COMPARISON OF STRATEGIES AND THRESHOLDS FOR VI CONJUGATE VACCINES AGAINST TYPHOID FEVER: A COST-EFFECTIVENESS MODELING STUDY

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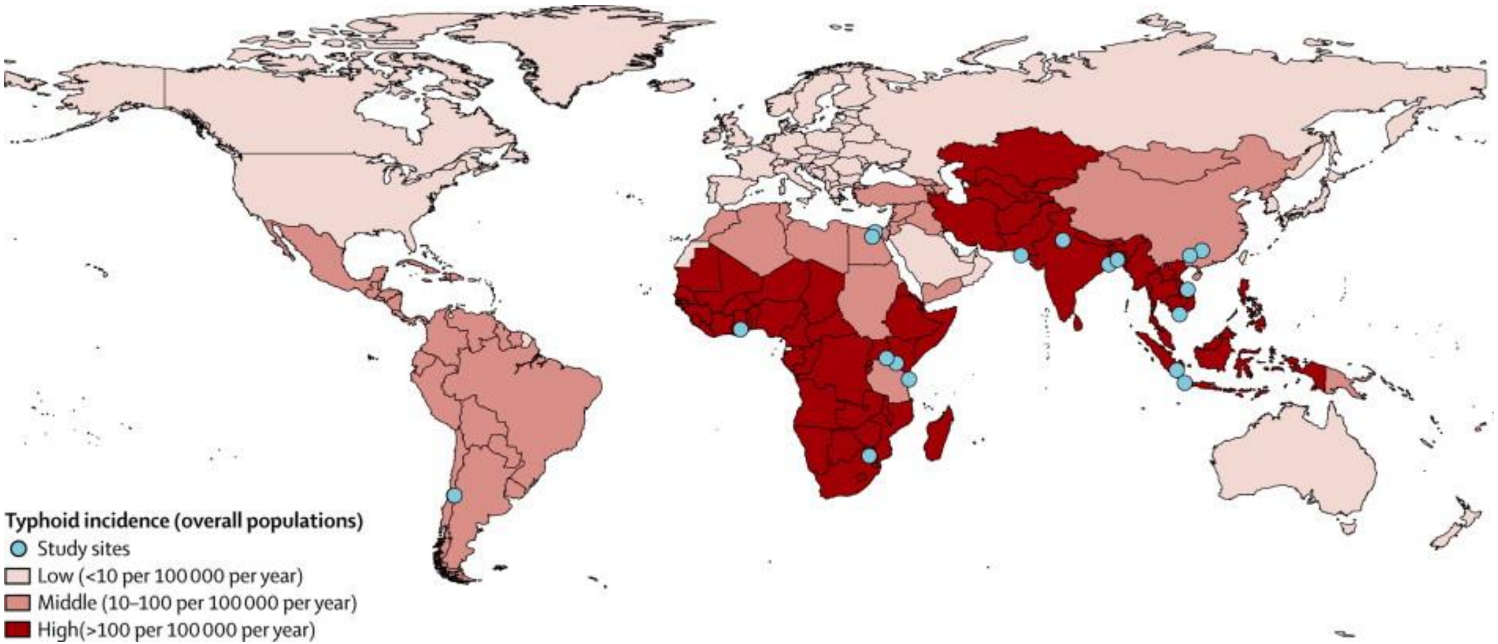
Burden of typhoid fever



Estimated global incidence of 12 million with annual mortality of 130,000

Mogasale V. et al., Lancet Glob Health (2014)

A new global strategy for typhoid fever?

- Current global public health strategy relies on passive surveillance
- Older vaccinations have significant limitations
- New generation typhoid conjugate vaccines presents opportunity
  - Potential >90% efficacy
  - Longer duration of immunity
  - Immunogenic in young children (<5 years)
- Increasing antimicrobial resistance with higher mortality may influence decision

Study questions

1) What is the health impact of typhoid conjugate vaccines implemented in routine EPI programs with or without school catch-up campaigns?

2) What are the cost-effective incidence thresholds for delivery of these vaccines?

3) What will the impact of rising drug resistance and associated mortality be on the value of these vaccines?

EPI; Expanded Program on Immunization

Methods

Methodological approach

Modeling approach

- Age-structured natural history and dynamic transmission model
- Cost-effectiveness analysis

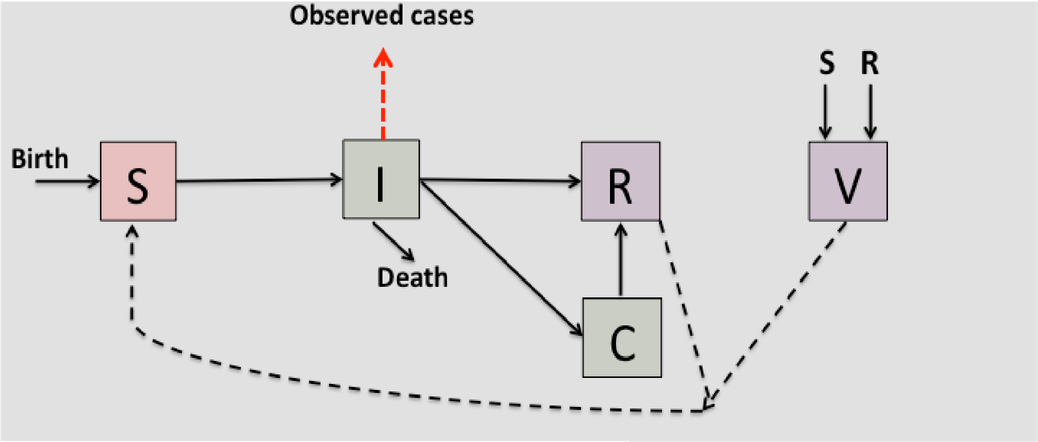
Data sources

- Meta-analysis of global typhoid burden
- Global burden of disease
- Natural history data from literature

Tested treatment strategies (10 year time horizon)

- Integration with Expanded Program on Immunization (EPI)
  - Routine immunization (<1 year)
  - 85% coverage
- EPI + school catch-up campaign
  - Routine EPI + school aged children (5-14 years)
  - 75% coverage

Dynamic transmission model



S- Fully susceptible
I- Infected
C- Carrier
R- Recovered (immune)
V- Vaccinated (immune)
W- Water in environment

<u>Modeling approach:</u>

- Age-structured
- Transmission (2 sources)
  - Short-cycle (person-to-person)
  - Long-cycle (public water supply)
- Sub-clinical infection
- Long-term carriage
- Waning immunity
- Rule of parsimony
- Model comparisons

Cost-effectiveness analysis

Incremental cost-effectiveness ratio (ICER)

- Compares two strategies
- Lower ICER is more cost-effective

$$ICER = \frac{Cost\ difference}{DALYs\ averted}$$

ICER calculation

- Cost: 2016 US$ (Societal perspective)
- Effectiveness: Disability adjusted life-years (DALYs)
- Highly cost-effective: ICER< $1035 (GDP per capita of low-income country)
- Cost-effective: ICER < 3x GDP per capita

Disability and mortality, cost, and vaccination

Disability and mortality inputs for model

Disease state	Case-years	Disability weight
Acute infectious disease, moderate	35%	0.05
Acute infectious disease, severe	48%	0.13
Abdominal pain and distension[a]	17%	0.32
Gastrointestinal bleeding	<1%	0.33
Mortality	1%	--

[a]Includes intestinal perforation

Cost inputs for model

Parameter	Base case
Typhoid conjugate vaccine (per dose)	$ 2.50
EPI-based delivery (per dose)	$ 0.50
School catch-up delivery (per dose)	$ 1.00
Total cost for EPI (per child)	$ 6.00
Total cost for catch-up (per child)	$ 7.00
Vaccine coverage (%)	75-85

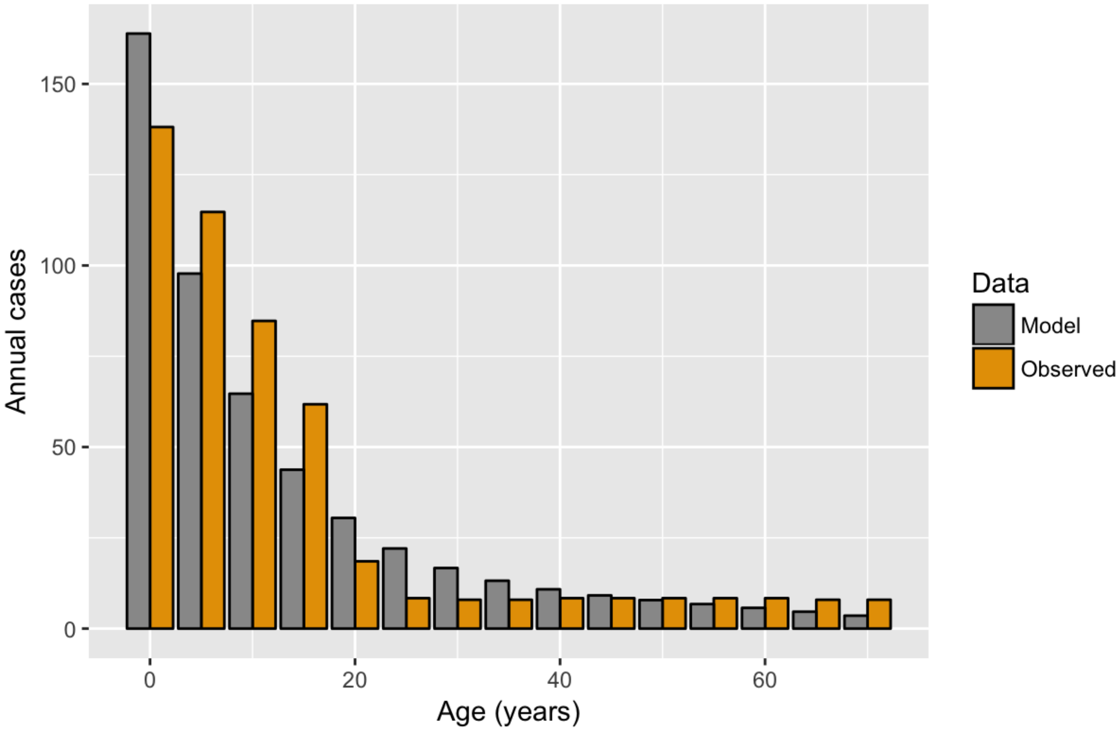
EPI; Expanded Program on Immunization

Typhoid conjugate vaccine assumptions

- 91% efficacy
- 20 year immunity duration

Results

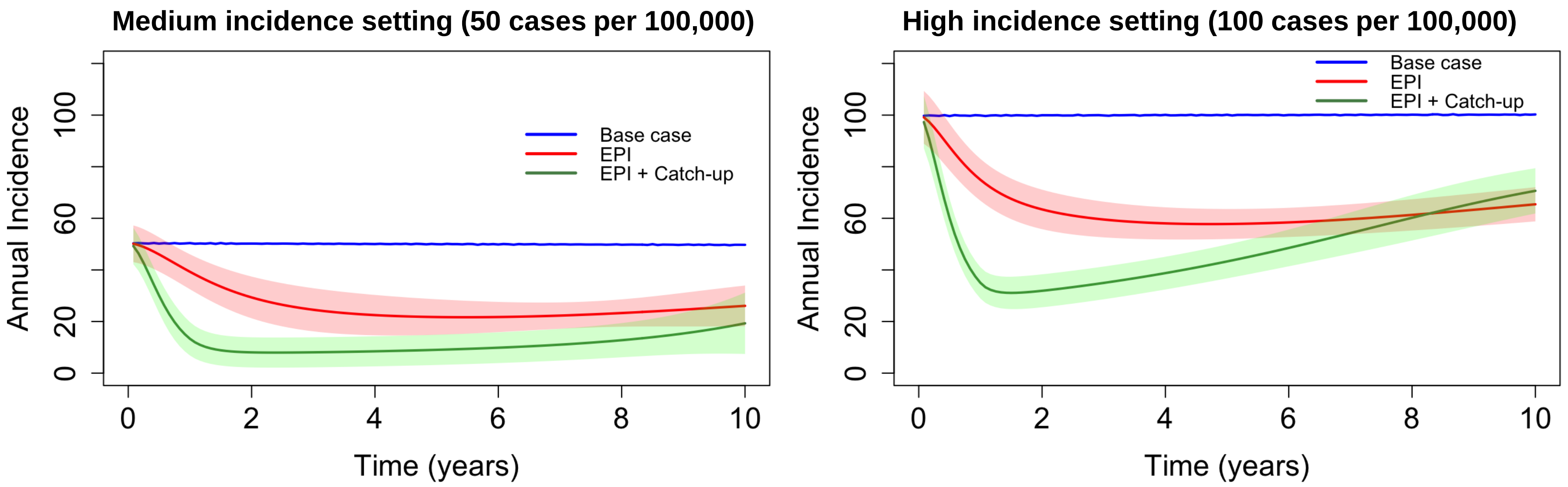
Model calibration



<u>Main points:</u>

- Transmission model was fit to age distribution
- Model was fit across low, medium, and high incidence settings
- Model reproduced data

Typhoid vaccination may substantially reduce incidence



EPI; Expanded Program on Immunization

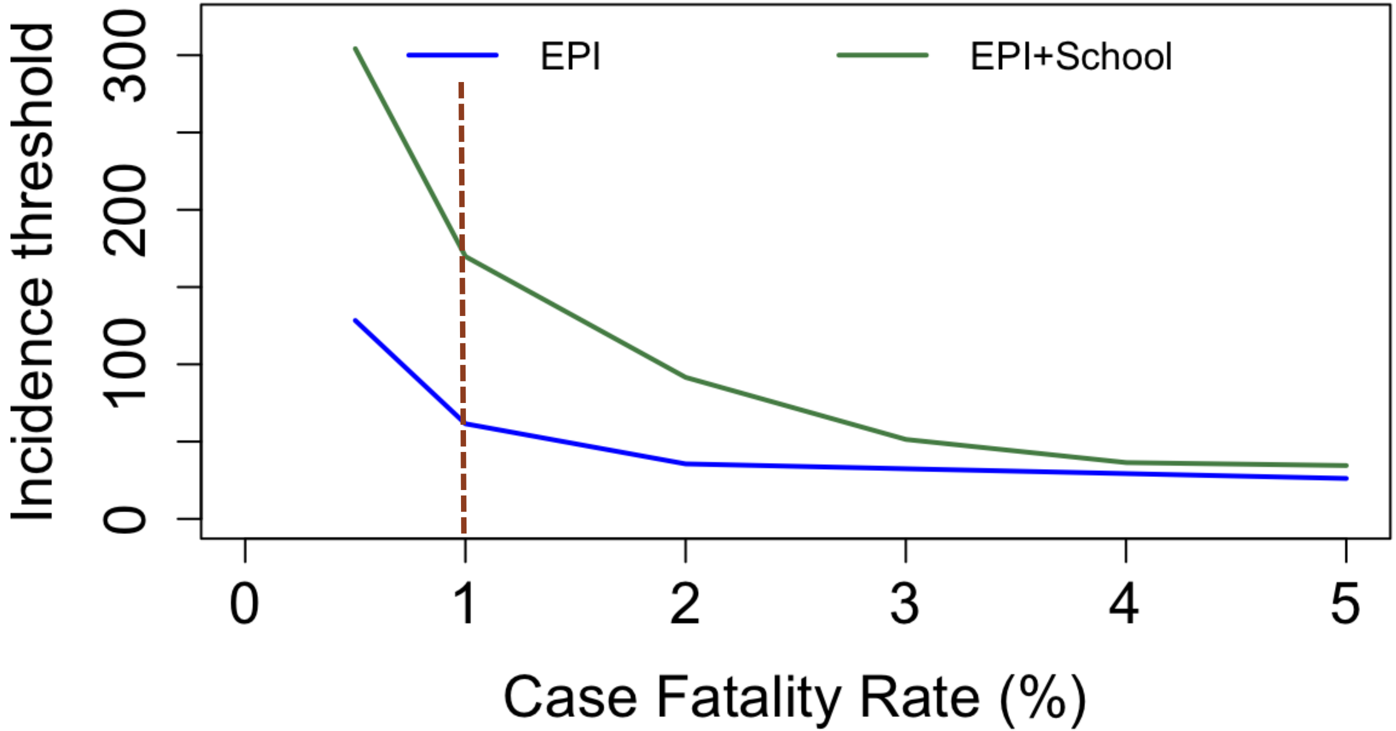
Conjugate vaccines highly cost-effective in medium incidence setting

EPI vaccination strategy → highly cost-effective in medium incidence settings (>**50 cases per 100,000**)

EPI vaccination + school catch-up campaign → highly cost-effective in high incidence settings (>**150 cases per 100,000**)

Analysis used a willingness-to-pay optimized for low-income country

Antimicrobial resistance may affect incidence thresholds



Limitations

- Substantial country-specific heterogeneity, uncertainty around typhoid biology, and constraints of common modeling assumptions
- General relationship between incidence and age distribution of typhoid cases
- Economic threshold (willingness-to-pay) may vary for countries; context- or budget-specific analyses can be done
- Vaccine cost and mortality are influential parameters

Conclusion

- Typhoid Vi conjugate vaccines through EPI may be highly cost-effective in moderate incidence settings (50 annual cases per 100,000).

- Typhoid vaccination through EPI with school catch-up campaign may be highly cost-effective in high incidence settings (150 annual cases per 100,000).

- These results were sensitive to case fatality rates, underscoring the need to consider rising antimicrobial resistance in vaccine decision making.

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Key collaborators

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