RESEARCH ARTICLE

World Health Organization Estimates of the Global and Regional Disease Burden of 22 Foodborne Bacterial, Protozoal, and Viral Diseases, 2010: A Data Synthesis

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Abstract

Background

Foodborne diseases are important worldwide, resulting in considerable morbidity and mortality. To our knowledge, we present the first global and regional estimates of the disease burden of the most important foodborne bacterial, protozoal, and viral diseases.

Methods and Findings

We synthesized data on the number of foodborne illnesses, sequelae, deaths, and Disability Adjusted Life Years (DALYs), for all diseases with sufficient data to support global and regional estimates, by age and region. The data sources included varied by pathogen and included systematic reviews, cohort studies, surveillance studies and other burden of disease assessments. We sought relevant data circa 2010, and included sources from 1990–2012. The number of studies per pathogen ranged from as few as 5 studies for bacterial intoxications through to 494 studies for diarrheal pathogens. To estimate mortality for *Mycobacterium bovis* infections and morbidity and mortality for invasive non-typhoidal *Salmonella enterica* infections, we excluded cases attributed to HIV infection. We excluded stillbirths in our estimates. We estimate that the 22 diseases included in our study resulted

in two billion (95% uncertainty interval [UI] 1.5–2.9 billion) cases, over one million (95% UI 0.89–1.4 million) deaths, and 78.7 million (95% UI 65.0–97.7 million) DALYs in 2010. To estimate the burden due to contaminated food, we then applied proportions of infections that were estimated to be foodborne from a global expert elicitation. Waterborne transmission of disease was not included. We estimate that 29% (95% UI 23–36%) of cases caused by diseases in our study, or 582 million (95% UI 401–922 million), were transmitted by contaminated food, resulting in 25.2 million (95% UI 17.5–37.0 million) DALYs. Norovirus was the leading cause of foodborne illness causing 125 million (95% UI 70–251 million) cases, while *Campylobacter* spp. caused 96 million (95% UI 52–177 million) foodborne illnesses. Of all foodborne diseases, diarrheal and invasive infections due to non-typhoidal *S. enterica* infections resulted in the highest burden, causing 4.07 million (95% UI 2.49–6.27 million) DALYs. Regionally, DALYs per 100,000 population were highest in the African region followed by the South East Asian region. Considerable burden of foodborne disease is borne by children less than five years of age. Major limitations of our study include data gaps, particularly in middle- and high-mortality countries, and uncertainty around the proportion of diseases that were foodborne.

Conclusions

Foodborne diseases result in a large disease burden, particularly in children. Although it is known that diarrheal diseases are a major burden in children, we have demonstrated for the first time the importance of contaminated food as a cause. There is a need to focus food safety interventions on preventing foodborne diseases, particularly in low- and middle-income settings.

Introduction

Foodborne diseases are globally important, as they result in considerable morbidity, mortality, and economic costs [1,2]. Many different diseases, including those due to bacteria, viruses, parasites, chemicals, and prions, may be transmitted to humans by contaminated food [3]. Outbreaks and sporadic cases of foodborne disease are regular occurrences in all countries of the world. In recent decades, globalization of the food supply has also meant that pathogens causing foodborne diseases are rapidly transported across international borders [4]. Foodborne disease outbreaks have led to adverse impacts on trade and food security [5,6]. In response to foodborne diseases, national governments and international bodies have established elaborate systems to control and improve food safety [7].

Recognizing that contaminated food is an important cause of human disease, estimates of disease burden of the various foodborne diseases has been sought to enable advocacy for improved food safety and to assist governments to prioritize efforts for enhancing food safety. Although several countries have estimated the number of cases, sequelae, deaths, and Disability Adjusted Life Years (DALYs) resulting from foodborne diseases at the national level, most have not [8]. Furthermore, global and regional estimates of the burden of foodborne diseases have not been available [1,2]. In 2007, the World Health Organization (WHO) established the Foodborne Disease Burden Epidemiology Reference Group (FERG) to estimate the global and regional burden of disease attributable to food from all causes [9]. FERG consists of thematic task forces to estimate the human health burden of (1) enteric bacterial and viral infections, (2)

parasitic infections, and (3) illnesses due to chemicals and toxins. The Director General of WHO nominated members of the FERG following an open call for applications to governments, in the scientific press, and through global networks [1]. The Enteric Diseases Task Force (EDTF) of the FERG comprised 14 experts in the epidemiology of viral, bacterial and parasitic infections transmitted by food, and was supported by various resource advisors who were expert in various aspects of infectious disease transmission.

Methods

In this study, the EDTF estimates the global and regional disease health burden in 2010 resulting from the most common foodborne diseases. For a glossary of terms used in this paper see S1 Text.

FERG EDTF reviewed the epidemiology of all bacterial and viral diseases potentially transmitted by food and identified those for inclusion based on public health importance and data availability. We excluded enteroaggertative *Escherichia coli*, *Vibrio parahaemolyticus*, *V. vulnificus*, and *Yersinia* spp., which are infrequent causes of foodborne diseases, due to a lack of sufficient data for global estimation, ie–not commonly reported in systematic reviews of etiological agents of diarrhea [10]. After excluding these agents, we included 19 bacterial or viral diseases in our study. Of these 19 diseases, four are distinct manifestations of *Salmonella enterica* infection: invasive infections due to *S. enterica* serotype Typhi (*Salmonella* Typhi); invasive infections due to *S. enterica* serotype Paratyphi A (*Salmonella* Paratyphi A); invasive infections due to non-typhoidal *S. enterica* (iNTS); and diarrheal disease due to non-typhoidal *S. enterica* (NTS). We then determined that our approach for estimating the burden for diarrheal diseases could also be applied to protozoal diseases and included 3 protozoal diseases.

Diarrhea is a dominant feature for 14 of these diseases—ten caused by bacteria, three by protozoa, and one by a virus. One or more extra-intestinal manifestations including bacteremia, hepatitis, and meningitis are the dominant feature for the other eight diseases—seven caused by bacteria and one caused by a virus.

To identify data for estimation of incidence, mortality and sequelae for different agents, we conducted literature reviews to identify relevant studies, consulted with academics and expert committees, and evaluated systematic reviews that were conducted circa 2010. Where data sources were not available, the EDTF recommended that WHO commission systematic reviews into incidence and outcomes of specific agents, which were subsequently published in the peer-reviewed literature [11–22]. Where multiple data sources were available for a single agent, the EDTF made decisions to use the most contemporaneous and comprehensive sources, or incorporate both into the estimation process. In the following sections, we outline how we synthesized data in accordance with a documented framework reported elsewhere [23]. Table 1 summarizes our approach, while S2 Text provides a comprehensive description of the methods and distribution for all parameters used for estimating cases, sequelae, deaths and DALYs for each of the 22 diseases.

Estimating Cases, Sequelae, and Deaths for Diarrheal Diseases

For diarrheal diseases caused by *Campylobacter* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Giardia lamblia*, norovirus, NTS, and *Shigella* spp., national estimates of foodborne diseases were only available from a limited number of countries. We therefore used two approaches, documented in Pires *et al.* [11], depending on the level of development of the country. The first approach, based on national estimates of the incidence of foodborne diseases from seven studies published between 2005–2014, was applied to the 61 countries in low-mortality (European Region (EUR) and

Table 1. Summary of enteric pathogens included and methods of estimating incidence of infection. For more information, see S2 Text.

Disease	Pathogens	Methods	Reference
Diarrheal Disease	*Campylobacter* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Giardia lamblia*, norovirus, nontyphoidal *Salmonella enterica*, *Shigella* spp	Synthesis of seven national studies into foodborne disease incidence for low-mortality countries in Region A combined with systematic reviews for middle- and high-mortality countries that was derived from 136 outpatient and community studies and 254 inpatient studies among children <5 years of age, and 97 inpatient, outpatient, and community studies among persons ≥5 years of age	[11]
Diarrheal Disease	*Vibrio cholerae* (cholera)	Data synthesis of WHO cholera reports and publicly available data sources.	[24]
Diarrheal Disease	Shiga-toxin producing *E. coli*	Systematic review of 16 published studies	[19]
Intoxications	*Bacillus cereus*, *Clostridium perfringens*, *Staphylococcus aureus*	Estimation from seven national studies in low-mortality sub-region A countries only	[11]
Intoxications	*Clostridium botulinum*	Estimation from five national studies in 55 EUR and AMR sub-region A countries only*	See S2 Text
Invasive enteric disease	Hepatitis A virus	Conversion of mortality data from Global Burden of Disease 2010 for hepatitis A to incidence	[25]
Invasive enteric disease	Typhoid, Paratyphoid fevers	Data from Global Burden of Disease 2010	[26]
Invasive enteric disease	Invasive non-typhoidal *Salmonella enterica* (iNTS)	Systematic review of 10 published studies of incidence of invasive infections	[22]
Invasive enteric disease	*Mycobacterium bovis*	Systematic review of 140 data sources combined with incidence estimates for human TB infections.	[16,17]
Invasive enteric disease	*Brucella* spp.	Systematic review of 29 published studies of incidence combined with information from countries free of *Brucella* in livestock.	[15]
Invasive enteric disease	*Listeria* spp.	Systematic review of 87 published studies, including 43 containing data on incidence	[18]

* EUR— European Region; AMR— Region of the Americas

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other subregion A [27]) countries [3,28–35]. For countries with national estimates of incidence and mortality, we used these data. We used the median and associated uncertainty intervals for diarrheal diseases for the subregion to estimate incidence and mortality of diarrheal diseases for other countries within the subregion without national data [10].

The second approach was applied to the remaining 133 countries not in EUR or other subregion A categories (see S1 Text for a country list by subregion). For this approach, we modified the WHO Child Health Epidemiology Reference Group (CHERG) method to estimate diarrheal incidence and mortality for all age groups [10]. First, we estimated the overall incidence of diarrhea from all causes (i.e., "envelope" of diarrheal incidence) for 2010 by combining estimates of diarrheal incidence for children <5 years of age and persons ≥5 years of age [13,36]. We used the overall diarrheal mortality (i.e., envelope for diarrheal deaths) derived by WHO [37] for 2010. We derived an etiological proportion for each disease by region from systematic reviews of stool sample isolation or detection proportions from inpatient, outpatient, and community-based studies of persons with diarrhea. We followed the CHERG standard approach because there is limited information on pathogens among people who have died, and assumed that the distribution of pathogens observed among inpatients hospitalized with severe diarrhea represented the pathogen prevalence among diarrheal deaths [10]. To derive etiological proportions for children <5 years of age, we assumed that the distribution of pathogens in outpatient and community studies represented the pathogen prevalence among diarrheal

episodes for those who did not die. We made the same assumption for persons ≥5 years of age but due to sparseness of data also included inpatient studies. For more details of methods, see Pires *et al.* [11]. For some pathogens we assumed that different etiological agents, such as *Shigella* spp., NTS and *Campylobacter* spp., had similar clinical profiles (S2 Text).

Estimates for cholera were based on the incidence among populations at risk for cholera in endemic and non-endemic countries [24]. The case fatality ratio (CFR) for cholera was 1% in Western Pacific Region (WPR) subregion B, 1% in South-East Asian Region (SEAR) subregion B (except 1.5% in Bangladesh), 1.3% in Eastern Mediterranean Region (EMR) subregion B, 3% in SEAR subregion D, 3.2% in EMR subregion D, and 3.8% in African Region (AFR) [24]. For all other countries, we assumed cholera occurred only among international travellers and did not result in deaths. In this instance, we applied the median incidence from non-endemic countries with available data for cholera.

Shiga-toxin producing *E. coli* (STEC) infection incidence and mortality were based on a systematic review described elsewhere [19]. Sequelae, more common among O157 infections, were hemolytic uremic syndrome (HUS) and end stage renal disease (ESRD). Based on review, we estimated 0.8% of O157 infections and 0.03% of infections caused by other serotypes result in HUS, and 3% of HUS cases result in ESRD. We estimated that the CFR for HUS was 3.7%; for ESRD the CFR was 20% in the 35 subregion A countries and 100% in other countries.

We used data on the incidence and mortality of foodborne intoxications caused by *Bacillus cereus*, *Clostridium perfringens*, and *Staphylococcus aureus* from national studies conducted in low-mortality countries. We applied the median incidence from national studies to the 61 countries in EUR and other subregion A countries. We did not attempt to estimate burden due to these three foodborne intoxications in high- and middle-mortality countries due to the absence of data on diseases caused by these pathogens in these countries. The median CFR from national studies was 0.003% for *C. perfringens* and 0.0025% for *S. aureus*; there were no *B. cereus* deaths. We considered that 31% of Guillain-Barré Syndrome (GBS) cases globally were associated with antecedent *Campylobacter* infection and that the CFR for GBS was 4.1% [38,39].

Estimating Cases, Sequelae, and Deaths of Extra-Intestinal Diseases

For diseases caused by hepatitis A virus, *Brucella* spp., *Listeria monocytogenes*, *Mycobacterium bovis*, iNTS, *Salmonella* Paratyphi A, and *Salmonella* Typhi we used a variety of approaches depending on availability of data.

We used Institute of Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) 2010 data to estimate the burden of disease for typhoid, paratyphoid, and hepatitis A [25]. IHME provided country-specific age-standardized prevalence data of typhoid and paratyphoid fever. These data were converted to incidence by dividing by duration, and partitioned into typhoid and paratyphoid assuming a 1.0 to 0.23 ratio [40]. Country-specific hepatitis A mortality data, stratified by age and sex, were converted to incidence assuming a CFR of 0.2%.

Rates of iNTS are highly correlated with HIV prevalence and malaria risk [22]. To estimate iNTS incidence globally, we used age-specific estimates of incidence from a systematic review [22] to construct a random effect log linear model using covariates of country specific HIV and malaria deaths, and the log of Gross Domestic Product. As data were sparse, we predicted incidence for all ages, which was converted to age-specific incidence based on age profiles for iNTS cases in low and high incidence settings [22]. From this, we predicted iNTS incidence among persons not infected with HIV [41,42]. To estimate deaths, we assumed that the CFR for iNTS in non-HIV infected individuals was a uniform distribution with a range 5–20% in sub-region B-E countries and range 3.9–6.6% in sub-region A countries [43].

Estimates for *M. bovis* infections were based on a systematic review where the proportion of human tuberculosis (TB) infections due to *M. bovis* ranged from 0.3% in Region of the Americas (AMR) to 2.8% in AFR [17]. We identified 51 countries that were free from *M. bovis* in cattle based on European Union certification and the World Organization for Animal Health [44]. All countries in a region except those free from *M. bovis* in cattle were assumed to have the same proportion of human TB infections due to *M. bovis*. To account for internationally acquired infections, all countries free of *M. bovis* in cattle were assigned the lowest observed proportion of human TB infections due to *M. bovis* (0.3%). To derive estimates of human *M. bovis* incidence, we multiplied WHO country-specific human TB incidence by the estimate of the proportion of human TB infections that were due to *M. bovis* [45]. To estimate mortality associated with *M. bovis* that accounted for HIV co-morbidity we used estimates of mortality due to human TB in HIV negative persons from WHO. We adjusted mortality data by assuming that the CFR for *M. bovis* was 20% lower than human TB, as *M. bovis* infections are more likely to be extrapulmonary [16].

To estimate the incidence and mortality for brucellosis we updated a systematic review and included additional data on 32 countries that were considered *Brucella*-free in livestock (free of *B. arbortus* in cattle and *B. melitensis* in sheep and goats) [15]. We imputed incidence data to countries without estimates using a Bayesian log-normal random effects model, except for countries that were *Brucella*-free in livestock [23]. To account for internationally acquired infections, all countries that were *Brucella*-free in livestock were assigned the median incidence of human brucellosis reported from these countries. The CFR for brucellosis was 0.05%, and 40% of cases resulted in chronic infections and 10% of cases in males resulted in orchitis [14].

We estimated the incidence and mortality for listeriosis using a systematic review that is described elsewhere [18]. In accordance with standard burden of disease practice, we excluded stillbirths, in our baseline burden estimates. The CFR was 14.9% for perinatal cases and 25.9% for other cases.

Incidence and mortality data for botulism were only available from countries in Europe and North America. We limited our estimation to the 55 countries in EUR and AMR subregion A, which was based on the median incidence derived from countries with national estimates of botulism. We estimated that 35% of botulism cases were severe and that the CFR of severe botulism was 15%.

Estimation of Foodborne Proportion

We assumed that all infections from *L. monocytogenes*, *M. bovis*, and from the four foodborne intoxications (*B. cereus*, *C. botulinum*, *C. perfringens*, and *S. aureus*) were foodborne. To estimate the proportion of the other enteric diseases that were transmitted by contaminated food, we relied upon results of a FERG structured expert elicitation [46]. In this expert elicitation, foodborne and waterborne were considered separate transmission pathways. Proportions of brucellosis and hepatitis A infections and intestinal protozoa acquired from contaminated food were estimated using global panels of experts. Foodborne proportions for the remaining enteric diseases were estimated using a panel of experts for each region separately, although several experts were serving on more than one panel.

Disability Weights

Disability weights for each clinical outcome for the enteric diseases were taken from the GBD 2010 study [47]. Disability weights for listeriosis meningitis and neurological sequelae were derived from GBD 2010 disability weights using a multiplicative methodology and expert judgment. Disability weights for individual conditions are specified in S2 Text.

Data Analysis

The FERG approach to computing DALYs from the estimated cases, sequelae, deaths, and other parameters described in this paper is described in more detail elsewhere, including the modelling of uncertainty intervals incorporating (where relevant) uncertainty of estimated foodborne proportions [23]. Estimates were produced using the 2012 revisions for United Nations country-level population data for 2010 [48]. Calculations followed disease-specific models defined by incidence and probability parameters, each with a distribution [23]. Uncertainty around input parameters were propagated using Monte Carlo simulations; 10,000 values were sampled from each input parameter to calculate 10,000 estimates of cases, deaths or DALYs. The 2.5th and 97.5th percentile of each set of the 10,000 estimates yielded a 95% Uncertainty Interval (UI). Further details of analyses and modelling of DALYs and components described in this paper are in S2 Text.

Results

Cases

We estimated that the 22 diseases in our study caused 2.0 billion (95% UI 1.5–3.0 billion) illnesses in 2010, 39% (95% UI 26–53%) in children <5 years of age. Among the 1.9 billion (95% UI 1.4–2.8 billion) cases of diarrheal diseases, norovirus was responsible for 684 million (95% UI 491–1,112 million) illnesses; the largest number of cases for any pathogen (Table 2). The pathogens resulting in the next largest number of cases were ETEC, *Shigella* spp., *G. lamblia*, *Campylobacter* spp. and NTS. *Campylobacter* spp. cases included 31,700 (95% UI 25,400–40,200) GBS cases. There were also 2.48 million (95% UI 1.69–5.38 million) STEC cases which included 3,330 (95% UI 2,160–6,550) with HUS and 200 (95% UI 15–760) with ESRD. Among the extra-intestinal diseases, the pathogens resulting in the most infections were hepatitis A virus, *Salmonella* Typhi and *Salmonella* Paratyphi A. *Brucella* spp. resulted in 0.83 million (95% UI 0.34–19.6 million) illnesses, which included almost 333,000 (95% UI 135,000–7,820,000) chronic infections and 83,300 (95% UI 33,800–1,960,000) episodes of orchitis. *L. monocytogenes* resulted in 14,200 (95% UI 6,100–91,200) illnesses which included 7830 (95% UI 3,400–50,500) cases of septicaemia, 3,920 (95% UI 1,650–24,900) cases of meningitis, and 666 (95% UI 207–4,710) cases with neurological sequelae.

Overall, 29% (95% UI 23–36%) of all 22 diseases were estimated to be transmitted by contaminated food equating to 582 million (95% UI 400–922 million) foodborne cases in 2010; 38% (95% UI 24–53%) in children <5 years of age. The pathogens resulting in the most foodborne cases were norovirus, *Campylobacter* spp., ETEC, NTS, and *Shigella* spp. A high proportion of foodborne infections caused by *V. cholerae*, *Salmonella* Typhi, and *Salmonella* Paratyphi A occurred in the African region (Table 3). A high proportion of foodborne infections caused by EPEC, *Cryptosporidium* spp., and *Campylobacter* spp. occurred among children <5 years of age (Table 4). Among the 11 diarrheal diseases, the rate ratio of foodborne cases occurring among children <5 years of age compared to those ≥5 years of age was 6.44 (95%UI 3.15–12.46).

Deaths

We estimated that the 22 diseases in our study caused 1.09 million (95% UI 0.89–1.37 million) deaths in 2010, 34% (95% UI 29–38%) in children <5 years of age. Among the diarrheal diseases, norovirus was responsible for the most deaths. Other diarrheal pathogens responsible for large numbers of deaths were EPEC, *V. cholerae*, and *Shigella* spp. The 37,600 (95% UI 27,700–55,100) deaths attributed to *Campylobacter* spp. included 1,310 (95% UI 887–1,880) deaths

Table 2. Median number of foodborne illnesses, deaths, and Disability Adjusted Life Years (DALYs), with 95% uncertainty intervals, 2010.

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	PROPORTION FOODBORNE (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYS (95% UI)
Diarrheal Disease	**1,912,159,038 (1,413,002,730–2,849,323,016)**	**715,196 (603,325–846,397)**	**55,139,959 (46,746,114–65,120,623)**	**0.29 (0.22–0.36)**	**548,285,159 (369,733,377–888,360,956)**	**199,892 (136,903–286,616)**	**15,780,400 (11,043,288–22,251,264)**
Campylobacter spp. *	166,175,078 (92,227,873–300,877,905)	37,604 (27,738–55,101)	3,733,822 (2,857,037–5,273,652)	0.58 (0.44–0.69)	95,613,970 (51,731,379–177,239,714)	21,374 (14,604–32,584)	2,141,926 (1,535,985–3,137,980)
Cryptosporidium spp.	64,003,709 (43,049,455–104,679,951)	27,553 (18,532–44,654)	2,159,331 (1,392,438–3,686,925)	0.13 (0.07–0.24)	8,584,805 (3,897,252–18,531,196)	3,759 (1,520–9,115)	296,156 (119,456–724,660)
Entamoeba histolytica	103,943,952 (47,018,659–210,632,459)	5,450 (2,194–17,127)	515,904 (222,446–1,552,466)	0.28 (0.14–0.44)	28,023,571 (10,261,254–68,567,590)	1,470 (453–5,554)	138,863 (47,339–503,775)
Enteropathogenic *E. coli*	81,082,327 (40,716,656–171,419,480)	122,760 (97,115–154,869)	9,717,390 (7,602,047–12,387,029)	0.30 (0.17–0.48)	23,797,284 (10,750,919–62,931,604)	37,077 (19,957–61,262)	2,938,407 (1,587,757–4,865,590)
Enterotoxigenic *E. coli*	240,886,759 (160,890,532–377,471,599)	73,857 (53,851–103,026)	5,887,541 (4,190,610–8,407,186)	0.36 (0.24–0.50)	86,502,735 (49,136,952–151,776,173)	26,170 (14,887–43,523)	2,084,229 (1,190,704–3,494,201)
Giardia spp.	183,842,615 (130,018,020–262,838,002)	0 (0–0)	171,100 (115,777–257,315)	0.15 (0.08–0.27)	28,236,123 (12,945,655–56,996,454)	0 (0–0)	26,270 (11,462–53,577)
Norovirus	684,850,131 (490,930,402–1,122,947,359)	212,489 (160,595–278,420)	15,105,714 (11,649,794–19,460,578)	0.18 (0.11–0.30)	124,803,946 (70,311,254–251,352,877)	34,929 (15,916–79,620)	2,496,078 (1,175,658–5,511,092)
Salmonella enterica, non-typhoidal	153,097,991 (64,733,607–382,208,079)	56,969 (43,272–88,129)	4,377,930 (3,242,020–7,175,522)	0.52 (0.35–0.67)	78,439,785 (31,579,011–210,875,866)	28,693 (17,070–49,768)	2,183,146 (1,314,295–3,981,424)
Shigella spp.	190,849,501 (97,832,995–363,915,689)	65,796 (46,317–97,036)	5,407,736 (3,771,300–8,107,456)	0.27 (0.13–0.44)	51,014,050 (20,405,214–118,927,631)	15,156 (6,839–30,072)	1,237,103 (554,204–2,520,126)
Shiga toxin-producing *E. coli*	2,481,511 (1,594,572–5,376,503)	269 (111–814)	26,827 (12,089–72,204)	0.48 (0.33–0.60)	1,176,854 (754,108–2,523,007)	128 (55–374)	12,953 (5,951–33,664)
Vibrio cholerae	3,183,394 (2,211,329–4,146,250)	105,170 (78,671–126,058)	7,347,635 (5,496,431–8,804,408)	0.24 (0.10–0.46)	763,451 (310,910–1,567,682)	24,649 (10,304–50,042)	1,722,312 (720,029–3,491,997)
Intoxications	**5,409,083 (2,187,762–12,929,293)**	**175 (70–407)**	**9,905 (3,993–23,527)**	**1.00**	**5,409,083 (2,187,762–12,929,293)**	**175 (70–407)**	**9,905 (3,993–23,527)**
*Bacillus cereus***	256,775 (43,875–807,547)	0 (0–0)	45 (7–171)	1.00	256,775 (43,875–807,547)	0 (0–0)	45 (7–171)
*Clostridium botulinum***	475 (183–990)	24 (7–65)	1,036 (299–2,805)	1.00	475 (183–990)	24 (7–65)	1,036 (299–2,805)
*Clostridium perfringens***	3,998,164 (837,262–11,529,642)	120 (25–351)	6,963 (1,423–20,493)	1.00	3,998,164 (837,262–11,529,642)	120 (25–351)	6,963 (1,423–20,493)
*Staphylococcus aureus***	1,073,339 (658,463–1,639,524)	25 (10–55)	1,575 (702–3,244)	1.00	1,073,339 (658,463–1,639,524)	25 (10–55)	1,575 (702–3,244)
Invasive enteric diseases	**77,929,723 (36,606,712–149,676,316)**	**371,002 (218,593–631,271)**	**23,070,841 (13,388,154–39,912,033)**	**0.34 (0.17–0.52)**	**25,569,838 (10,019,370–58,282,758)**	**146,981 (81,052–274,835)**	**9,107,557 (4,891,985–17,483,327)**

(Continued)

Table 2. (Continued)

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	PROPORTION FOODBORNE (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYS (95% UI)
Brucella spp.	832,633 (337,929–19,560,440)	4,145 (1,557–95,894)	264,073 (100,540–6,187,148)	0.47 (0.30–0.61)	393,239 (143,815–9,099,394)	1,957 (661–45,545)	124,884 (43,153–2,910,416)
Hepatitis A	46,864,406 (14,417,704–111,771,902)	93,961 (29,602–221,677)	4,580,758 (1,599,296–10,408,164)	0.30 (0.14–0.49)	13,709,836 (3,630,847–38,524,946)	27,731 (7,169–77,320)	1,353,767 (383,684–3,672,726)
Listeria monocytogenes	14,169 (6,112–91,175)	3,175 (1,339–20,428)	118,340 (49,634–754,680)	1.00	14,169 (6,112–91,175)	3,175 (1,339–20,428)	118,340 (49,634–754,680)
Mycobacterium bovis	121,268 (99,852–150,239)	10,545 (7,894–14,472)	607,775 (458,364–826,115)	1.00	121,268 (99,852–150,239)	10,545 (7,894–14,472)	607,775 (458,364–826,115)
Salmonella enterica, invasive non-typhoidal	596,824 (596,824–596,824)	63,312 (38,986–94,193)	3,895,547 (2,401,034–5,790,874)	0.48 (0.28–0.64)	284,972 (167,455–384,321)	29,391 (14,948–50,463)	1,794,575 (886,443–3,107,172)
Salmonella enterica Paratyphi A	4,826,477 (1,782,796–10,323,273)	33,325 (12,309–71,278)	2,367,164 (875,236–5,066,375)	0.37 (0.19–0.58)	1,741,120 (536,650–4,310,983)	12,069 (3,784–29,521)	855,730 (268,879–2,100,120)
Salmonella enterica Typhi	20,984,683 (7,751,285–44,883,794)	144,890 (53,519–309,903)	10,292,017 (3,805,373–22,027,716)	0.37 (0.19–0.58)	7,570,087 (2,333,263–18,743,406)	52,472 (16,454–128,350)	3,720,565 (1,169,040–9,130,956)
TOTAL	**2,000,626,631 (1,494,986,030–2,942,534,533)**	**1,092,584 (892,999–1,374,238)**	**78,730,084 (64,963,913–97,740,062)**	**0.29 (0.23–0.36)**	**581,902,722 (400,741,151–922,031,380)**	**350,686 (240,030–524,042)**	**25,175,035 (17,547,264–37,021,003)**

* Includes Guillain-Barré Syndrome cases and deaths.

** 61 EUR and other subregion A (low mortality) countries only.

*** EUR and subregion A (low mortality) countries only, excluding WPR A countries.

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from GBS. Among the extra-intestinal enteric diseases, the pathogens resulting in the most deaths were *Salmonella* Typhi, hepatitis A virus, iNTS and *Salmonella* Paratyphi A.

Overall, the 22 diseases in our study resulted in 351,000 (95% UI 240,000–524,000) deaths due to contaminated food in 2010; 33% (95% UI 27–40%) in children <5 years of age. The enteric pathogens resulting in the most foodborne deaths were *Salmonella* Typhi, EPEC, norovirus, iNTS, NTS, and hepatitis A. The mortality rates of foodborne diseases were consistently highest in the African region followed by the South Eastern Asian region (Table 3). Among the 11 diarrheal diseases due to contaminated food, the rate ratio of deaths in children <5 years of age compared to those ≥5 years of age was 8.37 (95%UI 5.90–11.4). For all 22 diseases, the rate ratio of deaths in children <5 years of age compared to those ≥5 years of age was 4.85 (95%UI 3.54–6.59).

DALYs

We estimated that the 22 diseases in our study caused 78.7 million (95% UI 65.0–97.7 million) DALYS in 2010, 43% (95% UI 38–48%) in children <5 years of age. The pathogens resulting in the most DALYs were norovirus, *Salmonella* Typhi, EPEC, *V. cholerae*, ETEC, and hepatitis A (Table 2).

Table 3. Median rates of foodborne illnesses, deaths and Disability Adjusted Life Years (DALYs) per 100,000 persons, by region, with 95% uncertainty intervals, 2010.

PATHOGEN*	African Region (AFR)			Region of the Americas (AMR)			Eastern Mediterranean Region (EMR)		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)
Diarrheal Disease	9,830 (3,969–21,567)	9 (5–14)	687 (369–1,106)	7,900 (4,497–13,850)	0.5 (0.3–0.7)	44 (30–63)	16,387 (7,729–34,176)	4 (2–6)	354 (218–544)
Campylobacter spp.**	2,221 (335–8,482)	0.8 (0.4–1)	70 (41–112)	1,389 (490–3,207)	0.07 (0.04–0.1)	13 (8–18)	1,873 (488–5,608)	1 (0.6–1)	90 (56–130)
Cryptosporidium spp.	205 (35–813)	0.2 (0.04–0.4)	13 (3–37)	114 (32–355)	0.007 (0.002–0.02)	0.6 (0.2–2)	346 (52–1,287)	0.04 (0.004–0.2)	4 (0.4–20)
Entamoeba histolytica	796 (98–3,868)	0.05 (0.009–0.4)	5 (0.9–39)	212 (16–1,209)	0.001 (0–0.009)	0.3 (0.03–1)	737 (79–3,110)	0.02 (0.002–0.2)	2 (0.3–14)
Enteropathogenic *E. coli*	454 (125–1,215)	2 (0.6–3)	140 (50–282)	189 (35–730)	0.06 (0.01–0.1)	5 (1–12)	430 (116–1,222)	0.7 (0.2–2)	57 (18–131)
Enterotoxigenic *E. coli*	982 (312–2,480)	1 (0.6–3)	109 (46–216)	1,281 (299–3,295)	0.05 (0.01–0.1)	5 (1–12)	4,971 (1,685–10,849)	0.4 (0.1–1)	35 (11–89)
Giardia spp.	809 (172–2,574)	0 (0–0)	0.8 (0.2–3)	309 (62–1,249)	0 (0–0)	0.3 (0.05–1)	670 (133–2,193)	0 (0–0)	0.6 (0.1–2)
Norovirus	1,749 (491–5,060)	1 (0.3–3)	81 (24–185)	2,491 (898–6,186)	0.1 (0.04–0.3)	9 (3–23)	2,796 (744–7,376)	0.4 (0.1–1)	33 (9–76)
Salmonella enterica, non-typhoidal	896 (175–2,994)	1 (0.5–2)	89 (42–147)	1,002 (378–1,990)	0.1 (0.06–0.2)	7 (4–12)	1,610 (147–14,052)	0.6 (0.3–1)	54 (26–87)
Shigella spp.	523 (45–2,865)	0.5 (0.1–2)	43 (8–124)	278 (35–1,443)	0.02 (0.003–0.05)	1 (0.3–5)	627 (55–4,648)	0.4 (0.07–1)	38 (6–117)
Shiga toxin-producing *E. coli*	5 (2–9)	0 (0–0.002)	0.05 (0.02–0.1)	16 (9–30)	0.004 (0.001–0.01)	0.3 (0.1–0.9)	65 (37–97)	0.002 (0–0.004)	0.2 (0.1–0.5)
Vibrio cholerae	43 (13–101)	2 (0.5–4)	1 12 (35–252)	0.02 (0.008–0.05)	0 (0–0)	0 (0–0)	9 (0.4–28)	0.3 (0.01–1)	20 (0.7–69)
Invasive enteric diseases	**425 (156–976)**	**5 (3–8)**	**307 (160–508)**	**31 (11–81)**	**0.3 (0.2–0.6)**	**16 (8–35)**	**394 (80–1,056)**	**2 (0.7–4)**	**108 (41–250)**
Brucella spp.	3 (0.4–110)	0.02 (0.002–0.5)	1 (0.1–34)	3 (1–37)	0.01 (0.005–0.2)	0.9 (0.3–12)	33 (10–187)	0.2 (0.05–0.9)	11 (3–60)
Hepatitis A	232 (60–643)	0.5 (0.1–1)	23 (7–60)	12 (3–33)	0.02 (0.006–0.07)	1 (0.3–3)	237 (17–772)	0.5 (0.04–2)	23 (2–74)
Listeria monocytogenes	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)	0.3 (0.1–1)	0.07 (0.03–0.3)	3 (1–11)	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)
Mycobacterium bovis	7 (4–9)	0.5 (0.3–0.7)	30 (19–42)	0.1 (0.05–0.2)	0.007 (0.003–0.01)	0.4 (0.2–0.8)	1 (0.8–2)	0.2 (0.08–0.3)	9 (5–18)
Salmonella enterica., invasive non-typhoidal	25 (12–37)	3 (1–5)	169 (71–306)	0.7 (0.4–0.9)	0.06 (0.03–0.1)	3 (1–5)	1 (0.7–2)	0.1 (0.06–0.3)	8 (3–14)
Salmonella enterica Paratyphi A	25 (5–73)	0.2 (0.04–0.5)	12 (3–36)	2 (0.4–7)	0.02 (0.003–0.05)	1 (0.2–4)	17 (2–55)	0.1 (0.01–0.4)	9 (1–28)
Salmonella enterica Typhi	108 (24–317)	0.7 (0.2–2)	53 (12–155)	10 (2–32)	0.07 (0.01–0.2)	5 (0.9–16)	73 (9–240)	0.5 (0.06–2)	37 (5–122)
TOTAL	**10,304 (4,279–22,108)**	**14 (8–21)**	**1,001 (562–1,543)**	**7,937 (4,515–13,899)**	**0.8 (0.5–1)**	**61 (40–93)**	**16,865 (8,051–34,712)**	**6 (4–9)**	**470 (286–728)**

(Continued)

We estimate that the 22 diseases in our study resulted in 25.2 million (95% UI 17.5–37.0 million) DALYs due to contaminated food; 43% (95% UI 36–50%) in children <5 years of age. Fig 1 shows the relative burden of foodborne enteric infections, if iNTS and NTS were grouped together. The pathogen resulting in the most foodborne DALYs was nontyphoidal *S. enterica*, if iNTS were included (4.07 million DALYs; 95% UI 2.49–6.27 million DALYs). Other pathogens resulting in substantial foodborne DALYs included: *Salmonella* Typhi, EPEC, norovirus, and *Campylobacter* spp. The rates of DALYs for foodborne diseases were highest in the African region. Overall, the 22 diseases transmitted by contaminated food resulted in 10.8 million (95% UI 7.59–15.3 million) DALYs in children <5 years of age compared to 14.3 million (95% UI 9.42–22.5 million) DALYs in those ≥5 years of age.

Table 3. (*Continued*)

PATHOGEN*	European Region (EUR)			South-East Asian Region (SEAR)			Western Pacific Region (WPR)			GLOBAL		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)
Diarrheal Disease	2,483 (1,439–4,136)	0.3 (0.2–0.4)	23 (16–30)	7,074 (2,570–19,537)	5 (2–9)	363 (177–649)	6,302 (2,501–17,289)	0.3 (0.1–0.5)	33 (17–54)	7,968 (5,373–12,911)	3 (2–4)	229 (160–323)
Campylobacter spp.**	522 (363–687)	0.05 (0.03–0.09)	9 (6–13)	1,152 (200–3,372)	0.4 (0.1–0.9)	33 (9–83)	876 (359–3,855)	0.04 (0.02–0.1)	10 (4–17)	1,390 (752–2,576)	0.3 (0.2–0.5)	31 (22–46)
Cryptosporidium spp.	21 (4–70)	0.003 (0–0.009)	0.2 (0.03–0.6)	78 (10–474)	0.09 (0.01–0.4)	6 (0.9–29)	32 (2–170)	0.003 (0–0.03)	0.3 (0.02–3)	125 (57–269)	0.05 (0.02–0.1)	4 (2–11)
Entamoeba histolytica	0 (0–0)	0 (0–0)	0 (0–0)	256 (27–1,188)	0.03 (0.004–0.2)	3 (0.3–17)	229 (0–1,598)	0.001 (0–0.003)	0.3 (0–1)	407 (149–997)	0.02 (0.007–0.08)	2 (0.7–7)
Enteropathogenic *E. coli*	8 (3–16)	0 (0–0)	0.005 (0.002–0.01)	594 (62–2,775)	0.9 (0.2–2)	66 (15–146)	166 (8–395)	0.06 (0.003–0.1)	5 (0.2–12)	346 (156–915)	0.5 (0.3–0.9)	43 (23–71)
Enterotoxigenic *E. coli*	6 (2–13)	0 (0–0)	0.004 (0.001–0.01)	1,075 (229–3,521)	0.6 (0.1–1)	42 (10–104)	555 (43–2,430)	0.04 (0.003–0.1)	4 (0.3–10)	1,257 (714–2,206)	0.4 (0.2–0.6)	30 (17–51)
Giardia spp.	54 (16–123)	0 (0–0)	0.03 (0.009–0.1)	159 (16–903)	0 (0–0)	0.1 (0.01–0.9)	354 (8–1,519)	0 (0–0)	0.3 (0.005–1)	410 (188–828)	0 (0–0)	0.4 (0.2–0.8)
Norovirus	1,652 (630–3,294)	0.05 (0.02–0.1)	4 (1–8)	841 (113–5,631)	1 (0.2–3)	71 (15–230)	1,305 (189–6,441)	0.05 (0.004–0.2)	4 (0.4–17)	1,814 (1,022–3,653)	0.5 (0.2–1)	36 (17–80)
Salmonella enterica, non-typhoidal	186 (118–275)	0.1 (0.08–0.2)	8 (5–14)	908 (88–4,758)	0.7 (0.2–2)	49 (11–147)	898 (170–6,428)	0.02 (0.01–0.03)	2 (1–7)	1,140 (459–3,065)	0.4 (0.2–0.7)	32 (19–58)
Shigella spp.	3 (0.9–8)	0.003 (0–0.01)	0.2 (0.03–0.8)	1,084 (177–3,927)	0.3 (0.07–1)	25 (5–83)	689 (19–2,549)	0.04 (0.002–0.1)	4 (0.1–10)	741 (297–1,728)	0.2 (0.1–0.4)	18 (8–37)
Shiga toxin-producing *E. coli*	18 (9–28)	0.003 (0.001–0.006)	0.3 (0.1–0.8)	19 (2–95)	0.002 (0–0.01)	0.2 (0.02–1)	3 (2–6)	0 (0–0.001)	0.05 (0.02–0.1)	17 (11–37)	0.002 (0–0.005)	0.2 (0.09–0.5)
Vibrio cholerae	0.03 (0.01–0.06)	0 (0–0)	0 (0–0)	17 (0.7–52)	0.4 (0.007–2)	30 (0.5–109)	0.2 (0.01–0.5)	0.002 (0–0.005)	0.1 (0.005–0.3)	11 (5–23)	0.4 (0.1–0.7)	25 (10–51)
Invasive enteric diseases	19 (9–51)	0.2 (0.1–0.3)	10 (7–19)	872 (169–2,288)	4 (1–9)	250 (81–598)	163 (30–391)	0.9 (0.3–2)	58 (19–134)	372 (146–847)	2 (1–4)	132 (71–254)
Brucella spp.	4 (1–33)	0.02 (0.006–0.2)	1 (0.4–11)	2 (0.02–302)	0.01 (0–1)	0.8 (0.006–96)	2 (0.5–61)	0.01 (0.002–0.3)	0.6 (0.1–19)	6 (2–132)	0.03 (0.01–0.7)	2 (0.6–42)
Hepatitis A	11 (3–28)	0.02 (0.006–0.06)	1 (0.3–3)	494 (57–1,590)	1 (0.1–3)	48 (6–151)	51 (3–164)	0.1 (0.006–0.3)	5 (0.3–15)	199 (53–560)	0.4 (0.1–1)	20 (6–53)
Listeria monocytogenes	0.2 (0.2–0.3)	0.04 (0.03–0.06)	2 (1–2)	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)	0.2 (0.1–0.4)	0.04 (0.03–0.09)	1 (1–3)	0.2 (0.09–1)	0.05 (0.02–0.3)	2 (0.7–11)
Mycobacterium bovis	0.2 (0.1–0.3)	0.02 (0.01–0.03)	0.9 (0.7–1)	2 (0.9–4)	0.2 (0.1–0.5)	13 (6–26)	0.8 (0.4–1)	0.04 (0.02–0.07)	2 (1–4)	2 (1–2)	0.2 (0.1–0.2)	9 (7–12)
Salmonella enterica., invasive non-typhoidal	0.8 (0.6–1)	0.07 (0.04–0.1)	3 (2–5)	2 (0.3–2)	0.2 (0.03–0.3)	9 (2–16)	1 (0.5–2)	0.1 (0.05–0.2)	6 (2–10)	4 (2–6)	0.4 (0.2–0.7)	26 (13–45)
Salmonella enterica Paratyphi A	0.2 (0.03–1)	0.002 (0–0.008)	0.1 (0.01–0.6)	58 (11–167)	0.4 (0.1–1)	29 (7–83)	18 (3–47)	0.1 (0.02–0.3)	8 (1–20)	25 (8–63)	0.2 (0.05–0.4)	12 (4–31)
Salmonella enterica Typhi	1 (0.1–5)	0.007 (0–0.03)	0.5 (0.05–2)	250 (50–725)	2 (0.4–5)	128 (29–361)	77 (12–203)	0.5 (0.07–1)	33 (5–87)	110 (34–272)	0.8 (0.2–2)	54 (17–133)
TOTAL	2,506 (1,455–4,168)	0.5 (0.3–0.6)	32 (24–45)	8,068 (3,294–20,663)	9 (4–17)	622 (306–1,145)	6,491 (2,630–17,528)	1 (0.6–2)	93 (45–175)	8,369 (5,723–13,318)	5 (3–8)	366 (255–538)

* Table does not include four foodborne intoxications due to *Clostridium botulinum*, *C. perfringens*, *S. aureus*, and *Bacillus cereus* due to a lack of data for global estimation.

** Includes Guillain-Barré Syndrome cases and deaths.

Discussion

To our knowledge, we estimate for the first time the substantial worldwide burden of foodborne bacterial, viral, and protozoal diseases in humans, particularly among children. Although children <5 years of age represent only 9% of the global population, we found that 43% of the disease burden from contaminated food occurred in this group. Foodborne illnesses from diarrheal and invasive non-typhoidal *S. enterica* resulted in the largest disease burden reflecting the ubiquitous nature of *Salmonella*, the severe nature of illness, and the fact that young children are commonly infected [19]. Large human disease burdens are also imposed by foodborne infections due to norovirus and typhoid. It is important to recognize that diseases with lower burden may still warrant intervention. In particular, certain foodborne diseases may represent

Table 4. Median number of foodborne illnesses, deaths, and Disability Adjusted Life Years (DALYs) by age group, with 95% uncertainty intervals, 2010.

PATHOGEN*	Age Group: <5 Years of Age			Age Group: ≥5 Years of Age			Ratio <5:≥5		
	ILLNESSES Number (95% UI)	DEATHS Number (95% UI)	DALYs Number (95% UI)	ILLNESSES Number (95% UI)	DEATHS Number (95% UI)	DALYs Number (95% UI)	ILLNESSES Ratio <5:≥5 (95% UI)	DEATHS Ratio <5:≥5 (95% UI)	DALYs Ratio <5:≥5 (95% UI)
Diarrheal Disease	**216,839,210 (148,937,428– 309,926,253)**	**91,621 (62,442– 132,707)**	**8,547,149 (5,903,945– 12,254,175)**	**327,209,075 (179,670,939– 643,705,133)**	**107,500 (69,907– 163,979)**	**7,205,002 (4,790,026– 10,747,526)**	**0.66 (0.32– 1.28)**	**0.86 (0.60– 1.16)**	**1.19 (0.86– 1.60)**
Campylobacter spp.**	47,988,357 (22,436,891– 102,663,926)	13,861 (8,754– 23,670)	1,383,499 (911,878– 2,279,897)	42,883,268 (18,350,672– 112,061,441)	7,436 (4,930– 9,974)	750,578 (540,003– 956,663)	1.11 (0.34– 3.47)	1.91 (1.21– 3.08)	1.87 (1.26– 2.92)
Cryptosporidium spp.	5,986,213 (2,569,532– 12,738,924)	1,989 (678– 5,683)	185,057 (64,847– 518,497)	2,253,036 (774,628– 8,639,265)	1,673 (638– 4,149)	104,794 (40,408– 256,055)	2.61 (0.69– 8.01)	1.23 (0.42– 2.72)	1.83 (0.65– 3.93)
Entamoeba histolytica	8,480,759 (1,593,697– 30,849,576)	896 (90– 4,852)	92,213 (15,997– 444,002)	17,828,477 (5,378,578– 50,963,825)	524 (218– 1,110)	43,984 (20,149– 85,551)	0.48 (0.08– 2.38)	1.75 (0.18– 8.71)	2.14 (0.38– 9.49)
Enteropathogenic *E. coli*	17,312,780 (6,767,766– 54,104,398)	22,156 (11,944– 37,473)	2,004,543 (1,084,856– 3,389,584)	5,458,601 (2,145,370– 16,561,005)	14,647 (7,305– 25,447)	911,012 (457,215– 1,575,768)	3.20 (0.85– 11.78)	1.52 (1.03– 2.29)	2.21 (1.52– 3.29)
Enterotoxigenic *E. coli*	38,352,806 (21,144,875– 64,795,160)	14,056 (7,045– 26,784)	1,303,490 (668,837– 2,446,758)	46,811,878 (20,306,649– 103,801,449)	11,933 (6,382– 18,887)	767,975 (419,834– 1,204,273)	0.82 (0.35– 1.96)	1.21 (0.63– 2.10)	1.74 (0.95– 2.93)
Giardia spp.	18,773,028 (8,075,497– 38,649,748)	0 (0–0)	20,677 (8,552– 44,101)	8,693,968 (3,337,657– 24,195,602)	0 (0–0)	5,016 (1,945– 13,791)	2.11 (0.84– 5.22)	N/A	4.04 (1.57– 10.28)
Norovirus	34,582,700 (19,595,826– 59,592,939)	8,992 (4,251– 19,347)	844,376 (406,822– 1,776,252)	89,056,582 (46,054,795– 206,532,318)	25,807 (11,201– 61,642)	1,638,925 (730,924– 3,844,771)	0.38 (0.19– 0.73)	0.35 (0.22– 0.54)	0.52 (0.33– 0.78)
Salmonella enterica, non-typhoidal	15,274,234 (6,514,539– 41,696,874)	12,531 (6,562– 30,779)	1,149,675 (609,216– 2,792,992)	60,293,254 (18,488,275– 189,066,838)	15,807 (8,762– 21,942)	1,016,047 (576,408– 1,405,079)	0.26 (0.06– 1.16)	0.84 (0.44– 1.83)	1.19 (0.64– 2.57)
Shigella spp.	15,516,627 (5,416,319– 38,620,351)	8,863 (3,250– 20,925)	819,280 (309,576– 1,909,450)	34,049,173 (10,186,959– 95,312,884)	6,060 (2,734– 11,511)	404,144 (188,009– 749,866)	0.45 (0.13– 1.70)	1.49 (0.60– 3.26)	2.06 (0.87– 4.43)
Shiga toxin-producing *E. coli*	339,905 (217,805– 728,708)	63 (30– 170)	6,969 (3,278– 17,751)	836,948 (536,302– 1,794,298)	65 (24– 204)	5,989 (2,654– 15,877)	0.41 (0.41– 0.41)	0.96 (0.81– 1.31)	1.16 (1.09– 1.29)
Vibrio cholerae	114,518 (46,636– 235,152)	3,697 (1,546– 7,506)	331,395 (138,538– 672,643)	648,933 (264,273– 1,332,530)	20,952 (8,758– 42,535)	1,390,973 (581,491– 2,820,499)	0.18 (0.18– 0.18)	0.18 (0.18– 0.18)	0.24 (0.24– 0.24)
Invasive enteric diseases	**4,336,215 (1,675,945– 9,422,681)**	**23,727 (11,866– 45,950)**	**2,180,916 (1,085,765– 4,219,254)**	**21,182,632 (8,375,340– 49,059,198)**	**123,026 (69,306– 230,318)**	**6,900,776 (3,799,471– 13,355,093)**	**0.21 (0.15– 0.23)**	**0.19 (0.14– 0.22)**	**0.32 (0.23– 0.35)**
Brucella spp.	4,144 (1,527– 93,225)	21 (7– 463)	1,988 (687– 44,999)	389,106 (142,279– 9,006,169)	1,936 (654– 45,081)	122,904 (42,484– 2,865,643)	0.01 (0.01– 0.01)	0.01 (0.01– 0.01)	0.02 (0.02– 0.02)
Hepatitis A	2,165,243 (573,433– 6,084,381)	4,380 (1,132– 12,211)	411,592 (112,767– 1,130,290)	11,544,593 (3,057,415– 32,440,565)	23,351 (6,036– 65,109)	941,278 (269,448– 2,538,627)	0.19 (0.19– 0.19)	0.19 (0.19– 0.19)	0.44 (0.39– 0.46)
Listeria monocytogenes	1,240 (393– 10,502)	330 (126– 2,138)	30,750 (11,700– 198,862)	12,936 (5,716– 80,766)	2,851 (1,200– 18,271)	87,569 (36,830– 561,221)	0.10 (0.07– 0.13)	0.11 (0.08– 0.16)	0.34 (0.24– 0.49)

(Continued)

Table 4. (*Continued*)

PATHOGEN*	Age Group: <5 Years of Age			Age Group: ≥5 Years of Age			Ratio <5:≥5		
	ILLNESSES Number (95% UI)	DEATHS Number (95% UI)	DALYs Number (95% UI)	ILLNESSES Number (95% UI)	DEATHS Number (95% UI)	DALYs Number (95% UI)	ILLNESSES Ratio <5:≥5 (95% UI)	DEATHS Ratio <5:≥5 (95% UI)	DALYs Ratio <5:≥5 (95% UI)
Mycobacterium bovis	869 (732–1,049)	76 (58–101)	7,134 (5,477–9,496)	120,398 (99,119–149,188)	10,470 (7,836–14,372)	600,639 (452,917–816,737)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.01 (0.01–0.01)
Salmonella enterica, invasive non-typhoidal	45,549 (25,019–62,638)	4,700 (2,268–8,188)	421,523 (203,340–733,940)	239,467 (142,115–321,539)	24,692 (12,655–42,246)	1,373,635 (684,718–2,373,326)	0.19 (0.17–0.20)	0.19 (0.17–0.20)	0.31 (0.29–0.32)
Salmonella enterica Paratyphi A	357,814 (110,286–885,942)	2,480 (778–6,067)	227,507 (71,530–557,578)	1,383,306 (426,364–3,425,041)	9,588 (3,007–23,454)	627,953 (197,302–1,541,909)	0.26 (0.26–0.26)	0.26 (0.26–0.26)	0.36 (0.36–0.36)
Salmonella enterica Typhi	1,555,715 (479,504–3,851,923)	10,783 (3,381–26,377)	989,159 (311,001–2,424,250)	6,014,372 (1,853,758–14,891,483)	41,689 (13,072–101,973)	2,730,232 (857,835–6,703,954)	0.26 (0.26–0.26)	0.26 (0.26–0.26)	0.36 (0.36–0.36)
TOTAL	**221,451,463 (153,244,508–315,075,166)**	**116,613 (80,862–165,379)**	**10,831,919 (7,587,557–15,271,603)**	**350,711,509 (199,599,319–673,777,073)**	**232,916 (152,283–368,498)**	**14,250,088 (9,419,295–22,483,691)**	**0.63 (0.32–1.18)**	**0.50 (0.36–0.68)**	**0.76 (0.56–1.01)**

* Table does not include four foodborne intoxications due to *Clostridium botulinum*, *C. perfringens*, *S. aureus*, and *Bacillus cereus* due to a lack of data for global estimation.

** Includes Guillain-Barré Syndrome cases and deaths.

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a larger problem in some regions. For example, the most substantial burden due to foodborne cholera occurs in African and Asian regions. Similarly, the burden of brucellosis and *M. bovis* infections were highest in the Middle Eastern and African regions.

To develop these comprehensive estimates of the disease burden of foodborne diseases, we adopted an innovative approach to incorporate the highest quality data available for each foodborne disease [11]. Due to their quality, we gave highest priority to studies with national estimates of foodborne diseases. Since studies with national estimates were only available in a few countries, we adapted the CHERG approach for estimating the disease burden of diarrheal diseases [10,36]. This approach was facilitated by the availability of estimates of the envelope of diarrheal deaths, along with recent advances in diarrheal disease diagnosis, such as widespread application of polymerase chain reaction (PCR) for norovirus detection [20,49].

In our study, norovirus resulted in the largest number of cases of foodborne diseases and overall burden, highlighting the global importance of this agent [20]. However, the disease model we used in the 135 middle- and high-mortality counties included only norovirus infections that resulted in a diarrheal illness. If we also included estimates for norovirus infections that resulted in vomiting without diarrhea, there would be an estimated additional 163 million norovirus cases in these countries [50]. We also found, similar to what has been reported in national studies, that in the countries where we applied the modified CHERG approach, the etiological cause of almost half of diarrheal cases and deaths remained unknown. This was likely due, in large part, to pathogens that are possibly foodborne but with insufficient data for estimation, and unknown agents not yet discovered. In this study, we focused our attention on the burden due to pathogens that were known to be transmitted by contaminated food.

When we examined the human health impact of different pathogens, various serotypes of *Salmonella* resulted in the greatest foodborne burden. If we consider the combined burden
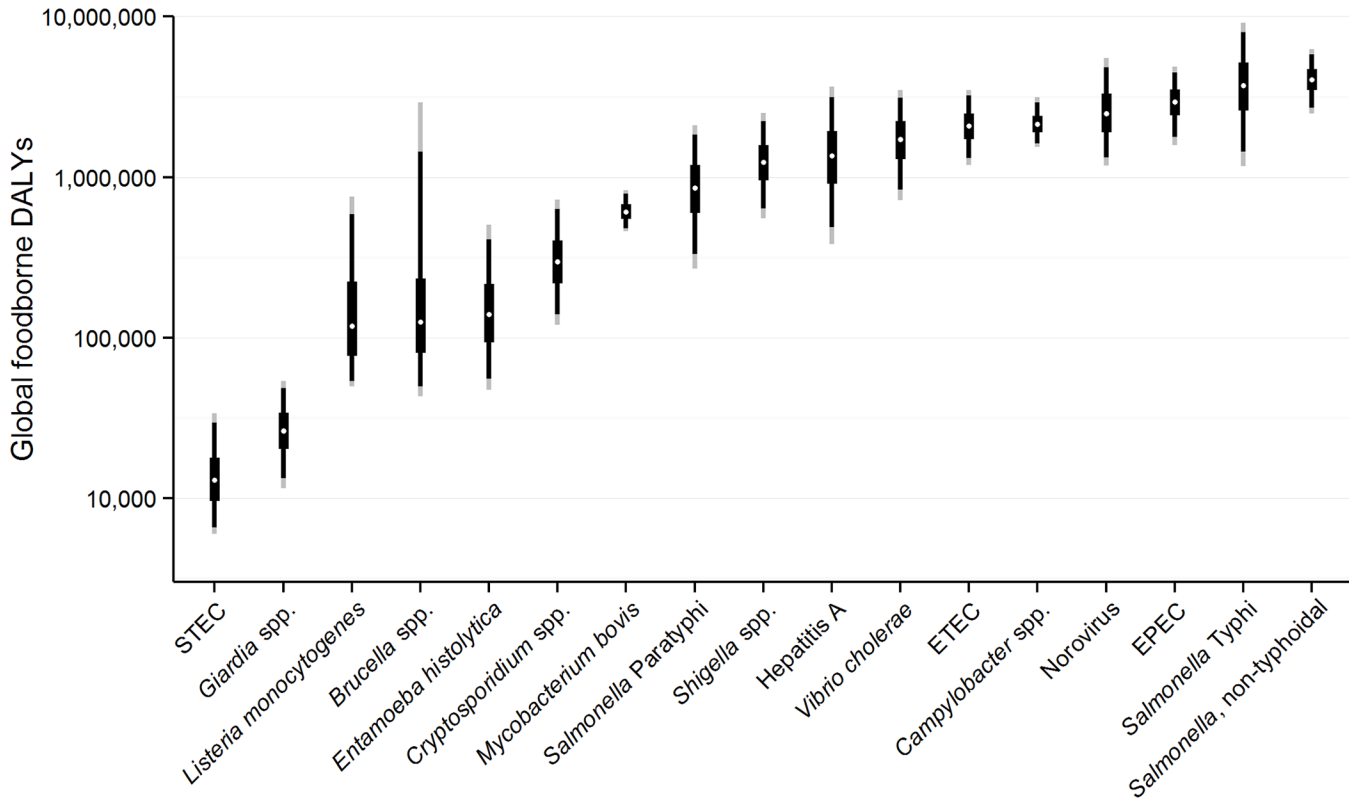
Fig 1. Disability Adjusted Life Years for each pathogen acquired from contaminated food ranked from lowest to highest with 95% Uncertainty Intervals, 2010. Note figure is on a logarithmic scale. The figure shows the median (white dot); Inter-Quartile Range = 50%UI = 25%/75% percentiles (thick black line); 90% UI = 5%/95% percentiles (thin black line); 95% UI = 2.5%/97.5% percentiles (thin grey line). Note, figure does not include four foodborne intoxications due to *Clostridium botulinum*, *C. perfringens*, *S. aureus*, and *Bacillus cereus* due to a lack of data for global estimation. In addition, data for non-typhoidal *Salmonella enterica* infections and invasive non-typhoidal *S. enterica* have been combined.

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attributable to *S. enterica* from all invasive (including iNTS, *Salmonella* Typhi and *Salmonella* Paratyphi A) and diarrheal infections, there were an estimated 8.76 million (95% UI 5.01–15.6 million) DALYs from all transmission sources and 6.43 million (95% UI 3.08–13.2 million) DALYs from contaminated food. This highlights the significant public health importance of *Salmonella* infections and the urgency of control, particularly for invasive infections in low- and middle-income settings where most of the mortality occurs [51–53].

Twelve of the diseases included in our study were also included in the GBD 2010 study [25,26,54]. For three diseases (typhoid, paratyphoid and hepatitis A) we used GBD 2010 data to derive estimates of incidence. For the other nine diarrheal diseases, we elected to conduct our own analysis or used updated data from commissioned systematic reviews to derive estimates. Our study builds upon the GBD 2010 study by providing estimates of the proportion of each disease acquired from food; we also provide, in addition to estimates of deaths, estimates of the number of illnesses for each of the diseases [26]. Before we applied our estimate of foodborne proportions to each pathogen, our estimates of the disease burden for a few pathogens, in terms of the estimated number of deaths and DALYs were relatively similar for diseases in common with GBD 2010 and FERG.

However, there were important differences in other estimates. The GBD 2010 study estimates of deaths due to *E. histolytica*, *Cryptosporidium* spp., and *Campylobacter* spp. were 10 times, 4 times and 3 times greater, respectively, than the FERG estimates [25]. The FERG

estimate for DALYs for nontyphoidal *S. enterica* combining diarrheal and invasive infections was 4 times greater than GBD 2010 [54]. The FERG estimates are relatively similar to previous global estimates of cholera, typhoid fever, salmonellosis, and shigellosis [19,24,40,55]. The GBD 2010 study estimates included 'cysts and liver abscesses' as a complication of typhoid fever, which has been questioned [56]. However, we understood this categorization to be a proxy for serious typhoid fever and incorporated these data into our estimates. The CFR for each of the diseases included in our estimate are comparable to those reported in national studies. There is a continuing need for high quality studies assessing the foodborne disease burden at the national level. Our methodology for estimating the disease burden attributable to foodborne transmission can be used in future studies.

In comparing the overall burden of our findings, the diseases we included in our study resulted in 79 million DALYs in 2010. This represent approximately 3% of the 2.49 billion DALYs reported in the GBD 2010 study [54]. The GBD 2010 study estimated that approximately 25% of DALYs globally were due to deaths and disability in children younger than 5 years of age, while we estimated that 43% of the DALYs in our study were among children <5 years of age.

There are obvious policy implications of our findings. Countries and international agencies must prioritize food safety to prevent foodborne illness, particularly among young children. The highest burden of disease due to contaminated food was in the African region, largely due to iNTS in children. The considerable regional difference in the burden of foodborne diseases suggests that current control methods exist to avoid an important proportion of the current burden. Our results should stimulate research into the epidemiology of foodborne diseases, with a view to informing prevention efforts. There is an urgent need to identify and implement effective food hygiene interventions in low- and middle-income countries.

A limitation of our estimates of the consequences for human health of foodborne diseases is that, due to data gaps particularly in middle- and high-mortality countries, we included only a few sequelae in our estimates. We did not include data on post-infectious sequelae, such as reactive arthritis and irritable bowel syndrome following foodborne infections. Studies of the burden of enteric pathogens in low-mortality countries highlight that excluding these sequelae under-represents the true burden of disease, but reliable data were not available from middle- and high-mortality countries [57]. Where we did include sequelae, there were insufficient data to account for age-specific effects. We also excluded stillbirths; this exclusion only affected disease burden estimates for *L. monocytogenes*. A recent review estimated that listeriosis, which we assume is all foodborne, causes 273 stillbirths globally annually [18].

We were unable to distinguish between the effects on health from the condition under study and that of co-morbid conditions, which is common to many studies of human health. For example, salmonellosis and *M. bovis* infections may occur as HIV co-infections. If FERG included deaths among HIV-infected persons, there would have substantial additional deaths due to invasive nontyphoidal *S. enterica* deaths, some of which could presumably be averted by improvements in food safety. For some other pathogens in our estimates, such as *L. monocytogenes* and *Cryptosporidium* spp., we were unable to account for the excess mortality due to HIV infection due to a lack of reliable data.

Another important limitation of our attempt to quantify the disease burden due of foodborne disease is the inherent difficulty in estimating the proportion of illness acquired from food [58]. We relied on a structured expert elicitation study for these estimates. We were unable to estimate differences in mode of transmission by age, despite this potentially being important. Expert elicitation studies can result in highly variable proportions attributed to food, depending on the nature of experts included in elicitation studies [59,60]. Without specific studies attributing sources of infection, it is difficult to obtain accurate estimates of

foodborne transmission, but this finding regarding the need for more attribution studies is an important outcome of our study [61]. For example, the FERG expert elicitation study estimated that 18% of norovirus was foodborne compared with 14% estimated from a recent study based on outbreak genotyping [21].

The major limitation of our study was the lack of reliable data from many regions of the world. In particular, for the most populous regions of the world we had the least data for some pathogens [10]. We tried to use the best data available and attempted to make reasoned assumptions wherever possible [8]. For some agents, such as toxin-mediated illnesses, we elected to limit our estimates to countries where diseases were endemic or where there was sufficient data. Further data on burden of enteric diseases from low- and middle-income settings, particularly high quality epidemiological data, are needed to improve our understanding of foodborne diseases [8,11].

Despite these limitations, our estimates of the disease burden due to 22 foodborne diseases should provide policy makers with information for advocacy for improved regulation and control of foodborne diseases. Of particular importance, we estimate that almost half of the burden of foodborne disease occurs in children under 5 years of age. This previously underappreciated disease burden requires greater attention from governments and resourcing to improve food safety. In our study we highlight regions where diseases, such as tuberculosis and brucellosis are still transmitted by contaminated food. Our results highlight the benefits of countries conducting national studies estimating and attributing the incidence, hospitalizations and deaths due to foodborne diseases to improve understanding of burden and improve control measures. Our regional estimates could be used to fill data gaps for countries attempting to estimate the burden of disease due to contaminated food.

Supporting Information

S1 Text. Glossary and regions.
(DOCX)

S2 Text. Information sheets for foodborne agents.
(DOCX)

Acknowledgments

Author Contributions

Conceived and designed the experiments: MDK SMP REB BD DD AF CLFW TH KHK RL CFL PRT AHH FJA. Performed the experiments: SMP JAC BD CLFW TH AJH CFL FJA. Analyzed the data: MDK SMP JAC BD CLFW TH AJH CFL FJA. Wrote the first draft of the

manuscript: FJA MDK. Contributed to the writing of the manuscript: MDK SMP REB MC JAC BD DD AF CLFW TH AJH KHK RL CFL PRT AHH FJA. Agree with the manuscript's results and conclusions: MDK SMP REB MC JAC BD DD AF CLFW TH AJH KHK RL CFL PRT AHH FJA. All authors have read, and confirm that they meet, ICMJE criteria for authorship.

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Editors' Summary

Background

Foodborne diseases are responsible for a large burden of illness (morbidity) and death (mortality) in both resource-rich and resource-poor countries. More than 200 diseases can be transmitted to people through the ingestion of food contaminated with microorganisms (bacteria, viruses, and parasites) or with chemicals. Contamination of food can occur at any stage of food production—on farms where crops are grown and animals raised, in factories where food is processed, and during food storage and preparation in shops, restaurants and the home. Contamination can arise because of pollution of the water, soil or air or through poor food-handling practices such as failing to wash one's hands before preparing food. Many foodborne diseases (for example, norovirus, *Escherichia coli*, and campylobacter infections) present with gastrointestinal symptoms—stomach cramps, diarrhea, and vomiting. However, some foodborne illnesses cause symptoms affecting other parts of the body and some have serious sequelae (abnormal bodily conditions or diseases arising from a pre-existing disease). For example, infection with some strains of *E. coli* can lead to kidney failure.

Why Was This Study Done?

Accurate regional and global estimates of the disease burden of foodborne illnesses are needed to guide governmental and international efforts to improve food safety. However, estimates of the number of cases of foodborne illness, sequelae, deaths, and disability adjusted life years (a DALY represents the disease-related loss of one year of full health because of premature death or disability; DALYs provide a measure of the burden of a disease) are only available for a few countries. Consequently, in 2007, the World Health Organization (WHO) established the Foodborne Disease Burden Epidemiology Reference Group (FERG) to estimate the global and regional burden of disease attributable to foodborne illnesses. Here, researchers involved in one of the constituent task forces of FERG—the Enteric Diseases Task Force—undertake a data synthesis (the combination of information from many different sources) to provide global and regional estimates of the disease burden of several important foodborne bacterial, protozoal (parasitic), and viral diseases.

What Did the Researchers Do and Find?

The researchers combined national estimates of foodborne diseases and data from systematic reviews (studies that identify all the research on a given topic using predefined criteria), national surveillance programs, and other sources to estimate the number of illnesses, sequelae, deaths and DALYs globally and regionally for 22 diseases with sufficient data to support such estimations. Together, these 17 bacterial infections, two viral infections, and three protozoal infections caused 2 billion cases of illness, more than 1 million deaths, and almost 80 million DALYs in 2010. Using information on the proportions of infections considered to be foodborne by expert panels, the researchers estimated that nearly a third of these cases of illness (582 million cases), resulting in 25 million DALYs, were transmitted by contaminated food. Notably, 38% of the cases of foodborne illness, 33% of deaths from these diseases, and 43% of the disease burden from contaminated food (11 million DALYs) occurred in children under 5 years old. The leading cause of foodborne illness was norovirus (125 million cases), closely followed by campylobacter (96 million);

diarrheal and invasive infections caused by non-typhoidal *Salmonella enterica* infections caused the largest burden of disease (4.07 million DALYs). Finally, the burden of foodborne illness was highest in WHO's African region.

What Do These Findings Mean?

The lack of reliable data on the 22 illnesses considered in this analysis for many regions of the world, including some of the most populous regions, and uncertainty about the proportion of the cases of each illness that is foodborne may limit the accuracy of these findings. Nevertheless, these results provide new information about the regional and global disease burden caused by foodborne illnesses. In particular, these estimates reveal an unexpectedly high disease burden caused by foodborne illnesses among young children. Thus, although children under the age of 5 years represent only 9% of the global population, nearly half of the disease burden from contaminated food may occur in this age group. Overall, the findings of this study suggest that governments and international agencies should prioritize food safety to prevent foodborne illness, particularly among young children, and highlight the need to identify effective food hygiene interventions that can be implemented in low- and middle-income countries.

Additional Information

This list of resources contains links that can be accessed when viewing the PDF on a device or via the online version of the article at http://dx.doi.org/10.1371/journal.pmed.1001921.

- The World Health Organization provides information about foodborne diseases, food safety and the estimation of the global burden of foodborne diseases (available in several languages)

- The US National Institute of Allergy and Infectious Diseases provides detailed information about several foodborne illnesses

- The US Centers for Disease Control and Prevention provides information about foodborne disease outbreaks in the US and elsewhere and information about food safety in the US

- The UK National Health Service Choices website provides information about food poisoning (another name for foodborne illness) and about food safety

- STOP Foodborne Illness STOP Foodborne Illness, a US non-profit public-health organization, provides personal stories about foodborne illness