country funds between 1988 and 2008 for both approaches. Figure A4 shows the resulting overall single and multi-country funds allocated to each income group for each approach. The analysis in the main paper allocates multi-country funds according to population less than 5 years of age.

As noted in the text, valuation data remain limited. For the United States, Miller et al. (1996) estimated a value of \$1.7 million (i.e., 1994 estimate of \$1.2 million converted to 2008 USD) per

paralytic poliomyelitis case prevented.[16] This estimate derived from the average compensation awards for VAPP assuming the value reflected the treatment costs and all non health-care-related costs (i.e., including loss of productivity and other “intangible” costs).[16, Table 1] In contrast, using data from Brazil related to the acute costs of treating paralytic poliomyelitis victims and estimated follow-up costs over a 10-year period,[21] Musgrove (1988) estimated total treatment costs for Latin America of approximately \$13,000 assuming a discount rate of 12%[4]. Bart et al. (1996) assumed “cost of treatment and rehabilitation” of \$370 for developing countries and \$37,000 for industrialized countries.[5, Table 1] Kahn and Ehreth (2003) assumed “medical care cost per polio case” equal to the median GDP per capita in each income group to obtain estimates of \$525, \$2,500, and \$5,600, for the low-, lower middle-, and upper middle-income groups, respectively, \$31,000 in high-income countries in the Americas, and \$19,000 in the “other developed regions.”[8] Tucker et al. (2001)[22] based their estimates of “medical and non-medical (but not intangible)” VAPP costs on the average compensation awards paid in the US, adjusted downwards to reflect lower medical costs in Australia and exclusion of intangible costs, yielding an estimate of \$760,000 per VAPP case. Griffiths et al. estimated direct treatment costs for South Africa of \$5,600 using a 3% discount rate.[23] They also included indirect, discounted costs of \$240,000 based on loss of human capital assumptions. Our post-eradication model assumed average treatment costs of \$600, \$6,000, and \$60,000 for each paralytic poliomyelitis case (including fatal cases or cases receiving no treatment), respectively for low-, lower middle-, and upper middle-income countries and societal willingness-to-pay estimates of \$6,300, \$20,000, and \$75,000 for low-, lower middle-, and upper middle-income countries, respectively, assuming the value of each DALY averted equals the average gross national income.[1, 2, 24]

The DALY values used as the best estimates shown in Table 1 differ from the values in the prior post-eradication model,[1, 2] because we recalculated average life-expectancy for the 104 countries in the model instead of using the entire global income groups, and because we considered life expectancy over a different time period. In addition, the best-estimate willingness-to-pay values in Table 1 of \$12,000 (low-), \$44,000 (lower middle-) and \$110,000 (upper middle-income countries) also differ from our prior work[1, 2] because we recalculated average GNI per capita for the 104 countries in the model and used the most recent available data from 2005, 2006, or 2007 based on the Atlas method.[25] Given the importance of these inputs with respect to the overall results, we emphasize that while we expect that the true values lie within the ranges that we present, the lack of better valuation information represents an important limitation.

## **A6. Sensitivity analyses**

The base case analysis makes several conservative assumptions, which we explored using sensitivity analyses. First, the pre-1988 incidence of less than 270,000 cases per year remains below several estimates from the literature.[26-34] Second, the costs include substantial national contributions in addition to the external funds and all costs associated with routine vaccination at the estimated coverage levels. Third, the base case analysis does not include the potentially enormous positive externalities associated with the GPEI or consider its more controversial impacts on public health infrastructure.[6, 35-41] As shown in the next section and mentioned in the paper, inclusion of externalities (e.g., mortality reduction from Vitamin A administration

during SIAs alone) significantly increases the net benefits of the GPEI. Finally, the choice of the analytical time horizon and scope conservatively restricts the net benefits to only those countries that still had endemic polio in 1988, and ignores any indirect benefits of the GPEI received by countries excluded from the model. We also explored some less conservative assumptions (i.e., the year of interruption of WPV transmission, the discount rate, and the assumptions about future IPV prices).

### **A6.1. Characterization of benefits of Vitamin A supplementation**

We extracted information from Vitamin A usage during polio NIDs from the SIA database[42] of WHO’s Immunization, Vaccines, and Biologicals division and used an approach similar to the one used by Ching et al. (2000)[40] to characterize the Vitamin A-associated mortality reduction. We did not attempt to estimate the benefits associated with reduced morbidity (e.g., Bitot spots and blindness) due to lack of available data.[40]

Overall, 138 countries conducted or planned to conduct 1,003 Vitamin A campaigns between 1973 and 2009, administering a minimum of 2.4 billion Vitamin A supplements during 781 campaigns with information about the number of children reached available.[42] Of these, 1.3 billion supplements were administered during 352 campaigns whose dates coincided with polio SIAs (thus, as part of a GPEI SIA) and occurred in the 104 countries in our model, all between 1993 and 2009 (Figure A5). In addition, approximately 13 million Vitamin A supplements were administered in conjunction with polio SIAs in countries not in the model, all in Latin America.

We based our estimates of the mortality reduction associated with Vitamin A use during polio SIAs on the data in Figure A5. We computed estimates for two distinct scenarios (‘conservative’ and ‘maximum’) to reflect uncertainty about the true mortality reduction and valuation of mortality prevention. Ching et al. (2000) assume 23% reduction in mortality compared to the mortality in absence of Vitamin A supplementation for children receiving 2 Vitamin A supplements per year, and 11.5% reduction for children receiving only 1 dose per year,[40] based on data from 8 randomized controlled trials.[43] Given the possibility that children received only one Vitamin A supplement in a given year, or only one supplement during a polio SIA and the other in a non-polio campaign, we vary the reduction level from  $r = 5.75\%$  (‘conservative’) to  $r = 11.5\%$  (‘maximum’) per supplement. The observed mortality rate  $m_{obs}$  in the presence of Vitamin A supplementation equals:

$$m_{obs} = (1 - r) \times m_{abs}$$

where  $r$  is the reduction per supplement in the mortality in absence of Vitamin A supplementation ( $m_{abs}$ ). Thus, we estimated the number of deaths prevented ( $D$ ) as

$$D = r \times m_{abs} \times c = (r / (1-r)) \times m_{obs} \times c$$

where  $c$  is the number of supplements administered.

Vitamin A campaigns typically target children aged 6 to 59 months, with few exceptions. For the ‘conservative’ scenario, for  $m_{obs}$  we took the estimated annualized mortality among children

aged 1 to 4 years, while for the ‘maximum’ scenario, we used the estimated annualized mortality among children aged 0 to 4 years, which are typically much higher since the risk of death is highest during the first year of age. We estimated the annualized mortality rates as follows:

$$\text{‘conservative’ } m_{\text{obs}} = -\log[1-(m_5 - m_1)/1000]/4$$

$$\text{‘maximum’ } m_{\text{obs}} = -\log[1-m_5/1000]/5$$

where  $m_1$  is infant mortality (“infant deaths per 1,000 live births”),  $m_5$  is the under-five mortality (“deaths under age five per 1,000 live births”) (both sexes combined, medium variants), [11] and  $\log$  denotes the natural logarithm. Moreover, for the ‘conservative’ scenario we assumed 0 children reached for campaigns with missing data about the number of children reached, while for the ‘maximum’ scenario we assumed the targeted number of children (if available) for campaigns with missing data about the number of children reached. Figure A6 shows the estimated deaths prevented, totaling between 1.1 (‘conservative’) and 5.4 (‘maximum’) million between 1993 and 2009.

To translate mortality into monetary values, we first computed the number of DALYs averted per death prevented in the year and country of each campaign and then used the same values for the societal willingness-to-pay per DALY averted as in Table 1. DALYs averted per death prevented depend on the life expectancy at birth or later, depending on the age of death. Age of death has little impact on DALY estimates since life expectancy at birth normally does not differ much from life expectancy at age 5. However, since childhood mortality reduction substantially impacts life expectancy, we varied the assumption about the life expectancy estimates we used. For the ‘conservative’ scenario, we used life expectancy at birth estimated for the first year a country administered Vitamin A during polio SIAs for all years, while for the ‘maximum’ scenario we used life expectancy at birth estimated for the year that each Vitamin A campaign was conducted. Finally, for the ‘conservative’ scenario, we subtracted \$0.13 for each Vitamin A supplement administered based on the incremental costs per child reached with Vitamin A estimated in Ching et al. (2000). [40] This leads to total costs of \$180 million (1988 net present value) for all Vitamin A supplements administered in the 104 countries during 1993-2009. For the ‘maximum’ scenario, we did not subtract these costs, reflecting the assumption that GPEI resources already fully accounted for them. Table A7 summarizes the intermediate and final results for both scenarios.

## **A6.2 Other sensitivity analyses**

The true amount countries spent internally in addition to external funds in the context of the eradication effort remains uncertain. However, a wide range for the ratio of internal to external funds from 0 to 2 showed only moderate impact on the overall results, because the cost savings associated with prevented cases dominate the overall net benefits compared to the vaccination and program costs.

The base case calibration of the true incidence to the model incidence in 1987 (i.e., 270,000) yielded a somewhat lower (more conservative) estimate for the incidence before 1988 than some existing estimates of approximately 350,000 cases per year. [29-34] If we calibrate the incidence in 1987 to 350,000 by adjusting the model so that it also yields 350,000 cases in 1987 (e.g., by

increasing the paralysis-to-infection ratio in the model from 0.005 to approximately 0.0073), then the underreporting factor effectively increases from 7 to almost 9 true cases per reported case, which increases the incremental net benefits of the interventions by approximately \$17 billion.

We recognize that the assumed decrease in annual costs and cases between 2010 and  $T_{WPV}=2012$  in the base case arguably represents an optimistic assumption for the time required to interrupt WPV transmission everywhere. If we assume instead that the financial costs remain at the level of the projected requirements for 2010 (i.e., approaching \$2 billion per year for external and internal costs) and the cases remain at 2,000 per year until 2015, then the net benefits decrease by between approximately \$2.1 and \$2.9 billion. Overall, this represents a relatively small impact compared to the total net benefits because (1) the net present value of current costs remain relatively small from a 1988 perspective and (2) the accrued benefits of prevented cases far outweigh the program costs, even at this stage, although delay in achieving eradication is financially costly and achieving eradication faster is better.[9]

Projections for the cost of IPV and its administration after OPV cessation continue to evolve, particularly with new research aimed at reducing IPV costs,[44] with estimates of the upper and lower bounds of the expected prices of IPV shown in Table 1. We find that the incremental net benefits for *GEPI then universal IPV* increase by approximately \$1.6 billion for the lower bound and decrease by approximately \$1.8 billion for the upper bound.

For the comparator, we explored the assumption that coverage levels remained constant at their 1987 levels instead of the actual observed improvement in coverage we used for the base case. That assumption implies a larger number of paralytic cases per year than actually occurred, which means more cases for the interventions to prevent and significantly higher net benefits.

Due to lack of available detailed data on costs and/or health impacts, we could not quantify the economic benefits of morbidity reductions associated with Vitamin A supplementation, mortality or morbidity reductions associated with GPEI support of measles vaccination efforts, or other components of PolioPlus campaigns that most likely led to real health benefits in some areas (e.g., bed nets, deworming treatment). We could not quantify the role of the GPEI laboratory network in the development and maintenance of surveillance and laboratory capacity for other infectious diseases, including measles and other vaccine-preventable diseases, or the associated benefits.[6] Similarly, we could not characterize the important intangible benefits related to the large body of polio-related research that may benefit future efforts to control or eradicate other diseases or the benefits of global cooperation toward a common public health goal.

Although not discussed in the paper, we note that using different assumptions could lead to different results. For example, in the context of a very low value of preventing disease, we would expect that a policy of low control would emerge as economically optimal.[45, 46] Applying the lowest possible value, which corresponds to the unethical, theoretical assumption of zero societal willingness-to-pay to treat paralytic cases or prevent associated suffering and economic loss, would imply negative net benefits for the 104 countries, indicating that the interventions would not pay for themselves solely during the first 20 years of the post-eradication era if we do not value the prevention of paralysis. However, assuming zero value for the

prevention of paralysis implies that no economic justification exists for any polio vaccination, which is clearly not realistic, and not consistent with the actual revealed preferences of countries to vaccinate their populations.

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Table A1: List of countries included in the analysis (direct recipients of funds from Global Polio Eradication Initiative cost database,[47] unless noted otherwise).

Country	Income level[12]	WHO Region[48]	Year of first coverage estimate[13]
Afghanistan	LOW	EMR	1980
Albania	LMI	EUR	1980
Algeria	LMI	AFR	1981
Angola	LOW	AFR	1985
Armenia <sup>a</sup>	LOW	EUR	1992
Azerbaijan	LOW	EUR	1992
Bangladesh	LOW	SEAR	1981
Belarus <sup>b</sup>	LMI	EUR	1992
Benin	LOW	AFR	1985
Bhutan	LOW	SEAR	1980
Bosnia and Herzegovina <sup>b</sup>	LMI	EUR	1992
Botswana	UMI	AFR	1980
Bulgaria	LMI	EUR	1980
Burkina Faso	LOW	AFR	1985
Burundi	LOW	AFR	1981
Cambodia	LOW	WPR	1984
Cameroon	LOW	AFR	1981
Cape Verde	LMI	AFR	1983
Central African Republic	LOW	AFR	1980
Chad	LOW	AFR	1984
China	LMI	WPR	1982
Comoros	LOW	AFR	1984
Congo	LOW	AFR	1980
Côte d'Ivoire	LOW	AFR	1984
Democratic People's Republic of Korea	LOW	SEAR	1980
Democratic Republic of the Congo	LOW	AFR	1980
Djibouti	LMI	EMR	1982
Egypt	LMI	EMR	1980
Equatorial Guinea	LOW	AFR	1985
Eritrea	LOW	AFR	1993
Ethiopia	LOW	AFR	1980
Federated States of Micronesia	LMI	WPR	1987
Fiji <sup>b</sup>	LMI	WPR	1980
Gabon	UMI	AFR	1985
Gambia	LOW	AFR	1980
Georgia	LOW	EUR	1992
Ghana	LOW	AFR	1980
Guinea	LOW	AFR	1982
Guinea-Bissau	LOW	AFR	1983
India	LOW	SEAR	1980
Indonesia	LOW	SEAR	1981

Iran (Islamic Republic of)	LMI	EMR	1980
Iraq	LMI	EMR	1980
Jordan <sup>a</sup>	LMI	EMR	1980
Kazakhstan <sup>a</sup>	LMI	EUR	1992
Kenya	LOW	AFR	1984
Kyrgyzstan <sup>a</sup>	LOW	EUR	1992
Lao People's Democratic Republic	LOW	WPR	1981
Lebanon	UMI	EMR	1981
Lesotho	LOW	AFR	1980
Liberia	LOW	AFR	2000
Madagascar	LOW	AFR	1982
Malawi	LOW	AFR	1980
Maldives <sup>b</sup>	LMI	SEAR	1980
Mali	LOW	AFR	1985
Mauritania	LOW	AFR	1981
Mauritius	UMI	AFR	1980
Moldova	LOW	EUR	1992
Mongolia	LOW	WPR	1980
Montenegro <sup>b</sup>	LMI	EUR	2006
Morocco	LMI	EMR	1982
Mozambique	LOW	AFR	1981
Myanmar	LOW	SEAR	1982
Namibia	LMI	AFR	1991
Nepal	LOW	SEAR	1982
Niger	LOW	AFR	1981
Nigeria	LOW	AFR	1984
Oman	UMI	EMR	1980
Pakistan	LOW	EMR	1980
Papua New Guinea	LOW	WPR	1980
Philippines	LMI	WPR	1980
Romania	LMI	EUR	1985
Russian Federation	LMI	EUR	1992 <sup>c</sup>
Rwanda	LOW	AFR	1981
Samoa <sup>b</sup>	LMI	WPR	1980
Sao Tome and Principe	LOW	AFR	1981
Senegal	LOW	AFR	1986
Serbia	LMI	EUR	1992
Sierra Leone	LOW	AFR	1999
Solomon Islands <sup>b</sup>	LOW	WPR	
Somalia	LOW	EMR	1980
South Africa	LMI	AFR	1983
Sri Lanka	LMI	SEAR	1980
Sudan	LOW	EMR	1980
Swaziland	LMI	AFR	1981

Syrian Arab Republic <sup>a</sup>	LMI	EMR	1980
Tajikistan	LOW	EUR	1992
Thailand <sup>b</sup>	LMI	SEAR	1980
The former Yugoslav Republic of Macedonia <sup>b</sup>	LMI	EUR	1993
Timor-Leste <sup>b</sup>	LOW	SEAR	2002
Togo	LOW	AFR	1981
Tonga <sup>b</sup>	LMI	WPR	1980
Tunisia <sup>b</sup>	LMI	EMR	1983
Turkey	LMI	EUR	1980
Turkmenistan	LMI	EUR	1992
Uganda	LOW	AFR	1981
Ukraine	LOW	EUR	1992
United Republic of Tanzania	LOW	AFR	1980
Uzbekistan	LOW	EUR	1992
Vanuatu <sup>b</sup>	LMI	WPR	1982
Viet Nam	LOW	WPR	1983
Yemen	LOW	EMR	1980
Zambia	LOW	AFR	1983
Zimbabwe	LOW	AFR	1981

Acronyms: AFR=African region; EMR=Eastern Mediterranean region; EUR=European region; LOW=low-income; LMI=lower middle-income; NA=not applicable (country not a member of any WHO region); SEAR=South-East Asian region; UMI=upper middle-income; WPR=Western Pacific region

<sup>a</sup> Not a direct recipient of country-level funds, but beneficiary of operation MECACAR

<sup>b</sup> Not a direct recipient of country-level funds, but LMI country outside AMR

<sup>c</sup> However, we use country-reported POL3 coverage data[49] available from 1986 as a best estimate for the POL3 coverage.

**Table A2: List of countries excluded from the analysis.**

Country	Income level[12]	WHO Region[48]	Reason for exclusion
Argentina	UMI	AMR	AMR country
Aruba	HIGH	NA	High-income country
Australia	HIGH	WPR	High-income country
Austria	HIGH	EUR	High-income country
Bahamas	HIGH	AMR	AMR country
Bahrain	HIGH	EMR	High-income country
Barbados	UMI	AMR	AMR country
Belgium	HIGH	EUR	High-income country
Belize	LMI	AMR	AMR country
Bolivia	LMI	AMR	AMR country
Brazil	UMI	AMR	AMR country
Brunei Darussalam	HIGH	WPR	High-income country
Canada	HIGH	AMR	AMR country
Channel Islands	HIGH	NA	High-income country
Chile	UMI	AMR	AMR country
China, Hong Kong Special Administrative Region	HIGH	NA	High-income country
China, Macao Special Administrative Region	HIGH	NA	High-income country
Colombia	LMI	AMR	AMR country
Costa Rica	UMI	AMR	AMR country
Croatia	UMI	EUR	UMI country and not a direct recipient of country-level funds
Cuba	LMI	AMR	AMR country
Cyprus	HIGH	EUR	High-income country
Czech Republic	UMI	EUR	UMI country and not a direct recipient of country-level funds
Denmark	HIGH	EUR	High-income country
Dominican Republic	LMI	AMR	AMR country
Ecuador	LMI	AMR	AMR country
El Salvador	LMI	AMR	AMR country
Estonia	UMI	EUR	UMI country and not a direct recipient of country-level funds
Finland	HIGH	EUR	High-income country
France	HIGH	EUR	High-income country
French Guiana	HIGH	NA	High-income country
French Polynesia	HIGH	NA	High-income country
Germany	HIGH	EUR	High-income country
Greece	HIGH	EUR	High-income country
Grenada	UMI	AMR	AMR country
Guadeloupe	HIGH	NA	High-income country
Guam	HIGH	NA	High-income country
Guatemala	LMI	AMR	AMR country
Guyana	LMI	AMR	AMR country

Haiti	LOW	AMR	AMR country
Honduras	LMI	AMR	AMR country
Hungary	UMI	EUR	UMI country and not a direct recipient of country-level funds
Iceland	HIGH	EUR	High-income country
Ireland	HIGH	EUR	High-income country
Israel	HIGH	EUR	High-income country
Italy	HIGH	EUR	High-income country
Jamaica	LMI	AMR	AMR country
Japan	HIGH	WPR	High-income country
Kuwait	HIGH	EMR	High-income country
Latvia	UMI	EUR	UMI country and not a direct recipient of country-level funds
Libyan Arab Jamahiriya	UMI	EMR	UMI country and not a direct recipient of country-level funds
Lithuania	UMI	EUR	UMI country and not a direct recipient of country-level funds
Luxembourg	HIGH	EUR	High-income country
Malaysia	UMI	WPR	UMI country and not a direct recipient of country-level funds
Malta	UMI	EUR	UMI country and not a direct recipient of country-level funds
Martinique	HIGH	NA	High-income country
Mexico	UMI	AMR	AMR country
Netherlands	HIGH	EUR	High-income country
Netherlands Antilles	HIGH	NA	High-income country
New Caledonia	HIGH	NA	High-income country
New Zealand	HIGH	WPR	High-income country
Nicaragua	LOW	AMR	AMR country
Norway	HIGH	EUR	High-income country
Occupied Palestinian Territory	LMI	NA	Coverage data unavailable
Panama	UMI	AMR	AMR country
Paraguay	LMI	AMR	AMR country
Peru	LMI	AMR	AMR country
Poland	UMI	EUR	UMI country and not a direct recipient of country-level funds
Portugal	HIGH	EUR	High-income country
Puerto Rico	UMI	NA	UMI country and not a direct recipient of country-level funds/AMR country
Qatar	HIGH	EMR	High-income country
Republic of Korea	HIGH	WPR	High-income country
Réunion	HIGH	NA	High-income country
Saint Lucia	UMI	AMR	AMR country
Saint Vincent and the Grenadines	LMI	AMR	AMR country
Saudi Arabia	UMI	EMR	UMI country and not a direct recipient of country-level funds
Singapore	HIGH	WPR	High-income country
Slovakia	UMI	EUR	UMI country and not a direct recipient of country-level funds
Slovenia	HIGH	EUR	High-income country
Spain	HIGH	EUR	High-income country
Suriname	LMI	AMR	AMR country
Sweden	HIGH	EUR	High-income country
Switzerland	HIGH	EUR	High-income country

Trinidad and Tobago	UMI	AMR	AMR country
United Arab Emirates	HIGH	EMR	High-income country
United Kingdom	HIGH	EUR	High-income country
United States of America	HIGH	AMR	AMR country
United States Virgin Islands	HIGH	NA	High-income country
Uruguay	UMI	AMR	AMR country
Venezuela (Bolivarian Republic of)	UMI	AMR	AMR country

Acronyms: AMR=American region; EMR=Eastern Mediterranean region; EUR=European region; HIGH=high-income; LOW=low-income; LMI=lower middle-income; NA=not applicable (country not a member of any WHO region); UMI=upper middle-income; WPR=Western Pacific region

**Table A3: Distribution of children under five years of age across the income groups[11, 12] for the countries included in the base case analysis**

Income group	1988	2008	2035
Low income	60%	69%	72%
Lower middle income	40%	31%	27%
Upper middle income	0.24%	0.22%	0.21%

**Table A4: Inputs to the infection transmission model used to estimate incidence for the comparator scenarios.**

<i>Sym- bol</i>	<i>Name in diagram</i>	<i>Base case value [unit]</i>	<i>Interpretation</i>	<i>Source(s)</i>
$S$	Fully susceptible	-	Individuals never infected or successfully vaccinated	-
$I^{opv}$	OPV infected	-	Previously fully susceptible individuals experiencing an OPV infection (vaccine recipient or contact)	-
$I$	WPV infected	-	Previously fully susceptible individuals experiencing a WPV infection	-
$RL$	Recent live	-	Individuals recently recovered from OPV or WPV infection	-
$HL$	Historic live	-	Individuals recovered from OPV or WPV infection several years ago	-
$RL^{wpv}$	RL OPV infected	-	Recently live poliovirus infected individuals experiencing a WPV infection (vaccine recipient or contact)	-
$HL^{wpv}$	HL OPV infected	-	Historically live poliovirus infected individuals experiencing a WPV infection (vaccine recipient or contact)	-
$RL^{opv}$	RL OPV infected	-	Recently live poliovirus infected individuals experiencing an OPV infection (vaccine recipient or contact)	-
$HL^{opv}$	HL OPV infected	-	Historically live poliovirus infected individuals experiencing an OPV infection (vaccine recipient or contact)	-
$vc$	routine coverage	time series [%]	Proportion of newborns receiving 3 or more doses of OPV (1980 to 2007)	WHO/UNICEF (2008)[13]
$b$	births	time series [people]	Annual number of live births (1980 to $T_{end}$ )	UN (2008)[11]
$\mu$	mu	time series [1/year]	Population change parameter (1980 to $T_{end}$ )	Derived from UN (2008)[11]
$N_0$	initial population	country-dependent [people]	Population size of each country in 1980	UN (2008)[11]
$R_0$	$R_0$ - LOW - LMI - UMI	11.5 [dmnl] 9.5 [dmnl] 7.5 [dmnl]	Basic reproductive number for WPV; See Table A5 for values in China, India, Indonesia and the Russian Federation	Duintjer Tebbens et al. (2005)[18]
$R_0^{rel}$	relative $R_0$	0.4 [dmnl]	$R_0$ of OPV virus divided by $R_0$ of WPV	Various sources[19, 50]
$tr$	take rate - LOW - LMI & UMI	71 [%] 85 [%]	Proportion of fully vaccinated infants becoming directly infected with the vaccine virus ; See Table A5 for values in China, India, Indonesia and the Russian	Duintjer Tebbens et al. (2005)[18]

$D$	d	35/365 [year]	Federation Average duration of WPV infection	Various sources[18, 51]
$D^{opv}$	drel OPV	0.5 [dmnl]	Infectious period of OPV infection divided by infectious period of WPV infection	Various sources[18, 51]
$D^{rl}$	drel RL	7/35 [dmnl]	Infectious period for “recent live” compartment divided by infectious period for fully susceptibles	Various sources[18, 51]
$D^{hl}$	drel HL	9/35 [dmnl]	Infectious period for “historic live” compartment divided by infectious period for fully susceptibles	Various sources[18, 51]
$s^{rl}$	srel RL	0.25 [dmnl]	Susceptibility for “recent live” compartment relative to fully susceptibles	Duintjer Tebbens et al. (2005)[18]
$s^{hl}$	srel HL	0.80 [dmnl]	Susceptibility for “historic live” compartment relative to fully susceptibles	Duintjer Tebbens et al. (2005)[18]
$i^{rl}$	irel RL	0.10 [dmnl]	Infectiousness for “recent live” compartment relative to fully susceptibles	Duintjer Tebbens et al. (2005)[18]
$i^{hl}$	irel HL	0.50 [dmnl]	Infectiousness for “historic live” compartment relative to fully susceptibles	Duintjer Tebbens et al. (2005)[18]
$p_{wpv}$	paralysis to infection ratio	1/200 [case/person]	Average number of paralytic poliomyelitis cases per WPV infection in susceptibles	Various sources[18, 26, 52, 53]
$p_{opv1}$	VAPP to primary infection ratio	1.87/10 <sup>6</sup> [case/person]	Average number of paralytic poliomyelitis cases per OPV recipient infection	Duintjer Tebbens et al. (2006)[33]
$p_{opv2}$	VAPP to secondary infection ratio	3.71/10 <sup>6</sup> [case/person]	Average number of paralytic poliomyelitis cases per contact OPV infection	Duintjer Tebbens et al. (2006)[33]

Acronyms: LOW=low-income; LMI=lower middle-income; OPV=oral poliovirus vaccine; VAPP=vaccine-associated paralytic polio; UMI=upper middle-income; UN=United Nations; UNICEF=United Nations Children’s Fund; WHO=World Health Organization; WPV=wild poliovirus

**Table A5: Country-specific inputs to the infection transmission model differing from the income level values in Table A4**

<i>Sym- bol</i>	<i>Name in diagram</i>	<i>Base case value [unit]</i>	<i>Interpretation</i>	<i>Source(s)</i>
$R_0$	$R_0$		Basic reproductive	Duintjer Tebbens et
	- India	13 [dmnl]	number for wild	al. (2005)[18]
	- Indonesia	10 [dmnl]	polioviruses	
	- China & Russian Federation	8.5 [dmnl]		
$tr$	take rate		Proportion of fully	Duintjer Tebbens et
	- India	40 [%]	vaccinated infants	al. (2005)[18]
	- Indonesia	98 [%]	becoming directly	
	- China & Russian Federation	95 [%]	infected with the vaccine virus	

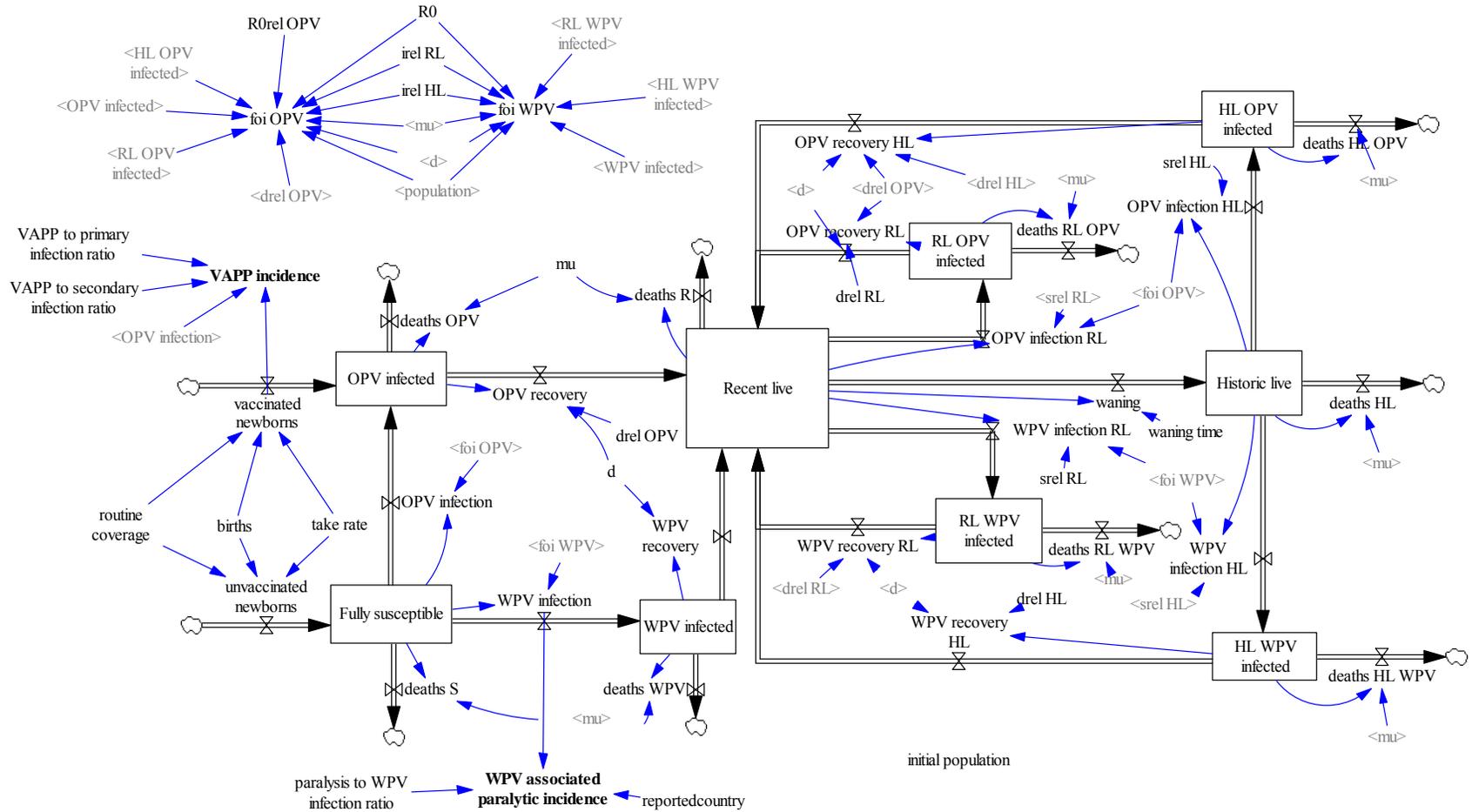
**Table A6: Allocation of multi-country funds between 1988 and 2008 (in 2008 USD) to the different income groups in the model**

Income group	Based on population less than 5 years of age[11]	Based on observed distribution of single-country funds by income group
Low income	1,400,752,688	1,871,528,614
Lower middle income	546,013,195	80,154,931
Upper middle income	6,669,793	1,752,132
Total	1,953,435,677	1,953,435,677

**Table A7: Results from analysis of Vitamin A supplementation during polio campaigns[42] in 104 modeled countries during 1993-2009 reflecting the different assumptions for the ‘Conservative’ and ‘Maximum’ scenarios (see text)**

	<i>‘Conservative’ scenario</i>	<i>‘Maximum’ scenario</i>
Number of Vitamin A supplements	1.3 billion	1.4 billion
Incremental costs (1988 net present value)	\$180 million	\$0
Deaths prevented	1.1 million	5.4 million
Disability adjusted life-years saved	28 million	140 million
Net benefits of Vitamin A supplementation (1988 net present value)	\$17 billion	\$90 billion

**Figure A1: Schematic of the infection transmission model used to estimate incidence for the comparator scenarios (see table A4 for interpretation of model input names)**



**Figure A2: Overall effectively underreporting correction factor (ratio of estimated to reported total cases) for different assumptions about completeness of reporting, and corresponding estimated incidence.**

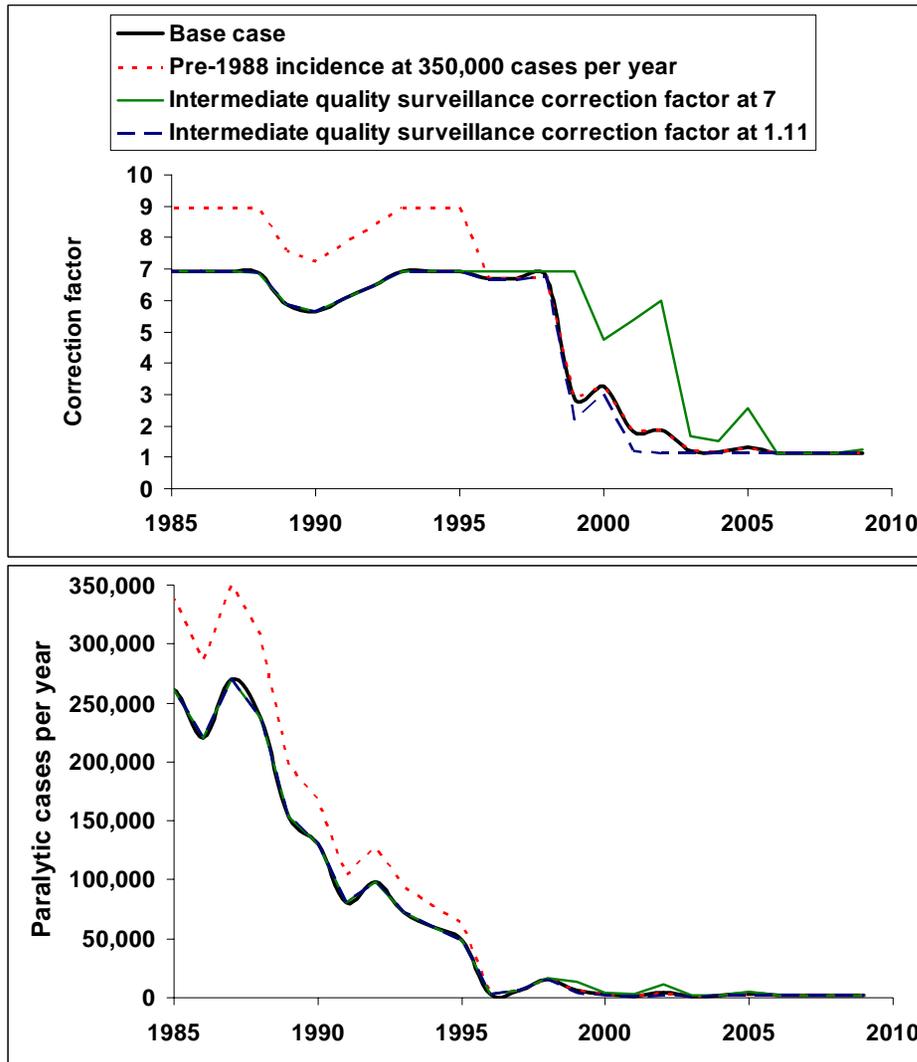
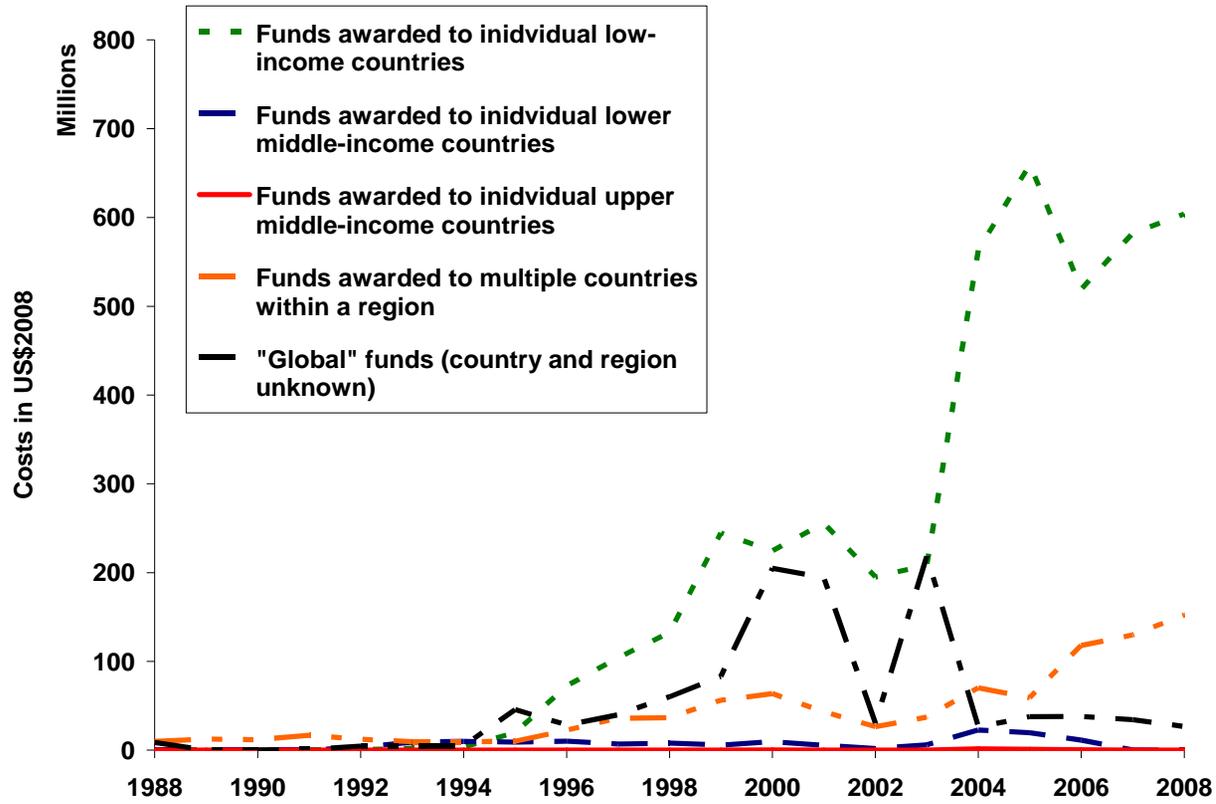
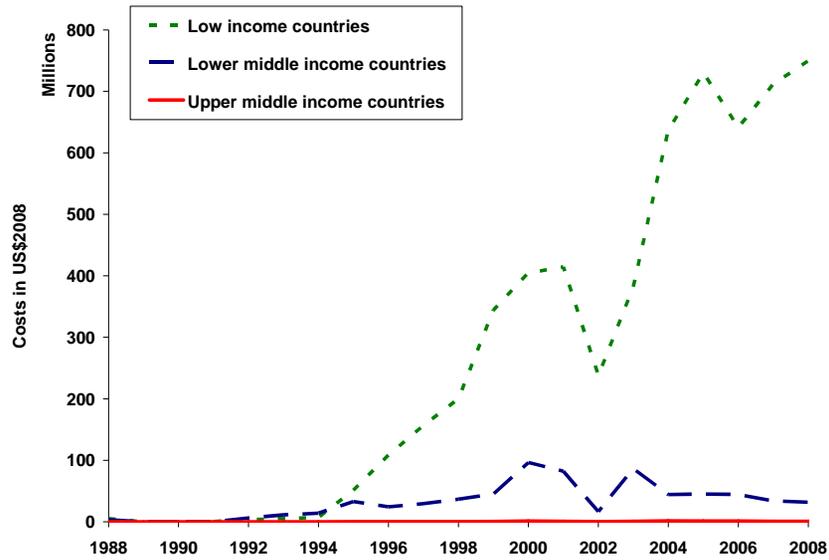


Figure A3: Breakdown of included costs from the Global Polio Eradication Initiative database[47] by recipient.

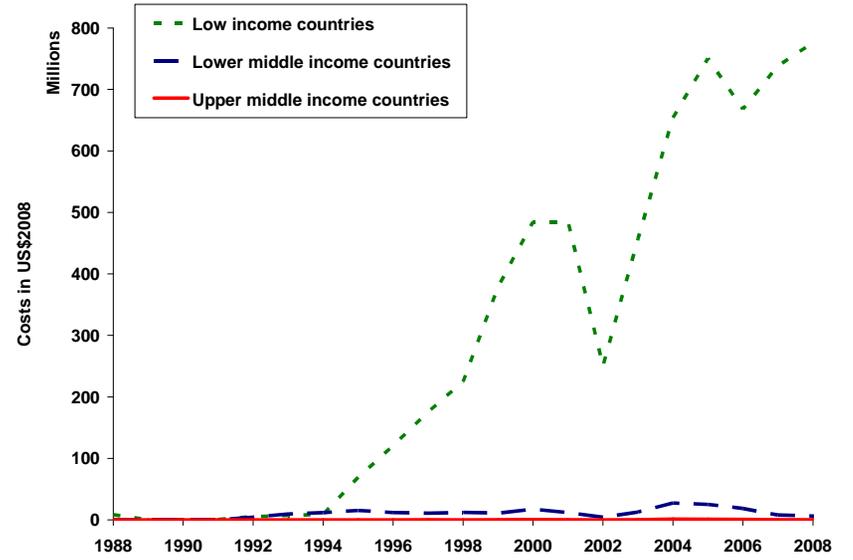


**Figure A4: Overall external funds awarded, by income group**

(a) Based on population less than 5 years of age



(b) Based on observed distribution of single-country funds by income group



**Figure A5: Number of Vitamin A supplements administered in conjunction with polio campaigns in the 104 countries in the model[42]**

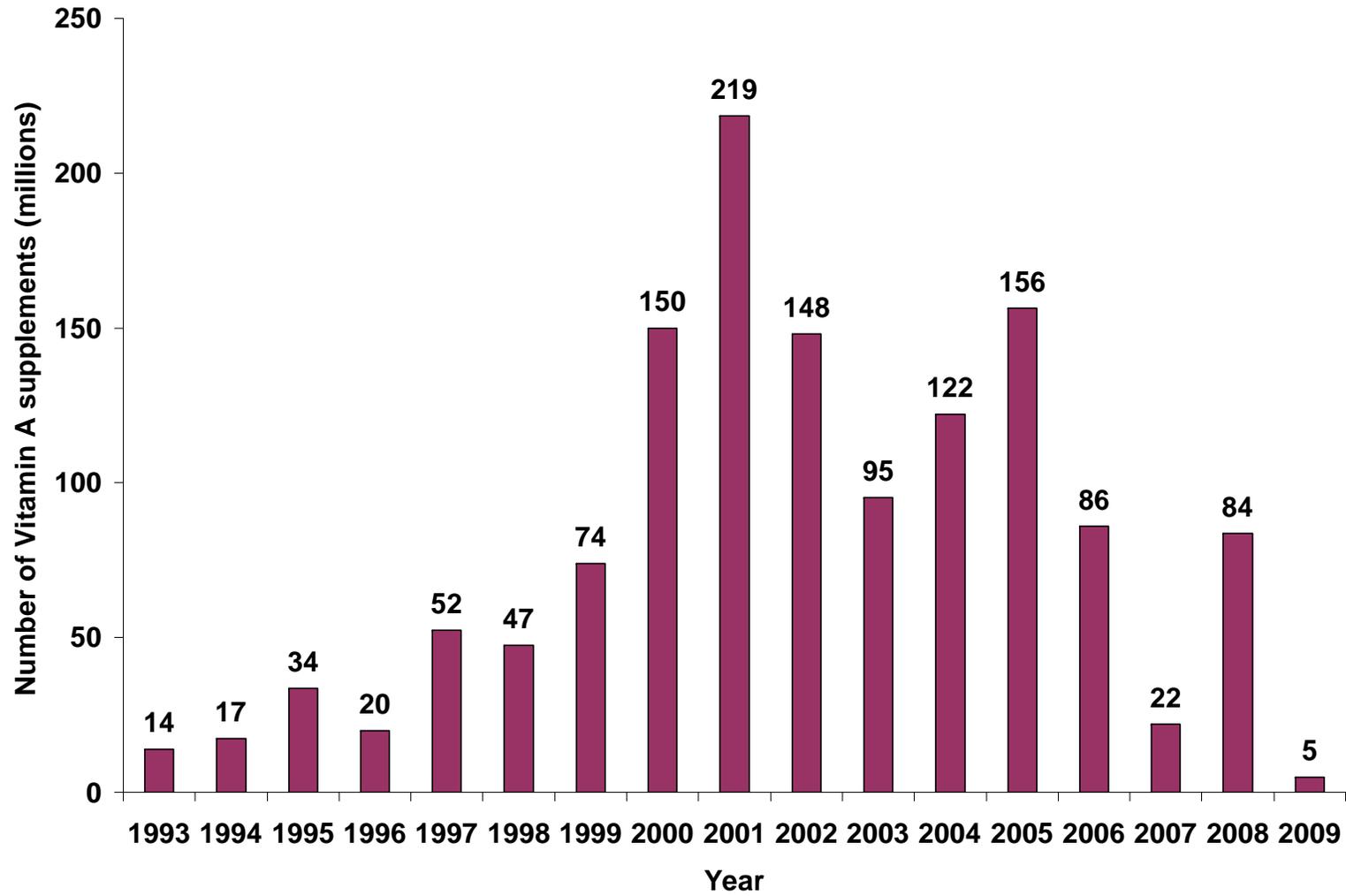


Figure A6: Estimated annual numbers of deaths prevented due to Vitamin A administered in conjunction with polio campaigns in the 104 modeled countries

