Previous efforts to model typhoid burden

RESEARCH ARTICLE

The burden of typhoid fever in low- and middle-income countries: A meta-regression approach

Marina Antillón¹*, Joshua L. Warren², Forrest W. Crawford², Daniel M. Weinberger¹, Esra Küürüm³, Gi Deok Pak⁴, Florian Marks⁵, Virginia E. Pitzer⁶


Estimating the incidence of typhoid fever and other febrile illnesses in developing countries

John A Crump ³, Fouad G Youssef, Stephen P Luby, Momtaz O Wasfy, Josefa M Rangel, Maha Taalat, Said A Oun, Frank J Mahoney

The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017

GBD 2017 Typhoid and Paratyphoid Collaborators ¹. Show footnotes
Additional population-based studies of typhoid fever

- Studies in previous model (published 1980-2013) (32 studies, 22 locations)
- Studies in new model (published 1980-2021) (43 studies, 60 locations)
Comparison to most recent incidence data

- SEAP
- SETA
- STRATAA
- Lao PDR & Myanmar
Objective

• Interpolate data from incidence studies (overall and for specific age-groups) to predict typhoid incidence at the national level, particularly for countries where no blood-culture-confirmed incidence evidence is available.
  • All LICs, LMICs, and UMICs – 145 countries
• Explore ways to estimate subnational variation in typhoid incidence
• Quantify uncertainty
  • It may not be necessary (or possible) to have a precise estimate of incidence, but knowing whether incidence is likely to be low (<10 per 100K person-years), medium (10-100 per 100K person-years), high (100-500 per 100K person-years), or very high (>500 per 100K person-years) is important for informing policy decisions
Approach

Data

• Population-based incidence studies with blood-culture confirmed cases
• Age groups noted: overall incidence, 0-2, 2-5, 5-15, 15+ years, or any combination of these
• Contextual information: catchment population, % individuals enrolled, blood culture volume collected.
• Widely available economic, environmental, and demographic covariates, which we map to the location of the study.

Methods

• Statistical model
• Bayesian approach to account for all sources of uncertainty.
• Using adjusted reported incidence from studies that report it
Adjustments to crude incidence data

**Adjusted "true" typhoid fever incidence**

**Cases who sought care for fever at study facilities**

**Cases who were enrolled and had blood collected for culturing**

**Observed blood-culture-confirmed cases and person-time under surveillance**

Adjustment for healthcare seeking (assumed to be 100% for active surveillance studies, estimated for passive surveillance studies)

Adjustment for proportion who met fever criteria who were enrolled

Adjustment for blood culture sensitivity (by age group)

## Predictors included

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Resolution</th>
<th>Mean and range in estimation sample</th>
<th>Source</th>
</tr>
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<tbody>
<tr>
<td>Population density</td>
<td>1/4x1/4 degree</td>
<td>3,643 (0-18,467)</td>
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<td>GDP per capita PPP, 2015 USD</td>
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Model fit

0-2

2-4

6-15

15+
Global burden of typhoid fever: 19.3 million cases, 90% CI (6.5-64.2M)
Age-specific incidence

Incidence per 100K persons
ages 0-1

Incidence per 100K persons
ages 2-4

Incidence per 100K persons
ages 5-15

Incidence per 100K persons
ages 15+
Work in progress, future directions

Ongoing efforts
- Further assessing model convergence
- Consider additional covariates and/or spatial random effects
- Potentially include serosurveillance data

Beyond scope
- Antibiotic resistance
- Additional outcomes: hospitalizations, complications, etc.
- Typhoid fever as a proportion of all fevers, enteric infections, etc.
- Asymptomatic/subclinical infection
Thank you!

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Marina Antillon, Ottavia Prunas, Virginia Pitzer
Predictors of typhoid incidence
Model details

- Generalized linear mixed-effects model
  - **Age-group** and **location-specific** incidence modeled as a function of predictor variables and random effects

\[
\log(\lambda_{aj}) = B_{0j} + B_{aj} + \log(\text{person-time}_{aj})
\]

**Intercept:**
Overall incidence

**Slope:**
Relative incidence for age group \(a\)

**Covariates**

**Incidence in reference age group (5-15 yo)**

**IRR for other age groups vs reference**
Probability of categories of overall incidence:

- Probability of Low Incidence: <10 per 100,000 Person-Years
- Probability of Medium Incidence: 10-<100 per 100,000 Person-Years
- Probability of High Incidence: 100-<500 per 100,000 Person-Years
- Probability of Very High Incidence: 500+ per 100,000 Person-Years