A Bayesian approach for estimating typhoid fever incidence from passive surveillance data

11th International Conference on Typhoid & Other Invasive Salmonelloses
March 26-28, 2018

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Yale School of Public Health
Advisor: Virginia E. Pitzer, ScD
The need for adjusted incidence estimates

- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence

Facility-based laboratory-confirmed case estimates of typhoid are likely lower than actual number. Only a fraction of individuals with typhoid seek care at a healthcare facility. Only a fraction of individuals with typhoid who seek care receive a blood culture diagnostic test. Only a fraction of individuals with typhoid who receive a blood culture test positive for typhoid.
The need for adjusted incidence estimates

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The need for adjusted incidence estimates

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➤ Only a fraction of individuals with typhoid seek care at a healthcare facility
The need for adjusted incidence estimates

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➤ Only a fraction of individuals with typhoid seek care at a healthcare facility
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Typhoid Reporting Pyramid
Infections reported are only a fraction of the true number

- Blood culture confirmed infections
- Blood cultures tested
- People who seek care for a fever
- Symptomatic infections
- All typhoid infections (including asymptomatic individuals)
Typhoid Reporting Pyramid
Infections reported are only a fraction of the true number

Blood culture confirmed infections
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Blood culture confirmed infections

Blood cultures tested

People who seek care for a fever

Symptomatic infections

All typhoid infections (including asymptomatic individuals)
Typhoid Reporting Pyramid

Blood culture confirmed infections

Blood cultures tested

People who seek care for a fever

Symptomatic infections

All typhoid infections (including asymptomatic individuals)
Typhoid Reporting Pyramid

- **Symptomatic infections**
- All typhoid infections (including asymptomatic individuals)
- People who seek care for a fever
- Blood cultures tested
- Blood culture confirmed infections

People who seek care for a fever, all typhoid infections (including asymptomatic individuals), blood cultures tested, blood culture confirmed infections.
Typhoid Reporting Pyramid

- **People who seek care for a fever**
  - Symptomatic infections
  - All typhoid infections (including asymptomatic individuals)
  - Blood cultures tested
  - Blood culture confirmed infections
Typhoid Reporting Pyramid

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STRATEgic Typhoid alliance across Africa and Asia (STRATAA)

WEDNESDAY, MARCH 27

8:30-10:30 STRATAA/TyVAC

SYMPOSIUM SESSION CHAILED BY:
Andrew J. Pollard, University of Oxford & Kathleen Neuzil,
University of Maryland School of Medicine

Burden of Enteric Fever in Africa and Asia from Three Urban Centres: A Multicentre,
Prospective Epidemiological Study with over 600,000 Person-Years of Observation
James Meiring, University of Oxford

• A 2-year prospective epidemiological study

• 3 sites:
  o Dhaka, Bangladesh
  o Patan, Nepal
  o Blantyre, Malawi

• Passive surveillance, serosurveillance, and healthcare utilisation
  surveys nested within demographic census population
Estimating symptomatic typhoid infection incidence

- Symptomatic infections
- All typhoid infections (including asymptomatic individuals)
- People who seek care for a fever
- Blood cultures tested
- Blood culture confirmed infections
- People who seek care for a fever
- All typhoid infections (including asymptomatic individuals)
**Typhoid nested in febrile pyramid**

- **Symptomatic infections**
  - People with febrile illness
  - Laboratory tests for organism
    - People who seek care for a fever
      - Laboratory-confirmed infections
        - Blood culture tested
          - Blood culture confirmed infections
            - All typhoid infections (including asymptomatic individuals)
Observed (STRATAA) data

- **Symptomatic infections**
  - All typhoid infections (including asymptomatic individuals)

- **People who seek care for a fever**

- **People with febrile illness**

- **Laboratory tests for organism**

- **Laboratory-confirmed cases**
  - Blood culture confirmed infections
  - Blood cultures tested
  - People who seek care for a fever

- **Strategic Typhoid alliance across Africa and Asia**
Additional Sources of Information

- People who seek care for a fever
- People with febrile illness
- Laboratory tests for organism
- Blood cultures tested
- Blood culture confirmed infections
- Laboratory-confirmed cases
- Symptomatic infections
- All typhoid infections (including asymptomatic individuals)

- Age
- Days with fever
- Blood culture volume
- Antimicrobial use

STRATAA
Strategic Typhoid alliance across Africa and Asia
Symptomatic infections

Laboratory-confirmed cases

Blood culture confirmed infections

Blood cultures tested

People who seek care for a fever

People who seek care for a fever

Laboratory tests for organism

People with febrile illness

All typhoid infections (including asymptomatic individuals)

Probability of seeking healthcare

• Blood culture volume
• Antimicrobial use

• Age
• Days with fever

• Age
• Country
Probability of having a blood culture

- People with febrile illness
- People who seek care for a fever
- Laboratory tests for organism
- Laboratory-confirmed cases

All typhoid infections (including asymptomatic individuals)

Symptomatic infections

Blood culture confirmed infections

Blood cultures tested

People who seek care for a fever

Laboratory tests for organism

Laboratory-confirmed cases

- Blood culture volume
- Antimicrobial use
- Age
- Country
Probability of testing positive

- All typhoid infections (including asymptomatic individuals)
- Symptomatic infections
- People who seek care for a fever
- Laboratory tests for organism
- Laboratory-confirmed cases

• Blood culture volume
• Antimicrobial use
• Age
• Days with fever
• Age
• Country

People with febrile illness
People who seek care for a fever
Laboratory tests for organism
Laboratory-confirmed cases
Blood cultures tested
Blood culture confirmed infections
All typhoid infections (including asymptomatic individuals)
Serosurveillance: An upper bound on estimates

- Laboratory-confirmed cases
  - Blood culture confirmed infections
    - People who seek care for a fever
      - People with febrile illness
        - All typhoid infections (including asymptomatic individuals)
          - Laboratory tests for organism
            - Blood cultures tested
              - People who seek care for a fever
                - Blood culture volume
                  - Antimicrobial use
                    - Age
                      - Days with fever
                        - Age
                          - Country
                            - Serological surveillance

Bayesian inference

• Combines past experience with new data to form the current state of knowledge
• Quantifies uncertainty about estimates
Bayesian Framework

People who sought care for a fever

Symptomatic infections

Blood cultures collected & tested

Blood culture confirmed infections

Blood culture (BC) positive infections

STRATAA passive surveillance

Probability of having BC drawn

STRATAA passive surveillance
Probability of blood culture by age

Probability of having positive BC result

STRATAA passive surveillance
Blood culture sensitivity by volume

Probability of seeking healthcare

STRATAA Healthcare Utilisation Survey

“True” Symptomatic Infections

Blood culture confirmed → Symptomatic infections

Intervening processes

People who sought care for a fever

Blood cultures collected & tested

Blood culture confirmed infections

Blood culture (BC) positive infections

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Probability of having positive BC result

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Blood culture sensitivity by volume

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“True” Symptomatic Infections

Bayesian Framework

People who sought care for a fever

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Probability of having positive BC result
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Blood culture sensitivity by volume

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Probability of blood culture by age

Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

“True” Symptomatic Infections

All adjustment factors

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<tr>
<th>Country</th>
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Lower probabilities | Higher probabilities
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Lower probabilities

Higher probabilities

about the same
All adjustment factors

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Lower probabilities: Bangladesh, Nepal, Malawi

Higher probabilities: Bangladesh, Nepal

About the same: Bangladesh, Nepal

Malawi is lower: Malawi
All adjustment factors

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- Malawi is lower
- Nepal is lower
- Lower probabilities
- Higher probabilities

about the same
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Lower probabilities: Bangladesh <5, Nepal test, Malawi seek HC
Higher probabilities: Bangladesh BC test, Nepal seek HC

about the same
Malawi is lower
Nepal is lower
Malawi is higher
Adjustments to Incidence Rates

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Incidence Rate per 100,000 person-years

Adjustment: None, BC sensitivity, BC sensitivity, BC test, BC sensitivity, BC test, Healthcare seeking

*BC = Blood Culture

**STRATAA**

*Strategic Typhoid alliance across Africa and Asia*
Overall results

- 8- to 12-fold adjustments

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*per 100,000 person-years
# Overall results: Bangladesh

- Bangladesh has the highest crude incidence rates, but the lowest adjustment ratio

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*per 100,000 person-years
## Overall results: Nepal

- Nepal has the highest adjustment ratio

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*per 100,000 person-years
Overall results: Malawi

- Malawi is somewhere in between

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*per 100,000 person-years
Adjusted rates vary by age

- Adults (15+ years) had the lowest incidence rates
- Children 5-14 years had the highest incidence rates

**Observed vs. Adjusted Incidence Rates**

<table>
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<tr>
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Incidence Rate per 100,000 person-years

- **<5 years**
  - Bangladesh: Low
  - Nepal: Low
  - Malawi: Low

- **5-14 years**
  - Bangladesh: Moderate
  - Nepal: High
  - Malawi: Moderate

- **>15 years**
  - Bangladesh: Low
  - Nepal: Low
  - Malawi: Low

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**Observed vs. Adjusted**

- **Observed**
  - Bangladesh: Low
  - Nepal: Low
  - Malawi: Low

- **Adjusted**
  - Bangladesh: Moderate
  - Nepal: High
  - Malawi: Moderate

STRATAA
Strategic Typhoid alliance across Africa and Asia
Implications

- Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population.
Implications

- Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population

- Our model provides a method to estimate incidence while accounting for the reporting process
  - Improved understanding of intervening processes
  - Can be updated with additional information or contexts
Implications

• Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population

• Our model provides a method to estimate incidence while accounting for the reporting process
  — Improved understanding of intervening processes
  — Can be updated with additional information or contexts

• These upward-adjusted estimates can be used for analysis and/or decision-making for typhoid control
Acknowledgements

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Blantyre, Malawi
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Kathmandu, Nepal
Buddha Basnyat, Mila Shakya, Abhilasha Karkey, Sabina Dongol, Amit Aryja, Anup Adhikari, Maheshwar Ghimire, Pallavi Gurung,

Archana, Maharjan
Cambridge, UK
Gordon Dougan, Zoe Dyson, Emily Lees, Ankur Mutreja, Derek Pickard, Stephen Reece

Ho Chi Minh, Vietnam
Stephen Baker, Thomas Darton, Christiane Dolocek, Tan Trinh Van, Nhu Tran Hoang, Tran Vu Thieu Nga

Melbourne, Australia
Sarah Dunstan, Kat Holt, Mike Inouye, Artika Nath, Louise Judd

New Haven, USA
Virginia Pitzer, Maile Thayer Phillips, Yu-Han Kao, Neil Saad
Bayesian inference

- Bayesian inference combines past experience (prior) with new data (likelihood) to form the current state of knowledge (posterior)

\[
\text{posterior} \propto \text{likelihood} \times \text{prior}
\]

- Observed data
- Information from additional sources
Bayesian Framework

Blood culture confirmed cases

Blood cultures collected & tested

People who sought care for a fever

Total Symptomatic Cases

Blood culture (BC) positive infections
STRATAA passive surveillance

Probability of having positive BC result
STRATAA passive surveillance
Blood culture sensitivity by volume

Probability of having BC drawn
STRATAA passive surveillance
Probability of blood culture by age

Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

“True” Symptomatic Infections

Bayesian Framework

$N_{BC+} \sim \text{Poisson}(\lambda \cdot p_{sens} \cdot p_{BC} \cdot p_{HC} | \text{per person years})$

$p_{sens,i} = \exp(\gamma_0 + \gamma_1 \cdot BCvol_i) \cdot (1 - 0.34 \cdot abx_i)$

$p_{BC} \sim \text{Beta}(\alpha_{BC}, \beta_{BC})$

$p_{HC} \sim \text{Beta}(\alpha_{HC}, \beta_{HC})$

$N_{true} \sim \text{Poisson}(\lambda | \text{per person years})$

*Non-informative priors unless otherwise specified*