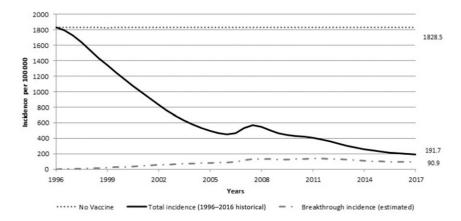# Supplemental Information: Detailed Model Input Parameters

SUPPLEMENTAL FIGURE 4
Projected natural and breakthrough varicella incidence in the United States, all ages, 1996 to 2017. Source: MSD data on file (2021). Data values shown are for 2017 and used to calculate the percentage of total varicella cases that are breakthrough cases.

Adverse Event	Incidence of Adverse Event per 100 000 Doses, by Vaccine									
	DTaP	HepA	HepB	Hib	Influenza	MMR	PCV13	Polio (IPV)	Rotavirus	Varicella
Anaphylaxis	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	—	0.1
Arthralgia	—	—	—	—	—	1000	—	—	—	—
Aseptic meningitis	—	—	—	—	—	0.1	—	—	—	—
Vaccine-related encephalitis	—	—	—	—	—	0.1	—	—	—	—
Guillain-Barre syndrome	—	—	—	—	0.1	—	—	—	—	—
Hypotonic hyporesponsive episodes	8	—	—	—	—	—	—	—	—	—
Injection site reaction (severe)	2000	2000	2000	2000	2000	2000	2000	2000	—	2000
Intussusception	—	—	—	—	—	—	—	—	1	—
Mild complication (eg, fever, rash, systemic reaction)	—	—	—	—	925	—	—	—	—	1000
Mild gastroenteritis or vomiting	—	—	—	—	—	—	—	—	225	—
Parotitis	—	—	—	—	—	1600	—	—	—	—
Protracted crying or screaming	63	—	—	—	—	—	—	—	—	—
Seizure	10	—	—	—	—	33	0.5	—	—	—
Thrombocytopenic purpura	—	—	—	—	—	3	—	—	—	—

—, not applicable. Default adverse event incidence data were obtained from Ekwueme et al (2000)[40] and (Zhou et al 2005)[6] for DTaP; Meltzer et al (2001)[41] and Zhou et al (2014)[14] for HepA; Zhou et al (2014) for Hep B; Zhou et al (2005)[6] for Hib; Prosser et al (2006) for influenza; Zhou et al (2004)[32] for MMR; Zhou et al (2014)[7] for PCV13; Miller et al (1996)[35] and Zhou et al (2014)[78] for IPV; Widdowson et al (2007)[34] and Zhou et al (2014)[7] for rotavirus; and Zhou et al (2005)[6] and Zhou et al (2008)[31] for varicella vaccines. A rate of 1 anaphylaxis event per 1 000 000 doses was assumed for all injected vaccines (Bohlke et al 2003;[77] Erlewyn-Lajeunesse et al 2012;[97] McNeil et al 2016).[116] Two percent of doses for all injected vaccines were assumed to cause severe injection site reactions per expert opinion and review of package inserts for pediatric vaccines.

SUPPLEMENTAL TABLE 6 Costs and QALY Losses per Adverse Event

Adverse Event (Vaccine)	Cost per Adverse Event, USD[a]	QALY Loss per Adverse Event	Sources and Assumptions
Anaphylaxis (all injected vaccines)	7970	0.0200	The default cost for anaphylaxis was calculated based on the resource use from previous economic analyses of DTaP (Ekwueme et al 2000[41]; Zhou et al 2005).[6] These previous studies assumed that 100% of anaphylaxis patients were hospitalized and had an outpatient visit. The default QALY loss for anaphylaxis was obtained from Kamiya et al (2016),[47] citing Lee et al (2005).[51]
Arthralgia (MMR)	179	0.0001	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33,] which assumed that 1% of patients were hospitalized with a mean of 0.5 outpatient visits. Assumed same QALY loss as mild complication, which was obtained from Tu et al (2014).[48]
Aseptic meningitis (MMR)	7210	0.0232	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33,] which assumed that 25% of patients were hospitalized with a mean of 1.3 outpatient visits. The default disutility for aseptic meningitis was assumed to be the same as the utility loss for meningitis caused by invasive pneumococcal disease, which was reported in Rubin et al (2010).[45]
Vaccine-related encephalitis (MMR)	44 558	0.0539	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33] which assumed that 100% of patients were hospitalized with a mean of 3.62 outpatient visits. The default QALY loss was calculated by adding the QALY loss for acute encephalitis and for encephalitis that results in lifetime disability. The QALY for acute encephalitis was obtained from Anyiwe et al (2019)[46] which assumed a disutility value of 0.21 for a 2 wk duration, resulting in a QALY loss of 0.01. The disutility for encephalitis that results in lifetime disability was obtained from Philipson et al (2017; citing WHO [2004])[52] which assumed a disutility of 0.56. The model assumed that this disutility would occur for the remaining 50 wk of the year, resulting in a QALY loss of 0.54. Fowler et al (2010)[53] reported that 8.5% of encephalitis cases result in long-term disability. This percentage was applied to the QALY loss for encephalitis resulting in long-term disability and then added to the QALY loss for acute encephalitis to calculate the assumed QALY loss for vaccine-related encephalitis.

Adverse Event (Vaccine)	Cost per Adverse Event, USD[a]	QALY Loss per Adverse Event	Sources and Assumptions
Guillain-Barre syndrome (influenza)	32 882	0.1410	Obtained from a previous cost-effectiveness model for influenza (Prosser et al 2006)[43] and inflated from 2003 to 2019 USD using the US PCE health care inflation factor. The default QALY loss for Guillain-Barre syndrome was obtained from Prosser et al (2006).[43]
Hypotonic hyporesponsive episodes (DTaP)	1622	0.0001	Based on resource use of DTaP-related episodes reported by Ekwueme et al (2000)[41] and Zhou et al (2005),[6] which reported that 12.5% of patients are hospitalized and 50% of patients have an outpatient visit. The default disutility and duration of disutility for hypotonic hyporesponsive episodes was assumed to be the same as a mild complication, which was obtained from Tu et al (2014).[48]
Injection site reaction (severe) (all injected vaccines)	75	0.0014	Based on a previous cost-effectiveness model for influenza, which assumed a physician visit for an injection site reaction (Prosser et al 2006).[43] The default disutility and duration was assumed to be 0.5 for 1 day per expert opinion, which is similar to QALY loss for injection site reaction for Tdap vaccine in adolescents (0.001) (Kamiya et al 2016).[47]
Intussusception (rotavirus)	6094	0.0232	Obtained from a previous economic analysis of rotavirus vaccine (Widdowson et al 2007)[35] and inflated from 2004 to 2019 USD using the US PCE healthcare inflation factor. The default QALY loss was assumed the same as aseptic meningitis (Rubin et al 2010).[45]
Mild complication (eg, fever, rash, systematic reaction) (influenza, pertussis)	75	0.0001	Based on resource use from a previous economic analysis of varicella vaccine (Zhou et al 2008),[32] which assumed an outpatient visit. The default QALY loss for a mild complication was based on fever obtained from Tu et al (2014).[48]
Mild gastroenteritis or vomiting (rotavirus)	75	0.0006	Obtained from a previous economic analysis of rotavirus vaccine (Widdowson et al 2007)[35] and inflated from 2004 to 2019 USD using the US PCE healthcare inflation factor. The default disutility for mild gastroenteritis or vomiting of 0.219 was based on the disutility for nonhospitalized diarrhea (Martin et al 2009).[50] The default duration applied was 1-day per expert opinion.
Parotitis (MMR)	141	0.0002	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33] which assumed that 1% of patients were hospitalized with a mean of 0.1 outpatient visits. The default QALY loss for parotitis was assumed to be slightly higher than mild complication per expert opinion.
Protracted crying or screaming (DTap)	31	0.0001	Based on resource use of DTaP-related protracted crying or screaming reported by Ekwueme et al (2000)[41] and Zhou et al (2005),[6] which reported that 0.5% of patients are hospitalized and 10% of patients have an outpatient visit. The default QALY loss for protracted crying or screaming was assumed to be the same as a mild complication (Tu et al 2014).[48]
Seizure (DTaP, MMR, PCV13)	891	0.0004	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33] which assumed that 10% of patients were hospitalized with a mean of 1 outpatient visit. The default QALY loss for a seizure was obtained from Tu et al (2014).[48]
Thrombocytopenic purpura (MMR)	14 098	0.0232	Based on resource use from a previous economic analysis of MMR (Zhou et al 2004),[33] which assumed that 40% of patients were hospitalized with a mean of 5.91 outpatient visits. The default QALY loss for thrombocytopenic purpura was assumed to be the same as aseptic meningitis (Rubin et al 2010).[45]

CMS, Centers for Medicare and Medicaid Services; CPT, Current Procedural Terminology; PCE, personal consumption expenditures.

[a] Hospitalization costs (if applicable) were obtained from Zhou et al (2004)[33] and inflated from 2001 to 2019 USD using the US PCE health care inflation factor. Outpatient visit costs (if applicable) were obtained from the 2019 Physician Fee Schedule (CPT 99213) (CMS.gov, 2019).[30]

SUPPLEMENTAL TABLE 7 Diphtheria Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %	Sources	Cost per Case, USD	Sources
Hospitalized case	100.0	Ekwueme et al (2000)[41]	14 994.66	Ekwueme et al (2000)[41] citing Hatziandreu et al (1994)[104a]
Outpatient case	0.0		NA	
Percentage of medically attended cases resulting in death	10.0	Zhou et al (2005)[6]	NA	NA

NA, not applicable; PCE, personal consumption expenditures.

[a] Inflated to 2019 USD using the US PCE health care inflation factor.

SUPPLEMENTAL TABLE 8 Hepatitis A Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %					Sources	Cost per Case, USD	Sources
	0–4 y	5–14 y	15–39 y	40–59 y	≥60 y			
Icteric infection	7.6	51.2	83.2	83.2	83.2	Rein et al (2007)[45] and	NA	NA
Hospitalized case (not fulminant)	5.0	17.0	23.0	23.0	23.0	Dhankhar et al (2015)[96] citing Armstrong and Bell (2002)[74] and CDC (2001)[81]	12 091.79	Dhankhar et al (2015)[96] citing Rein et al (2007)[130a]
Fulminant case (without transplant)	0.052	0.007	0.093	0.755	1.098		35 985.13	
Liver transplant	0.010	0.001	0.017	0.142	0.027		376 104 (year of transplant) and 33 674 (annual cost remaining lifetime)	Berge et al (2000)[77]
Outpatient case	94.4	83.0	76.9	76.1	75.9		1223.80	Dhankhar et al (2015)[96] citing Rein et al (2007)[130a]
Anicteric and asymptomatic infection	92.4	48.8	16.8	16.8	16.8		NA	
NMA case	100.0	100.0	100.0	100.0	100.0		0	Assumed
Percentage of cases resulting in death						Dhankhar et al (2015)[96] citing Rein et al (2007)[130] and Wolfe et al (2009)[139]		
Icteric infection	0.008	0.001	0.014	0.109	0.736		NA	NA
Anicteric infection	0.000	0.000	0.000	0.000	0.000		NA	NA
Percentage of liver transplants resulting in death								
Year of transplant	11.6	11.6	11.6	11.6	11.6		NA	NA
Subsequent years	4.4	4.4	4.4	4.4	4.4		NA	

CDC, Centers for Disease Control and Prevention; PCE, personal consumption expenditures; NA, not applicable; NMA, nonmedically attended.

[a] Inflated to 2019 USD using the US PCE health care inflation factor.

Case Severity	Case Severity Distribution, %					Sources	Cost per Case, USD	Sources
	<1 m	1 m–1 y	1–4 y	5–14 y	≥15 y			
Acute symptomatic	1.0	6.0	6.0	30.0	30.0	Zhou et al (2005)[6]		Miriti et al (2008)[118a]
Fulminant case	0.1	0.1	0.6	0.6	0.6	citing Margolis et al	22 899	
Hospitalized case	62.7	62.7	62.2	62.2	62.2	(1995)[114]	10 631	
Outpatient case (jaundice)	37.2	37.2	37.2	37.2	37.2		483	
Acute symptomatic	99.0	94.0	94.0	70.0	70.0		0.00	
Percentage of cases resulting in long-term sequelae								
Chronic HepB (among acute cases)	90.0	90.0	30.0	6.0	6.0	CDC (Pertusis)[85]	NA	NA
Liver transplant (among fulminant cases)	12.0	12.0	12.0	12.0	12.0	Miriti et al (2008)[118]	164 779 (year of transplant); 31 948 (annual cost remaining lifetime)	Nguyen et al (2019)[124] and Berge et al (2000)[77]
Percentage of fulminant cases resulting in death	70.0	70.0	70.0	70.0	70.0	Zhou et al (2005)[6] citing Mulley et al (1982)[120], Bloom et al (1993)[65], Margolis et al (1995)[114], Arevalo and Washington (1988)[73], and Krahn and Detsky (1993)[107]	NA	NA
Annual transitions from chronic HepB and associated complications								
Chronic HepB						Miriti et al (2008)[118]		
Compensated cirrhosis	0.5	0.5	0.5	0.5	0.5		NA	NA
HCC	0.02	0.02	0.02	0.02	0.02		NA	NA
Compensated cirrhosis							24 562	Nguyen et al (2019)[124a]
Decompensated cirrhosis	3.4	3.4	3.4	3.4	3.4			
HCC	2.5	2.5	2.5	2.5	2.5			
Death	3.8	3.8	3.8	3.8	3.8			
Decompensated cirrhosis							152 096	Nguyen et al (2019)[124a]
HCC	2.5	2.5	2.5	2.5	2.5			
Liver transplant	1.0	1.0	1.0	1.0	1.0			
Death	26.4	26.4	26.4	26.4	26.4			
HCC							117 153	Nguyen et al (2019)[124a]
Liver transplant	2.0	2.0	2.0	2.0	2.0			
Death	71.1	71.1	71.1	71.1	71.1			
Annual probability of hospitalization for acute exacerbation among those with chronic HepB	0.1	0.1	0.1	0.1	0.1		18 391	Miriti et al (2008)[118] citing US Department of Health and Human Services (2003)[135a]
Percentage of liver transplants resulting in death							NA	NA
Year of transplant	11.6	11.6	11.6%	11.6	11.6	Dhankhar et al (2015)[9]	NA	NA
Subsequent years	4.4	4.4	4.4%	4.	4.4	citing Wolfe et al (2009)[139]	NA	NA

CDC, Centers for Disease Control and Prevention; HCC, hepatocellular carcinoma; HepB, hepatitis B; NA, not applicable; USD, United States dollars.
[a] Inflated to 2019 USD using the US PCE health care inflation factor.

SUPPLEMENTAL TABLE 10 Hib Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %						Sources	Cost per Case, USD	Sources
	Prevaccine			Postvaccine					
	0–5 m	6–11 m	≥1 y	0–5 m	6–11 m	≥1 y			
Meningitis case	68.2	65.1	54.6	39.6	54.9	32.3	Zhou et al (2002)[141]	29 055	Rubin et al (2010)[45] citing Ray et al (2006)[129] and Stoecker et al (2016)[132a]
Epiglottitis case	0.7	0.7	19.4	0.0	0.0	3.2		15 831	Zhou et al (2002)[141] citing Boyle et al (1994)[79a]
Bacteremia case	8.6	9.5	6.7	32.2	18.5	29.8		20 246	
Pneumonia case	9.6	10.5	7.5	7.9	2.8	9.2		16 423	
Cellulitis case	10.5	11.6	8.2	2.3	2.8	5.7		5940	
Arthritis case	1.6	1.7	2.4	0.0	1.4	0.4		4211	
Other invasive case	0.8	0.9	1.2	18.1	19.7	19.4		13 706	
Percentage of Hib meningitis cases resulting in long-term sequelae									Zhou et al (2002)[141] citing Prouty and Lakin (2000)[128] and Chambers and Wolman (1998)[92a]
Major cognitive difficulties	9.3	9.3	9.3	9.3	9.3	9.3	(Christie et al 2017)[94]	121 509 (annual cost for 50 y)	
Major hearing loss	8.2	8.2	8.2	8.2	8.2	8.2	(Jit, 2010)	25 188 (special education cost applied from ages 3–18 y); 46 766 (1-time cost)	
Percentage of Hib cases resulting in death	3.8	3.8	3.8	3.8	3.8	3.8	Zhou et al (2002)[141] citing Cochi et al (1985)[95]	NA	

NA, not applicable; PCE, personal consumption expenditures.
[a] Inflated to 2019 USD using the US PCE health care inflation factor.

SUPPLEMENTAL TABLE 11 Influenza Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

ase Severity	Case Severity Distribution, %			Cost Per Case, USD		
	0–4 y	5–10 y	Sources	0–4 y	5–10 y	Sources
Hospitalized case	0.7	0.7	Hart et al (2018)[102]	41 480.90	18 782.46	Hart et al (2018)[102a]
ED visit case	8.2	14.0		711.65	614.80	Talbird et al (2017)[134a]
Outpatient case	51.0	38.6	531.08	334.33	Hart et al (2018)[102a]	
NMA case	40.1	46.7	NA	0.00	0.00	NA
Percentage of medically attended cases resulting in death	0.02	0.02	Rolfes et al (2019)[131]	NA	NA	NA

ED, emergency department; PCE, personal consumption expenditures; NA, not applicable; NMA, nonmedically attended.
[a] Inflated to 2019 USD using the US PCE health care inflation factor.

SUPPLEMENTAL TABLE 12 Measles Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %					Sources	Cost per Case, USD					Sources
	<1 y	1 y	2–4 y	5–19 y	≥20 y		<1 y	1 y	2–4 y	5–19 y	≥20 y	
Encephalitis case	0.1	0.1	0.1	0.1	0.2	Zhou et al (2004)[33]	46 076	46 076	46 076	46 076	46 076	Zhou et al (2004)[33a]
Pneumonia case	7.0	7.2	5.2	1.6	4.7		16 340	16 084	14 470	12 438	15 074	
Otitis media case	12.0	13.5	8.7	2.2	1.4		1450	1356	1258	770	1500	
Uncomplicated or diarrhea case	81.0	79.2	86.0	96.1	1.4	623	638	492	230	548		
Percentage of encephalitis cases resulting in long-term disability	8.5	8.5	8.5	8.5	8.5	Fowler et al (2010)[53]	128 114 (annual cost for duration of 50 y)					Zhou et al (2008)[32a]
Percentage of reported cases resulting in death	0.08	0.08	0.08	0.08	0.08	Zhou et al (2004)[33] citing Pelletier et al (1998)[127]	NA	NA	NA	NA	NA	NA

NA, not applicable; PCE, personal consumption expenditures.
[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 13 Mumps Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

| Case Severity | Case Severity Distribution, % | | | Cost Per Case, USD | | |
	<15 y	≥15 y	Sources	<15 y	≥15 y	Sources
Complicated case	11.5	48.5	Zhou et al (2004)[33]	5882.90	1850.04	Zhou et al (2004)[33a]
Uncomplicated case	88.5	51.5		151.98	151.98	
Percentage of reported cases resulting in death	0.001	0.001	Zhou et al (2004)[33]	NA	NA	

NA, not applicable; PCE, personal consumption expenditures.

[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 14 Pertussis Case Severity Distribution, Disease-Related Deaths, and Costs per Case

Case Severity	Case Severity Distribution, %	Sources	Cost per Case, USD	Sources
Hospitalized case	4.5	Ekwueme et al (2000)[41] citing Farizo et al (1992)[99] and Sutter and Cochi (1992)[133]	15 178.71	Ekwueme et al (2000)[41a]
Outpatient case	95.5	91.20		
Percentage of medically-attended cases resulting in death	0.04	CDC (Pertusis)[90]	NA	

CDC, Centers of Disease Control and Prevention; PCE, personal consumption expenditures; NA, not applicable; NMA, nonmedically attended.

[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 15 Pneumococcal Disease Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Parameter	Age Groups (y)												Sources
	<1	1–4	5–17	18–24	25–34	35–44	45–54	55–64	65–74	75–84	85–94	95+	
Case severity, %[a]													
Acute otitis media case													
Complex case	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	Kaur et al (2017)[15]
Simple case	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	
Percentage of meningitis cases resulting in long-term sequelae													
Major cognitive difficulties	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	Christie et al (2017)[94]
Major hearing loss	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	Jit (2010)[64]
Percentage of cases resulting in death													
IPD case (meningitis or bacteremia)	2.7	2.7	2.7	11.7	11.7	11.7	11.7	11.7	11.7	11.7	11.7	11.7	Moore et al (2015)[119]
Hospitalized pneumococcal pneumonia	0.3	0.2	0.7	1.7	2.4	3.5	4.9	5.5	6.7	8.2	11.6	15.4	<18 y: Hayes et al (2018)[105], ≥18 y: Wuerth et al (2016)[140]
Acute otitis media													
Complex case	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	Kaur et al (2017)[15]
Simple case	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	88.9	

Parameter	Age Groups, y						Source
	<5	5–17	18–34	35–49	50–64	≥65	
Cost per case, USD							
IPD							
Hospitalized case - meningitis	29 055	21 709	27 947	32 097	43 495	29 341	<50: Rubin et al (2010)[45] citing Ray et al (2006)[129], ≥50: Stoecker et al (2016)[132b]
Hospitalized case - bacteremia	5544	21 709	27 947	32 097	43 495	29 341	
Pneumococcal pneumonia							
Hospitalization	8722	5987	10 022	11 313	37 849	25 230	Rubin et al (2010)[45b]
Outpatient visit	279	369	369	369	138	275	
Acute otitis media							
Complex case	1007	1007	1007	1007	1007	1007	
Simple case	121	121	121	121	121	121	

IPD, invasive pneumococcal disease; PCE, personal consumption expenditures.
a Case severity distribution for IPD and pneumococcal pneumonia determined from disease incidence data.
b Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 16 Polio Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %	Sources	Cost per Case, USD	Sources
Paralytic case	100.0	Roush and Murphy (2007)[4] and CDC (1999)[3]	71 927	Duintjer Tebbens et al (2010)[97a]
Nonparalytic case	0.0	0.00	CDC (2015)[84]	
Percentage of paralytic cases resulting in permanent paralysis	0.5	WHO (2019)[138]	73 292 (annual cost for remaining lifetime)	National Spinal Cord Injury Statistics Center (2016)[123a]
Percentage of paralytic cases resulting in death	2.0	CDC (2015)[84]	NA	NA

CDC, Centers for Disease Control and Prevention; PCE, personal consumption expenditures; NA, not applicable; WHO, World Health Organization.
[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 17 Rotavirus Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity[a]	Case Severity Distribution	Sources	Cost per Case, USD	Sources
Hospitalization	NA	NA	4996.04	Leshem et al (2014)[108b]
ED visit	NA	406.13		
Outpatient visit	NA	NA	86.36	
NMA case	NA	NA	0.00	
Percentage of medically attended cases resulting in death	0.0043%	Widdowson et al (2007)[35]	NA	

ED, emergency department; PCE, personal consumption expenditures; NA, not applicable; NMA, nonmedically attended; USD.
[a] Case severity for rotavirus determined from incidence rates for each severity level.
[b] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 18 Rubella Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %						Sources	Cost Per Case, USD	Sources
	Prevaccine			Postvaccine					
	<1 y	1–14 y	≥15 y	<1 y	1–14 y	≥15 y			
CRS	0.17	0.00	0.00	88.89	0.00	0.00	Prevaccine: Roush and Murphy (2007)[4]; postvaccine: CDC (Pertusis),[88] CDC (2016 Annual Tables),[85] CDC (Hepatitis B),[86] Adams et al (2017),[72] and Adams et al (2016)[71]	74 179	Zhou et al (2004)[33] citing White et al (1985)[136a]
Complicated case	0.04	0.04	30.05	0.04	0.04	30.05	Zhou et al (2004)[33]	<15 y: 26 037; ≥15 y: 1534	
Uncomplicated case	99.79	99.96	69.96	11.07	99.96	69.96		51	
Percentage of CRS cases resulting in long-term sequelae									
Intellectual disability — moderate	27.1	27.1	27.1	27.1	27.1	27.1	Zhou et al (2004)[33]	46 546 (annual cost for 50-y duration)	Zhou et al (2004)[33] citing Chambers and Wolman (1998)[92] and Prouty and Lakin (2000)[128a]
Intellectual disability — severe	5.9	5.9	5.9	5.9	5.9	5.9		122 974 (annual cost for 50-y duration)	
Learning disabilities	47.0	47.0	47.0	47.0	47.0	47.0		25 102 (annual cost applied from age 3–18 y)	
Percentage of cases resulting in death									
CRS (first year)	10.600	10.600	10.600	10.600	10.600	10.600	Zhou et al (2004)[33]	NA	NA

SUPPLEMENTAL TABLE 19 Tetanus Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity	Case Severity Distribution, %	Sources	Cost per Case, USD	Sources
Hospitalized case	100.0	Ekwueme et al (2000)[41]	92 418.68	Ekwueme et al (2000)[41] citing Hatziandreu et al (1994)[104a]
Outpatient visit	0.0		NA	
Percentage of medically attended cases resulting in death	15.0	Zhou et al (2005)[6]	NA	

NA, not applicable; PCE, personal consumption expenditures; NMA, nonmedically attended.

[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 20 Varicella Case Severity Distribution, Disease-Related Deaths, and Direct Medical Costs per Case

Case Severity, %	Case Severity Distribution, y							Sources	Cost per Case, USD	Sources
	<1	1–4	5–9	10–14	15–19	20–29	≥30			
Natural varicella	52.6	52.6	52.6	52.6	52.6	52.6	52.6	MSD data on file (2021)		
Hospitalization, uncomplicated varicella	0.65	0.23	0.11	0.22	0.22	2.11	2.11	Zhou et al (2008)[32] citing MarketScan data, Lopez et al (2006),[112] Galil et al (2002),[99] and Berge et al (2000)[77]	4234.89	Zhou et al (2008)[32] citing MarketScan data, Lieu et al (1994),[110] and Zhou et al (2005)[6a]
Pneumonia	0.33	0.04	0.01	0.06	0.06	0.93	0.93		5378.83	
Encephalitis	0.02	0.01	0.01	0.04	0.04	0.12	0.12		15 402.38	
ED visit	1.5	0.4	0.2	0.1	0.4	0.8	2.4		233.68	
Outpatient visit	78.8	16.7	9.4	7.1	17.5	33.2	95.5		82.23	
Breakthrough varicella (postvaccine only)	47.4	47.4	47.4	47.4	47.4	47.4	47.4	NA		
Hospitalization, uncomplicated varicella	0.1	0.0	0.0	0.0	0.0	0.4	0.4	Rates of complication and resource use are assumed to be 20% of those for natural varicella (Brisson and Edmunds, 2003)[79]	4234.89	Zhou et al (2008)[32] citing MarketScan data, Lieu et al (1994),[110] and Zhou et al (2005)[6a]
Pneumonia	0.07	0.01	0.00	0.01	0.01	0.19	0.19		5378.83	
Encephalitis	0.00	0.00	0.00	0.01	0.01	0.02	0.02		15 402.38	
ED visit case	0.3	0.1	0.0	0.0	0.1	0.2	0.5		233.68	
Outpatient case	15.8	3.3	1.9	1.4	3.5	6.6	19.1		82.23	
Percentage of encephalitis cases resulting in long-term disability	8.5	8.5	8.5	8.5	8.5	8.5	8.5	Fowler et al (2010)[52]	128 114 (annual cost for 50-y duration)	Zhou et al (2008)[32] citing Lieu et al (1994)[110]
Percentage of cases resulting in death										
Natural varicella	0.004	0.001	0.001	0.002	0.006	0.021	0.021	Zhou et al (2008)[32] citing Galil et al (2002)[100] and Berge et al (2000)[77]	NA	NA
Breakthrough varicella	0.001	0.000	0.000	0.000	0.001	0.004	0.004		NA	NA

ED, emergency department; PCE, personal consumption expenditures: NA, not applicable.

[a] Inflated to 2019 USD using the US PCE healthcare inflation factor.

SUPPLEMENTAL TABLE 21 Quality of Life Inputs

Disease	Disutility	Duration of Disutility, y	QALY Loss	Source
Diphtheria	0.23	0.03	0.006	Philipson et al (2017)[52] citing WHO (2004)[137] and CDC (2012)[82]
HepA				
Liver transplant	0.27	Remaining lifetime	0.270 per year	Dhankhar et al (2015)[96] citing Rein et al (2007),[130]
Icteric case	0.36	Hospitalized: 0.19 Outpatient: 0.09	Hospitalized: 0.066; outpatient: 0.034	Luyten et al (2011),[113] Chong et al (2003),[93] and Berge et al (2000)[77]
Anicteric case	0.17	0.01	0.001	
HepB				
Acute case	0.29	0.02	0.006	Chahal et al (2019)[91]
Fulminant case	0.62	0.04	0.024	
Chronic HepB	0.14	Remaining lifetime	0.14 per year	
Compensated cirrhosis	0.33	(or until transition)	0.33 per year	
Decompensated cirrhosis	0.62		0.620 per year	
Hepatocellular carcinoma	0.56	0.560 per year		
Liver transplant	0.35	Remaining lifetime	0.350 per year	
Hib				
Hib infection	0.62	0.03	0.017	Philipson et al (2017)[52] citing WHO (2004)[137] and CDC (2014)[83]
Major cognitive difficulties	0.38	Remaining lifetime	0.380 per year	Oostenbrink et al (2002)[126]
Major hearing loss	0.09	Remaining lifetime	0.090 per year	Oostenbrink et al (2002)[126]
Influenza				
Hospitalized case	0.076	—	0.076	Prosser et al (2006)[43]
Non-hospitalized case	0.005	—	0.005	
Measles				
Measles case	0.15	0.04	0.006	Philipson et al (2017)[52] citing WHO (2004)[137] and CDC (2015)[84]
Long-term disability caused by encephalitis	0.56	50.00	0.560 per year	
Mumps	0.15	0.03	0.004	Philipson et al (2017)[52] citing WHO (2004)[137] and National Health Service (Mumps)[122]
Pertussis	0.19	0.08	0.015	Philipson et al (2017)[52] citing Greer and Fisman (2011)[101] and CDC (2015)[84]
Pneumococcal disease				
IPD meningitis	0.023	1.0	0.023	Rubin et al (2010)[45] citing Bennett et al (2000)[76] and Oh et al (1996)[125]
IPD bacteremia	0.008	1.0	0.008	
All-cause pneumonia hospitalizations	0.006	1.0	0.006	
All-cause pneumonia outpatient visits	0.004	1.0	0.004	
All-cause acute otitis media	0.005	1.0	0.005	
Major cognitive difficulties	0.380	Remaining lifetime	0.380 per year	Oostenbrink et al (2002)[126]
Major hearing loss	0.090	Remaining lifetime	0.090 per year	Oostenbrink et al (2002)[126]
Polio				
Paralytic polio	0.369	0.50	0.185	Khan and Ehreth (2003),[106] Harvard Medical School (2019)[103]
Permanent paralysis	0.369	Remaining lifetime	0.369 per year	Khan and Ehreth (2003)[106]
Nonparalytic polio	0.001	1.00	0.001	Prosser et al (2006)[43]
Rotavirus				
Hospitalization	0.58	0.01	0.003	Martin et al (2009)[50] citing Martin et al (2008)[115]
ED visit	0.22	0.02	0.004	
Outpatient visit	0.22	0.02	0.004	
Nonmedically attended case	0.22	0.01	0.003	
Rubella				
Rubella infection	0.15	0.02	0.003	Philipson et al (2017)[52] citing WHO (2004)[137] and National Health Service (Rubella)[121]
CRS	0.35	Remaining lifetime	0.350 per year	Philipson et al (2017)[52] citing WHO (2004)[137]
Tetanus	0.64	0.08	0.049	Philipson et al (2017)[52] citing WHO (2004)[137] and CDC (2015)[84]
Varicella				
Natural varicella	0.005	1.00	0.005	Zhou et al (2008)[32] citing Brisson and Edmunds (2003)[80]
Breakthrough varicella	0.001	1.00	0.001	
Long-term disability caused by encephalitis	0.560	50.00	0.560 per year	

ABCs, Active Bacterial Core surveillance; CDC, Centers for Disease Control and Prevention; NNDSS, National Notifiable Diseases Surveillance System; WHO, World Health Organization; —, not applicable.

SUPPLEMENTAL TABLE 22 Productivity Loss per Case, by Disease

Disease	Productivity Lost per Case, d	Sources and Assumptions
Diphtheria	6.1	Zhou et al (2014)[7]
Tetanus	16.7	Zhou et al (2014)[7]
Pertussis		
Hospitalized	10.3	Zhou et al (2014)[7]
Outpatient	1.0	Assumption
NMA	0.5	Assumption
HepA		
Anicteric	1.5	Hankin-Wei et al (2016)[34]
Icteric, hospitalized	33.2	MSD data on file (2020); based on data from Berge et al (2000)[77]
Icteric, outpatient	15.5	
HepB		Assumed same as for HepA cases; individuals who developed
Hospitalized (including fulminant)	33.2	decompensated cirrhosis and HCC were assumed to incur a full year of
Outpatient	15.5	productivity loss (Barbosa et al 2014)[75]
Decompensated cirrhosis	365	
HCC	365	
Hib		Zhou et al (2002)[141]; productivity lost for hospitalized cases was assumed to
Meningitis	7.2	be equal to the length of hospitalization (days) reported in Zhou et al
Epiglottitis	4.3	(2002)[140]; nonhospitalized cases were assumed to incur 1 caregiver day
Bacteremia	3.0	of time lost; an average number of caregiver days lost per Hib outcome
Pneumonia	4.8	was calculated based on the hospitalization rate for Hib outcomes
Cellulitis	2.1	reported in Zhou et al (2002).[141]
Arthritis	1.5	
Other invasive disease	3.2	
Influenza	1.1	Li and Leader (2007)[109]
Measles		Zhou et al (2004)[33]
Encephalitis	8.7	
Pneumonia	4.5	
Otitis media	4.0	
Uncomplicated or diarrhea case	3.5	
Mumps		Zhou et al (2004)[33]
Complicated	5.6	
Uncomplicated	4.0	
Rubella		Zhou et al (2004)[33]
Complicated	5.1	
Uncomplicated	2.8	
Pneumococcal disease		
IPD Meningitis	10.6	Lieu et al (2000)[111]
IPD Bacteremia	2.2	Lieu et al (2000)[111]
Hospitalized pneumococcal pneumonia	1.9	Lieu et al (2000)[111]
Outpatient pneumococcal pneumonia	1.0	Assumption
AOM - complex	4.4	Lieu et al (2000)[111]
AOM - simple	1.0	Estimated from Lieu et al (2000)[111] and Ray et al (2006)[129]
Polio		
Paralytic	182.6	Assumed 6 mo caregiver time loss based on Harvard Medical School (2019)[103] estimate of 6 mo to 2 y for return of motor function
Nonparalytic	0.5	Assumed 0.5 d work loss based on CDC ("What is polio?")[88] estimate that about 25% of cases of polio result in flu-like symptoms for 2 to 5 days
Rotavirus		
Hospitalized	1.6	Mast et al (2010)[116]; caregiver time lost for hospitalized cases was equal to
ED	1.8	the length of the hospitalization (1.6 d) reported in Mast et al (2010)[116] to avoid potential double-counting for hospitalized cases first treated in outpatient or ED setting
Outpatient	1.7	
NMA	1.0	Widdowson et al (2007)[35]
Varicella		
Natural varicella (hospitalized or outpatient)	<15 y: 0.6; ≥15 y: 5.7	Calculated based on rates of hospitalization from Zhou et al (2008)[32] and workdays lost for inpatient and outpatient cases estimated in Brisson and Edmunds (2003)[80]
Breakthrough varicella (hospitalized or outpatient)	<15 y: 0.6; ≥15 y: 5.7	

SUPPLEMENTAL TABLE 22 Continued

Disease	Productivity Lost per Case, d	Sources and Assumptions
Encephalitis	8.7	Assumed equal to length of measles encephalitis hospitalization reported by Zhou et al (2004)[33]
Pneumonia	4.5	Assumed equal to length of measles pneumonia hospitalization reported by Zhou et al (2004)[33]

AOM, acute otitis media; ED, emergency department; HCC, hepatocellular carcinoma; NMA, nonmedically attended.

SUPPLEMENTAL TABLE 23 Percent Reduction in Annual Productivity for Long-Term Complications

Disease	Reduction in Annual Productivity, %
HepA	
Liver transplant	27.0
HepB	
Chronic HepB	14.0
Compensated cirrhosis	33.0
Decompensated cirrhosis	62.0
HCC	56.0
Liver transplant	35.0
Hib	
Major cognitive difficulties	38.0
Major hearing loss	9.0
Measles	
Long-term disability caused by encephalitis	56.0
Rubella	
CRS	35.0
Varicella	
Long-term disability caused by encephalitis	56.0

Long-term complications were assumed to incur a percentage reduction in annual caregiver or patient productivity for patients' remaining lifetime or the duration of the complication. The percentage reduction in annual productivity values were assumed to be equal to the disutility (ie, percentage reduction in health-related quality-of-life) values applied for each long-term complication. CRS, congenital rubella syndrome; HCC, hepatocellular carcinoma.

SUPPLEMENTAL TABLE 24 Market and Nonmarket Productivity, by Age Group

Age Group, y	Annual Productivity, USD[a]	Daily Productivity, USD[b]	Sources and Assumptions
0–14	0	169.93	Annual age-specific market productivity (for value of time lost from
15–24	21 798	59.72	work) and nonmarket productivity (for value of time lost from
25–34	69 922	191.57	household and volunteer activities) estimates were obtained from
35–44	94 068	257.72	Grosse et al (2019).[31] Productivity amounts were inflated to 2019
45–54	90 102	246.85	USD using the employment cost index US Bureau of Labor
55–64	73 494	201.35	Statistics (2019).[23] Daily productivity costs for caregivers are
65–74	41 621	114.03	based on the average daily productivity for people aged 15 years
75–89	17 314	47.43	and over, weighted by 2017 population size for each age.
90–100	0	0.00	

[a] Annual productivity estimates were used to calculate indirect costs (discounted lifetime productivity loss) of disease-related mortality (Supplemental Table 25).
[b] Daily productivity estimates were used to calculate indirect costs of time spent with disease cases and caregiver time for vaccination.

SUPPLEMENTAL TABLE 25 Age-Specific Life Expectancy and Calculated Lifetime Productivity Lost from Premature Death

Age, y	Probability of All-Cause Mortality[a]	Remaining Life Expectancy, y[b]	Discounted Lifetime Productivity Lost for Deaths, USD[c]
<1	0.003931	78.6	1 050 863
10	0.000093	69.1	1 423 405
20	0.000795	59.4	1 799 992
30	0.001351	49.9	1 922 680
40	0.001936	40.7	1 660 684
50	0.004030	31.6	1 187 093
60	0.009093	23.2	688 413
70	0.018428	15.7	301 582
80	0.048163	9.1	108 207
90	0.141733	4.4	0
100[d]	1.000000	0.5	0

[a] CDC ("Underlying Cause of Death 1999-2017").[55]
[b] Arias and Xu (2019).[56]
[c] Calculated using age-specific data (by 1-year intervals, not all shown here) and discounted with an annual rate of 3%. Annual productivity is assumed to be $0 for ages 90 years and older.
[d] Calculations for death truncated at age 100.

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