APPENDIX

The following text briefly describes the model, based on the appendix of a prior publication (with references renumbered).[42] Figures A1-2 provide the model structure and Table A1 describes the generic inputs of the model (i.e., inputs that remain the same for any population).

"The differential equation-based poliovirus transmission and OPV evolution model (DEB model) [33] tracks the movement of people between demographic age groups (grouped into mixing age groups that mix preferentially amongst themselves), and for each serotype between oropharyngeal and intestinal infection stages (resulting in potential oropharyngeal and fecal-oral transmission, respectively), immunity states, and waning stages. Figure A1 provides an overview of the model structure based on prior work.[33] Figure A1a depicts the immunity states with the flows that move individuals in and out of them and Figure A1b details how effectively vaccinated or infected individuals progress through different stages of infection and, in the event of infection with OPV, through OPV evolution stages. The model assumes that active immunity from prior vaccination or infection results in permanent protection from polio (disease), but only partial protection from subsequent infection and participation in transmission, depending on the nature of immunity (IPV-induced vs. LPV-induced or both) and time since the last exposure (i.e. waning stage). The model includes 5 waning stages, 6 fecal-oral and 6 oropharyngeal infection stages (2 latent and 4 infectious, with varying degrees of infectiousness), and also accounts for a delay between IPV receipt and development of the immune response that moves individuals to the next IPV immunity state. In Figure A1a, we note that the model assumes identical properties for "IPV and LPV" and "≥ 2 LPV infections" and that the recent waning stages of these immunity states represent the highest degree of immunity to transmission in the model. The model further tracks OPV evolution by moving individuals infected with the OPV parent strain (stage 0) through 20 successive reversion stages that can each transmit and that come with increasing paralysis-to-infection ratios and relative basic reproduction numbers ($R_0$ values) compared to homotypic WPVs. The last reversion stage (stage 19) represents fully-reverted VDPVs with assumed paralysis-to-infection ratio and $R_0$ equivalent to homotypic WPVs. For WPVs or any OPV reversion stage, the DEB model mimics die-out by setting the force-of-infection for the given strain to 0 whenever its effective prevalence of infections resides below a calibrated threshold of 5 per million people. Consequently, OPV-related viruses can only continue to transmit and thus evolve to cVDPVs through successive infections when low enough population immunity to transmission permits circulation of the OPV viruses introduced in the population through vaccination. We fixed the die-out process, model structure, and numerical model inputs that characterize them across all populations we modeled and Table A1 includes the corresponding generic model inputs. […]

"Figure A2 summarizes the results of the model calibration process, based on prior work.[33] With the generic model inputs from Table A1 fixed, we compared our model behavior against i) data on children with non-polio acute flaccid paralysis who reported no receipt of OPV for northern India (modeled separately for Western Uttar Pradesh (WUP) and Bihar) and northwest (NW) Nigeria; ii) data on polio incidence and die-out of endemic WPV transmission for all situations and serotypes (shown in Figure A2 for WPV1 and WPV3 in northern India and northwest Nigeria and for all 3 WPV serotypes in the USA); iii) data from WPV importation outbreak behavior in the Netherlands, Tajikistan, and Albania; iv) data on age distributions of cases for all situations in which meaningful data was available (shown in Figure A2 for the

Netherlands, Tajikistan, and Albania); v) available serogical data on the effect of secondary OPV immunity in the USA and Cuba (not shown); vi) indigenous emergence of cVDPVs (shown in Figure A2 for northern India, NW Nigeria (both serotype 2), Haiti, and Madura in Indonesia (both serotype 1); and vii) no indigenous emergence of cVDPVs in all other situations and serotypes (die-out of serotype 1 OPV-related viruses shows in Figure A2 for Cuba and Haiti). We subsequently applied the model to successfully reproduce the asymptomatic transmission of an imported WPV1 in Israel in 2013.[25]" [42, online supplement pp. 1-2]

**Table A1: Generic inputs of the DEB model[33, 40] (adopted from the online supplement of Duinter Tebbens et al., 2017[42])**

| Model input (symbol) | Best estimate | Source |
|---|---|---|
| Relative susceptibility ($\sigma$) of recent immunity states (for PV1;PV2;PV3) | | [23, 39] |
| - Maternally immune | 0.78;0.79;0.77 | |
| - 1 successful IPV | 0.91;0.92;0.90 | |
| - 2 successful IPV | 0.80;0.80;0.79 | |
| - ≥ 3 successful IPV | 0.72;0.72;0.71 | |
| - 1 LPV infection | 0.42;0.43;0.41 | |
| - ≥ 2 LPV infections | 0.21;0.22;0.20 | |
| - IPV and LPV | 0.21;0.22;0.20 | |
| Duration of latent period ($\xi^{fec}$ or $\xi^{oro}$, in days) | ~ 3[a] | [23, 39] |
| Duration of fecal infectiousness ($\gamma^{fec}$, in days) of recent immunity states (for PV1;PV2;PV3) | | [23, 39] |
| - Fully susceptible | 28.0;27.8;28.3 | |
| - Maternally immune | 24.6;24.6;24.6 | |
| - 1 successful IPV, | 24.5;24.4;24.7 | |
| - 2 successful IPV | 21.1;20.8;21.3 | |
| - ≥ 3 successful IPV | 18.0;17.7;18.2 | |
| - 1 LPV infection | 11.6;10.5;10.5 | |
| - ≥ 2 LPV infections | 10.1;8.9;8.9 | |
| - IPV and LPV | 10.1;8.9;8.9 | |
| Duration of oropharyngeal infectiousness ($\gamma^{oro}$, in days) of recent immunity states (no serotype differences) | | [23, 39] |
| - Fully susceptible | 13.4 | |
| - Maternally immune | 11.9 | |
| - 1 successful IPV | 9.9 | |
| - 2 successful IPV | 6.6 | |
| - ≥ 3 successful IPV | 6.1 | |
| - 1 LPV infection | 5.0 | |
| - ≥ 2 LPV infections | 3.7 | |
| - IPV and LPV | 3.7 | |
| Relative fecal infectiousness ($\pi^{fec}$) of recent immunity states (for PV1;PV2;PV3) | | [23, 39] |
| - Maternally immune | 0.96;0.96;0.95 | |
| - 1 successful IPV | 0.92;0.92;0.91 | |
| - 2 successful IPV | 0.70;0.69;0.68 | |
| - ≥ 3 successful IPV | 0.61;0.59;0.59 | |
| - 1 LPV infection | 0.39;0.43;0.43 | |
| - ≥ 2 LPV infections | 0.20;0.23;0.23 | |
| - IPV and LPV | 0.20;0.23;0.23 | |
| Relative oropharyngeal infectiousness ($\pi^{oro}$) of recent immunity states (no serotype differences) | | [23, 39] |
| - Maternally immune | 0.68 | |
| - 1 successful IPV | 0.30 | |

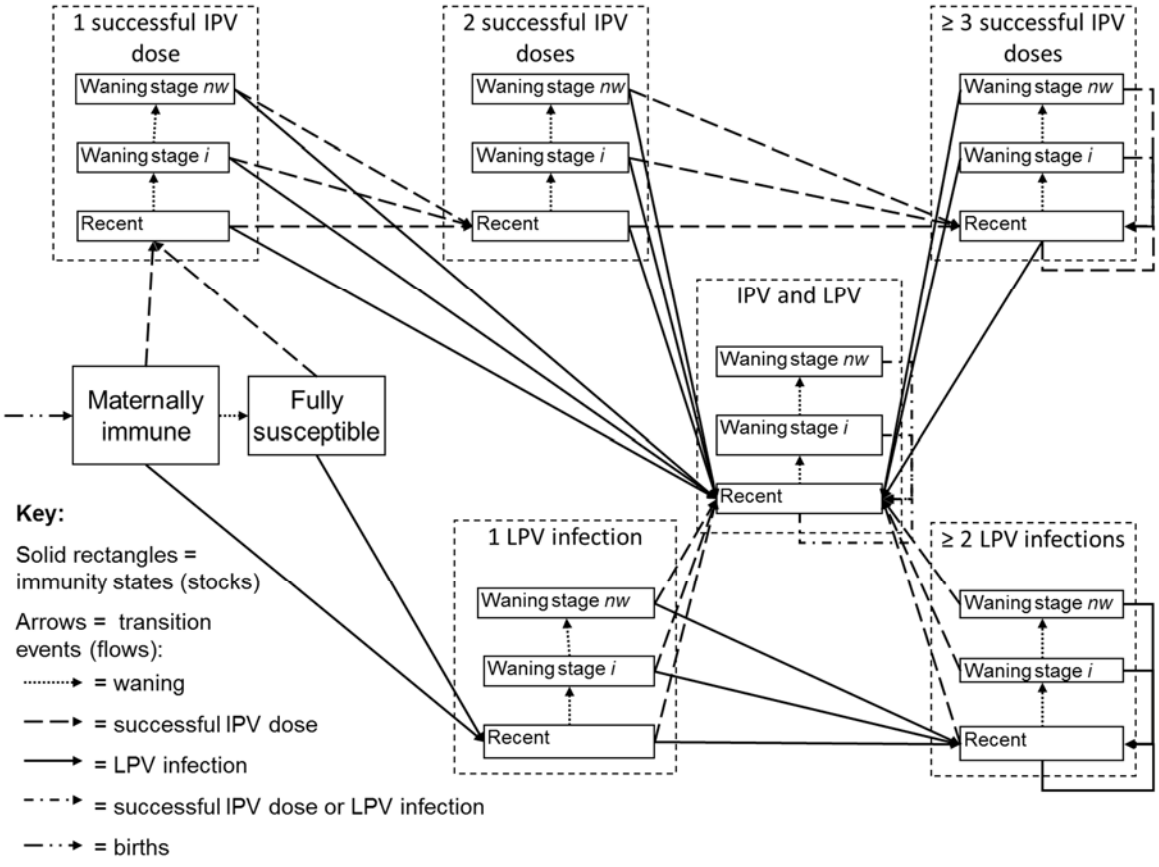
| | | |
|---|---|---|
| - 2 successful IPV | 0.17 | |
| - ≥ 3 successful IPV | 0.12 | |
| - 1 LPV infection | 0.33 | |
| - ≥ 2 LPV infections | 0.21 | |
| - IPV and LPV | 0.21 | |
| Number of infection stages | | |
| - Latent period ($r$) | 2 | |
| - Infectious period ($s$) | 4 | |
| Relative weight of infection stages, compared to average weight over the infectious period ($\theta_j$, $j$=0,…,$r$+$s$-1) | | [23, 39] |
| - Infection stage 0 and 1 (latent stages) | 0 | |
| - Infectious stage 2 | 12/17 | |
| - Infectious stage 3 | 40/17 | |
| - Infectious stage 4 | 12/17 | |
| - Infectious stage 5 | 4/17 | |
| IPV immunity delay ($\varphi$, in days) | 7 | [44] |
| Number of waning stages ($nw$) | 5 | |
| Shape of waning function ($z_w$) | 5 | [23, 39] |
| Average time to reach last waning stage ($\rho$, in days) | | [23, 39] |
| - Type 1&2 | 4×365 | |
| - Type 3 | 3×365 | |
| Average time for maternal immunes to wane to fully susceptible ($\rho_{MI}$, in days) | 0.25×365 | [23, 39] |
| Relative susceptibility ($\sigma$) for last waning stage (no serotype differences) | | [23, 39] |
| - 1 successful IPV | 1.0 | |
| - 2 successful IPV | 1.0 | |
| - ≥ 3 successful IPV | 1.0 | |
| - 1 LPV infection | 0.8 | |
| - ≥ 2 LPV infections | 0.7 | |
| - IPV and LPV | 0.7 | |
| Duration of fecal infectiousness ($\gamma^{fec}$, in days) of last waning stage (for PV1;PV2;PV3) | | [23, 39] |
| - 1 successful IPV | 26.6;26.4;26.9 | |
| - 2 successful IPV | 25.2;25.0;25.5 | |
| - ≥ 3 successful IPV | 23.8;23.6;24.1 | |
| - 1 LPV infection | 14.0;13.9;14.1 | |
| - ≥ 2 LPV infections | 11.4;11.4;11.6 | |
| - IPV and LPV | 11.4;11.4;11.6 | |
| Duration of oropharyngeal infectiousness ($\gamma^{oro}$, in days) of last waning stage (no serotype differences) | | [23, 39] |
| - 1 successful IPV | 11.4 | |
| - 2 successful IPV | 6.7 | |
| - ≥ 3 successful IPV | 6.6 | |
| - 1 LPV infection | 6.7 | |
| - ≥ 2 LPV infections | 4.0 | |
| - IPV and LPV | 4.0 | |
| Relative fecal infectiousness ($\pi^{fec}$) of last waning stage (no serotype differences) | | [23, 39] |
| - 1 successful IPV | 0.95 | |
| - 2 successful IPV | 0.9 | |
| - ≥ 3 successful IPV | 0.85 | |
| - 1 LPV infection | 0.5 | |
| - ≥ 2 LPV infections | 0.3 | |
| - IPV and LPV | 0.3 | |
| Relative oropharyngeal infectiousness ($\pi^{oro}$) of last waning stage (no serotype differences) | | [23, 39] |

| | | |
|---|---|---|
| - 1 successful IPV<br>- 2 successful IPV<br>- ≥ 3 successful IPV<br>- 1 LPV infection<br>- ≥ 2 LPV infections<br>- IPV and LPV | 0.43<br>0.25<br>0.13<br>0.5<br>0.3<br>0.3 | |
| Number of reversion stages ($h$) | 20 | |
| Shape of reversion function with respect to:<br>- $R_0$ ($z_r$)<br>- ln(PIR) ($z_p$) | <br>1<br>2.5 | |
| Average time to reach last reversion stage ($\varepsilon$, in days) (for PV1;PV2;PV3) | 620.5; 408; 620.5 | [40] |
| Paralysis-to-infection ratio for fully susceptible individuals infected with OPV ($PIR_0$) (for PV1; PV2;PV3) | $0.26\times10^{-6}$; $1.2\times10^{-6}$; $1.8\times10^{-6}$ | |
| Paralysis-to-infection ratio for fully susceptible individuals infected with FRPV ($PIR_{h-1}$) (for PV1; PV2;PV3) | 0.005; 0.0005; 0.001 | [33, 44, 45] |
| Relative $R_0$ of OPV vs. FRPV ($\tau_0$) (for PV1; PV2; PV3) | 0.37;0.55;0.25 | [23, 33, 39] |
| Effective infectious proportion below which we assume 0 force-of-infection (transmission threshold $EPI^*$) | 5/1,000,000 | |
| Relative PIR for maternally immunes compared to fully susceptible individuals ($RPIR_{MI}$) | 0.5 | |
| Ratio of $R_0$ by serotype in the same setting (PV1:PV2:PV3) | 1:0.9:0.75 | [40] |
| Average incubation period ($\delta$, in days) | 10 | [44, 46] |
| Demographics for all situations | Time series 1950-2100 | [47] |

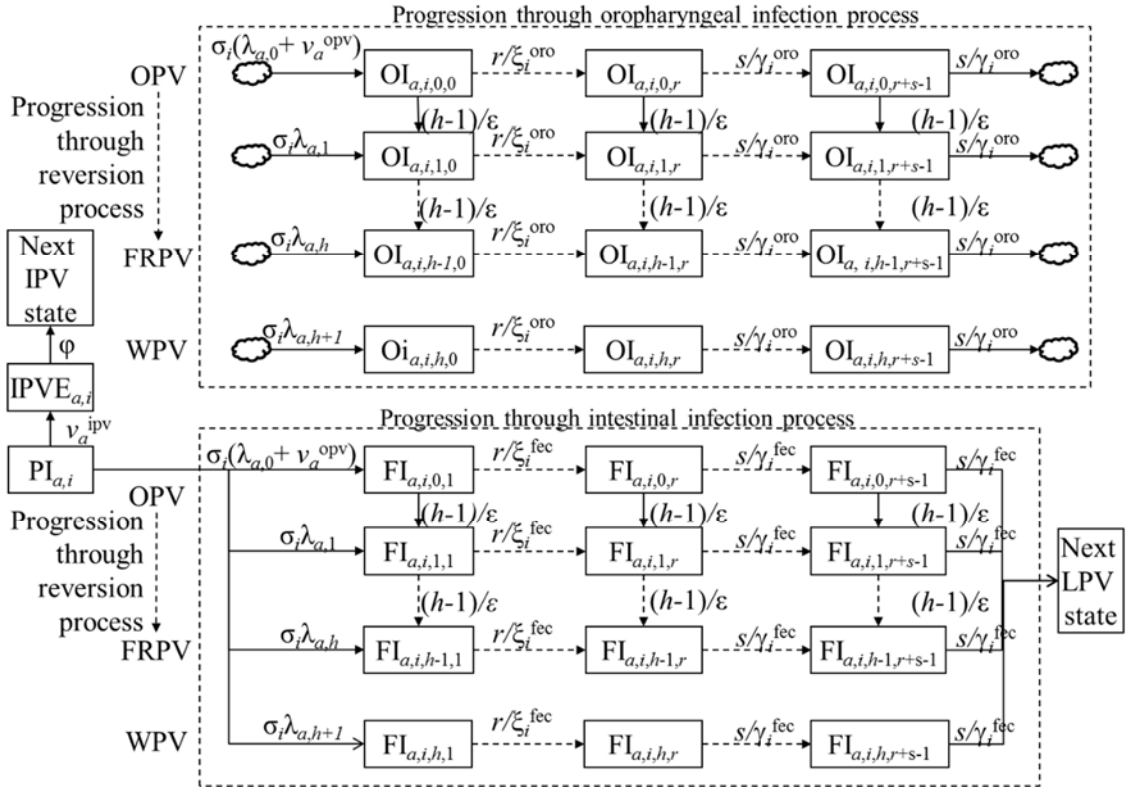
**Acronyms:** CDC = (U.S.) Centers for Disease Control and prevention; cVDPV = circulating vaccine-derived poliovirus; DEB = differential equation-based FRPV = fully-reverted poliovirus; GPLN = Global Polio Laboratory Network; IPV = inactivated poliovirus vaccine; LPV = live poliovirus; OPV = oral poliovirus vaccine; PIR = paralysis-to-infection ratio; PV(1,2,3) = poliovirus (type 1, 2, or 3, respectively); $R_0$ = basic reproductive number; UN = United Nations; USA = United States of America; VAPP = vaccine-associated paralytic poliomyelitis; VP1 = viral protein 1; WPV(1,2,3) = wild poliovirus (type 1, 2, or 3, respectively)

**Notes:** [a] Mean estimates obtained from experts and used in the model for the different immunity states, serotypes, and excretion modes vary between 2.85 and 3.37 days

**Figure A1: Schematic of the DEB model structure, adopted from Duintjer Tebbens et al. (2013)[33, p. 706]**
**(a) Immunity states and flows between them due to epidemiological events**



**(b) Progression through infection and reversion stages**




**"Acronyms:** FRPV = fully-reverted poliovirus; IPV = inactivated poliovirus vaccine; OPV = oral poliovirus vaccine; WPV = wild poliovirus**; Symbols:** $PI_{a,i}$ = partially infectible in age group *a* and immunity state *I*; $IPVE_{a,i}$ = IPV-exposed individual from immunity state *i* and age group *a*; $FI_{a,i,j,k}$ ($OI_{a,i,j,k}$) = individual in age group a from immunity state *i*, infected with virus strain *j* and in fecal (oropharyngeal) infection stage *k*; $\lambda_{a,j}$ = force-of–infection to age group *a* for virus strain *j;* $\nu_a^{ipv}$ ($\nu_a^{opv}$) = force-of-IPV(OPV)-vaccination to age group *a* as a result of routine and supplementary immunization; $\sigma_i$ = relative susceptibility for immunity state *i*; $\xi_i^{fec}$ ($\xi_i^{oro}$) = average duration of the fecal (oropharyngeal) latent period for immunity state *i*; $\gamma_i^{fec}$ ($\gamma_i^{oro}$) = average duration of the fecal (oropharyngeal) infectious period for immunity state *i*; $\varphi$ = IPV immunity delay; *h* = number of reversion stages; *r* = number of latent stages; *s* = number of infectious stages" [33, p. 706]

**Figure A2: Summary results from the model calibration process, adapted from Duintjer Tebbens et al. (2013)[33]**