FOOD SAFETY

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The Global Burden of Nontyphoidal Salmonella Gastroenteritis

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To estimate the global burden of nontyphoidal Salmonella gastroenteritis, we synthesized existing data from laboratory-based surveillance and special studies, with a hierarchical preference to (1) prospective population-based studies, (2) "multiplier studies," (3) disease notifications, (4) returning traveler data, and (5) extrapolation. We applied incidence estimates to population projections for the 21 Global Burden of Disease regions to calculate regional numbers of cases, which were summed to provide a global number of cases. Uncertainty calculations were performed using Monte Carlo simulation. We estimated that 93.8 million cases (5th to 95th percentile, 61.8–131.6 million) of gastroenteritis due to Salmonella species occur globally each year, with 155,000 deaths (5th to 95th percentile, 39,000–303,000 deaths). Of these, we estimated 80.3 million cases were foodborne. Salmonella infection represents a considerable burden in both developing and developed countries. Efforts to reduce transmission of salmonellae by food and other routes must be implemented on a global scale.

Salmonella species are a leading bacterial cause of acute gastroenteritis. Although the global human health impact of Salmonella infections has not been estimated, gastroenteritis is a major cause of morbidity and mortality, worldwide, both in children <5 years old [1, 2] and in the general population [3]. In a study from four developed countries, Scallan et al [3] estimated that the incidence of diarrheal disease ranged from 0.44 to 0.99 episodes per person-year; conservatively, such an incidence would translate into an order of 2.8 billion cases of diarrheal illness each year worldwide. Accurate estimates of the burden of diarrheal diseases caused by Salmonella species and other foodborne pathogens are needed to effectively set public health goals and allocate resources to reduce disease burden. Recently, the World Health Organization (WHO) established the Foodborne Disease Burden Epidemiology Reference Group to provide global foodborne disease estimates [4].

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1058-4838/2010/5006-0014\$15.00 DOI: 10.1086/650733 Although laboratory-based surveillance provides useful trend information, it underestimates disease burden [5–12]. To be ascertained in a laboratory-based surveillance system, an ill person must seek medical care, submit a specimen (usually stool), the laboratory must test for the pathogen and report a positive finding, and the laboratory-confirmed infection must be ascertained by public health authorities. Therefore, cases in laboratory-based surveillance represent a fraction of the total community cases. Several countries have conducted either prospective population-based studies, or cross-sectional surveys to determine the extent of the underascertainment within laboratory-based surveillance [6, 11, 13–16]. However, global estimates are difficult to calculate because many countries, particularly developing countries, have insufficient surveillance data.

In 2000, Crump et al [17] estimated the global burden of typhoid fever by summarizing available data and extrapolating to countries and regions where data were lacking. The WHO has recommended a similar approach for estimating the global burden of foodborne disease [18]. Thus, we synthesized existing data from the literature, special studies and laboratory-based surveillance to estimate the global burden of nontyphoidal *Salmonella* gastroenteritis.

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METHODS

Regional incidence. We classified the world population into 21 regions, as designated by the 2005 Global Burden of Disease, Injuries and Risk Factors Study (GBD; Table 1) [19]. We used the United Nations Department of Economic and Social Affairs, Population Division year 2005 median fertility variant regional population estimates [20], and included the regional populations as point estimates (ie, without uncertainty) in the stochastic model.

We used a hierarchy of data sources to estimate the incidence of Salmonella gastroenteritis for each GBD region (Table 1). The ideal source was a prospective population-based study, in which a cohort of individuals was followed up to determine illness and collect specimens, and which estimated the incidence of Salmonella infection in the population. If such a study existed from a country within a GBD region, that incidence estimate was extrapolated to the entire region. If these data were not available, we used data from "multiplier studies" conducted in the region. Multiplier studies calculate the incidence of Salmonella by multiplying the incidence of laboratory-confirmed infections, ascertained from laboratory-based surveillance, by a Salmonella-specific multiplier which adjusts for under-ascertainment. If a multiplier study existed from a country within a GBD region, that incidence estimate was extrapolated to the entire region.

If neither a prospective population-based study nor a multiplier study existed in a GBD region, we used disease notification data from countries in the region, averaged among the countries within the region. To account for underascertainment, notification data were multiplied by a Salmonella-specific multiplier estimate obtained from the literature. If disease notification data were not available, we used an estimate of the incidence of Salmonella in foreign travelers returning from one or more countries in the region, with two adjustments. Because the incidence in foreign travelers represents only the fraction of travelers who seek care and submit stool once back in their home country, we adjusted for under-ascertainment using a Salmonella-specific multiplier estimate from the literature. Because the susceptibility of foreign travelers to infection is likely greater than the susceptibility of the resident population, potentially due to lack of prior exposure to regional serotypes or to differing exposure risks, we created a "correction factor" by comparing incidence estimates from returning travelers to those from the resident population, by region, where data allowed. In GBD regions where none of the above data sources were available, data were extrapolated from the geographically closest GBD region with either prospective population-based and multiplier study data, because such data were considered superior to the other data sources.

Disease notification data were obtained from institutional Web sites. Estimates of the incidence and underascertainment of *Salmonella* were identified from the published scientific literature for the period 1966–2007 using the keyword "*Salmonella*" and any one of the following keywords: "incidence," "prevalence," "public health," "mortality," "population surveillance," "surveillance," "burden," "distribution," "area," "location," "developing countries," "developed countries," "country," "epidemiology," "geography," and permutations of the word "monitor-." Additional articles were obtained through consultation with experts and cross-referencing citations from articles identified above. We also consulted members of WHO Global Salm-Surv, an international network of laboratories and individuals involved in surveillance, isolation, identification and antimicrobial resistance testing of *Salmonella* to identify unpublished studies [21].

Global incidence. For each GBD region, the estimated population was multiplied by the estimated incidence of Salmonella gastroenteritis. The resulting annual number of cases was summed across all regions to yield the annual number of cases of Salmonella gastroenteritis worldwide. This calculation was performed repeatedly using Monte Carlo simulation to account for uncertainties in the estimated incidences. Each incidence estimate was modeled as a PERT distribution [22]. The PERT distribution is a smooth curve, which places emphasis on values nearer to the most likely value and is often used to model expert opinion data. The incidence estimate reported in the literature was used as the most likely value in the corresponding PERT distribution. For the majority of incidence estimates, confidence intervals were reported in the literature, and were thus used as the minimum and maximum values in the PERT distribution. Where there was >1 confidence interval per region, the lowest and highest values reported were used as the minimum and maximum values. Because disease notification data did not have confidence intervals, in regions where we used such data, we used the lowest and highest country-specific incidences within the region as the minimum and maximum values.

A distribution of estimates of the annual number of cases of gastroenteritis due to *Salmonella* worldwide was generated in @RISK, version 4.5.2 (Palisade Corporation), with 10,000 iterations and Latin Hypercube sampling. To determine the annual number of deaths, we used two published case fatality rates to parameterize a uniform distribution: 0.0003% [15] and 0.003% [23]. A sensitivity analysis was conducted to determine which parameters had the most influence on the estimated annual number of cases, by ranking correlation coefficients between each of the input parameters and the annual number of cases. Scenarios were run to explore the impact of the most influential model parameter, select model assumptions, and the potential impact of regions whose resulting incidence appeared markedly lower than the geographically surrounding regions.

To estimate the proportion of estimated cases of Salmonella

| Table 1 | . Tł | ie Globa | l Burden | of | Salmonella | Gastroente | eritis, | , Circa | 2006, | Shown | by 200 | 5 Global | Burden | of | Disease, | Injuries | and | Risk |
|---------|------|----------|----------|----|------------|------------|---------|---------|--------|----------|---------|----------|--------|----|----------|----------|-----|------|
| Factors | Stud | y (GBD) | Region a | nd | Grouped by | the 6 Wor | ld He | ealth O | rganiz | ation (\ | NHO) Si | ubregion | IS | | | | | |

| | | Existin | ng sources of incidence data | Estimated global burden, mean value | | | |
|------------------------------|---------------|----------------------|------------------------------|-------------------------------------|------------|--------------------------|--------------|
| | 2006 | Inciden | ice per 100,000 person-years | No. of | No. of | Incidence per 100.000 | |
| GBD region | Population | Type of data | Most likely value (range) | Reference(s) | cases | deaths | person-years |
| EMRO | | | | | | | |
| North Africa/Middle East | 410,800,000 | Multiplier | 124 (58–267) | [27] | 563,000 | 900 | 140 |
| Total | 410,800,000 | | | | 563,000 | 900 | 140 |
| AFRO | | | | | | | |
| Sub-Saharan Africa, Central | 84,412,000 | Returning traveler | 93 (43–205) | [30] | 85,000 | 100 | 100 |
| Sub-Saharan Africa, East | 314,208,000 | Returning traveler | 471 (294–755) | [30] | 1,488,000 | 2500 | 470 |
| Sub-Saharan Africa, Southern | 68,021,000 | Returning traveler | 69 (48–98) | [30] | 46,000 | <100 | 70 |
| Sub-Saharan Africa, West | 300,598,000 | Returning traveler | 279 (180–432) | [30] | 839,000 | 1400 | 280 |
| Total | 767,239,000 | | | | 2,458,000 | 4100 | 320 |
| WPRO | | | | | | | |
| Asia Pacific, High Income | 180,468,000 | Multiplier | 32 (15–69) | [13] | 64,000 | 100 | 40 |
| Asia, Central | 76,815,000 | Returning traveler | 39 (28–53) | [30] | 29,000 | <100 | 40 |
| Asia, East | 1,344,125,000 | Multiplier | 3600 (1688–7763) | a | 53,429,000 | 88,200 | 3980 |
| Australasia | 24,407,000 | Multiplier | 257 (79–480) | [11] | 66,000 | 100 | 270 |
| Oceania | 9,002,000 | Extrapolation | 257 (79–480) | [11] | 24,000 | <100 | 270 |
| Total | 1,634,817,000 | | | | 53,610,000 | 88,500 | 3280 |
| SEARO | | | | | | | |
| Asia, South | 1,498,563,000 | Returning traveler | 474 (330–681) | [30] | 7,034,000 | 11,600 | 470 |
| Asia Southeast | 573,711,000 | Extrapolation | 3,600 (1688–7763) | ^a | 22,805,000 | 37,600 | 3980 |
| Total | 2,072,274,000 | | | | 29,839,000 | 49,200 | 1440 |
| EURO | | | | | | | |
| Europe, Central | 118,750,000 | Disease notification | 160 (39–322) | [28] | 2,835,000 | 4700 | 2390 |
| Europe, Eastern | 211,614,000 | Disease notification | 40 (23–69) | [28] | 1,265,000 | 2100 | 600 |
| Europe, Western | 407,707,000 | Population | 220 (110–430) | [6] | 965,000 | 1600 | 240 |
| Total | 738,071,000 | | | | 5,065,000 | 8400 | 690 |
| AMRO | | | | | | | |
| North America, High Income | 332,117,000 | Multiplier | 495 (250-870) | [14, 15] | 1,716,000 | 2800 | 520 |
| Caribbean | 40,525,000 | Returning traveler | 107 (86–134) | [30] | 42,000 | <100 | 110 |
| Latin America, Andean | 49,517,000 | Returning traveler | 80 (60–106) | [30] | 39,000 | <100 | 80 |
| Latin America, Central | 215,172,000 | Returning traveler | 108 (77–150) | [30] | 229,000 | 400 | 110 |
| Latin America, Southern | 58,371,000 | Returning traveler | 80 (60–106) | [30] | 46,000 | <100 | 80 |
| Latin America, Tropical | 192,735,000 | Returning traveler | 80 (60-106) | [30] | 151,000 | 300 | 80 |
| Total | 888,437,000 | | | | 2,222,000 | 3,700 | 250 |
| Global total ^b | 6,511,638,000 | | | | 93,757,000 | 155,000 | 1140 |

NOTE. GBD regions crudely grouped into WHO sub-regions, based on majority overlap of countries between regions. Disease notification, disease notification data plus underascertainment multiplier; extrapolation, extrapolation from regions in close geographic proximity; multiplier, multiplier study (laboratory-based incidence adjusted for underascertainment); population, prospective population-based incidence study; returning traveler; returning traveler data, plus underascertainment multiplier and susceptible traveler correction factor.

^a Ran Lu, Branch of Enteric Infection Disease Control and Prevention, Chinese Center for Disease Control and Prevention, unpublished data

^b Numbers may not add due to rounding.

gastroenteritis that were foodborne, we used the average "proportion foodborne" from 6 published estimates of the foodborne proportion [5, 8, 11, 24–26]. The proportion of foodborne cases was multiplied by the annual number of cases to estimate the annual number of foodborne gastroenteritis cases due to *Salmonella* species. Because of the uncertainty associated with such source attribution values, we also calculated estimates using the lowest (55%) [24] and highest (95%) [5, 26] proportions in the published literature.

RESULTS

Availability of data. We found 14,806 articles with the keyword "Salmonella," which, when linked with the secondary keywords, reduced to 1,619 articles, of which 724 were related to humans. From these we identified one prospective, population-based study, from England in the 1990s, which estimated the community incidence of Salmonella infection [6]. This incidence was extrapolated to the "Europe, Western" region.



Figure 1. Distribution of plausible values for the estimated annual number of cases of *Salmonella* gastroenteritis worldwide, circa 2006, showing 5th and 95th percentiles.

Six countries in 5 GBD regions had "multiplier studies," which used laboratory-confirmed incidences adjusted for under-ascertainment. The estimated incidence of *Salmonella* from Australia [11] was extrapolated to the "Australasia" region, Jordan [27] to the "North Africa/Middle East" region, Japan [13] to the "Asia Pacific, High Income" region, and China (Ran Lu, Branch of Enteric Infection Disease Control and Prevention, Chinese Center for Disease Control and Prevention, unpublished data) to the "Asia, East" region. The estimated incidence from the United States [15] and Canada [14] were averaged, and extrapolated to the "North America, High Income" region.

Two GBD regions had available disease notification data for one or more country within the region. Data from the European Food Safety Authority [28] for 2005 were used, with the exception of Slovenia, for which 2004 data were used. Disease notification data from countries within regions were averaged, and multiplied by a *Salmonella*-specific multiplier from the Netherlands [29], and the resulting incidence estimate applied to the respective "Europe, Central" and "Europe, Eastern" regions.

Eleven GBD regions had information available on the incidence of *Salmonella* gastroenteritis in returning Swedish travelers [30]. These incidences were multiplied by the *Salmonella*specific multiplier from the Netherlands [29], and then by the correction factor to account for differences in the susceptibility between traveling Swedes and the resident population in a given region. The correction factor was calculated by taking advantage of the fact that 2 incidence estimates were available for 1 region ("North Africa/Middle East"): one from a multiplier study from Jordan [27], and one from Swedish travelers [30], corrected for under-ascertainment. The ratio of these 2 estimates (0.0678) was used to correct for the hypothesized increased susceptibility of traveling Swedes versus regional residents.

For the final 2 GBD regions, it was necessary to extrapolate

from neighboring regions. The calculated incidence from the Australia multiplier study [11] was extrapolated to the "Oceania" region, and the calculated incidence from the China multiplier study (Ran Lu, Branch of Enteric Infection Disease Control and Prevention, Chinese Center for Disease Control and Prevention; unpublished data) was extrapolated to the "Asia, Southeast" region.

The distribution of estimates for the annual number of cases of Salmonella gastroenteritis worldwide is shown in Figure 1. Overall, we estimate that 93,757,000 cases of gastroenteritis due to nontyphoidal Salmonella occur annually (Table 1), ranging from 61,768,000 (5th percentile) to 131,634,000 (95th percentile). The estimated annual number of deaths and the incidence per 100,000 persons are shown by GBD region, WHO subregion, and overall (Table 1). We estimate that nontyphoidal Salmonella causes 155,000 deaths (5th to 95th percentile, 39,000–303,000 deaths) each year, worldwide. By applying the average of published values of the proportion of Salmonella infections that is foodborne (86%), we estimated that, of the 93,757,000 cases, ~80,318,000 are foodborne, and that the number of foodborne cases is likely between 51,566,000 (assuming 55% are foodborne) and 89,069,000 (assuming 95% are foodborne).

The input parameter with the most influence on the estimated annual number of cases was the incidence estimate for the "Asia, East" region (Table 2). To illustrate its impact, we ran the 4 scenarios: 1 with a 10-fold decreased incidence, 1 with a 2-fold decreased incidence, and 2 using data from other sources considered lower in the hierarchy (returning traveler data and extrapolation from Japan). We also assessed the impact of our assumption that travelers to a region are ~15 times more susceptible than regional residents, by decreasing our suscep-

 Table 2.
 Correlation between the Input Parameters and the

 Distribution of the Annual Number of Cases of Salmonella Gastroenteritis Worldwide, Showing the Top 5 Variables

| R | ank | Proportion | Correlation coefficient |
|---|-----|---|-------------------------|
| 1 | | Incidence estimate for "Asia, East" region | 0.917 |
| 2 | | Incidence estimate for "Asia, Southeast region ^a | 0.391 |
| 3 | | | |
| | А | Incidence estimate for "Asia, South" region | 0.059 |
| | В | Incidence estimate from "Europe, Central" region | 0.055 |
| 4 | | Incidence estimate for "North America, High In- come" region | 0.024 |
| 5 | | | |
| | A | Incidence estimate for "Sub-Saharan Africa, East" region | 0.016 |
| | В | Incidence estimate from "Europe, East" region | 0.016 |
| | С | Incidence estimate from "Europe, West" region | 0.015 |

^a Incidence for "Asia, Southeast" estimated by extrapolating from "Asia, East."

tible traveler correction factor 2-fold (ie, travelers \sim 7 times more susceptible) and 7-fold (ie, travelers \sim 2 times more susceptible). Because the incidence estimate for the "Asia, South" region was markedly lower than its geographic counterparts, we assessed its impact using both a 2-fold and a 10-fold increase (Table 3).

DISCUSSION

The global human health impact of nontyphoidal *Salmonella* is high, with an estimated 93.8 million illnesses, of which an estimated 80.3 million are foodborne, and 155,000 deaths each year. The estimated total number of cases is plausible given previously published diarrheal disease estimates [3], which suggest that the total annual number of diarrheal illnesses may be on the order of 2.8 billion worldwide. If so, *Salmonella* infections represent ~3% of these illnesses. Worldwide, mass production and distribution of food disseminates pathogens rapidly; this, combined with the challenge of multidrug resistance related to antibiotic use, creates new challenges for controlling and preventing *Salmonella* infection. Improving food safety and reducing the burden of *Salmonella* infection means promoting and implementing effective food safety interventions on a global scale.

We estimated the global burden of *Salmonella* gastroenteritis by using the best available data in each of the 21 GBD regions. Our hierarchical approach allowed us to use published data, as well as information from special studies and surveillance to inform estimates of the disease burden. These methods may be useful for other foodborne pathogens, particularly since data on other pathogens, such as *Campylobacter, Shigella*, and *Yersinia* species, will likely have the same data availability issues as encountered with *Salmonella* species. We considered prospective population-based incidence studies the gold standard for determining the incidence and used them in preference to other data sources. However, these studies are complex and expensive, so few countries have used them to estimate the incidence of enteric disease [6, 16].

In lieu of a prospective study, investigators in several countries have conducted multiplier studies that estimate the incidence of *Salmonella* gastroenteritis by multiplying the incidence of laboratory-confirmed infections by a multiplier to correct for underascertainment. The multiplier is derived from crosssectional surveys of the general population and clinical diagnostic laboratories. Multiplier studies, which estimate the frequency at which cases are lost to surveillance at each surveillance step (care seeking, specimen submission, laboratory testing), have been conducted in Australia [11], Canada [14], the United States [15], Jordan [27], Japan [13], and China (Chinese Center for Disease Control and Prevention; unpublished data).

For 2 GBD regions, both European, there were no prospective, population-based or multiplier studies, but available disease notification data allowed us to estimate the disease burden by determining the average incidence of laboratory-confirmed Salmonella infection and adjusting for underascertainment using values from the literature. Salmonella-specific multipliers range from 3.2 in England [6], 7 in Australia [31], 14.3 in the Netherlands [29], 25 in Canada [14], 38 in the United States [15], to 64 in Japan [13]. Because of geographic proximity, the Netherlands Salmonella-specific multiplier of 14.3 [29] was used to adjust for underascertainment in these 2 European regions. It is very unlikely, however, that the completeness and ascertainment of laboratory-confirmed cases of Salmonella infection would be the same across all European countries given varying methods of surveillance and levels of socioeconomic development. Thus, the Netherlands multiplier probably provides a conservative estimate of the population incidence.

To overcome the lack of regional incidence data in Africa, Asia (central, south, and southeast), Latin America, and the Caribbean, we used a novel approach, using data from a Swed-

Table 3. Estimated Annual Global Burden of Salmonella Gastroenteritis, Circa 2006, under Different Scenarios

| Variable | Mean no. of cases | Mean no. of deaths | Mean incidence per 100,000 person-years |
|---|----------------------|-----------------------|---|
| Results from Table 1 | 93,757,000 | 155,000 | 1140 |
| Scenario | | | |
| Estimated incidence in "Asia, South" increased by a factor of 10 | 157,059,000 | 259,000 | 2400 |
| Susceptible traveler correction factor decreased by a factor of 7 | 153,916,000 | 254,000 | 2400 |
| Susceptible traveler correction factor decreased by a factor of 2 | 103,783,000 | 171,000 | 1600 |
| Estimated incidence in "Asia, South" increased by a factor of 2 | 100,790,000 | 166,000 | 1600 |
| Estimated incidence in "Asia, East" decreased by a factor of 2 | 55,639,000 | 92,000 | 850 |
| Estimated incidence in "Asia, East" decreased by a factor of 10 | 25,145,000 | 42,000 | 390 |
| Estimated incidence in "Asia, East" derived from returning traveler data | 22,545,000 | 37,000 | 350 |
| Estimated incidence in "Asia, East" derived from extrapolation (from "Asia Pacific, High Income") | 18,136,000 | 30,000 | 280 |

ish study on travel-associated Salmonella infections (adjusted for underascertainment) to estimate the incidence of laboratory-confirmed cases in these regions. The concept of using such data as a measure of relative risk between regions was first proposed by Ekdahl et al [30] in the Swedish traveler study. We hypothesized that acquired immunity to specific Salmonella serovars that are prevalent may mean that travelers are more likely than residents to be infected with Salmonella. To compensate, we derived a correction factor by comparing the incidence in Swedish travelers returning from the "North Africa/ Middle East" region to the incidence estimate calculated for the Jordan population, finding that the incidence in travelers was 15 times greater. However, it is likely that local populations of countries which are less developed than Jordan are relatively more malnourished and susceptible to Salmonella infections than their Jordanian counterparts. In such populations, the local susceptibility may approach that of travelers to the area; thus, estimates for such regions presented here would significantly underestimate the true incidence.

We recognize that the methods used here do not capture the full extent of the actual uncertainty associated with the data. For example, we did not capture the uncertainty associated with data coverage in a region, and thus did not distinguish between regions which had information from only one country versus multiple countries. As well, we did not distinguish between variability and uncertainty. However, we made the best use of existing data to estimate the global burden of *Salmonella* gastroenteritis and attempted to capture the main sources of uncertainly. Further advancements are needed to better characterize uncertainly in such models.

There is currently no consensus or guidance available on the weight of evidence or uncertainty associated with different types of burden of illness studies (for instance, prospective versus laboratory-based incidence calculations) or extrapolations between countries or regions. Clearly, however, there is a scale of declining weight of evidence and increasing uncertainty as we move from prospective studies and extrapolate away from the country in which the study was conducted. Future work should consider accounting for this by, for instance, increasing the spread of the uncertainty distributions based on study type, as well as increasing the uncertainty in the results for some regions as a function of the nature of the extrapolation performed.

We used a range of possible case fatality rate values, from 0.0003% [15] to 0.003% [23], to estimate the annual deaths. However, the case-fatality rate—and, thus, the estimated number of deaths per year due to *Salmonella* infection—may be higher in countries where nutrition is poor and access to health care limited. Unfortunately, few published data exist with which to improve these estimates; thus the estimated number of deaths reported here should be considered a conservative value.

We limited this study to assessing the human health burden

of gastroenteritis caused by *Salmonella* as measured by numbers of cases and deaths. We did not attempt to estimate its impact in terms of hospitalization, disability, long-term sequelae, or economic costs because of lack of data. These factors impact hugely on the human health burden, and should be considered in future. We also did not account for invasive *Salmonella* infection, which poses a significant burden, particularly in HIVprevalent regions, such as sub-Saharan Africa.

We estimated the number of foodborne cases by averaging published values of the estimated proportion of Salmonella infections that were foodborne [5, 8, 11, 24-26], and applying that average to our estimated number of cases. This crude approach is subject to several limitations. First, since we applied a single proportion to the total number of cases, we assumed that the proportion of Salmonella cases that were foodborne was the same across all world regions. However, the proportion likely varies widely between countries and regions. More information on the country- and region-specific foodborne transmission of Salmonella is needed, particularly for developing regions, where the importance of waterborne transmission is likely greater, due to more frequent contamination at the source and during household storage, and lack of disinfection. Information from developing countries is particularly needed since all published estimates of the proportion of Salmonella infections that are foodborne currently come from developed countries. We recognize that the proportion that is foodborne is likely lower in developing countries because the proportion waterborne is likely higher. However, in the absence of regional estimates we extrapolated an average of all published estimates of the proportion that is foodborne to arrive at a global value.

The major limitation of this study is the significant reliance of its results on the unpublished Chinese incidence estimate. To address this, we explored the impact of using returning traveler data and extrapolating from the "Asia Pacific, High Income" region in lieu of the China data. Unfortunately, both alternate data sources have their own inherent biases. A main criticism of analyses such as this one is the use of data primarily from developed countries, thus yielding values that significantly underestimate the true incidence of disease. Through WHO Global Salm-Surv, an international network of epidemiologists and laboratory scientists, we were able to identify an unpublished study from China which we felt more accurately depicted the incidence of Salmonella infection in this populous region, compared to either the returning traveler data and extrapolation. The Chinese estimate is significantly higher than the other multiplier studies, although this is likely due to true population differences in rates of illness. It is also higher than the returning traveler data for the "Asia, East" and other adjacent regions, although this is likely due to the bias associated with returning traveler data as discussed above. Unfortunately, other sources of information (eg, disease notification data) with which to

validate our choice of estimate were unavailable for the "Asia, East" region. Thus, we chose the data we felt most accurately represented the incidence in the region.

Salmonella causes considerable burden globally. Although subject to several limitations, these data provide important information for priority setting in specific regions. They also highlight the need for improved public health surveillance for human foodborne illness in some regions. There were no publicly available notification data from some regions, including those with a large proportion of the global population, such as South/South-East Asia, and South America, which account for 39% of the world population. This lack of good surveillance information significantly impacts the quality of the global estimate. Assessing the true burden of *Salmonella* infection should be prioritized in countries within these regions, for example via capacity-building initiatives such as WHO Global *Salm*-Surv, to improve global burden estimates and better inform priority setting.

GLOBAL BURDEN OF SALMONELLA WORKING GROUP

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