

Impact of Switch to IPV on Rotavirus Vaccine Performance

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Efficacy of oral rotavirus vaccines is lower in resource-limited areas

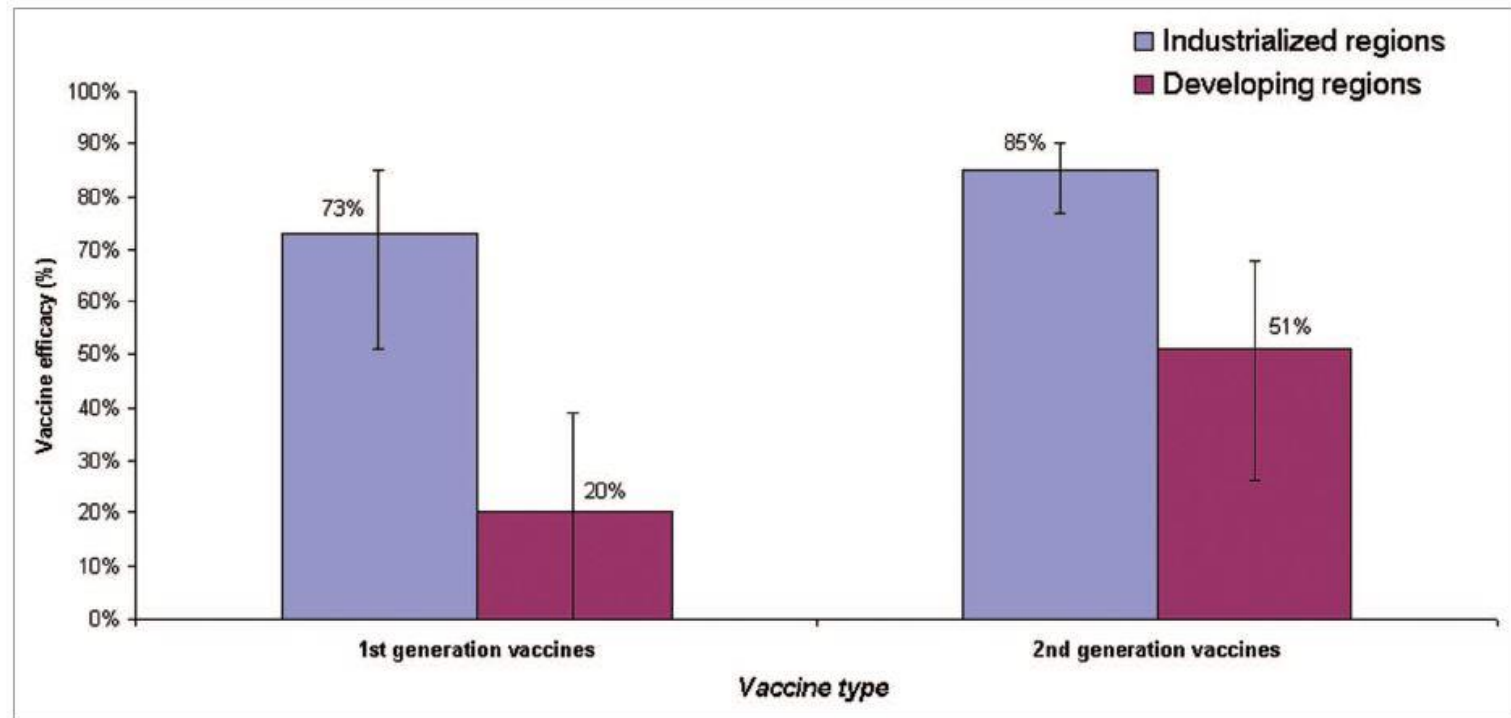
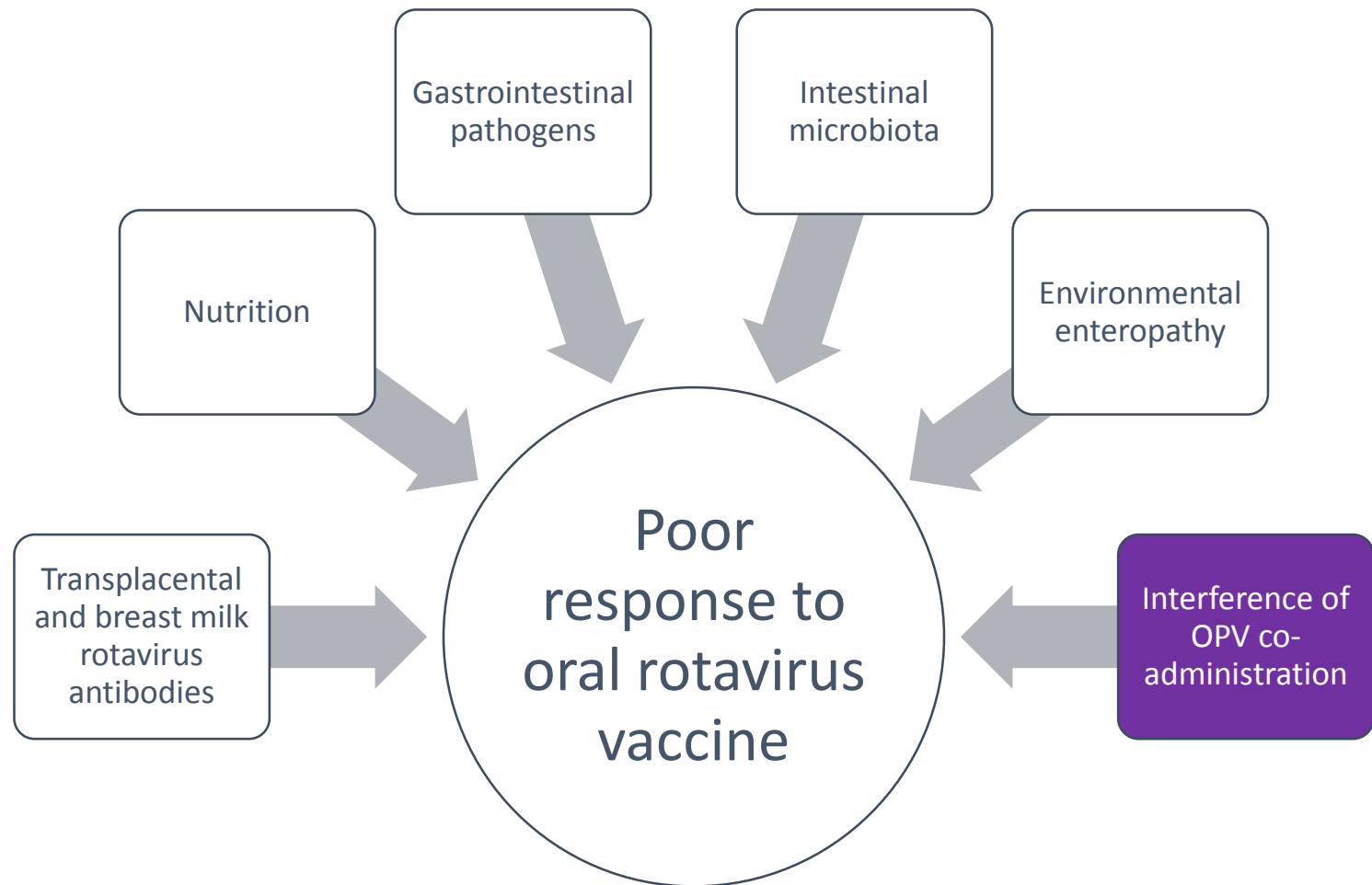
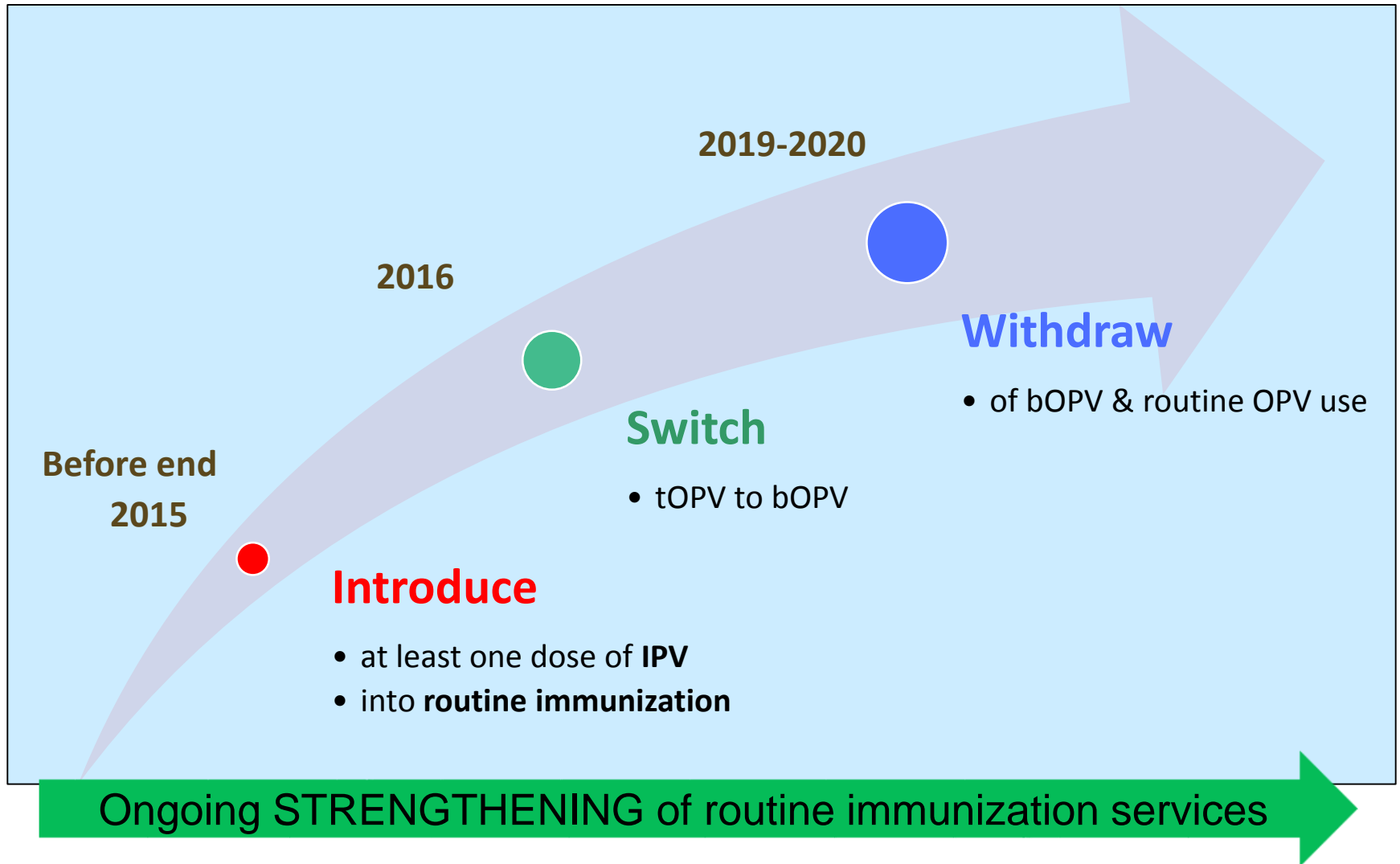


Figure 1. Pooled estimates of efficacy against severe rotavirus disease by income settings for first and second generation rotavirus vaccines. These estimates are the pooled estimates and 95% confidence limits are generated from studies outlined in Tables 2 and 3 (refer to Methods).

Multiple factors affect rotavirus vaccine efficacy in resource-limited areas



The Polio Eradication & Endgame Strategic Plan 2013-2018



1. Does co-administration of rotavirus vaccine affect the performance of oral polio vaccine?

Seroprotection rates to polio antigens with and without RIX 4414 co-administration, Bangladesh

Antibody	Timing	Sero-protection rate % (95% CI)
Anti-poliovirus type 1	RIX4414 + OPV	86.4 (76;94)
	Placebo + OPV	90.1 (81;96)
Anti-poliovirus type 2	RIX4414 + OPV	98.5 (92;100)
	Placebo + OPV	97.1 (90;100)
Anti-poliovirus type 3	RIX4414 + OPV	69.6 (57;80)
	Placebo + OPV	68.1 (56;79)

Seroresponse to polio vaccine with and without pentavalent rotavirus vaccine co-administration, Latin America

Antibody	Timing	Sero-protection rate
Anti-poliovirus type 1	RotaTeq + OPV	98.9 %
	Placebo + OPV	99.4%
Anti-poliovirus type 2	RotaTeq + OPV	99.7%
	Placebo + OPV	99.7%
Anti-poliovirus type 3	RotaTeq + OPV	98.3%
	Placebo + OPV	98.4%

1. Does co-administration of rotavirus vaccine affect the performance of oral polio vaccine?

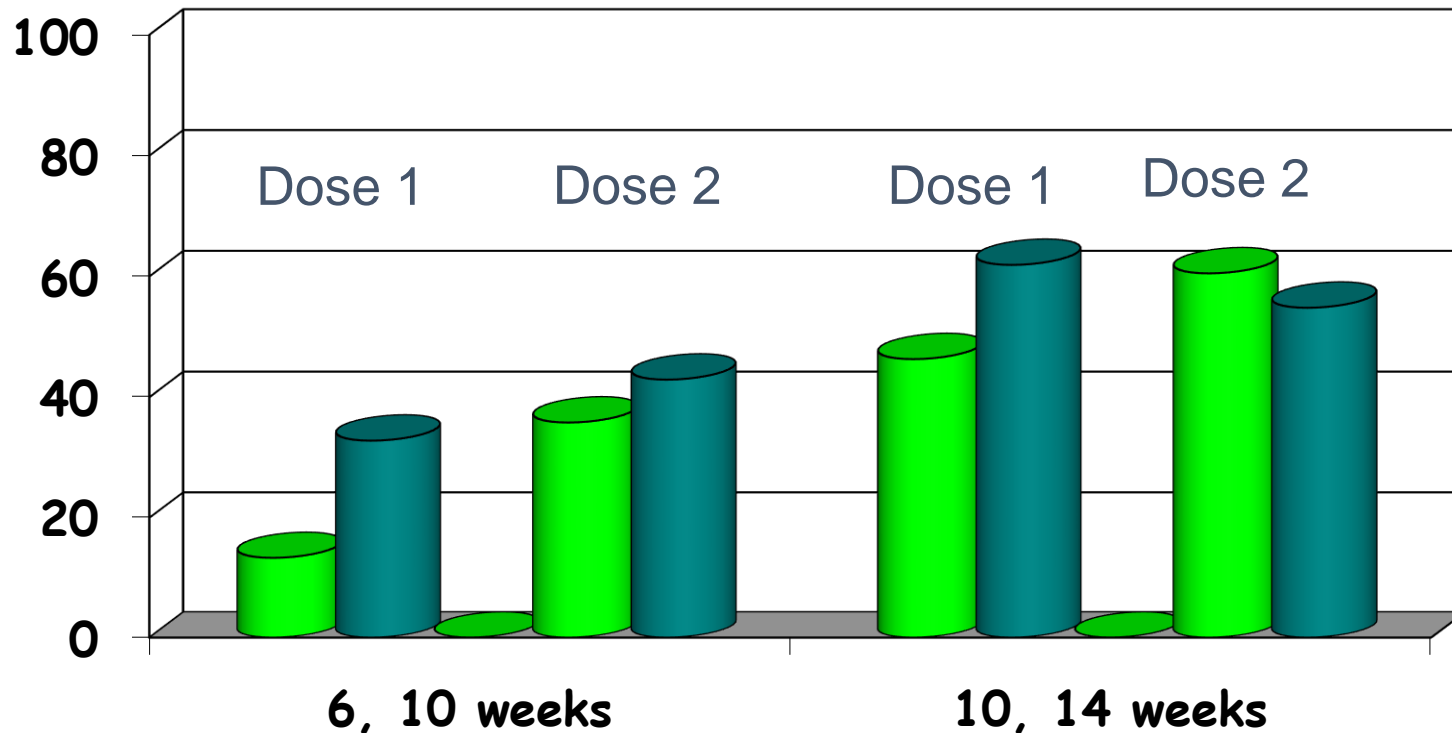
No!

2. Does co-administration of trivalent oral polio vaccine (tOPV) affect performance of rotavirus vaccine?

Seroconversion rates to RIX 4414 with tOPV or IPV in South African Infants

Sero-conversion rates per groups

■ HRV^{5.2ffu} + tOPV ■ HRV^{5.2ffu} + IPV

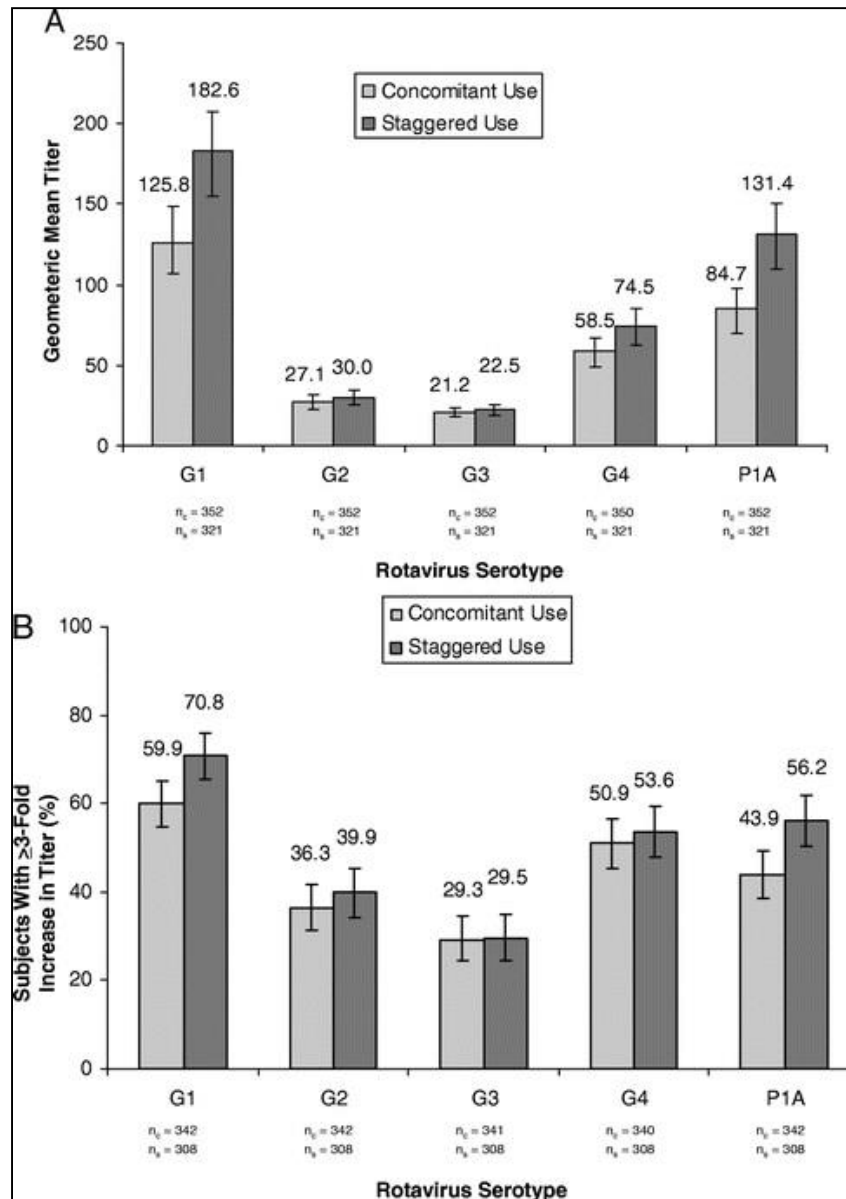


Interference of tOPV on serum IgA antibody response to RIX 4414 in Bangladesh

Treatment group	N	n	Seroconversion rate % (95% CI)	P value
RIX4414 + tOPV	69	39	57 (44; 68)	0.113
RIX4414	66	44	67 (54; 78)	

Sero-conversion rate, cut-off \leq 20U/ml

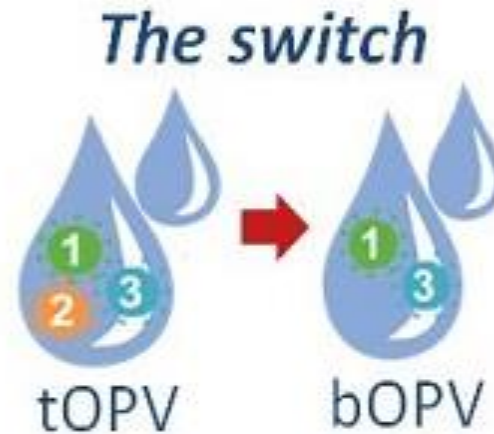
Serum neutralizing antibodies to RotaTeq with concomitant or staggered tOPV use in Latin America



2. Does co-administration of trivalent oral polio vaccine (tOPV) affect performance of rotavirus vaccine?

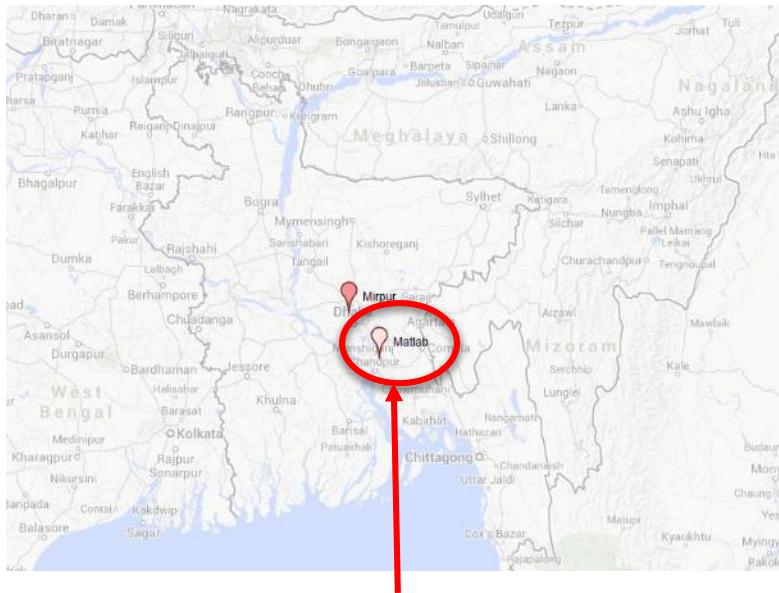
Yes!

3. Does interference with rotavirus vaccine performance also occur with co-administration of bOPV and mOPV?



- Type 2 component of tOPV replicates most efficiently
- Removal of type 2 might reduce interference on rotavirus vaccine?

RCT* of different OPV formulations in healthy infants in Bangladesh from May – December 2012

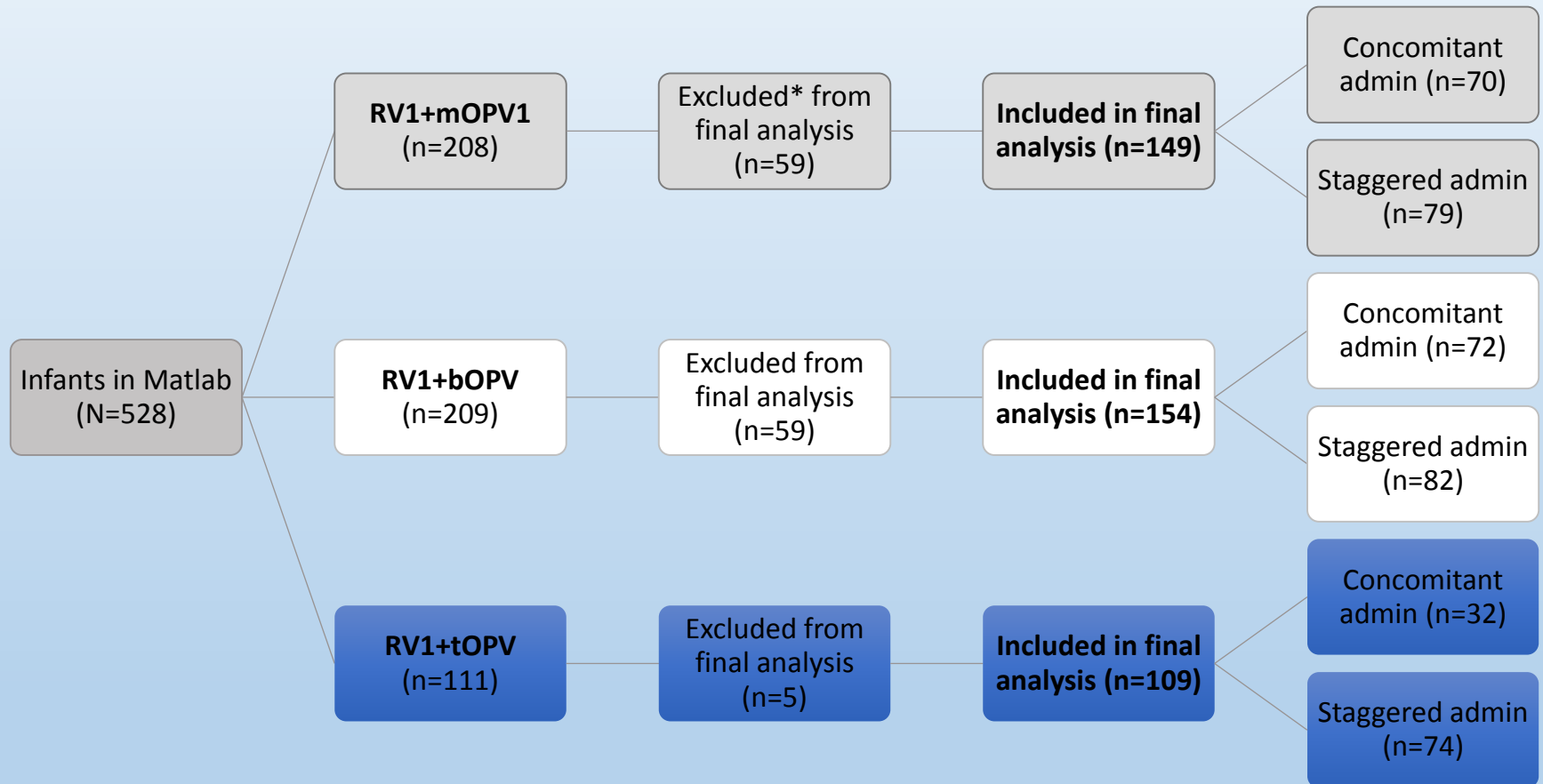


Note: Infants in Matlab received RV1; infants in Mirpur did not.



Source: "Washing Utensils And Vegetables" by Anwar Huq, University of Maryland Biotechnology Institute, Baltimore, Maryland, United States. - Bradbury J: Beyond the Fire-Hazard Mentality of Medicine: The Ecology of Infectious Diseases. PLoS Biol 1/2/2003: e22. <http://dx.doi.org/10.1371/journal.pbio.0000022>. Licensed under CC BY 2.5 via Wikimedia Commons - http://commons.wikimedia.org/wiki/File:Washing_Utensils_And_Vegetables.png#media/File:Washing_Utensils_And_Vegetables.png

Post-hoc analysis



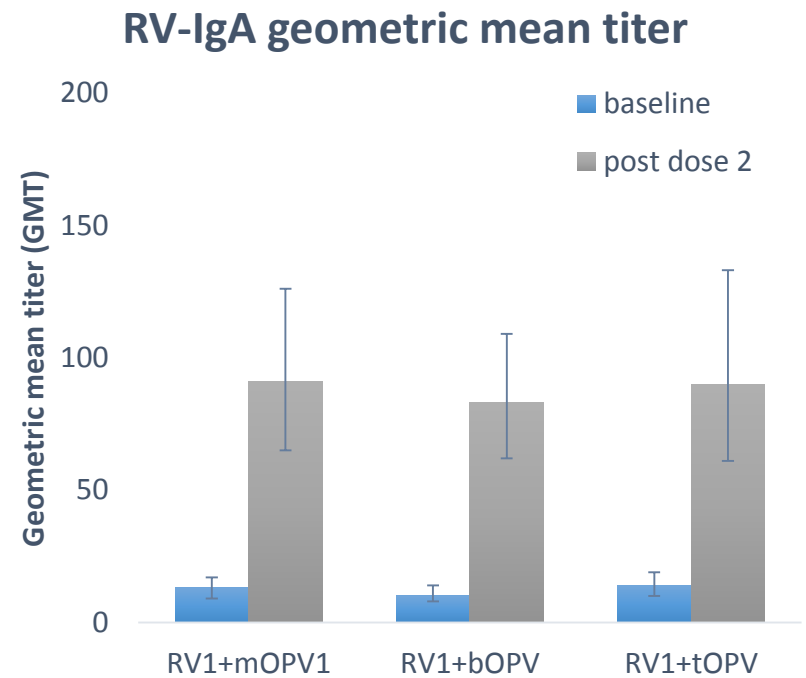
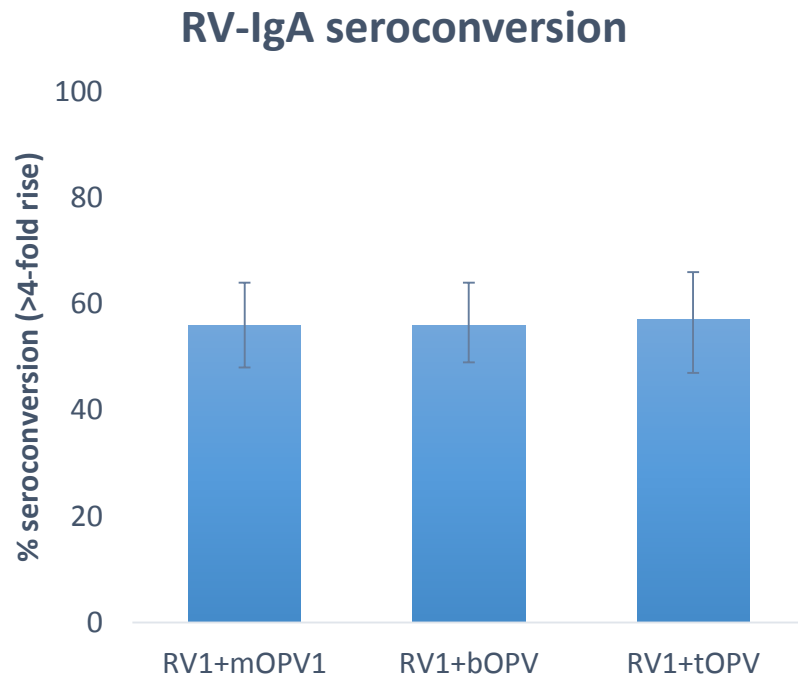
Exclusion criteria:

- Unknown RV1 admin
- Missing serological data
- 2nd RV dose <3 weeks to final blood collection

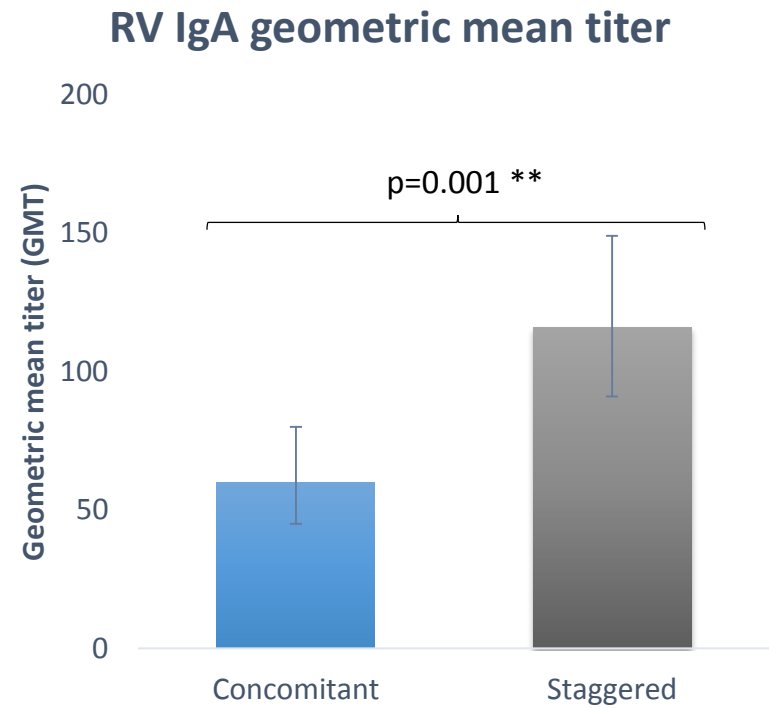
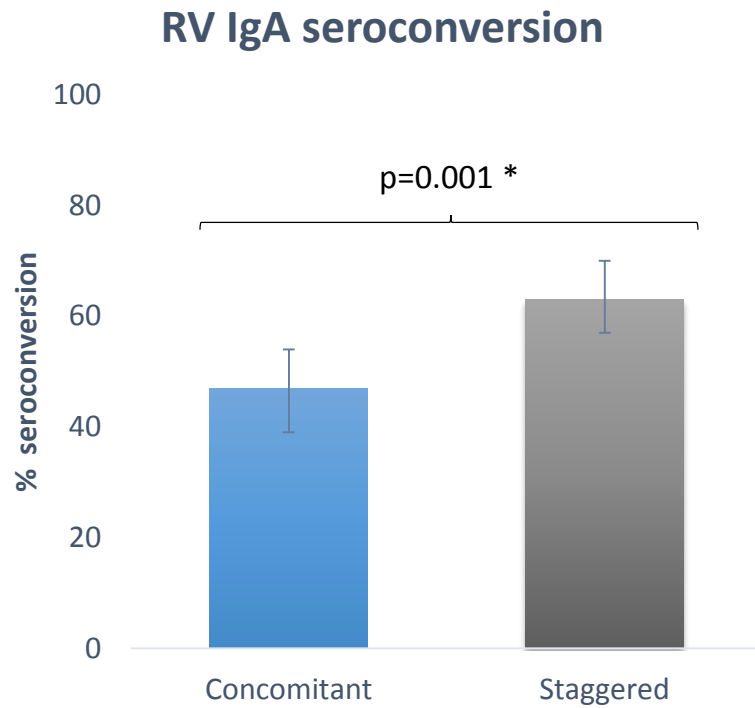
Groups were similar at baseline

Characteristics (Baseline)	RV1+mOPV1 n=149	RV1+bOPV n=154	RV1+tOPV n=106
Sex, male (%)	70 (47%)	84 (54%)	61 (58%)
Age (days)			
Mean (SD)	45.9 (2.5)	45.6 (2.4)	45.3 (2.5)
Median (range)	46.0 (42-50)	45.6 (42-50)	45.0 (42-50)
Mother's education <5 years (%)	66 (44%)	77 (50%)	45 (43%)
Malnutrition (%)			
Stunting, anytime	15 (10%)	21 (14%)	18 (17%)
Wasting, anytime	60 (40%)	62 (40%)	37 (35%)
Full breastfeeding (%)	149 (100%)	154 (100%)	105 (99%)
Rotavirus IgA			
% Seropositive (IgA >40) at baseline (95% CI)	32% (24-39)	30% (23-37)	35% (26-44)
IgA (GMT) at baseline (95% CI)	13 (9-17)	10 (8-14)	14 (10-19)

No difference in RV1 immunogenicity by OPV type



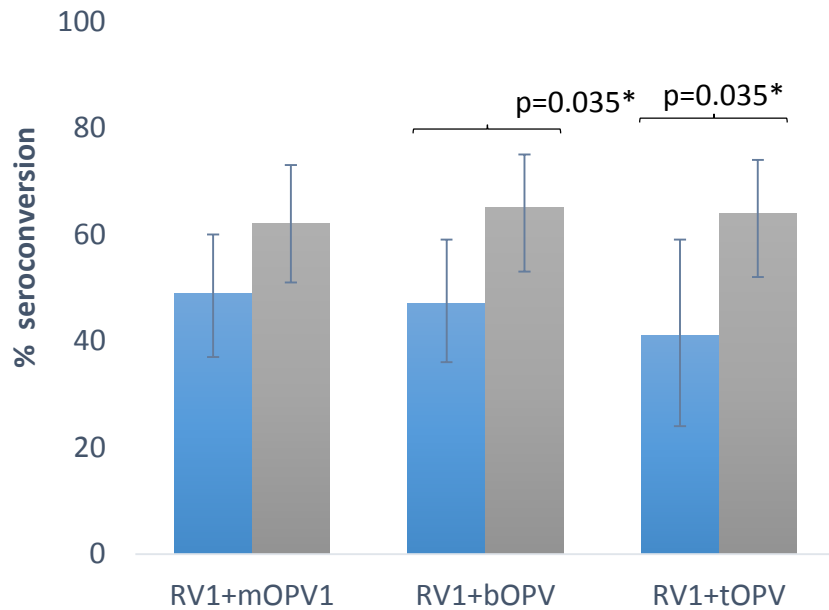
Lower RV1 immunogenicity when OPV given concomitantly...



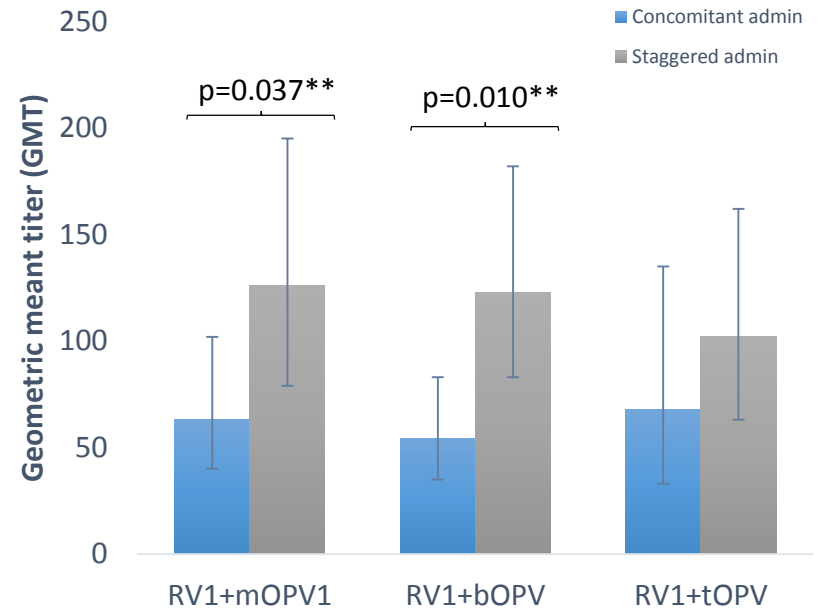
*Chi-square test. **Non-parametric Wilcoxon test.

... regardless of OPV formulation.

RV-IgA seroconversion



RV-IgA geometric mean titer



*Chi-square test. **Non-parametric Wilcoxon test.

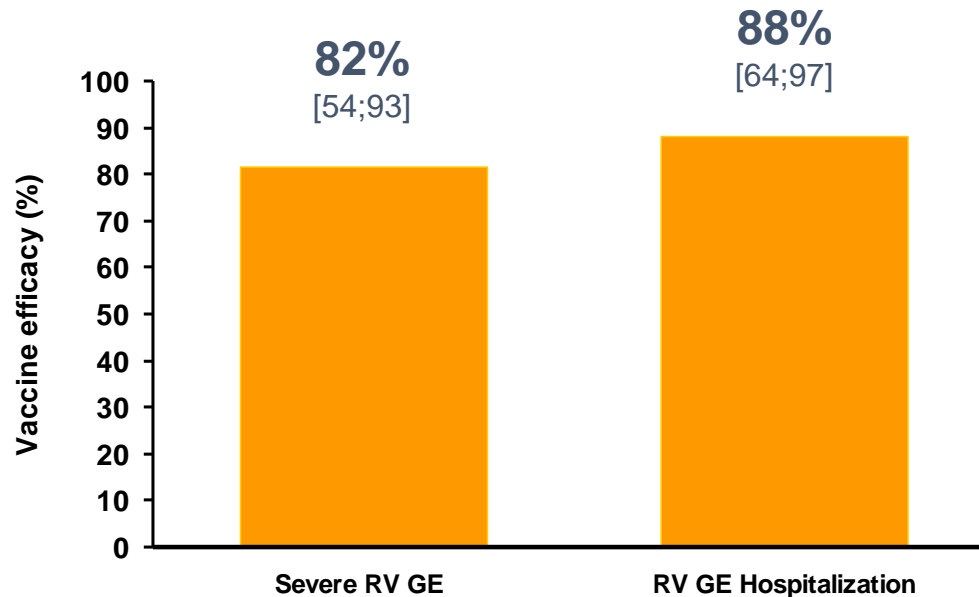
Serum IgA antibody response among infants given RV1 with bOPV versus IPV in Chile

	bOPV	IPV	P value
Seroconversion	50%	65%	0.004
Log IgA Titer	1.8	2.1	0.007

3. Does interference with rotavirus vaccine performance also occur with co-administration of bOPV and mOPV?

Yes!

4. What is the impact of OPV interference on rotavirus vaccine efficacy?



- Trial of RV1 co-administered with OPV in Latin America
- Efficacy similar to high efficacy of 85% demonstrated in the Latin American study without OPV co-administration

Summary

- Co-administered rotavirus vaccines **do not interfere** with the immune response of polio vaccines
- Co-administered oral polio vaccines **interferes** with the immune response to rotavirus vaccine
- Interference appears to be **similar** with all formulations of OPV (tOPV, bOPV, and mOPV)
- Switch to IPV will **likely be beneficial** for performance of rotavirus vaccines