

Duration of Immunity and Booster responses in Nepal

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TyVAC Typhoid Vaccine
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CENTER FOR VACCINE DEVELOPMENT • OXFORD VACCINE GROUP • PATH



Photo: PATH/Asad Zaidi

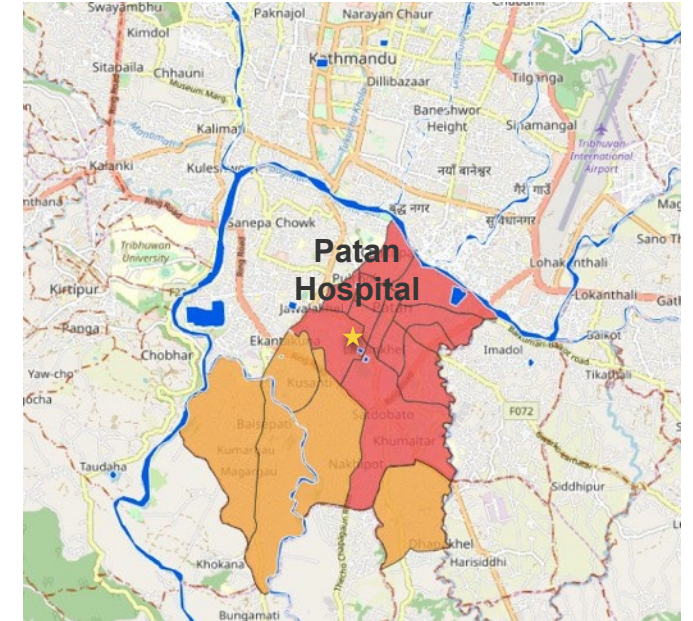
Study Overview

TyVAC-Nepal











- Study Design: Participant and observer blinded 1:1 RCT
- Study Participants: 20,019 children aged 9 months to < 16 years
- Randomised to receive:
 - Typhoid conjugate vaccine (Typbar TCV, Bharat Biotech) or
 - Group A meningococcal vaccine (MenAfriVac, SII)
- Duration: 2 years

TyVOID-Nepal

- Study Design: Prospective cohort study alongside community surveillance following an RCT.
- Study Participants: Children vaccinated in TyVAC RCT and population of catchment area.



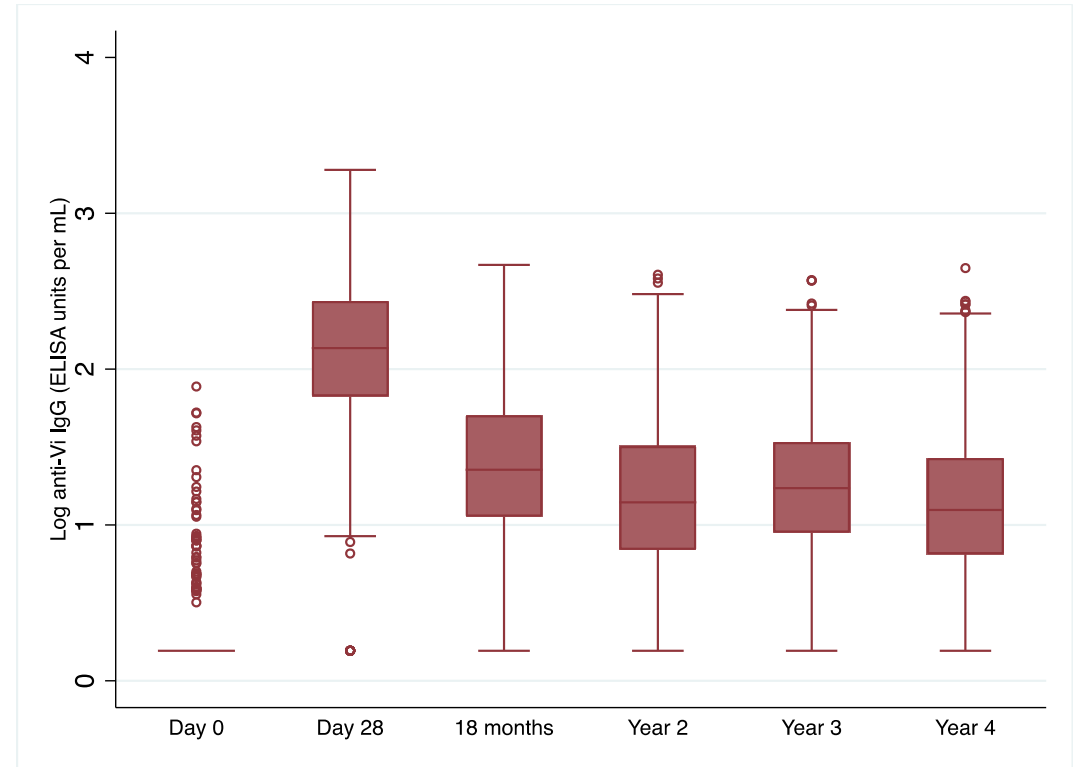
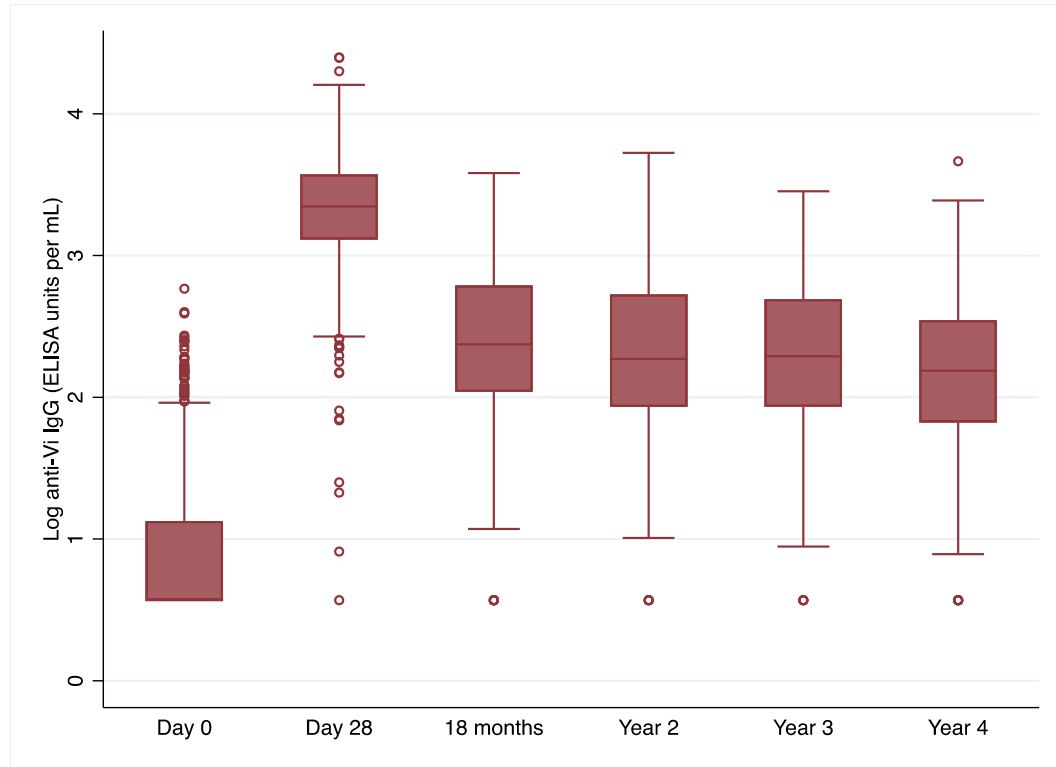
TyVAC Nepal & TyVOID Nepal: Immunogenicity sub-study

	TyVAC Nepal						TyVOID Nepal	
	Baseline	28 days	18 months	24 months	36 months		42 – 50 months	50 – 60 months
TCV received								
TCV arm						Early cohort		
MenA arm						Late cohort		
Blood samples collected								
TCV arm	1000	709	539	134	405	Early cohort	500	500
MenA arm	500	388	299	247	52	Late cohort	250	250

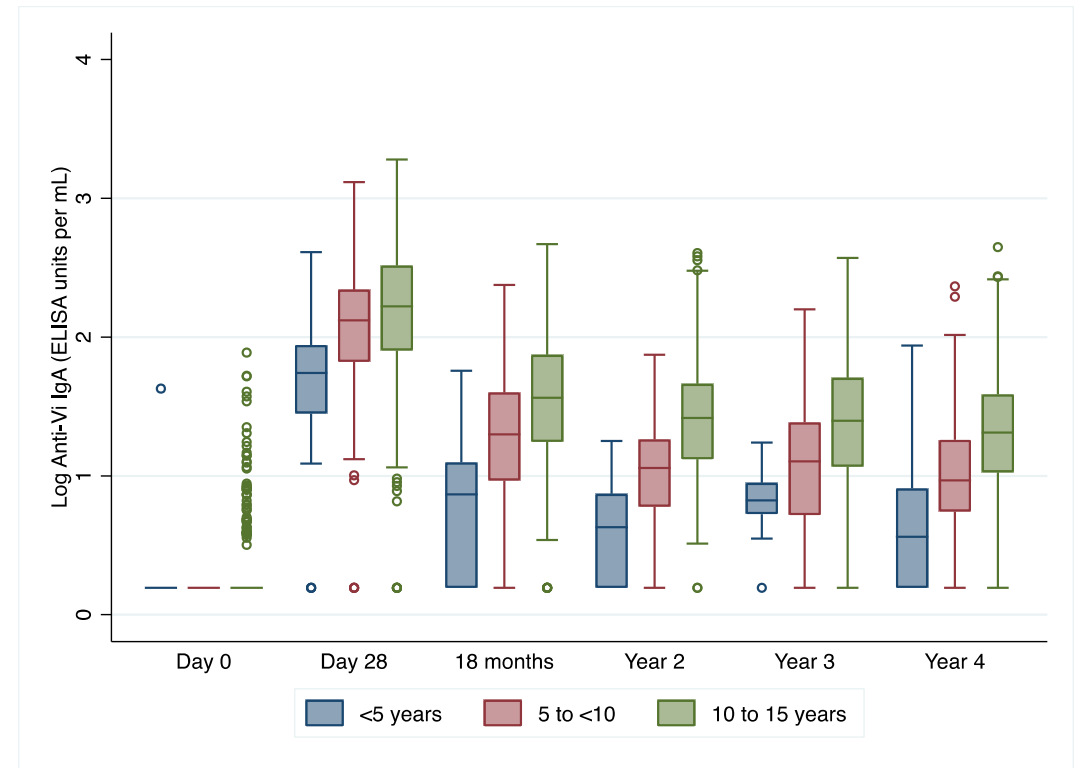
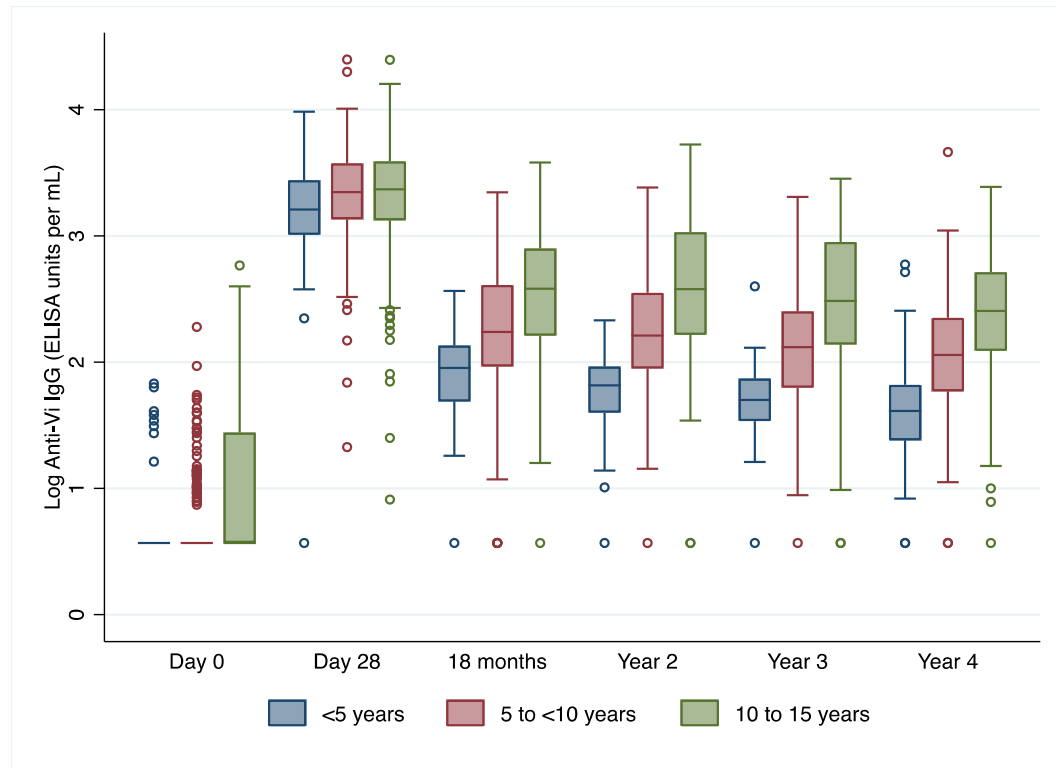
Vi IgG and Vi IgA Levels in the Immunogenicity Cohort

		TCV						MenA			
		TyVAC					TyVOID Early cohort	TyVAC			TyVOID Late cohort
Time point		D0	D28	M18	Year 2	Year 3	Year 4	D0	Year 2	Year 3	Year 4
FU time-yrs Median (Range)					2.12 (1.84 -2.32)	3.10 (2.83 – 3.70)	4.04 (3.97– 4.1)		2.12 (1.83 - 2.28)	3.09 (2.83 – 3.70)	1.128 (0.8 - 1.9)
IgG	GMC (95% CI) (EU/mL)	7.21 (6.69 – 7.11)	2037.90 (1904.64– 2180.48)	241.29 (220.23 – 264.36)	214.18 (180.52 – 254.11)	200.91 (170.39 - 236.89)	146.46 (132.3- 162.0)	6.48 (5.89– 7.13)	6.83 (5.62 – 8.31)	6.41 (5.45 – 7.53)	241.29 (208.5 - 279.23)
	No with 4 fold rise from baseline/ total no.(%)		677/683 (99.1)	573/601 (95.34)	189/199 (94.97)	200/222 (90.09)	318/350 (90.8)		3/104 (2.80)	8/135 (5.93)	161/173 (93.06)
IgA	GMC (95% CI) (EU/mL)	1.79 (1.72 – 1.87)	122.04 (111.83 – 133.17)	22.86 (20.81 – 25.12)	14.34 (12.29 – 16.74)	17.08 (14.76 – 19.76)	13.02 (11.76 – 14.42)	1.74 (1.67 – 1.83)	1.77 (1.65 – 1.90)	1.90 (1.73 – 2.08)	22.33 (19.29 – 25.84)
	No with 4 fold rise from baseline/ total no.(%)		664/683 (99.10)	479/539 (88.87)	163/199 (81.91)	182/222 (81.98)	252/323 (78.0)		0/107 (0.00)	3/132 (2.22)	136/164 (82.9)

Boxplots for Anti-Vi IgG & Anti-Vi IgA Titres over 4-Year Study Period in the TCV cohort















Boxplots for Anti-Vi IgG & IgA Titres over 4-Year Study Period, By Age Category (<5, 5-<10, ≥10)



TyVAC Nepal: Two dose study

Methods

	Day 0 Primary Dose (Visit 1)	28 days Post- primary (Visit 2)	15 month age Booster dose (Visit 3)	28 days Post-booster (Visit 4)
Permissible window	-2 weeks /+1 month 29 days	-7 /+21 day	-2 weeks /+1 month 29 days	-7 /+21 days
9 month age	 		 	
12 month age	 		 	

Data Analysis

The Covid-19 pandemic heavily affected the study's follow-up visits. Many participant follow-ups out-of-the window.

- **Analysis 1:** All participants: regardless of their visit time.
- **Analysis 2:** Excluding out-of-the-window participants and also the V4 visits if V3 was out-of-window.

Proportions of visits made within per protocol window

	9-month	12-month
Visit 1 (Follow-ups per protocol window/ Total follow-ups)	50/50	50/50
Visit 2 (Follow-ups per protocol window/ Total follow-ups)	27/38	32/32
Visit 3 (Follow-ups per protocol window/ Total follow-ups)	32/43	16/37
Visit 4 (Follow-ups per protocol window/ Total follow-ups)	20/38	10/33

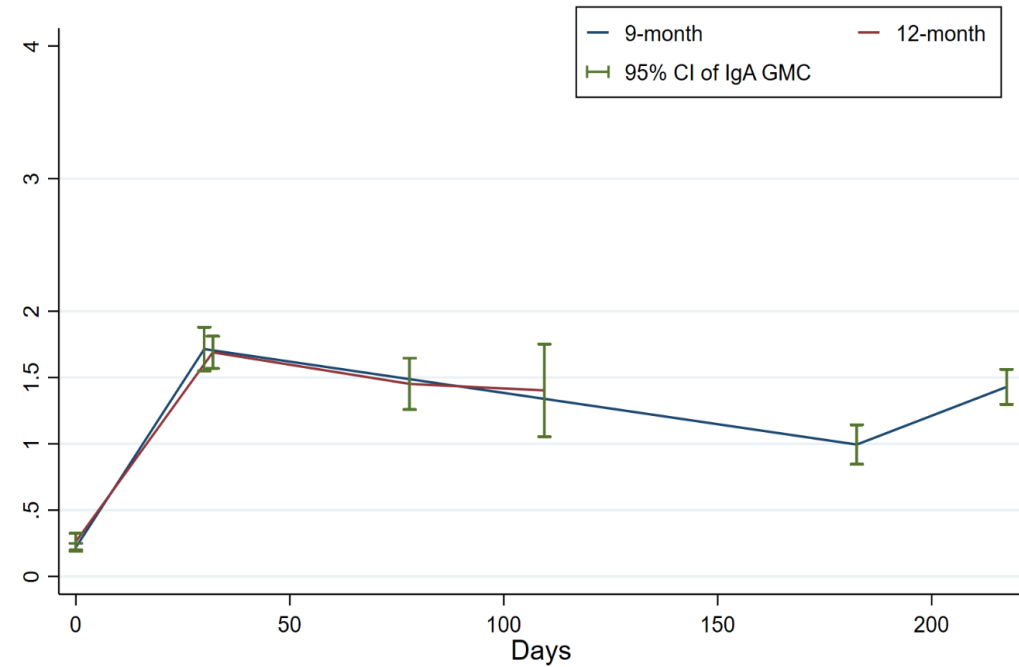
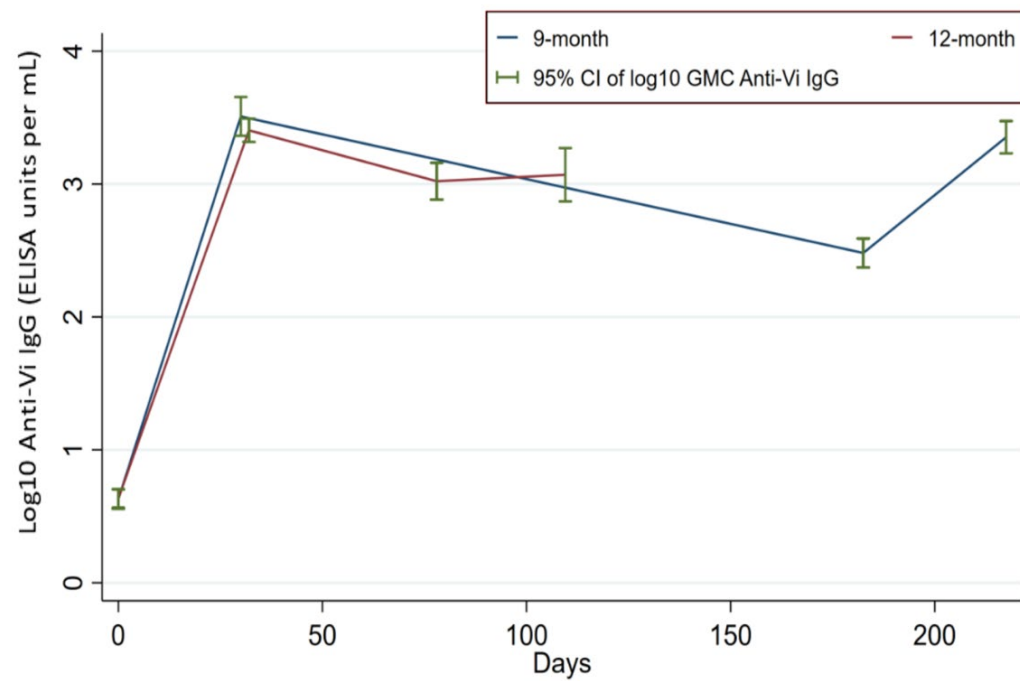
Fold increase of Anti-Vi IgG and IgA titers between Visit 1 to 2, Visit 1 to 3 , Visit 3 to 4, Visit 1 to 4

Fold Increase	9-month				12-month			
	Visit 1 to 2	Visit 1 to 3	Visit 3 to 4	Visit 1 to 4	Visit 1 to 2	Visit 1 to 3	Visit 3 to 4	Visit 1 to 4
IgG								
Mean fold increase (95% CI)	1087.12 (616.49 - 1557.75)	87.90 (64.19 - 111.61)	10.03 (5.99 - 14.07)	684.72 (420.19 - 949.24)	713.43 (544.21 - 882.65)	309.10 (186.41 - 431.79)	1.15 (0.73 - 1.57)	309.10 (186.41 - 431.79)
4-fold increase (%)	27/27 (100%)	32/32 (100%)	16/20 (80%)	20/20 (100%)	32/32 (100%)	16/16 (100%)	0/8 (0%)	10/10 (100%)
IgA								
Mean fold increase (95% CI)	51.57 (18.02 - 85.13)	9.59 (5.52 - 13.66)	4.26 (2.77 - 5.75)	21.41 (13.47 - 29.34)	100.61 (26.20 - 227.43)	22.36 (11.46 - 33.26)	0.97 (0.65 - 1.29)	22.83 (8.04 to 37.62)
4-fold increase (%)	27/27 (100%)	24/32 (75%)	9/20 (45%)	20/20 (100%)	31/32 (96.88%)	14/16 (87.5%)	0/8 (0%)	8/10 (80%)

Anti- Vi IGA and IgG titers at Visits 1, 2, 3, and 4.

	9-month group				12-month group			
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 1	Visit 2	Visit 3	Visit 4
IgG								
Geometric mean concentration (95% CI), EU/mL	4.27 (3.60 - 5.06)	3223.51 (2302.10 - 4513.71)	302.848 (235.845 - 388.89)	2249.26 (1701.02 - 2974.19)	4.30 (3.67 - 5.04)	2533.10 (2069.10 - 3101.15)	1049.01 (762.07 - 1443.99)	1173.43 (740.17 - 1860.31)
IgA								
Geometric mean concentration (95% CI) EU/mL	1.66 (1.54 - 1.77)	51.80 (35.42 - 75.75)	9.88 (7.01 - 13.92)	26.87 (19.84 - 36.39)	1.83 (1.58 - 2.11)	48.96 (37.02- 64.73)	28.31 (18.11 - 44.25)	25.29 (11.32 - 56.52)

Geometric mean IgG and IgA (95% CI) of 9-month and 12-month groups in median days of the four visits



Discussion Points

TyVAC Nepal & TyVOID Nepal: Immunogenicity sub-study

- Overall high level of antibody titres persisted to 4 years post-vaccination.
- Sustained antibody titres in children ≥ 5 years 4 years post-vaccination.
- Faster decay of antibodies, especially IgA, in the youngest age group , and needs further study.

TyVAC-Nepal: 2 dose study

- Vi-TT is highly immunogenic at both 9 and 12 months of age.
- Stronger response to a booster in 9m group than 12m group, likely as a result of the longer interval between doses.
- If it is found that a second dose is needed, it may be best administered after a long interval and preferably before the period of heightened risk after school entry.

Acknowledgements

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- WHO IPD & WHO Country office, Nepal





17th Asian Conference on Diarrhoeal Disease and Nutrition
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Kathmandu, Nepal



Partner Organization:



Learn more at:

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