

Modeling strategies to increase population immunity and prevent poliovirus transmission in two high-risk areas in northern India

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This appendix summarizes changes we made to include IPV in the India model,[16,17] and provides supplemental results. We use the same acronyms and we refer to the tables and figures in the main paper here. We also provide additional tables and figures preceded by an “A” to distinguish them from those in the main text. The IPV scenarios include potential administration of a dose of OPV and IPV at the same time in RI. Due to limited information available on seroconversion rates of IPV for northern India, we relied on the results of recent reviews (see Table 1).[5,19]

Notation

We define the following and refer to Duintjer Tebbens et al. (2013)[16] for further details on these quantities and their place within the full set of model equations:

Indices

a = model age group ($a = 0, \dots, na-1$, where $na=8$ and age group 0 represents infants from 0-2 months, inclusive (maternally immune infants only exist in age group 0))

e = excretion and transmission mode ($e = 0$ (fecal) or 1 (oropharyngeal))

i = immunity state ($i = 0$ (fully susceptible), 1 (maternally immune), 2 (1 successful IPV), 3 (2 successful IPV), 4 (≥ 3 successful IPV), 5 (1 LPV infection), 6 (≥ 2 LPV infections), 7 (IPV and LPV))

j = virus strain ($j = 0$ (OPV), 1, ..., $h-2$ (OPV-related), $h-1$ (FRPV), h (WPV), where $h=20$)

k = infection stage ($k = 0$ (first latent stage), $r-1$ (last latent stage), r (first infectious stage), ..., $r+s-1$ (last infectious stage), where $r=2$ and $s=4$)

w = waning stage ($w = 0$ (recent), ..., $nw-1$, where $nw=5$; note that fully susceptibles and maternally immunes only exist in waning stage 0)

Symbols for state variables

$IPVE_{a,i,w}$ = successfully IPV-vaccinated individuals from immunity state i , age group a , and waning stage w yet to acquire the properties of the next IPV state (i.e., IPV-exposed individuals)

$LI_{a,i,w,j,k,e}$ = individuals from immunity state i , age group a , and waning stage w infected with live virus strain j and residing in infection stage k of excretion mode e (i.e., live-virus-infected individuals)

$PI_{a,i,w}$ = partially infectible individuals in immunity state i , age group a , and waning stage w

Other symbols

b = birth rate [1/(people \times day)]

$\gamma_{i,w,e}$ = total duration of infectious period (in all infectious stages) for immunity state i , waning stage w , and excretion mode e [day]

evc_a^{IPV} or evc_a^{OPV} = effective vaccination coverage with IPV or OPV = fraction of the population receiving an effective IPV or OPV dose upon entering situation-specific age group a (i.e., a dose that takes if given to a fully susceptible individual)

$evc_a^{IPV}(IPV1)$ = effective vaccination coverage with IPV that moves fully susceptibles or maternally immunes to the 1 successful IPV state

$evc_a^{IPV}(IPV2)$ = effective vaccination coverage with IPV that moves fully susceptibles or maternally immunes to the 2 successful IPV state

$evc_a^{IPV}(IPV3)$ = effective vaccination coverage with IPV that moves fully susceptibles or maternally immunes to the ≥ 3 successful IPV state

evr_a^{IPV} or evr_a^{OPV} = effective IPV or OPV vaccination rate = fraction of the population in situation-specific age group a receiving an effective IPV (OPV) dose per day (i.e., a dose that takes if given to a fully susceptible) [1/day]

ε = average time to reach last reversion stage [days]

φ = IPV immunity delay [days]

$\lambda_{a,j}$ = force-of-infection to situation-specific age group a due to virus strain j [1/days]

mf = fraction of newborns born with maternal immunity

μ_a = fraction of people in situation-specific age group a that die (or emigrate) per day [1/days]

N = total population size [people]

ρ = average time to reach the last waning stage [days]

$\sigma_{i,w}$ = relative susceptibility for immunity state i in waning stage w

w_a = width of age group a (with $w_0 = \rho_{MI} = 0.25 \times 365$ days) [day]

$\xi_{i,w,e}$ = duration of latent period for immunity state i , waning stage w , and excretion mode e [day]

Equations

The equations for partially infectible individuals remain unchanged, but we now consider flows directly to 2 or 3 successful IPV doses as a result of the cumulative effect of multiple RI IPV doses modeled at 3 months of age, which leads to the following new equation of IPV-exposeds (IPVE, i.e., the brief state in which successfully IPV-vaccinated individuals reside before entering the appropriate IPV immunity state). Moreover, since we consider the possibility of both OPV and IPV vaccination during the same schedule, IPVE individuals may get vaccinated with RI OPV, hence new equation of live-virus-infecteds (LI).

$$\begin{aligned}
\frac{dIPVE_{a,i,w}(t)}{dt} = & b(t)N(t)evc_0^{IPV}(t) \left((1 - mf(t))1_{\{i=0\}} + mf(t)1_{\{i=1\}} \right) 1_{\{a=0\}} \\
& + \left((1 - \sigma_{i,w}evc_{a-1}^{OPV}(t)) (IPVE_{a-1,i,w}(t) + IPVE_{0,1,0}(t)1_{\{a=1,i=0\}}) \right. \\
& + evc_{a-1}^{IPV}(IPV1)(t) (PI_{0,0,0}(t) + PI_{0,1,0}(t)) 1_{\{a=1,i=0\}} \\
& + evc_{a-1}^{IPV}(IPV2)(t) (PI_{0,0,0}(t) + PI_{0,1,0}(t)) 1_{\{a=1,i=2\}} \\
& + evc_{a-1}^{IPV}(IPV3)(t) (PI_{0,0,0}(t) + PI_{0,1,0}(t)) 1_{\{a=1,i=3\}} + evc_{a-1}^{IPV}(t)PI_{a-1,i,w}(t) \\
& + evc_{a-1}^{IPV}(t)PI_{0,1,0}(t)1_{\{a=1,i=0\}} \left. \right) \frac{1_{\{a>0\}}}{w_{a-1}} + IPVE_{a,i,w-1}(t) \frac{nw-1}{\rho} 1_{\{w>0,i>1\}} \\
& + evr_a^{IPV}(t)PI_{a,i,w}(t) \\
& - \left\{ \mu_a(t) + \frac{1_{\{a<na-1\}}}{w_a} + \sum_{j=0}^h \sigma_{i,w}\lambda_{a,j}(t) + \sigma_{i,w}evr_a^{OPV}(t) \right. \\
& + \left. \frac{nw-1}{\rho} 1_{\{w<nw-1,i>1\}} + \frac{1}{\varphi} \right\} IPVE_{a,i,w}(t)
\end{aligned}$$

$$\begin{aligned}
& \frac{dLI_{a,i,w,j,k,e}(t)}{dt} = b(t)N(t)evc_0^{OPV}(t) \left((1 - mf(t))1_{\{i=0\}} + \sigma_{0,1}mf(t)1_{\{i=1\}} \right) 1_{\{a=0,j=0,k=0\}} \\
& + (LI_{a-1,i,w,j,k,e}(t) + LI_{0,1,0,j,k,e}(t)1_{\{a=1,i=0\}} \\
& + \sigma_{i,w}evc_{a-1}^{OPV}(t)IPVE_{a-1,i,w}(t)1_{\{j=0,k=0\}} \\
& + evc_0^{OPV}(t)IPVE_{0,1,0}(t)1_{\{a=1,i=0,j=0,k=0\}} + \sigma_{i,w}evc_{a-1}^{OPV}(t)PI_{a-1,i,w}(t)1_{\{j=0,k=0\}} \\
& + evc_0^{OPV}(t)PI_{0,1,0}(t)1_{\{a=1,i=0,j=0,k=0\}}) \frac{1_{\{a>0\}}}{w_{a-1}} \\
& + (evr_a^{OPV}(t)1_{\{j=0\}} + \lambda_{a,j}(t)) \sigma_{i,w}PI_{a,i,w}(t)1_{\{k=0\}} \\
& + (evr_a^{OPV}(t)1_{\{j=0\}} + \lambda_{a,j}(t)) \sigma_{i,w}IPVE_{a,i,w}(t)1_{\{k=0\}} \\
& + \frac{LI_{a,i,w,j,k-1,e}(t)r}{\xi_{i,w,e}} 1_{\{0 < k \leq r\}} + \frac{LI_{a,i,w,j,k-1,e}(t)s}{\gamma_{i,w,e}} 1_{\{k > r\}} \\
& + \frac{LI_{a,i,w,j-1,k,e}(t)(h-1)}{\varepsilon} 1_{\{0 < j < h\}} \\
& - \left\{ \mu_a(t) + \frac{1_{\{a < na-1\}}}{w_a} + \frac{r}{\xi_{i,w,e}} 1_{\{k < r\}} + \frac{s}{\gamma_{i,w,e}} 1_{\{k \geq r\}} \right. \\
& \left. + \frac{(h-1)}{\varepsilon} 1_{\{j < h-1\}} \right\} LI_{a,i,w,j,k,e}(t)
\end{aligned}$$

Use of three IPV doses in RI

Similar to RI with OPV, we assume that primary (non-birth) RI with IPV occurs at the time that infants age from the maternally immune 0 to 2-month age group into the 3 to 11-month age group. We model the cumulative effect of the 3 primary doses and all possible combinations of priming, taking, or remaining susceptible after each dose. Thus, previously fully susceptible (FS) or maternally immune (MI) individuals vaccinated with IPV may remain FS or MI, or move to the 1 successful IPV state (IPV1, i.e., primed), 2 successful IPV state (IPV2), ≥ 3 successful IPV state (IPV3) following an effective “take” with 0, 1, 2, or 3 IPV doses, respectively (Table A1).

Table A1. Routes of acquiring immunity with a three-dose IPV schedule. The quantities between brackets indicate the proportion of the group following the indicated route.

Group	Stay FS or MI	Move to IPV1	Move to IPV2	Move to IPV3
1 dose	No prime with dose 1 [(1-p1)]	Prime with dose 1 [p1]	None	none
2 doses	No prime with dose 1, no prime with dose 2 [(1-p1)×(1-p1)]	No prime with dose 1, prime with dose 2 [(1-p1)×p1]; Prime with dose 1, no take with dose 2	Prime w dose 1, take w dose 2 [p1×p2]	none

		$[p1 \times (1-p2)]$		
3 doses	No prime with dose 1, 2, or 3 $[(1-p1) \times (1-p1) \times (1-p1)]$	Prime with dose 1, no take with doses 2 and 3 $[p1 \times (1-p2) \times (1-p2)]$; No prime with dose 1, prime with dose 2, no take with dose 3 $[(1-p1) \times p1 \times (1-p2)]$; No prime with doses 1 and 2, prime with dose 3 $[(1-p1) \times (1-p1) \times p1]$	No prime with dose 1, prime with dose 2, take with dose 3 $[(1-p1) \times p1 \times p2]$; Prime with dose 1, no take with dose 2, take with dose 3 $[p1 \times (1-p2) \times p2]$; Prime with dose 1, take with dose 2, no take with dose 3 $[p1 \times p2 \times (1-p3)]$	Prime with dose 1, take with doses 2 and 3 $[p1 \times p2 \times p3]$

We assume a cumulative take rate after three doses of IPV of 0.95 for the base case and probabilities $p1$ of priming, $p2$ of “take” given one successful prior IPV dose, and $p3$ of “take” given two successful prior IPV doses equal to the average per-dose take rate $1 - \sqrt[3]{1 - tr_{IPV}} = 0.63$. We characterize the effective vaccination coverage of IPV for fully susceptible and maternally immune individuals (evc^{IPV}) as: $evc^{IPV} = evc^{IPV}(IPV1) + evc^{IPV}(IPV2) + evc^{IPV}(IPV3)$, where

$$evc^{IPV}(IPV1) = dcov1 \times p1 + dcov2 \times ((1 - p1) \times p1 + p1 \times (1 - p2)) + dcov3 \times (p1 \times (1 - p2)^2 + (1 - p1) \times p1 \times (1 - p2) + (1 - p1)^2 \times p1)$$

$$evc^{IPV}(IPV2) = dcov2 \times p1 \times p2 + dcov3 \times ((1 - p1) \times p1 \times p2 + p1 \times (1 - p2) \times p2 + p1 \times p2 \times (1 - p3))$$

$$evc^{IPV}(IPV3) = dcov3 \times p1 \times p2 \times p3$$

where $dcovi$ represents the proportion of children receiving exactly i (non-birth) RI doses. We assume that any number of successful IPV doses move previously immune individuals (i.e., individuals with 1 or more prior LPV infections, because no IPV-immunes do exist in the model prior to the age of RI IPV vaccination) to the IPV and LPV immunity state, which we model with the same properties as the ≥ 2 LPV infections immunity state.[16,17]

Use of one IPV dose in RI added to three non-birth OPV doses

We model the cumulative effect of an added IPV dose to the 3 primary OPV doses as a boost in take by one IPV dose. We use the average per-dose IPV take rate (tr^{IPV}) of 0.63 to calculate the combined per dose take rates similar to the methods used for OPV based on the cumulative take rate after 3 doses (i.e., $tr_d = 1 - (1 - tr)^d$, for d doses and an average per-dose take rate equal to tr). As

above, we consider the coverage of individuals vaccinated with 1, 2 or 3 primary OPV doses to estimate the take rate for a simultaneous OPV and IPV third dose assuming: $tr_d^{OPVIPV} = 1 - (1 - tr_d^{OPV}) \times (1 - tr^{IPV})$. We assume that children receive IPV simultaneously with the first non-birth OPV dose that they receive (regardless of the age at which they receive the first OPV dose), so that any child receiving at least one non-birth OPV dose also receives the added IPV dose. The effective vaccination coverage for fully susceptible and maternally immune individuals becomes: $evc^{OPVIPV} = evc^{OPV} + evc^{IPV}$, where

$$evc^{OPV} = dcov1 \times tr_1^{OPV} + dcov2 \times tr_2^{OPV} + dcov3 \times tr_3^{OPV}$$

and

$$evc^{IPV} = dcov1 \times (tr_1^{OPVIPV} - tr_1^{OPV}) + dcov2 \times (tr_2^{OPVIPV} - tr_2^{OPV}) + dcov3 \times (tr_3^{OPVIPV} - tr_3^{OPV})$$

evc^{IPV} moves fully susceptible or maternally immune individuals to the 1 successful IPV dose group but previously LPV-immunes to the ≥ 2 LPV infections immunity state.

Use of a IPV dose in RI instead of the third non-birth OPV dose

We assume that infants receive the immunity from any OPV and IPV they receive as they age into the 3-11 month age group. We model the cumulative effect of 2 primary OPV doses in the same way as three cumulative doses, except with the coverage of third OPV dose ($dcov3$) equal to 0 (i.e., we replace the third OPV dose with an IPV dose). We use the average per-dose IPV take rate (tr^{IPV}) of 0.63 to calculate the effect of the one IPV dose assuming vaccine recipients get this dose at the same coverage level as the coverage of the third OPV dose. Thus, previously fully susceptible or maternally immune individuals vaccinated with that IPV dose may remain fully susceptible or maternally immune, or move to the 1 IPV state (primed) with $evc^{IPV}(IPV1) = dcov3 \times p1$. Previously LPV-immune individuals move to the IPV and LPV immunity state at the average per-dose take rate, without multiplication by relative susceptibility, consistent with the assumption that IPV doses boost immunes at the same rate that they prime susceptible individuals.

Gradually replace non-birth OPV doses with IPV in RI

We assume that infants receive the immunity from any OPV and IPV doses that they receive as they age into the 3-11-month age group. We replace 3 primary OPV doses with one IPV dose per year. For the first replacement, we use the approach for one IPV dose instead of the third non-birth OPV dose described above. For the second replacement, we model the effect of one OPV dose as $evc^{OPV} = dcov1 \times tr_1^{OPV}$ followed by two IPV doses: using an IPV dose instead of the second OPV dose with coverage $dcov2$, and using a second IPV dose instead of the third OPV dose with coverage $dcov3$. Thus, previously fully susceptible or maternally immune individuals vaccinated with IPV may remain fully susceptible or maternally immune, or move to the 1 IPV state (primed) or 2 IVP state following an effective “take” with 0, 1, or 2 IPV doses respectively: $evc^{IPV} = evc^{IPV}(IPV1) + evc^{IPV}(IPV2)$, where $evc^{IPV}(IPV1) = dcov1 \times p1 + dcov2 \times ((1 - p1) \times p1 + p1 \times (1 - p2))$ and $evc^{IPV}(IPV2) = cov2 \times p1 \times p2$. As above,

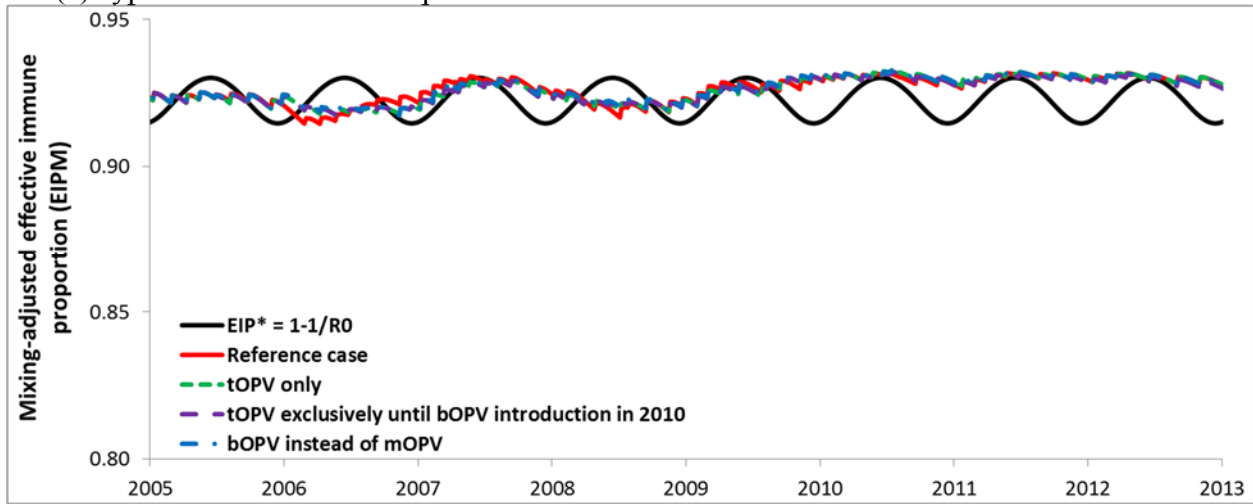
LPV-immunes move to the IPV and LPV immunity state following IPV at the appropriate rates. For the final replacement of the last dose, we follow the approach for the use of three IPV doses in RI described above.

Additional results

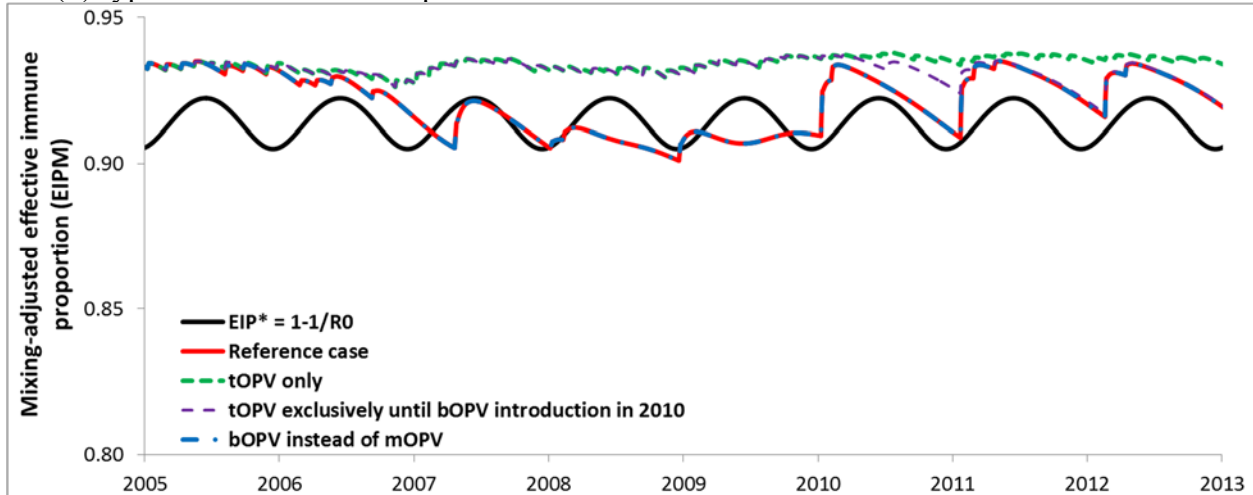
Figures A1 and A2 show the results comparable to Figures 1 and 2 for WUP. Figure A3 shows the results for both areas for all three serotypes for the scenarios shown in Figure 3a. Figure A4 shows the results for both areas for all three serotypes for the scenarios shown in Figure 3b. Figure A5 shows the results for both areas for all three serotypes for the scenarios shown in Figure 3c. Figure A6 shows that some variability in the IPV take rate does not significantly impact the results and that the timing of OPV2 cessation (e.g., in 2015 instead of 2016) shifts the starting point of the drop in population immunity. Figure A7 shows the EIPM of reference case compared to the threshold EIP* for both areas for all three serotypes.

Figure A1: The impact of the hypothetical retrospective scenarios on population immunity in Western Uttar Pradesh (WUP)

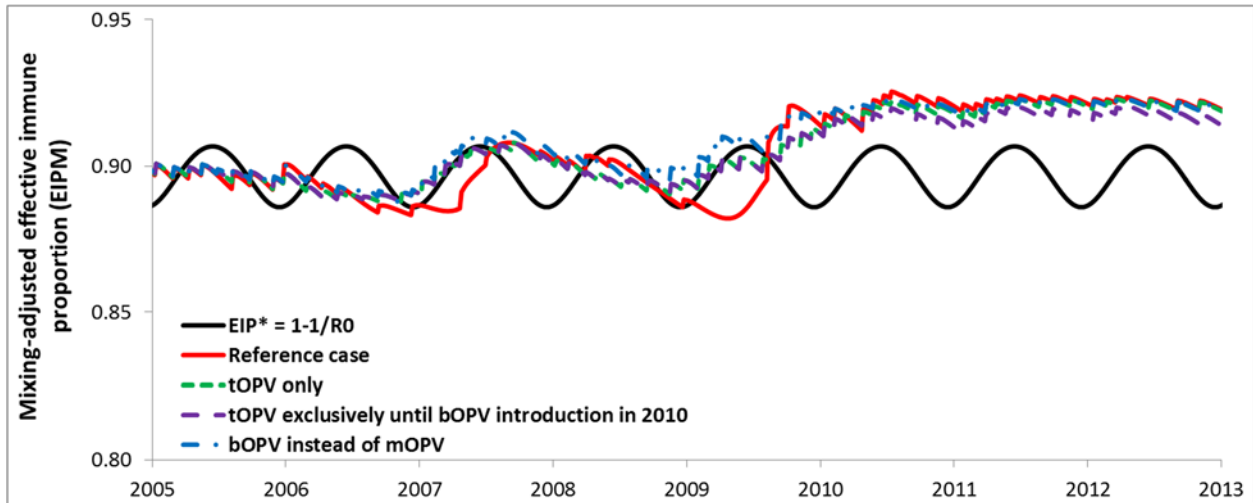
(a) type 1 scenarios in the top of Table 2



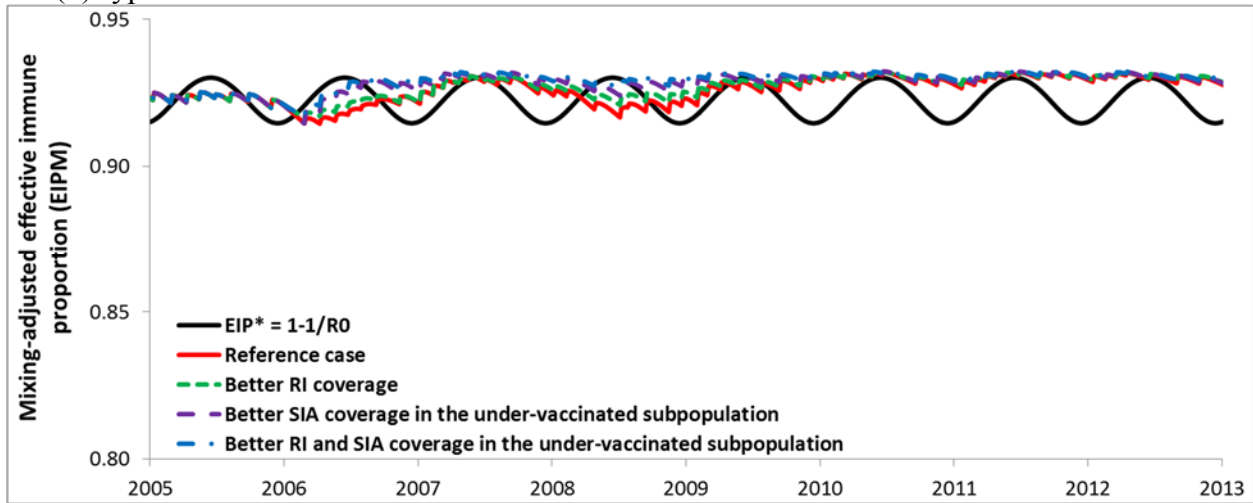
(b) type 2 scenarios in the top of Table 2



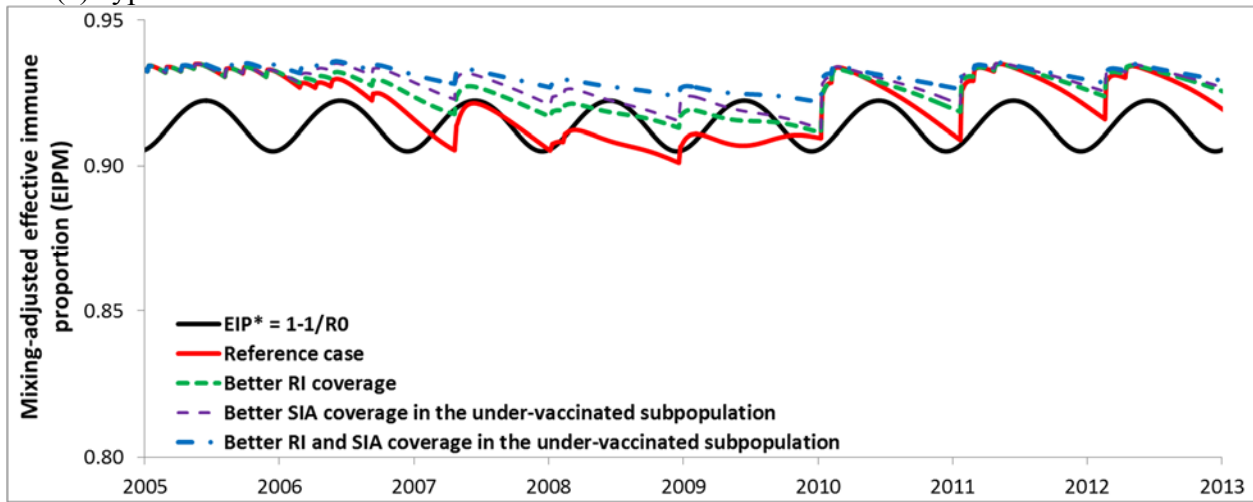
(c) type 3 scenarios in the top of Table 2



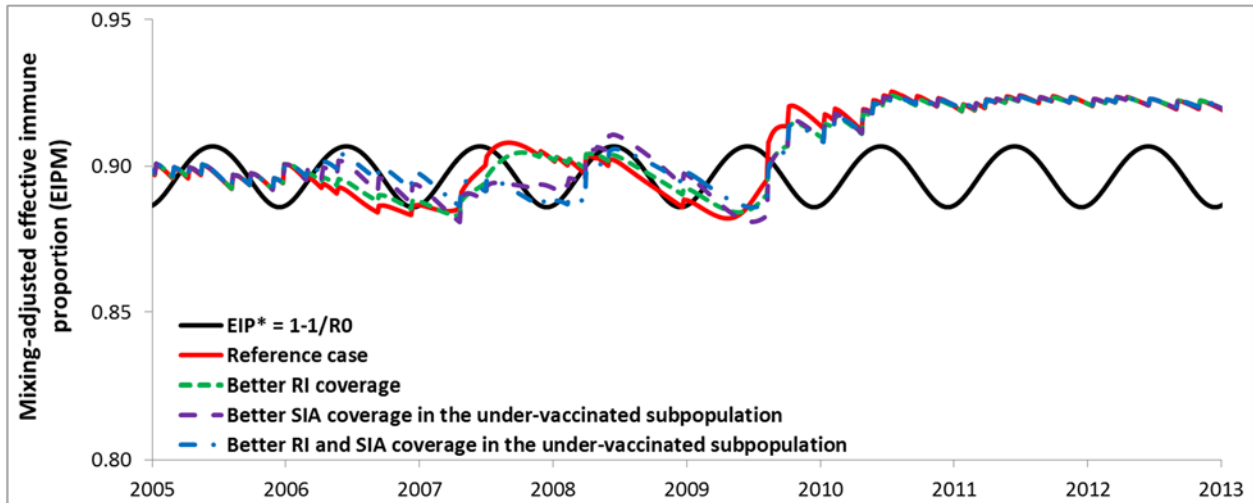
(d) type 1 scenarios in the middle of Table 2



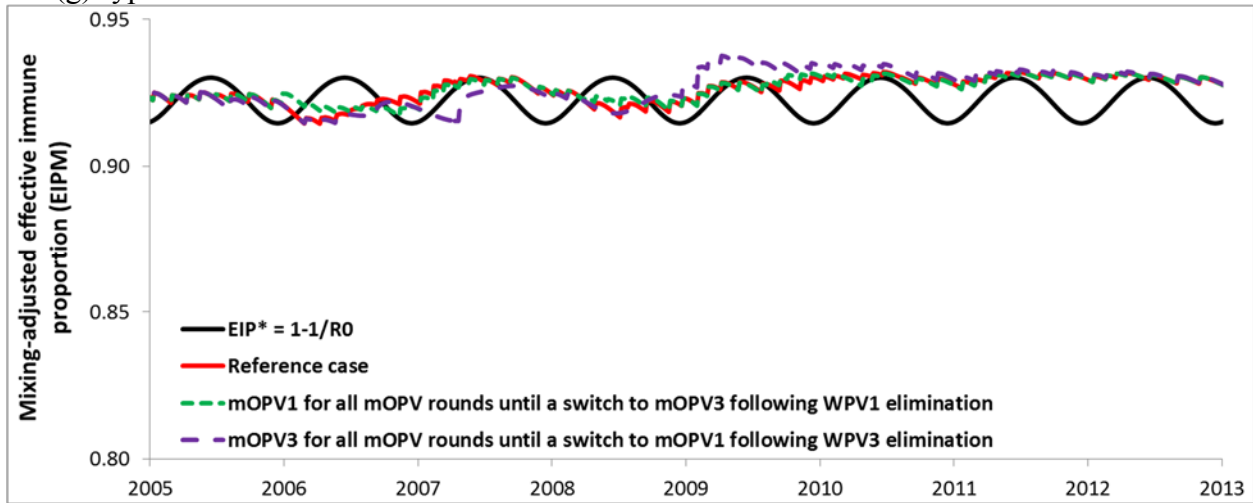
(e) type 2 scenarios in the middle of Table 2



(f) type 3 scenarios in the middle of Table 2



(g) type 1 scenarios in the bottom of Table 2



(h) type 3 scenarios in the bottom of Table 2

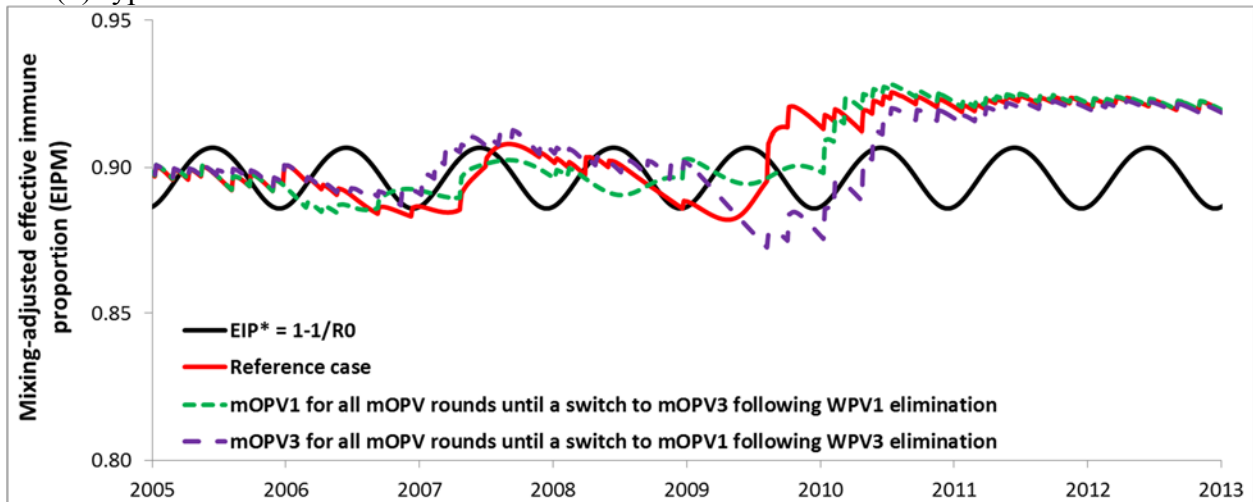
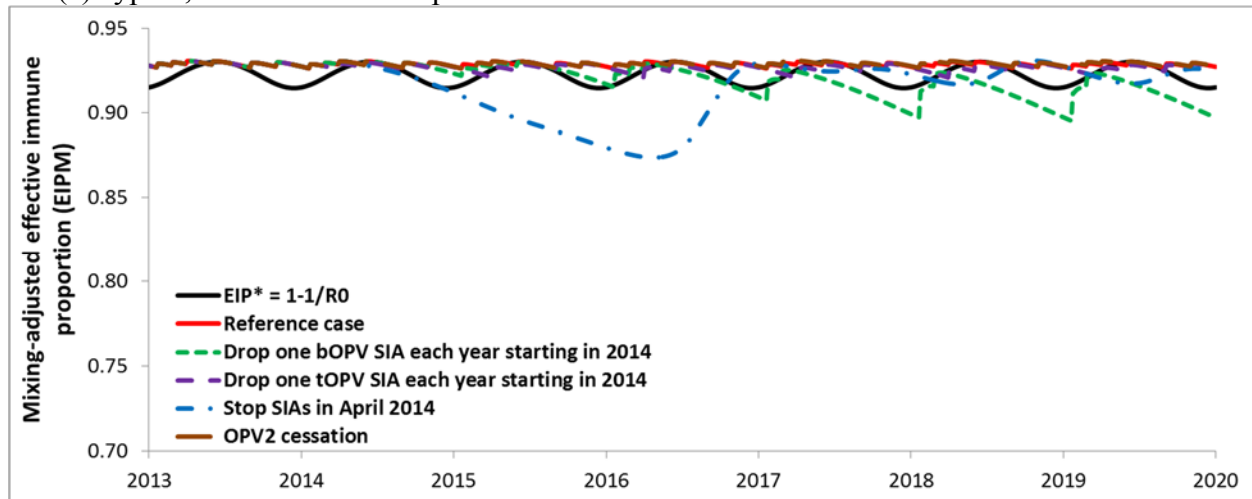
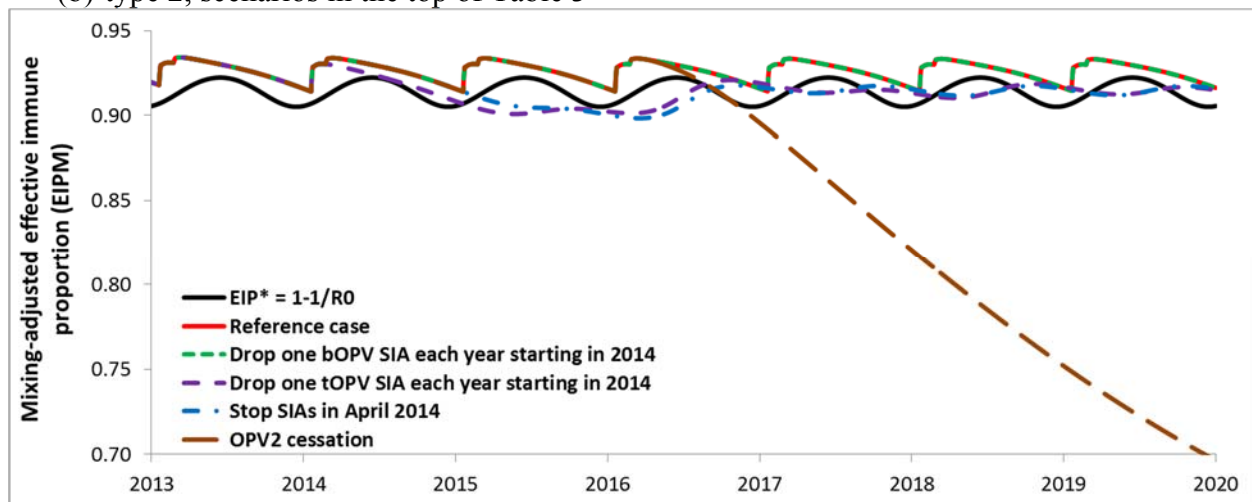


Figure A2: The impact of selected prospective scenarios on population immunity in Western Uttar Pradesh (WUP)

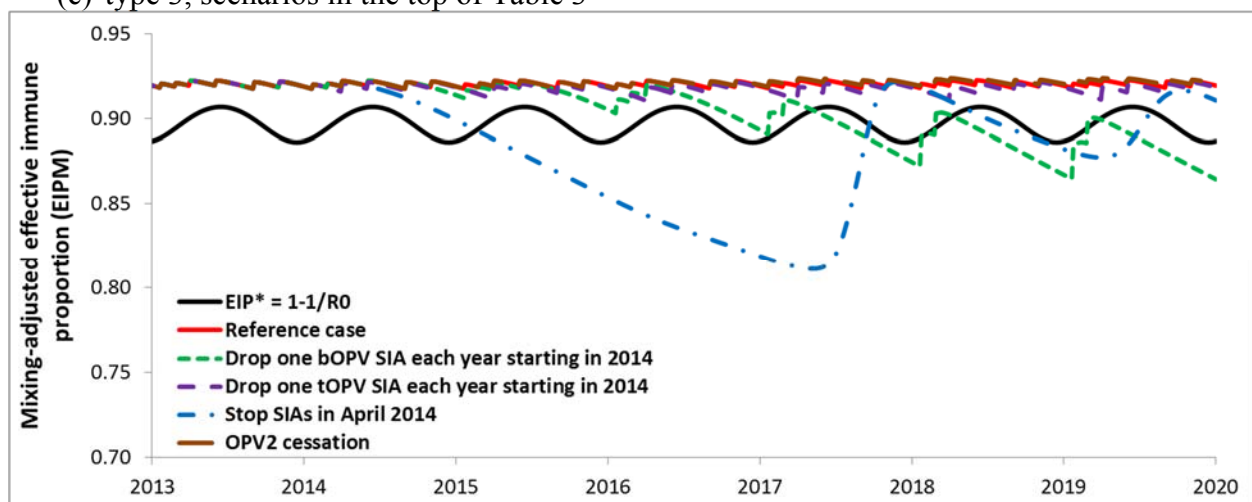
(a) type 1, scenarios in the top of Table 3



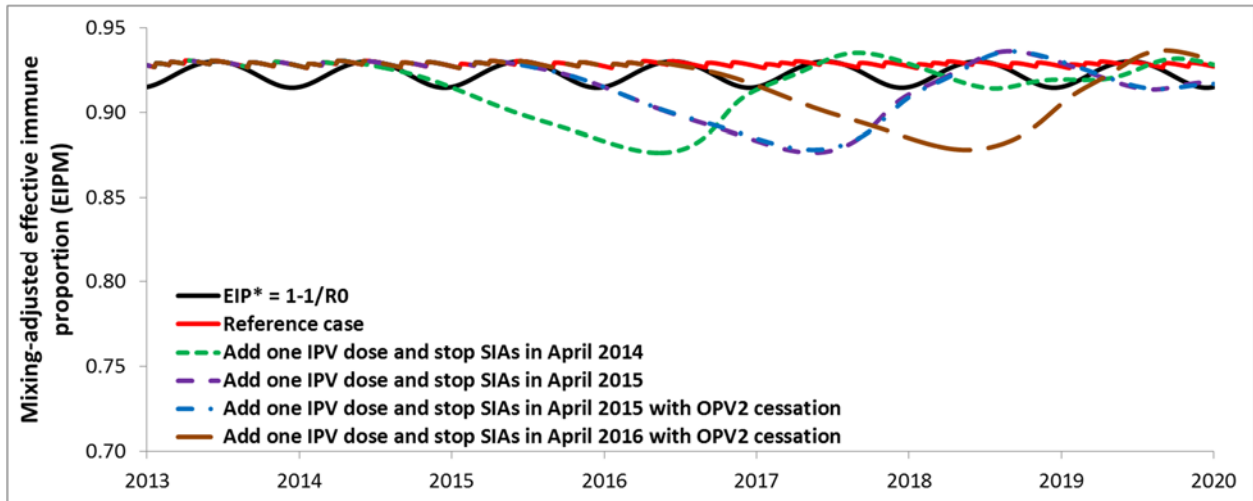
(b) type 2, scenarios in the top of Table 3



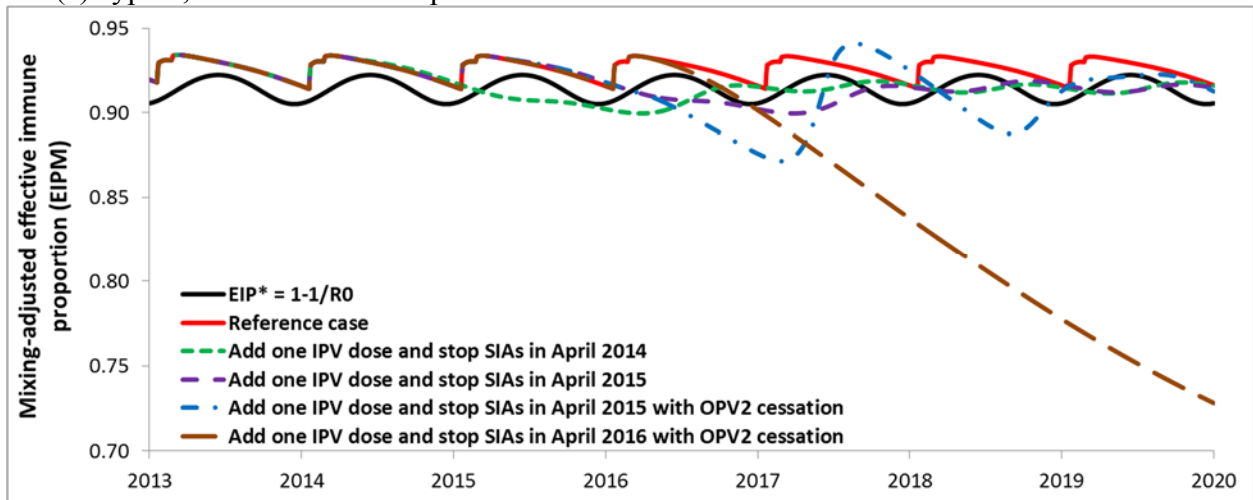
(c) type 3, scenarios in the top of Table 3



(d) type 1, scenarios in the top of Table 3



(e) type 2, scenarios in the top of Table 3



(f) type 3, scenarios in the top of Table 3

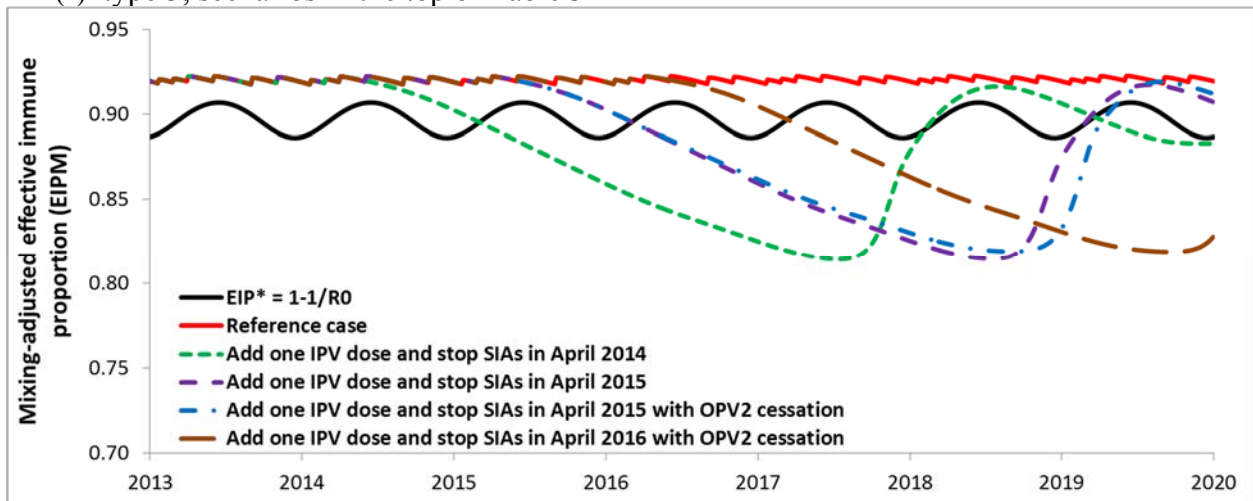
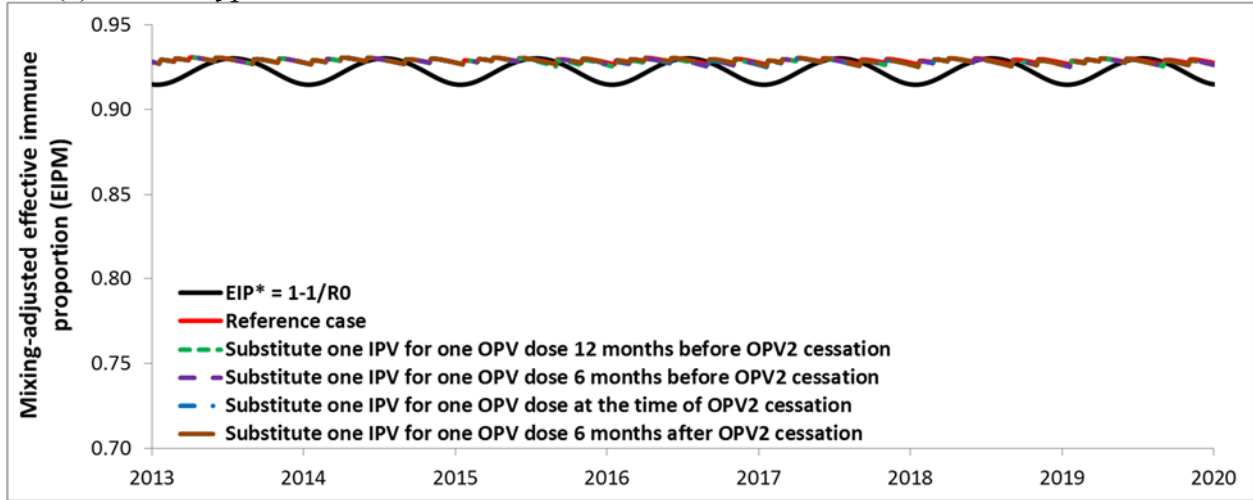
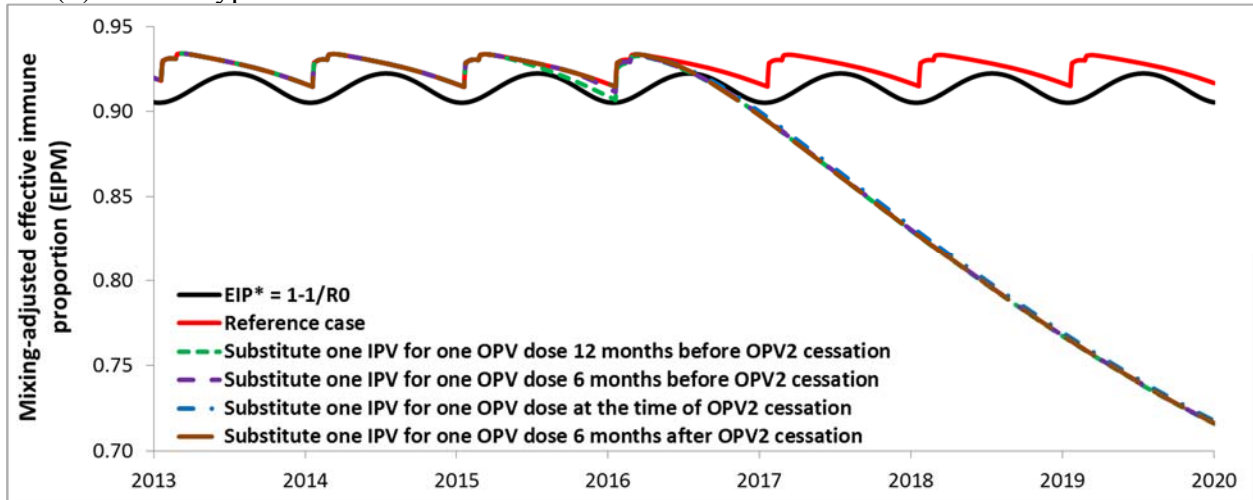


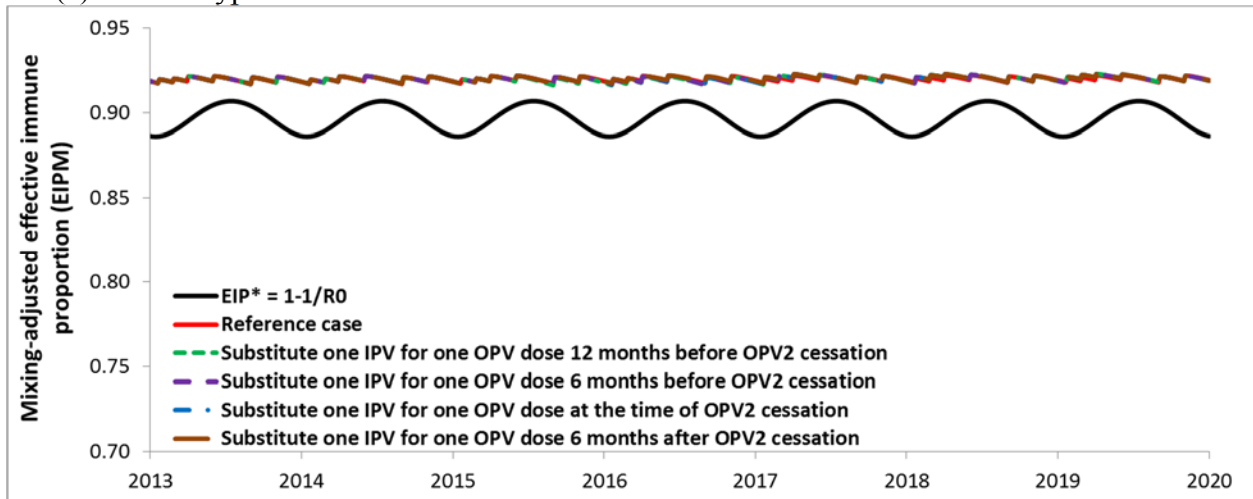
Figure A3: The impact of the prospective scenarios on population immunity in northern India
(a) Bihar – type 1



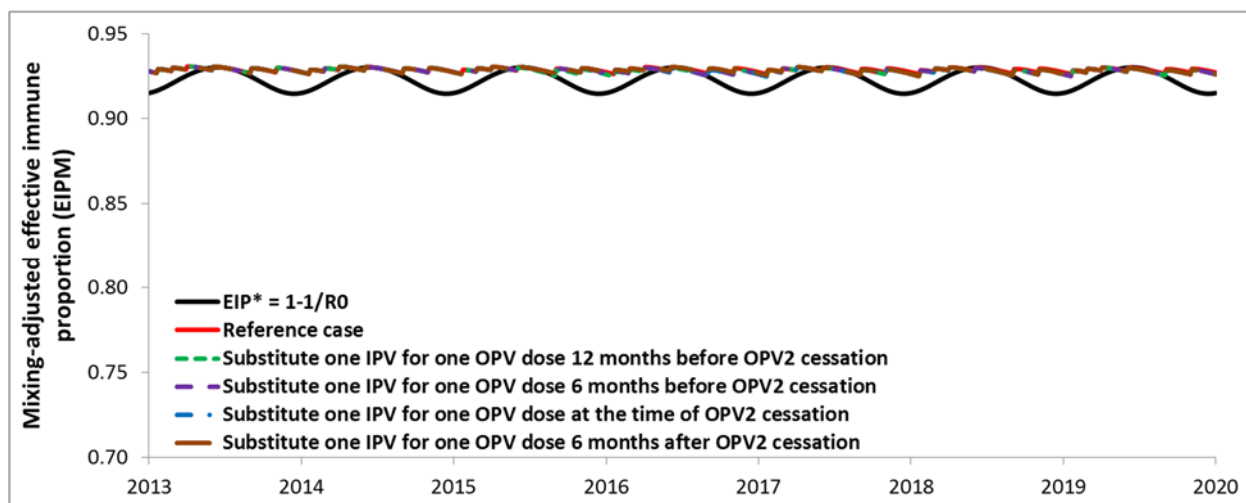
(b) Bihar – type 2



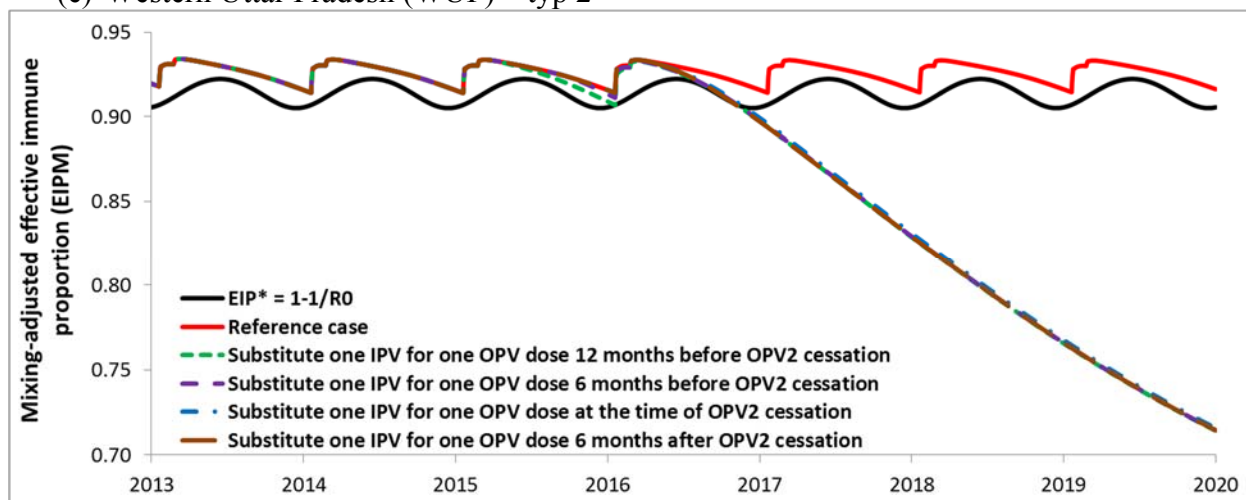
(c) Bihar – type 3



(d) Western Uttar Pradesh (WUP) – type 1



(e) Western Uttar Pradesh (WUP) – typ 2



(f) Western Uttar Pradesh (WUP) – type 3

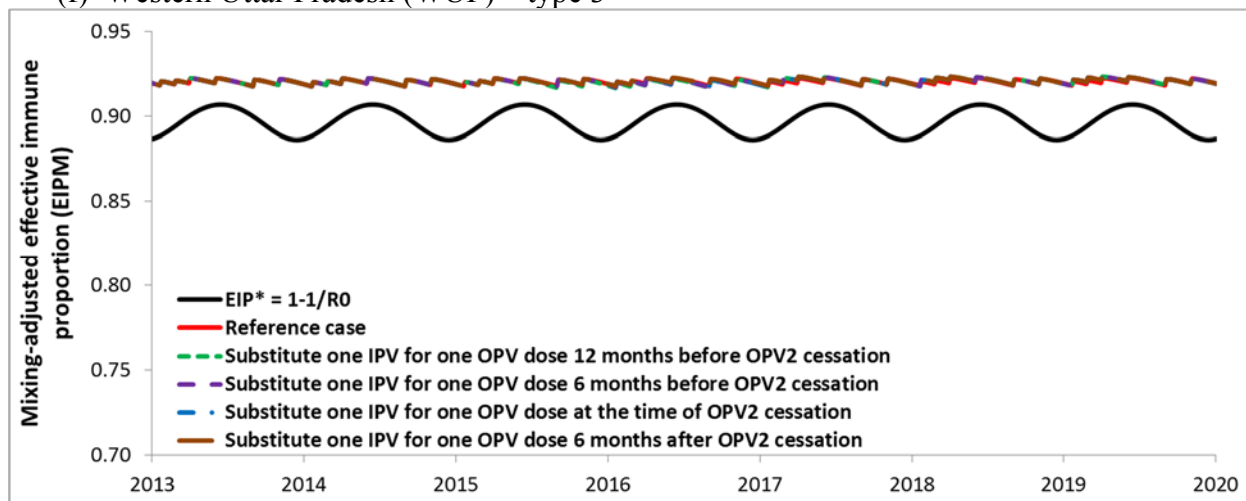
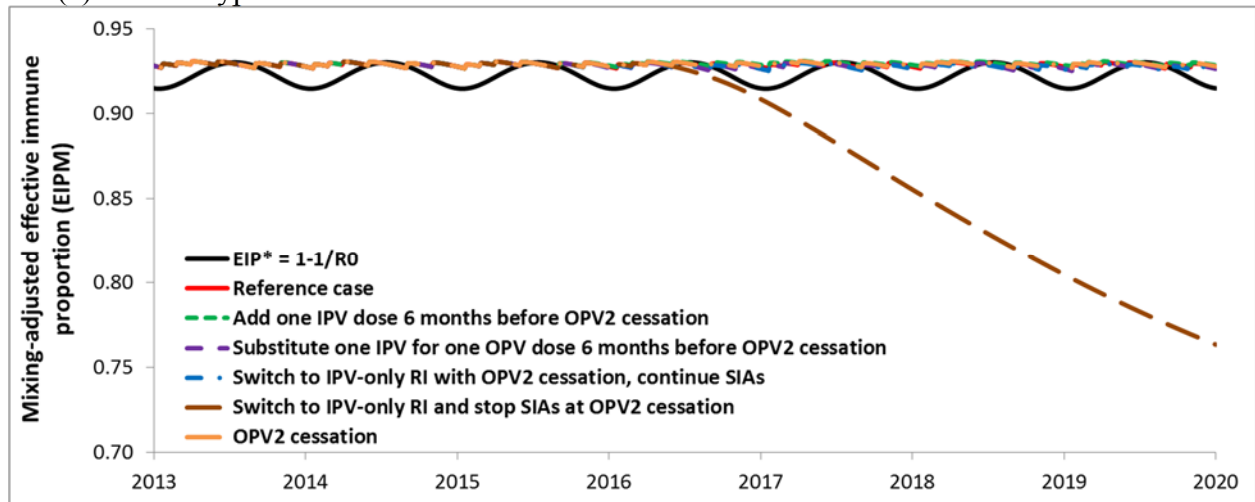
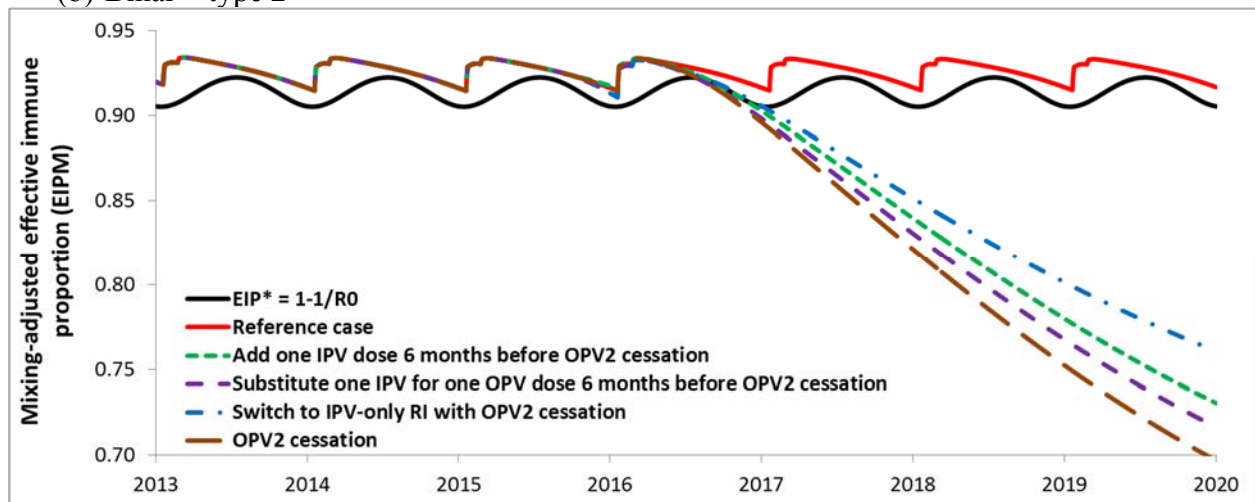


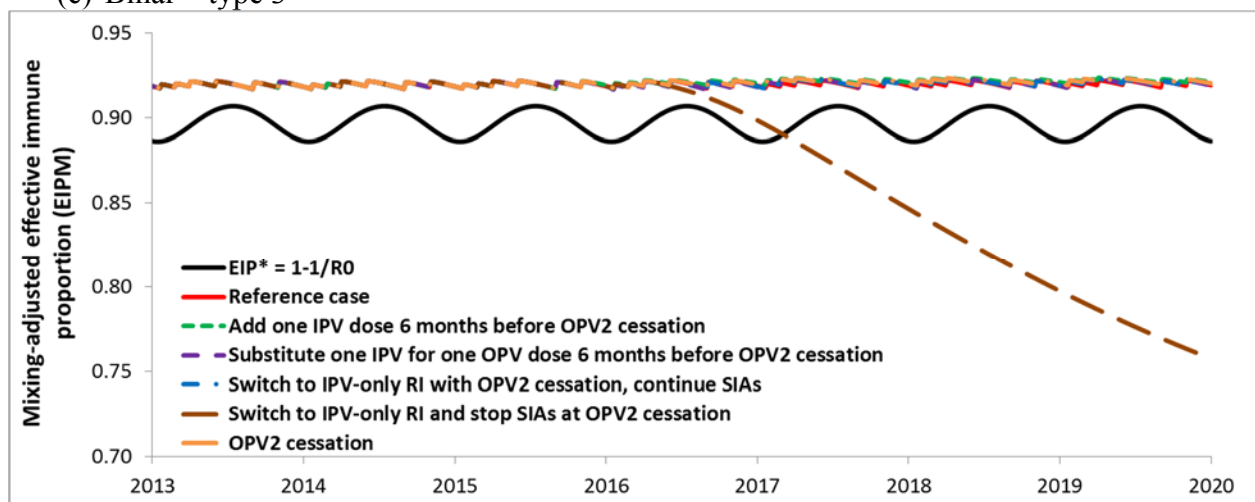
Figure A4: The impact of the prospective scenarios on population immunity in northern India
(a) Bihar – type 1



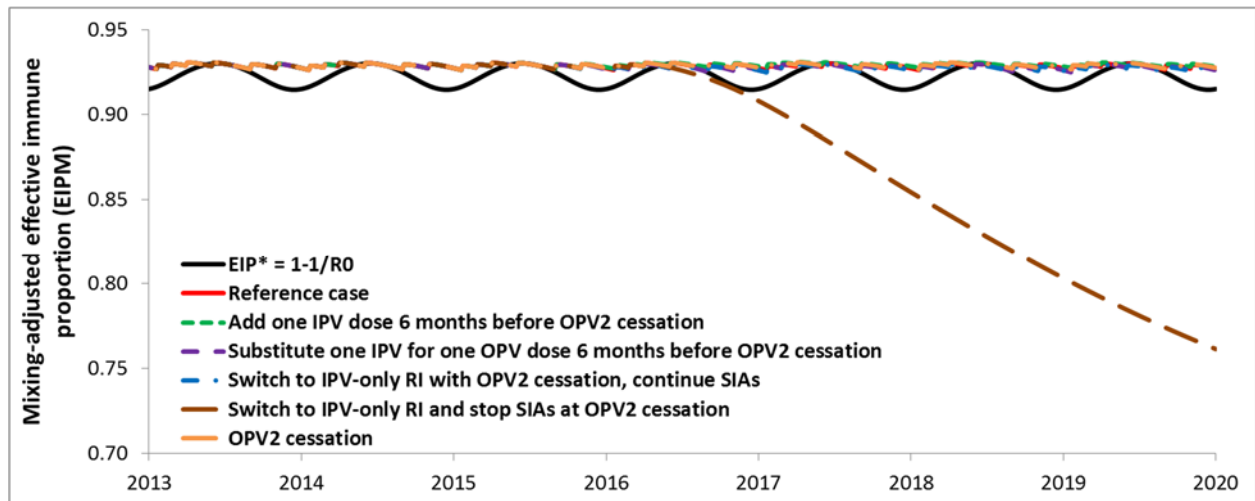
(b) Bihar – type 2



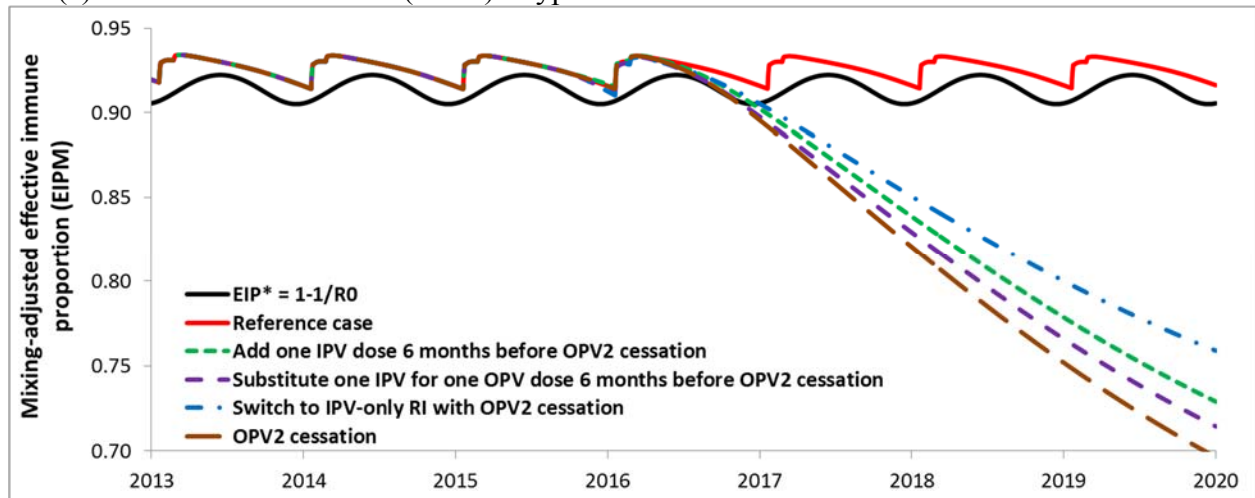
(c) Bihar – type 3



(d) Western Uttar Pradesh (WUP) – type 1



(e) Western Uttar Pradesh (WUP) – type 2



(f) Western Uttar Pradesh (WUP) – type 3

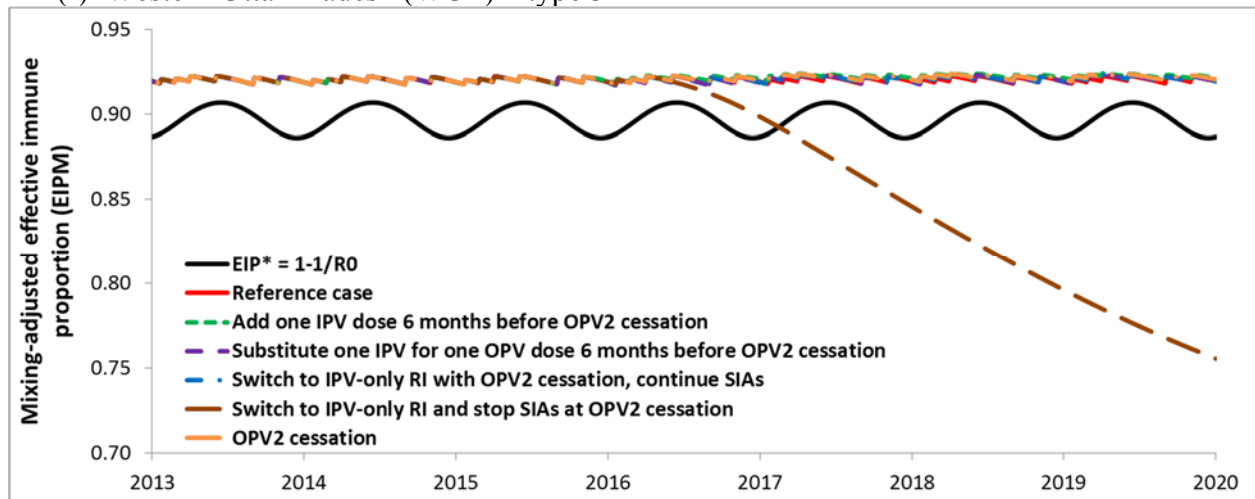
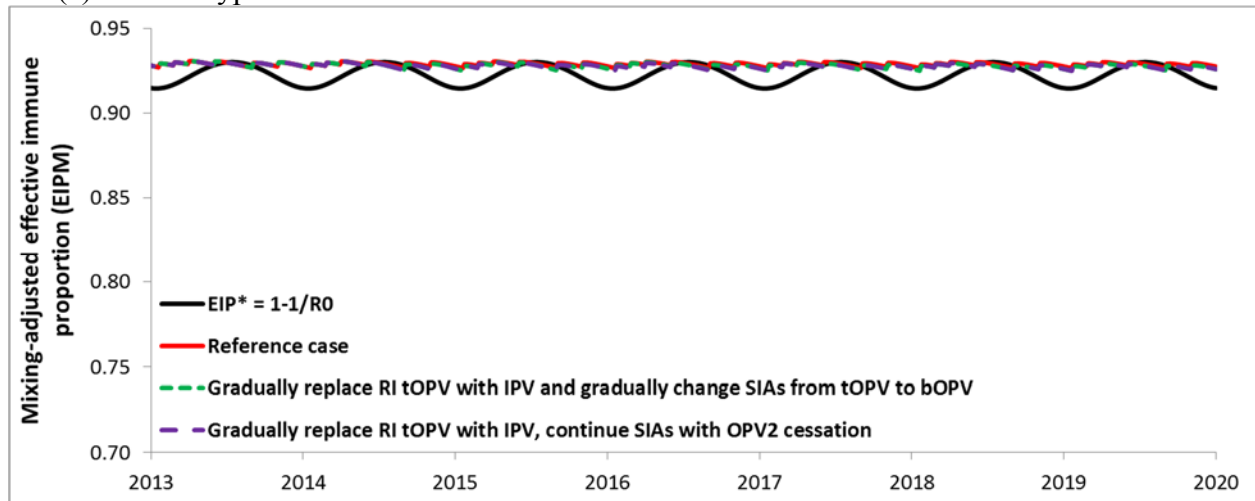
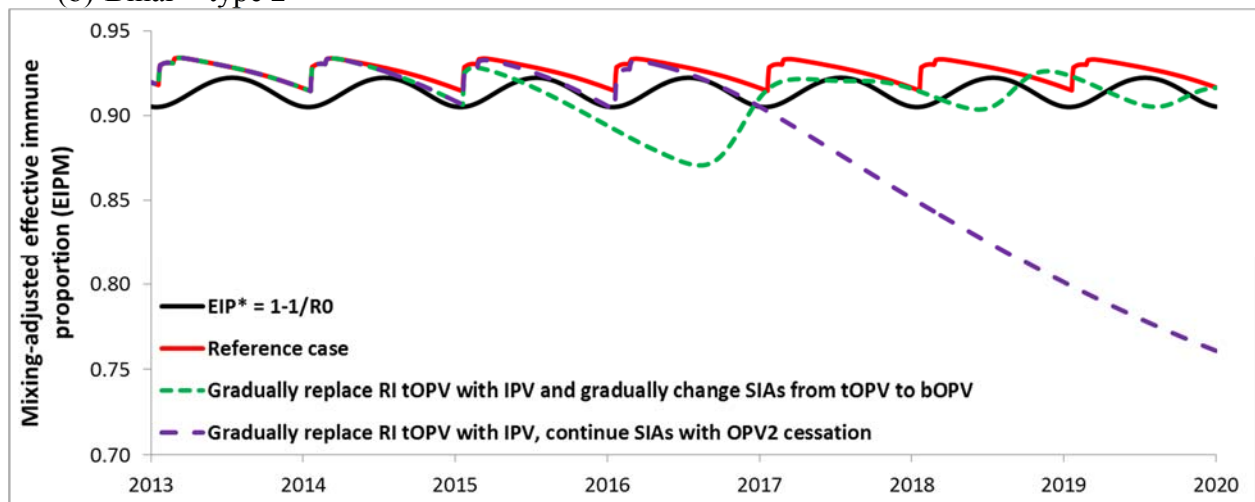


Figure A5: The impact of selected prospective scenarios on population immunity in northern India

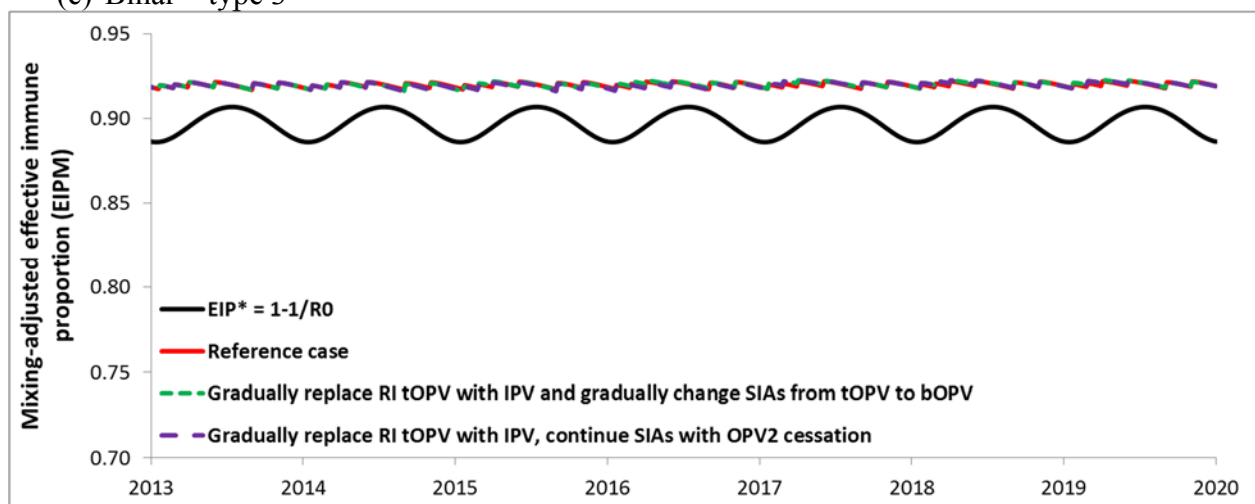
(a) Bihar – type 1



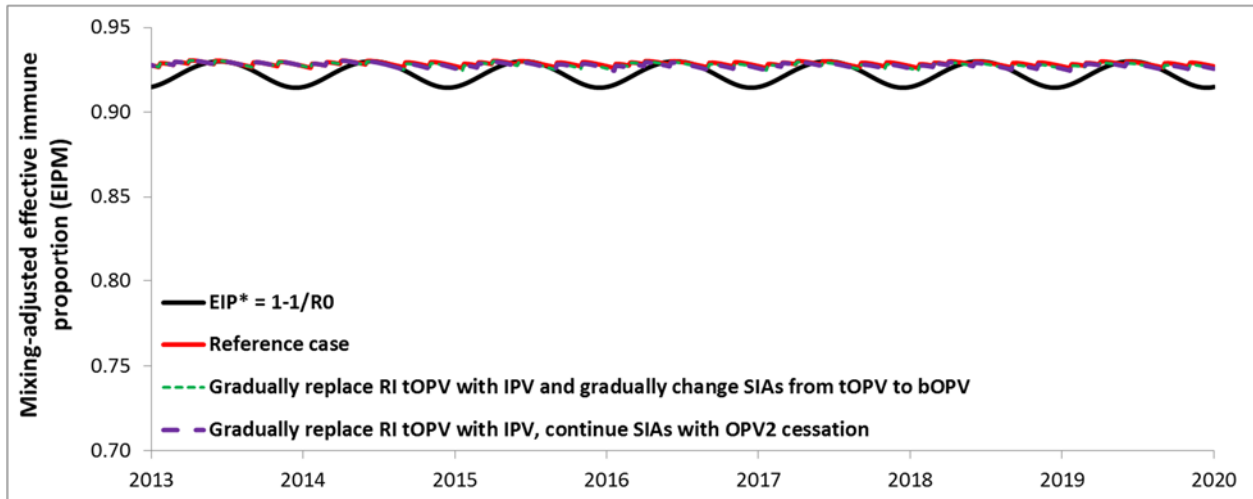
(b) Bihar – type 2



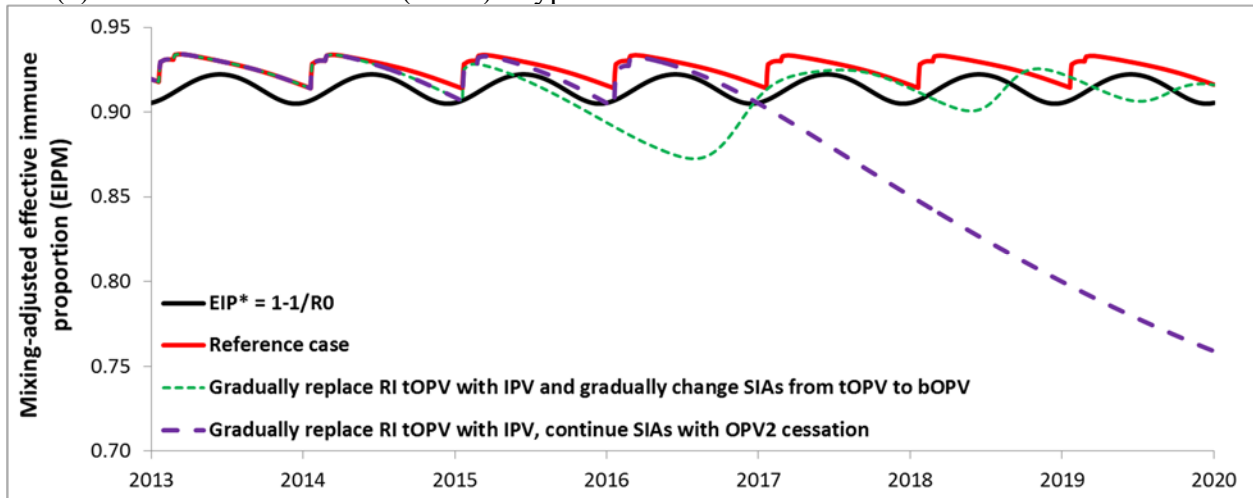
(c) Bihar – type 3



(d) Western Uttar Pradesh (WUP) – type 1



(e) Western Uttar Pradesh (WUP) – type 2



(f) Western Uttar Pradesh (WUP) – type 3

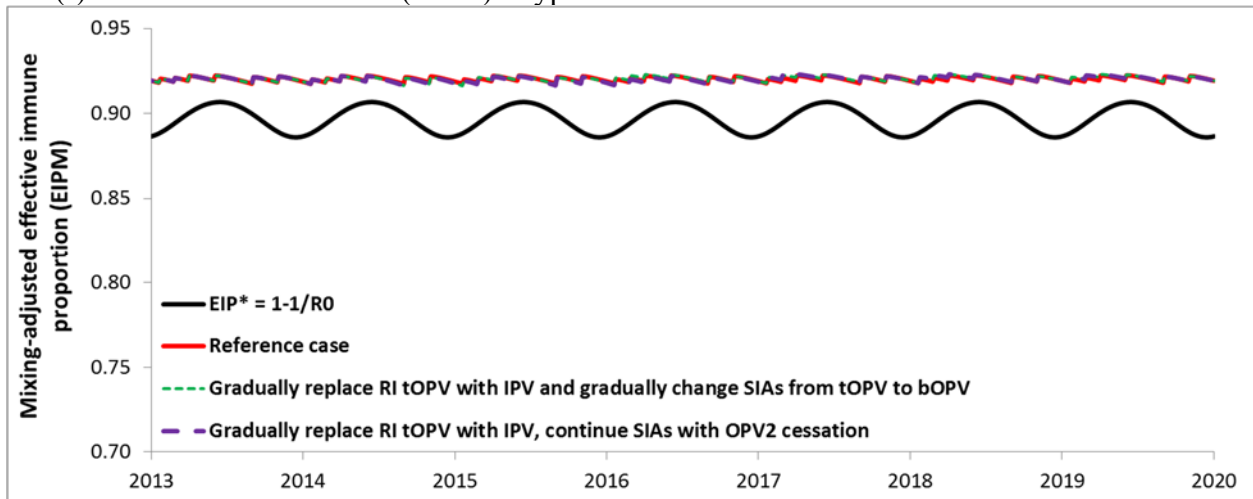
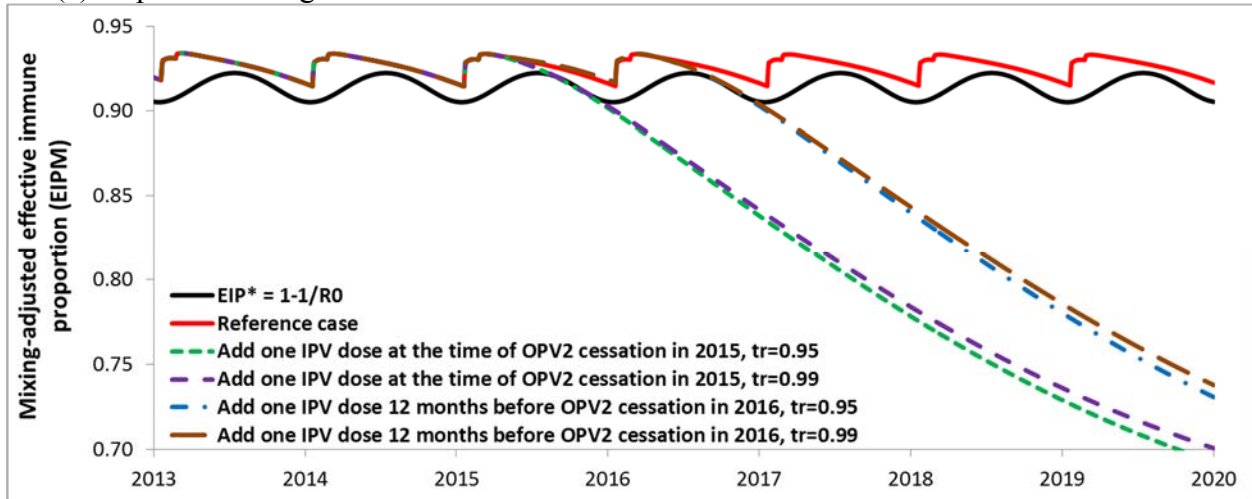


Figure A6: Sensitivity analysis for the take rate of one IPV dose take rate for type 2 and date of OPV2 cessation for both areas

(a) impact of timing of OPV2 cessation and IPV take rate in Bihar



(b) impact of timing of OPV2 cessation and IPV take rate in WUP

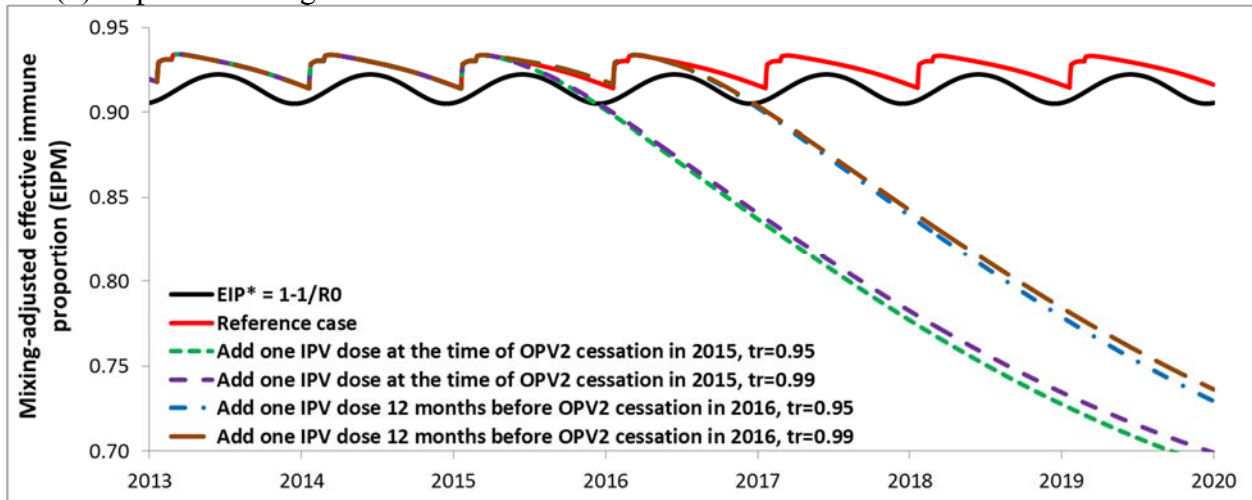
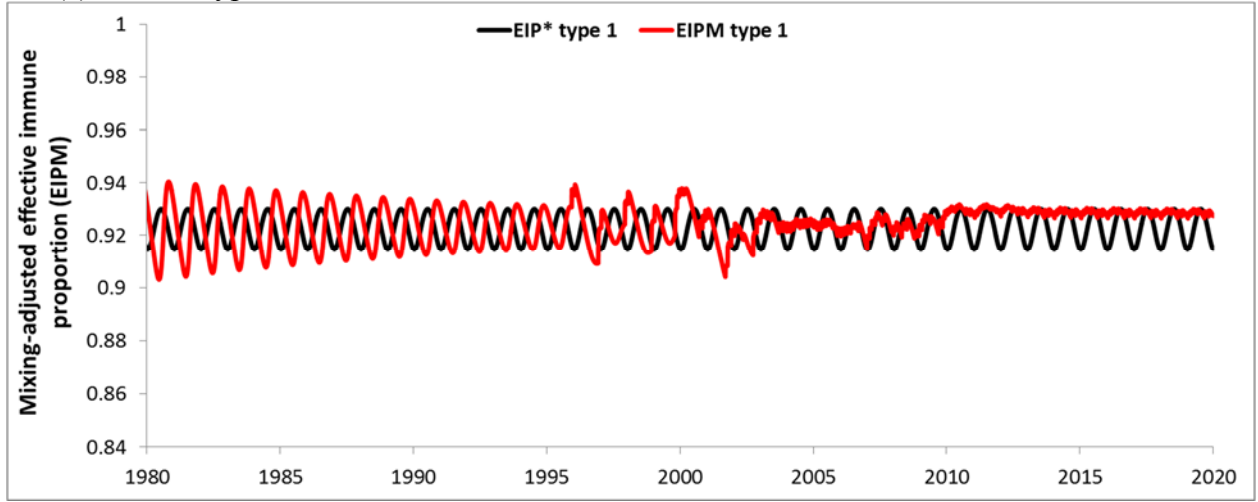
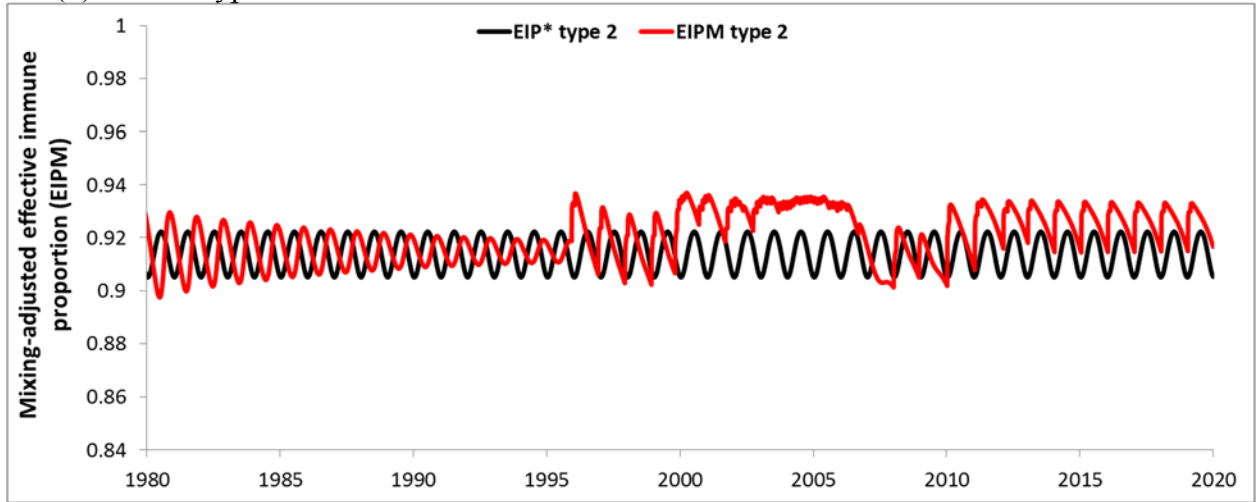


Figure A7: Effective immune proportion ($EIPM$) of reference case compared to the threshold (EIP^*) for northern India.

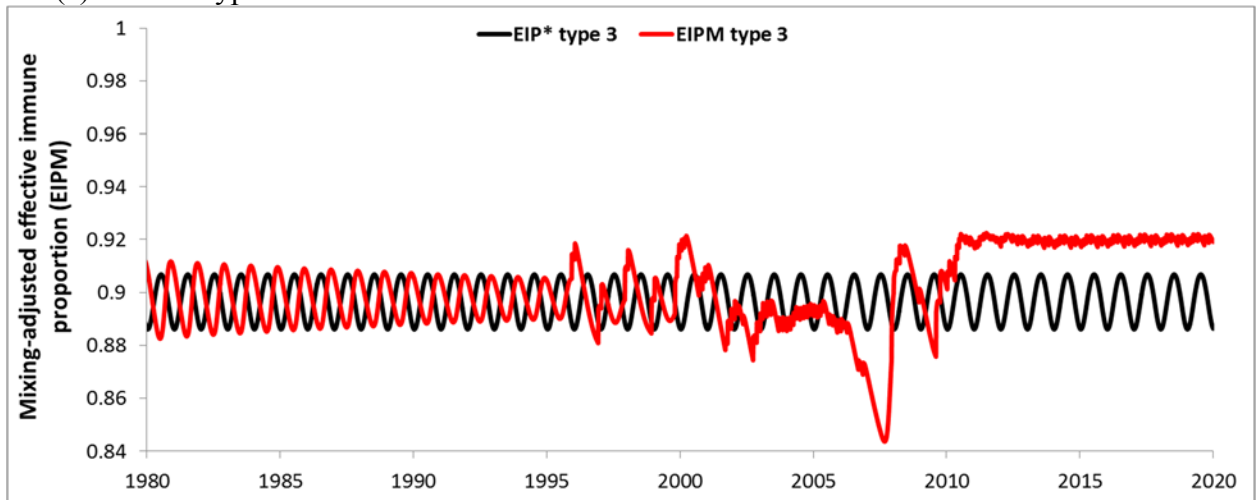
(a) Bihar – type 1



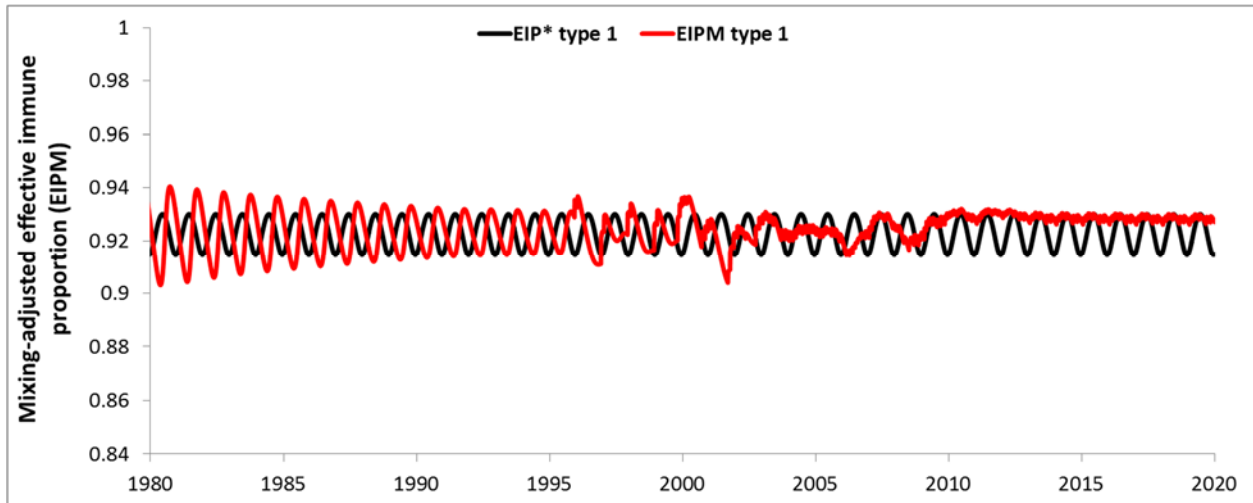
(b) Bihar – type 2



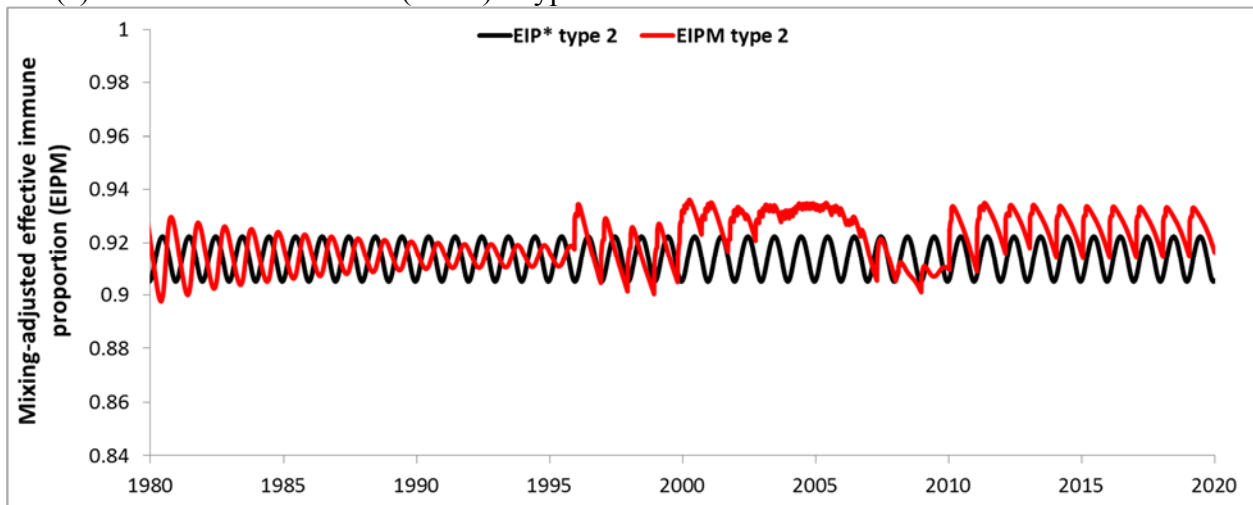
(c) Bihar – type 3



(d) Western Uttar Pradesh (WUP) – type 1



(e) Western Uttar Pradesh (WUP) – type 2



(f) Western Uttar Pradesh (WUP) – type 3

