Appendix for Managing population immunity to reduce or eliminate the risks of circulation following the importation of live polioviruses

Authors: Kimberly M. Thompson, Dominika A. Kalkowska, Radboud J. Duintjer Tebbens

We characterize the historic and future population immunity in three countries with IPV-only immunization schedules: the US,[15] Israel[4] and The Netherlands[15] and extend these models out through 2020. We updated some of the generic assumptions in these models for consistency with more recent applications.[4, 19, 20, 23, 24] These updates included changing to the 2012 revision of the United Nations World Population Prospects data,[32] decreasing the relative R_0 for type 3 compared to types 1 and 2, and increasing the reversion time of OPV-viruses to evolve to fully-reverted vaccine-derived polioviruses.[23] The model simulates the complex dynamic process of individuals in different immunity states becoming infected and then clearing their infections. To simulate die-out in the deterministic model, transmission occurs in a (sub)population as long as the infectiousness-weighted prevalence of infectious individuals remains above a certain "transmission threshold" calibrated based on the experience with poliovirus die-out and cVDPV emergence in diverse situations.[4, 15] The model tracks infections and estimates cases based on assumed serotype-specific paralysis-to-infection ratios for first infections.[4, 15]

Overall, population immunity varies over time due to seasonality, and changes can occur gradually or rapidly. For example, routine immunization (RI) adds immunity to the population consistently over time, and thus changes in RI lead to relatively gradual changes in overall population immunity. In contrast, supplemental immunization activities (SIAs) and outbreaks lead to large surges of immunity, due to their impact on many individuals over a short period of time.[4, 15, 17-20, 22-24] All IPV-using countries primarily rely on RI, but they could use SIAs.

US Model

We characterized the transition from OPV to a sequential IPV/OPV schedule from 1997-1999 and an IPV-only schedule from 2000 forward using a previously-developed approach to assign appropriate proportions of infants to different IPV and/or LPV immunity states.[20, 23] Going forward, we assume an increase in the national coverage with 3 or more polio doses from approximately 0.9 in 1996[15] to 0.93 by 2006.[33] We extrapolate partial coverage with 1 or 2 doses out into the future based on the reported dropout rate between 1 and 3 doses of diphtheria-tetanus-pertussis (DTP) vaccine.[33]

Israel Model

The main text describes the model, and Figure A1 shows population immunity in Israel model going back to 1950.

The Netherlands Model

Table A1 shows the changes to The Netherlands model used for consistency with more recent applications of the model.[4, 19, 20, 23] The Netherlands model includes two subpopulations, as noted in the main text. For the orthodox reformed communities, some uncertainty remains about

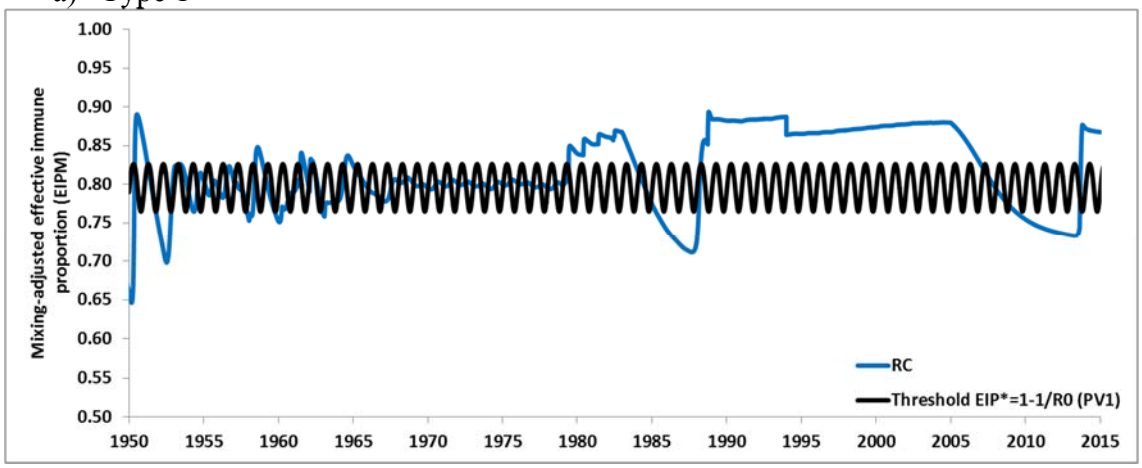
the average coverage level, which varies significantly by denomination. One study reported a minimum of 60% coverage with at least one combined DTP-IPV or measles-mumps-rubella (MMR) dose among mostly orthodox reformed minorities based on two surveys.[34] However, this average may overestimate the coverage in the subpopulation of orthodox reformed communities that we modeled, as it includes over 95% coverage among respondents from one denomination that may not fall under the orthodox minority. The denominations categorized as low or medium coverage represent a total of 200,000 people, with a population-weighted coverage of around 50%. Moreover, coverage with 3 or more polio doses probably remains somewhat lower than coverage with at least one DTP-IPV or MMR dose. Consequently, as noted in the main text, from 1994 forward, we use a best estimate of 40% relative coverage compared to the general population with a range of 20%-60%. We calculated both the subpopulation-and-age-mixing adjusted population immunity (EIPM) for The Netherlands as a whole, and the age-mixing adjusted EIPM for each individual subpopulation.[20] We find that the assumed very strong preferential mixing in the orthodox reformed communities implies that the population immunity in that subpopulation drives the overall population immunity in The Netherlands. Figure A2 shows the resulting refit model for the 1992-1993 WPV3 outbreak. Similar to the outbreak curves, the breakdown of cases by age and subpopulation also did not change significantly. For the run-up, WPV3 transmission more realistically continues with cases until 1969 in the updated model compared to 1960 in the prior fit.[15]

Table A1: Changes to The Netherlands model used for consistency with more recent applications of the model.[4, 19, 20, 23]

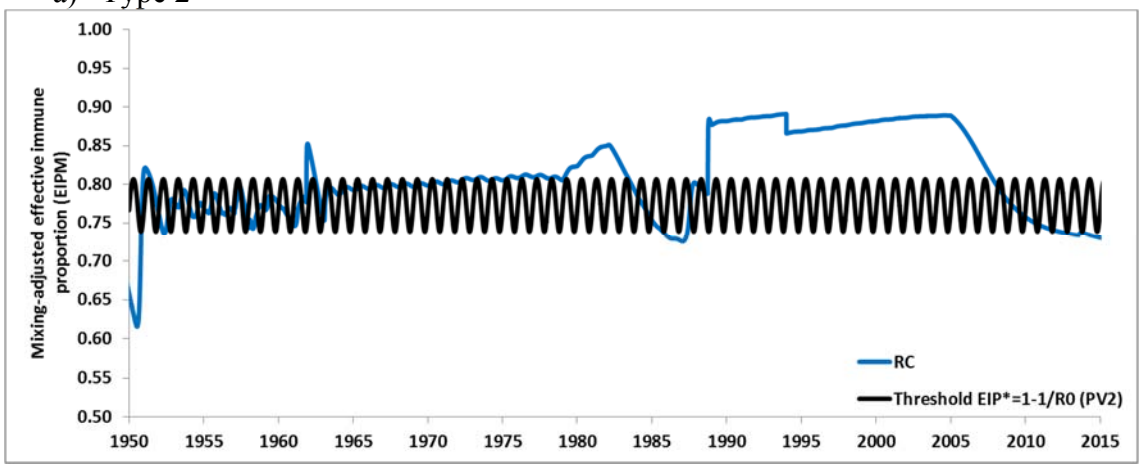
Model input/assumption	**Duintjer Tebbens et al. (2013)[15]**	**Updated model**	**Explanation**
Basic for demographic data	World Population Prospects: The 2010 Revision[35]	World Population Prospects: The 2012 Revision[32]	Generic input change[23]
Average time to reach last reversion stag (ε, in days) (for PV1; PV2; PV3)	547.5; 360; 547.5	620.5; 408; 620.5	Generic input change[23]
Characterization of IPV RI	Any successful vaccination leads to immunity state "1 successful IPV"	Divert appropriate proportions to each IPV immunity state	Improved IPV RI characterization[19]
R_0 (PV1;PV2;PV3)	5;4.5;4	5.33;4.8;4	Preserve same R_0 for PV3 in context of generically changed relative R_0 for PV3 vs. PV1[23]
Booster IPV doses in orthodox reformed communities	At same coverage as primary IPV doses	No booster IPV doses	More realistic characterization in the context of recalibrated model
Relative RI coverage in orthodox reformed communities vs. general populations	0.2	0.4	See Methods
Proportion of transmissions via oropharyngeal route (p^{oro})	0.95	0.9	More realistic characterization in the context of recalibrated model and comparison to assumed values for USA and Israel model
Average per-dose take rate for IPV (any serotype)	0.9	0.75	More realistic characterization in the context of recalibrated model and comparison to assumed values for USA and Israel model
Mixing age groups	0-4, 5-14, 15-39, 40+ years	0-4, 5-14, 15+ years	Characterization consistent with USA and Israel model and most other modeled situations[15]
Timing of annual introductions	Variable; stop introductions in 1960	Day 91 of each year (April 1). stop introductions in 1978	Corrected so that timing of annual introductions on same day of each year[15] and continues until reported WPV1 outbreak in 1978[36]
Day of introduction for the 1992-1993 outbreak	July 18. 1992	June 29, 1992	Fitted values within previously characterized range[14]

Figure A1. Population immunity in Israel by serotype for the RC compared to the threshold (EIP*)

a) Type 1



a) Type 2



b) Type 3

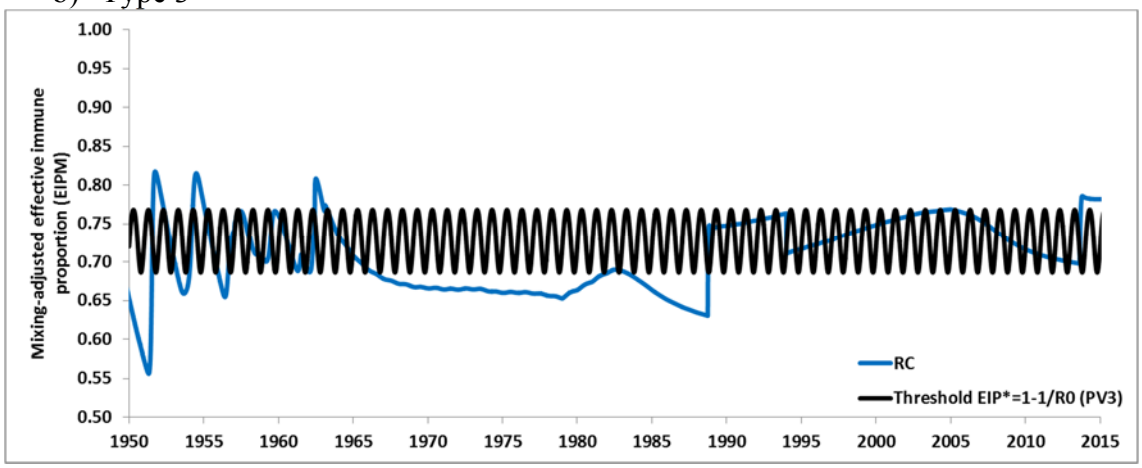


Figure A2. Updated model result of the 1992-1993 WPV3 outbreak in The Netherlands compared to the previously published model[15]