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Vaccine-Associated Paralytic Poliomyelitis: A Review of the Epidemiology and Estimation of the Global Burden

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Abstract

Background.—Vaccine-associated paralytic poliomyelitis (VAPP) is a rare adverse event associated with oral poliovirus vaccine (OPV). This review summarizes the epidemiology and provides a global burden estimate.

Methods.—A literature review was conducted to abstract the epidemiology and calculate the risk of VAPP. A bootstrap method was applied to calculate global VAPP burden estimates.

Results.—Trends in VAPP epidemiology varied by country income level. In the low-income country, the majority of cases occurred in individuals who had received >3 doses of OPV (63%), whereas in middle and high-income countries, most cases occurred in recipients after their first OPV dose or unvaccinated contacts (81%). Using all risk estimates, VAPP risk was 4.7 cases per million births (range, 2.4–9.7), leading to a global annual burden estimate of 498 cases (range, 255–1018). If the analysis is limited to estimates from countries that currently use OPV, the VAPP risk is 3.8 cases per million births (range, 2.9–4.7) and a burden of 399 cases (range, 306–490).

Conclusions.—Because many high-income countries have replaced OPV with inactivated poliovirus vaccine, the VAPP burden is concentrated in lower-income countries. The planned universal introduction of inactivated poliovirus vaccine is likely to substantially decrease the global VAPP burden by 80%–90%.

Keywords

inactivated poliovirus vaccine (IPV); oral poliovirus vaccine (OPV); OPV cessation; OPV withdrawal; polio endgame; polio eradication; poliomyelitis; vaccine-associated paralytic poliomyelitis (VAPP)

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The oral poliovirus vaccine (OPV) containing live-attenuated poliovirus strains types 1, 2, and 3 has served as the primary tool to eradicate polio worldwide. Following OPV administration to susceptible individuals, the polio vaccine strains establish an infection and replicate in the pharynx and the intestine for 4–6 weeks, allowing the recipient to develop humoral and mucosal immunity [1]. During replication, the Sabin strains mutate toward more genetically stable variants, sometimes reverting to neurovirulent variants that may enter the central nervous system and cause paralysis clinically indistinguishable from poliomyelitis caused by wild poliovirus (WPV); this is called vaccine-associated paralytic poliomyelitis (VAPP) [2]. VAPP occurs in recently vaccinated individuals (recipient VAPP) and in susceptible individuals indirectly exposed to vaccine virus, such as close contacts of individuals recently vaccinated or community contacts (contact VAPP).

Previous studies, primarily from industrialized countries, reported that individuals with immunodeficiency disorders and individuals receiving their first dose of OPV were at highest risk of developing VAPP (ranging from 13% to 55% of cases in the United States and Belarus) [3–8]. Administration of intramuscular injections before receiving OPV has also been shown to provoke VAPP [9]. Due to differences in transmissibility and attenuation of each vaccine strain serotype, type 3 has been more often associated with recipient VAPP, type 2 has been more often observed in immunodeficient individuals and cases with contact VAPP, and type 1 has been less often associated with VAPP cases [10].

In 2002, the World Health Organization (WHO) estimated the global burden of VAPP to be 250–500 cases based on the assumption that the risk of VAPP is 1 case per 2–4 million births (RW Sutter, unpublished data). This estimate was based on the results of 2 previous VAPP studies done in the United States and India, but does not represent findings from the larger body of literature on the risk of VAPP.

As part of the new polio endgame, the expanded use of inactivated poliovirus vaccine (IPV) and the withdrawal of Sabin type 2 vaccine virus (OPV2) will impact both the risk and epidemiology of VAPP. First, in November 2012, the Strategic Advisory Group of Experts on Immunization recommended that all countries exclusively using OPV introduce at least 1 dose of IPV into the primary immunization schedule in addition to the OPV primary series [11]. Second, since type 2 WPV was eradicated in 1999 and type 2 vaccine-derived polioviruses are causing an increasing number of paralytic cases and outbreaks in countries free of WPV since 2000, the Global Polio Eradication Initiative (GPEI) is planning a phased withdrawal of OPV types, starting with type 2 strains (OPV2). Experience from countries that replaced OPV with IPV in the primary immunization schedule demonstrates that VAPP is eliminated following the switch [12].Furthermore, studies from countries that adopted a sequential immunization schedule in which infants received multiple IPV doses followed by multiple OPV doses also demonstrated that VAPP was eliminated [13]. However, no studies have specifically evaluated the risk of VAPP in countries that adopted the newly recommended global polio immunization schedule (3 doses of OPV plus a single dose of IPV at 14 weeks of age).

The primary objectives of this literature review are to (1) compare the epidemiology of VAPP in different countries, (2) compare the risk of VAPP in previously published

VAPP studies from different countries, and (3) estimate the current global VAPP burden in countries exclusively using OPV.

METHODS

Extraction of Information From Peer-Reviewed Literature

A literature review was conducted using electronic search software (PubMed), applying the following search criteria: “vaccine associated” All Fields AND (“poliomyelitis” MeSH Terms OR “poliomyelitis” All Fields OR “polio” All Fields). Of the articles retrieved by the search, articles that contained information on the number of VAPP cases in a defined geographic population during a specific time period were included. If more than 1 article covering the same period of time in the same population was identified, the results of the articles were integrated for analysis. From each study, the following information was abstracted when available: number of VAPP cases (overall, recipient and contact), gender, age, previous vaccination history, serotype(s) isolated, and immune status.

Case Definitions

Because there is no global standard case definition for VAPP, studies with different case definitions and criteria were included in this review. A VAPP case was most often defined as a case of acute flaccid paralysis (AFP) with residual paralysis (compatible with paralytic poliomyelitis) lasting at least 60 days, and occurring in an OPV recipient between 4 and 40 days after the dose of OPV was administered, or in a person who has had known contact with a vaccine recipient between 7 and 60–75 days after the dose of OPV was administered. Isolation of vaccine-related poliovirus from any stool samples and no isolation of wild poliovirus was frequently used as criteria, but was not diagnostic in itself [4]. Last, in many countries, a panel of experts was established to review and classify all polio compatible cases as either VAPP or other nonpolio AFP syndromes based on clinical and epidemiological characteristics of the cases.

Risk Calculations

Risk of VAPP was calculated for each country using 2 methods: VAPP per million OPV doses and VAPP per million births. The risk of VAPP per OPV doses was calculated by dividing the number of VAPP cases reported by a country during a certain time period by the total number of OPV doses administered during the same time period as reported by the study. VAPP per million births was calculated by dividing the number of VAPP cases during a specific time period by the number of surviving infants reported for the same time period, according to the United Nations (UN) population estimations [14]. Because population statistics for surviving infants are only available starting from 1980, for studies which reported cases prior to 1980, the number of surviving infants in 1980 was used as a proxy for the preceding years. When sufficient data were available, the risk was estimated for overall, recipient, and contact VAPP cases. Countries were classified by income level based on the World Bank List of Economies; because information was only available from 1970 onward, studies conducted prior to this time were classified based on their income level in 1970 [15].

Estimation of the Global Burden of VAPP

Estimates of risk of VAPP per million births based upon VAPP cases reported in the literature were used to calculate 2 estimates of the annual global burden of VAPP. In the first estimation, a single risk estimate was chosen for each country for which a VAPP study was available. In countries with multiple studies, the risk estimate from the most recently published article was selected because the epidemiologic and laboratory methods and sensitivity of AFP surveillance have substantially improved over time. A second estimation of the global VAPP burden was made using risk estimates from countries that still use OPV exclusively (India and Cuba). It is hypothesized that the second estimate more accurately reflects the global burden because the epidemiological and hygienic conditions of India (low income) and Cuba (middle income) more accurate represent those existing in currently OPV-using countries and differs from the overrepresentation of studies from Europe and the Americas in the literature. It should be noted that because of high coverage and unique polio immunization practices (twice annual national campaigns where all children under 3 years of age are vaccinated together) in Cuba, the VAPP risk in Cuba might not reflect the risk in all middle-income countries. The risk of VAPP per million births was chosen instead of the risk of VAPP per OPV doses administered to estimate the global VAPP burden. This method was chosen because there is evidence that the VAPP incidence per OPV doses administered method underestimates VAPP risk in some countries that deliver numerous OPV doses to already immune children during immunization campaigns.

The bootstrap method was applied to define a minimum and maximum estimation of the risk of VAPP per million surviving infants in the first estimation. In order to minimize the influence of outliers in the risk calculations, the boundaries for the lower and upper limits were calculated by taking the interquartile range of all risk calculations from the chosen studies. Thus, the multiplier of the lower bound represents the 25th percentile of the calculated VAPP risk values, and the upper bound represents the 75th percentile of these values. The lower and upper estimates were then each multiplied by the official UN population estimates of surviving infants in 2012 in the 125 countries which used OPV exclusively, to obtain a range of estimated VAPP cases that occurred in 2012. Because estimates from only 2 countries were available for the second calculation, these estimates were used as a lower and upper bound and a median was calculated.

RESULTS

Literature Review

The initial search returned 305 articles, of which 31 articles provided detailed VAPP information from 1 or multiple countries reported during a specific reporting period and were included in the review.

Epidemiology

The number of VAPP cases by country and time period reported in the 31 articles are summarized in Table 1 [4–8, 16–41]. Of the recipient and contact VAPP cases that reported the gender (418/1427), 60% of cases were reported in males (251) and 40% in females (167). In the 7 studies that investigated the immune status of the VAPP cases, 16% of VAPP

cases had immune deficiencies, although there was a high variability by country, from 3% (4/121) in the United States (1961–1972) to 55% (6/11) in Belarus (1996–2002) [8, 17].

The serotype, age, and OPV vaccination history for recipient and contact VAPP cases are reported in Tables 2 and 3, respectively. The serotype of the vaccine strain isolated from VAPP cases was analyzed in studies from countries that exclusively used trivalent OPV (tOPV) to avoid the inherent bias of monovalent vaccines toward a single causative serotype. Information on serotype isolation was available for 38% of all VAPP cases (536/1427). Of the recipient cases (n = 223), type 3 Sabin poliovirus was isolated from 42% of cases, type 2 from 26%, type 1 in 17% of cases, and multiple serotypes in 15%. Of the contact cases (n = 313), type 3 was isolated in 37% of cases, type 2 in 31% of cases, type 1 in 20%, and multiple serotypes in 12% of cases.

Information on age was available for 61% (864/1427) of the total VAPP cases. Among recipients (n = 414), 71% of VAPP cases were reported in children <1 year, 14% in children aged 1–4 years, 5% in persons aged 5–19, and 10% in adults ≥20 years of age. For contact VAPP cases (n = 450), 35% of contact VAPP cases were reported in children <1 year, 33% in children aged 1–4 years, 8% in persons aged 5–19 years, and 24% in adults aged ≥20 years.

OPV vaccination history was available for 49% (697/1427) of the total VAPP cases. Among recipients (n = 347), 74% of VAPP cases occurred after the individual received their first dose of OPV, and 8%, 7%, and 11% occurred after receiving their second, third, or 4 or more doses, respectively. In contacts (n = 350), 52% of the cases had never been vaccinated with OPV and 11%, 8%, and 28% reported receiving 1, 2, or 3 or more previous OPV doses, respectively.

Overall, a small number of recipient and contact VAPP cases reported a history of previous vaccination with IPV [4, 34, 37, 40]. Almost all of these cases were in individuals who had been vaccinated with IPV before the availability of enhanced-potency IPV in the late 1960s, including 6 cases from the WHO consultative study and 1 case in Norway [34, 40]. In 2 studies from the United States, 12 individuals reported possible history of IPV vaccination, but whether or not the vaccination occurred prior to the availability of enhanced-potency IPV was not stated [4, 37].

Epidemiology by Country Income Level

Trends in the age and OPV vaccination history of VAPP cases varied by country income level (Tables 2 and 3). In the only low-income country with data available (India), the highest number of VAPP cases occurred in children 1–4 years of age (52% of recipients and 64% of contacts). In middle-income countries, infants <1 year of age were most affected (91% of recipients and 61% of contacts). In high-income countries, the age distribution was different for recipient and contact VAPP. Among recipients in high-income countries, infants <1 year of age were most affected (61%), but for contacts in high-income countries, adults >20 years of age were most affected (63%).

In the 1 low-income country (India), the majority of VAPP cases occurred in children who had received more than 3 doses of OPV prior to onset (53% of recipients and 68% of contacts). In contrast, in both middle- and high-income countries, VAPP was highest in recipients receiving their first dose or in unvaccinated contacts, and VAPP risk declined with each subsequent dose of OPV.

In all middle- and high-income countries, type 3 OPV was the predominant serotype isolated, and type 1 was rarely isolated from VAPP cases.

Global Burden Estimates

The risk of VAPP for each individual study by per million doses distributed and per million births is shown in Table 4. Romania (1970–1984) reported the highest risk, with 1 case per 35 000 OPV doses administered and 43.7 VAPP cases per million births. Brazil (1995–2001) recorded the lowest risk, with 1 case per 10.7 million doses and 0.41 cases per million births [21, 39].

Using a single estimation from every country in the review, the global burden of VAPP in 2012 was estimated to be approximately 498 cases of VAPP (interquartile range, 256–1018) (Table 5). Using estimates from studies conducted in countries that currently use OPV exclusively, the burden of VAPP was estimated to be 398 cases (range, 306–491).

DISCUSSION

With rapid progress toward eradication, many high- and middle-income countries have introduced IPV in the past 2 decades, either exclusively or in a sequential schedule. This trend resulted in a concentration of the VAPP burden in low-income countries that still exclusively use OPV. This review reveals that the majority of published VAPP studies were conducted in high- and middle-income countries in the European and American regions. However, only 7% of the birth cohort exclusively using OPV lives in Europe and the Americas. In contrast, over 90% of the VAPP burden is concentrated in low- and lower-middle-income countries in South East Asia, Africa, the Western Pacific, and Eastern Mediterranean regions. Data on the risk and epidemiology of VAPP in these countries are limited.

Our review of previously published VAPP studies demonstrates that the epidemiology and relative risk of VAPP varies widely depending on context. The age and vaccination history of VAPP cases differs in low-, middle-, and high-income countries. The overall risk of VAPP also differs depending on the country and its customary immunization practices.

In the only low-income country in this review (India), VAPP was highest in children 1–4 years of age, whereas in middle- and high-income countries, the risk of VAPP was highest in infants <1 year of age. This difference might be explained by the lower immunogenicity of OPV in low-income countries. Multiple clinical trials have found lower immunogenicity for OPV in developing countries compared with high income countries [42]. The reasons for lower OPV immunogenicity in developing countries are not fully understood; however, it is has been hypothesized to be related to a higher prevalence of protective maternal

antibodies and a high force of other competing intestinal infections. In order for VAPP to occur, an OPV dose must successfully establish an infection in the gut and replicate, therefore, the first “immunizing” dose might not occur until the child has already received several doses of OPV. The higher prevalence and higher titer of protective antipolio maternal antibodies observed among infants in developing countries during the first 3 months of age might prevent OPV from establishing an infection and therefore prevent the development of VAPP [10]. In high-income countries, high OPV immunogenicity and delivery of the first dose of OPV after 2 months (when maternal antibodies are lower) may increase the risk for VAPP following the first dose. Better diagnosis and higher survival of individuals with immune deficiencies in developed countries may also increase the risk of VAPP in middle- and high-income countries. In Belarus and the 2 studies in the United States, VAPP in immunodeficient individuals accounted for a high proportion of the VAPP cases (55% and 13%–18%, respectively) [3, 23].

In countries using tOPV, type 3 was the predominant serotype isolated from the stool of recipient and contact VAPP cases. Type 2 was the second most prevalent, and type 1 consistently represented a low percentage of total VAPP risk. The higher frequency of type 2 and 3 VAPP when compared to type 1 may be related to the fewer nucleotide substitutions responsible for the attenuated phenotype in types 2 and 3 virus strains [10].

Certain countries reported rates of VAPP 5–10 fold higher than the median: Romania (43.7 and 31.4), Belarus (16.9), and Hungary (14.7), most of which can be explained by the existence of specific population risk factors. In Romania, a thorough investigation demonstrated that high prevalence of intramuscular injections of antibiotics leading to “provocation polio” could explain the high risk of VAPP [9]. In Belarus, an unusually high number of VAPP cases had been diagnosed with immune-deficiency disorders (55%). In Hungary, the use of monovalent type 3 in campaigns and, potentially, high rates of intramuscular injections could partially explain the increased VAPP risk [6, 24]. There is no evidence that the high risk of VAPP observed in these studies is representative of the risk of VAPP in the majority of OPV-using countries globally.

Factors related to the serotype of OPV vaccine administered and population immunity are known to influence the risk of VAPP. Monovalent vaccines were used for a short time in many of the countries reporting VAPP cases in this review [5, 8, 24, 28, 41]. Only Hungary continued the use of monovalent OPVs (mOPVs) for 20 years in campaigns. Based upon the data from these studies, the highest rate of VAPP was associated with mOPV3 and the lowest with mOPV1 [6]. Administration of tOPV appears to be associated with lower risk of VAPP than mOPV3, and higher risk than mOPV1. Limited data from Hungary also suggest a higher rate of VAPP associated with the use of bivalent OPV compared to tOPV [6].

The overall immunity of the population is likely to play a role in the risk of VAPP. Countries that accumulate large pools of susceptible individuals are most likely to have an increased risk of contact VAPP. Large pools of susceptible populations can accumulate in all age groups through historically low OPV coverage and absence of natural immunity from wild poliovirus in polio-free regions [43].

Beyond VAPP, another consequence of prolonged vaccine virus replication is the emergence of circulating vaccine-derived polioviruses (cVDPVs), which have regained the transmissibility and neurovirulence of WPVs [44]. Because VDPVs were not discovered until 2000, it is possible that some previous VDPV cases were misclassified as VAPP cases. However, it is unlikely that misclassified cVDPVs cases had a large impact on the estimated risk of VAPP because in most studies, epidemiological investigations reported little to no evidence for the spatial and temporal clustering of VAPP cases (which would be expected in a cVDPV outbreak).

Because the majority of paralytic cases and outbreaks caused by VDPVs are due to type 2 VDPV and there is an ongoing risk of the reestablishment of endemic Sabin type 2 transmission, withdrawal of type 2 from OPV has become a priority of the GPEI [45]. This review found that 26% of recipient VAPP and 31% of contact VAPP were associated with type 2 vaccine virus in studies only using tOPV. Therefore, removal of type 2 serotype from OPV provided globally in routine immunization and campaigns could decrease the overall risk of VAPP by at least 25%–30%. Furthermore, the addition of 1 dose of IPV with DTP3 contact will decrease the overall VAPP burden since IPV has shown to be protective against VAPP. Adding a dose of IPV might decrease VAPP by as much as 80%–90% given that data from this review suggest that few VAPP cases occur before the age of the third diphtheria-tetanus-pertussis (DTP3) immunization contact in low-income countries.

Limitations

An important limitation of this study is that the number of cases reported by each country depends on the sensitivity of surveillance systems to detect VAPP cases and the case definition used. Also, because some countries used surveillance for acute flaccid paralysis to report VAPP cases, individuals older than 15 years old may not have been included as potential cases. Additionally, confirmation of residual paralysis 60 days following onset was not always included. Another limitation is that in some studies, when laboratory data were unavailable, cases were categorized as vaccine-associated on a clinical basis alone, which may have led to overestimation of VAPP risk in countries where WPV was still circulating. Furthermore, molecular technologies were not available before the 1990s, and some WPV could have been incorrectly characterized as vaccine polioviruses.

Despite the limitations of the available scientific evidence, it is evident that VAPP is a rare complication of OPV use. Our estimate of the global burden suggests that approximately 300–500 persons experience the paralytic consequences of VAPP each year in countries currently exclusively using OPV for routine polio immunization. The ongoing threat of paralysis from wild poliovirus is evidenced by the recently recorded large number of cases resulting from importations into previously polio-free areas. However, as the world moves closer and closer toward global eradication, the burden of VAPP will become increasingly unacceptable. Therefore, the Polio Eradication and Endgame Strategic Plan: 2013–2018 calls for the introduction of at least 1 dose of IPV in all OPV-using countries before OPV2 withdrawal [45]. Implementation of this plan should significantly decrease the global VAPP burden, and represents another major step toward a polio-free world. Following IPV

introduction, further studies should be conducted to evaluate the effect on the burden of VAPP.

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Table 1.

Overview of Studies Reporting the Incidence and Risk of Vaccine-Associated Paralytic Polio (VAPP)

Reference	Country	Surveillance Period	Vaccine(s)	Birth Cohort (Millions)[a]	OPV Doses (Millions)[b]	Overall VAPP	Recipient VAPP	Contact VAPP
Diamanti et al [16]	Albania	1980–1995	tOPV	1.17	11.00	11	5	6
Samoilovich et al [17]	Belarus	1996–2002	tOPV	0.65	8.20	11	9	2
Oliveira and Struchiner [18, 19] Dias-Tosta and Kückelhaus [20]	Brazil	1989–1995	tOPV	23.95	NA	30	14	16
Teixeira-Rocha etal [21]	Brazil	1995–2001	tOPV	24.41	106.67	10	8	2
Varughese et al [22]	Canada	1965–1988	tOPV	8.82	0.00	16	4	12
Alvis et al [23]	Columbia	1988–1998	tOPV	9.73	22.50	9	NA	NA
Mas Lago et al [5]	Cuba	1963–2006	mOPV1, bOPV2/3, tOPV	6.87	14.84	20	20	0
Driesel et al [24]	East Germany	1960–1990	mOPV1, mOPV2, mOPV3	NA	50.00	28	NA	NA
Begg et al [25] Smith and Wherry [26]	England/Wales	1970–1984	tOPV	9.78	NA	19	10	9
Joce et al [27]	England/Wales	1985–1991	tOPV	5.36	18.40	13	9	4
Estívariz et al [6] Dömok et al [28]	Hungary	1961–1981	mOPV1, mOPV2, mOPV3, bOPV1/3, tOPV	3.13	34.67	46	32	14
Kohler et al [29]	India	1999	tOPV	25.53	733.40	181	60	121
Kohler et al [30]	India	2000–2001	tOPV	51.04	NA	238	NA	NA
Fiore et al [31]	Italy	1996–1997	tOPV	1.06	NA	5	NA	NA
Hao et al [32] Ministry of Health, Labor and Welfare of Japan [7]	Japan	1971–2000	tOPV	44.67	66.40	33	18	15
Andrus et al [33]	Latin America	1989–1991	tOPV	29.31	431.61	139	85	54
Örstavik et al [34]	Norway	1965–1969	tOPV	0.25	NA	5	2	3
Strebel et al [35]	Romania	1984–1992	tOPV	2.96	12.96	93	45	48
Ivanova [36]	Russia	1998–2005	tOPV	11.02	205.00	66	66	25
Schonberger et al [8]	United States	1961–1972	mOPV1, mOPV2, mOPV3, tOPV	41.44	551.00	121	79	42
Nkowane et al [4]	United States	1973–1984	tOPV	42.01	274.10	105	46	59
Strebel et al [37]	United States	1980–1989	tOPV	36.89	203.50	80	39	41

Reference	Country	Surveillance Period	Vaccine(s)	Birth Cohort (Millions)[a]	OPV Doses (Millions)[b]	Overall VAPP	Recipient VAPP	Contact VAPP
WHO Consultative Group [38–41]	No. 1	1970–1984	tOPV	NA	7.45	0	0	0
	No. 2	1970–1984	IPV primary, tOPV booster	NA	NA	0	0	0
	No. 3	1970–1984	tOPV	11.06	56.33	30	15	15
	No. 4	1970–1984	mOPV1, mOPV3, mOPV2	2.19	18.76	16	9	7
	No. 5	1970–1984	tOPV	34.94	56.99	22	15	7
	No. 6	1970–1984	tOPV	NA	NA	0	0	0
	No. 7	1970–1984	mOPV1, mOPV2, mOPV3, tOPV	10.13	19.35	98	18	80
	No. 8	1970–1984	mOPV1, mOPV2, mOPV3, tOPV	5.56	8.41	243	106	137
	No. 9	1970–1984	tOPV	NA	6.46	1	0	1
	No. 10	1970–1984	tOPV	52.37	351.21	102	41	61
	No. 11	1970–1984	tOPV (part), IPV +tOPV (part)	5.49	22.65	9	2	7
	No. 12	1970–1984	IPV, tOPV in outbreaks	NA	NA	0	0	0
	No. 13	1970–1984	IPV	NA	NA	0	0	0

Abbreviations: IPV, inactivated poliovirus vaccine; mOPV, monovalent OPV; NA, not available; OPV, oral poliovirus vaccine; tOPV, trivalent OPV; WHO, World Health Organization.

[a]Source: United Nations Population Estimation 2012 Revision [14].

[b]Source: OPV doses administered used was the number provided by each individual study.

Table 2.

Recipient VAPP Epidemiology: Virus Serotype Associated, Age Distribution, and OPV Vaccination History of Recipient VAPP Cases

		Serotype[a]				Age				OPV Vaccination History			
Country (Years)	**Recipient VAPP**	**I**	**II**	**III**	**Multiple**	**<1 y**	**1–4 y**	**5–19 y**	**20 + yrs**	**1st**	**2nd**	**3rd**	**4 or More**
Low Income	60	19	9	25	7	25	31	4	0	9	4	15	32
		32%	15%	42%	12%	42%	52%	7%	0%	15%	7%	25%	53%
India (1999)	60	19	9	25	7	25	31	4	0	9	4	15	32
Middle Income	438	10	14	16	17	156	15	0	0	161	10	5	1
		18%	25%	28%	30%	91%	9%	0%	0%	91%	6%	3%	1%
Albania (1980–1995)	5	0	1	0	0	4	1	0	0	3	1	1	0
Belarus (1996–2002)	9	1	1	2	3	NA	NA	NA	NA	6	0	2	1
Brazil (1989–1995)	14	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Brazil (1995–2001)	8	2	1	2	3	8	0	0	0	4	4	0	0
Cuba (1963–2006)[a]	20	1	14	4	1	20	0	0	0	19	1	0	0
Hungary (1961–1981)[a]	32	3	2	27	0	21	11	0	0	31	1	0	0
Latin America (1989–1991)	85	6	5	10	5	NA	NA	NA	NA	24	NA	NA	NA
Romania (1984–1992)	45	NA	NA	NA	NA	42	3	0	0	39	3	2	0
Russia (1998–2005)	66	NA	NA	NA	NA	61	NA	NA	NA	59	NA	NA	NA
WHO No. 3 (1970–1984)	15	1	1	1	3	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 4 (1970–1984)[a,b]	9	0	0	8	0	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 5 (1970–1984)	15	0	5	1	3	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 7 (1970–1984)[a]	18	3	2	3	5	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 8 (1970–1984)[a]	106	1	7	17	21	NA	NA	NA	NA	NA	NA	NA	NA
High Income	209	9	35	52	10	111	11	18	43	88	13	5	4
		8%	33%	49%	9%	61%	6%	10%	23%	80%	12%	5%	%
Canada (1965–1988)	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
England / Wales (1970–1984)	10	NA	NA	NA	NA	9	0	0	1	NA	NA	NA	NA
England/Wales (1985–1991)	9	0	3	3	1	8	0	1	0	6	2	0	1
Japan (1971–2000)	18	1	7	4	6	12	6	0	0	15	3	0	0
Norway (1965–1969)	2	0	1	0	1	0	1	0	1	NA	NA	NA	NA

		Serotype[a]				Age				OPV Vaccination History			
Country (Years)	**Recipient VAPP**	**I**	**II**	**III**	**Multiple**	**<1 y**	**1–4 y**	**5–19 y**	**20 + yrs**	**1st**	**2nd**	**3rd**	**4 or More**
USA (1961 −1972)[a]	79	3	3	7	2	23	0	16	40	NA	NA	NA	NA
USA (1973–1984)	46	7	16	23	0	31	3	1	0	38	4	2	1
USA (1980–1989)	39	1	8	22	0	28	1	0	1	29	4	3	2
WHO No. 10 (1970–1984)[b,c]	41	1	2	7	13	5	3	1	2	NA	NA	NA	NA
WHO No. 11 (1970–1984)	2	0	0	0	2	NA	NA	NA	NA	NA	NA	NA	NA
Total	707	38	58	93	34	292	57	22	43	258	27	25	37
		17%	26%	42%	15%	71%	14%	5%	10%	74%	8%	7%	11%

Abbreviations: Abbreviations: NA, not available; OPV, oral poliovirus vaccine; VAPP, vaccine-associated paralytic polio; WHO, World Health Organization.

[a]Results from the following studies were excluded from calculation of serotype subtotals and totals because monovalent vaccines were used in country during the surveillance period: Cuba (1963–2006), Hungary (1961–1981), WHO No. 4 (1970–1984), WHO No. 7 (1970–1984), and WHO No. 8 (1970–1984).

[b]Results from study were excluded from calculation of subtotals and totals to avoid double-counting data from the same country in the same period reported by 2 separate studies.

[c]Individuals reported in the article aged 15–24 years were categorized as older than 20 years.

Table 3.

Contact VAPP Epidemiology: Virus Serotype Associated, Age Distribution, and OPV Vaccination History of Contact VAPP Cases

		Serotype[a]				Age				OPV Vaccination History			
Country (Years)	**Contact VAPP**	**I**	**II**	**III**	**Multiple**	**<1 y**	**1–4 y**	**5–19y**	**20 + yrs**	**Never Vaccinated**	**1**	**2**	**3 or More**
Low Income	121	40	30	35	16	26	77	18	0	12	12	15	82
		33%	25%	29%	13%	21%	64%	15%	0%	10%	10%	12%	68%
India (1999)	121	40	30	35	16	26	77	18	0	12	12	15	82
Middle Income	406	16	25	26	10	101	58	4	2	50	16	12	11
		21%	32%	34%	13%	61%	35%	2%	1%	56%	18%	13%	12%
Albania (1980–1995)	6	0	3	2	0	2	4	0	0	0	0	2	4
Brazil (1989–1995)	16	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Brazil (1995–2001)	2	0	0	1	1	2	0	0	0	2	0	0	0
Belarus (1996–2002)	2	0	2	0	0	NA	NA	NA	NA	2	0	0	0
Hungary (1961–1981)	14	0	5	8	0	11	3	0	0	10	3	1	0
Latin America (1989–1991)	54	15	13	19	7	NA	NA	NA	NA	NA	NA	NA	NA
Romania (1984–1992)	48	NA	NA	NA	NA	30	18	0	0	17	13	9	7
Russia (1998–2005)[b]	25	NA	NA	NA	NA	20	5	0	0	19	NA	NA	NA
WHO No. 3 (1970–1984)[c]	15	1	4	3	2	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 4 (1970–1984)[d]	*7*	*0*	*2*	*4*	*0*	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 5 (1970–1984)[c]	7	0	3	1	0	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 7 (1970–1984)[c]	80	6	38	11	8	36	28	4	2	NA	NA	NA	NA
WHO No. 8 (1970–1984)[c]	137	3	34	14	11	NA	NA	NA	NA	NA	NA	NA	NA
High Income	193	7	41	54	13	29	15	16	104	120	12	2	6
		6%	36%	47%	11%	18%	9%	10%	63%	86%	9%	1%	4%
Canada (1965–1988)	12	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
England and Wales (1970–1984)	9	NA	NA	NA	NA	0	0	2	7	NA	NA	NA	NA
England/Wales (1985–1991)	4	0	1	2	0	0	0	4	0	4	0	0	0
Japan (1971–2000)	15	1	10	3	1	5	5	1	4	15	0	0	0
Norway (1965–1969)	3	0	1	2	0	NA	NA	NA	NA	NA	NA	NA	NA
USA (1961–1972)	42	7	17	16	0	15	0	4	23	35	1	0	1

Country (Years)	Contact VAPP	Serotype[a]			Age					OPV Vaccination History			
		I	II	III	Multiple	<1 y	1–4 y	5–19y	20 + yrs	Never Vaccinated	1	2	3 or More
USA (1973–1984)	59	3	11	20	0	3	5	5	43	38	6	0	5
USA (1980–1989)	41	1	8	13	0	6	5	0	26	28	5	2	0
WHO No. 9 (1970–1984)[d]	1	0	0	0	1	0	0	0	1	NA	NA	NA	NA
WHO No. 10 (1970–1984)[c,d,e]	*61*	*2*	*10*	*14*	*11*	NA	NA	NA	NA	NA	NA	NA	NA
WHO No. 11 (1970–1984)[d]	7	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total	720	63	96	115	39	156	150	38	106	182	40	29	99
Percentage		20%	31%	37%	12%	35%	33%	8%	24%	52%	11%	8%	28%

No contact cases were reported in Cuba (1963–2006), WHO No. 1, WHO No. 2, WHO No. 6, WHO No. 12, and WHO No. 13.

Abbreviations: NA, not available; OPV, oral poliovirus vaccine; VAPP, vaccine-associated paralytic polio; WHO, World Health Organization.

[a]Results from the following studies were excluded from calculation of serotype subtotals and totals because monovalent vaccines were used in country during the surveillance period: Hungary (1961–1981), WHO No. 4 (1970–1984), WHO No. 7 (1970–1984), WHO No. 8 (1970–1984).

[b]Five cases were reported in children older than 1 year, but specific age group was not specified. Cases classified as 1–4 years.

[c]Cases reported as possible contacts were included. Cases reported as “no known contact” were not included.

[d]Results from study were excluded from calculation of subtotals and totals to avoid double-counting data from the same country in the same period reported by 2 separate studies.

[e]Individuals reported in the article aged 15–24 years were categorized as older than 20 years.

Table 4.

Risk of VAPP (in Descending Order of Highest to Lowest Risk by Birth Cohort)

			VAPP Cases Per Million Births		
Country	**Surveillance Period**	**Million OPV Doses Per VAPP Case Total[a]**	**Total**	**Recipient**	**Contact**
WHO No. 8	1970–1984	0.035	43.73	19.08	24.66
Romania	1984–1992	0.14	31.39	15.19	16.20
Norway	1965–1969	NA	20.03	8.01	12.02
Belarus	1996–2002	0.75	16.86	13.80	3.07
Hungary	1961–1981	0.754	14.69	10.22	4.47
WHO No. 7	1970–1984	0.20	9.67	1.78	7.90
Albania	1980–1995	1.00	9.42	4.28	5.14
Russia	1998–2005	3.11	8.26	5.99	2.27
WHO No. 4	1970–1984	1.17	7.32	4.12	3.20
India	1999	4.05	7.09	2.35	4.74
Latin America	1989–1991	3.11	4.74	2.90	1.84
Italy	1996–1997	NA	4.73	NA	NA
India	2000–2001	NA	4.66	NA	NA
United States	1961–1972	4.55	2.92	1.91	1.01
Cuba	1963–2006	0.74	2.91	2.91	NA
WHO No. 3	1970–1984	1.88	2.71	1.36	1.36
United States	1973–1984	2.61	2.50	1.09	1.40
England / Wales	1985–1991	1.42	2.43	1.68	0.75
United States	1980–1989	2.54	2.17	1.06	1.11
WHO No. 10	1970–1984	3.44	1.95	0.78	1.16
England / Wales	1970–1984	NA	1.94	1.02	0.92
Canada	1965–1988	NA	1.81	0.45	1.36
WHO No. 11	1970–1984	2.52	1.64	0.36	1.28
Brazil	1988–1998	NA	1.25	0.58	0.67
Japan	1971–2000	2.01	0.74	0.40	0.34
WHO No. 5	1970–1984	2.59	0.63	0.43	0.20
Brazil	1995–2001	10.67	0.41	0.33	0.08

Country	Surveillance Period	Million OPV Doses Per VAPP Case Total[a]	VAPP Cases Per Million Births		
			Total	Recipient	Contact
East Germany	1960–1990	1.79	NA	NA	NA

Abbreviations: NA, not available; OPV, oral poliovirus vaccine; VAPP, vaccine-associated paralytic polio; WHO, World Health Organization.

[a] Number for million OPV doses used was the number provided in the published study.

Table 5.

Estimations Global VAPP Burden in 2012

	Estimate Using Multiple Countries[a]		Estimate Using Data From Exclusively OPV Using Countries[b]	
	Cases Per Million Births	**Estimated Cases 2012**	**Cases Per Million Births**	**Estimated Cases 2012**
Lower (25th percentile)	2.43	256	2.91	306
Median	4.73	498	3.79	399
Upper (75th percentile)	9.67	1018	4.66	490

Abbreviations: OPV, oral poliovirus vaccine; VAPP, vaccine-associated paralytic polio; WHO, World Health Organization.

[a]Studies included in calculation: Albania (1980–1995), Belarus (1996–2002), Brazil (1995–2001), Canada (1965–1988), Cuba (1963–2006), England/Wales (1985–1991), Hungary (1961–1981), India (2000–2001), Italy (1996–1997), Japan (1971–2000), Latin America (1989–1991), Norway (1965–1969), Romania (1984–1992), Russia (1998–2005), United States (1980–1989), WHO No. 3 (1970–1984), and WHO No. 7 (1970–1984).

[b]Studies included in calculation: Cuba (1963–2006) and India (2000–2001).