



Longer-term efficacy of typhoid conjugate vaccine in Malawi

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13th International Conference on Typhoid & Other Invasive Salmonellosis

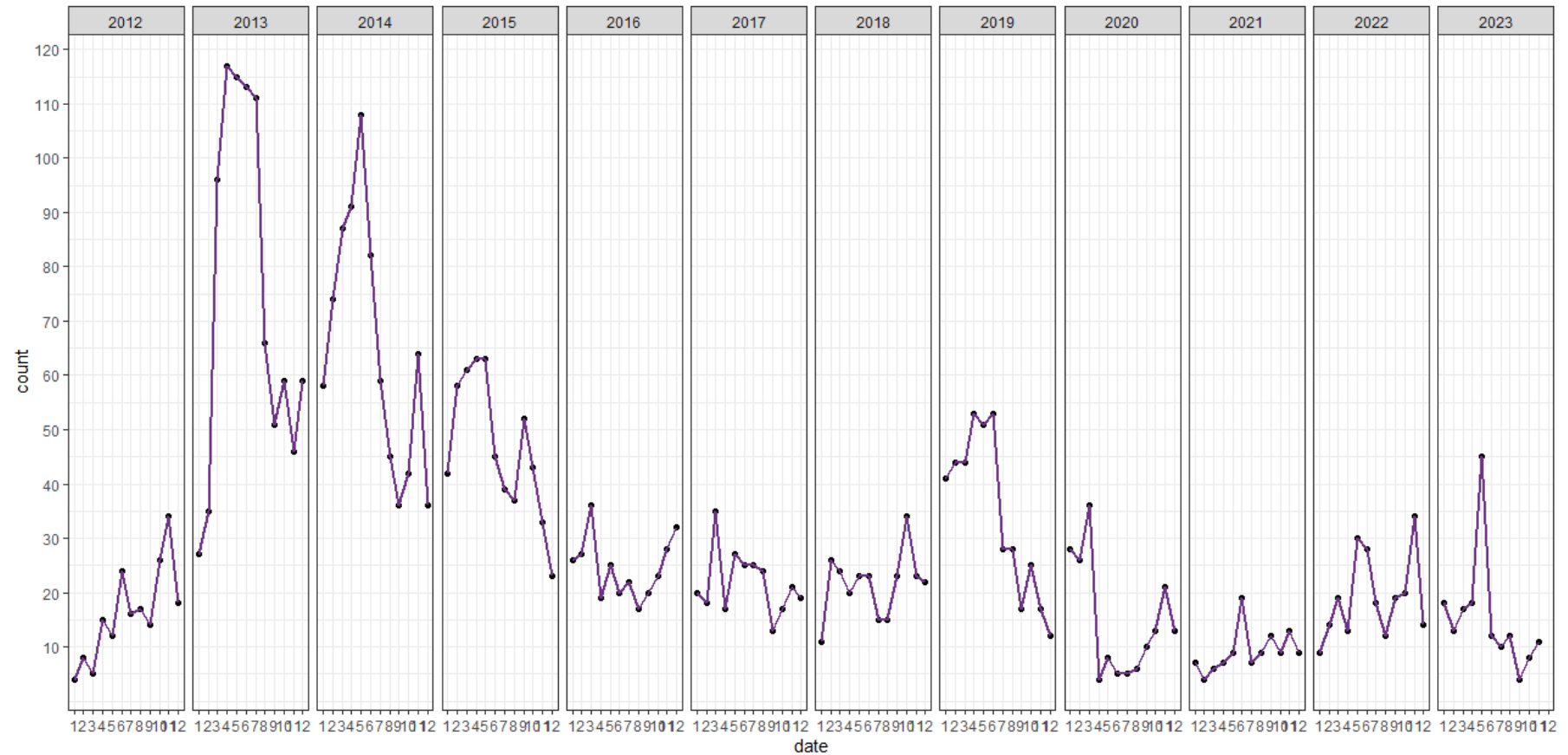


TyVAC Typhoid Vaccine
Acceleration Consortium
CENTER FOR VACCINE DEVELOPMENT • OXFORD VACCINE GROUP • PATH

Typhoid cases - Malawi



High incidence of MDR typhoid 2016-2019 (STRATAA) *444/100,000 PYO



*Meiring et al, Lancet 2021

TyVAC trial of TCV: Study design and objectives



#Design	Typhoid conjugate vaccine (TCV)	Control vaccine	Study dates	Target no. vaccinated	Age
Individually randomized	Typhar™ TCV (Bharat Biotech)	Group A meningococcal vaccine (MenA)	Feb 2018 – Sep 2022	28,000 1:1 ratio	9 months – 12 years

*Sub-study of 600 age-stratified children.

Primary objective

- **Vaccine efficacy:** Blood-culture confirmed typhoid incidence, TCV vs MenA
- **48-month final analysis:** Data lock Sept 30, 2022

Secondary and exploratory objectives

- Safety, tolerability, and immunogenicity
- **Durability, age-band efficacy**



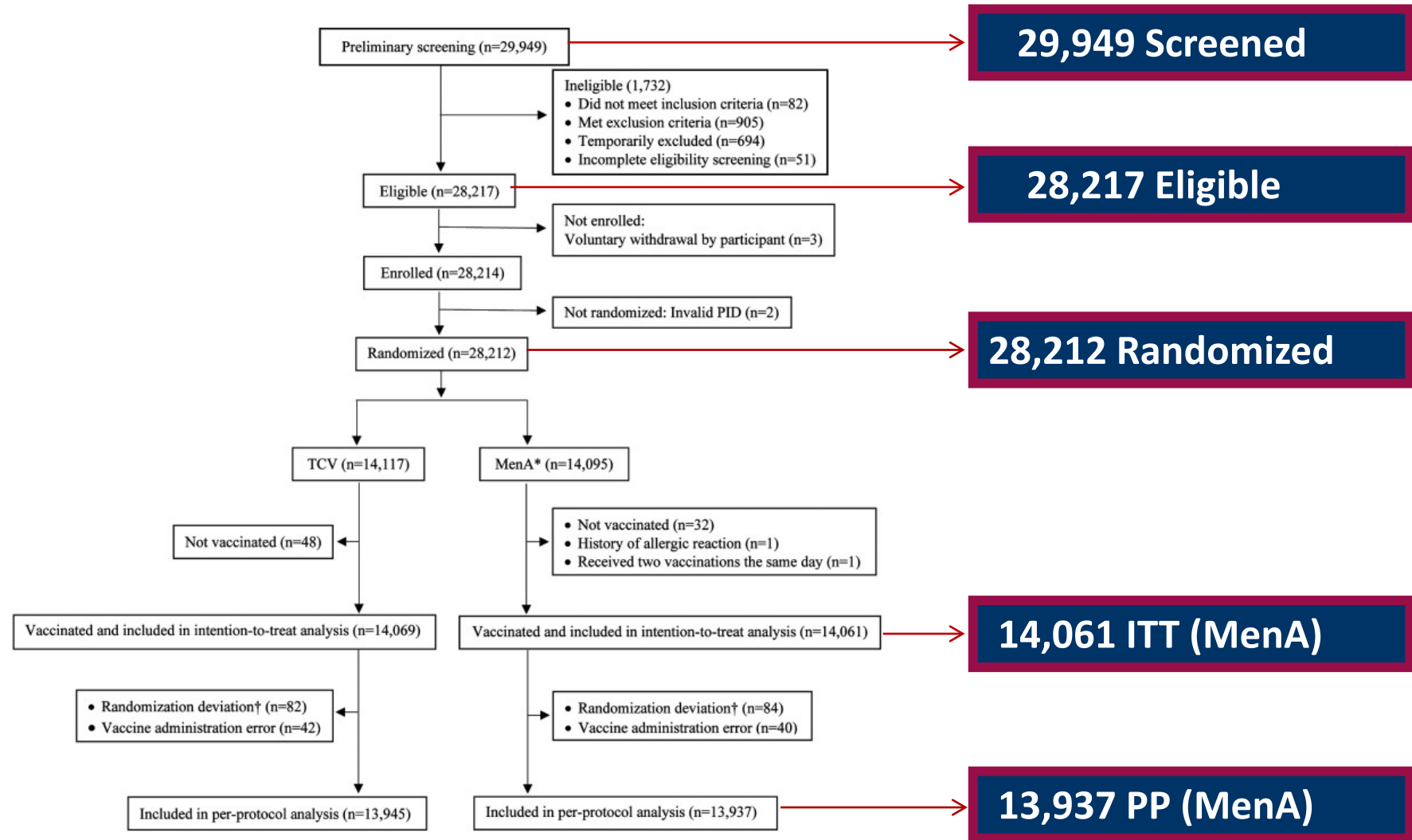
Protocol: Meiring et al, *Clin Infect Dis* 2019.

*Safety & immuno: Nampota et al, *Lancet GH* 2023.

Consort diagram



Patel PD, Patel P, Liang Y et al.
 Safety and efficacy of a typhoid conjugate vaccine in Malawian children
New England Journal of Medicine.
 2021;385:1104-1115.



14,069 ITT (TCV)

13,945 PP (TCV)

14,061 ITT (MenA)

13,937 PP (MenA)

Typhoid vaccine trial results @18-24 months



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ORIGINAL ARTICLE

Safety and Efficacy of a Typhoid Conjugate Vaccine in Malawian Children

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N ENGL J MED 385;12 NEJM.ORG SEPTEMBER 16, 2021



*Safe & immunogenic



**80.7% efficacious @ 18-24 months



*Co-administration (Measles Rubella)



Durability of protection



Efficacy in youngest children

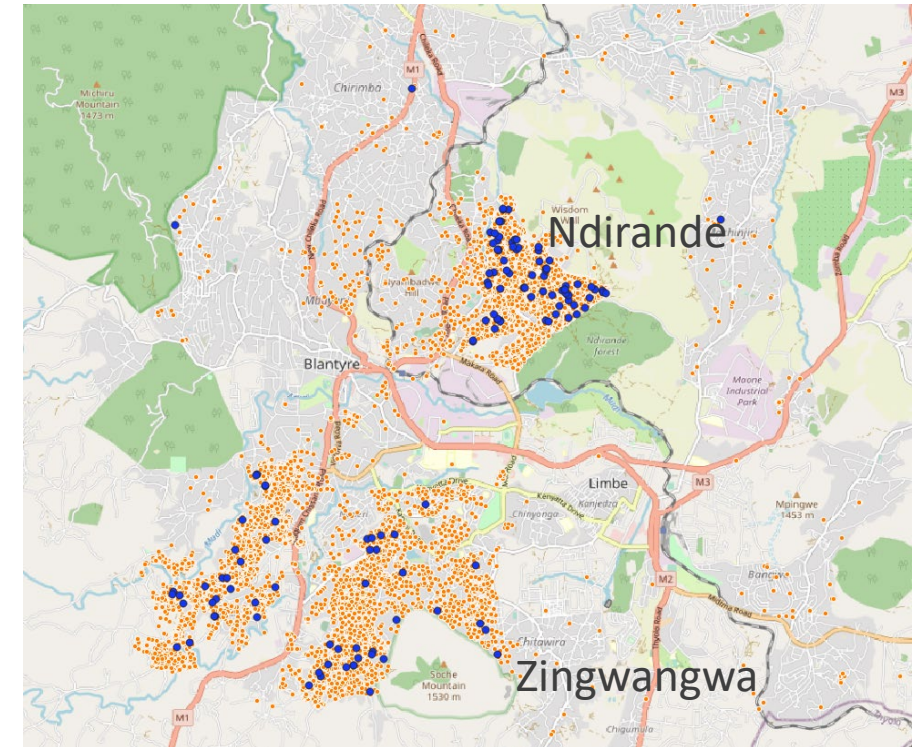
** Patel et al, *NEJM* 2021 (Malawi).

*Immuno & safety: Nampota et al, *Lancet GH* 2023.

Passive surveillance data, 48-month analysis



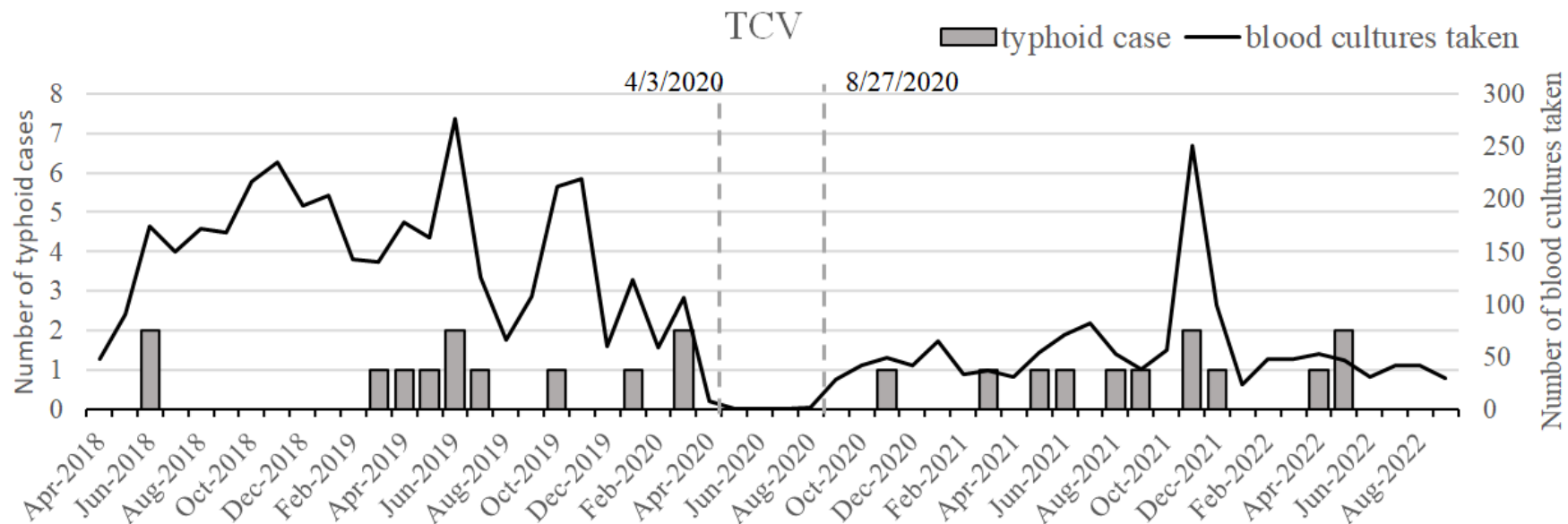
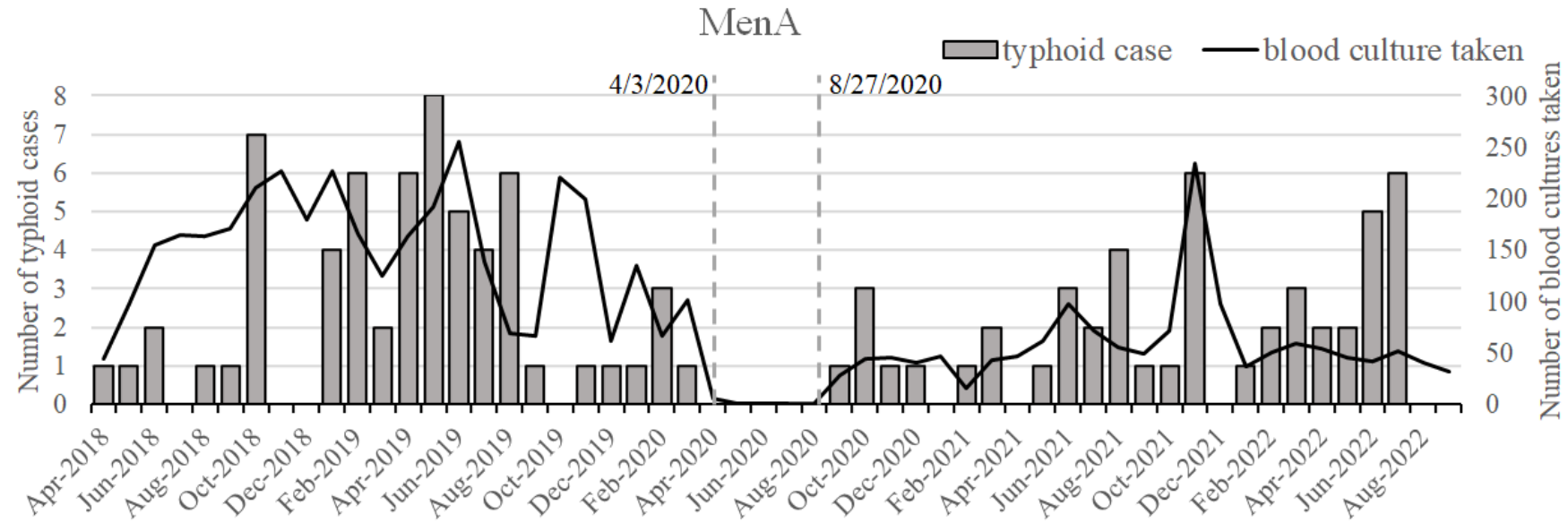
Enhanced passive surveillance for typhoid	Count
Screened passive surveillance visits	39,174
Eligible (T >= 38° or 3 days reported fever)	10,777
Blood cultures collected (96% of fever)	10,136
Typhoid cases (1.3% of cultures)	136
*SAEs (all deemed unrelated to vaccine)	554
Deaths (one typhoid death (MenA group))	34



Map of Blantyre showing vaccine coverage (orange dots) and typhoid cases (blue dots) among vaccinated children.



Blood cultures and typhoid cases over time



*Final ITT analysis – 48-52 months follow-up



28,130 children 9 months – 12 years	TCV n=14,069	MenA n=14,061
Follow-up time person-years	60,500	60,220
Typhoid cases culture positive	24	110
Incidence /100,000 pyo (95%CI)	39.7 (25.4, 59)	182.7 (150.1, 220.2)

Vaccine Efficacy: 78.3% (95% CI: 66.3% - 86.1%)

No. Needed to Vaccinate: 163 (95% CI: 129 - 222)

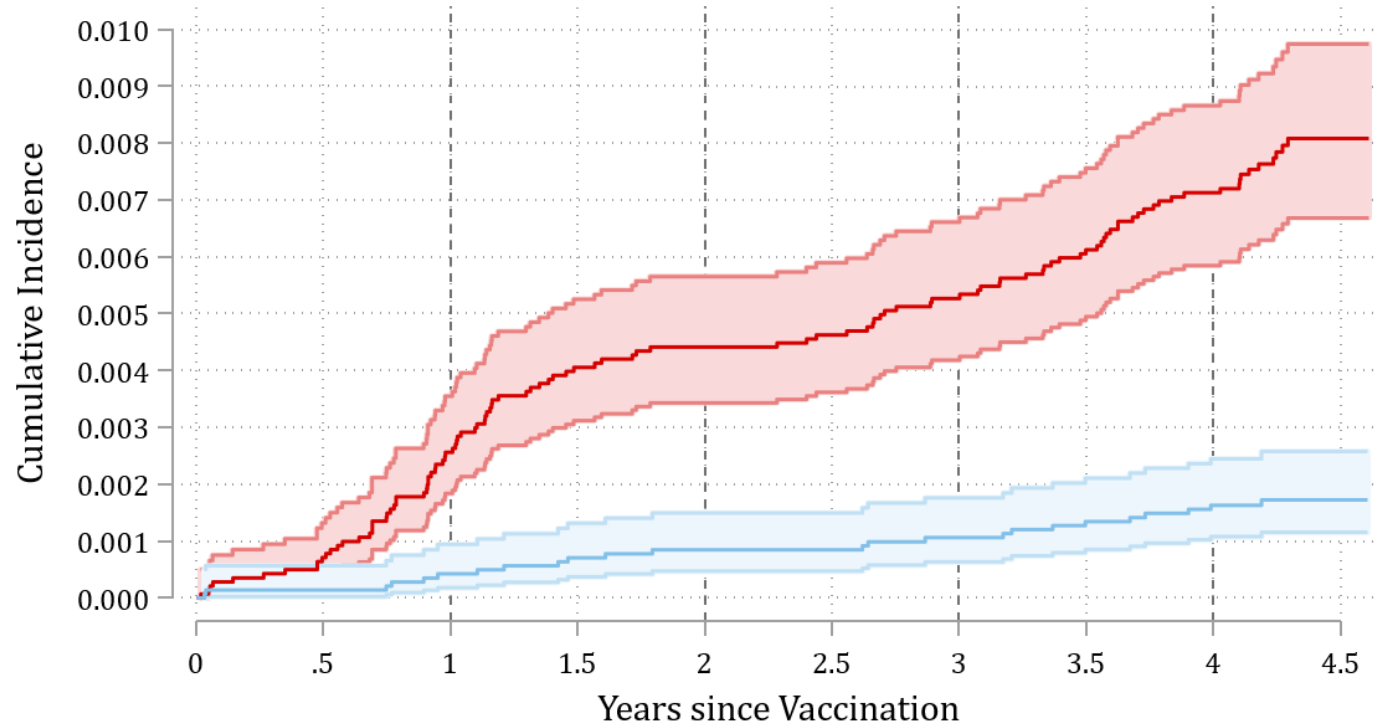


*Patel P, Liang et al, Lancet 2023 (in press).

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4411421.



Kaplan Meier for ITT population



110 typhoid cases in MenA arm

24 typhoid cases in TCV arm

Maximum number at risk

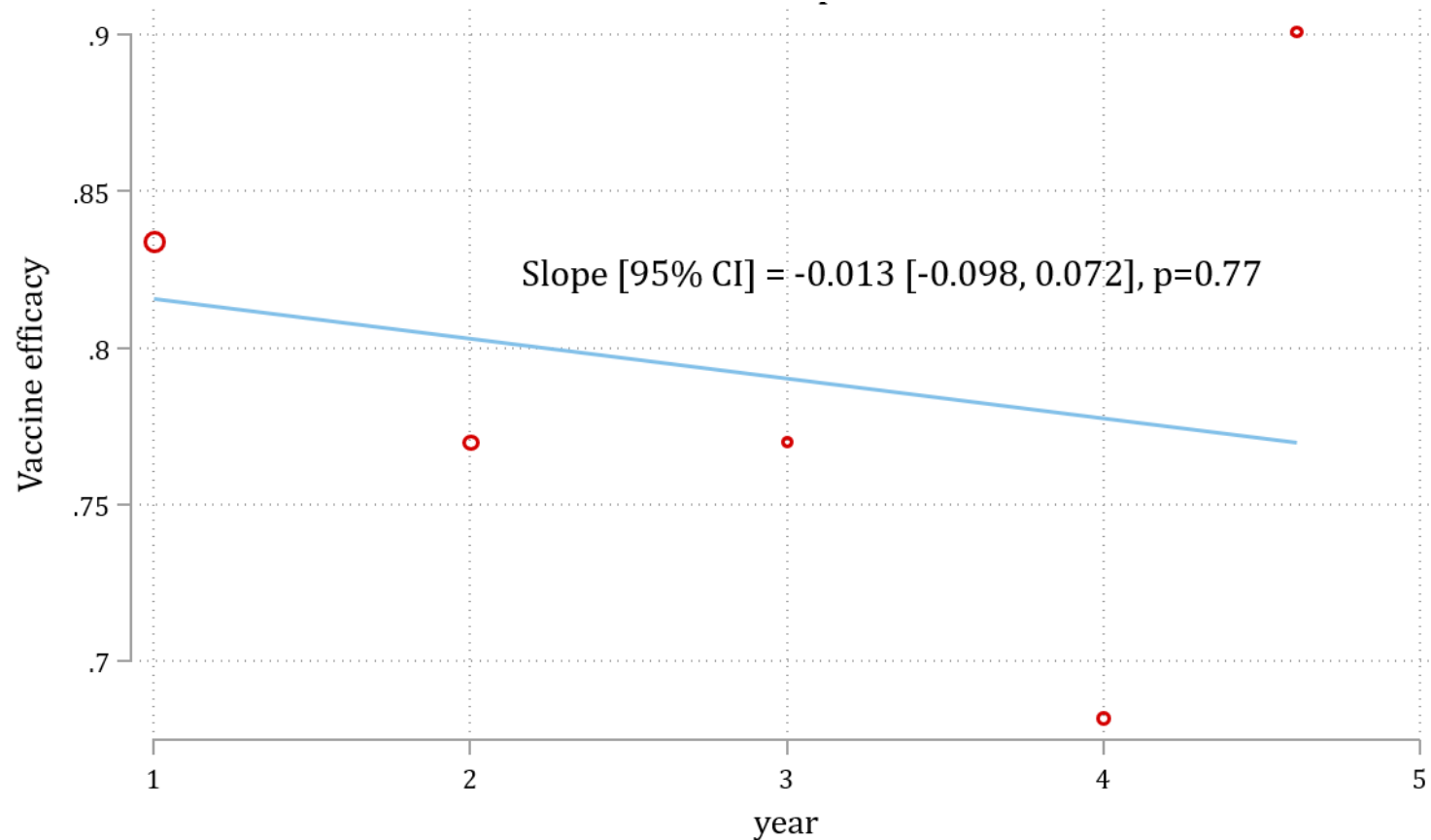
MenA:	14061	14035	14006	13982	13976	13971	13929	13907	13893	1616
TCV:	14069	14057	14050	14045	14043	14041	13996	13985	13980	1655

p<0.001

■ 95% CI — MenA
■ 95% CI — TCV



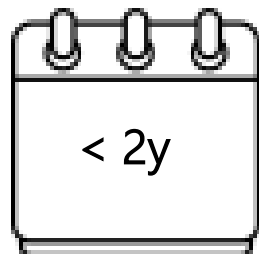
Meta-regression of vaccine efficacy over 5 annual intervals



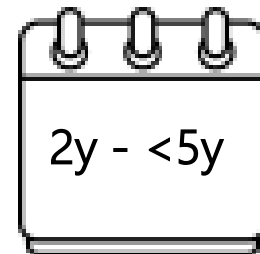
Weights: Inverse-variance

Vaccine efficacy estimated to **fall** by 1.3% per annum

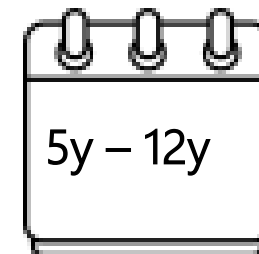
Efficacy by age at vaccination



< 2y



2y - <5y



5y - 12y

	< 2y		2y - <5y		5y - 12y	
	TCV	MenA	TCV	MenA	TCV	MenA
No. participants	1555	1600	3503	3579	9011	8882
Typhoid cases	4	14	5	25	15	71
Incidence (per 100,000 PYO)	60.7 (22.8, 161.8)	206.7 (122.4, 349.0)	33.3 (13.9, 80.1)	163.4 (110.4, 241.9)	38.6 (23.2, 64.0)	186.1 (147.5, 234.8)
Vaccine efficacy	70.6% [6.4%, 93%]		79.6% [45.8%, 93.9%]		79.3% [63.5%, 89.0%]	

Conclusion



- ✓ Safe & immunogenic
- ✓ 78.3% efficacious @ 4+ years
- ✓ Co-administration (MR)
- ✓ *Durability of protection
- ✓ *Efficacy in youngest children

*Patel P , Liang et al, 2023. Available as Lancet pre-print 2023.
[https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4411421.](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4411421)

National TCV roll out - History made in Malawi

Largest national vaccine campaign

TCV Target: 9 million children (9 months – 14 years)

Estimated vaccine coverage during national campaign

76.9%

TCV

9m-14y

83%

MR

9-59m

86%

OPV

0-59m

78.3%

Vitamin A

6-59m

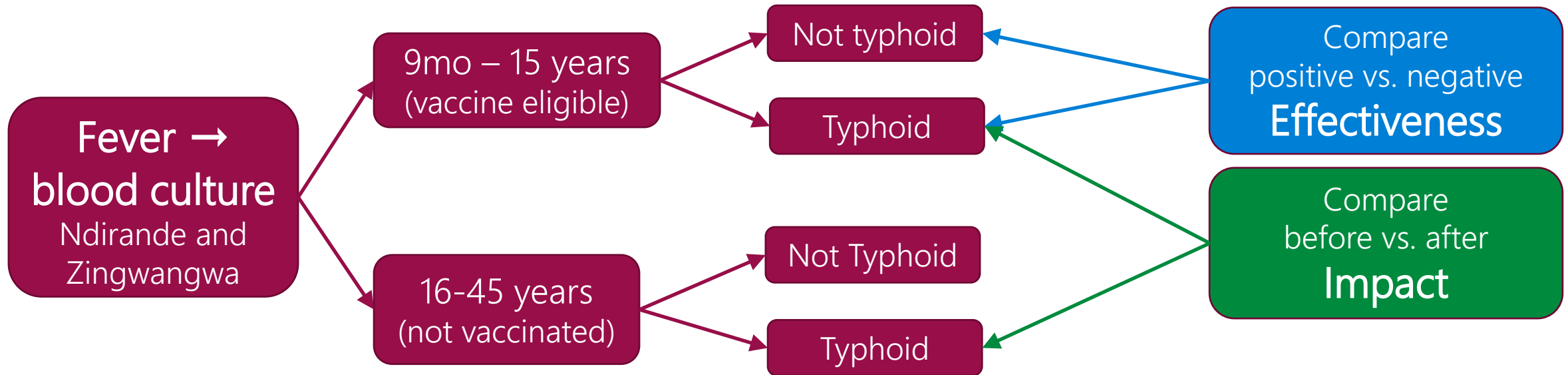
Challenges

- Infrastructure damage (Cyclone Freddy)
- Vaccinator fatigue (COVID, cholera, polio)
- Community fatigue





MITIMA Measuring the Effectiveness and Impact of TCV Introduction in Malawi



Aims:

Effectiveness – case control study, test-negative design.

Impact – ecological, proportionate reduction in typhoid incidence before and after.



THE AGA KHAN UNIVERSITY



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TyVAC works closely with global partners





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Supplementary