TECHNICAL APPENDIX
For

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Uncertainty and sensitivity analyses of a decision analytic model for post-eradication polio risk management.

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A1. INTRODUCTION

This technical appendix includes more details about the methods and additional results that we provide to complete the results highlighted in the main paper. We follow the same structure and use the same acronyms (section A6 provides a list) as in the main paper. The results in this appendix focus on income group aggregates over a 20-year time horizon with 3% discount rate (unless noted otherwise). We expand on the results presented in the main paper and refer to the "base case" as the simulation that maintains the general assumptions while varying many uncertain inputs probabilistically and that yielded the main results presented elsewhere.[1]

A2. BASE CASE METHODS AND ASSUMPTIONS

This section includes several subsections that provide supplemental information related to the methods that we describe in the main paper.

A2.1 Logic for random outbreak generation

We performed all of the analyses using Mathematica™ (contact the corresponding author to review the code). To generate the random number of outbreaks in a given stochastic iteration, we draw from different Poisson distributions, depending on the year, income group, and decisions, using the inverse cumulative Poisson distribution functions applied to the same sets of random numbers for each decision permutation. Having generated a list of numbers of outbreaks for each income group, year, and decision permutation, we then determine the characteristics for each outbreak (i.e., population size, R_0, coverage since last SIAs, and partially infectible reduction in the event of continued SIAs), while ensuring that each decision permutation draws similar characteristics. Thus, we must generate these characteristics for *m* outbreaks, where *m* equals the maximum number of outbreaks in a given year and income group over all decision permutations.

To determine population sizes, we randomly draw a population size from the list of country population sizes in a given income group and year (i.e., poplist(i,j) based on UN population projections[2]). The base case then uses one of five outbreak population sizes for which we ran the dynamic outbreak sub-model,[3] assigning population sizes according to the key in Table A1. For context, the last column provides the proportion of the global population in 2010 living in

countries of each category, although in the overall model these probabilities will vary depending on the year and income group.

We clarify the above logic using the subroutines below with the following symbols:

i = income group (low (LOW), lower middle (LMI), upper middle (UMI), and high-income (HIGH))
j = year (T_0, T_0+1,...,T_0+20)
d = permutation of decisions regarding routine and supplemental immunization, containment, and population immunity at T_0 (assume D possible permutations)
λ = outbreak Poisson rate
N_outbreaks = random number of outbreaks
poplist = list of population sizes, sorted in descending order
N_poplist = number of entries in poplist
Total_poplist = sum of all entries in poplist
Pop_outbreak = outbreak population size
u = realization of a U[0,1] distributed random variable
k, found, cum, n, ob, p, m = temporary variables
m = Max(N_outbreaks(i,j,1,iteration), N_outbreaks(i,j,2,iteration),...,N_outbreaks(i,j,D,iteration))

We used the following logic (shown here as an excerpt in the form of computer code) to generate the random number of outbreaks in an iteration following a Poisson distribution:

```
For i = 1 to 4 do
        For j = T0 to T0+19 Do
                u(i,j) ~ U[0,1]
                For d = 1 to D Do
                        found = False
                        n = 0
                        While Not(found) Do
                                cum = 0
                                For k = 1 to n
                                        cum = cum + Exp{- λ(i,j,d)}× λ(i,j,d)^k/k!}
                                End For
                                If u(i,j) ≤ cum Then
                                        N_outbreaks(i,j,d,iteration) = n
                                Else
                                        n = n + 1
                                End If
                        End While
                End For
        End For
End For
```

We used the following logic to generate population sizes for each outbreak in an iteration:

```
For ob = 1 to m
        u ~ U[0,1]
        p[0] = 0
        k = 0
        found = False
        While And(Not(found),k ≤ N_poplist(i,j)) Do
                k = k + 1
                p[k] = p[k-1] + poplist(i,j)[k]/Total_pop(i,j)
                If p[k] < u Then
                        Pop_outbreak(i,j,ob,iteration) = poplist(i,j)[k]
                        found = True
                End If
        End While
End For
```

Table A1: Key for the assignment of randomly generated outbreak population sizes to outbreak population sizes in the outbreak sub-model.[3]

Size of randomly determined outbreak population	*Population size actually used in the outbreak model*	*Proportion of world population in 2010 living in countries in given population size bracket*[*]
< 1,000,000	500,000	0.2 %
1,000,000 - 7,500,000	5,000,000	3.5 %
7,500,000 – 25,000,000	10,000,000	9.3 %
25,000,000 - 75,000,000	50,000,000	17.4 %
≥ 75,000,000	100,000,000	69.6 %

[*] Based on UN population data[2] combined with income group stratification[4]

We also randomly sample the R_0 value and pre-outbreak routine immunization coverage for each outbreak, and in the case of continues SIAs, we also sample a different reduction in partially inectibles relative to the average population immunity for each outbreak, as described in the methods of the main paper We resample the cVDPV risk case for every income group but hold it constant during each simulated year. Table A2 shows the discrete probability distributions for these inputs. As shown in Table A2, the base case assigns equal probability to the two medium cases for R_0 (we explored the impacts of different probabilities as described in the results section of the main paper). We sample all other distributed inputs from continuous probability distribution functions (Table 1).

Table A2: Discrete random variables in the model (not including outbreak population size and reduction in partially infectibles in the event of continued supplemental immunization activities).

Model input	*Probability*	*Low-income group*	*Lower middle-income group*	*Upper middle-income group*	*High-income group*[*]
R_0 case					
- Lowest	0.0	8	6	4	2
- Low-medium	0.5	10	8	6	4
- High-medium	0.5	13	11	9	6
- Highest	0.0	16	14	12	9
Coverage case[**]					
- Projected averages	0.8	0.68	0.90	0.92	0.94
- Low	0.1	0.40	0.70	0.70	0.85
- Lowest	0.1	0.25	0.50	0.60	0.80
cVDPV risk case[*]					
- Low-risk case	0.5	Initial cVDPV outbreak rate based on historical occurrence of cVDPV events only			
- High-risk case	0.5	Initial cVDPV outbreak rate based on historical occurrence of cVDPV and aVDPV events			

[*] For the high-income group, we did not model a different risk for the cVDPV low-risk and high-risk cases

[**] The routine immunization levels apply to the time period between the last regulars SIAs and an outbreak (see methods section in the main paper)

A2.2 Interpretation of ICER and INB

The following equations relate incremental cost-effectiveness ratios (ICERs) to incremental net benefits (INB)

ICER = Incremental Costs/ Incremental Effectiveness
INB = Incremental Effectiveness x WTP – Incremental Costs,

where WTP equals the willingness to pay per prevented paralytic case and the incremental costs include treatment cost of paralytic cases. Table A3 shows the appropriate interpretation of the incremental ICERs and INBs in the context of different signs of the incremental effectiveness. With positive effectiveness, positive costs yield a positive ICER and smaller ICERs indicate more cost-effective interventions. If the ICER is smaller than the per-capita GNI for each DALY averted by the prevented paralytic cases, then the INB will be greater than 0 (assuming a WTP equal to the per-capita GNI for each DALY averted) and some may consider the alternative "very cost-effective" compared to the comparator program.[(5)] With positive effectiveness but negative costs, ICER becomes negative, INB positive, and we identify the alternative as "cost and life-saving." However, a negative ICER can also indicate a "dominated" alternative, implying negative effectiveness but positive costs. A dominated case always yields a negative INB, and equivalently means that the alternative represents a "financial and life-costing" intervention relative to the comparator.

Table A3: Interpretation of incremental cost-effectiveness ratio (ICER) and incremental net benefit (INB) for the alternative (alt) vs. the comparator (comp) as a function of the signs of the incremental effectiveness (IE) and incremental costs (IC)

	IE > 0	IE < 0
IC < 0	"Cost and life-saving" ICER(alt vs. comp) < 0 INB (alt vs. comp) > 0 Always better to opt for the alternative	"Cost-saving but life-costing" ICER(alt vs. comp) > 0 INB (alt vs. comp) = function of WTP, with INB > 0 if ICER > WTP Choice depends on trade-offs
IC > 0	"Life-saving at a cost" ICER(alt vs. comp) > 0 INB (alt vs. comp) = function of WTP, with INB > 0 if ICER < WTP Choice depends on trade-offs	"Dominated" ICER(alt vs. comp) < 0 INB (alt vs. comp) < 0 Always better to stay with the comparator

IE = Cases(comp) – Cases(alt)
IC = Costs(alt) – Costs(comp)

A2.3 Calculation of DALYs and WTP per paralytic case

To compute the WTP values corresponding to the average per-capita GNI for each DALY, we first estimate the number of DALYs averted per prevented paralytic case for each income group, based on the 2002 World Bank classification.[4] We use the simplest formula for DALYs, which attributes equal weight to disability or life lost at any age ($K = 0$), although it discounts future loss at a fixed rate:[6]

$$\text{DALYs per paralytic case} = (1 - \text{Exp}[-r \times L]) \times fr / L + (1 - \text{Exp}[-r \times L]) \times (1-fr) \times Dpp / L$$

where r = discount rate
L = standard life expectation at average age of onset
fr = fatality rate for paralytic polio
Dpp = disability weight for paralytic polio

The first term represents the number of years of life lost per death due to paralytic polio, the second term represents the years lived with the disability of permanent paralysis. We use the disability weight of $Dpp = 0.369$ for poliomyelitis from the Global Burden of Disease assessment.[6] We estimate $fr = 0.15$ based on reported paralytic polio cases in the US in 1952, the year of greatest incidence.[7] We further assume an average age of onset of 0 years such that we can use life expectancy at birth for L. For the income group stratification of 2002, this results in average values for L during 2010-2030 of approximately 64, 73, 76, and 80 for the low, lower middle, upper middle, and high-income groups, respectively.[8]

Based on World Bank GNI estimates for 2002,[9] which we converted from assumed US$2006 to US$2002, the average per capita GNI for the 2002 income groups[4] equals $403, $1,227, $4,567, and $24,146 for the low, lower middle, upper middle, and high-income groups, respectively. Table A4 shows the resulting DALY and WTP estimates for different values of fr and r. Clearly, the choice of discount rate plays an influential role in the results. For the base case, we use r = 0.03, although we also use the estimates with different discount rates for the relevant sensitivity

analyses that vary discount rate. We do not vary *fr* or the assumption of the average of onset of 0 years (which has little impact given discounting and the fact that life expectancy typically increases by age during the first years of life).[10]

Table A4: Disability-adjusted life years (DALYs) and willingness-to-pay (WTP) per paralytic polio case for different assumptions about the discount rate and the fatality rate per paralytic polio case (shaded row shows the inputs used for the base case).

Fatality rate	Discount rate	DALYs per paralytic case				WTP per paralytic case prevented (US$2002)			
		LOW	LMI	UMI	HIGH	LOW	LMI	UMI	HIGH
0.05	0	26.04	29.24	30.44	32.04	10,486	35,886	139,029	773,729
	0.03	11.45	11.86	11.99	12.14	4,612	14,552	54,740	293,141
	0.07	5.66	5.69	5.69	5.70	2,280	6,980	26,005	137,655
0.15	0	30.14	33.85	35.24	37.09	12,138	41,539	160,930	895,617
	0.03	13.26	13.73	13.87	14.05	5,339	16,845	63,364	339,320
	0.07	6.55	6.58	6.59	6.60	2,639	8,080	30,102	159,340
0.25	0	34.24	38.45	40.03	42.14	13,790	47,193	182,832	1,017,505
	0.03	15.06	15.59	15.76	15.97	6,065	19,137	71,987	385,500
	0.07	7.45	7.48	7.49	7.50	2,999	9,180	34,199	181,025

A2.4 Calculation of the correlation ratios (CRs)

Mathematically, the correlation ratio (CR) of the model output to a given input equals the squared product moment correlation between the model output and the conditional expectation of the model output to that input. The conditional expectation represents the best regression of the model output on the input, and the squared correlation is the highest possible squared correlation between the model output and any function of the input.[11, 12] To compute the CR, we approximate the conditional expectation of the model output to the given input by fitting a polynomial function of the input up to degree five and applying the "early stopping" heuristic to prevent overfitting.[12] We applied this heuristic both with the first and the second half-sample (i.e., of 5,000 iterations each) as the training sample, and then chose the polynomial function that yielded the lowest maximum squared correlation with the full sample among the two polynomial functions obtained for each choice of training sample. This polynomial function provided our approximation of the conditional expectation, and the squared correlation between the model output and the approximated conditional expectation provided our CR estimates.

A3. ADDITIONAL BASE CASE RESULTS

This section includes several subsections that provide supplemental information related to the base case results. It includes additional figures and summary statistics of the distributions of costs and cases and discussion about the probabilities of observations in the tails. It also addresses analyses of departures from the base case assumptions, including use of different discount rates, WTP, maximum outbreak population sizes, surveillance and response policies, containment policies and population immunity at T_0.

A3.1 Distribution of paralytic cases and costs

Figure A1 and Figure A2 show the cumulative distribution functions (CDFs) and probability density functions (PDFs), respectively, of the expected aggregate costs (on the left) and the expected aggregate number of paralytic cases (on the right) for the major immunization options and the four income groups. The x-axis in each panel extends to the largest 99th percentile among the four routine vaccination options. We hold the inputs reflecting major assumptions, preferences, and policy choices at their base case values, while randomly sampling outbreaks and uncertain inputs as described. In the low-income group, routine IPV represents the most costly option, but in the middle income group OPV with SIAs emerges as more costly than IPV. This occurs because of the differences in administration costs per dose during SIAs, which we based on reported estimates of 0.23, 0.64, and 1.9 US$2002 in low, lower middle and upper middle-income countries, respectively,[13] and because of the reduced schedule of only two IPV doses. No routine represents by far the least costly option, and OPV without SIAs remains much less expensive than IPV or OPV with SIAs in all three low and middle-income groups. Given that the outbreak-dependent response cost represents the main country-level cost component with no routine immunization (and only passive surveillance), no routine yields the most variable costs.

Figure A1: Cumulative distribution functions of the aggregated country-level costs (including treatment costs) and paralytic cases in the base case. Dash-dotted line = OPV with SIAs; dashed line = OPV without SIAs; dotted line = IPV; solid line = no routine. The x-axes run up to the largest 99th percentile among the distributions in the same panel.

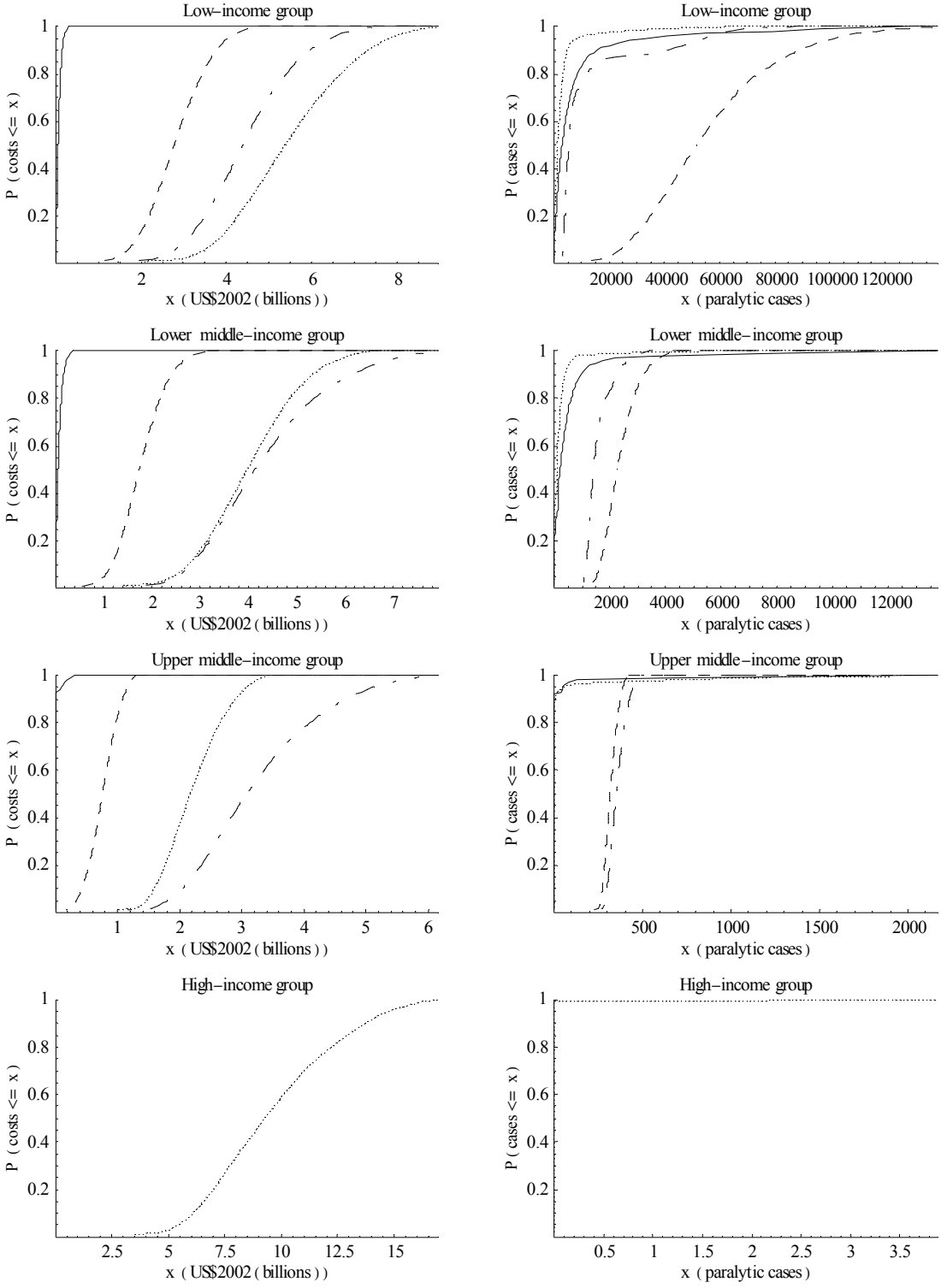


Figure A2: Probability density functions of the aggregated country-level costs (including treatment costs) and paralytic cases in the base case. Dash-dotted line = OPV with SIAs; dashed line = OPV without SIAs; dotted line = IPV; solid line = no routine. The x-axes run up to the largest 99th percentile among the distributions in the same panel.

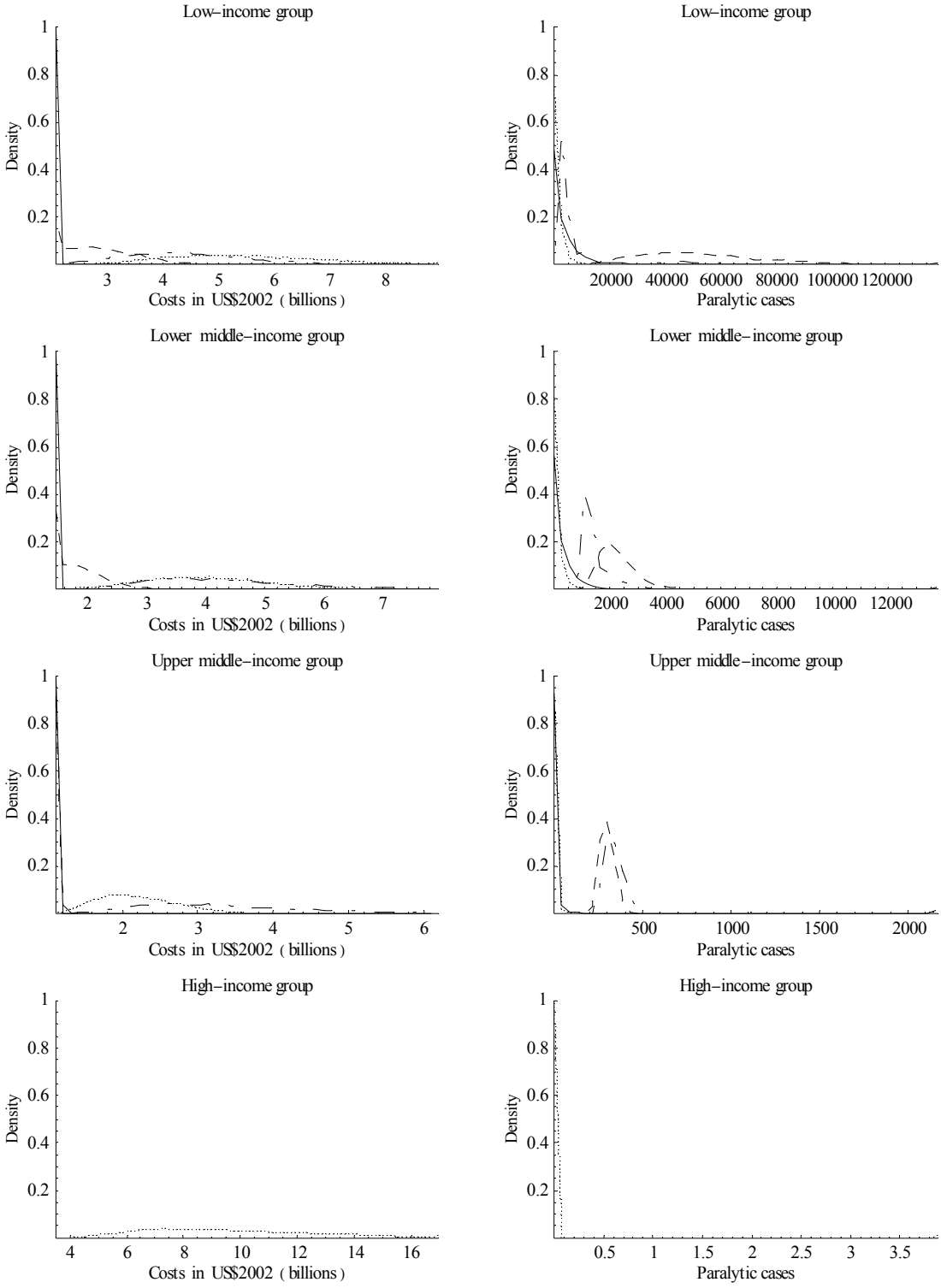


Table A5 provides summary statistics for the results, including the mean (μ), standard deviation (σ), coefficient of variation (CV = σ/μ expressed as a percent), and selected percentiles. The CVs clearly demonstrate the relatively larger variability of the costs of the no routine options and range from 113% to ~ 530%, compared to IPV or OPV immunization costs, whose CVs range from 22% to 32%.

Table A5: Summary statistics of output distributions for costs (including treatment costs for paralytic cases) and paralytic cases in the base case.

COSTS (billions US$2002)										
Income level, immunization policy	*Mean*	*Standard deviation*	*CV*	*2.5th percentile*	*5th percentile*	*50th percentile*	*95th percentile*	*97.5th percentile*	*99th percentile*	*99.9th percentile*
LOW, OPV, SIAs	4.51	1.13	25%	2.56	2.82	4.41	6.55	7.01	7.45	8.36
LOW, OPV, no SIAs	2.87	0.75	26%	1.55	1.72	2.81	4.15	4.44	4.79	5.79
LOW, IPV, no SIAs	5.53	1.37	25%	3.23	3.50	5.40	7.96	8.42	8.97	10.13
LOW, no routine, no SIAs	0.09	0.10	113%	0.00	0.00	0.07	0.22	0.28	0.36	0.86
LMI, OPV, SIAs	4.38	1.31	30%	2.40	2.60	4.16	6.89	7.40	7.94	9.00
LMI, OPV, no SIAs	1.80	0.50	28%	0.94	1.06	1.76	2.68	2.90	3.16	4.13
LMI, IPV, no SIAs	4.05	1.00	25%	2.28	2.51	4.00	5.81	6.15	6.56	7.40
LMI, no routine, no SIAs	0.08	0.11	130%	0.00	0.00	0.06	0.25	0.30	0.39	0.85
UMI, OPV, SIAs	3.30	1.04	32%	1.72	1.88	3.13	5.24	5.71	6.19	7.04
UMI, OPV, no SIAs	0.78	0.25	31%	0.32	0.38	0.78	1.20	1.26	1.31	1.45
UMI, IPV, no SIAs	2.24	0.50	22%	1.40	1.50	2.19	3.14	3.30	3.45	3.70
UMI, no routine, no SIAs	0.02	0.10	528%	0.00	0.00	0.00	0.14	0.24	0.39	1.14
HIGH, IPV, no SIAs	9.71	2.92	30%	5.13	5.58	9.33	15.06	15.97	16.96	18.70
PARALYTIC CASES										
LOW, OPV, SIAs	12,759	18,498	145%	2,918	3,098	5,281	56,757	65,379	88,490	124,227
LOW, OPV, no SIAs	56,783	25,789	45%	20,337	24,104	52,240	105,566	120,788	138,974	177,089
LOW, IPV, no SIAs	4,181	26,822	642%	0	0	1,202	9,882	31,727	63,369	212,334
LOW, no routine, no SIAs	11,305	57,945	513%	0	0	2,983	40,913	87,511	131,018	520,553
LMI, OPV, SIAs	1,592	509	32%	1,081	1,116	1,422	2,629	3,008	3,410	4,638
LMI, OPV, no SIAs	2,393	654	27%	1,446	1,544	2,279	3,613	3,982	4,412	5,488
LMI, IPV, no SIAs	333	1,958	588%	0	0	105	599	1,082	5,834	26,799
LMI, no routine, no SIAs	777	4,774	614%	0	0	220	1,720	5,226	13,756	44,974
UMI, OPV, SIAs	359	51	14%	281	290	353	449	466	488	612
UMI, OPV, no SIAs	322	40	12%	257	264	318	392	407	420	457
UMI, IPV, no SIAs	81	587	720%	0	0	0	99	931	2,167	8,840
UMI, no routine, no SIAs	55	428	778%	0	0	0	57	185	2,023	5,369
HIGH, IPV, no SIAs	1	9	1237%	0	0	0	0	0	4	142

Considering the number of paralytic cases, Figure A1, Figure A2 and Table A5 show important differences with respect to the income groups and routine immunization policies. A policy of OPV without SIAs clearly yields the largest expected number of paralytic cases in the low and lower middle-income groups, but we observe longer tails of the distribution with no routine or IPV. These longer tails yield higher numbers of paralytic cases for the upper percentiles and higher CVs (e.g., CV ≤ 145% with OPV, CV > 500% with no routine or IPV). In the low-income group, OPV with SIAs leads to a similar number of expected cases as no routine given that SIAs will typically limit the size of frequent cVDPV outbreaks, but in the lower middle-income group the VAPP and cVDPV outbreak burden with OPV and SIAs tends to exceed that from outbreaks with IPV or no routine immunization. In the upper middle-income group, very few outbreaks take off even with routine OPV without SIAs. Consequently, the burden (almost all VAPP) remains greater with SIAs than without. Figure A1 reveals the highly skewed distribution of the numbers of cases in high-income countries, which includes a very high probability of 0 cases and only an approximately 2% probability of a positive number of cases.

Note that the x-axis extends only to the 99th percentile; the simulation of 10,000 iterations yielded a maximum of 289 paralytic cases).

A3.2 Distribution of differences in outcomes between immunization policies

Table A6 provides estimates of the difference in numbers of paralytic cases found when comparing the immunization policies. We use distributions to characterize the estimated number of cases with each policy, and we define p(diff > 0) as the probability of observing more cases with policy 1 than with policy 2 (i.e., the number of iterations where diff > 0 divided by 10,000). Thus, as shown in Table A6, we estimate a probability of approximately 96-98% that more cases would occur with a policy of OPV without SIAs than with no routine. Since both no routine and IPV yield some probability of zero cases, we added a column to indicate the probability of observing no difference between them, denoted p(diff=0). Looking at the results for the upper middle-income group, we estimate an approximately 6% probability of observing more cases with IPV than with no routine (which implies an approximately 100%-6% - 81% = 13% probability of observing more cases with no routine than with IPV). This probability of approximately 6% of more cases with IPV than with no routine arises due to the assumed risk of a release from an IPV production site. Given that in those 6% of the iterations the outbreaks tend to be large (especially if they occur long after cessation), they result in a positive expected difference in cases for IPV minus no routine, which according to an expected ICER criterion would imply that no routine dominates IPV immunization.

Table A6: Comparisons of the difference in numbers of estimated paralytic cases for different immunization policies. (diff = number of cases with policy 1 – number of cases with policy 2; Mean diff = *E*[number of cases with policy 1 – number of cases with policy 2])

Policy 1:	*OPV without SIAs*		*OPV without SIAs*		*IPV*		
Policy 2:	*No routine*		*IPV*		*no routine*		
	Mean diff	*p(diff > 0)*	*Mean diff*	*p(diff > 0)*	*Mean diff*	*P(diff = 0)*	*p(diff > 0)*
Low income group	4,500	0.960	53,000	0.987	-7,100	0.066	0.036
Lower middle-income group	1,600	0.965	2,100	0.982	-440	0.111	0.023
Upper middle-income group	270	0.977	240	0.963	26	0.814	0.057

For all income groups, very small (i.e., less than 4%) positive probabilities exist that no routine or IPV yields more cases than OPV without SIAs, and despite the larger tails with IPV or no routine, the expected values remain higher for OPV without SIAs (Table A6).

Figure A3 provides the full cumulative distributions of the difference in number of paralytic cases between the main immunization options for the low and middle-income groups, revealing long tails in the differences. Figure A4 highlights a distribution not included in Figure A3 (i.e., the difference in paralytic cases with IPV minus OPV with SIAs in the low-income group). Although in only approximately 7% of iterations we observed a higher number of cases with IPV

than with OPV and SIAs, which would imply that the option of OPV with SIAs dominates IPV, in 93% of iterations we observed more cases with OPV with SIAs. The expected difference remains negative (i.e., ~ -8,500 cases). The negative INB of IPV vs. OPV with SIAs in the low-income group remains very robust against possible changes in the sign of the effectiveness, with an expected INB of approximately -1 billion US$2002 and a standard error of less than 0.1.

Figure A3: Cumulative distribution functions of the difference in paralytic cases between the immunization policies in the base case. The x-axes run from the 0.1 to the 99.9 percentile. OPV indicates OPV without SIAs.

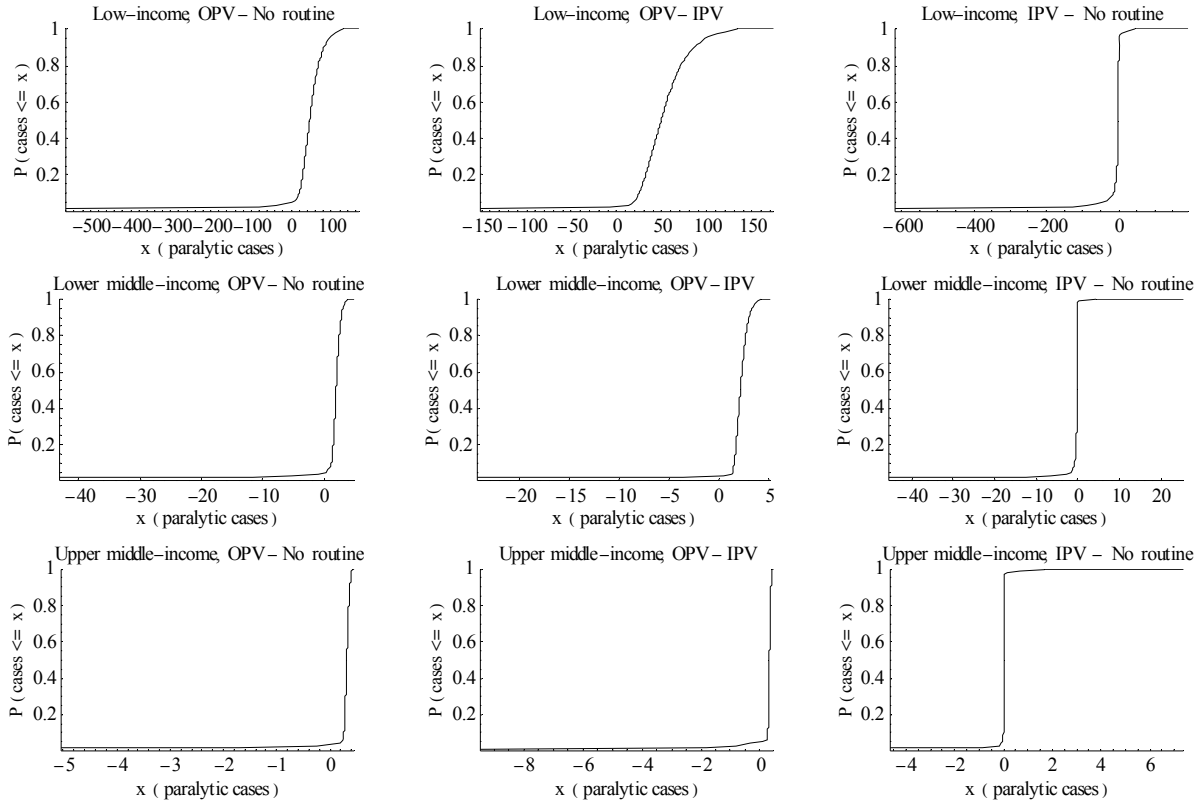


Figure A4: Cumulative distribution of the number of paralytic cases with IPV minus OPV with SIAs in the low-income group. The x-axes run from the 0.1 to the 99.9 percentile.

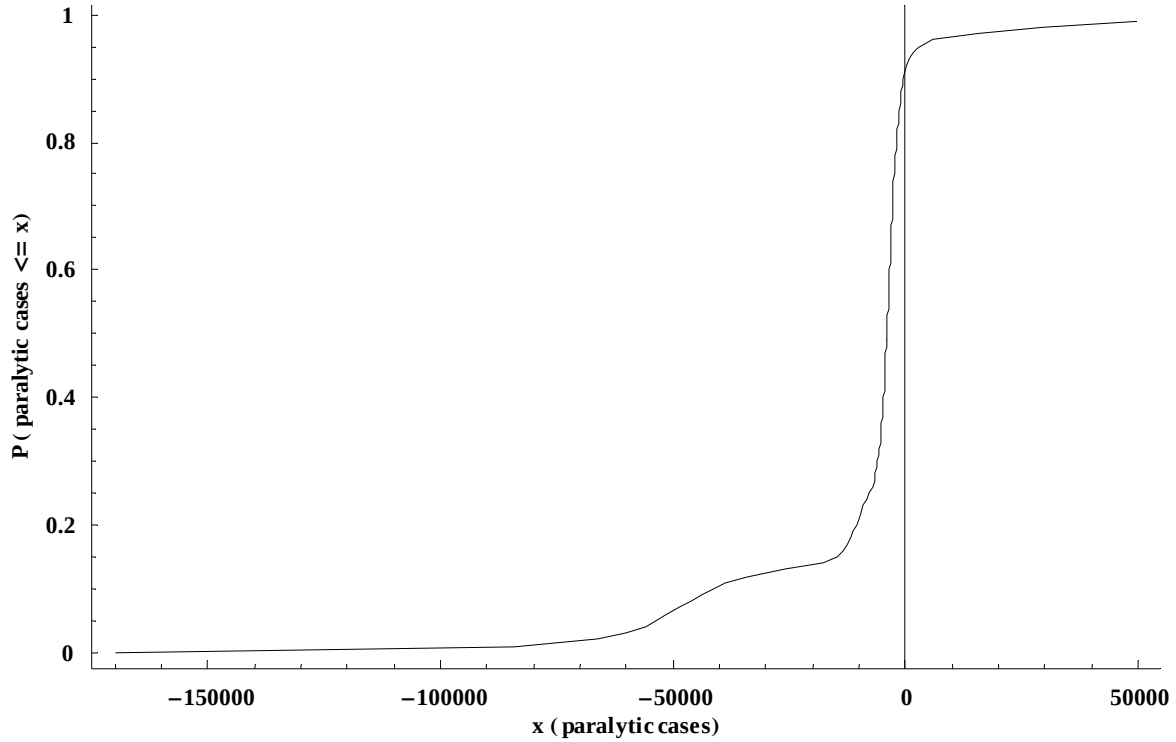


Table A7 shows the probabilities of positive or negative INBs corresponding to the distributions shown in Figure 2 in the main paper as well as the comparison of IPV vs. no routine. This table emphasizes the very high likelihood of positive INBs of no routine vs. OPV (without SIAs), and of negative INBs of IPV vs. OPV (without SIAs) or no routine, based on 10,000 iterations.

Table A7: Expected value and probability of negative or positive incremental net benefits (P(<0) or P(>0), respectively) for different policy comparisons.

	No routine vs. OPV (without SIAs)			*IPV vs. OPV (without SIAs)*			*IPV vs. no routine*		
	Mean	*P(< 0)*	*P(> 0)*	*Mean*	*P(< 0)*	*P(> 0)*	*Mean*	*P(< 0)*	*P(> 0)*
Low-income group	3.020	0.002	0.998	-2.383	0.940	0.060	-5.403	>0.999	<0.001
Lower middle-income group	1.749	0.001	0.999	-2.215	0.982	0.018	-3.964	>0.999	<0.001
Upper middle-income group	0.781	0.005	0.996	-1.448	>0.999	<0.001	-2.218	>0.999	<0.001

A3.3 Departures from the base case assumptions

This subsection provides further breakdowns of the results presented in Table 2 in the main paper.

A3.3.1 Impact of the discount rate

Table A8 shows how the discount rate affects the major model outcomes. Given continued greater costs and disease burden with continued OPV (without SIAs) than with no routine (see Figure 3b in the main paper), lowering the discount rate results in higher INBs throughout the 20-year time horizon. Similarly, the substantial costs in every year for routine IPV immunization drive the negative INBs, causing more negative INBs as the discount rate decreases. However, the ICER depends more on the effectiveness, which remains positive over time in the low and lower middle-income groups but becomes negative in the upper middle-income group at the end of the 20-year time horizon (see Figure 3b in the main paper). Thus, while the results remain robust with respect to INBs, the impact of the discount rate on the attractiveness as interpreted through ICERs remains ambiguous.

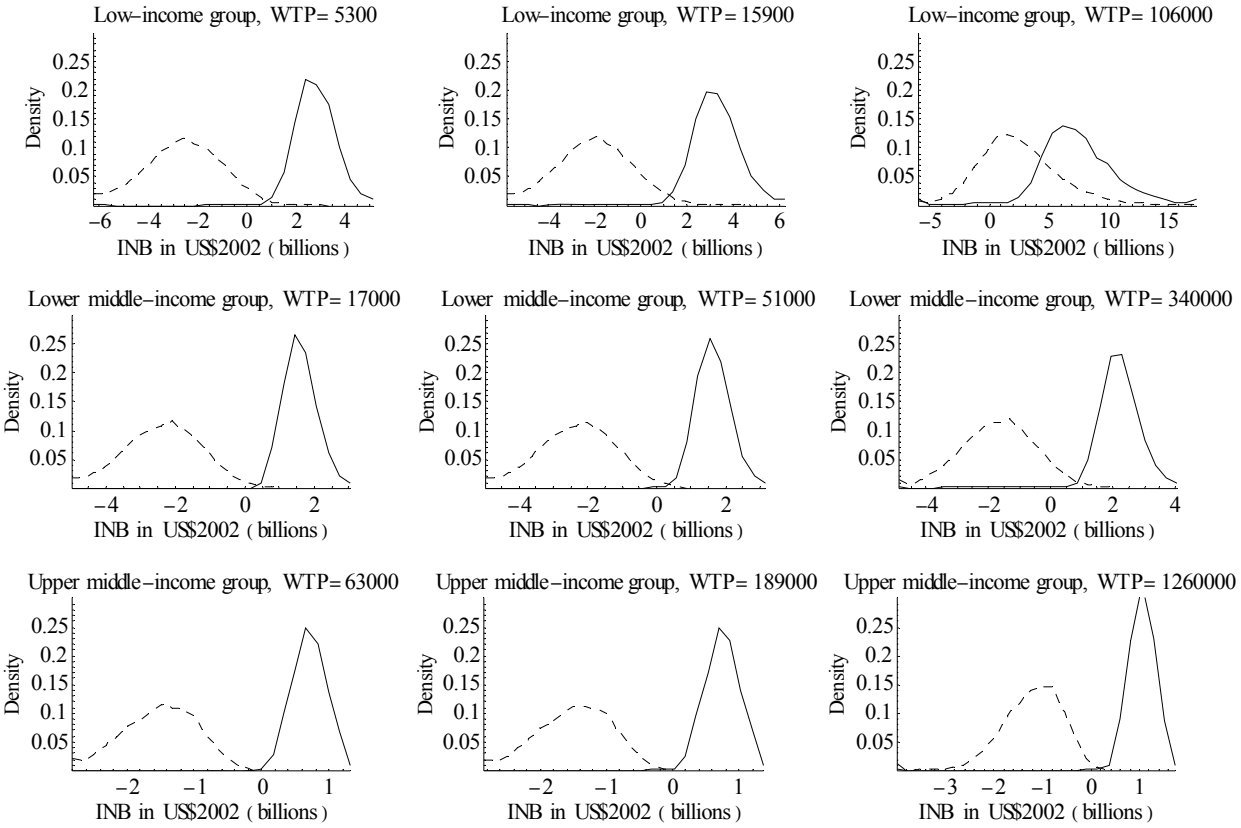
Table A8: Impact of discount rate on expected aggregate cost-effectiveness ratios (ICERs) and incremental net benefits (INBs).

Policy comparison, income group	*ICER (US$2002 per paralytic case) with discount rate of:*			*INB (billions US$2002) with discount rate of:*		
	0%	*3% (base case)*	*7%*	*0%*	*3% (base case)*	*7%*
No routine vs. OPV (without SIAs), LOW	Cost and life-saving	Cost and life-saving	Cost and life-saving	4.43	3.02	2.11
No routine vs. OPV (without SIAs), LMI	Cost and life-saving	Cost and life-saving	Cost and life-saving	2.34	1.75	1.28
No routine vs. OPV (without SIAs), UMI	Cost and life-saving	Cost and life-saving	Cost and life-saving	1.04	0.78	0.58
IPV vs. OPV (without SIAs), LOW	46,169	50,603	57,634	-2.55	-2.38	-1.90
IPV vs. OPV (without SIAs), LMI	1,063,075	1,092,184	1,138,418	-2.78	-2.21	-1.68
IPV vs. OPV (without SIAs), UMI	6,516,348	6,045,445	5,595,423	-1.84	-1.44	-1.08

A3.3.2 Impact of the valuation of paralytic cases

Figure A5 shows that increasing the WTP value by 3 or 20 times the per capita GNI per DALY averted (i.e., instead of 1) brings the INB distributions for IPV and no routine closer together. For example, valuing each DALY averted due to prevented paralytic cases at 20 times the per capita GNI in the low-income group results in more overlap of the distributions, indicating more probability that IPV vs. OPV without SIAs emerges as more attractive than no routine vs. OPV without SIAs. In other words, if one accepts an ICER of at least 20 times the GNI per capita for each DALY averted, than IPV becomes a more viable option relative to no routine.

Figure A5: Probability density functions of aggregate incremental net benefit (INB) of no routine vs. OPV without SIAs (solid lines) and IPV vs. OPV without SIAs (dashed lines) with WTP values (in US$2002 per paralytic case) corresponding to 1 (left panes; same as base case), 3 (middle panes), or 20 (right panes) times the per-capita GNI per averted disability-adjusted life-year. The x-axes run from smallest 1st to largest 99th percentile among the two distributions in each panel.



A3.3.3 Impact of the maximum possible outbreak population size

We generate discrete outbreak population sizes based on the actual distribution of population sizes among countries (see methods section in the main paper and Table A1). This approach remains somewhat artificial since poliovirus outbreaks may affect only certain areas of a country, or likewise affect more than one country. In the base case, we match any outbreak that occurs in a country of more than 75 million inhabitants (~69% of outbreaks; see Table A1) to the relevant sub-model run with a population of 100 million, implicitly assuming that the outbreak and response will not go beyond this population (even if the outbreak occurs in a very large country such as China).

Table A9 evaluates the impact on the aggregate number of cases of allowing outbreak population sizes of up to 250 million for outbreaks in countries with over 200 million people (i.e., in 2010 there will consist of China, India, Indonesia, and the United States, representing 45% of the

global population), while using an outbreak population size of 100 million in the sub-model for outbreaks in countries with 75 to 200 million people (i.e., 24% of the global population in 2010). The impact on the expected number of paralytic cases remains moderate given that for large outbreak populations the response often controls the outbreak before it reaches the large number of susceptibles in the population. However, this comes at the expense of using many doses of mOPV, yielding more response VAPP cases and high costs, which are most notable with no routine because for that policy response costs represent the only country-level costs. Table A10 illustrates the effect of the maximum outbreak population size on ICERs and INBs.

Table A9: Impact of the maximum possible outbreak population size on the expected costs, including treatment costs, and number of paralytic cases (5^{th} – 95^{th} percentiles).

Income group, immunization policy	*Costs in billions US$2002 with maximum outbreak population size of:*		*Paralytic cases with maximum outbreak population size of:*	
	100 million (base case)	*250 million*	*100 million (base case)*	*250 million*
LOW, OPV, SIAs	4.51 (2.8 - 6.6)	4.6 (2.86 - 6.61)	12759 (3098 - 56757)	16003 (3103 - 86598)
LOW, OPV, no SIAs	2.87 (1.72 - 4.15)	3.7 (2.19 - 5.7)	56783 (24104 - 105566)	61882 (25581 - 115680)
LOW, IPV, no SIAs	5.53 (3.5 - 7.96)	5.58 (3.56 - 8.01)	4181 (0 - 9882)	5740 (0 - 11350)
LOW, no routine, no SIAs	0.09 (0 - 0.22)	0.17 (0 - 0.44)	11305 (0 - 40913)	15531 (0 - 50157)
LMI, OPV, SIAs	4.38 (2.6 - 6.89)	4.39 (2.61 - 6.91)	1592 (1116 - 2629)	1609 (1117 - 2704)
LMI, OPV, no SIAs	1.8 (1.06 - 2.68)	2.41 (1.35 - 3.88)	2393 (1544 - 3613)	2546 (1597 - 3904)
LMI, IPV, no SIAs	4.05 (2.51 - 5.81)	4.1 (2.55 - 5.86)	333 (0 - 599)	431 (0 - 638)
LMI, no routine, no SIAs	0.08 (0 - 0.25)	0.16 (0 - 0.49)	777 (0 - 1720)	889 (0 - 1900)
UMI, OPV, SIAs	3.3 (1.88 - 5.24)	3.3 (1.88 - 5.24)	359 (290 - 449)	357 (290 - 443)
UMI, OPV, no SIAs	0.78 (0.38 - 1.2)	0.79 (0.38 - 1.22)	322 (264 - 392)	323 (264 - 396)
UMI, IPV, no SIAs	2.24 (1.5 - 3.14)	2.24 (1.5 - 3.15)	81 (0 - 99)	104 (0 - 106)
UMI, no routine, no SIAs	0.02 (0 - 0.14)	0.03 (0 - 0.14)	55 (0 - 57)	56 (0 - 55)
HIGH, IPV, no SIAs	9.71 (5.58 - 15.06)	9.72 (5.58 - 15.06)	1 (0 - 0)	1 (0 – 0)

Table A10: Impact of the maximum possible outbreak population size on expected cost-effectiveness ratios (ICERs) and incremental net benefits (INBs) for the major policy comparisons

Policy comparison, income group	*ICER (US$2002 per paralytic case) with maximum outbreak population size of:*		*INB (billion US$2002) with maximum outbreak population size of:*	
	100 million (base case)	*250 million*	*100 million (base case)*	*250 million*
No routine vs. OPV (without SIAs), LOW	Cost and life-saving	Cost and life-saving	3.02	3.78
No routine vs. OPV (without SIAs), LMI	Cost and life-saving	Cost and life-saving	1.75	2.28
No routine vs. OPV (without SIAs), UMI	Cost and life-saving	Cost and life-saving	0.78	0.78
IPV vs. OPV (without SIAs), LOW	51,103	34,026	-2.38	-1.58
IPV vs. OPV (without SIAs), LMI	1,092,184	799,356	-2.21	-1.65
IPV vs. OPV (without SIAs), UMI	6,045,445	6,621,907	-1.44	-1.44

A3.3.4 Impact of the surveillance policy

Surveillance impacts the timeliness of outbreak detection and therefore of the response. For the base case, we assumed detection of any outbreak at the time of onset of the 5th paralytic case, corresponding to our model interpretation of passive surveillance, which comes at no country-level costs.[3] Alternatively, the current intensive AFP surveillance system might continue and maintain the ability to identify single paralytic cases and detect outbreaks by the time of onset of the first paralytic case. Note that we include the time from onset until laboratory confirmation in the response delay time, which we discuss below.

Table A11 displays the impressive reduction in expected aggregate disease burden with AFP compared to passive surveillance. However, this comes at a substantial cost, and consequently the cost-effectiveness of adding AFP surveillance appears poor for any income group and immunization policy. However, maintaining AFP surveillance can either improve or reduce the attractiveness of no routine or IPV vs. OPV without SIAs compared to the base case with passive surveillance, depending on which expected burden it reduces most (i.e., that of OPV or the alternative) (Table A12). For these comparisons, the costs of AFP surveillance cancel out since they occur both with the comparator and with the alternative.

Table A11: Expected aggregate cost (including treatment costs) and paralytic cases, and cost-effectiveness ratios (ICERs) for acute flaccid paralysis (AFP) vs. passive surveillance,

by routine immunization policy and income group. The costs only include field surveillance costs and do not account for any changes in the global costs of the polio laboratory network.

Routine immunization policy, income group	*Costs (billions US$2002)*		*Paralytic Cases*		*ICER of AFP surveillance (US$2002/ paralytic case)*
	AFP	*Passive (base case)*	*AFP*	*Passive (base case)*	
LOW, OPV without SIAs	3.89	2.84	17,181	56,783	26,614
LOW, IPV	6.58	5.53	1,933	4,181	471,950
LOW, no routine	1.14	0.08	4,923	11,305	165,149
LMI, OPV without SIAs	2.45	1.79	1,563	2,393	789,323
LMI, IPV	4.70	4.05	125	333	3,484,655
LMI, no routine	0.73	0.08	211	777	1,144,031
UMI, OPV without SIAs	1.11	0.77	319	322	110,776,597
UMI, IPV	2.58	2.23	33	81	7,779,150
UMI, no routine	0.36	0.02	14	55	8,344,580
HIGH, IPV	10.48	9.71	0	1	1,666,636,572

Table A12: Impact of the surveillance policy on expected cost-effectiveness ratios (ICERs) and incremental net benefits (INBs) for the major policy comparisons.

Policy comparison, income group	*ICER (US$2002 per paralytic case)*		*INB (billion US$2002)*	
	AFP	*Passive (base case)*	*AFP*	*Passive (base case)*
No routine vs. OPV (without SIAs), LOW	Cost and life-saving	Cost and life-saving	2.83	3.02
No routine vs. OPV (without SIAs), LMI	Cost and life-saving	Cost and life-saving	1.75	1.75
No routine vs. OPV (without SIAs), UMI	Cost and life-saving	Cost and life-saving	0.78	0.78
IPV vs. OPV (without SIAs), LOW	176,284	51,103	-2.60	-2.38
IPV vs. OPV (without SIAs), LMI	1,566,244	1,097,184	-2.22	-2.21
IPV vs. OPV (without SIAs), UMI	5,120,177	6,095,445	-1.43	-1.44

Table A13 explores the impact of a hypothetical global environmental surveillance system on the expected disease burden for the different routine immunization policies. This analysis remains preliminary given that no such system currently exists or is planned for and therefore it remains difficult to quantify its costs and sensitivity.[13] Here, we assumed that the environmental

surveillance system would detect the 5000th effective infection. When counting effective infections, this approach assigns lower weight to infecteds with shorter duration of infection or lower viral output due to prior immunity than to previously fully susceptible infecteds.[3] Although all reductions in expected burden compared to passive surveillance remain small, Table A13 shows that with routine IPV immunization, environmental surveillance offers the greatest potential to detect infections before 5 paralytic cases occur due to the amount of virus that IPV-vaccinees typically excrete.

Table A13: The impact of a hypothetical global environmental surveillance system on the expected disease burden.

Income group, routine immunization policy	*Expected paralytic cases with only passive surveillance (base case)*	*Expected paralytic cases with passive and environmental surveillance*	*Reduction*
LOW, OPV without SIAs	56,783	56,783	0.0%
LOW, IPV	4,181	4,166	0.4%
LOW, no routine	11,305	11,305	0.0%
LMI, OPV without SIAs	2,393	2,393	0.0%
LMI, IPV	333	311	6.6%
LMI, no routine	777	777	0.0%
UMI, OPV without SIAs	322	322	0.0%
UMI, IPV	81	77	5.5%
UMI, no routine	55	55	0.0%
HIGH, IPV	1	1	6.6%

A3.3.5 Impact of the response delay

The response delay equals the time from outbreak detection to initialization of the first mass immunization response round and represents the key controllable characteristic of polio outbreak response.[14] Not surprisingly, we observe a great impact of the response delay on the expected effectiveness (

Table A14). As with AFP surveillance, the impact of the response delay on policy comparisons depends on the immunization policy with the largest reduction in the number of cases, which yields an ambiguous impact of this policy choice on the incremental ICERs and INBs in

Table A14. These results do not associate a financial cost with the ability to respond faster, although clearly access to a stockpile would influence the response delay.

Table A14: Impact of response delay on the expected cost-effectiveness ratios (ICERs) and incremental net benefits (INBs) for the major policy comparisons.

Policy comparison, income group	*Cases prevented*		*ICER (US$2002 per paralytic case)*		*INB (billions US$2002)*	
	45 days	*70 days (base case)*	*45 days*	*70 days (base case)*	*45 days*	*70 days (base case)*
No routine vs. OPV (without SIAs), LOW	15,450	45,478	Cost and life-saving	Cost and life-saving	2.85	3.02
No routine vs. OPV (without SIAs), LMI	1,671	1,616	Cost and life-saving	Cost and life-saving	1.75	1.75
No routine vs. OPV (without SIAs), UMI	306	267	Cost and life-saving	Cost and life-saving	0.78	0.78
IPV vs. OPV (without SIAs), LOW	16,829	52,603	159,229	50,603	-2.59	-2.38
IPV vs. OPV (without SIAs), LMI	1,748	2,060	1,287,889	1,092,184	-2.22	-2.21
IPV vs. OPV (without SIAs), UMI	279	240	5,202,765	6,045,445	-1.43	-1.44

Although neither the surveillance nor the response delay dramatically alter the incremental ICERs or INBs for policy comparisons, both dramatically limit the consequences associated with any individual immunization option.

A3.3.6 Impact of the containment policy

In our model, a failure to maintain containment guidelines[15] leads to a 5-fold increase in the risk of unintentional poliovirus release.[16] Thus, not maintaining containment substantially increases the expected disease burden long after OPV cessation, especially with routine IPV given the risks associated with handling wild poliovirus for IPV production (

Table A15).[16] However, the effect of this risk on the ICERs and INBs of policy comparisons remains small given the small number of *additional prevented* cases with IPV or no routine compared to OPV without SIAs (Table A16). The only exception arises in the comparison of IPV to OPV in the upper middle-income group, for which we modeled a high baseline risk of IPV production site release given the greater probability of domestic IPV production in that group. The number of prevented cases here changes sign, and the ICER becomes "dominated." In contrast, the INB does not show a large impact to this change due to the unchanged IPV immunization costs.

Table A15: The impact of the containment policy system on the expected disease burden.

Income group, routine immunization policy	*Expected paralytic cases with maintained containment (base case)*	*Expected paralytic cases without maintained containment*	*Increase*
LOW, OPV without SIAs	56,783	56,809	0.0%
LOW, IPV	4,181	14,403	244.5%
LOW, no routine	11,305	14,114	24.8%
LMI, OPV without SIAs	2,393	2,393	0.0%
LMI, IPV	333	1,069	221.1%
LMI, no routine	777	939	20.8%
UMI, OPV without SIAs	322	322	0.0%
UMI, IPV	81	388	376.2%
UMI, no routine	55	117	113.2%
HIGH, IPV	1	3	248.1%

Table A16: Impact of containment policy on the expected cost-effectiveness ratios (ICERs) and incremental net benefits (INBs) for the major policy comparisons.*

Policy comparison, income group	*Cases prevented*		*ICER (US$2002 per paralytic case)*		*INB (billions US$2002)*	
	Maintained (base case)	*Not maintained*	*Maintained (base case)*	*Not maintained*	*Maintained (base case)*	*Not maintained*
No routine vs. OPV (without SIAs), LOW	45,478	42,695	Cost and life-saving	Cost and life-saving	3.02	3.00
No routine vs. OPV (without SIAs), LMI	1,616	1,454	Cost and life-saving	Cost and life-saving	1.75	1.74
No routine vs. OPV (without SIAs), UMI	267	204	Cost and life-saving	Cost and life-saving	0.78	0.76
IPV vs. OPV (without SIAs), LOW	52,603	42,406	50,603	63,081	-2.38	-2.45
IPV vs. IPV (without SIAs), LMI	2,060	1,324	1,092,184	1,707,375	-2.21	-2.24
IPV vs. OPV (without SIAs), UMI	240	-66	6,093,089	Dominated	-1.44	-1.49

* The estimates do not include expected global costs of 6.7 million US$2002 over the 20-year time horizon for enforcing containment, which cancel out because both the comparator and the alternative policies assume the same containment policy in this table (keeping "without containment" fixed for the comparator program does not change the ICERs and INBs much since containment yields little impact on total cases with continued OPV).

In Table A17, we show how the outcomes change if we model the IPV production site release rate in the upper middle-income group as equal to this rate in the lower income groups (i.e., instead of the base case for which we used a rate one order of magnitude greater than that of the lower income groups; see Table 1 in the main paper). While altering the assumption about the likelihood of domestic IPV production changes the comparison of no IPV vs. no routine from cost-ineffective to "dominated," unlike the failure to maintain containment this does not change the comparison of IPV vs. OPV without SIAs to "dominated."

Table A17: Impact of the assumption that upper middle-income countries may produce IPV domestically and face the base case risk (0.01) or lower risk (0.001) of uninentional IPV production site release per 100 million people per year.

Aggregate upper-middle income group outcomes	*Base case*	*Lower IPV-release risk*
Cost (including treatment costs; billions US$2002)		
OPV (without SIAs)	0.78	0.78
IPV	2.23	2.22
No routine	0.02	0.02
Paralytic cases		
OPV (without SIAs)	322	323
IPV	81	27
No routine	55	52
Incremental cost-effectiveness ratio (US$2002/paralytic case)		
IPV vs. OPV (without SIAs)	6,028,687	4,877,290
IPV vs. No routine	Dominated	86,712,573
Incremental net benefits (billions US$2002)		
IPV vs. OPV (without SIAs)	-1.43	-1.42
IPV vs. No routine	-2.21	-2.20

A3.3.7 Impact of the population immunity at T_0

Maximizing population immunity at T_0 reduces the probability and size of outbreaks occurring soon after T_0 (i.e., during the time period of greatest risk due to cVDPVs). The methods section in the main paper describes the different scenarios (RPI, MPI and TIAs) we modeled for the level of population immunity at T_0. Table A18 shows how this plays out in terms of the expected aggregate costs and cases, and gives the ICERs of enhancing population immunity at T_0 for the OPV-cessation scenarios. While achieving maximum population at T_0 (i.e., through a global immunization day) may prevent thousands of expected paralytic cases, due to the substantial costs this appears less cost-effective than enhancing population immunity through targeted campaigns in high-risk areas, which would not prevent as many cases, but offers protection at a much smaller cost. For all combinations of income groups and routine immunization policies, neither option to maximize population immunity appears very cost-

effective based on the average per-capita GNI per DALY averted criterion. In the upper middle-income group with no routine, the expected burden of VAPP cases associated with a full immunization day exceeds the expected number of prevented cases after T_0 compared to the realistic population immunity scenario, making this option "dominated."

Table A18: Expected aggregate costs (including treatment costs) and paralytic cases, and cost-effectiveness ratios (ICERs) for increasing population immunity at T_0 by routine immunization policy and income group.*

Routine immunization policy, income group	*Costs (billions US$2002)*			*Paralytic Cases*			*ICER of increasing population immunity(US$2002/ paralytic case)*	
	RPI	*MPI*	*TIAs*	*RPI*	*MPI*	*TIAs*	*MPI vs. RPI*	*TIAs vs RPI*
No routine, LOW	0.09	0.32	0.13	11,305	6,097	8,947	44,426	19,363
No routine, LMI	0.08	0.43	0.09	777	431	723	1,001,160	216,756
No routine, UMI	0.02	0.35	NA	55	61	NA	Dominated	NA
IPV, LOW	5.53	5.78	5.58	4,181	2,105	3,011	118,759	42,317
IPV, LMI	4.05	4.42	4.07	333	222	308	3,327,465	533,083
IPV, UMI	2.24	2.57	NA	81	71	NA	32,657,610	NA

* The base case assumed the RPI scenario. Alternatives include costs (i.e., approximately 302, 417, and 338 million US$2002 in the low, lower middle, and upper middle-income groups, respectively, to achieve MPI through a global immunization day, or approximately 63 and 18 million US$2002 in the low and lower middle-income groups, respectively, to conduct TIAs) and VAPP cases (i.e., approximately 260, 94, and 25 cases in the low, lower middle, and upper middle-income groups, respectively, to achieve MPI through a global immunization day, or approximately 54 and 4 cases in the low and lower middle, groups, respectively, to conduct TIAs) related to any immunization push prior to T0. MPI = maximum population immunity; NA = not applicable, since we assumed targeted immunization activities only for high-risk areas in low and lower middle-income countries; RPI = realistic population immunity; TIAs = targeted immunization activities)

Table A19 shows the impact of the additional immunization activities on the comparison of IPV or no routine versus OPV without SIAs with RPI fixed for the comparator (i.e., OPV without SIAs). Consistent with the high ICERs in Table A18, the attractiveness of IPV or no routine vs. OPV without SIAs does not substantially improve, or reduce, upon addition of activities to enhance population immunity at T_0.

Table A19: Impact of the population immunity at T_0 on the expected cost-effectiveness ratios (ICERs) and incremental net benefits (INBs) for the major policy comparisons, assuming OPV without SIAs and with RPI as the comparator program.

Routine immunization policy, income group	*ICER of given policy vs. OPV without SIAs and RPI (US$2002 per paralytic case)*			*INB of given policy vs. OPV without SIAs and RPI (billions US$2002)*		
	RPI (base case)	*MPI*	*TIAs*	*RPI (base case)*	*MPI*	*TIAs*
No routine, LOW	Cost and life-saving	Cost and life-saving	Cost and life-saving	2.96	2.75	2.92
No routine, LMI	Cost and life-saving	Cost and life-saving	Cost and life-saving	1.72	1.38	1.71
No routine, UMI	Cost and life-saving	Cost and life-saving	NA*	0.77	0.44	NA
IPV, LOW	51,814	54,357	51,608	-2.45	-2.68	-2.49
IPV, LMI	1,107,728	1,221,369	1,100,785	-2.25	-2.61	-2.26
IPV, UMI	6,083,098	7,158,454	NA	-1.45	-1.78	NA

* NA = not applicable, since we assumed targeted immunization activities only for high-risk areas in low and lower middle-income countries.

A3.4 Sensitivity analysis results for discretely distributed inputs

Table A20 shows the effect of the three inputs that we modeled as discrete random variables for the base case on the expected number of cases. Table A20 evaluates the model at the 8 possible combinations of upper and lower values of these inputs following design-of-experiments concepts,[12] while keeping all other inputs continuously distributed (following the distributions in Table 1 in the main paper). The way we discretely modeled these inputs (with R_0 and the coverage also varying not only with each iteration but also with each outbreak) forces us to single them out from the larger probabilistic sensitivity analysis (which we discuss below). Table A20 shows the expected number of paralytic cases for each of the 8 model evaluations and for each of the income groups and routine immunization policies, as well as for the base case. The last rows show the average effects (i.e., the average model output with an input at the high value minus the average model output with that input at the low value, divided by two). Clearly, regardless of the income group or immunization policy, R_0 emerges as the input with the greatest effect, followed by the coverage case (except with continued SIAs, where routine immunization coverage has a relatively low effect), and the cVDPV risk case. Table A20 assumes the low-medium and high-medium cases from Table A2 as low and high values for R_0. If we extend the range for R_0 to the lowest and highest cases, we find the same importance ranking, although the absolute values of the main effects substantially increase (Table A21).

Table A20: Main effect (ME) of R_0, the cVDPV risk case, and routine immunization coverage on the aggregate expected number of cases. Row y_0 gives the result from the base case.

				OPV with SIAs			OPV (without SIAs)			IPV				No routine		
	R0 case	cVDPV risk case	Coverage case	LOW	LMI	UMI	LOW	LMI	UMI	LOW	LMI	UMI	HIGH*	LOW	LMI	UMI
y1	Low-medium	Low-risk	Lowest	5,186	1,370	359	21,641	1,686	317	3,971	150	10	0	4,597	163	7
y2	High-medium	Low-risk	Lowest	10,544	1,574	361	211,726	7,630	369	12,255	1,444	475	3	20,365	1,808	148
y3	Low-medium	High-risk	Lowest	8,692	1,404	359	32,928	1,992	317	4,238	177	10	0	5,142	221	7
y4	High-medium	High-risk	Lowest	30,618	2,235	366	337,019	11,504	400	14,688	1,677	477	3	25,370	2,306	152
y5	Low-medium	Low-risk	Projected	4,999	1,368	359	7,570	1,176	317	1,340	16	2	0	3,534	72	5
y6	High-medium	Low-risk	Projected	9,797	1,525	361	55,178	2,296	318	5,634	452	102	1	15,973	1,087	100
y7	Low-medium	High-risk	Projected	7,930	1,396	359	10,409	1,176	317	1,477	16	2	0	3,888	89	5
y8	High-medium	High-risk	Projected	27,598	2,034	365	86,584	2,968	318	6,820	559	102	1	19,158	1,343	102
y0	Random (base case)			12,759	1,592	359	56,783	2,393	322	4,181	333	81	1	11,305	777	55
ME**(R0 case)				12,938	457.465	4.491	154,490	4,592	34	7,093	943	283	2	15,926	1,500	119
ME(cVDPV risk case)				11,078	307.729	2.358	42,706	1,213	8	1,006	92	1	0	2,272	207	1
ME(coverage case)				-1,179	-65.398	-0.536	-110,893	-3,799	-34	-4,970	-601	-191	-1	-3,231	-477	-26

* For high-income countries, the outbreak rates remain equal for the cVDPV high-risk and low-risk cases
** ME(R0) = (y2+y4+y6+y8-y1-y3-y5-y7)/4; ME(cVDPV risk case) = (y3+y4+y7+y8-y1-y2-y5-y6)/4; ME(coverage case) = (y5+y6+y7+y8-y1-y2-y3-y4)/4

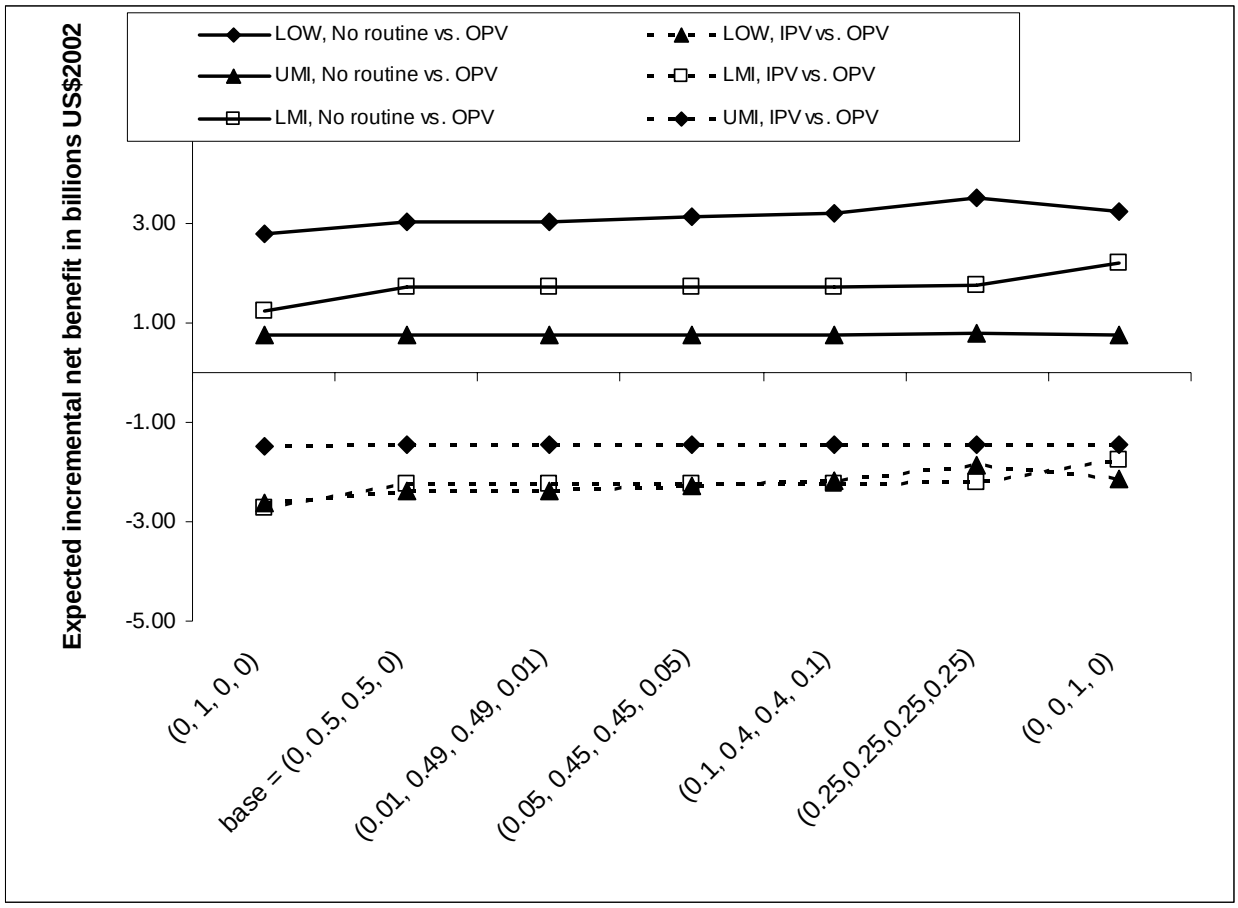
Table A21: Main effect (ME) of R0, the cVDPV risk case, and routine immunization coverage on the aggregate expected number of cases, with R0 ranges from lowest to highest case. Row y0 gives the result from the base case.

				OPV with SIAs			OPV (without SIAs)			IPV				No routine		
	R0 case	cVDPV risk case	Coverage case	LOW	LMI	UMI	LOW	LMI	UMI	LOW	LMI	UMI	HIGH*	LOW	LMI	UMI
y1	Lowest	Low-risk	Lowest	4,220	1,359	359	6,607	1,176	317	934	8	0	0	877	12	1
y2	Highest	Low-risk	Lowest	18,763	3,555	430	766,001	86,706	1,192	30,683	6,238	1,727	138	51,276	10,707	1,166
y3	Lowest	High-risk	Lowest	4,742	1,359	359	8,868	1,176	317	1,017	8	0	0	1,021	12	1
y4	Highest	High-risk	Lowest	63,689	10,261	589	1,223,510	138,034	1,713	42,830	8,662	1,752	138	72,534	15,130	1,203
y5	Lowest	Low-risk	Projected	4,192	1,359	359	4,218	1,175	317	260	1	0	0	695	8	1
y6	Highest	Low-risk	Projected	17,105	3,291	419	311,348	18,895	477	16,665	2,796	611	74	39,082	7,041	870
y7	Lowest	High-risk	Projected	4,628	1,359	359	5,044	1,175	317	312	1	0	0	806	8	1
y8	Highest	High-risk	Projected	57,087	9,192	555	496,331	29,529	573	23,527	4,021	623	74	53,662	9,653	890
y0	Random (base case)			12,759	1,592	359	56,783	2,393	322	4,181	333	81	1	11,305	777	55
ME**(R0 case)				34,716	5,216	139.81	693,113	67,116	672	27,796	5,425	1,178	106	53,288	10,623	1,031
ME(cVDPV risk case)				21,467	3,152	73.62	161,395	15,491	154	4,786	912	9.25	0.00	9,023	1,759	14
ME(coverage case)				-2,100	-333	-11.37	-297,011	-44,079	-463	-8,675	-2,024	-561	-32	-7,866	-2,288	-152

* For high-income countries, the outbreak rates remain equal for the cVDPV high-risk and low-risk cases
** ME(R0) = (y2+y4+y6+y8-y1-y3-y5-y7)/4; ME(cVDPV risk case) = (y3+y4+y7+y8-y1-y2-y5-y6)/4; ME(coverage case) = (y5+y6+y7+y8-y1-y2-y3-y4)/4

Figure 4 in the main paper isolates the distribution of R_0 and demonstrates its important impact on the expected number of paralytic cases. Figure A6 shows the impact of changing the R_0 distribution on the major INB results of the model. Given the prominence of the unchanged vaccination costs in the INBs and the fact that we change the distribution for R_0 simultaneously for the comparator and the alternative, we observe a less dramatic effect of R_0 than for the expected number of paralytic cases. At most, the INBs increases by 42% between the "low-medium only" distribution (i.e., p=(0,1,0,0)) and the "equal probability" distribution (i.e., p=(0.25, 0.25, 0.25, 0.25)) for IPV vs. OPV without SIAs in the lower middle-income group.

Figure A6: Impact of assumptions about the R_0 distribution on the expected aggregate incremental net benefits.*



* The notation indicates the probability weights assigned to the lowest, low-medium, high-medium, and highest R_0 case. E.g. (0,0.5,0.5,0) indicates 50% probability of drawing low-medium or high-medium R_0 for a given outbreak, and 0% probability of drawing lowest or highest R_0. The income group dependent values for each R_0 case are 8, 6, 4, and 2 in the low (LOW), lower middle (LMI), upper middle (UMI), and high (HIGH) income group, respectively, for the lowest case; 10, 8, 6, and 4 in LOW, LMI, UMI, and HIGH, respectively, for the low-medium case; 13, 11, 9, and 6 in LOW, LMI, UMI, respectively for the high-medium case; and 16, 14, 12, and 9 in LOW, LMI, UMI, and HIGH, respectively, for the highest case.

A3.5 Breakdowns of sensitivity analysis results for continuously distributed inputs

The main paper provided sensitivity analysis results for the aggregate low and middle-income groups. Here, we provide the breakdowns by income group and the results focusing on only the numbers of paralytic cases.

A3.5.1 Input sensitivity to the incremental net benefits by income group

Table A22 shows the 8 inputs with the most influence on the INBs of no routine and IPV vs. OPV without SIAs in each income group (except for the high-income group where we did not evaluate these policy comparisons). Consistent with the results aggregated over all income groups in Tables 3 and 4 in the main paper, cost inputs dominate the rankings, although

fracpopopvwithsias remains important in each of the two lowest income groups and inputs related to low-probability outbreaks (e.g., *biorel[3]*, *pobrexcrbase*) also have some smaller impact.

Table A22: Inputs (from Table 1 in the main paper) that correlate most strongly with the incremental net benefits (INB), by income group.

Rank[*]	*INB of no routine vs. OPV without SIAs*					*INB of IPV vs. OPV without SIAs*				
	#	*Input symbol*	*RC*	*PMC*	*CR*	*#*	*Input name*	*RC*	*PMC*	*CR*
Low-income group:										
1	42	nvcopv1	0.741	0.669	0.447	43	nvcipvsingle1	-0.707	-0.711	0.506
2	3	fracpopopvwithsias	0.394	0.380	0.167	41	vpipv1	-0.421	-0.434	0.188
3	82	relnvccostresponse	0.198	0.198	0.039	42	nvcopv1	0.351	0.362	0.131
4	48	corrfactor1	0.158	0.158	0.025	3	fracpopopvwithsias	0.222	0.231	0.061
5	40	vpopv1	0.109	0.101	0.010	46	wastipv1	-0.179	-0.201	0.040
6	28	biorel[3]	-0.059	-0.397	0.157	82	relnvccostresponse	0.110	0.115	0.013
7	46	wastipv1	0.034	0.030	0.001	48	corrfactor1	0.091	0.095	0.009
8	30	pobrelbase	-0.027	-0.030	0.001	40	vpopv1	0.028	0.032	0.001
Lower middle-income group:										
1	53	nvcopv2	0.746	0.695	0.483	54	nvcipvsingle2	-0.601	-0.612	0.374
2	3	fracpopopvwithsias	0.345	0.353	0.141	52	vpipv2	-0.581	-0.591	0.350
3	82	relnvccostresponse	0.220	0.240	0.058	53	nvcopv2	0.308	0.322	0.104
4	59	corrfactor2	0.204	0.209	0.044	57	wastipv2	-0.274	-0.300	0.093
5	51	vpopv2	0.102	0.097	0.010	3	fracpopopvwithsias	0.168	0.176	0.034
6	28	biorel[3]	-0.053	-0.276	0.076	82	relnvccostresponse	0.114	0.121	0.015
7	56	wastopv2	0.045	0.041	0.002	59	corrfactor2	0.084	0.088	0.008
8	6	h[2,3]	-0.038	-0.036	0.001	51	vpopv2	0.061	0.063	0.004
Upper middle-income group:										
1	64	nvcopv3	0.949	0.887	0.786	65	nvcipvsingle3	-0.764	-0.774	0.599
2	62	vpopv3	0.038	0.032	0.001	64	nvcopv3	0.413	0.422	0.179
3	2	contactvapprate	0.032	0.033	0.002	63	vpipv3	-0.397	-0.410	0.168
4	14	pobexcrbase	-0.029	-0.202	0.041	68	wastipv3	-0.071	-0.076	0.006
5	12	dprol	-0.022	-0.024	0.001	62	vpopv3	0.033	0.029	0.001
6	28	biorel[3]	-0.020	-0.113	0.013	18	rrivdpvtend1	-0.025	-0.017	0.000
7	3	fracpopopvwithsias	0.019	0.017	0.000	2	contactvapprate	0.025	0.023	0.001
8	1	recipvapprate	0.016	0.011	0.000	12	dprol	-0.017	-0.021	0.000

[*]Based on absolute values of the rank correlation
CR = correlation ratio; PMC = (Pearson's) product moment correlation; RC = (Spearman's) rank correlation

A3.5.2 Input sensitivity to the number of paralytic cases by income group

Typically, we found three or fewer inputs dominating the uncertainty in the number of paralytic cases for individual policy options. Table A23 and

Table A24 show the 3 inputs with the largest influence on the number of paralytic cases with continued OPV use and OPV cessation, respectively. Typically, inputs related to the number of VAPP cases (*contactvapprate*, *recipvapprate*) and the rate of cVDPV outbreaks (*fracpopopvwithsias, rrcvdpv[3]*) dominate the total burden with continued OPV (Table A23; the correlations with *pobrelbase* and *dprollow* remain very weak). With routine IPV, inputs related to the rate of cVDPV outbreaks (including *h[1,3]*, *h[2,3]*, *relhalflifeipv*, and those mentioned above) still impact the total burden, but also those related to the rate of IPV production site releases, and the probability of iVDPV outbreaks (i.e., *ipvrel[2or1]*, *ipvrel[4or3]*, *pobexcrbase*). With no routine, the uncertainty regarding the risk of intentional poliovirus release (i.e., *biorel[3]*) also emerges as important.

Table A23: Inputs (from Table 1 in the main paper) correlating most strongly with the number of paralytic cases given continued OPV.

Rank[*]	*Paralytic cases with OPV with SIAs*					*Paralytic cases with OPV without SIAs*				
	#	*Input symbol*	*RC*	*PMC*	*CR*	*#*	*Input name*	*RC*	*PMC*	*CR*
Low-income group:										
1	2	contactvapprate	0.353	0.025	0.001	3	fracpopopvwithsias	0.646	0.648	0.486
2	3	fracpopopvwithsias	-0.073	-0.054	0.004	13	dprollow	-0.020	-0.019	0.000
3	1	recipvapprate	0.028	0.007	0.000	1	recipvapprate	-0.019	-0.016	0.000
Lower middle-income group:										
1	2	contactvapprate	0.592	0.342	0.117	3	fracpopopvwithsias	0.577	0.586	0.396
2	1	recipvapprate	0.180	0.108	0.012	2	contactvapprate	0.260	0.248	0.062
3	3	fracpopopvwithsias	-0.030	-0.038	0.001	1	recipvapprate	0.072	0.069	0.005
Upper middle-income group:										
1	2	contactvapprate	0.925	0.890	0.792	2	contactvapprate	0.872	0.870	0.758
2	1	recipvapprate	0.290	0.283	0.080	1	recipvapprate	0.343	0.352	0.124
3	30	pobrelbase	-0.021	-0.019	0.000	4	rrcvdpv[3]	0.064	0.072	0.005

[*]Based on absolute values of the rank correlation

CR = correlation ratio; PMC = (Pearson's) product moment correlation; RC = (Spearman's) rank correlation

Table A24: Inputs (from Table 1 in the main paper) correlating most strongly with the number of paralytic cases given OPV cessation.

Rank[*]	*Paralytic cases with IPV*					*Paralytic cases with no routine*				
	#	*Input symbol*	*RC*	*PMC*	*CR*	*#*	*Input name*	*RC*	*PMC*	*CR*
Low-income group:										
1	3	fracpopopvwithsias	0.273	0.008	0.000	3	fracpopopvwithsias	0.264	0.019	0.000
2	25	ipvrel[2or1]	0.107	0.858	0.736	5	h[1,3]	0.236	0.042	0.002
3	5	h[1,3]	0.101	-0.005	0.000	28	biorel[3]	0.161	0.888	0.787
Lower middle-income group:										
1	3	fracpopopvwithsias	0.263	0.020	0.000	3	fracpopopvwithsias	0.265	0.020	0.000
2	6	h[2,3]	0.087	0.003	0.000	6	h[2,3]	0.205	0.019	0.001
3	8	relhalflifeipv	-0.082	-0.016	0.001	28	biorel[3]	0.123	0.845	0.718
Upper middle-income group:										
1	24	ipvrel[4or3]	0.114	0.095	0.009	4	rrcvdpv[3]	0.130	0.009	0.000
2	4	rrcvdpv[3]	0.108	0.015	0.000	14	pobexcrbase	0.095	0.405	0.184
3	30	pobrelbase	0.081	0.046	0.002	3	fracpopopvwithsias	0.086	-0.006	0.000
High-income group:										
1	14	pobexcrbase	0.098	0.060	0.007	NA				
2	24	ipvrel[4or3]	0.077	0.066	0.005					
3	21	reportedpertrueexcretors	-0.062	-0.031	0.001					

[*]Based on absolute values of the rank correlation
CR = correlation ratio; NA = not applicable because we did not model this option; PMC = (Pearson's) product moment correlation; RC = (Spearman's) rank correlation

A3.5.3 Further analysis of the effect of the rate of (un)intentional releases

Despite the small probability of more cases with IPV than with no routine (Table A6), the small risk of an unintentional release from an IPV production site leading to a large outbreak results in a greater expected number of cases with IPV than with no routine in the upper middle-income group (i.e., approximately 81 vs. 55 expected paralytic cases with IPV and no routine, respectively, in the base case). This implies that a hypothetical comparison of IPV vs. no routine in the upper middle-income group would determine that IPV remains "dominated" compared to no routine based on the expected ICER. To further analyze the impact of the rate of unintentional virus release from an IPV manufacturing site (i.e., input *ipvrel[4or3]* for the upper middle-income group), we performed a separate simulation in which we sampled *ipvrel[4or3]* from a uniform distribution on [0,0.05] instead of a lognormal distribution to ensure obtaining sufficient samples across its range. Figure A7 shows the relationship for the number of paralytic cases with IPV minus no routine. The regression line (which approximates the expected difference in paralytic cases for any given value of *ipvrel[4or3]*) starts out negative but becomes positive at a value of *ipvrel[4or3]* of approximately 0.009 releases per 100 million people per year. Thus, the expected positive difference in paralytic cases in the base case remains consistent with our estimated distribution for *ipvrel[4or3]* with mean above this threshold value (i.e., 0.01, see Table 1 in the main paper).

Figure A7: Scatter plot and approximate conditional expectation (or best regression) of the number paralytic cases for IPV minus no routine in the upper-middle income group to the rate of IPV production site releases given routine IPV use (in number of releases per 100 million people per year).

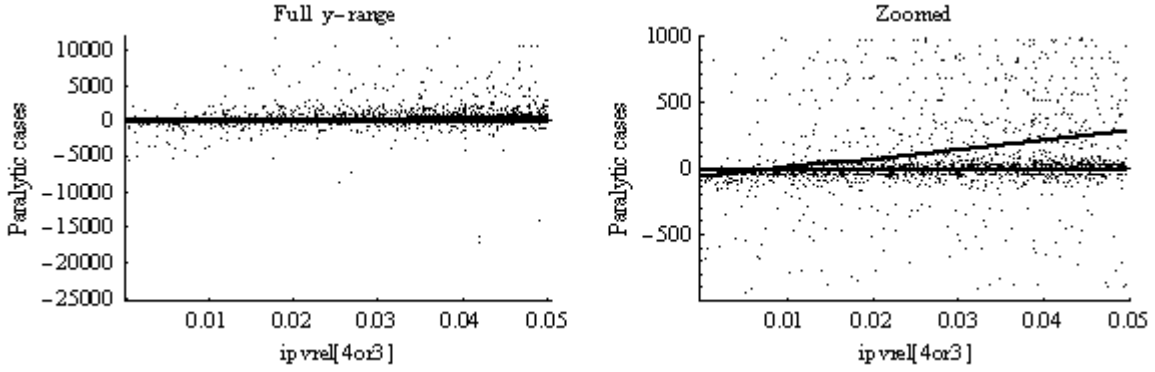


Table A25 shows the threshold values for the rate of unintentional IPV production site releases by income group, based on analyses similar to those above that take uniform distributions for the relevant input. While the threshold values for the rate of unintentional IPV production site releases remain almost equal in each income group, we assumed 10-fold lower mean rates in the base case for the low and lower middle-income group than for the upper middle-income group given the expectation that low and lower middle-income countries would not produce their own IPV. Therefore, the expected number of paralytic cases remains greater with no routine than with IPV in the lower two income groups.

Table A25: Threshold values (i.e., value above which the expected aggregate number of paralytic cases of the alternative exceeds that of the comparator) for the annual rate of unintentional releases from an IPV production site (*ipvrel*) and the annual rate of intentional releases given (*biorel*) per 100 million people.

Income group, scenario	*Estimated mean value for* ipvrel *given routine IPV*	*Threshold value of* ipvrel *(IPV vs. no routine)*
Low-income group	0.001	0.056
Lower middle-income group	0.001	0.057
Upper middle-income group	**0.01**	**0.0086**
Income group, scenario	*Estimated mean value for* biorel[3] *given no routine*	*Threshold value of* biorel[3] *(no routine vs. OPV without SIAs)*
Low-income group	0.001	0.007
Lower middle-income group	0.001	0.005
Upper middle-income group	0.001	0.018

Table A25 also includes threshold values for the rate of intentional releases with respect to the difference in paralytic cases with no routine and OPV (without SIAs). Based on separate simulations that used uniform distributions for the relevant the rate of intentional releases per

100 million people per year (*biorel[3]*), we found that this input must exceed its estimated mean value of 0.001 by at least a factor 5 for the number of cases with no routine to surpass the number of cases with OPV without SIAs.

A6. LIST OF ACRONYMS

AFP = acute flaccid paralysis surveillance
CR = correlation ratio
cVDPV = circulating vaccine-derived poliovirus
DALY = disability-adjusted life year
GNI = gross national income
HIGH = the high-income group
IPV = (enhanced potency) inactivated poliovirus vaccine
ICER = incremental cost-effectiveness ratio
INB = incremental net benefit
iVDPV = immunodeficient vaccine-derived poliovirus
LOW = the low-income group
LMI = the lower middle-income group
ME = main effect
MPI = maximum population immunity
NID = national immunization days
OPV = oral poliovirus vaccine
PMC = product moment correlation
RC = rank correlation
RPI = realistic population immunity
SIAs = supplemental immunization activities
TIAs = targeted immunization activities
UMI = the upper middle-income group
VAPP = vaccine-associated paralytic polio
WTP = willingness-to-pay per prevented paralytic polio case

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