Estimating the global burden of typhoid fever

John A Crump, MB, ChB, DTM&H
Foodborne and Diarrheal Diseases Branch
Centers for Disease Control and Prevention
Overview

• Existing typhoid fever burden estimates

• Methodology for typhoid fever burden
  – Incidence
  – Mortality
  – New estimate

• Limitations

• Future directions
Estimates of global typhoid burden

• 1984
  – Dr Dhiman Barua, WHO
  – PAHO meeting
  – Reviews of Infectious Diseases, 1986

• 1986
  – United States Institute of Medicine
  – Committee on Issues and Priorities for New Vaccine Development

• 1996
  – World Health Report
  – 16 million illnesses
  – 600,000 deaths (3.8% mortality)
Limitations of existing estimate

- Methods not outlined in detail
- Limited source data
- Do not adjust for age distribution
  - Incidence
  - Mortality
- Exclude China
Changes since 1984

- Growth of global population
- Changes in sanitary conditions
- Improved surveillance
- Initiation of population-based typhoid incidence studies
- Publication vaccine studies from new regions
- Improved understanding of age distribution of typhoid fever
- Formalization of methods for assessment of disease burden
Incidence: sources

- Literature search (Medline)
- National typhoid surveillance data
Incidence: results

• Literature search
  – 859 articles
  – 250 articles selected
  – 22 reliable, population-based

• National surveillance data
  – Developed countries
Incidence: data sources

- Reliable national surveillance data
- Limited national surveillance data
- Incidence study
Incidence: global population

• United Nations Sex and Age of the World’s Population
  – 2000 medium fertility variant estimate

• Standard age strata

• United Nations regions
The United Nations classification of major areas and regions

<table>
<thead>
<tr>
<th>Area</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Eastern Africa</td>
</tr>
<tr>
<td></td>
<td>Middle Africa</td>
</tr>
<tr>
<td></td>
<td>Northern Africa</td>
</tr>
<tr>
<td></td>
<td>Southern Africa</td>
</tr>
<tr>
<td></td>
<td>Western Africa</td>
</tr>
<tr>
<td>Asia</td>
<td>Eastern Asia</td>
</tr>
<tr>
<td></td>
<td>South-central Asia</td>
</tr>
<tr>
<td></td>
<td>South-eastern Asia</td>
</tr>
<tr>
<td></td>
<td>Western Asia</td>
</tr>
<tr>
<td>Europe</td>
<td>Eastern Europe</td>
</tr>
<tr>
<td></td>
<td>Northern Europe</td>
</tr>
<tr>
<td></td>
<td>Southern Europe</td>
</tr>
<tr>
<td></td>
<td>Western Europe</td>
</tr>
<tr>
<td>Latin America/Caribbean</td>
<td>Caribbean</td>
</tr>
<tr>
<td></td>
<td>Central America</td>
</tr>
<tr>
<td></td>
<td>South America</td>
</tr>
<tr>
<td>Northern America</td>
<td>Northern America</td>
</tr>
<tr>
<td>Oceania</td>
<td>Australia/New Zealand</td>
</tr>
<tr>
<td></td>
<td>Melanesia</td>
</tr>
<tr>
<td></td>
<td>Micronesia</td>
</tr>
<tr>
<td></td>
<td>Polynesia</td>
</tr>
</tbody>
</table>
Typhoid fever incidence by region

- <10/100,000/yr
- 10-100/100,000/yr
- 100-1,000/100,000/yr
Incidence: extrapolating data

• Extrapolate
  – One age group to others

• Age distribution of typhoid fever
  – Three incidence levels
  – Limited range of population-based typhoid incidence studies with data by age group
Age incidence profiles

- High (>100/100,000/year)
- Low (<10/100,000/year)

Proportion of cases

Age group

0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80+
Age incidence profiles

Proportion of cases

Age group

High (>100/100,000/year)
Medium (10-100/100,000/year)
Low (<10/100,000/year)
Incidence: calculation

- Global population divided into regions and age strata
- All data sources considered for each region
- Most conservative rates selected
- Incidence for each age stratum calculated from age distribution curves
<table>
<thead>
<tr>
<th>Age strata</th>
<th>Population</th>
<th>Source data incidence</th>
<th>Extrapolated incidence</th>
<th>Total cases by age stratum</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>21,995,000</td>
<td></td>
<td>83</td>
<td>18,255</td>
</tr>
<tr>
<td>5-9</td>
<td>20,613,000</td>
<td></td>
<td>48</td>
<td>9,894</td>
</tr>
<tr>
<td>10-14</td>
<td>20,258,000</td>
<td></td>
<td>44</td>
<td>8,914</td>
</tr>
<tr>
<td>15-19</td>
<td>19,285,000</td>
<td></td>
<td>38</td>
<td>7,328</td>
</tr>
<tr>
<td>20-24</td>
<td>16,926,000</td>
<td></td>
<td>23</td>
<td>3,893</td>
</tr>
<tr>
<td>25-29</td>
<td>14,236,000</td>
<td></td>
<td>20</td>
<td>2,847</td>
</tr>
<tr>
<td>30-34</td>
<td>12,562,000</td>
<td></td>
<td>18</td>
<td>2,261</td>
</tr>
<tr>
<td>35-39</td>
<td>10,892,000</td>
<td></td>
<td>15</td>
<td>1,634</td>
</tr>
<tr>
<td>40-44</td>
<td>9,490,000</td>
<td></td>
<td>11</td>
<td>1,044</td>
</tr>
<tr>
<td>45-49</td>
<td>7,823,000</td>
<td></td>
<td>9</td>
<td>704</td>
</tr>
<tr>
<td>50-54</td>
<td>5,807,000</td>
<td></td>
<td>8</td>
<td>465</td>
</tr>
<tr>
<td>55-59</td>
<td>4,255,000</td>
<td></td>
<td>7</td>
<td>298</td>
</tr>
<tr>
<td>60-64</td>
<td>3,746,000</td>
<td></td>
<td>7</td>
<td>262</td>
</tr>
<tr>
<td>65-69</td>
<td>2,990,000</td>
<td></td>
<td>6</td>
<td>179</td>
</tr>
<tr>
<td>70-74</td>
<td>2,160,000</td>
<td></td>
<td>7</td>
<td>151</td>
</tr>
<tr>
<td>75-79</td>
<td>1,211,000</td>
<td></td>
<td>4</td>
<td>48</td>
</tr>
<tr>
<td>80+</td>
<td>788,000</td>
<td></td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>58,210</strong></td>
</tr>
</tbody>
</table>
Incidence: estimate

• 11 million (10,825,486) illnesses/year
Mortality

• Lack population-based data

• Published studies
  – Hospital-based
  – Overestimate

• Infants and children
  – Mild illness
Mortality

• Highest incidence
  – Children <5 years
  – South-central and south-east Asia

• Conservative mortality 1%
Global typhoid burden

- 11 million (10,825,486) illnesses/year
- 110,000 (108,254) deaths/year
- South-central and south-eastern Asia
Limitations

• Few data points to extrapolate from

• Vaccine studies
  – High incidence areas

• Adjustments
  – Blood culture sensitivity
  – Antibiotic therapy
  – Mild illness
Future directions

• Standard method

• Sentinel surveillance tool
  – Incidence
  – Mortality

• Widely applied

• Integrated with disease burden estimates for other febrile illnesses
Acknowledgements

Centers for Disease Control and Prevention, Atlanta
Foodborne and Diarrheal Diseases Branch
  Eric D. Mintz, MD, MPH
  Stephen P. Luby, MD
  Robert V. Tauxe, MD, MPH
  Paul S. Mead, MD, MPH
Biostatistics and Informatics Branch
  R. Michael Hoekstra, PhD

World Health Organization, Geneva
Global Programme on Evidence for Health Policy
  Claudia Stein, MD, MSc
Department of Communicable Disease Surveillance and Response
  Claire-Lise Chaignat, MD
Age incidence of waterborne typhoid outbreaks

Cork, Ireland, 1920
Santa Ana, CA, 1923
Olean City, NY, 1928
Georgia Milltown, 1942
Dade Co, FL, 1973
Shefaram, Israel, 1985

Mahle WT, Levine MM. Pediatr Infect Dis J 1993;12:627-31
Culture methods for typhoid fever

- Bone marrow
- Blood culture
- Rose spot
- Rectal swab

Serologic tests for typhoid fever

- **Widal test**
  - O and H antigens
  - Limited use even when paired sera collected

- **Better rapid diagnostic tests**
  - Antibody and antigen detection
  - Need to be inexpensive, practical, sensitive, specific
  - Countries with endemic typhoid fever
Global burden of *Shigella*

- CDC and WHO
- Global population stratified
  - Age
  - Developed and industrialized
- Published studies of diarrhea incidence for each stratum
- Published studies of etiology of diarrhea for each stratum
- Calculated global burden
*Shigella* method is not appropriate for typhoid

- Syndrome of undifferentiated fever, not diarrhea
- Little data exist on fever incidence
- Even fewer data on the etiology of fever in developing countries
- Another approach is needed
Incidence: data sources

Reliable national surveillance data
Limited national surveillance data
Incidence study
Typhoid fever incidence by region

- <10/100,000/yr
- 10-100/100,000/yr
- 100-1,000/100,000/yr
Rationale for estimating global burden

Evaluation of policies for health improvement requires detailed, reliable assessment of the epidemiologic conditions and the burden of disease

Murray CJL, Lopez AD. Global burden of disease
Incidence: extrapolating data

• Extrapolate
  – One country in a region to others