

## Summary

Recent nOPV2 trials in the Gambia and Bangladesh have provided data on nOPV2 efficacy in African settings and concomitant administration with bOPV. Both provide evidence of reduced efficacy, the not for their combined effect.

Two dose seroconversion from baseline in the Gambia trial for seronegative infants was 85.6%. Combining with seronegative children, 66.7% seroconverted after two doses. All infants in the trial had (at least) one dose of IPV as a condition of participation.

In the Bangladesh concomitant trial, 2-dose per-protocol type 2 seroconversion was 89.1% in the nOPV2 only arm, and 65.8% in the nOPV-bOPV arm. Upon three doses these grew to 95.9% and 79.6%, respectively.

Per dose efficacy for seronegative infants in the Gambia trial, derived from cumulative 2-dose seroconversion, was 62.1%. The per-dose impairment of nOPV2-bOPV compared to nOPV2 alone in the Bangladesh trial, derived from the 3-dose results, was 62.7%.

Applying 62.1% with a 62.7% impairment, 3-dose seroconversion for type 2 from nOPV2 delivered with bOPV would be 77.2%. This is not that different that the 79.6% 3-dose results from the nOPV2-bOPV arm from the Bangladesh trial.

Currently, in the Nigeria model, 70% per-dose efficacy is being used for mOPV2 (Sabin 2) for Nigeria, and likewise for nOPV2. More subtly, R0 for nOPV2 is half that of Sabin.

We proposed the following:

Source	Efficacy per dose	Note
nOPV2 in RI (with bOPV)	0.389	$0.621 * 0.627$ , Gambia * Bangladesh impairment
nOPV2 in SIA (Nigeria)	0.621	Gambia per-dose efficacy from seronegative infants. Over the course of multiple doses, will converge on 1, reducing differences with Sabin 2
Sabin 2 in SIA (Nigeria)	0.7	This does not have the specific support, but some impairment of nOPV2 compared to Sabin 2 seems likely

Supporting plots (to be fleshed out later)

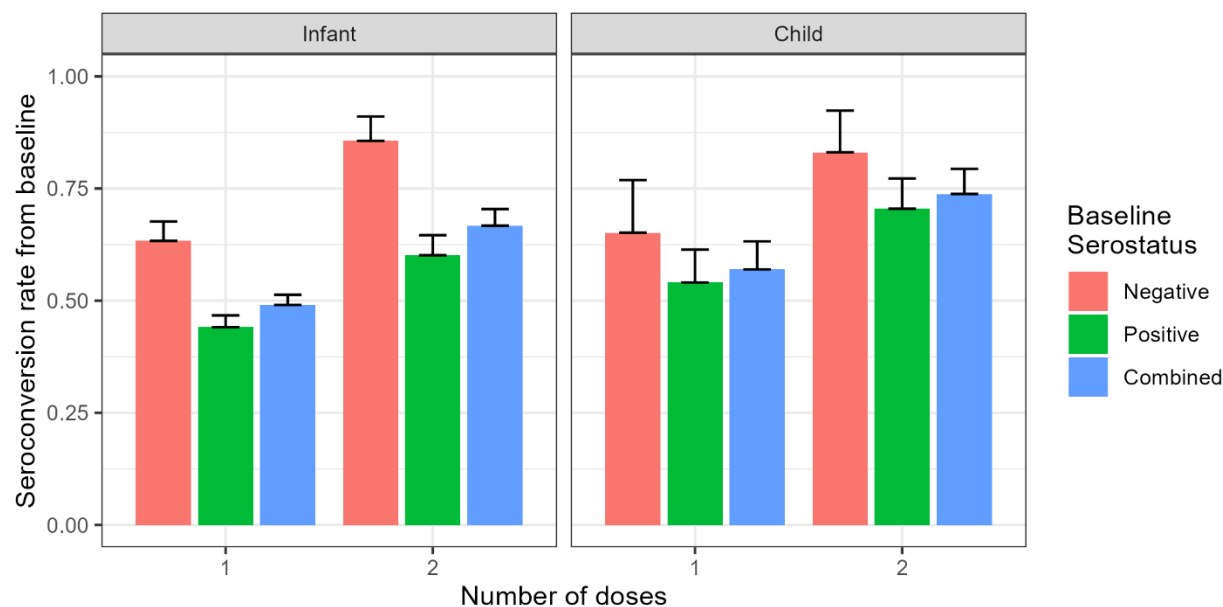


Figure 1: Gambia trial, cumulative seroconversion with upper confidence bound.

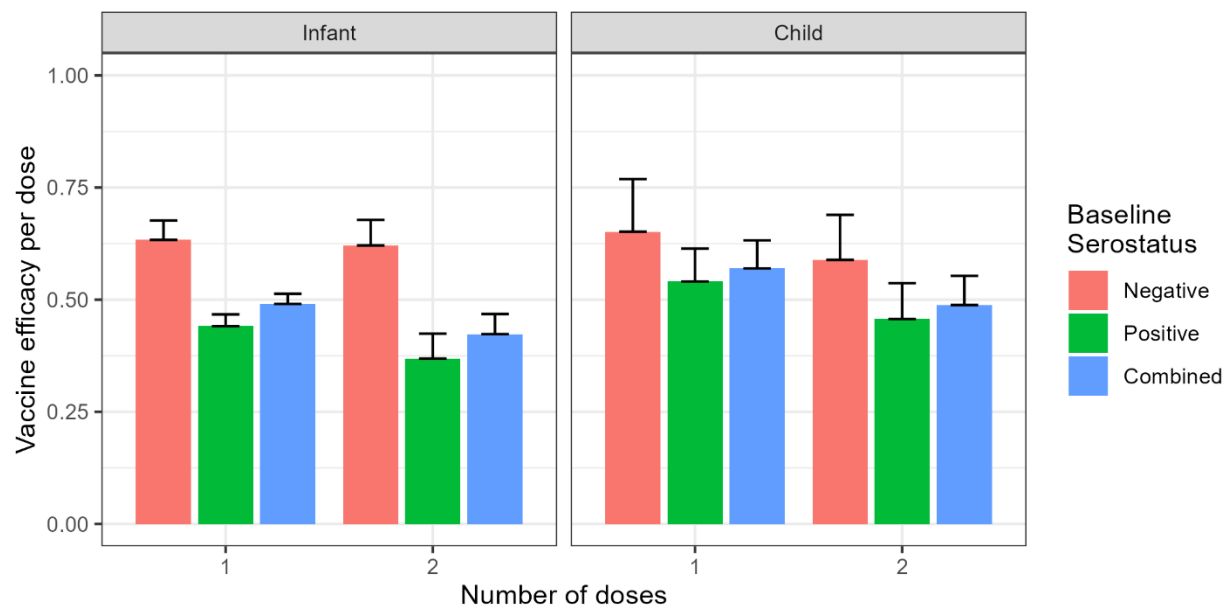


Figure 2: Gambia trial per dose efficacy of nOPV2, derived from cumulative seroconversion.

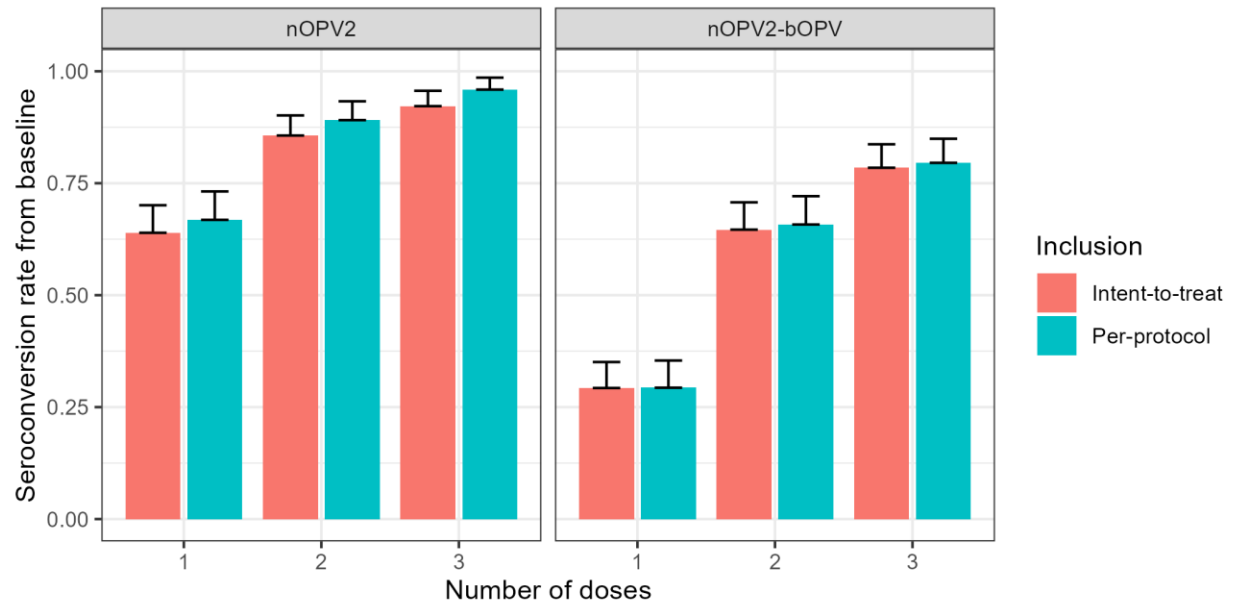


Figure 3: Bangladesh trial type 2 seroconversion.

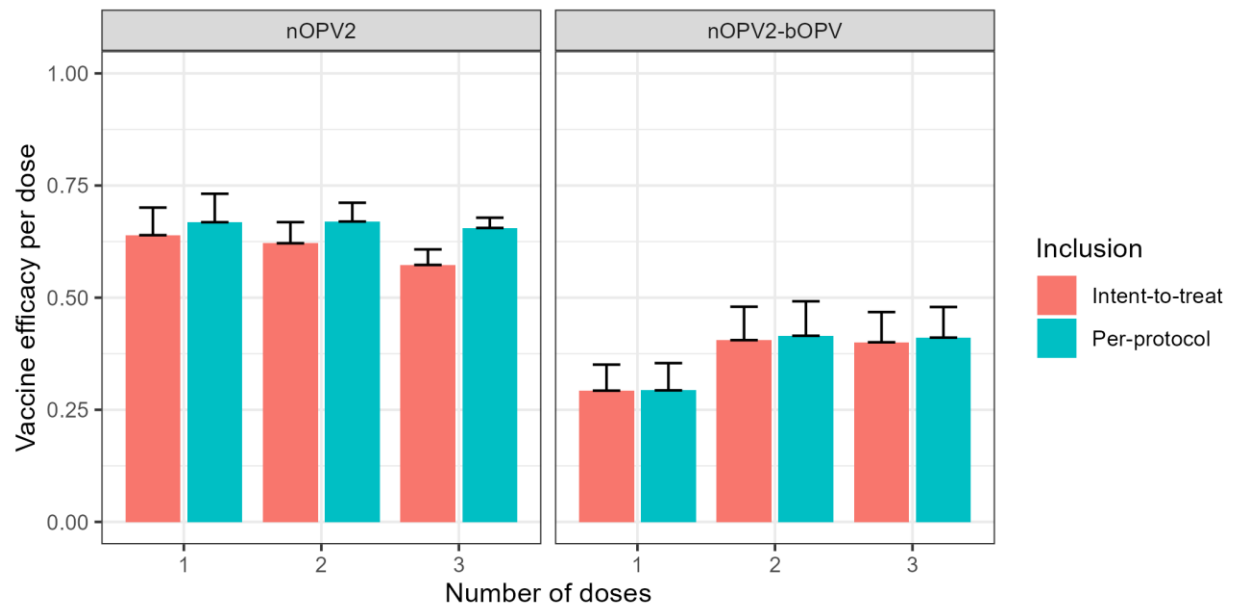


Figure 4: Bangladesh trial, per-dose efficacy derived from cumulative seroconversion.

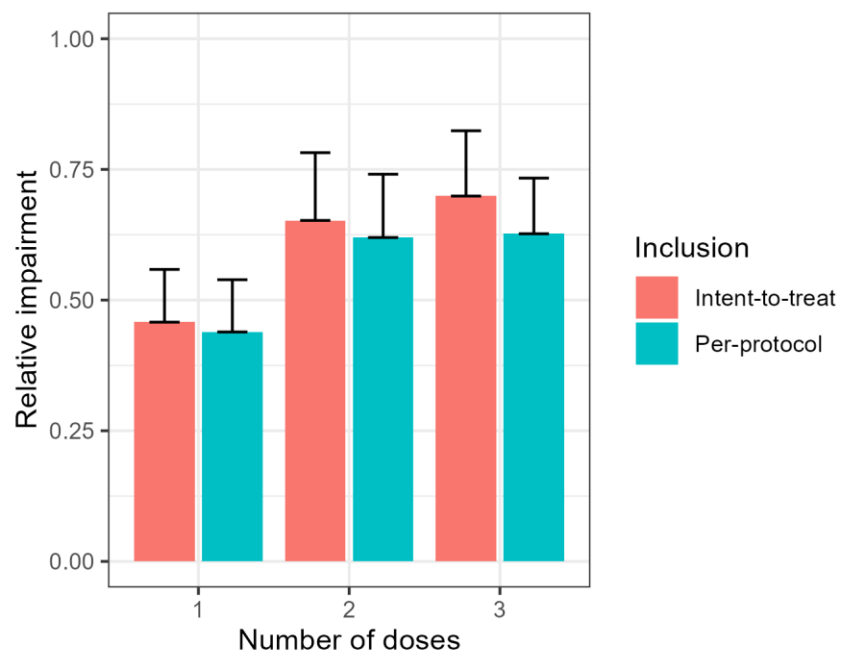


Figure 5: Bangladesh trial, relative impairment of nOPV2 when coadministered with nOPV2-bOPV, derived from cumulative results.

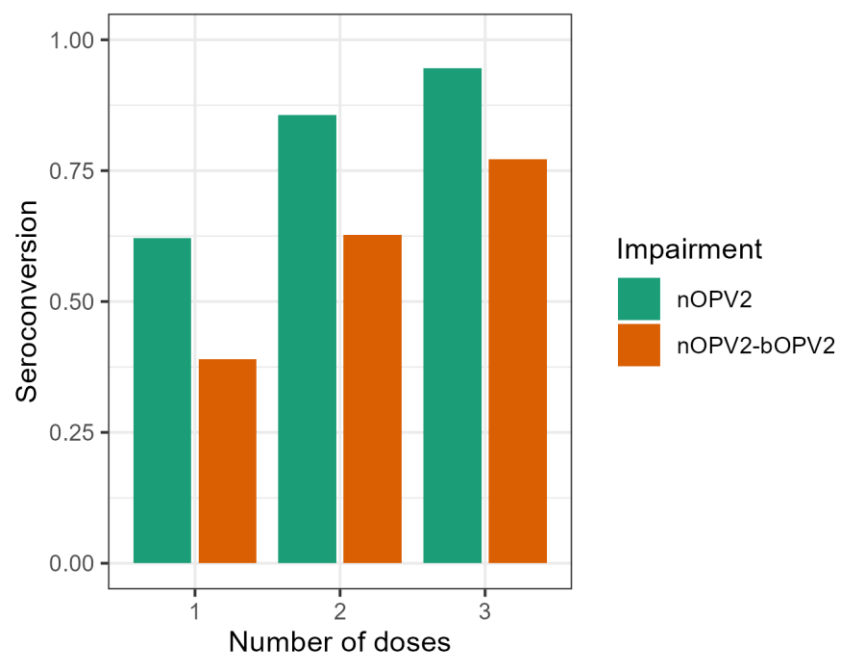
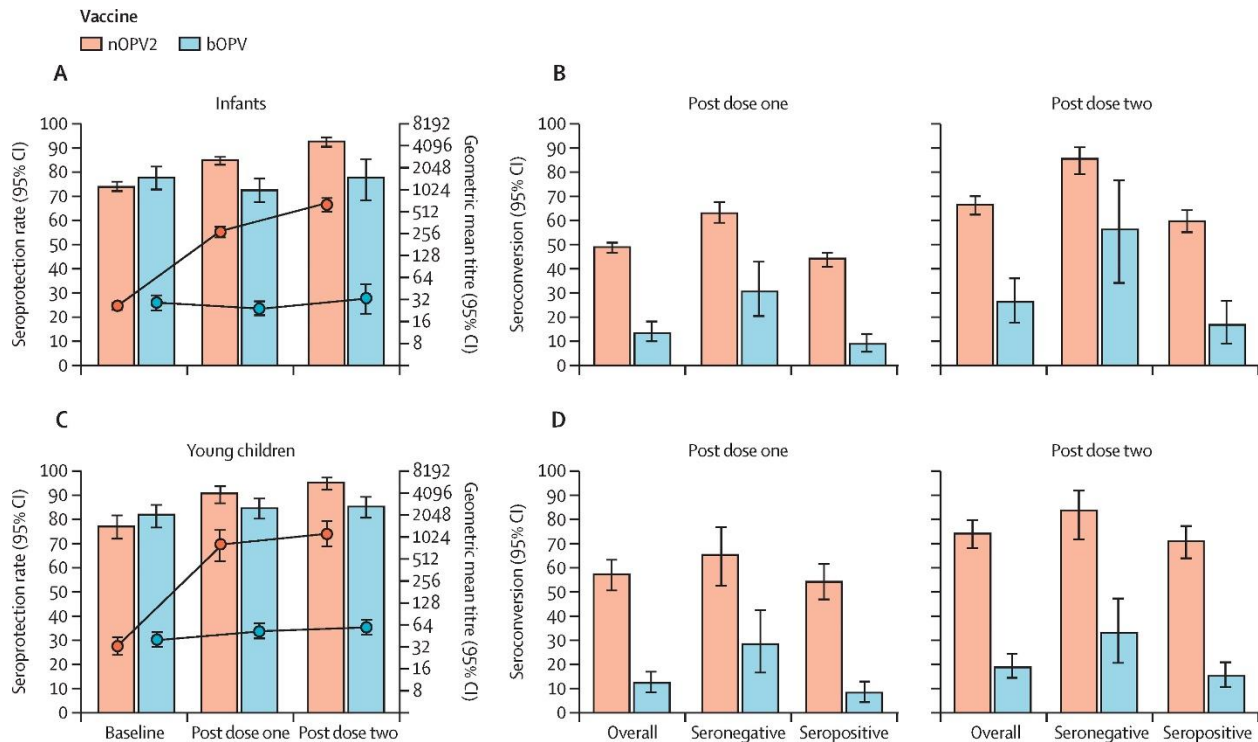


Figure 6: Effect of proposed impairment on seroconversion in RI.

## Other data

There are some knowledge gaps in comparing these studies, and we highlight one: heterotypic immunity, in this case apparent seroconversion to type 2 from a non-nOPV2 arm.

In the Gambia study, there was significant seroconversion found in the bOPV arm. It should be noted that vaccine exposure for the Gambia study was higher than that of the Bangladesh study. We did not adjust nOPV2 per-dose efficacy with the type 2 seroconversion results in the bOPV arm because seroconversion in the bOPV arm did not likely come from community exposure to OPV2.



In contrast, there was very little type 2 seroconversion in the Bangladesh study in the bOPV-only arms with little/no vaccine exposure.

**Supplementary Table 2: Immune response for poliovirus types 1, 2, and 3 by study group, per-protocol population**

	<b>Group A (nOPV2 only [n=230])</b>	<b>Group B (nOPV2 and bOPV [n=225])</b>	<b>Group C (bOPV only [n=231])</b>
<b>Poliovirus type 1</b>			
Immune response at 10 weeks after 1 dose	2 (1%, 0-3)	173 (77%, 71-82)	183 (79%, 74-84)
Cumulative immune response by 14 weeks after 2 doses	10 (4%, 2-8)	208 (92%, 88-95)	215 (93%, 89-96)
Cumulative immune response by 18 weeks after 3 doses	20 (9%, 6-13)	220 (98%, 95-99)	225 (97%, 94-99)
<b>Poliovirus type 2</b>			
Immune response at 10 weeks after 1 dose	147 (64%, 58-70)	66 (29%, 24-36)	0 (0%, 0-2)
Cumulative immune response by 14 weeks after 2 doses	196 (85%, 80-89)	148 (66%, 59-72)	4 (2%, 1-4)
Cumulative immune response by 18 weeks after 3 doses	211 (92%, 87-95)	179 (80%, 74-84)	17 (7%, 5-11)
<b>Poliovirus type 3</b>			
Immune response at 10 weeks after 1 dose	3 (1%, 0-4)	144 (64%, 58-70)	140 (61%, 54-67)
Cumulative immune response by 14 weeks after 2 doses	6 (3%, 1-6)	196 (87%, 82-91)	200 (87%, 82-90)
Cumulative immune response by 18 weeks after 3 doses	8 (3%, 2-7)	213 (95%, 91-97)	218 (94%, 91-97)

Data are the number of vaccine responders (%; 95% CI). nOPV2 = novel oral poliovirus vaccine type 2; bOPV = bivalent oral poliovirus vaccine.