The global burden of typhoid fever
John A. Crump, 1, 2 Stephen P. Luby, 1 & Eric D. Mintz 3

Objective To use new data to make a revised estimate of the global burden of typhoid fever, an accurate understanding of which is necessary to guide public health decisions for disease control and prevention efforts.

Methods Population-based studies using confirmation by blood culture of typhoid fever cases were sought by computer search of the multilingual scientific literature. Where there were no eligible studies, data were extrapolated from neighbouring countries and regions. Age–incidence curves were used to model rates measured among narrow age cohorts to the general population. One-way sensitivity analysis was performed to explore the sensitivity of the estimate to the assumptions. The burden of paratyphoid fever was derived by a proportional method.

Findings A total of 22 eligible studies were identified. Regions with high incidence of typhoid fever (≥100/100 000 cases/year) include south-central Asia and south-east Asia. Regions of medium incidence (10–100/100 000 cases/year) include the rest of Asia, Africa, Latin America and the Caribbean, and Oceania, except for Australia and New Zealand. Europe, North America, and the rest of the developed world have low incidence of typhoid fever (<10/100 000 cases/year). We estimate that typhoid fever caused 21 650 974 illnesses and 216 510 deaths during 2000 and that paratyphoid fever caused 5 412 744 illnesses.

Conclusion New data and improved understanding of typhoid fever epidemiology enabled us to refine the global typhoid burden estimate, which remains considerable. More detailed incidence studies in selected countries and regions, particularly Africa, are needed to further improve the estimate.

Keywords Typhoid fever/epidemiology/blood; Paratyphoid fever/epidemiology; Salmonella enterica/ isolation and purification; Cohort studies; Population surveillance; Cost of illness; Sensitivity and specificity (source: MeSH, NLM).

Mots clés Fièvre typhoïde/épidémiologie; Paratyphoïde, Fièvre/épidémiologie; Salmonelle entérique/ isolement et purification; Étude cohorte; Surveillance population; Coût maladie; Sensibilité et spécificité (Épidémiologie) (source: MeSH, INSERM).

Palabras clave Fiebre tifoidea/epidemiología; Fiebre paratifoidea/epidemiología; Salmonella enterica/ aislamiento y purificación; Estudios de cohortes; Vigilancia de la población; Costo de la enfermedad; Sensibilidad y especificidad (fuente: DeCS, BIREME).

Introduction
The existing estimate of the global burden of typhoid fever is 16 million illnesses and 600 000 deaths annually (1). This estimate was presented at a meeting of the Pan American Health Organization in 1984 and subsequently published in 1986 (2). Although similar estimates were published around the same time (3) and are widely quoted in the typhoid fever literature, the 1984 estimate is subject to several limitations. For example, the methods were not outlined in detail, so the study cannot be reproduced. Furthermore, limited data sources were available at the time the estimate was made and the initial estimate excluded China. The estimate also does not account for the current understanding of the age distribution of typhoid fever.

A variety of changes have taken place since 1984 to indicate that updating the estimate of the global burden of typhoid fever is now both necessary and feasible. The denominator population has changed considerably with the growth of the global population (4). Programmes such as those to improve the safety of water supplies and sanitary conditions have modified the risk of infection (5). Available typhoid fever incidence data has grown with efforts to improve global disease surveillance (6), the initiation of population-based typhoid fever incidence studies (7, 8), and the publication of vaccine studies from new regions (9). Advances in understanding of the age distribution of typhoid fever allow incidence rates measured among narrow age cohorts to be more accurately extrapolated to the general population (8). The formalization of methods for the assessment of disease burden provides a framework for standardized methods (10).

In light of the above changes and in an effort to provide a more contemporary and precise picture of the disease globally, we developed and applied a method to generate a revised estimate of the disease burden of typhoid fever.

Methods
Typhoid fever incidence data
Studies that potentially contained data on the incidence of typhoid fever were sought by a computer search of the multilingual

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Ref. No. 03-002295
(Submitted: 12 February 03 – Final revised version received: 20 August 03 – Accepted: 02 September 03)
scientific literature published between 1966 and 2001. A set of 8620 articles, obtained using the keywords “typhoid”, “typhoid fever”, “enteric fever”, and “Salmonella Typhi” was linked with a set of 1357515 articles obtained using at least one of the following keywords that dealt with disease burden: “incidence”, “prevalence”, “public health”, “death rate”, “mortality”, “surveillance”, “burden”, “suffering”, “distribution”, “area”, “location”, and “country”, and permutations of the root words “epidemiol-”, “monitor-”, and “geograph-”. The resulting cross-linked set contained 1342 articles, from which 23 articles relating to 22 studies relevant to the stated goal of the search were selected (available on request). Additional (mainly pre-1966) references were sought from citations listed in these 23 articles and from the archives of the authors and experts in the field.

Attempts were made to obtain a full print copy of each article. Studies were selected for inclusion in the global burden estimate if they used blood culture confirmation of cases and used a method that captured cases at all levels of the health-care system (for example, rural clinics, private physicians, hospitals) or by regular household visits. Where more than one eligible study for a country or region was available, the most recent study was selected. If more than one contemporary study was available for a region, the study with the lowest incidence of typhoid fever was selected. This was done in an attempt to account for bias caused by the preferential selection of sites with a high incidence of typhoid fever for studies on typhoid fever vaccine. Although epidemics play a part in typhoid fever epidemiology, studies that were conducted during typhoid fever epidemics were not considered because they did not reflect usual typhoid fever incidence. The volume of source data contributing to the estimate was calculated as person-years of surveillance.

Global population data
The world’s population was classified into age and regional strata according to the designations of the United Nations Department of Economic and Social Affairs, Population Division. Briefly, it was divided into seventeen 5-year age strata from 0–4 years, to >80 years) and 21 regions (eastern Africa, central Africa, northern Africa, southern Africa, western Africa, eastern Asia, south-central Asia, southeast Asia, western Asia, eastern Europe, northern Europe, southern Europe, western Europe, Caribbean, central America, South America, North America, Australia/New Zealand, Melanesia, Micronesia, and Polynesia). Year 2000 medium fertility variant estimates were used (4).

Extrapolating between countries
Because eligible studies of typhoid fever incidence were not available for every country or region, it was necessary to extrapolate typhoid fever incidence from one country to another within a region and sometimes from one region to another. Extrapolations between countries and regions were based on geographical proximity and United Nations socioeconomic indicators (11).

Extrapolating between age groups
A large proportion of eligible studies of typhoid fever incidence were conducted among age cohorts representing a narrow age range (for example, school-aged children). Therefore, to adjust the incidence obtained from such measurements to that of the general population in a region, typhoid fever age-incidence curves were generated for high (>100/100 000 cases/year), medium (10–100/100 000 cases/year), and low (<10/100 000 cases/year) incidence settings. An age-distribution curve for high incidence typhoid fever was generated from the most rigorous population-based study conducted in a high incidence setting (8). The age-distribution curve for low incidence typhoid fever was generated from the United States national typhoid fever surveillance system (Centers for Disease Control and Prevention, unpublished data, 2000) and was validated by comparison with national typhoid fever surveillance system data from other low incidence regions in western Europe and Australasia. The age-distribution curve for medium incidence typhoid fever was modelled by deriving mean age-specific typhoid incidences from the age-distribution curves for high- and low-incidence typhoid fever. The resulting curves are shown in Fig. 1; the curves are corrected to an overall proportion of 1 to allow comparison of relative age-specific rates.

Estimating the global burden of typhoid fever
After incidence rates were extrapolated within and between regions and between age groups, the total number of typhoid fever cases in 2000 was calculated by age stratum for each region. The sum of total cases by region was calculated as the crude global typhoid fever burden. Because eligible studies of typhoid fever incidence usually used a single blood culture collection to confirm cases, it was necessary to adjust the crude estimate for the global typhoid fever burden to account for under-detection of cases resulting from the limited sensitivity of blood culture for diagnosis of typhoid fever. The blood culture adjustment factor was derived from published literature (12–14). The lower reported sensitivity of 50% (13) was selected in an effort to account for the impact of antimicrobial use on blood culture sensitivity. The specificity of blood culture for the diagnosis of typhoid fever was assumed to be 100%.

Case-fatality rate
Studies on the incidence of typhoid fever were further reviewed for population-based case-fatality rate estimates. Hospital-based typhoid fever case series and case-fatality rate data from countries with reliable national typhoid fever surveillance systems that employ blood culture confirmation were reviewed. Expert opinion was sought from persons and groups working in the fields of typhoid fever, enteric diseases, and infectious diseases epidemiology. The resulting case-fatality rate estimates were applied to the global total typhoid fever cases to estimate the total number of annual typhoid fever deaths.

Estimating the global burden of paratyphoid fever
Because there is very little reliable, population-based data on the incidence of paratyphoid fever, we sought to estimate incidence...
to the global burden of typhoid fever. To do this we used the 1997 global survey of Salmonella serotyping practices and results, which was conducted by WHO and the United States Centers for Disease Control and Prevention (CDC), WHO Collaborating Center for Foodborne Disease Surveillance. In this survey, each WHO Member State was sent a questionnaire asking whether or not a given country had public health surveillance for Salmonella infections (typhoid and/or non-typhoid) and whether or not serotyping was performed as part of the surveillance. Member States were then asked to provide information on the total number of Salmonella isolates for 1990 and 1995, and to list, by serotype and number of isolates, the 15 most commonly isolated Salmonella serotypes from people in 1990 and 1995 (15). The ratio derived from the survey was validated by comparison with ratios seen in population-based studies of typhoid fever incidence that also reported data on paratyphoid fever.

Sensitivity analysis
One-way sensitivity analysis was conducted by varying source data inputs from the least conservative (highest) to the most conservative (lowest) figures on typhoid fever incidence, and by adjusting age-incidence curves, by varying the sensitivity of a single blood culture, and by varying the typhoid fever case-fatality rate.

Results
Typhoid fever incidence data
In total, 22 studies of typhoid fever incidence employed blood culture confirmation of cases and used a method that captured cases at all levels of the health-care system or by regular household visits. The 22 studies represent approximately 1.8 million person-years of surveillance and include data from 13 countries. Of the 21 regions, only 6 (29%) contained countries with national typhoid fever surveillance systems that routinely use blood culture confirmation and detection of cases by enhanced passive surveillance (Table 1). The countries wealthy enough to support highly developed national typhoid fever surveillance systems generally experience a low incidence of typhoid fever and contribute little to the global burden of typhoid fever.

Global population data
The United Nations medium fertility variant year 2000 global population estimate is 6 091 349 000. The distribution of the global population by area and region is listed in Table 2.

Extrapolating between countries
The 22 studies contain data for 13 countries representing 9 (43%) of the 21 United Nations regions. An additional four (19%) of the regions include countries with national typhoid fever surveillance systems that routinely use blood culture confirmation and detection of cases by enhanced passive surveillance. Because data points were available for only 13 (62%) of the regions (Table 1), extrapolation between regions was done on the basis of geographical proximity and socioeconomic conditions (11). This method was used to classify regions into high, medium, and low incidence (Fig. 2).

Extrapolating between age groups
For 18 (86%) of the 22 eligible typhoid fever incidence studies, incidence was measured in a narrow age cohort only. For these studies, incidence was calculated for the overall population by extrapolating using the appropriate age-incidence curve developed for high, medium, and low incidence settings using published studies (8) and national surveillance data (Fig. 1). Overall regional typhoid fever rates are listed in Table 2 and are classified into high (>100/100 000 cases/year), medium (10-100/100 000 cases/year), and low (<10/100 000 cases/year) incidence settings.

Estimating the global burden of typhoid fever
After making age and country extrapolations, typhoid fever incidence was compiled by region and area, and then applied to corresponding population estimates to derive a crude total of 10 825 487. To account for the sensitivity of blood culture for diagnosing typhoid fever, we applied an adjustment factor of 2 to our crude global total typhoid case burden. This adjustment produced a global typhoid fever case burden estimate of 21 650 974 (Table 2).

Case-fatality rate
No population-based studies on typhoid fever incidence were found that both captured case-fatality rate data and were large enough to accurately estimate case-fatality rate. A conservative case-fatality rate of 1% was chosen on the basis of conservative estimates from hospital-based typhoid fever studies (16), mortality data from countries with reliable national typhoid fever surveillance systems that employ blood culture confirmation of cases (17), and expert opinion. When applied to the global typhoid fever case burden estimate of 21 650 974, the case-fatality rate yields 216 510 deaths annually.

Estimating the global burden of paratyphoid fever
The 1997 global survey of Salmonella serotyping practices and results achieved country response rates by WHO region ranging from 34% to 70%. Worldwide, 3572 Salmonella Typhi isolates and 888 Paratyphi isolates were reported (15). This corresponds to 0.25 paratyphoid fever illnesses for every typhoid fever illness. The ratio was validated by review of the 8 (36%) of 22 population-based typhoid fever incidence studies that also report paratyphoid fever data (9, 18–24). The number of paratyphoid fever illnesses ranged from 0.11 to 0.35 for every typhoid fever illness. By applying the proportion 0.25 to the global typhoid fever estimate, we derived an estimate of 5 412 744 paratyphoid fever cases.

Sensitivity analysis
The results of the one-way sensitivity analysis are summarized in Table 3.

Discussion
Changes in the global epidemiology of typhoid fever
We estimate that typhoid fever caused 21 650 974 illnesses and 216 510 deaths during 2000 and that paratyphoid fever caused 5 412 744 illnesses. The previous estimates of 16 million illnesses and 600 000 deaths were made 16 years ago. The growth of the global population by approximately 20%, from 4.8 billion to 6.1 billion, contributes to the larger contemporary global typhoid fever burden. However, methodological differences may play a substantial role that is difficult to assess. For example, the differences in the methodology used to obtain the estimates confound efforts to draw inferences about the apparent increase of the global typhoid fever burden. In fact, there is some evidence that
typhoid fever incidence rates have declined over the past several decades. For Chile (5, 18, 25, 26), Egypt (27, 28), India (14, 29, 30), the former Soviet Union (20–22, 31), and Viet Nam (7, 32), multiple data points available over time from each country indicate a secular trend towards declining typhoid fever incidence for all countries except Viet Nam; this trend is consistent with improvements in sanitary conditions and reductions in diarrhoeal disease morbidity and mortality reported from some countries and regions (5, 33). Accurately tracking changes of global typhoid burden, therefore, will require the adoption of a standard method for generating estimates.

**Limitations of the revised global typhoid fever burden estimate**

To further refine the estimate of the global burden of typhoid fever, improvements are needed in both the quantity and quality of source data. Only 22 studies were eligible to contribute incidence data to our estimate. The 1.8 million person-years of surveillance available to make this estimate represent <0.001% of the approximately 250 billion person-years that have occurred since 1950. Whole regions lacked either eligible population-based studies of typhoid fever incidence or surveillance systems that might measure typhoid fever incidence at the population level. The lack of data is most notable for eastern, central, and western Africa. Population-based studies from Egypt in the northern Africa region are in the middle incidence range, but a single study from South Africa places the southern Africa region in the high incidence range. In contrast to hospital-based studies conducted in south-central and south-east Asia, where *Salmonella Typhi* is a leading cause of bloodstream infection (34), in similar studies conducted in sub-Saharan Africa the organism has not predominated (35–37). This may suggest that the typhoid situation in the rest of the African continent might reflect more closely that seen in Egypt than that seen in

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**Table 1. Typhoid surveillance and incidence studies by geographical location**

<table>
<thead>
<tr>
<th>United Nations classification of Area/Region</th>
<th>Regional typhoid surveillance</th>
<th>Typhoid incidence studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Country Number Year(s)</td>
<td>Reference</td>
</tr>
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<td></td>
<td></td>
</tr>
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<td>–</td>
</tr>
<tr>
<td>Middle Africa</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>Northern Africa</td>
<td>No</td>
<td>Egypt</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>No</td>
<td>South Africa</td>
</tr>
<tr>
<td>Western Africa</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Asia</td>
<td>No</td>
<td>China</td>
</tr>
<tr>
<td>South-central Asia</td>
<td>No</td>
<td>India</td>
</tr>
<tr>
<td>South-eastern Asia</td>
<td>No</td>
<td>Nepal</td>
</tr>
<tr>
<td>Southern Asia</td>
<td>No</td>
<td>Indonesia</td>
</tr>
<tr>
<td>Western Asia</td>
<td>No</td>
<td>Viet Nam</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>No</td>
<td>Poland</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td>Western Europe</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td><strong>Latin America/Caribbean</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>Central America</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>South America</td>
<td>Yes</td>
<td>Guyana</td>
</tr>
<tr>
<td><strong>Northern America</strong></td>
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<td></td>
</tr>
<tr>
<td>Northern America</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td><strong>Oceania</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia/New Zealand</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td>Melanesia</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>Micronesia</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>Polynesia</td>
<td>No</td>
<td>Tonga</td>
</tr>
</tbody>
</table>

\* Region contains at least one country with national typhoid fever surveillance systems that employ blood culture confirmation of cases. 
\* Most recent study contributes to country or region incidence estimate. 
\* No eligible typhoid incidence studies.
South Africa. However, this uncertainty remains a key concern in terms of the reliability of our estimate. Population-based studies of typhoid fever incidence are needed elsewhere in Africa to clarify the typhoid fever situation for the continent. Such epidemiological data are needed to guide decision-making by public health officials for disease prevention and control programmes.

We also faced issues of data quality. Several of the studies that contribute to the new estimate of global typhoid fever burden were conducted during the 1950s, 1960s, and 1970s (20–23, 27–31, 38, 39). Since these studies were conducted, changes in the determinants of typhoid fever incidence, such as improvements in water supply and sanitary conditions (5), raise questions about the validity of these historical data for the year 2000 estimate. We elected to consider all eligible studies because of the limited number of data points available, but where multiple studies were reported for the same country, we chose the most recent estimate to limit the effect of secular changes in typhoid fever incidence.

Reliance on typhoid vaccine studies to contribute data to our global typhoid burden estimate also raises concerns over data quality. To achieve favourable sample sizes, typhoid vaccine studies are preferentially conducted at sites that are known to experience high incidence of typhoid fever, introducing a bias towards overestimation of incidence in the region where the study was conducted. We attempted to account for this bias by selecting the most conservative regional incidence rates for our calculations.

In one-way sensitivity analysis, the sensitivity of the diagnostic test has the greatest impact on the variability of the estimate of global typhoid fever burden. The authors of the 1984 estimate do not report making an adjustment for diagnostic test sensitivity. This adjustment probably accounts for the largest

### Table 2. Crude typhoid fever incidence rates by region, 2000

<table>
<thead>
<tr>
<th>Area/Region</th>
<th>Typhoid cases</th>
<th>Population</th>
<th>Crude Incidence*</th>
<th>Incidence classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Africa</td>
<td>98 560</td>
<td>255 500 000</td>
<td>39</td>
<td>Medium</td>
</tr>
<tr>
<td>Middle Africa</td>
<td>36 857</td>
<td>95 385 000</td>
<td>39</td>
<td>Medium</td>
</tr>
<tr>
<td>Northern Africa</td>
<td>58 210</td>
<td>175 037 000</td>
<td>33</td>
<td>Medium</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>123 473</td>
<td>52 887 000</td>
<td>233</td>
<td>High</td>
</tr>
<tr>
<td>Western Africa</td>
<td>91 737</td>
<td>241 102 000</td>
<td>38</td>
<td>Medium</td>
</tr>
<tr>
<td>Area total</td>
<td>408 837</td>
<td>819 911 000</td>
<td>50</td>
<td>Medium</td>
</tr>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Eastern Asia</td>
<td>182 927</td>
<td>1 483 111 000</td>
<td>12</td>
<td>Medium</td>
</tr>
<tr>
<td>South-central Asia</td>
<td>9 299 064</td>
<td>1 495 977 000</td>
<td>622</td>
<td>High</td>
</tr>
<tr>
<td>South-eastern Asia</td>
<td>575 407</td>
<td>521 983 000</td>
<td>110</td>
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</tr>
<tr>
<td>Western Asia</td>
<td>61 481</td>
<td>187 463 000</td>
<td>33</td>
<td>Medium</td>
</tr>
<tr>
<td>Area total</td>
<td>10 118 879</td>
<td>3 688 534 000</td>
<td>274</td>
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</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
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<tr>
<td>Eastern Europe</td>
<td>15 940</td>
<td>306 654 000</td>
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</tr>
<tr>
<td>Northern Europe</td>
<td>143</td>
<td>93 736 000</td>
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<tr>
<td>Southern Europe</td>
<td>2785</td>
<td>144 861 000</td>
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<tr>
<td>Western Europe</td>
<td>276</td>
<td>184 077 000</td>
<td>&lt;1</td>
<td>Low</td>
</tr>
<tr>
<td>Area total</td>
<td>19 144</td>
<td>729 328 000</td>
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<td><strong>Latin America/Caribbean</strong></td>
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<td>19 889</td>
<td>37 757 000</td>
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<td>Central America</td>
<td>79 164</td>
<td>135 497 000</td>
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<td>Medium</td>
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<tr>
<td>South America</td>
<td>174 465</td>
<td>341 434 000</td>
<td>51</td>
<td>Medium</td>
</tr>
<tr>
<td>Area total</td>
<td>273 518</td>
<td>514 688 000</td>
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<tr>
<td><strong>Northern America</strong></td>
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<tr>
<td>Northern America</td>
<td>453</td>
<td>308 636 000</td>
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<tr>
<td>Area total</td>
<td>453</td>
<td>308 636 000</td>
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<td>Low</td>
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<tr>
<td>Australia/New Zealand</td>
<td>62</td>
<td>22 598 000</td>
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<tr>
<td>Melanesia</td>
<td>3897</td>
<td>6 489 000</td>
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<td>Micronesia</td>
<td>326</td>
<td>539 000</td>
<td>60</td>
<td>Medium</td>
</tr>
<tr>
<td>Polynesia</td>
<td>371</td>
<td>626 000</td>
<td>59</td>
<td>Medium</td>
</tr>
<tr>
<td>Area total</td>
<td>4656</td>
<td>30 252 000</td>
<td>15</td>
<td>Medium</td>
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<tr>
<td><strong>Global</strong></td>
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<tr>
<td>Crude total</td>
<td>10 825 487</td>
<td>6 091 349 000</td>
<td>178</td>
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</tr>
<tr>
<td>Adjusted total</td>
<td>21 650 974</td>
<td>6 091 349 000</td>
<td>355</td>
<td></td>
</tr>
</tbody>
</table>

* Per 100 000 persons per year.

b Region incidence estimate derived by extrapolation.
Research

John A. Crump et al.  Global burden of typhoid fever

Table 3. Sensitivity analysis of typhoid fever incidence and case-fatality rate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data input</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence data selection</td>
<td>Most conservative (lowest)</td>
<td>10 825 487</td>
</tr>
<tr>
<td></td>
<td>Least conservative (highest)</td>
<td>16 371 420</td>
</tr>
<tr>
<td>Age incidence adjustment</td>
<td>Adjusted (high, medium, low)</td>
<td>10 825 487</td>
</tr>
<tr>
<td></td>
<td>Adjusted (high, low)</td>
<td>11 110 627</td>
</tr>
<tr>
<td></td>
<td>Not adjusted</td>
<td>13 433 150</td>
</tr>
<tr>
<td>Blood culture sensitivity (%)</td>
<td>100</td>
<td>10 825 487</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>14 433 983</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>21 650 974</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>43 301 948</td>
</tr>
<tr>
<td>Case-fatality rate (%)</td>
<td>5</td>
<td>1 082 549</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>216 510</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>21 651</td>
</tr>
</tbody>
</table>

methodological and quantitative difference between our estimate and the old one. Blood culture sensitivity is determined by the combined effects of the volume of blood collected, the timing of collection, and antimicrobial use (12–14). We could not account for these factors for the studies that contributed to our global typhoid burden estimate because they were not routinely reported. Instead, we chose to apply a conservative sensitivity of 50% to all studies. The impact of the global epidemic of antimicrobial use (40) on the detection of typhoid fever cases by blood culture is not well characterized but could have considerable impact on culture-based approaches to case confirmation. The estimated number of deaths due to typhoid fever is important for decision-makers in public health policy, yet case-fatality rate data from population-based studies of typhoid fever are lacking. The reliability of the case-fatality rate of 1% selected for this estimate should be evaluated in population-based studies to facilitate a more accurate estimation of the number of deaths due to typhoid fever.

The challenge of global surveillance for febrile illnesses

The etiologies and incidence of febrile illnesses such as typhoid fever have proved difficult to determine. The implementation of population-based typhoid fever and febrile illness surveillance studies in selected regions could add considerably to the accuracy of the global typhoid fever burden estimate. Recently described rapid methods for estimating typhoid fever incidence may make this feasible (41). An accurate picture of the global epidemiology of typhoid fever will be necessary to prioritize the use of scarce health-care resources for disease control and to efficiently target the use of vaccines (32) and other preventive measures for typhoid fever.

Acknowledgements

We acknowledge the invaluable advice and assistance of Claire-Lise Chaignat, Department of Communicable Disease Surveillance and Response, and Claudia Stein, Evidence for Information and Policy, WHO, Geneva, Switzerland. We also acknowledge Robert V. Tauxe, Foodborne and Diarrhoeal Diseases Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA for his helpful comments and suggestions on the manuscript.

Conflicts of interest: none declared.
Résumé
La charge mondiale de typhoïde
Objectif Utiliser de nouvelles données pour procéder à une estimation révisée de la charge mondiale de typhoïde, qu’il est nécessaire de connaître avec précision pour orienter les décisions de santé publique en matière de prévention et de lutte.
Méthodes Les études en population avec confirmation des cas de typhoïde par hémoculture ont été identifiées par une recherche documentaire informatisée de la littérature scientifique multilingue. Lorsqu’aucune étude ne répondait aux critères de recherche, les données étaient extrapolées à partir des pays et régions voisins. Des courbes d’incidence en fonction de l’âge ont été utilisées pour traduire dans la population générale les taux mesurés sur des cohortes correspondant à des tranches d’âge étroites. Une analyse de sensibilité unilatérale a été effectuée pour déterminer la sensibilité de l’estimation aux hypothèses de départ. La charge de paratyphoïde a été dérivée de celle de la typhoïde selon une méthode proportionnelle.
Résultats Au total, 22 études répondant aux critères de recherche ont été identifiées. Les régions de forte incidence de la typhoïde (>100 cas pour 100 000 habitants par an) sont l’Asie du Sud et du centre et l’Asie du Sud-Est. Les régions d’incidence moyenne (10-100 cas pour 100 000 habitants par an) sont le reste de l’Asie, l’Afrique, l’Amérique latine, les Caraïbes et l’Océanie à l’exception de l’Australie et de la Nouvelle-Zélande. En Europe, en Amérique du Nord et dans le reste du monde développé, l’incidence de la typhoïde est faible (<10 cas pour 100 000 habitants par an). D’après nos estimations, la typhoïde a provoqué 21 650 974 cas de maladie et 216 510 décès en 2000 et la paratyphoïde 5 412 744 cas de maladie.
Conclusion De nouvelles données, jointes à une amélioration de la connaissance de l’épidémiologie de la typhoïde, nous ont permis d’affiner l’estimation de la charge mondiale de typhoïde, laquelle reste considérable. Des études plus détaillées de l’incidence de la maladie dans certains pays et régions, notamment en Afrique, sont nécessaires pour obtenir une estimation encore plus exacte.

Resumen
La carga mundial de fiebre tifoidea
Objetivo Usar nuevos datos para hacer una estimación revisada de la carga mundial de fiebre tifoidea, a fin de determinar exactamente qué debe hacerse para orientar las decisiones de salud pública encaminadas a controlar y prevenir la enfermedad.
Métodos Se hizo una búsqueda computadorizada en la literatura científica multilingüe para encontrar estudios poblacionales en los que se confirmara el diagnóstico de fiebre tifoidea mediante hemocultivo. En los casos en que ningún estudio reunía las condiciones requeridas, los datos se extrapolaron a partir de los países y regiones vecinas. Se usaron curvas de edad-incidencia para, a partir de las mediciones realizadas en cohortes estrechas de edad, modelizar las tasas correspondientes a la población general. Se hizo un análisis de sensibilidad unidireccional para determinar la sensibilidad del cálculo a los supuestos utilizados. La carga de fiebre paratifoidea se calculó mediante un método proporcional.
Resultados Se hallaron en total 22 estudios que reunían los requisitos establecidos. Las regiones con alta incidencia de fiebre tifoidea (más de 100/100 000 casos/año) son Asia centromeridional y Asia sudoriental. Las regiones de incidencia media (10–100/100 000 casos/año) comprenden el resto de Asia, África, América Latina y el Caribe y Oceanía, salvo Australia y Nueva Zelanda. Europa, América del Norte y el resto del mundo desarrollado tienen una baja incidencia de fiebre tifoidea (menos de 10/100 000 casos/año). Calculamos que la fiebre tifoidea causó 21 650 974 casos y 216 510 defunciones durante el año 2000, y la fiebre paratifoidea 5 412 744 casos.
Conclusion Los nuevos datos y el mejor conocimiento de la epidemiología de la fiebre tifoidea nos permitieron calcular con mayor precisión la carga mundial de esa enfermedad, que sigue siendo considerable. Es necesario realizar estudios de incidencia más detallados en determinados países y regiones, sobre todo en África, para obtener estimaciones aún más precisas.
References