An assessment of the human health impact of seven leading foodborne pathogens in the United States using disability adjusted life years

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SUMMARY

We explored the overall impact of foodborne disease caused by seven leading foodborne pathogens in the United States using the disability adjusted life year (DALY). We defined health states for each pathogen (acute illness and sequelae) and estimated the average annual incidence of each health state using data from public health surveillance and previously published estimates from studies in the United States, Canada and Europe. These pathogens caused about 112 000 DALYs annually due to foodborne illnesses acquired in the United States. Non-typhoidal Salmonella (32 900) and Toxoplasma (32 700) caused the most DALYs, followed by Campylobacter (22 500), norovirus (9 900), Listeria monocytogenes (8 800), Clostridium perfringens (4 000), and Escherichia coli O157 (1 200). These estimates can be used to prioritize food safety interventions. Future estimates of the burden of foodborne disease in DALYs would be improved by addressing important data gaps and by the development and validation of US-specific disability weights for foodborne diseases.

Key words: Campylobacter, foodborne infections, Salmonella.

INTRODUCTION

Foodborne diseases are an important public health problem in the United States, where each year 31 known pathogens cause an estimated 9.4 million illnesses, 56 961 hospitalizations, and 1 351 deaths through contaminated foods [1]. Of these 31 known pathogens, norovirus was estimated to cause the most foodborne illnesses, while non-typhoidal Salmonella (NTS) was the leading cause of hospitalization and death. Overall, 90% of domestically acquired foodborne illnesses, hospitalizations, and deaths caused by known pathogens were attributed to seven pathogens: Campylobacter, Clostridium perfringens, Escherichia coli O157, Listeria monocytogenes, NTS, norovirus, and Toxoplasma gondii. These foodborne infections can also result in long-term complications and sequelae, the burden of which is substantial [2, 3].
Understanding the overall human health impact of foodborne disease is important for prioritizing food safety policies and interventions. However, comparing multiple, distinct health outcomes across a range of foodborne diseases that cause a wide variety of different symptoms, complications, and long-term sequelae is challenging. The aim of this study was to explore the overall human health impact of foodborne disease caused by the seven leading foodborne pathogens in the United States using the disability adjusted life year (DALY), a measure developed by the World Health Organization that combines data on premature mortality and on morbidity from acute illness and sequelae into a single statistic summarizing years of healthy life lost [4].

METHODS
DALY
The DALY aggregates the loss of life and health due to illness compared with ‘perfect’ health, using time as the common metric [4]. Therefore, the number of DALYs for all incident cases of illness caused by a specific foodborne pathogen can be calculated by summing the number of healthy years of life lost (YLL) due to premature mortality and the number of years lost due to disability (YLD) for each health state associated with that pathogen:

\[ \text{DALY} = \text{YLL} + \text{YLD}. \]

For each health state, the YLL is calculated by multiplying the number of deaths (D) by the remaining life expectancy at the age at which death occurs in years (E):

\[ \text{YLL} = D \times E. \]

YLD is calculated, for each health state, by multiplying the number of incident cases (N) by the estimated average duration of the health state (T) by a disability weight (DW) which reflects the severity of the disease. The disability weight is measured on a scale from 0 and 1, where perfect health is the best outcome (weight = 0), and death is the most severe outcome (weight = 1):

\[ \text{YLD} = N \times T \times DW. \]

Health states
We defined health states for each pathogen (Supplementary Table S1) [2, 5–7]. The most common acute health state for Campylobacter, C. perfringens, E. coli O157, NTS, and norovirus was acute gastroenteritis, with severity ranging from mild illness (no medical care sought) to death. Sequelae included Guillain–Barré syndrome (GBS; from infection with Campylobacter), reactive arthritis (ReA; Campylobacter and NTS), post-infectious irritable bowel syndrome (PI-IBS; Campylobacter and NTS), and haemolytic uraemic syndrome (HUS) and end-stage renal disease (ESRD; E. coli O157). Important long-term sequelae were not considered to occur following infection with C. perfringens or norovirus. Two categories of infection with Listeria were considered. Health states of pregnancy-associated listeriosis included meningitis, bacteraemia, and neurological disorders, all in the neonate, as well as abortion or stillbirth, and neonatal death; health states of listeriosis not associated with pregnancy were meningitis, bacteraemia, and death. Similarly, two categories of infection with Toxoplasma were considered. Acquired toxoplasmosis was considered to result in mild or severe illness, chorioretinitis, and death. Sequelae of congenital toxoplasmosis included chorioretinitis, intracranial calcifications, hydrocephalus, and central nervous system abnormalities.

Data sources and approach
The average annual incidence of each health state was estimated using data from public health surveillance and previously published studies (Supplementary Table S2). When US data were not available, we used published studies from Europe or Canada. We used the incidence approach to estimating DALYs, in which disease burden is defined as the expected sum of current and future DALYs resulting from all incident cases of disease over a 1-year period. We assumed that all persons hospitalized would have previously sought medical care. We modelled the uncertainty in these estimates using @Risk (Palisades Corporation, USA) with probability distributions for all data inputs. When multiple data points were derived from published studies, we selected the middle value and used uniform minimum variance unbiased (UMVU) estimators to determine the minimum and maximum values. For proportions based on a single data point, we used a 50% relative increase/decrease on an odds scale to determine the minimum and maximum values. All model parameters and probability distributions are detailed in Supplementary Table S2.

Acute illness and death
For each disease, except congenital toxoplasmosis, we based our estimates of the average annual numbers of
acute illnesses, hospitalizations, and deaths on previously published estimates by Scallan et al. of foodborne illness in the United States [1]. These estimates were based on statistical models using data from 2000 to 2008 and on the 2006 US population; therefore, the reference year for these estimates should be considered circa 2006. [1]. In generating posterior distributions for the purposes of this analysis, we used the negative binomial distribution with parameters chosen to approximate the distributions in the original paper (Supplementary Table S2).

All estimated Campylobacter, C. perfringens, E. coli O157, NTS, and norovirus illnesses, hospitalizations, and deaths were assumed to include acute gastroenteritis. The same statistical models used to estimate foodborne illness in the United States [1] were used to estimate the average annual number of ill persons who sought medical care for each pathogen, with the exception of norovirus, for which we used the estimated average annual rate of emergency room and outpatient visits for norovirus in the United States [8].

We used FoodNet surveillance data from 2005 to 2008 to estimate the proportion of listeriosis that was pregnancy-associated and applied that proportion to the estimated number of cases of invasive listeriosis from Scallan et al. [1], where a pregnancy-associated case was defined as isolation of Listeria from a pregnant woman, a fetus, or an infant aged <31 days. Data from the CDC’s Listeria Initiative from 2005 to 2012 were used to estimate the proportion of pregnancy-associated illnesses that resulted in stillbirth and the proportions of live-born infants and patients with non-pregnancy-associated listeriosis who developed meningitis or bacteraemia. Meningitis and bacteraemia were defined as isolation of Listeria from cerebrospinal fluid (CSF) and blood, respectively.

For toxoplasmosis, we considered mild and severe illnesses as occurring in non-hospitalized and hospitalized persons, respectively. We estimated the annual number of cases of toxoplasmosis due to congenital infection in the United States based on an extrapolation of regional studies [9–11] and estimated the number of foodborne cases by applying the estimated proportion due to foodborne transmission [12, 13].

Sequelae

Guillain-Barré syndrome. We estimated the incidence of Campylobacter-associated GBS using European studies that linked surveillance data on laboratory-confirmed Campylobacter infections with hospital discharge registers or other medical records containing a GBS diagnosis. The rate of GBS was 20/100 000 Campylobacter cases in the UK [14], 23–30/100 000 in Sweden [15, 16], and 33/100 000 in Denmark [17]. We estimated the excess risk of GBS in Campylobacter cases by subtracting the expected rate in the US population (0-3/100 000) [18] from the estimated rate in Campylobacter cases. To estimate the number of deaths, we applied the case-fatality rate from all US GBS cases (2.2%) [18] to the estimated number of Campylobacter-associated GBS cases.

Haemolytic uremic syndrome. FoodNet data from 2000 to 2006 were used to estimate the average annual rate of E. coli O157-associated HUS [19]. We estimated the rate based on the number of HUS patients with culture-confirmed or serological evidence of E. coli O157 infection and applied it to the 2006 US population. The death rate in HUS patients was also derived from these data and applied to the estimated number of HUS cases. As post-diarrhoeal HUS cases would have been included in the estimated number of HUS cases. For the proportion of HUS cases that progressed to ERSD we used an estimate (3%) based on data from a review of HUS patient studies [20].

Post-infectious irritable bowel syndrome. Our estimate of Campylobacter and NTS-associated PI-IBS was based on a meta-analysis of case-control studies [21]. We used the weighted mean (9%) of the estimated attributable risks and applied this to the estimated number of acute gastroenteritis illnesses for each pathogen.

Reactive arthritis. We based our estimates of Campylobacter-associated ReA (7%) on a Finnish population-based study that diagnosed ReA by physical examination and compared the incidence among case-patients with matched controls [22]. The proportion of persons with salmonellosis who developed ReA (8%) was based on a review of outbreaks [23]. We applied these proportions to the estimated number of physician visits for each pathogen. We based our estimate of medical care-seeking of ReA patients (44%) on a US study [24].

Sequelae of listeriosis. Estimates of the proportion of children who developed neurological disorders following pregnancy-associated listeriosis came from a case-series review [25].
Sequelae of toxoplasmosis. Estimates of acquired toxoplasmosis-associated chorioretinitis were based on estimated rates of symptomatic retinitis in persons infected with *Toxoplasma* (0.3–0.7%) during an outbreak in Canada [26, 27]. The proportions of congenital toxoplasmosis cases that developed intracranial calcifications, CNS abnormalities, hydrocephalus, and chorioretinitis (with onset soon after birth and later in life) were based on a Dutch review of studies [5].

Disability weights

No disability weights were available from the United States for the relevant health states; therefore, we relied on disability weights from published Dutch studies (Supplementary Table S4). For acute gastroenteritis, we used Dutch disability weights generated using an annual profile method [28]. We accepted their disability weight of zero for mild gastroenteritis of 1 day or 5 days based on relevance criteria (more than 50% of their population panel was unwilling to trade time to be restored to full health).

YLL

To estimate YLL, we multiplied the estimated numbers of deaths by the population life expectancy at the age at which death occurred. The age distributions at time of death for persons with *Campylobacter*, *E. coli* O157, *Listeria*, and NTS infections were available from FoodNet surveillance from 1996 to 2012 (2000–2012 for persons with *E. coli* O157 who developed HUS) (Supplementary Table S3). YLL due to fetal and neonatal deaths were taken as the mean US life expectancy for males and females aged <1 year (78 years). For toxoplasmosis and GBS, data on age at death were obtained from the annual multiple cause-of-death data from US death certificates from 1999 to 2010. For *C. perfringens* illnesses, data on age at death were obtained from published case-series data and outbreak reports [29–31]. The number of deaths by age group for norovirus were estimated based on a published study [32]. Age-specific life expectancies were obtained from the 2006 US life tables for ages 0–99 years (Supplementary Table S3).

RESULTS

Incidence of health states

Table 1 shows the estimated annual number of acute episodes of domestically acquired foodborne illness for the five pathogens causing gastroenteritis – NTS,
Campylobacter, E. coli O157, C. perfringens, and norovirus – including the number of medical care visits, hospitalizations, and deaths. We estimated 230 cases [90% credibility interval (CrI) 80–470] of pregnancy-associated listeriosis of which 50 (90% CrI 20–90) resulted in stillbirth. Of live-born infants, we estimated 90 (90% CrI 30–170) cases developed bacteraemia, 40 (90% CrI 10–80) developed meningitis, and 10 (90% CrI 0–30) infants died. Of 1360 (90% CrI 460–2600) cases not associated with pregnancy, we estimated that 1100 (90% CrI 380–2160) developed bacteraemia, 210 (90% CrI 70–400) developed meningitis, and 250 (90% CrI 10–740) resulted in death. In addition to the 86700 (90% CrI 64600–111400) cases and 330 (90% CrI 200–480) deaths associated with acquired toxoplasmosis, we estimated 1100 (90% CrI 290–1900) foodborne congenital cases resulting in eight (90% CrI 2–20) deaths.

PI-IBS was the most common sequela from domestically acquired foodborne illness, with an estimated 89900 and 74000 cases attributed to NTS and Campylobacter, respectively (Table 2).

ReA was the second most common sequela with 18400 NTS- and 15200 Campylobacter-associated cases. We estimated almost 2700 cases of chorioretinitis from acquired (93%) and congenital (7%) toxoplasmosis.

**DALY estimates**

NTS (32900) and Toxoplasma (32700) caused the most DALYs due to domestically acquired foodborne illnesses (Table 3), followed by Campylobacter (22500), norovirus (9900), Listeria (8800), C. perfringens (4000), and E. coli O157 (1200) (Table 3). YLL was the main driver of DALYs for Listeria (98%) and E. coli O157 (64%) (Fig. 1). YLD due to sequelae accounted for most of the DALYs for Campylobacter (74%), NTS (61%), Toxoplasma (59%). Of the YLD due to sequelae from toxoplasmosis, most were due to acquired cases of chorioretinitis. YLD from acute illness was the main driver of DALYs for C. perfringens (77%) and foodborne norovirus (76%).
We assessed the overall human health impact of foodborne disease from seven leading foodborne pathogens in the United States using the DALY approach, which allowed a ranking of pathogen-specific foodborne illness risks. NTS and *Toxoplasma* infections resulted in the highest number of DALYs each year due to domestically acquired foodborne illness, followed by *Campylobacter*, *norovirus*, *Listeria*, *C. perfringens*, and *E. coli* O157.

NTS has long been an important cause of foodborne illness in the United States, and the incidence of laboratory-confirmed infections reported to public health surveillance systems has remained relatively stable for almost a decade [33]. While NTS infection has a low case-fatality ratio compared to some other foodborne infections, such as *Listeria*, the high number of illnesses results in it being the leading cause of domestically acquired foodborne deaths among known pathogens, contributing to a number of YLL second only to foodborne toxoplasmosis. Nonetheless, most DALYs for *Salmonella* infection are due to years spent with disability, specifically time lived with PI-IBS. The assumption that symptoms last for an average of 5 years [34] was an important factor contributing to the high number of YLD attributable to PI-IBS.

*Toxoplasma* infects many persons in the United States, although most infections are asymptomatic or cause a self-limited illness [35]. However, in persons with immunocompromising conditions, such as human immunodeficiency virus or organ transplant, reactivated and untreated toxoplasmosis has a high mortality rate, and most of these deaths occur in

### Table 3. Estimated disability adjusted life years (DALYs) from domestically acquired foodborne illnesses, by pathogen, including the number of years lived with disability (YLD) and the number of years of life lost (YLL) due to mortality, United States*

<table>
<thead>
<tr>
<th>Pathogen (estimated % foodborne†)</th>
<th>YLD</th>
<th>YLL</th>
<th>DALY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>90% CrI</td>
<td>Mean</td>
</tr>
<tr>
<td><em>Campylobacter</em> (80%)</td>
<td>20 100</td>
<td>8800–36 100</td>
<td>2300</td>
</tr>
<tr>
<td>Acute gastroenteritis</td>
<td>3600</td>
<td>1100–7300</td>
<td>2,200</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>960</td>
<td>220–2100</td>
<td>–</td>
</tr>
<tr>
<td>PI irritable bowel syndrome‡</td>
<td>15 500</td>
<td>5200–30 900</td>
<td>–</td>
</tr>
<tr>
<td>Guillain–Barré syndrome</td>
<td>50</td>
<td>20–110</td>
<td>100</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em> (100%)</td>
<td>3000</td>
<td>550–7200</td>
<td>900</td>
</tr>
<tr>
<td><em>Escherichia coli</em> O157 (68%)</td>
<td>430</td>
<td>280–590</td>
<td>800</td>
</tr>
<tr>
<td>Acute gastroenteritis</td>
<td>370</td>
<td>230–530</td>
<td>400</td>
</tr>
<tr>
<td>Acute cholera</td>
<td>60</td>
<td>30–100</td>
<td>400</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em> (100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy-associated</td>
<td>100</td>
<td>30–220</td>
<td>4,300</td>
</tr>
<tr>
<td>Not associated with pregnancy</td>
<td>80</td>
<td>30–150</td>
<td>4,300</td>
</tr>
<tr>
<td><em>Salmonella</em>, non-typhoidal (94%)‡</td>
<td>24 300</td>
<td>15 500–35 400</td>
<td>8600</td>
</tr>
<tr>
<td>Acute gastroenteritis</td>
<td>4200</td>
<td>3000–5700</td>
<td>8,600</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>1200</td>
<td>620–1900</td>
<td>–</td>
</tr>
<tr>
<td>PI irritable bowel syndrome</td>
<td>18 900</td>
<td>10 300–29 900</td>
<td>–</td>
</tr>
<tr>
<td><em>Norovirus</em> (26%)</td>
<td>7500</td>
<td>5700–9500</td>
<td>2400</td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em> (50%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td>3900</td>
<td>1000–6900</td>
<td>630</td>
</tr>
<tr>
<td>Acquired</td>
<td>15 900</td>
<td>8400–25 700</td>
<td>12 300</td>
</tr>
</tbody>
</table>

CrI, Credible interval; PI, post-infectious.
* Modal or mean value shown; numbers >1000 rounded to the nearest hundred, numbers from 10 to 1000 rounded to the nearest ten, numbers <10 not rounded.
† The estimated number of DALYs shown in this table are for domestically acquired foodborne illnesses only. Estimated percent foodborne from Scallan et al. [1].
‡ Includes all *S. enterica* serotypes other than Typhi.

**DISCUSSION**

We assessed the overall human health impact of foodborne disease from seven leading foodborne pathogens in the United States using the DALY approach, which allowed a ranking of pathogen-specific foodborne illness risks. NTS and *Toxoplasma* infections resulted in the highest number of DALYs each year due to domestically acquired foodborne illness, followed by *Campylobacter*, *norovirus*, *Listeria*, *C. perfringens*, and *E. coli* O157.

NTS has long been an important cause of foodborne illness in the United States, and the incidence of laboratory-confirmed infections reported to public health surveillance systems has remained relatively stable for almost a decade [33]. While NTS infection has a low case-fatality ratio compared to some other foodborne infections, such as *Listeria*, the high number of illnesses results in it being the leading cause of domestically acquired foodborne deaths among known pathogens, contributing to a number of YLL second only to foodborne toxoplasmosis. Nonetheless, most DALYs for *Salmonella* infection are due to years spent with disability, specifically time lived with PI-IBS. The assumption that symptoms last for an average of 5 years [34] was an important factor contributing to the high number of YLD attributable to PI-IBS.

*Toxoplasma* infects many persons in the United States, although most infections are asymptomatic or cause a self-limited illness [35]. However, in persons with immunocompromising conditions, such as human immunodeficiency virus or organ transplant, reactivated and untreated toxoplasmosis has a high mortality rate, and most of these deaths occur in
younger adults aged <65 years [36]. As such, premature death contributed 39% of DALYs for foodborne toxoplasmosis. We did not estimate the number of stillbirths that occurred due to congenital toxoplasmosis. Including these would have increased the number of premature deaths and the contribution of YLL to the total DALYs. The other main contributor to DALYs for foodborne toxoplasmosis is the years of life lived with chorioretinitis, an eye inflammation that can lead to severe visual impairment [27].

Public health efforts to reduce the incidence of foodborne toxoplasmosis have focused on improving meat quality and educating consumers about safe food handling [37].

The major drivers of DALYs varied by pathogen. Premature death was the most important contributor for *Listeria* and *E. coli O157*. *Listeria* has a high case-fatality rate in older adults, and pregnancy-associated cases can result in fetal loss or infant death. Most DALYs lost due to *E. coli O157* were also due to YLL, because a high proportion of the deaths are in young children. DALYs lost due to foodborne norovirus and *C. perfringens* were mostly due to the large number of acute illnesses, each contributing only a small number of YLD but summing to a substantial burden. Similar to *Salmonella*, PI-IBS was the main driver of the number of DALYs lost for foodborne campylobacteriosis. Estimates of the prevalence of IBS in the general population of developed countries range from 10% to 20% [38, 39] of which 6–18% is estimated to be post-infectious [40]. Based on our estimates, prevalent cases of *Campylobacter*- and NTS-associated PI-IBS would account for about 2% of IBS in the United States.

Other studies assessing the relative importance of foodborne pathogens in the United States have resulted in similar rankings. Using quality adjusted life years (QALYs), another measure of disease burden that includes both the quality and the quantity of life lived, and cost of illness estimates, Hoffman et al. ranked NTS as the leading contributor to QALY losses due to 14 pathogens causing foodborne illness, followed by *Campylobacter*, *Toxoplasma*, *Listeria*, norovirus, and *E. coli O157* [41], while Scharff attributed the largest economic burden to NTS followed by *Toxoplasma*, norovirus, *Listeria*, *Campylobacter*, and *E. coli O157* [42]. In both studies, *C. perfringens* was ranked eighth, below *Yersinia*, which was not included in our study. In The Netherlands, using the DALY approach, *Toxoplasma*, *Campylobacter*, *Salmonella*, and *Staphylococcus aureus* toxins were responsible for the majority of the burden associated with foodborne disease due to 14 pathogens [2]. A study in New Zealand of DALYs attributable to six pathogens transmitted commonly through food ranked *Campylobacter* highest, followed by *Listeria*, norovirus, *Salmonella*, *Yersinia*, and STEC. [3]
DALYs can vary markedly based on disability weights. For mild gastroenteritis, had we assigned the Dutch disability weight for ‘Gastroenteritis, mild, 5 days’ (0.010) rather than the weight based on relevance criteria (zero), norovirus would have ranked first rather than sixth in number of DALYs. However, had we assigned the Dutch disability weight for ‘Gastroenteritis, mild, 1 day’ (0.002), the rank order of pathogens would have remained unchanged.

These estimates have additional important limitations. There are important data gaps, especially with regard to sequelae. Therefore, we relied heavily on estimates from studies in other industrialized countries. Other possibly important sequelae for which conclusive demonstration of causality is lacking were not included in our estimates. For example, there is some evidence to suggest that inflammatory bowel disease, a term used to describe chronic intestinal diseases, primarily Crohn’s disease and ulcerative colitis, can be triggered by bacterial enteric infections [43]. Moreover, there are reports of PI-IBS associated with norovirus [44]. We based our estimates of the average annual numbers of acute norovirus illnesses, hospitalizations, and deaths on estimates published by Scallan et al. in 2011 [1]; however, subsequent CDC publications have estimated a greater number of deaths attributable to norovirus [32]. In addition, we assumed that the age at death for foodborne norovirus was the same as that for all norovirus deaths. However, outbreak surveillance suggests that foodborne norovirus illnesses often involve younger adults compared to non-foodborne norovirus illnesses which more often affect the elderly. In generating posterior distributions for the estimated number of illnesses, hospitalizations, and deaths from the original CDC estimates of domestically acquired foodborne illness [1], we used the negative binomial distribution with parameters chosen to approximate the distribution in the original paper. The mean values generated were close to, and often exactly the same as, the estimates in the original paper; however, the variance did differ from the original estimates, particularly for deaths, which were often highly skewed. Because data on disability weights are lacking for US residents, we used weights from The Netherlands, although weights may vary between countries.

The most common causes of foodborne illness in the United States have tremendous costs in terms of morbidity and mortality. DALYs are one way to quantify these effects in a manner that allows comparison across illnesses caused by pathogens with different symptoms, complications, and sequelae. These analyses can help target preventive interventions to mitigate these effects. These estimates could be improved with better data distinguishing between mild, moderate, and severe disease; estimates of premature mortality that account for the impact of co-morbidities; and US-based estimates of disease sequelae. As additional data become available and as the incidence of illness changes, these estimates can be further refined.

SUPPLEMENTARY MATERIAL

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DECLARATION OF INTEREST

None.

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