Introduction of Typhoid Conjugate Vaccines: Opportunities and Challenges

Kathleen Neuzil, MD, MPH
Center for Vaccine Development
University of Maryland School of Medicine

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Outline

• Give a brief introduction of TyVAC
• Outline broadly opportunities and challenges for introduction of typhoid 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.
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

Feasey et al. CID 2015: 51; S362
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.

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

Carl Britto, Rhodes Scholar, Oxford Vaccine Group
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

UNICEF and WHO. 2015
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.
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
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
Rapid Emergence of MDR H58 Lineage of S. Typhi in Blantyre, Malawi
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
CONTINUED HIGH LEVEL OF INTRODUCTIONS IN NEXT STRATEGY PERIOD

Introductions by vaccine by year

over 150 introductions

source: SDPv10
# Plans for impact studies of TCVs in selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Design</th>
<th>Vaccinated age group</th>
<th>Number vaccinated</th>
<th>Control vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>Individually-randomized controlled trial</td>
<td>6 months – 12 years</td>
<td>~23,000</td>
<td>Meningitis A</td>
</tr>
<tr>
<td>Nepal</td>
<td>Individually-randomized controlled trial</td>
<td>6 months – 15 years</td>
<td>~20,000</td>
<td>Meningitis A</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>Cluster-randomized controlled trial</td>
<td>6 months – 15 years</td>
<td>~43,000</td>
<td>Undecided</td>
</tr>
</tbody>
</table>
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

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