

Introduction of Typhoid Conjugate Vaccines: Opportunities and Challenges

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TyVAC Typhoid Vaccine
Acceleration Consortium

Outline

- Give a brief introduction of TyVAC
- Outline broadly opportunities and challenges conjugate vaccines



The Typhoid Vaccine Acceleration Consortium (TyVAC) is led by the Center for Vaccine Development at the University of Maryland School of Medicine, the Oxford Vaccine Group at the University of Oxford, and PATH. TyVAC is funded by the Bill & Melinda Gates Foundation.



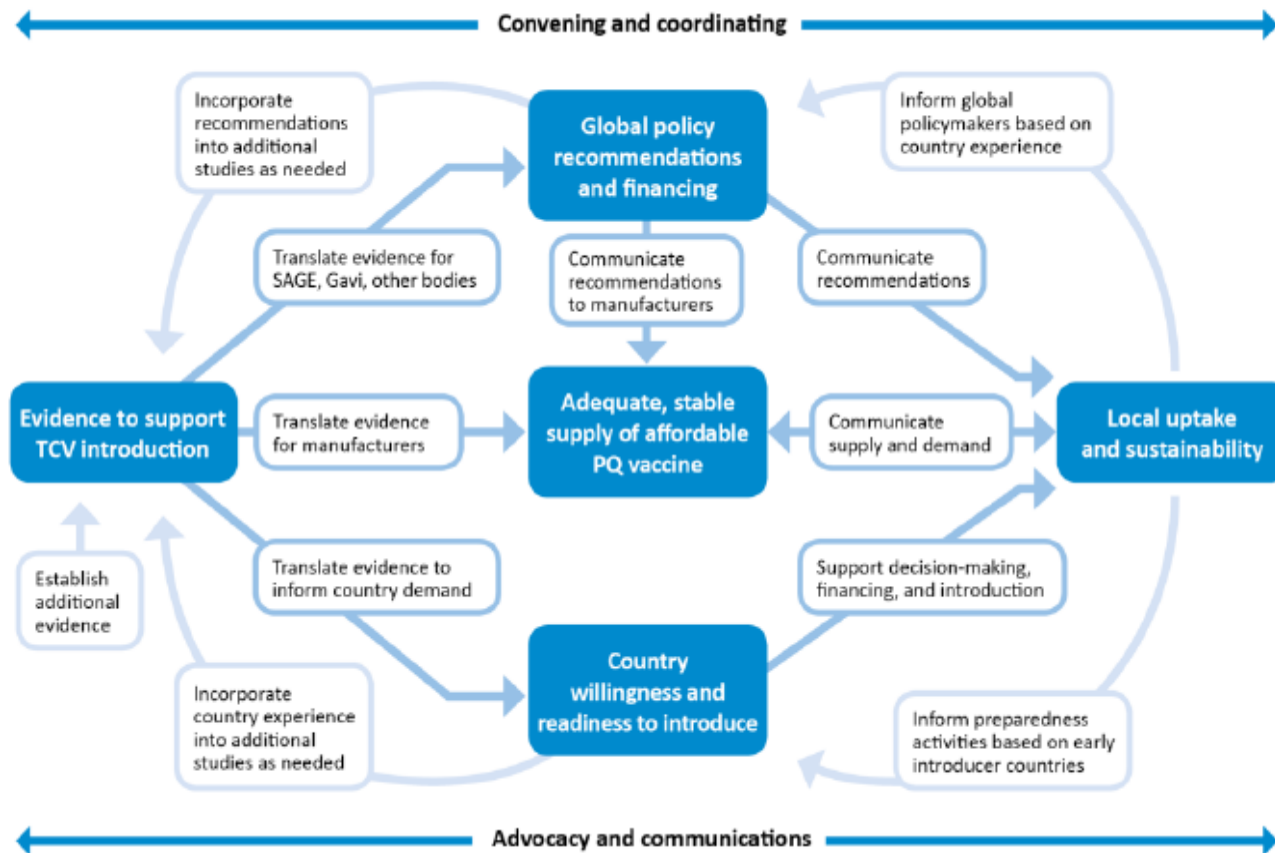
TyVAC's mission

- Reduce the global burden of typhoid by accelerating the introduction of typhoid conjugate vaccines (TCVs), particularly in low resource countries.



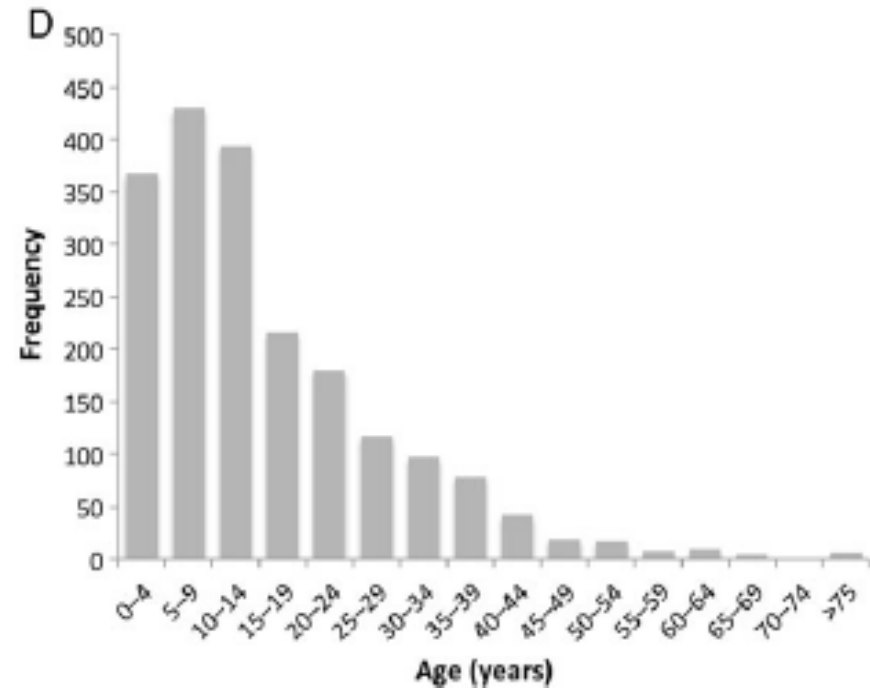
PATH/Molly Mart

How? A Framework for Accelerating TCV Introduction



Where are we in 2017?

- Typhoid continues to be a substantial public health threat.
- Increasing recognition of the burden in young children.



Aggregate age distribution for *S. typhi*, Malawi

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- Increasing recognition of the burden in young children.
- Outbreaks of typhoid continue.

Zimbabwe typhoid outbreak: 1800 cases since October

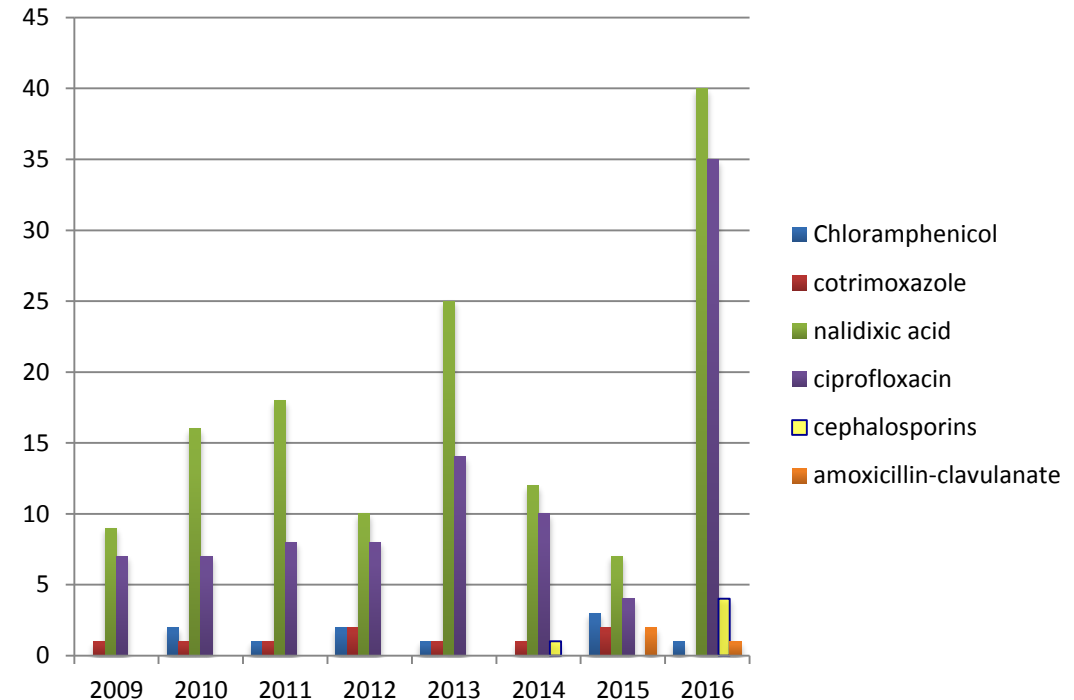
by [News Desk](#) April 2, 2017



Where are we in 2017?

- Typhoid continues to be a substantial public health threat.
- Increasing recognition of the burden in young children.
- Outbreaks of typhoid continue.
- Antimicrobial resistance to the most effective treatments is on the rise.

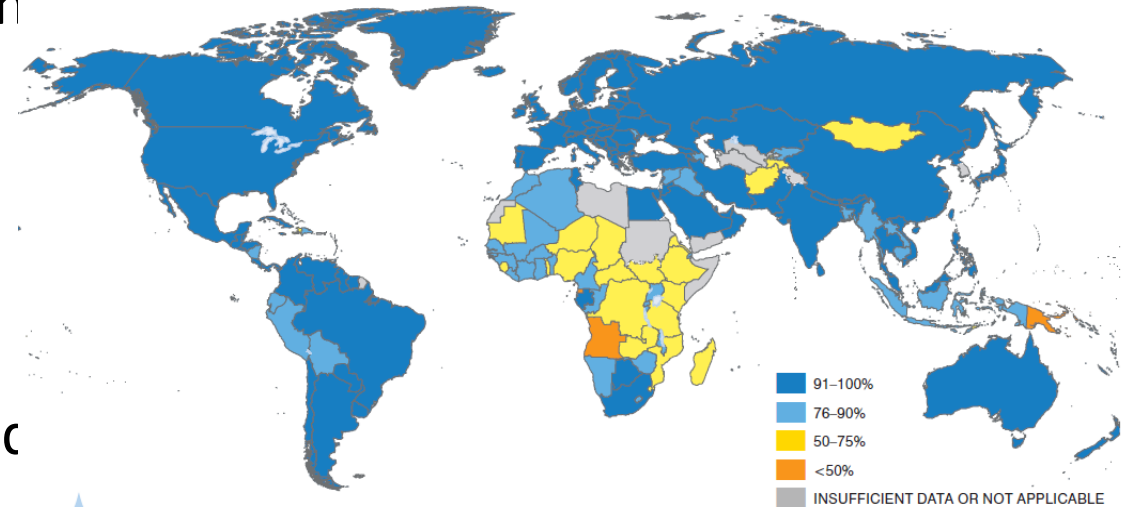
Rise in AMR, Patan Hospital, Nepal
Children < 13 years



Where are we in 2017?

- Typhoid continues to be a substantial public health threat.
- Increasing recognition of the burden in young children.
- Outbreaks of typhoid continue.
- Antimicrobial resistance to the most effective treatments is on the rise.
- Improvements in water, sanitation, and hygiene continue to lag in many parts of the world

Percent of population with improved drinking water sources, 2015



2008, 83, 49–60

No. 6



**World Health
Organization**

Organisation mondiale de la Santé

Weekly epidemiological record Relevé épidémiologique hebdomadaire

8 FEBRUARY 2008, 83rd YEAR / 8 FÉVRIER 2008, 83^e ANNÉE

No. 6, 2008, 83, 49–60

<http://www.who.int/wer>

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WHO position paper

**Typhoid vaccines:
WHO position paper**

**Vaccins antityphoïdiques:
note d'information de l'OMS**

WHO Position Paper Summary, 2008



In view of the continued high burden of typhoid fever and increasing antibiotic resistance, and given the safety, efficacy, feasibility and affordability of 2 licensed vaccines (Vi and Ty21a), countries should consider the programmatic use of typhoid vaccines for controlling endemic disease. In most countries, the control of the disease will require vaccination only of high-risk groups and populations. Given the epidemic potential of typhoid fever, and observations on the effectiveness of vaccination in interrupting outbreaks, typhoid fever vaccination is recommended also for outbreak control.

Gavi Vaccine Investment Strategy, 2008 (2013)

The WG agreed that the majority of the available vaccine products are **not ideal for implementation in GAVI countries due to a limited duration of protection which may require revaccination of the entire cohort every 3 years...** The WG expressed a strong preference for the conjugate vaccine product (currently in late stages of development) which could be administered through routine vaccination strategy. However, in light of the prospect of only one available conjugate vaccine product, the WG also noted that sole source supply is not ideal for the GAVI market.

Why TCVs?

- Two typhoid vaccines are currently available, but are underutilized in high-burden countries despite typhoid's substantial and detrimental impact and World Health Organization (WHO) recommendation for their use.
- New TCVs have the potential to overcome certain challenges that have impeded the uptake of earlier vaccines through:
 - Suitability for children under the age of two
 - Inclusion in routine immunization programs.
 - Longer lasting protection

Considerations for Delivery Strategy

- Risk-based vs universal age-based approach
- Routine +/- catch-up
- Endemic and outbreak



PATH/Doune Porter.

Challenges of delivery strategies that target “high risk:

- Is risk determined by individual basis or population/regional/country basis?
 - Medium or high risk settings?
 - Perception/stigma of “high burden” or “high risk”
- Difficulty in identifying high risk individuals
 - What percentage of population is “at risk”?
 - Can risk factors be reliably identified in advance?
 - Population expansion and movement
- Programmatic difficulty of reaching high risk
 - Must reach high risk individuals prior to exposure

PATH/Rocky
Prajapati.

Rapid Emergence of MDR H58 Lineage of *S. Typhi* in Blantyre, Malawi

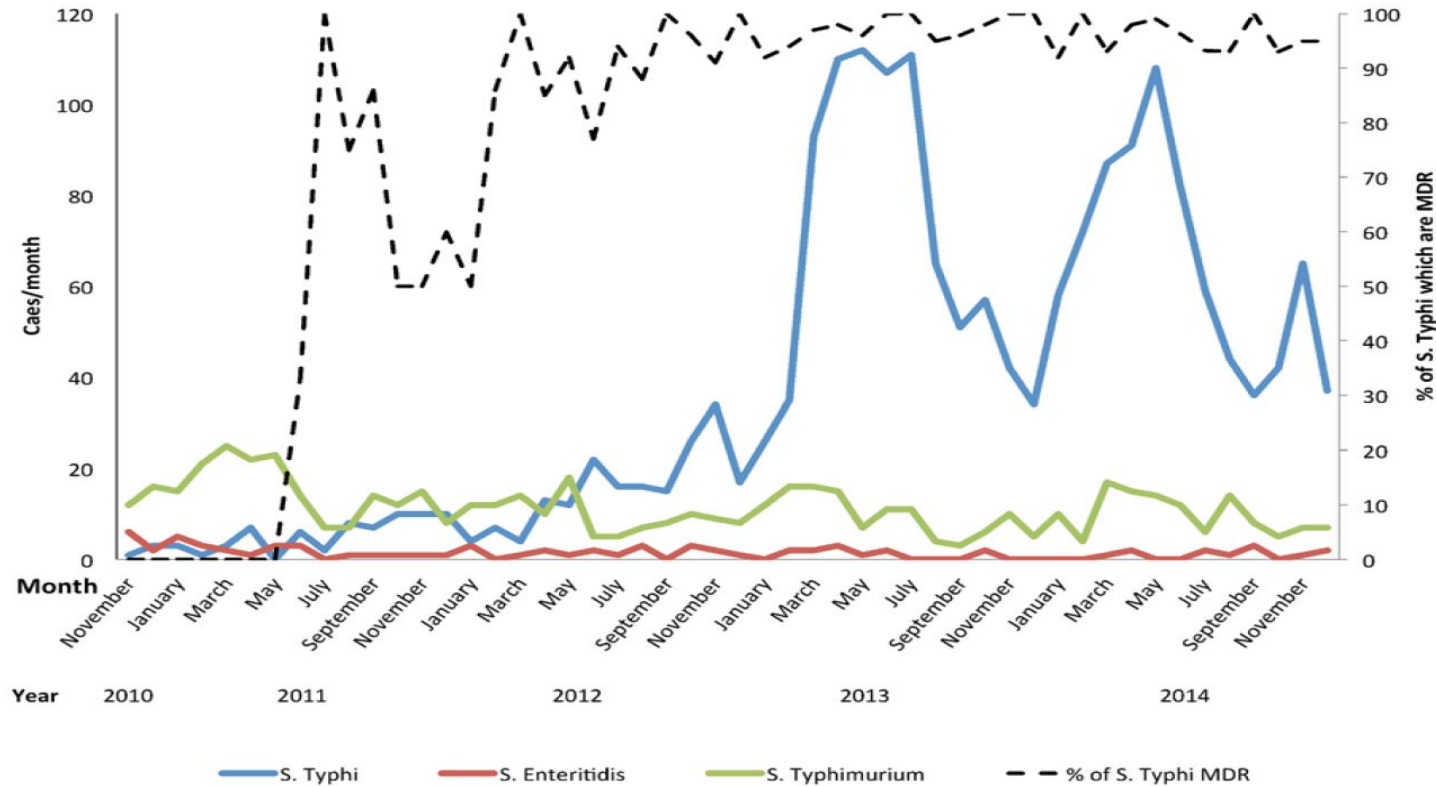


Fig 1. Monthly trends in bloodstream invasive *Salmonella* diagnosed at QECH from November 2010-October 2014.

What about routine immunization?

- TCV offers advantage of vaccinating at younger age
 - Advantages of protecting individual before exposure (not just before “peak”)
 - More total cases of disease prevented
 - Duration of protection is critical factor
 - Compatible with EPI
- Challenges remain
 - Vaccine supply
 - Vaccine cost
 - Increasing number of vaccines at 9-12 months
 - Measles-containing vaccine, Meningitis A, Japanese encephalitis, Yellow Fever, IPV, Malaria, Booster doses/ alternative schedules)

- Models/Cost-effectiveness analyses will be important to inform decisions

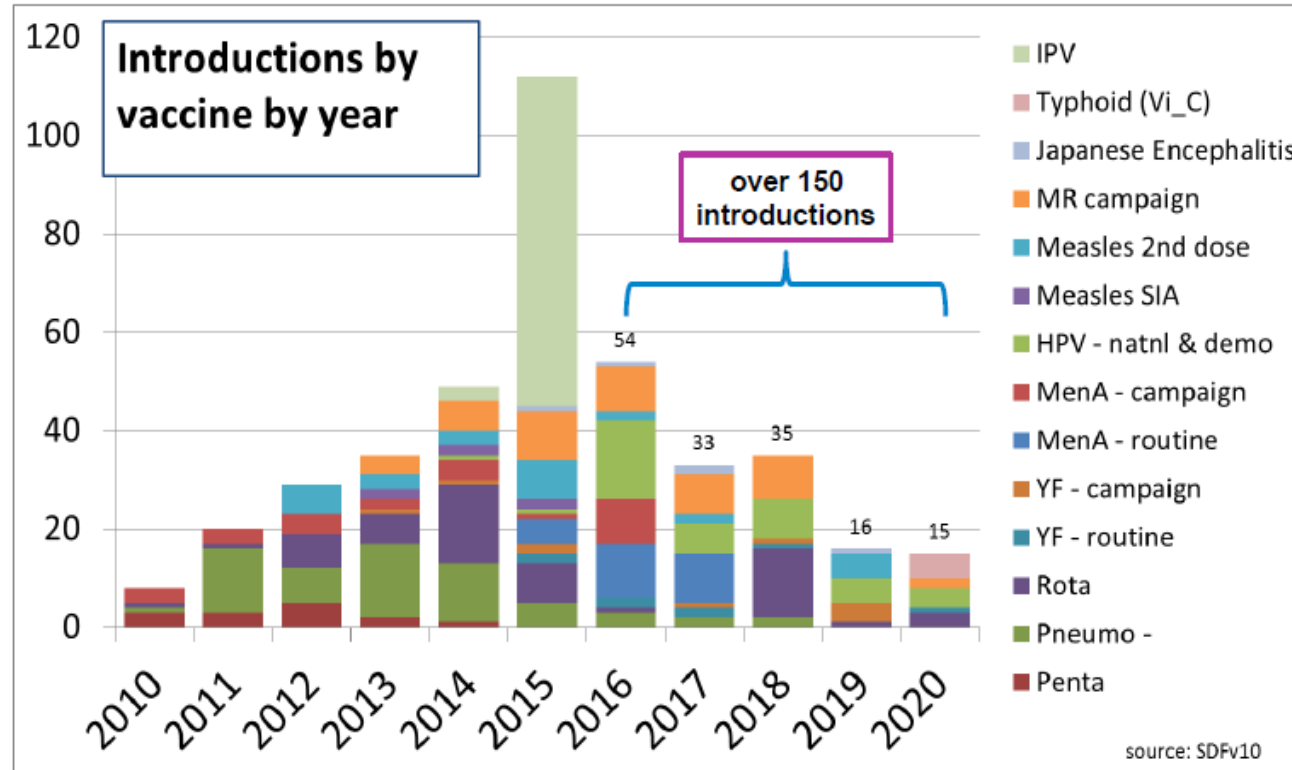
Considerations for Delivery Strategy

- Risk-based vs universal age-based approach
- Routine +/- catch-up
 - Local epidemiology and modelling
 - “Catch-up” necessary for any short-term impact or community protection
- Endemic vs outbreak
 - Endemic and outbreak
 - Supply
 - Stockpile



PATH/Doune Porter.

CONTINUED HIGH LEVEL OF INTRODUCTIONS IN NEXT STRATEGY PERIOD



Plans for impact studies of TCVs in selected countries

	Design	Vaccinated age group	Number vaccinated	Control vaccine
Malawi	Individually-randomized controlled trial	6 months – 12 years	~23,000	Meningitis A
Nepal	Individually-randomized controlled trial	6 months – 15 years	~20,000	Meningitis A
Bangladesh	Cluster-randomized controlled trial	6 months – 15 years	~43,000	Undecided

TyVAC's multidisciplinary strategy to combat typhoid

Serves as a coordinating body for typhoid-related research and control activities

Fosters supportive global policies

Ensures typhoid and TCVs are recognized as global, regional, and national health priorities

Provides data on impact, effectiveness, appropriate vaccination strategies, and associated costs

Supports countries in decision-making and preparation for sustained TCV introduction

Summary

- Value of vaccination for typhoid is considerable:
 - Reduce morbidity and mortality
 - Combat antibiotic resistance
 - Outbreak control
- TCVs offer the potential for greater impact and feasibility
- Multidisciplinary, collaborative approach is necessary for success



TyVAC Collaborating Partners



Yale SCHOOL OF PUBLIC HEALTH