Cost-effectiveness of typhoid conjugate vaccine strategies across five settings in Africa and Asia

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• **Goal**: To estimate the cost-effectiveness of five TCV delivery strategies in five settings with different epidemiological and health economic characteristics.

• **Delivery strategies**
  
  I. Routine vaccination at 9 month of age
  II. Routine vaccination at 9 mo + catch-up campaign 9m-5y
  III. Routine vaccination at 9 mo + catch-up campaign 9m-15y
  IV. Routine vaccination at 9 mo + catch-up campaign 9m-25y
  V. Routine vaccination at 9 mo + catch-up campaign all ages

• Sites were selected based on availability of both incidence data and cost-of-illness data.
<table>
<thead>
<tr>
<th>Location (year)</th>
<th>Setting</th>
<th>Incidence (adjusted)</th>
<th>Cost of Illness (Outpatient and Inpatient)</th>
<th>Cost of Vaccine Delivery</th>
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</thead>
</table>
| Kolkata, India (2004)   | Urban   | Medium 160 (290) per 100,000 | Low/Medium OP: $18.69  
 IP: $928.43  | Low  
 Routine: $3.55  
 Campaign: $1.67  |
| Delhi, India (1996)     | Urban   | High 750 (2,200) per 100,000 | High OP: $222.12  
 IP: $4,840.50  | Low  
 Routine: $3.55  
 Campaign: $1.67  |
| Dong Thap, Vietnam (1995) | Rural | Medium-high 200 (550) per 100,000 | Low/High OP: $10.70  
 IP: $1,241.32  | High  
 Routine: $8.33  
 Campaign: $9.02  |
| Kibera, Kenya (2010)    | Urban   | Medium-high 250 (900) per 100,000 | Low  
 OP: $4.78  
 IP: $103.87  | Low  
 Routine: $3.60  
 Campaign: $3.60  |
| Lwak, Kenya (2010)      | Rural   | Low 30 (100) per 100,000 | Low  
 OP: $4.78  
 IP: $103.87  | Low  
 Routine: $3.60  
 Campaign: $3.60  |
Typhoid transmission & treatment model

Essential features:

• Loss of immunity to subclinical infection
• Primary vs secondary infection
• Chronic carriers
• Link to treatment model
• Assume deaths only occur among hospitalized patients (conservative)
Fitting the model to age-specific incidence

- Fit using Stan (Hamiltonian Monte Carlo)
- We drew 5,000 samples from the joint posterior distribution of model parameters
Base case assumptions

- Vaccine price: $1/dose
- Single dose
- Efficacy = Vi-rEPA
- 80% coverage for routine vaccination
- 70% coverage for campaigns
- Null comparator: no vaccination
- Time horizon: 10 years

Scenario analyses:

- Vaccine price of $2/dose and $5/dose
- Two doses required to fully immunize children <5 years of age
Modeling vaccination with TCV

• **Vaccine efficacy**
  =95% (87.0-99.7%) during 1st year for (based on Vi-rEPA)

• **Duration of immunity**
  =19 years (6-147 yrs) (estimated based on Vi-rEPA)

Cost-Effectiveness Analysis

- Healthcare provider perspective
  - Direct medical costs only

- Net benefit framework to evaluate the probability that each strategy was optimal across a range of willingness-to-pay (WTP) thresholds while accounting for parameter uncertainty
  - Low emphasis on WHO thresholds

- Sensitivity analysis to assess contribution of each parameter to uncertainty in determining the optimal strategy
  - Net monetary benefit (NMB) at WTP equal to 1xGDP
Cost-effectiveness acceptability curves

- WTP = I$0 (Cost-saving)
- WTP = 1xGDP (Very cost-effective)
- WTP = 3xGDP (Cost-effective)

Kolkata
Delhi
Dong Thap
Kibera
Lwak
Cost-effectiveness acceptability curves

Kolkata

Delhi

Dong Thap

Kibera

Lwak
Scenario analysis: Vaccine price

Kolkata

Delhi

Dong Thap

Kibera

Lwak
Scenario analysis: Price & number of doses

Kolkata

Delhi

Dong Thap

Kibera

Lwak

Willingness-to-pay per disability-adjusted life-year averted, $
• Random forest analysis (robust to correlation between parameters)
• **Number of doses required** and **probability of hospitalization**
  were the primary sources of uncertainty in most settings
Conclusions

- Routine vaccination at 9 months old would be "cost-effective", "very cost-effective", or even "cost-saving" in most settings.

- However, additional benefits gained by including one-time catch-up campaigns would be economically justified.
  - Optimal delivery strategy varied by country and willingness to pay.
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We’re hiring! Two faculty positions available in laboratory- and field-based epidemiology
Additional slides
ICER of routine vaccination vs status quo

The chart shows the probability of different outcomes for routine vaccination compared to the status quo in various locations: Kolkata, Delhi, Dong Thap, Kibera, and Lwak.

- **Cost Saving** is represented by red color.
- **Very Cost Effective** is represented by blue color.
- **Cost Effective** is represented by green color.
- **Not Cost Effective** is represented by purple color.

The chart indicates that routine vaccination is likely to be cost saving or very cost effective in most locations.
• Substantial decline in incidence, with additional benefit of catch-up campaigns

• Possible rebound in incidence 10-20 years following campaign, particularly in high incidence settings
CEACs at current market price

Kolkata

Delhi

Dong Thap

Kibera

Lwak

Current price = 1,800 rupees

= I$106 in India

= I$78 in VN

= I$57 in Kenya

(converted to international dollars based on PPP conversion factor for each country in 2015)
Passive surveillance estimated to detect 42% (22-58%) fewer cases on average than active surveillance.

Not all individuals meeting the case definition may consent/have blood drawn for culture, and this may vary by age.

Blood culture sensitivity is only ~50-70% and varies depending on the volume of blood drawn. Lower volumes of blood often drawn for children <5 years old.
Adjusted incidence is much greater for Kibera than Kolkata (particularly in <5 yr olds) because:

- A low percentage of those meeting the case definition had blood culture performed, particularly among children <5 yrs
- A low volume of blood (1-3 mL) was collected from children <5 yrs old, and sensitivity was estimated to be lower
Typhoid dynamic model structure

Essential features:
- Loss of immunity to subclinical infection
- Primary vs secondary infection
- Chronic carriers
- Balance between “short cycle” transmission via contamination of food, etc in the immediate environment
- …and “long cycle” transmission via contaminated water
  - May be more seasonal