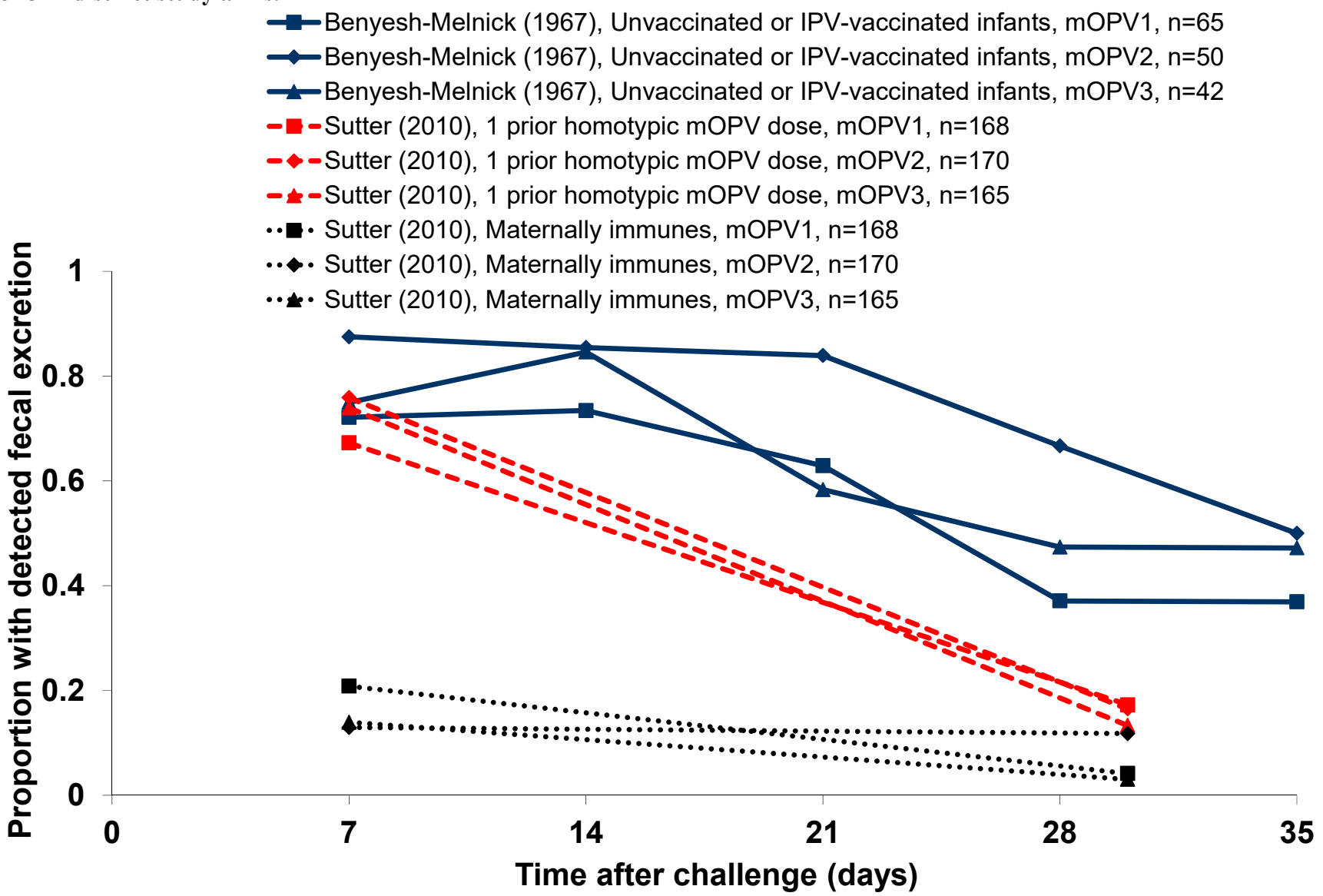
APPENDIX

Table A1 documents details on the study arms that we included and assigned to immunity states for the summary results on relative susceptibility, probability and concentration of fecal excretion over time, average duration of fecal excretion, and oropharyngeal excretion in the main paper. Figure A1shows the fecal excretion patterns from 2 studies[19, 53] that included separate study arms for each mOPV type. Figure A2 shows the proportions with fecal excretion for the only study[100] for which we could reliably stratify by time since primary vaccination. However, the relationship between time since primary vaccination and proportion excreting remains unambiguous after controlling for pre-challenge antibody titer.

Figure A1: Serotype-specific proportions with fecal excretion as a function of time among subjects challenged with mOPV1, 2, or 3 in distinct study arms.[19, 53]



Acronyms: IPV = inactivated poliovirus vaccine; mOPV1,2,3 = monovalent oral poliovirus vaccine type 1, 2, 3, respectively

Figure A2: Ambiguous relationship between age since entering immunity state and proportion excreting oral poliovirus vaccine (OPV) based on Nishio et al. (1984).[100]

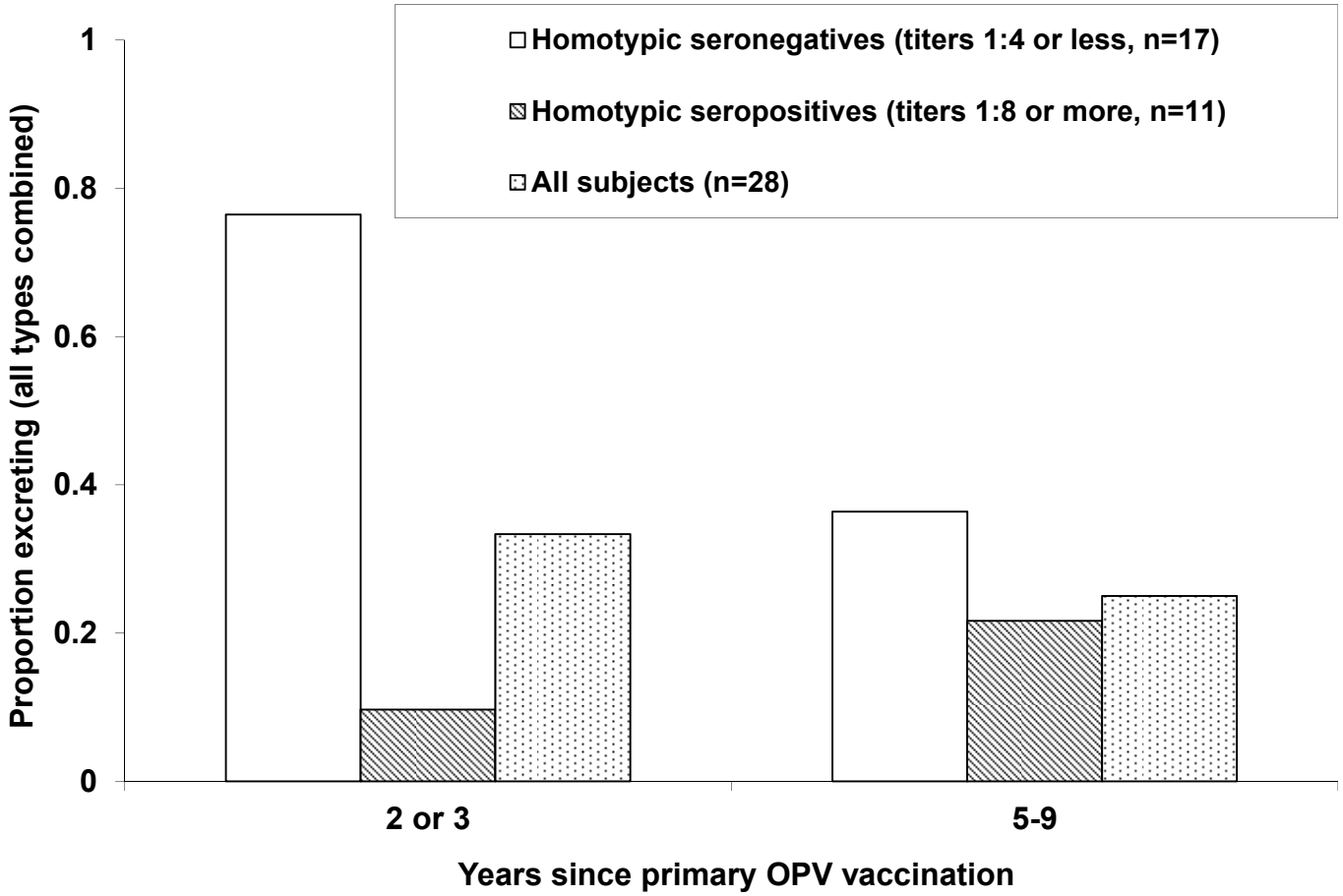


Table A1: Details of assignment of OPV challenge study data to immunity states to estimate relative susceptibility, probability and concentration of fecal excretion over time, average time until last positive stool specimen, and oropharyngeal excretion for "recent" immunity states.

Study (first author, year[ref #])	Sample collection time(s) to determine relative susceptibility	"Recent" immunity states assessed for one or more model inputs	Corresponding study arm(s) [age range at time of challenge] (n)	Notes	Topics
Abraham (1993)[56] and Ogra (1991)[58]	Cumulative (for 60 days)	Fully susceptible	Children with no prior vaccination [2 mo] (13[a])	Assumes negligible effect of maternal Ab at age of challenge (pre-challenge Ab status not reported)	Relative susceptibility
		≥ 3 successful IPV doses	Children with ≥ 3 prior eIPV doses [24 mo] (26[a])		Relative susceptibility
Cohen-Abbo (1995)[70]	~ 30 days after challenge	Fully susceptible	Unvaccinated children [2 mo] (84)		Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [3 or 4 mo] (62)	Approximately 52, 95, and 25% of subjects had seroconverted to PV1, PV2, and PV3, respectively after first tOPV dose	Relative susceptibility
		≥ 2 LPV infections	Children with 2 prior tOPV dose [4 or 6 mo] (68)	Approximately 85, 99, and 90% of subjects had seroconverted to PV1, PV2, and PV3, respectively, after first two tOPV doses	Relative susceptibility
Cuba IPV Study (2007)[62]	7 days after challenge	Fully susceptible	Polio-unvaccinated children [4-8 mo] (54)	Study design allows ruling out of secondary OPV exposure (no detectable Ab before challenge)	Relative susceptibility; cumulative mean virus titers in feces
		2 successful IPV doses	Children with 2 prior eIPV doses [4-8 mo] (72)	High pre-challenge seroconversion rates (PV1: 0.90; PV2: 89%; PV3: 90%)	Relative susceptibility; cumulative mean virus titers in feces
		≥ 3 successful IPV doses	Children with 3 prior eIPV doses [4-8 mo] (52)	High pre-challenge seroconversion rates (PV1: 0.94; PV2: 83%; PV3: 100%)	Relative susceptibility; cumulative mean virus titers in feces
Dick (1961)[41]	NA	Fully susceptible	Seronegative children with no prior IPV or 2 prior IPV [6-18 mo] (9+2 fed mOPV1)	Only virus excretion at titers of 10^2 log CID_{50} or more included in results	Probability of fecal excretion over time; oropharyngeal excretion
		Fully susceptible	Seronegative children with no prior IPV or 2 prior IPV [6-17 mo] (16 fed mOPV2)	Mean virus titers reported for 12 excretors after excluding children who were excreting at time of challenge or who did not frequent stools	Mean virus titers in feces over time

		2 successful IPV	Seropositive children with 2 prior IPV [5-15 mo] (16 fed mOPV2)	Mean virus titers for 10 excretors after excluding children who were excreting at time of challenge or who did not submit frequent stools	Mean virus titers in feces over time
Dong (1986)[50]	7 days after challenge	Fully susceptible	Unvaccinated children with reciprocal cord blood Ab titers ≤ 16 [3 days or 2 mo] (125 PV1; 55 PV2; 75 PV3)	Includes children from "test" and "control" groups challenged at 3 days and 2 mo, respectively	Relative susceptibility
		Maternally immune	Unvaccinated children with reciprocal cord blood Ab titers > 16 [3 days] (22 PV1; 66 PV2; 55 PV3)		Relative susceptibility
		1 LPV infection	Children with 1 prior (birth) tOPV dose [60 days] (108)	77, 96, and 78% were seropositive to PV1, PV2, and PV3, respectively, at time of challenge	Relative susceptibility
Former Soviet Union (Estonia) Drosdov (1960)[84]	NA	Fully susceptible	Seronegative children [< 3 years] (33 PV1; 10 PV2; 22 PV3)	Average time until last positive stool specimen only estimated for PV1 (16 subjects tabulated); Mean log titers over time from homotypic seronegatives fed mOPV1 (n=16), then mOPV3 (n=16), then mOPV2 (n=9)	Probability of fecal excretion over time (mOPV1); average time until last positive stool specimen; mean virus titers in feces over time
Egypt El-Sayed (2008)[51] and van der Sanden (2009)[83]	NA	1 LPV infection	Children with 1 prior mOPV1 at birth [30 days] (228 fed mOPV1)	55.4% of subjects had responded to the birth dose	Probability of fecal excretion over time
Ghendon (1961)[24]	Cumulative (for 4 weeks)	Fully susceptible	Triple seronegative children [1-3 yr.] (30)		Relative susceptibility; average time until past positive stool specimen; cumulative mean virus titers in feces
		2 successful IPV doses	Children seroconverted after 2xIPV [1-3 yr.] (31)	Children seropositive after but not before vaccination; LPV exposure cannot be ruled out	Relative susceptibility; average time until past positive stool specimen; cumulative mean virus titers in feces
		1 LPV infection	Children seroconverted after mOPV1 [1-3 yr.] (33)	Children seropositive after but not before vaccination; additional LPV exposure cannot be ruled out	Relative susceptibility; average time until past positive stool specimen; cumulative mean virus titers in feces
		≥ 2 LPV infections	Unvaccinated triple seropositive children and unvaccinated children with recent PV1 excretion [1-3 yr.] (32+19)	Assume children had history of multiple WPV infections, with last infection "recent"	Relative susceptibility; average time until past positive stool specimen; cumulative mean virus titers in feces
Ginter (1960)[88]	NA	Fully susceptible	Presumably previously unvaccinated young children [age	Titer results include excretors with pre-challenge Ab titers 1:4 and under as well as 2 type 2 and 1 type 3	Cumulative mean virus titer

			NR] (102)	excretors with pre-challenge Ab titers of 1:16	
Henry (1966)[25]	Cumulative (for 3 weeks)	Fully susceptible	Unvaccinated children [6 mo] (48 aggregated over all challenge doses)	All children had PV1 Ab (pre-challenge) below 10 IU/ml	Relative susceptibility; probability of fecal excretion over time; average time until past positive stool specimen; cumulative mean virus titers in feces
		≥ 3 successful IPV doses	Children with 3 prior IPV doses [6 mo] and children with 3 prior primary IPV doses and booster [16 mo] (43+49 aggregated over all challenge doses)	79% of subjects had some PV1 Ab response after primary course, and 100% after the booster; 86% of subjects that had not received booster excreted any challenge dose vs. 65% of subjects that had received booster	Relative susceptibility; probability of fecal excretion over time; average time until past positive stool specimen; cumulative mean virus titers in feces
		≥ 2 LPV infections	Children with 3 prior tOPV doses [16 mo] (50 aggregated over all challenge doses)	84% of subjects had some PV1 Ab response after the complete course of tOPV	Relative susceptibility; probability of fecal excretion over time; average time until past positive stool specimen; cumulative mean virus titers in feces
Horstmann (1959)[74]	NA	2 or ≥ 3 successful IPV doses	1 subject with only recent IPV-induced immunity [6 yrs] (1)		Oropharyngeal excretion
		1 or ≥ 3 LPV infections	1 subject with a recent LPV infection and a likely history of more LPV infection [9 yrs] (1)		Oropharyngeal excretion
Horstmann (1961)[85]	NA	Fully susceptible	Triple seronegative children with 1-4 prior IPV doses [0.5-5 years] (20 fed mOPV1,3.2; 27 fed mOPV1, bOPV, 29 fed tOPV twice);	Used less sensitive filter paper method to determine seronegativity and rectal swabs for virus isolation; include results for monovalent challenges only; interference noted given successive administration of mOPV types	Probability of fecal excretion over time
Ion-Nedelcu (1997)[63]	Cumulative (for 60 days)	Fully susceptible	Unvaccinated children [2-5 mo] (67)	History of LPV exposure cannot be ruled out	Relative susceptibility
		2 successful IPV doses	Children with 2 prior eIPV doses [4 mo] (78)	88% (PV1) to 91% (PV2 and 3) had pre-challenge neutralizing Ab; History of LPV exposure cannot be ruled out	Relative susceptibility
Kok (1992)[45]	7 days after challenge	Fully susceptible	Unvaccinated children [2-4 mo] (24)	Low susceptibility could reflect low-dose challenge (3.5-3.8 Log CID_{50}) or poor take due to other factors	Relative susceptibility
		≥ 2 LPV infections	Children with 3 prior tOPV doses [8-9 mo] (60)	92% of subjects had PV1-Ab titers ≥ 1:8 at time of challenge	Relative susceptibility; probability of fecal excretion over time
		2 successful IPV doses	Children with 2 prior eIPV doses [8-9 mo] (41)	Pre-challenge PV1-Ab ≥ 1:8 94%	Relative susceptibility
		≥ 3 successful IPV doses	Children with 3 prior eIPV doses [8-9 mo] (43)	Pre-challenge PV1-Ab ≥ 1:8 100%	Relative susceptibility

Kucharská (1985)[86]	NA	Fully susceptible	Unvaccinated infants [age NR] (36 fed mOPV1 then bOPV13)	No information available about Ab status of subjects; only use mOPV1 excretion results	Probability of fecal excretion over time
Laassri (2005)[64]c	7 days after challenge	Fully susceptible	Unvaccinated children [2 mo] (48)		Relative susceptibility
		≥ 2 LPV infections	Children with 2 prior tOPV doses [6 mo] (41)		Relative susceptibility
		2 successful IPV doses	Children with 2 prior IPV doses [6 mo] (42)		Relative susceptibility
Maldonado (1997)[73]	Cumulative for 8 weeks	Fully susceptible	Unvaccinated children [1.5-6 mo] (181)	Routine and mass vaccination combined	Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [1.5-6 mo] (181)	Approximately 70, 90, and 35% of subjects had PV1, PV2, and PV3 Ab response, respectively to first tOPV dose	Relative susceptibility
Mallet (1997)[71]	Day of peak excretion rate measured over sample collection period	Fully susceptible	Unvaccinated children [6-8 mo](21)	Combined for "Vero-OPV" and "PMK-OPV" groups	Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [7-9 mo] (21)	Combined for "Vero-OPV" and "PMK-OPV" groups; 88, 100, and 82% were seropositive to PV1, PV2, and PV3, respectively, at time of challenge	Relative susceptibility
		≥ 2 LPV infections	Children with 2 prior tOPV doses [8-10 mo] (21)	Combined for "Vero-OPV" and "PMK-OPV" groups; 94, 100, and 88% were seropositive to PV1, PV2, and PV3, respectively, at time of challenge	Relative susceptibility
Minor (2005)[57] and Ramsay (1994)[59]b	Cumulative (for 4 weeks)	Fully susceptible	Unvaccinated children [2 mo] (57)	PV3 results may be study artifact or effect of interference of strains in tOPV challenge, and leads to observed relative susceptibility > 1 for all immunity states; pre-challenge detectable (maternal) Ab range from 64%(PV3) to 90%(PV2), but with low titers	Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [3 mo] (57)	Pre-challenge Ab levels not available	Relative susceptibility
		1 successful IPV dose	Children with 1 prior eIPV dose [3 mo] (51)	Pre-challenge Ab levels not available	Relative susceptibility
		≥ 1 successful IPV doses and ≥ 1 LPV infections	Children with 1 prior eIPV then 1 tOPV dose [4 mo] (51)	Pre-challenge Ab levels not available	Relative susceptibility
Onorato (1991)[26] and Modlin (1991)[66]	NA	≥ 3 successful IPV doses	Children with 3 prior eIPV [~2 yrs] (48 fed low-dose and 45 fed high-dose mOPV1 combined)	100% had PV1 serum Ab at time of challenge (mean titers 15.5 IU)	Probability of excretion over time; average time until past positive stool specimen; cumulative mean virus titers in feces
		≥ 2 LPV	Children with 3 prior tOPV [~2 yrs]	100% had PV1 serum Ab at time of challenge (mean	Probability of excretion over time;

		infections	(34 fed low-dose and 45 fed high-dose mOPV1 combined)	titers 2.2 IU)	average time until past positive stool specimen; cumulative mean virus titers in feces
Parent du Châtelet (2003)[75]	Cumulative (for 4 wks)	Fully susceptible	PV3-seronegative children with 4 prior tOPV doses and 0, 1, or 3 prior eIPV doses [24 wks] (32)	Children had neutralizing Ab titers < 8 despite receipt of up to 7 doses of tOPV and eIPV; Response to 5.8 log CID_{50} mOPV3 challenge also very low	Relative susceptibility
		≥ 2 LPV infections	PV3-seropositive children with 4 prior tOPV doses [24 wks] (216)		Relative susceptibility; probability of excretion over time; average time until past positive stool specimen
		≥ 1 successful IPV doses and ≥ 1 LPV infections	PV3-seropositive children with 4 prior tOPV doses and 1 or 3 prior eIPV doses [24 wks] (202+205)		Relative susceptibility; probability of excretion over time; average time until past positive stool specimen
Piirainen (1999)[69] and Valtanen (2000)[82]	NA	≥ 3 successful IPV doses	Children with 3 prior regular eIPV or modified trypsin-inactivated IPV [17.5-19 mo] (45+41 fed mOPV3)	Average duration and mean virus titers based only on results from 45 children with prior eIPV	Probability of fecal excretion over time; average time until past positive stool specimen; mean virus titers in feces over time; cumulative mean virus titers in feces
PHLS (1965)[68]	Cumulative (for 6 wks)	Fully susceptible	Unvaccinated children receiving only non-polio vaccines [10-28 mo](23)		Relative susceptibility; average time until past positive stool specimen
		≥ 2 LPV infections	Children with 3 prior tOPV doses [10-28 mo] (53)	Waning before challenge relatively likely	Relative susceptibility; average time until past positive stool specimen
		≥ 3 successful IPV doses	Children with 3 prior IPV doses [10-28 mo] (69)	Standalone and combination IPV (Salk) lumped; waning or secondary OPV before challenge relatively likely	Relative susceptibility; average time until past positive stool specimen
Plotkin (1960)[43]	Cumulative (sampling interval NR)	Fully susceptible	Newborns with homotypic reciprocal transplacentally acquired Ab titers of 8 or less [<70 days] (48)		Relative susceptibility
		Maternally immune	Newborns with homotypic reciprocal transplacentally acquired Ab titers of 16 or more [<70 days] (55)		Relative susceptibility
Plotkin (1959)[55]	Cumulative	Fully susceptible	Newborns with homotypic transplacentally acquired Ab < 1:8 [0-60 days] (15 PV1+13 PV3)	CHAT and Wistar challenge combined for PV1; Jackson (PV2) data excluded because it failed to lead to any response, leaving < 10 PV2-challenged subjects (i.e., with P-712)	Relative susceptibility; average time until past positive stool specimen
		Maternally	Newborns with homotypic	CHAT and Wistar challenge combined for PV1;	Relative susceptibility; average time

		immune	transplacentally acquired Ab ≥ 1:8 [0-60 days] (31 PV1+15 PV3)	Jackson (PV2) data excluded because it failed to lead to any response	until past positive stool specimen
Sabin (1963)[52]	NA	≥ 1 successful IPV doses and ≥ 1 LPV infections	Children with 1 prior mOPV1 at birth and 1-3 prior IPV [6 mo] (10 fed mOPV1)	All subjects either had Ab response or virus recovered following birth mOPV1 dose	Probability of fecal excretion over time; average time until past positive stool specimen; mean virus titers in feces over time; cumulative mean virus titers in feces
Samoilovich (2003)[72]	Day of peak excretion rate measured over sample collection period	Fully susceptible	Unvaccinated children [2-22 mo] (28)	32, 42, and 42% were seropositive to PV1, PV2, and PV3, respectively and 18, 27, and 0% excreted PV1, PV2, and PV3, respectively, at time of challenge;	Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [4-24 mo] (32)	79, 100, and 79% were seropositive to PV1, PV2, and PV3, respectively at time of challenge;	Relative susceptibility
		≥ 2 LPV infections	Children with 2 prior tOPV doses [6-26 mo] (31)	100% were seropositive to each type at time of challenge	Relative susceptibility
Sutter (2010)[53]	NA	Maternally immune	Unvaccinated children [0 days] (≤ 168 fed mOPV1, ≤ 170 fed mOPV2, ≤ 165 fed mOPV3)	88, 85, and 66% were homotypic seropositive in cord blood in the mOPV1, 2, and 3 arms, respectively	Probability of fecal excretion over time
		1 LPV infection	Children with 1 prior mOPV1,2, or 3 at birth fed same vaccine again [30 days] (≤ 168 fed mOPV1, ≤ 170 fed mOPV2, ≤ 165 fed mOPV3)	20, 21, and 12% were homotypic seropositive at 30 days in the mOPV1, 2, and 3 arms, respectively	Probability of fecal excretion over time
Swartz (1972)[54]	7 days	Fully susceptible	Unvaccinated children [2 mo] (226)	51, 68, and 34% had low-titer Ab (presumable maternal) to PV1, PV2, and PV3, respectively, at time of challenge	Relative susceptibility
		1 LPV infection	Children with 1 prior tOPV dose [3.5 mo] (226)	72% had PV1 Ab at time of challenge (data for other serotypes not reported)	Relative susceptibility
		≥ 2 LPV infections	Children with 2 prior tOPV dose [5 mo] (226)	87% had PV1 Ab at time of challenge (data for other serotypes not reported)	Relative susceptibility
Swartz (2008)[78]	NA	≥ 1 successful IPV doses and ≥ 1 LPV infections	Children with 2 prior eIPV and 3 tOPV [15-17 mo] (75); children with 2 prior IPV and 2 tOPV [9-11 mo] (134)	Results for both study arms and all serotypes combined	Mean virus titers in feces over time
Vaccine Adm. Subcom. (1966)[81]	NA	Fully susceptible	Seronegative children with or without prior IPV [≤ 2 years] (316 fed mOPV1; 231 fed mOPV2; 254 fed mOPV3)	Results for children aged 5 mo or less and 6-35 mo not significantly different and combined	Probability of fecal excretion over time

Acronyms: CID_{50} = cell- or tissue-culture infectious doses; eIPV = enhanced inactivated poliovirus vaccine; IPV = inactivated poliovirus vaccine; IU = internalal units; LPV = live poliovirus; ml = milliliter; mo = month; mOPV1,2,3 = monovalent OPV type 1,2,3, respectively; NA = not applicable; NR = not reported; OPV = oral poliovirus vaccine PV(1,2,3) = poliovirus (type 1, 2, 3, respectively); tOPV = trivalent OPV

Notes:

[a] Cumulative numbers tested over sampling interval not reported, we assumed maximum number for any given time interval from Table 1 on p. 1108
[b] Results in table reflect original HPA isolation rates, which had unexplained, negligibly different rates than the isolation rates at NIBSC [(57)]
[c] Excretion after second dose not included in table given only about 50%