Estimate of Burden and Direct Healthcare Cost of Infectious Waterborne Disease in the United States

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Provision of safe drinking water in the United States is a great public health achievement. However, new waterborne disease challenges have emerged (e.g., aging infrastructure, chlorine-tolerant and biofilm-related pathogens, increased recreational water use). Comprehensive estimates of the health burden for all water exposure routes (ingestion, contact, inhalation) and sources (drinking, recreational, environmental) are needed. We estimated total illnesses, emergency department (ED) visits, hospitalizations, deaths, and direct healthcare costs for 17 waterborne infectious diseases. About 7.15 million waterborne illnesses occur annually (95% credible interval [CrI] 3.88 million–12.0 million), results in 601,000 ED visits (95% CrI 364,000–866,000), 118,000 hospitalizations (95% CrI 86,800–150,000), and 6,630 deaths (95% CrI 4,520–8,870) and incurring US $3.33 billion (95% CrI 1.37 billion–8.77 billion) in direct healthcare costs. Otitis externa and norovirus infection were the most common illnesses. Most hospitalizations and deaths were caused by biofilm-associated pathogens (nontuberculous mycobacteria, *Pseudomonas*, *Legionella*), costing US $2.39 billion annually.

At the beginning of the 20th century, diseases commonly transmitted by water, such as cholera and typhoid, were major causes of death in the United States (*1*). Reliable provision of treated, safe drinking water dramatically reduced the burden of these diseases and has been recognized as one of the greatest public health achievements of the 20th century (*2*). Despite this achievement, waterborne disease in the United States persists (*3*–*5*).

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In the United States, outbreaks associated with large public drinking water systems have sharply declined in the past 40 years (*3*,*6*), likely the result of improvements in regulation and operation. However, transmission of disease via drinking water systems still occurs, often attributable to aging infrastructure, operational challenges, and the private or unregulated water systems (e.g., private wells) that serve an estimated 43 million persons (*7*). At the same time, the complexity and scope of water use has increased; drinking, sanitation, hygiene, cooling, and heating needs are supported by 6 million miles of plumbing inside US buildings (i.e., premise plumbing) (*8*,*9*). Premise plumbing water quality can be compromised by long water residency times, reduced disinfectant levels, and inadequate hot water temperatures, creating environments where pathogens (e.g., nontuberculous mycobacteria [NTM], *Pseudomonas*, and *Legionella*) can amplify in biofilms (*10*). People can be exposed to these pathogens through contact, ingestion, or inhalation of aerosols (e.g., from showerheads, building cooling towers, or decorative fountains).

As leisure time has increased, swimming pools, waterparks, water playgrounds, and hot tubs have proliferated (*5*). These venues rely largely on chlorination as the major barrier against disease transmission. *Cryptosporidium* has emerged as the major cause of outbreaks associated with treated aquatic venues because it is extremely chlorine resistant and has a low infectious dose (*5*,*11*,*12*). Warmer oceans have led to *Vibrio*-associated wound infections farther north than previously documented (*13*).

Estimates of the overall burden of foodborne disease in the United States, including both known and unknown agents, have been useful in directing prevention

activities and setting public health goals (*14*,*15*). Quantifying the burden of infectious waterborne disease in the United States would also be beneficial.

Previous studies have attempted to estimate the burden of gastrointestinal illness (*16*,*17*) or all illness associated with drinking water (*18*) and untreated recreational water (*19*) in the United States, but the burden of disease from all water sources (drinking, recreational, environmental) and exposure routes (ingestion, contact, inhalation) has not been estimated. We present an estimate of the burden of waterborne disease in the United States that includes gastrointestinal, respiratory, and systemic disease; accounts for underdiagnosis; and includes all water sources and exposure routes.

Methods

We defined waterborne disease as disease in which water was the proximate vehicle for exposure to an infectious pathogen. Thus, diseases such as Legionnaires' disease (typically transmitted via inhaled water droplets containing *Legionella* bacteria) were considered waterborne. In contrast, arboviral diseases like malaria, for which standing water can increase the population of mosquitoes that transmit the parasite that causes malaria, were not considered waterborne. Algal toxins and chemical exposures were not considered. We determined the proportion of disease totals that were attributed to domestic waterborne exposure.

For this estimate, we chose diseases for which surveillance data, administrative data, or literature reports indicated that waterborne transmission for the disease in the United States was plausible, the disease was likely to cause substantial illness or death, and data were available to quantify associated health outcomes. Diseases included in this analysis were campylobacteriosis, cryptosporidiosis, giardiasis, Legionnaires' disease, NTM infection, norovirus infection, acute otitis externa, *Pseudomonas* pneumonia and septicemia, Shiga toxin–producing *Escherichia coli* (STEC) infection serotype O157, non-O157 serotype STEC infection, salmonellosis, shigellosis, and vibriosis (including infection by *Vibrio alginolyticus*, *V. parahaemolyticus*, *V. vulnificus*, and other species). To aid in quantifying the burden of respiratory diseases and enteric disease separately, we considered Legionnaires' disease, NTM infection, and *Pseudomonas* pneumonia primarily respiratory diseases, whereas we considered campylobacteriosis, cryptosporidiosis, giardiasis, norovirus infection, salmonellosis, and shigellosis primarily enteric diseases.

We employed methods similar to those of Scallan et al. (*14*,*15*) to estimate the number of illnesses, treat-and-release emergency department (ED) visits (i.e., visits in which the person was not admitted to the hospital), hospitalizations, and deaths attributed to waterborne transmission in the United States. We also quantified the direct healthcare costs of treat-and-release ED visits and hospitalizations, as measured by insurer and out-of-pocket payments. Our overall methods are described here; detailed methods are described in Appendices 1–3 (https://wwwnc.cdc.gov/EID/article/27/1/19-0676-App1.pdf; https://wwwnc.cdc.gov/EID/article/ 27/1/19-0676-App2.pdf; https://wwwnc.cdc.gov/EID/ article/27/1/19-0676-App3.pdf).

Data were for 2000–2015. All estimates were based on the 2014 US population (318.6 million persons); 2014 was the most recent year for which data were available for all surveillance sources. Estimates were derived from statistical models; each model input had uncertainty represented by a distribution of plausible values. Inputs are described in Appendix 1 and more details on the modeling process are described in Appendix 2. All estimates were rounded to 3 significant figures.

Illnesses

The initial model input was the number of reported or documented cases of illness for each disease, selected hierarchically: data from active surveillance systems were preferred, passive surveillance data were used if active surveillance data were not available, and administrative data were used if no active or passive surveillance system for the disease existed (Table 1). Administrative data sources included the Health Care Utilization Project (HCUP) National Inpatient Sample (HCUP NIS) hospitalization database, the HCUP National Emergency Department Sample (HCUP NEDS) ED visit database, and, in the case of otitis externa, the National Ambulatory Medical Care Survey (NAMCS), which surveys visits to physicians' offices. These administrative data sources use complex sample survey weighting methods and are considered nationally representative. We multiplied the initial reported or documented number of cases for each disease by a series of multipliers that accounted for underreporting and underdiagnosis (including illness severity, medical care-seeking, likelihood of specimen submission, proportion of laboratories capable of performing a diagnostic test, and test sensitivity).

Emergency Department Visits

The surveillance systems used do not tally treat-and-release ED visits but do capture the proportion of patients hospitalized with a given disease; we combined this proportion with the ratio of treat-and-release ED visits for each disease (reported in HCUP NEDS) to hospitalizations for that disease (in HCUP NIS) to calculate the estimated proportion of reported cases

Table 1. Data sources used to estimate the total number of illnesses for selected infectious diseases, United States*

Active surveillance data (name of surveillance system)	Passive surveillance data	Administrative data
Campylobacteriosis (FoodNet)	Giardiasis (NNDSS)	NTM infection (HCUP NEDS/NIS)
Cryptosporidiosis (FoodNet)	Legionnaires' disease (NNDSS)	Otitis externa (NAMCS, HCUP NEDS/NIS)
Norovirus (*20*,*21*)	*Vibrio* spp. infection (COVIS)	*Pseudomonas* pneumonia (HCUP NEDS/NIS)
Salmonellosis, nontyphoidal (FoodNet)	*Vibrio alginolyticus* infection (COVIS)	*Pseudomonas* septicemia (HCUP NEDS/NIS)
STEC infection, O157 (FoodNet)	*Vibrio parahaemolyticus* infection (COVIS)	
STEC infection, non-O157 (FoodNet)	*Vibrio vulnificus* infection (COVIS)	
Shigellosis (FoodNet)	Other *Vibrio* infection (COVIS)	

*COVIS, Cholera and Other Vibrio Illness Surveillance; FoodNet, Foodborne Diseases Active Surveillance Network; HCUP NEDS/NIS, Healthcare Cost and Utilization Project's National Emergency Department Sample and National Inpatient Sample; NAMCS, National Ambulatory Medical Care Survey; NNDSS, National Notifiable Diseases Surveillance System; NTM, nontuberculous mycobacterial; STEC, Shiga toxin–producing *Escherichia coli*.

with an ED visit. Although not all patients who visited the ED would have been reported or received a diagnosis, they were assumed to be more likely to receive a diagnosis than patients without an ED visit. Instead of applying the higher underdiagnosis factor used for illness, we used an underdiagnosis factor with a modal value of 2, consistent with previous estimates, and supported by a recent analysis comparing the incidence of bacterial gastroenteritis captured in surveillance and hospital discharge data (*14*,*22*,*23*).

Hospitalizations

We applied the proportion of patients hospitalized according to surveillance data to the estimated number of reported cases to calculate the estimated number of reported hospitalized patients. If surveillance data were not available, the number of hospitalizations reported in HCUP NIS for a particular disease was used. Hospitalized case-patients were assumed to be more likely to have received a diagnosis than nonhospitalized case-patients. Instead of applying the higher underdiagnosis factor used for illness, we used an underdiagnosis factor with a modal value of 2, consistent with previous estimates, and, for some bacterial enteric diseases, supported by recent work (*14*,*22*,*23*).

Deaths

We applied the proportion of case-patients who died, as reported by surveillance data, to the estimated number of reported cases to calculate the estimated number of reported deaths. If surveillance data were not available, we used the method of Gargano et al. (*24*). In brief, we combined the number of in-hospital deaths for each disease reported in HCUP NIS with the number of out-of-hospital deaths reported in death certificate records. We assumed that patients who died were more likely have received a diagnosis than patients who did not die. Instead of applying the higher underdiagnosis factor used for illness, we used an underdiagnosis factor with a modal value of 2, consistent with previous estimates (*14*,*22*).

Domestically Acquired Waterborne Disease

We used surveillance data, when available, to determine the proportion of persons with a given disease who traveled outside the United States during the incubation period. The remaining proportion of cases was considered domestically acquired. When this information was not available, we used literature estimates and expert consultation. We used recent attribution estimates for each disease (*25*; E.M. Beshearse, unpub. data), derived through structured expert judgment (SEJ), a formal process that answers questions for which data are sparse using expert opinions (*26*,*27*), to determine the proportion of disease attributable to waterborne transmission.

Uncertainty Estimates

For each input and multiplier in the model, we used a distribution that accounted for low, high, and midpoint estimates. This distribution accounted for the uncertainty in each input and multiplier and facilitated calculation of uncertainty intervals for final estimates. For diseases with surveillance data available, we used the methods of Scallan et al. to produce model inputs (*14*). For diseases with administrative data only (e.g., NTM infection and *Pseudomonas* pneumonia and septicemia), we used the mean hospitalization count from HCUP NIS and computed the illness count as the ratio of hospitalization count to hospitalization rate. We assumed the distribution of the hospitalization count to be normal, with the SD calculated from the reported 95% CI. As we did with surveillance data, we included the variation of hospitalization count over time in the model and assumed that the distribution for each multiplier followed the 4-parameter Program Evaluation and Review Technique (PERT) distribution (*28*), with disease-specific parameter values based on available publications.

Uncertainty in the final estimates is a cumulative effect of the uncertainty of each model input. Each multiplier was generated independently. Using 100,000 iterations, we obtained distributions of counts and used them to generate point estimates of means

and the corresponding 95% credible interval (CrI, the 2.5th percentile through the 97.5th percentile of the empirical distribution). We generated all-disease totals for each outcome by sampling from the distributions generated for each individual disease, using SAS 9.4 (https://www.sas.com) and R 3.5.1 (*29*).

Direct Healthcare Cost per ED Visit and Hospitalization

We used methods described previously (*30*,*31*) to calculate the direct cost of healthcare for ED visits and hospitalizations, using the 2012–2013 MarketScan research databases (IBM Watson Health, https://www.ibm.com/watson-health). These databases contain deidentified insurance billing data for tens of millions of persons covered by private, Medicare (which covers primarily persons ≥65 years of age), and Medicaid (which covers primarily persons with low incomes or disabilities) health insurance plans and contain information on insurance and out-of-pocket payments for hospitalizations, ED visits, doctors' office visits, laboratory testing, and outpatient drug prescriptions. We used these data to calculate the sum of insurer and out-of-pocket payments per hospitalization or visit, by insurance source. We calculated a weighted cost per hospitalization or visit by multiplying the mean total payments for each insurance source by the proportion of cases with the insurance source in HCUP NIS or HCUP NEDS. We assumed that persons with other sources of health insurance (e.g., Tricare, the US military health insurance plan) or no health insurance have the same costs as persons with private insurance. For ED visit costs, we used the data described by Adam et al. (*30*), except for norovirus infection (not examined by Adam et al.) and STEC O157 and non-O157 (categorized differently by Adam et al.) (Appendix 1).

Total Direct Health Care Costs of Domestically Acquired Waterborne Hospitalizations and ED Visits

We estimated the total direct healthcare cost of ED visits and hospitalizations attributed to waterborne transmission in the United States using the total number of ED visits and hospitalizations attributed to waterborne transmission in the United States. We multiplied these figures by the weighted average cost per ED visit or hospitalization, using 100,000 iterations, with uncertainty distributions as described (Appendix 1).

Results

Illnesses

We estimate that 33,600,000 (95% CrI 23,500,000–48,000,000) illnesses from the diseases in this analysis occurred in 2014, and of those, 7,150,000 (95% CrI 3,880,000–12,000,000; 21.3%) were attributed to waterborne transmission in the United States (Table 2). The diseases that caused the greatest number of domestically acquired waterborne illnesses were otitis externa (4,670,000 illnesses; 95% CrI 2,350,000–7,290,000) and norovirus infection (1,330,000 illnesses; 95% Cr 5,310–5,510,000), followed by giardiasis (415,000 illnesses; 95% CrI 140,000–816,000) and cryptosporidiosis (322,000 illnesses; 95% CrI 61,700–993,000). An estimated 96,000 domestically acquired waterborne respiratory illnesses occurred, and 2,330,000 domestically acquired waterborne enteric illnesses occurred.

Emergency Department Visits

An estimated 601,000 (95% CrI 364,000–866,000) treat-and-release emergency department visits for the included diseases were attributed to waterborne transmission in the United States in 2014 (Table 3). Otitis externa caused the largest number of visits (567,000; 95% CrI 337,000–823,000).

Hospitalizations

We estimate that these diseases were responsible for 118,000 (95% CrI 86,800–150,000) hospitalizations attributed to waterborne transmission in the United States (Table 3). The diseases with the largest number of hospitalizations were NTM infection (51,400 hospitalizations; 95% CrI 26,800–74,100), otitis externa (23,200 hospitalizations; 95% CrI 13,900–33,600), and *Pseudomonas* pneumonia (15,500 hospitalizations; 95% CrI 4,130–28,100). An estimated 77,700 respiratory hospitalizations were attributed to waterborne transmission, and 10,900 enteric hospitalizations were attributed to waterborne transmission.

Deaths

The diseases examined in this analysis were responsible for 6,630 deaths (95% CrI 4,520–8,870) attributed to waterborne transmission in the United States in 2014 (Table 3). The diseases with the largest number of deaths attributed to waterborne transmission in the United States were NTM infection (3,800, 95% CrI 1,950–5,620), Legionnaires' disease (995, 95% CrI 655–1,310), and *Pseudomonas* pneumonia (730, 95% CrI 185–1,460). An estimated 5,530 deaths from respiratory disease were attributed to waterborne transmission (83% of all domestically acquired waterborne deaths), and 131 deaths from enteric diseases were attributed to waterborne transmission.

Direct Healthcare Costs of ED Visits and Hospitalizations

Pseudomonas septicemia had the highest cost per hospital stay ($38,200; 95% CrI $6,340–$172,000), followed by Legionnaires' disease ($37,300, CrI $7,950–$149,000) (Table 4). Payments for ED visits and hospitalizations attributed to waterborne transmission in the United States totaled US $3.33 billion (95% CrI $1.37–$8.77 billion) in 2014 dollars (Table 5). This amount included $1.33 billion (95% CrI $361 million–$4.44 billion) in commercial insurer payments, $1.52 billion (95% CrI $338 million–$5.84 billion) in Medicare payments, and $284 million (95% CrI $62.7 million–$906 million) in Medicaid payments (Appendix 3 Tables 1–3). The costliest diseases were NTM infection ($1.53 billion; 95% CrI $272 million–$6.38 billion), otitis externa ($564 million; 95% CrI $187 million–$1.57 billion), and *Pseudomonas* pneumonia ($453 million; 95% CrI $49.9 million–$1.95 billion). An estimated $2.39 billion in direct healthcare costs from domestically acquired waterborne respiratory disease were incurred (72% of all costs from domestically acquired waterborne disease), as were $160 million in direct healthcare costs from domestically acquired waterborne enteric diseases.

Table 2. Estimated number of total cases of domestically acquired waterborne illness in 2014 for selected infectious diseases, United States*

Disease or syndrome	Estimated confirmed cases	Multipliers: Under-reporting	Multipliers: Under-diagnosis	Estimated total cases (95% CrI)	International travel, %	Waterborne, % (95% CrI)	Domestically acquired waterborne, no. (95% CrI)
Campylobacteriosis	54,000	1.0	28.3	1,540,000 (597,000–3,250,000)	14.4	13 (1–31)	171,000 (13,900–586,000)
Cryptosporidiosis	8,450	1.0	97.3	823,000 (243,000–2,160,000)	9.9	43 (17–73)	322,000 (61,700–993,000)
Giardiasis	17,900	1.30	45.9	1,070,000 (727,000–1,560,000)	12.3	44 (16–78)	415,000 (140,000–816,000)
Legionnaires' disease	5,030	1.0	2.3	11,400 (8,920–13,600)	1.0	97 (67–100)	11,000 (7,430–13,300)
NTM infection	25,700	1.0	3.8	97,000 (75,700–122,000)	1.0	72 (39–94)	68,900 (35,800–100,000)
Norovirus	NA	1.0	NA	21,800,000 (12,100,000–36,000,000)	1.1	6 (0–25)	1,330,000 (5,310–5,510,000)
Otitis externa†	1,720,000	1.0	3.4	5,980,000 (3,200,000–8,880,000)	1.3	79 (67–95)†	4,670,000 (2,350,000–7,290,000)
Pseudomonas pneumonia	15,800	1.0	2.0	31,700 (19,300–46,000)	1.0	51 (14–80)	15,900 (4,240–29,000)
Pseudomonas septicemia	13,000	1.0	2.0	26,100 (16,700–35,900)	1.0	22 (3–53)	5,760 (743–14,400)
Salmonellosis, nontyphoidal	46,400	1.0	29.1	1,350,000 (733,000–2,450,000)	9.7	6 (0–22)	77,000 (5,640–277,000)
STEC infection, serotype O157	3,530	1.0	18.2	64,200 (13,000–188,000)	4.0	5 (1–13)	3,360 (336–12,900)
STEC infection, serotype non-O157	4,550	1.0	48.1	219,000 (80,000–493,000)	15.3	6 (0–17)	11,400 (0–43,900)
Shigellosis	13,600	1.0	33.1	449,000 (97,800–1,350,000)	7.8	4 (1–21)	17,300 (1,080–77,500)
Vibrio spp. infection	1,230	NA	NA	172,000 (126,000–231,000)	NA	NA	34,600 (17,600–56,900)
V. alginolyticus	234	1.1	142.8	36,700 (23,600–54,800)	6.5	37 (13–71)	12,700 (4,100–25,400)
V. parahaemolyticus	593	1.1	141.6	92,400 (55,000–144,000)	6.7	24 (7–38)	20,800 (6,000–39,000)
V. vulnificus	133	1.1	1.7	249 (178–340)	1.5	77 (40–91)	188 (93–277)
Other *Vibrio*	271	1.1	142.8	42,600 (25,500–66,500)	14.4	2 (0–23)	879 (3–8,490)
Total illness	NA	NA	NA	33,600,000 (23,500,000–48,000,000)	NA	NA	7,150,000 (3,880,000–12,000,000)

*Estimates rounded to 3 significant figures. CrI, credible interval; NA, not applicable; NTM, nontuberculous mycobacteria; STEC, Shiga toxin–producing *Escherichia coli*.

†Combines the waterborne source attribution (*25*) for *Pseudomonas* spp. otitis externa (81%) and *Staphylococcus aureus* (75%) in a ratio of 2:1. More details provided in Appendix 1 (https://wwwnc.cdc.gov/EID/article/27/1/19-0676-App1.pdf).

Table 3. Estimated number of treat-and-release emergency department visits, hospitalizations, and deaths from domestically acquired waterborne transmission in 2014 for selected infectious diseases, United States*

	Treat-and-release ED visits†		Hospitalizations			Deaths		
Disease or syndrome	Total visits (95% CrI)	Domestic waterborne visits (95% CrI)	% Admitted to hospital	Total stays (95% CrI)	Domestic waterborne stays (95% CrI)	% Deaths	Total deaths (95% CrI)	Domestic waterborne deaths (95% CrI)
Campylobacteriosis	2,900 (1,620–4,630)	319 (31–966)	19.5	19,300 (8,790–34,900)	2,150 (192–6,900)	0.2	242 (0–1,150)	27 (0–146)
Cryptosporidiosis	1,260 (742–1,880)	492 (167–957)	19.2	2,870 (439–8,060)	1,120 (102–3,550)	0.3	61 (0–320)	24 (0–136)
Giardiasis	1,460 (902–2,090)	567 (185–1,120)	7.9	2,830 (1,760–4,070)	1,100 (364–2,180)	<0.1	4 (0–11)	1 (0–5)
Legionnaires' disease	691 (316–1,220)	667 (289–1,200)	98.1	11,200 (8,750–13,300)	10,800 (7,280–13,100)	9.0	1,030 (762–1,330)	995 (655–1,310)
NTM infection	7,150 (5,110–9,620)	5,080 (2,560–7,750)	74.8	72,400 (57,300–89,700)	51,400 (26,800–74,100)	5.5	5,350 (4,020–6,920)	3,800 (1,950–5,620)
Norovirus	429,000‡ (318,000–605,000)	26,300‡ (105–106,000)	0.4	78,100 (58,500–104,000)	4,780 (19–19,300)	<0.1	885 (742–1,120)	54 (0–219)
Otitis externa	726,000 (466,000–994,000)	567,000 (337,000–823,000)	0.9	29,700 (19,200–40,600)	23,200 (13,900–33,600)	<0.1	280 (144–452)	219 (107–367)
Pseudomonas pneumonia	580 (321–902)	291 (75–552)	97.2	30,800 (18,700–44,700)	15,500 (4,130–28,100)	4.6	1,450 (786–2,420)	730 (185–1,460)
Pseudomonas septicemia	164 (36–326)	36 (2–106)	97.2	25,300 (16,300–34,800)	5,590 (722–14,000)	12.1	3,140 (1,990–4,430)	695 (89–1,740)
Salmonellosis, nontyphoidal	3,410 (2,100–4,900)	194 (15–671)	28.4	26,600 (11,400–52,800)	1,520 (100–5,660)	0.5	421 (0–1,140)	24 (0–103)
STEC infection, serotype O157	252 (92–465)	12 (2–35)	38.5	2,640 (487–7,630)	138 (14–503)	0.7	36 (0–314)	2 (0–17)
STEC infection, serotype non-O157	75 (12–171)	4 (0–16)	16.0	1,420 (264–3,810)	74 (0–308)	0.2	16 (0–184)	1 (0–12)
Shigellosis	1,650 (540–2,870)	64 (5–311)	24.4	6,380 (929–20,300)	245 (12–1,140)	0.1	26 (0–218)	1 (0–9)
Vibrio spp. infection	366 (122–700)	76 (14–166)	NA	782 (567–1,030)	251 (153–362)	NA	113 (67–156)	60 (27–92)
V. alginolyticus	NA§	NA§	15.9	74 (38–141)	26 (8–58)	0.8	4 (0–11)	1 (0–5)
V. parahaemolyticus	NA§	NA§	22.3	264 (136–410)	60 (16–112)	1.4	16 (7–32)	4 (1–9)
V. vulnificus	NA§	NA‡	85.4	213 (147–297)	161 (79–241)	28.8	72 (38–104)	54 (24–85)
Other *Vibrio*	NA§	NA§	42.5	231 (134–350)	5 (0–46)	3.8	20 (11–33)	0 (0–4)
Total	1,180,000 (877,000–1,490,000)	601,000 (364,000–866,000)	NA	310,000 (263,000–360,000)	118,000 (86,800–150,000)	NA	13,100 (10,600–15,900)	6,630 (4,520–8,870)

*Estimates rounded to 3 significant figures. CrI, credible interval; ED, emergency department; NA, not applicable; NTM, nontuberculous mycobacterial; STEC, Shiga toxin–producing *Escherichia coli*.
†Treat-and-release ED visits were defined as visits in which the person was not admitted to the hospital.
‡For norovirus infection only, ED visits in which the person was admitted to the hospital were included, for consistency with previous published estimates.
§No International Classification of Diseases, 9th Revision, Clinical Modification, codes are available for *Vibrio* spp. infections, only a general code for "Vibriosis and cholera." ED visit estimates relied on administrative data that used these codes, and thus are presented only for *Vibrio* infection overall.

Discussion

Domestic waterborne transmission of 17 diseases in the United States caused ≈7.15 million (95% CrI 3.88–12.0 million) waterborne illnesses to occur annually during the study period, including 601,000 ED visits (95% CrI 364,000–866,000), 118,000 hospitalizations (95% CrI 86,800–150,000), and 6,630 deaths (95% CrI 4,520–8,870), and incurred $3.33 billion (95% CrI $1.31–$8.71 billion) in hospitalization and ED visit costs. This estimate includes drinking,

recreational, and environmental water exposures. Although the risk of illness from enteric pathogens readily controlled by water treatment processes still exists, this analysis highlights the expanding role of environmental pathogens (e.g., mycobacteria, *Pseudomonas*, *Legionella*) that can grow in drinking water distribution systems; plumbing in hospitals, homes, and other buildings; recreational water venues; and industrial water systems (e.g., cooling towers). This snapshot of waterborne disease transmission in the United States circa 2014 contrasts with historical waterborne disease transmission before the implementation of drinking water treatment and sanitation systems (e.g., cholera, typhoid fever, and other enteric pathogens) (*1*).

Few comparable waterborne disease burden estimates exist for the United States or other high-income countries. The World Health Organization (WHO) has estimated water, sanitation, and hygiene-related disease and injury (i.e., diarrhea, drowning, malnutrition) (*32*). WHO's estimated 6,600 annual US deaths from nondiarrheal infectious diseases is within the range of our estimate, although the infectious diseases included were not specified, making direct comparison difficult. Work from Australia used the WHO estimates to calculate the waterborne burden of 5 enteric pathogens, whereas estimates from Canada assessed the burden of AGI from drinking water and the burden of 5 enteric pathogens from private wells and small water systems (*33*–*35*). Work in Europe estimated the proportion of 9 primarily enteric diseases attributable to water (*36*). Prior estimates of the burden of waterborne disease in the United States focused on the burden of gastrointestinal illness associated with drinking water and an estimated 4–32 million cases of illness each year (*16*–*18*). Our estimate differs from previous work because it focuses on specific pathogens, includes nongastrointestinal diseases, and considers all waterborne exposure routes.

A previous estimate of foodborne disease found fewer illness, hospitalizations, and deaths from foodborne disease due to known pathogens (*14*), although it found more illness when unspecified agents were considered (*15*). For pathogens included in both estimates, underdiagnosis multipliers did not differ substantially, except for decreases in STEC multipliers because of improved laboratory capacity. The higher totals in this analysis reflect the diseases selected for inclusion, some of which cause severe respiratory diseases more likely to result in hospitalization and death than the diseases with primarily enteric effects that were included in the foodborne estimate. When estimates for the enteric pathogens included in both analyses are compared, the waterborne burden is lower than the foodborne burden. This difference could be because drinking and treated recreational water systems were designed to prevent enteric illness, and the intervention (disinfection) is relatively simple compared with the manifold interventions needed to prevent foodborne illness.

This work is subject to several limitations. First, we used a series of multipliers to generate estimates of

Table 4. Cost per hospital stay for selected diseases that can be transmitted by water, 2012–2013 IBM MarketScan health insurance databases, United States*

	Cost in 2014 US dollars (95% CrI)			
Disease/syndrome	Commercial insurance	Medicare	Medicaid	Overall
Campylobacteriosis	15,200 (1,520–47,100)	15,100 (1,630–55,300)	5,900 (85–29,000)	13,600 (3,850–35,800)
Cryptosporidiosis	17,900 (1,560–82,700)	17,300 (1,800–79,400)	10,700 (22–64,200)	16,100 (4,360–55,400)
Giardiasis	25,300 (1,790–168,000)	22,300 (1,890–96,900)	14,300 (159–88,000)	21,800 (6,160–99,200)
Legionnaires' disease	45,900 (2,320–306,000)	33,600 (4,210–183,000)	18,700 (17–99,300)	37,100 (7,950–149,000)
NTM infection	44,100 (1,650–244,000)	27,600 (1,720–152,000)	14,800 (49–69,100)	29,600 (6,350–120,000)
Norovirus infection†				6,080
Otitis externa	13,800 (1,480–56,500)	14,400 (1,490–65,100)	6,680 (43–36,900)	12,200 (3,320–42,400)
Pseudomonas pneumonia	45,100 (1,510–193,000)	28,200 (1,890–146,000)	11,600 (18–53,200)	29,300 (5,910–114,000)
Pseudomonas septicemia	63,600 (1,450–386,000)	34,400 (2,200–181,000)	19,800 (47–113,000)	38,200 (6,340–172,000)
Salmonellosis, nontyphoidal	17,200 (2,010–73,600)	17,100 (1,400–62,700)	6,940 (70–26,300)	14,900 (4,300–46,900)
STEC infection, serotype O157	25,900 (2,410–150,000)	17,200 (1,860–82,200)	4,530 (3–30,200)	19,000 (3,790–85,000)
STEC infection, serotype non-O157	23,600 (1,390–95,700)	31,900 (2,620–250,000)	5,020 (458–32,000)	24,200 (4,780–138,000)
Shigellosis	19,000 (2,910–85,300)	13,500 (1,610–39,600)	7,710 (37–51,300)	14,200 (4,130–48,000)
Vibrio spp. infection	17,400 (2,260–50,500)	18,400 (0,977–78,700)	4,600 (13–46,000)	16,000 (3,780–39,900)

*Estimates rounded to 3 significant figures. Overall cost calculated using the sum of insurer and out-of-pocket payments per stay for each payment source multiplied by the proportion of persons in the Health Care Utilization Project's Nationwide Inpatient Sample with each payment source, for the corresponding disease or syndrome. This produces a weighted average cost per stay that reflects the differing proportion of payment sources for each disease or syndrome. Persons who had a payment source other than commercial insurance, Medicare, or Medicaid (i.e., persons covered by Tricare (the healthcare plan for persons affiliated with the US armed services, who were uninsured, or who had an unknown source of insurance) were assumed to have a cost per stay equivalent to the commercial insurance cost per stay. NTM, nontuberculous mycobacterial; STEC, Shiga toxin–producing *Escherichia coli*.

†Norovirus costs were derived from previously published estimates that did not specify cost per insurance source or include uncertainty intervals.

disease, and accuracy of these estimates relies on the accuracy of the multipliers. Although we attempted to account for the uncertainty of each data point using uncertainty intervals, any systematic errors in multipliers will produce a biased estimate. For example, waterborne transmission is not the sole route of transmission for any of the diseases in this work; many of the included diseases can be transmitted through multiple pathways (e.g., cryptosporidiosis can be waterborne, foodborne, or transmitted directly from animals or humans). We also relied on structured expert judgment (SEJ) to estimate the proportions of diseases attributed to waterborne transmission. SEJ is an approach used when primary data are not available, and is subject to limitations including expert bias (*26*,*27*). For norovirus infection, the uncertainty interval for the waterborne attribution percentage was large, reflecting a lack of consensus among experts, and resulting in an estimate of illness with a wide credibility interval (1,330,000 [95% CrI 5,310–5,510,000] illnesses). Second, this analysis is limited to 17 infectious diseases with adequate surveillance or administrative data available and does not include all disease associated with waterborne transmission in the United States. Insufficient data were available

Table 5. Total direct healthcare cost of ED visits and hospitalizations from domestically acquired waterborne transmission of selected infectious diseases, United States, 2014*

	Value (95% CrI)						
	Treat-and-release ED visits†			Hospitalization			Direct healthcare cost, millions
Disease or syndrome	Cost per visit	Total no. visits	Total cost, millions	Cost per stay	Total no. hospital stays	Total cost, millions	
Campylobacteriosis	1,710 (137–5,810)	319 (31–966)	0.545 (0.0177–2.61)	13,600 (3,850–35,800)	2,150 (192–6,900)	30.0 (1.71–121)	30.5 (2.10–121)
Cryptosporidiosis	1,960 (238–6,270)	492 (167–957)	0.963 (0.0802–3.44)	16,100 (4,360–55,400)	1,120 (102–3,550)	17.9 (1.10–79.5)	18.9 (1.82–80.4)
Giardiasis	1,620 (196–7,510)	567 (185–1,120)	0.917 (0.0861–3.78)	21,800 (6,160–99,200)	1,100 (364–2,180)	23.9 (3.53–104)	24.8 (4.21–105)
Legionnaires' disease	691 (288–1,390)	667 (289–1,200)	0.460 (0.127–1.13)	37,100 (7,950–149,000)	10,800 (7,280–13,100)	401 (79.0–1,690)	402 (79.5–1,690)
NTM infection	1,610 (129–6,430)	5,080 (2,560–7,750)	8.17 (0.584–34.0)	29,600 (6,350–120,000)	51,400 (26,800–74,100)	1,520 (266–6,370)	1,530 (272–6,380)
Norovirus‡	1,140	26,300	30.1	6,080	4,780	29	59.1
Otitis externa	494 (120–1,430)	567,000 (337,000–823,000)	280 (60.2–846)	12,200 (3,320–42,400)	23,200 (13,900–33,600)	285 (67.8–1,040)	564 (187–1,570)
Pseudomonas pneumonia	856 (89–4,190)	291 (75–552)	0.249 (0.0162–1.27)	29,300 (5,910–114,000)	15,500 (4,130–28,100)	452 (49.8–1,950)	453 (49.9– 1,950)
Pseudomonas septicemia	923 (95–3,190)	36 (2–106)	0.0334 (0.000716–0.186)	38,200 (6,340–172,000)	5,590 (722–14,000)	214 (11.4–1,030)	214 (11.4–1,030)
Salmonellosis, nontyphoidal	1,230 (161–4,500)	194 (15–671)	0.240 (0.00734–1.24)	14,900 (4,300–46,900)	1,520 (100–5,660)	22.6 (0.870–110)	22.8 (1.08–110)
STEC infection, serotype O157	1,070 (109–2,350)	12 (2–35)	0.0130 (0.00734–0.051)	19,000 (3,790–85,000)	138 (14–503)	2.67 (0.129–14.5)	2.68 (0.141–14.5)
STEC infection, serotype non-O157	1,070 (109–2,350)	4 (0–16)	0.00440 (0–0.0223)	24,200 (4,780–138,000)	74 (0–308)	1.76 (0–11.0)	1.76 (0.00186–11.0)
Shigellosis	952 (115–3,980)	64 (5–311)	0.0609 (0.00171–0.349)	14,200 (4,130–48,000)	245 (13–1,140)	3.41 (0.106–18.9)	3.47 (0.140–19.0)
Vibrio spp. infection	1,030 (293–3,330)	76 (14–166)	0.0777 (0.00765–0.276)	16,000 (3,780–39,900)	251 (153–362)	4.02 (0.811–10.7)	4.10 (0.891–10.8)
Total cost			322 (100–889)			3,010 (1,120–8,410)	3,330 (1,370–8,770)

*Values are 2004 US dollars except as indicated. Estimates rounded to 3 significant figures. CrI, credible interval; ED, emergency department; NTM, nontuberculous mycobacterial; STEC, Shiga toxin-producing *E. coli*.

†Treat-and-release ED visits were defined as visits in which the person was not admitted to the hospital.

‡For norovirus only, costs were derived from previously published estimates that did not include uncertainty intervals. In addition, the number of ED visits includes visits in which the patient was admitted to the hospital.

to quantify the contribution of many viral diseases, including sapovirus, rotavirus, and astrovirus; or free-living ameba infections, which cause deaths in the United States each year (*5*). Noninfectious diseases (e.g., from exposure to harmful algal blooms, heavy metals, disinfection byproducts) were not considered. Third, these estimates used administrative data and relied on coding from the International Classification of Diseases, 9th Revision, Clinical Modification, which might not accurately capture the actual disease of the ill person. Fourth, the cost estimates consider only out-of-pocket and insurer payments and do not account for the total amount of time or wages lost to ill health, disability, early death, or other indirect costs. Physicians' office visits were not included, because data were not available. Payment totals might not reflect the actual cost incurred by healthcare providers. Fifth, this work did not make separate estimates for different age, demographic, or risk groups. Risks could differ by group (e.g., children swim more often and have higher rates of cryptosporidiosis), resulting in over- or underestimation of waterborne disease (*37*,*38*). Cost estimates did not consider the contribution of immunosuppressing conditions or other concurrent conditions to the healthcare costs incurred. Finally, some estimates used data from FoodNet. In 2007, Hispanic persons were underrepresented in FoodNet sites (*39*). Appendix 1 contains additional pathogen-specific limitations. Analytic strengths of these burden estimates include the use of active surveillance data when possible, estimates from a comprehensive structured expert judgment, and credible intervals to acknowledge the inherent uncertainty in the model inputs and outputs.

The data presented here reflect the changing picture of waterborne disease in the United States and underscore the role of environmental pathogens that grow in biofilms. An estimated 7.15 million (95% CrI 3.88 million–12.0 million) domestically acquired waterborne illnesses occur in the United States each year, highlighting the need to focus public health resources on the prevention and control of these diseases, including surveillance for the diseases in this estimate that do not have a dedicated national case surveillance system (e.g., NTM infections). These findings should serve as a foundation for improved disease surveillance, inform waterborne disease prevention priorities, and help measure progress in the prevention of waterborne disease in the United States.

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Estimate of Burden and Direct Healthcare Cost of Infectious Waterborne Disease in the United States

Appendix 1

Estimation and Uncertainty Model Inputs for Selected Diseases Transmitted through Water

Appendix 1 Table 1. Estimation and uncertainty model inputs for selected diseases transmitted through water, United States

Pathogen: *Campylobacter* spp.			
Model input	Data source(s)	Distribution*	Parameters
Reported/projected US illnesses	Number of illnesses caused by *Campylobacter* spp. infection reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–2015) (*1*) scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period.)	Empirical	By site and year (2012–2015), Appendix 1 Table 2
Population adjustment (year)	Incidence of *Campylobacter* infection in each FoodNet site by year applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed *Campylobacter* illnesses were enumerated by FoodNet active surveillance.		
Underdiagnosis (for number of illnesses)			
Proportion severe	Proportion of cases reporting bloody diarrhea from FoodNet surveillance of laboratory-confirmed *Campylobacter* infections (*3*). We used the same lower and upper endpoints derived from Scallan et al. (*3*).	PERT	Low, modal, high values: 0.36, 0.45, 0.52
Medical care seeking (severe)	Proportion (and 95% confidence interval [CI]) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) *(3)*.	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Campylobacter*, from the FoodNet Laboratory Survey (*4*). Uncertainty with this proportion (97%) was based on a 50% relative increase/decrease from 0.97 on an odds scale.	PERT	Low, modal, high values: 0.94, 0.97, 1.00
Positive predictive value	Because a substantial proportion of *Campylobacter* cases in 2014 were diagnosed by culture-independent diagnostic test (CIDT) only (*5*), and CIDTs have a lower specificity than culture-based methods, it was necessary to account for possible false-positive results from CIDT-only cases. For reported cases that were confirmed by CIDT alone, we used the positive predictive value (PPV) to convert CIDT cases to culture-confirmed cases. The PPV was defined as the probability of having a positive result in a culture-based test given a positive CIDT test. Further, because the PPV of PCR-	PERT	PCR: Low, modal, high values: 0.80, 0.85, 0.90 Non-PCR: Low, modal, high values: 0.37, 0.52, 0.73

Pathogen: *Campylobacter* spp.			
Model input	Data source(s)	Distribution*	Parameters
	based tests differ from non-PCR CIDT methods, we used separate PPVs for PCR and non-PCR CIDTs. Cases based on CIDT tests only were grouped into PCR and non-PCR. PPVs were derived from a previous publication that used data from FoodNet sites (*6*). Once CIDT-only cases were adjusted using the PPV to convert CIDT cases to the equivalent number of culture-confirmed cases, they were added to the number of reported culture-confirmed cases to obtain the adjusted total number of culture-confirmed cases. The PPVs were assumed to follow the PERT distribution.		
Culture-based test sensitivity	We used a laboratory test sensitivity rate of 70% based on studies of *Salmonella* (*7,8*) for the equivalent number of culture-confirmed cases. We assumed a lower bound of 60% and an upper bound of 90%.	PERT	Low, modal, high values: 0.60, 0.70, 0.90
Proportion with treat-and-release ED visit	Proportion of treat-and-release emergency department (ED) visits (i.e., visits where the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 008.43 (campylobacteriosis) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 008.43. This proportion was multiplied by the number of patients with FoodNet cases of *Campylobacter* infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 1,173, 1,636, 1,501 HCUP hospitalizations (2012–2014): 5,915, 6,515, 6,090 Proportion by year, 2012–2014: 0.20, 0.26, 0.25
Proportion hospitalized	Proportion of case-patients with FoodNet cases of *Campylobacter* infection who were hospitalized.	Empirical	By site and year (2012–2015); Table 3
Proportion who died	Proportion of case-patients with FoodNet cases of *Campylobacter* infection who died.	Empirical	By site and year (2012–2015); Table 4
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of case-patients with FoodNet cases of *Campylobacter* infection who reported travel outside the United States within 7 d of illness onset (2012–2015). Uncertainty with this proportion (15%) was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.10, 0.15, 0.21
Proportion waterborne	Structured expert judgement estimate for *Campylobacter* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.01, 0.11, 0.13, 0.31
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release emergency department visits for ICD-9-CM code 008.43 (campylobacteriosis), in 2014 US dollars, in 2012–2013 IBM MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,710 (137–5,810)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 008.43 (campylobacteriosis), in 2014 US dollars, in 2012–2013 IBM MarketScan research databases	Empirical	Mean (2.5th percentile, 97.5th percentile): 13,600 (3,850–35,800)
Pathogen-specific limitations and discussion	Diagnostic testing for campylobacteriosis is changing rapidly and the proportion of reported cases diagnosed by culture-independent diagnostic test alone is increasing. The positive predictive value of CIDTs varies by method (PCR vs. non-PCR) and by brand. We attempted to account for variation by method but were unable to account for variation by brand. The proportion of laboratories routinely testing for *Campylobacter* is based on a survey conducted from 1995 to 2000. It is likely that laboratory testing practices have changed since 2000. However, after consultation with CDC enteric disease experts, updated data were not available, and it was agreed that 97% of laboratories routinely testing for *Campylobacter* was a conservative estimate (because the higher the proportion of laboratories routinely testing for a pathogen, the lower the underdiagnosis multiplier).		

Pathogen: *Cryptosporidium* spp.			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by *Cryptosporidium* spp. infection reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–2015) (*1*); scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period).	Empirical	By site and year (2012–2015); Appendix 1 Table 2
Population adjustment (year)	Incidence of *Cryptosporidium* spp. infection in each FoodNet site by year applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99

Pathogen: *Cryptosporidium* spp.			
Model input	Data source(s)	Distribution	Parameters
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed *Cryptosporidium* spp. illnesses were enumerated by FoodNet active surveillance.	None	None
Underdiagnosis (for number of illnesses			
Percent severe	The proportion of laboratory-confirmed *Cryptosporidium* spp. cases reporting bloody diarrhea was assumed to be low.	PERT	Low, modal, high values: 0.0, 0.0, 0.05
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Cryptosporidium* spp., from the FoodNet Laboratory Survey (*4*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.27, 0.36, 0.46
Test sensitivity	Average from published studies (*3*). Uncertainty with this proportion (87%) was based on a 50% relative increase/decrease from 0.87 on an odds scale.	PERT	Low, modal, high values: 0.81, 0.87, 0.91
Proportion with treat-and-release ED visit	Proportion of treat-and-release ED visits (i.e., visits in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 007.4 (cryptosporidiosis) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 007.4. This proportion was multiplied by the number of patients with FoodNet cases of *Cryptosporidium* spp. infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 604, 658, 610 HCUP hospitalizations (2012–2014): 5,915, 6,515, 6,090 Proportion by year, 2012–2014: 0.33, 0.36, 0.33
Proportion hospitalized	Proportion of case-patients with FoodNet cases of *Cryptosporidium* spp. infection who were hospitalized.	Empirical	By site and year (2012–2015); Appendix 1 Table 3
Proportion who died	Proportion of case-patients with FoodNet cases of *Cryptosporidium* spp. infection who died.	Empirical	By site and year (2012–2015); Appendix 1 Table 4
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of emergency department visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of case-patients with FoodNet cases of *Cryptosporidium* spp. infection who reported travel outside the United States within 15 d of illness onset (2012–2015). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.067, 0.098, 0.138
Proportion waterborne	Structured expert judgement estimate for *Cryptosporidium* spp. infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.17, 0.43, 0.43, 0.73
Cost of treat-and-release emergency visits	Sum of insurer and out-of-pocket payments for treat-and-release emergency department visits for ICD-9-CM code 007.4, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,960 (238–6,270)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 007.4, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 16,100 (4,360–55,400)
Pathogen-specific limitations and discussion	Testing methods for *Cryptosporidium*, a parasite, differ from culture-based bacterial methods. Immunochromatographic testing was likely the most common diagnostic testing method in the time span of this analysis. Specificity of immunochromatographic testing varies by brand and ranges from 67% to 100%. We did not account for false positives because of a lack of data on testing methods, brands, and whether follow-up testing was performed.		

Pathogen: *Giardia duodenalis*			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by *Giardia duodenalis* reported to CDC's National Notifiable Diseases Surveillance System (NNDSS) (2008–2015) (*11*). Because not all states report giardiasis to NNDSS, estimates were scaled up to the total US population.	Empirical	By year (2008–2015): 19,153, 19,562, 19,984, 16,870, 15,224, 15,318, 14,657, 14,678
Population adjustment (year)	Population ratios applied to each year from 2008–2014 based on US Census population estimates for states that report giardiasis to NNDSS (*2*)	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*)	PERT	Low, modal, high values: 1.0, 1.3, 1.6
Underdiagnosis (for number of illnesses)			
Percent severe	Assumed to be mostly mild (*12*).	PERT	Low, modal, high values: 0.0, 0.0, 0.05
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Used the parameter generated by Scallan et al. (*3*), which was based on consultations with clinical and billing code experts. Uncertainty with this proportion (80%) was based on a 50% relative increase/decrease from 0.80 on an odds scale.	PERT	Low, modal, high values: 0.73, 0.80, 0.86
Test sensitivity	Average from published studies (*3*). We used uniform minimum variance unbiased (UMVU) estimators for lower and upper endpoints.	PERT	Low, modal, high values: 0.72, 0.83, 0.93
Proportion with treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 007.1 (giardiasis) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 007.1.	Empirical ratio	HCUP ED visits by year (2012–2014): 713, 712, 746 HCUP hospitalizations (2012–2014): 1,430, 1,425, 1,415 Proportion by year, 2012–2014: 0.5, 0.5, 0.53
Proportion hospitalized	Proportion of case-patients hospitalized, estimated using annual national estimates of hospitalization from the National Inpatient Sample (NIS) (2008–2014) using ICD-9-CM code 007.1 (giardiasis) compared with the number of illnesses reported in NNDSS (*11*).	Empirical	By year (2008–2014): 0.098, 0.094, 0.089, 0.094, 0.093, 0.097
Proportion who died	Proportion of case-patients who died, estimated using annual national estimates of in-hospital deaths from the NIS (2008–2015) using ICD-9-CM code 007.1 (giardiasis) compared with the total number of cases from NNDSS.	Empirical	Number of deaths by year (2008–2014): 2, 0, 1, 5, 3, 1, 2, 1 Proportion by year (per 100,000 cases): 10.4, 0, 5, 29.6, 19.7, 6.5, 13.6, 6.8
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	12.1% based on a published study (*13*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale	PERT	Low, modal, high values: 0.08, 0.12, 0.17
Proportion waterborne	Structured expert judgment estimate for giardiasis infection (*9*)	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.16, 0.43, 0.44, 0.78
Cost of treat-and-release emergency visits	Sum of insurer and out-of-pocket payments for treat-and-release emergency department visits for ICD-9-CM code 007.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*)	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,620 (196–7,510)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 007.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 21,800 (6,160–99,200)

Pathogen: *Giardia duodenalis*			
Model input	Data source(s)	Distribution	Parameters
Pathogen-specific limitations and discussion	Giardiasis is a nationally notifiable disease. However, each state has its own laws and regulations defining which diseases are reportable (https://wwwn.cdc.gov/nndss/data-collection.html). Clinical detection and diagnosis are challenging because many physicians lack familiarity with giardiasis, many symptoms (e.g., diarrhea) are nonspecific, and standard bacterial fecal cultures will not detect *Giardia* (*14–16*).		

Pathogen: *Legionella*			
Model input	Data source(s)	Distribution	Distribution values
Reported illnesses	Incidence of *Legionella* infection resulting in Legionnaires' disease reported to CDC's National Notifiable Diseases Surveillance System (NNDSS, 2008–2014 [*17*]).	Empirical	By year: 3181, 3522, 3346, 4202, 3688, 4954, 5166
Population adjustment (year)	Population ratios applied to each year from 2008–2014 based on US Census population estimates (*2*) and adjusted for increasing trend	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	All cases assumed to be reported	Constant	100%
Percent severe	All cases of infection assumed to be severe	Constant	100%
Underdiagnosis (for number of illnesses)			
Medical care seeking	Assumed to have a high rate of medical care seeking (97.9% hospitalized in cases reported to CDC's Active Bacterial Core surveillance program, 2011–2015) (*18*).	PERT	Low, modal, high values: 0.99, 0.995, 1.0
Specimen submission	In one healthcare system where universal testing of patients with community-acquired pneumonia for Legionnaires' disease was implemented, 56% of patients with Legionnaires' disease would have been tested using standard guidelines (*19*).	PERT	Low, modal, high values: 0.46, 0.56, 0.66
Laboratory testing	We assumed that all facilities would have access to laboratories capable of performing the urinary antigen test for *Legionella pneumophila* serogroup 1.	Constant	100%
Laboratory test sensitivity	71% based on published study of sensitivity of urinary antigen test for all *Legionella* species and serogroups (*20*)	PERT	Low, modal, high values: 0.791, 0.794, 0.797
Proportion with a treat-and-release ED visit	Ratio of treat-and-release ED visits to hospitalizations from the Health Care Utilization Project's National Emergency Department Sample and National Inpatient Sample, 2012–2014, using ICD-9-CM code 482.84 (Legionnaires' disease). This proportion was multiplied by the number of case-patients with NNDSS cases of Legionnaires' disease who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 333, 445, 250 HCUP hospitalizations (2012–2014): 3,680, 4,810, 4,170 Proportion by year, 2012–2014: 0.09, 0.09, 0.06
Proportion hospitalized	Proportion hospitalized (97.9%) in cases reported to CDC's Active Bacterial Core surveillance program, 2011–2013 (*18*)	Empirical	By year (2008–2014): 0.981, 0.981, 0.981, 0.980, 0.976, 0.987, 0.980
Proportion who died	Proportion of case-patients who died, reported to CDC's Active Bacterial Core surveillance program, 2011–2015 (*18*)	Empirical	By year: 0.096, 0.1058, 0.0843, 0.0775
Underdiagnosis (ED visits, hospitalizations, deaths)	Because nearly all case-patients were hospitalized, the underdiagnosis multiplier for ED visits, hospitalizations, and deaths was assumed to be the same as the underdiagnosis multiplier for illnesses.	PERT	Low, modal, high values: 1.9, 2.3, 2.8
Proportion travel-related	Proportion of persons with Legionnaires' disease who reported travel outside the United States within 10 d of illness onset (2005–2014) in CDC's Supplemental Legionnaires' Disease Surveillance System (*14*). Uncertainty with this proportion (1%) was based on a 50% relative increase/decrease from 0.01 on an odds scale.	PERT	Low, modal, high values: 0.0067, 0.01, 0.0149
Proportion waterborne	Structured expert judgment estimate for Legionnaires' disease (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.67, 1, 0.97, 1
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM code 482.84, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, from data reported by Adam et al. (10).	Empirical	Mean (2.5th percentile, 97.5th percentile): 691 (288–1,390)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 482.84, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 37,100 (7,950–149,000)

Pathogen: *Legionella*			
Model input	Data source(s)	Distribution	Distribution values
Pathogen-specific limitations and discussion	Previously reported costs for treat-and-release ED visits did not report visits for Medicaid because of small sample size. Medicaid visit costs were included in this estimation. As a consequence, the weighted average cost per treat-and-release ED visits is lower that what was reported by Adam et al. (*10*). In practice, Legionnaires' disease tends to be defined as a "severe" pneumonia, which is supported by the fact that nearly all reported case-patients have been hospitalized. Previous serologic studies, however, have shown that many persons not known to have a history of Legionnaires' disease have detectable titers of antibodies against *Legionella* (*21*). This indicates that less severe disease presentations may exist that have not been diagnosed or reported and would not be captured by this estimate.		

Pathogen: nontuberculous mycobacterial (NTM) infections			
Model input	Data source(s)	Distribution	Parameters
Reported hospitalizations	Number of case-patients hospitalized using annual national estimates from the National Inpatient Sample (NIS) (2012–2014) using International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 031 (031.0, pulmonary NTM infection; 031.1, cutaneous NTM infection; 031.2, disseminated NTM infection; 031.8, other specified NTM disease; 031.9, unspecified diseases due to mycobacteria).	Mixture of normals	By year (2012–2014): 18,130, 19,415, 19,525
Population adjustment (year)	Population ratios applied to each year, 2012–2014, based on US Census population estimates (*2*)	Degenerate	Adjustment by year (2012–2014): 1.01, 1.0, 1.0
Underreporting	All cases with an NTM ICD-9-CM code in the hospitalization record were assumed to be reported to NIS.		
Underdiagnosis (illnesses, ED visits, hospitalizations, deaths)	Strollo et al. estimated that 27% of NTM cases had the ICD-9-CM code in the hospitalization record (*22*); 1/0.27 = 3.704. Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 2.802, 3.704, 5.056
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for ICD-9-CM code 031 compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 031.	Empirical ratio	HCUP ED visits by year (2012–2014): 1,670, 1,846, 2,121 HCUP hospitalizations (2012–2014): 18,130, 19,415, 19,525 Proportion by year, 2012–2014: 0.09, 0.10, 0.11
Proportion hospitalized	After conferring with subject matter experts, we assumed 75% to be hospitalized. Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.667, 0.750, 0.818
Number of deaths	We used the method of Gargano et al. (*23*). In-hospital deaths that occurred in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 031 were combined with out-of-hospital deaths from the National Vital Statistics System (death certificates).	Empirical	Number of deaths by year (2012–2014): 965, 1150, 1035
Proportion travel-related	We assumed that NTM infections were similar to Legionnaires' disease, and used the proportion of patients with *Legionella* infection resulting in Legionnaires' disease who reported travel outside the United States within 30 d of illness onset (2005–2014) in CDC's Supplemental Legionnaires' Disease Surveillance System (*17*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.0067, 0.01, 0.0149
Proportion waterborne	Structured expert judgment estimate for NTM infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.39, 0.73, 0.72, 0.94
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM code 031, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,610 (129–6,430)

Pathogen: nontuberculous mycobacterial (NTM) infections			
Model input	Data source(s)	Distribution	Parameters
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 031, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 29,600 (6,350–120,000)
Pathogen-specific limitations and discussion	Pulmonary NTM infections are believed to be the most common manifestation of NTM infection (≈90% of infections are thought to be pulmonary). NTM diagnosis codes are not an exact match to manifestations because the wording for the pulmonary and disseminated codes contain both the manifestation and a species, so they might not accurately capture the true course of illness if clinicians choose the code for the species and not the manifestation. In the Marketscan databases we have observed that persons will often have a disseminated code for one hospitalization and a pulmonary code for the next hospitalization, or vice versa. We chose to not present numbers by individual diagnosis code because we believe the overall numbers are more reliable. The total cost of an NTM infection is likely higher than the cost per hospitalization reported here, because a single infection can have multiple hospitalizations. Because data on the proportion of persons with an NTM infection who have traveled outside of the United States recently were not available, we used the proportion from Legionnaires' disease surveillance. Dedicated surveillance for NTM infectious would address these data gaps. The illness and cost estimates in this work are in the range of with previous work. Previous estimates of the number of NTM infections in 2014 range from 50,976 (*24*) to 181,037 cases (*22*). We estimated 96,953 illnesses occurred (95% CrI 75,739–121,633). Strollo et al. estimated the US cost of pulmonary NTM infections in 2014 to be $1.7 billion, close to the $1.5 billion we estimated for all NTM infections (*22*).		

Pathogen: norovirus			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Incidence of illnesses caused by norovirus infection reported to 3 sites (Georgia, Maryland/DC, and Oregon) in the Kaiser Permanente health system (*25,26*).	Mixture of PERTs	69.5/1,000 person-years (Georgia), 76.9/1000 person-years (Oregon), 61.8/1000 person-years (metro DC area)
Population adjustment (year)	Scaled up to the 2014 US population (*2*).		
Underreporting	Assumed to be equivalent to active surveillance during the study period.	–	–
Underdiagnosis (for number of illnesses)			
Medical care seeking	The Hall and Grytdal incidence estimates were adjusted for the proportion (and 95% CI) of survey respondents among persons with diarrhea who sought medical care, from CDC's Foodborne Diseases Active Surveillance Network (FoodNet) Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*). No further adjustment was made.	NA	
Specimen submission	The Grytdal et al. estimate was adjusted for the proportion of persons with diarrhea who submitted a fecal sample for bacterial laboratory testing in the Kaiser Permanente health system, while the Hall et al. estimate was adjusted for the proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*). No further adjustment was made.		
Proportion with an ED visit	Estimated annual rate of ED visits per 1,000 persons, from Gastañaduy et al. (*27*). Unlike other diseases in this analysis, the ED visit estimate for norovirus infection includes visits in which the person was admitted to the hospital.	PERT	Low, modal, high values: 0.8, 1.35, 1.89
Number hospitalized	Estimated annual rate of hospitalizations per 100,000 person-years, from Lopman et al. (*28*), applied to the 2014 US population to produce the annual number of hospitalizations.	Empirical	By year (1997–2007): 45354, 53608, 67250, 56827, 51306, 69571, 86794, 62477, 67010, 112566, 108927

Pathogen: norovirus			
Model input	Data source(s)	Distribution	Parameters
Number who died	Estimated annual rate of deaths per 1,000 persons, from Hall et al. (*29*), applied to the 2014 US population.	Empirical	By year (1999–2007): 346, 850, 723, 857, 826, 668, 714, 717, 640
Proportion travel-related	Assumed to be low within the incubation period for norovirus.		Low, modal, high values: 0.005, 0.01, 0.02
Proportion waterborne	Structured expert judgment estimate for norovirus (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0, 0.03, 0.06, 0.25
Cost of treat-and-release ED visits	Previously reported costs for ED visits, converted to 2014 dollars (*27*).		
Cost of hospitalizations	Previously reported costs for hospitalizations, converted to 2014 dollars (*28*).		
Pathogen-specific limitations and discussion	For norovirus only, costs were derived from previously published costs that did not provide uncertainty intervals. Thus, cost estimates for norovirus do not include credible intervals. The previously published costs were not specifically calculated for norovirus infection and depend on the assumption that costs for norovirus infection are similar to costs for other causes of acute gastroenteritis. The proportion of persons with international travel during the incubation period for norovirus infection was assumed to be low and was not based on information from surveillance. The credible interval for the number of norovirus illnesses that are domestically acquired and waterborne is very wide, reflecting some uncertainty about the true proportion of norovirus infection that is waterborne. For norovirus only, ED visits that resulted in admission to the hospital were included in the count and cost calculation of ED visits. For other diseases, costs of ED visits that resulted in hospitalization were included in hospitalization costs, and not included in emergency visit costs. There were 4,778 hospitalizations for waterborne norovirus (some of these patients could have been admitted to the hospital without an ED visit) and 26,279 ED visits (both treat-and-release and admitted) for waterborne norovirus. If all hospitalizations are assumed to have originated with an ED visit (to estimate the largest possible effect of this double-counting), there could have been as few as 26,279 – 4,778 = 21,501 treat-and-release ED visits, and total costs for norovirus ED visits would be lower by $6,079 × 4,778 = $5,466,032.		

Syndrome: otitis externa			
Model input	Data source(s)	Distribution	Parameters
Total illnesses	Calculated using the total number of doctors' office visits and ED visits (both treat-and-release and admitted to the hospital) for otitis externa without concurrent otitis media, and the proportion of persons with otitis externa believed to seek medical care.	Nonparametric	Sum of physician office visits and ED visits
Population adjustment (year)	Population ratios applied to each year, 2012–2014, based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2014): 1.01, 1.0, 1.0
Underreporting	All doctors' office visits and ED visits that received an ICD-9-CM code of interest were assumed to be reported to NAMCS and HCUP NEDS.	–	–
Medical care seeking (under-diagnosis factor for illnesses)	A study of >50,000 beachgoers reported that, of beachgoers experiencing an earache after their beach visit, 29.55% sought medical care of any kind (*30*).	PERT	Low, modal, high values: 0.2185, 0.2955, 0.3861
Number of doctors' office visits	Because no national case surveillance system for otitis externa exists, most patients were not expected to be hospitalized, and because diagnosis of otitis externa does not generally rely on laboratory testing, we used the number of doctors' office visits for otitis externa as 1 initial input for the number of total illnesses. All visits in the National Ambulatory Medical Care Survey (for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) codes 380.10 (infective otitis externa, unspecified); 380.12 (acute swimmers' ear); and 380.14 (malignant otitis externa). Because it can be difficult to distinguish otitis externa from otitis media and a conservative estimate was desired, all visits with a concurrent diagnosis of	Mixture of normals	By year (2012–2014): 1,648,338; 1,484,991; 909,753

Syndrome: otitis externa			
Model input	Data source(s)	Distribution	Parameters
	ICD-9-CM code 381 (nonsuppurative otitis media and Eustachian tube disorders) or 382 (suppurative and unspecified otitis media) were excluded.		
Number of ED visits (both treat-and-release and admitted to the hospital; used for total illness estimate)	All ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for ICD-9-CM codes 380.10, 380.12, and 380.14 (excluding visits with a concurrent ICD-9-CM code of 381 or 382).	Mixture of normals	By year (2012–2014): 378,880; 375,869; 361,076
Number of treat-and-release ED visits	Treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for ICD-9-CM codes 380.10, 380.12, and 380.14 (excluding visits with a concurrent ICD-9-CM code of 381 or 382).	Nonparametric	By year (2012–2014): 367,049; 364,500; 349,206
Number hospitalized	Number of hospitalizations, from the Health Care Utilization Project's National Inpatient Sample, 2012–2014, for ICD-9-CM codes 380.10, 380.12, and 380.14 (excluding hospitalizations with a concurrent ICD-9-CM code of 381 or 382).	Empirical	By year (2012–2014): 15,110; 14,785; 14,400
Number who died	We used the method of Gargano et al. to estimate deaths (*23*). Briefly, in-hospital deaths for otitis externa without concurrent otitis media that occurred in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) were combined with out-of-hospital deaths from the National Vital Statistics System.	Empirical	By year (2012–2014):115, 130, 150
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	We assumed 7% of persons had traveled in the past week before developing otitis externa. Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.048, 0.07, 0.10
Proportion waterborne	One study estimated 50% of otitis externa is caused by *Pseudomonas* and 25% by *Staphylococcus aureus* (*31*). We used the structured expert judgment estimates for *Pseudomonas* otitis externa and *Staphylococcus aureus* otitis externa (*9*) and averaged the water attribution rates with a weight ratio of 2:1.	Nonparametric	2.5th percentile, median, mean, 97.5th percentile: 0.67, 0.8, 0.79, 0.95
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM codes 380.10, 380.12, and 380.14 (excluding visits with a concurrent ICD-9-CM code of 381 or 382), in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 494 (120–1,430)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM codes ICD-9-CM codes 380.10, 380.12, and 380.14 (excluding hospitalizations with a concurrent ICD-9-CM code of 381 or 382), in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 12,200 (3,320–42,400)
Pathogen-specific limitations and discussion	We excluded all ED and doctors' office visits with any report of otitis media (because otitis media and otitis externa can be difficult to distinguish clinically) so these numbers are likely an underestimate. Risk of otitis externa (commonly known as "swimmer's ear") is correlated with levels of *Pseudomonas* and other pathogens in water, and increases with bather load in recreational water venues (*32,33*). Risk of otitis externa in beachgoers who enter the water is 1.8 times higher than in beachgoers who do not enter the water (*30*). Otitis externa can be acutely painful and is also a public health problem. Swimming in natural waters has been estimated to cause nearly 1 million excess cases of swimmer's ear in the United States every year (*34*). Otitis externa represents a burden on the healthcare system (an estimated 2.4 million healthcare visits, and nearly half a million hours of clinician time each year [*35*]). Otitis externa also represents a possible source of antimicrobial overuse. Despite clinical guidelines recommending topical treatment for uncomplicated acute otitis externa, one third of outpatient visits involved prescription of systemic antimicrobials for this preventable condition (*36*). Finally, otitis externa is preventable, through keeping ears as dry as possible while swimming, and by making sure the ear is dry after swimming. Ear drops or a hair dryer set on low and held several inches away from the ear can aid in this process.		

Pathogen: *Pseudomonas* pneumonia			
Model input	Data source(s)	Distribution	Parameters
Reported hospitalizations	Number of patients hospitalized, using annual national estimates from the National Inpatient Sample (NIS) (2012–2014) with a primary diagnosis of International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 482.1 (pneumonia due to *Pseudomonas*).	Mixture of normals	By year (2012–2014): 17,040; 15,540; 13,240
Population adjustment (year)	Population ratios applied to each year during 2012–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2014): 1.01, 1.0, 1.0
Underreporting	All cases with a primary diagnosis of *Pseudomonas* pneumonia in the hospital billing record were assumed to be reported to NIS.	–	–
Underdiagnosis (illnesses, ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion hospitalized	After conferring with subject matter experts, we assumed 97% to be hospitalized. Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.95, 0.97, 0.99
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) with a primary diagnosis of ICD-9-CM code 482.1.	Empirical ratio	HCUP ED visits by year (2012–2014): 259, 296, 309 HCUP hospitalizations (2012–2014): 17,040; 15,540; 13,240 Proportion by year, 2012–2014: 0.02, 0.02, 0.02
Proportion who died	We used the method of Gargano et al. (*26*). In-hospital deaths that occurred in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) with a primary diagnosis of ICD-9-CM code 482.1 were combined with out-of-hospital deaths from the National Vital Statistics System (death certificates).	Empirical	By year (2012–2014): 790, 555, 450
Proportion travel-related	We assumed *Pseudomonas* pneumonia was similar to Legionnaires' disease, and used the proportion of case-patients with *Legionella* infection resulting in Legionnaires' disease who reported travel outside the United States within 30 d of illness onset (2005–2014) in CDC's Supplemental Legionnaires' Disease Surveillance System (*17*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.0067, 0.01, 0.0149
Proportion waterborne	Structured expert judgment estimate for *Pseudomonas* pneumonia (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.14, 0.52, 0.51, 0.8
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits with a primary diagnosis of ICD-9-CM code 482.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 856 (89–4,190)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations with a primary diagnosis of ICD-9-CM code 482.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 29,300 (5,910–114,000)
Pathogen-specific limitations and discussion	Because data on the proportion of persons with *Pseudomonas* pneumonia who have traveled outside the United States recently were not available, we used the proportion from Legionnaires' disease surveillance. Because a conservative estimate was desired, we included only hospitalizations and ED visits with a primary diagnosis of *Pseudomonas* pneumonia, which could have excluded some hospitalizations and visits because of waterborne transmission.		

Pathogen: *Pseudomonas* septicemia			
Model input	Data source(s)	Distribution	Parameters
Reported hospitalizations	Number of case-patients hospitalized using annual national estimates from the National Inpatient Sample (NIS) (2012–2014) with a primary diagnosis of International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 038.43 (Septicemia due to other gram-negative organisms – *Pseudomonas*).	Mixture of normals	By year (2012-2014): 17,040; 15,540; 13,240
Population adjustment (year)	Population ratios applied to each year from 2012–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2014): 1.01, 1.0, 1.0
Underreporting	All cases with a primary diagnosis of *Pseudomonas* septicemia in their hospitalization record were assumed to be reported to NIS.	–	–
Underdiagnosis (illnesses, ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion hospitalized	After conferring with CDC experts, we assumed 97% to be hospitalized. Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.95, 0.97, 0.99
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) with a primary diagnosis of ICD-9-CM code 038.43	Empirical ratio	HCUP ED visits by year (2012–2014): 79, 65, 100 HCUP hospitalizations (2012–2014): 11,865, 12,570, 13,300 Proportion by year, 2012–2014: 0.01, 0.01, 0.01
Proportion who died	We used the method of Gargano et al (*23*). In-hospital deaths that occurred in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) with a primary diagnosis of ICD-9-CM code 482.1 were combined with out-of-hospital deaths from the National Vital Statistics System (death certificates). Because death certificate data do not contain a specific code for *Pseudomonas* septicemia, we multiplied the number of deaths from "septicemia from other gram-negative organisms" by the proportion of septicemia from other gram-negative organisms attributed to *Pseudomonas* septicemia in HCUP NIS data.	Empirical	By year (2012–2014): 790, 555, 450
Proportion travel-related	We assumed *Pseudomonas* septicemia was similar to Legionnaires' disease, and used the proportion of patients with *Legionella* infection resulting in Legionnaires' disease who reported travel outside the United States within 30 d of illness onset (2005–2014) in CDC's Supplemental Legionnaires' Disease Surveillance System (*17*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.0067, 0.01, 0.0149
Proportion waterborne	Structured expert judgment estimate for *Pseudomonas* septicemia (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.03, 0.21, 0.22, 0.53
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits with a primary diagnosis of ICD-9-CM code 482.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 923 (95–3,190)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations with a primary diagnosis of ICD-9-CM code 482.1, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 38,200 (6,340–172,000)
Pathogen-specific limitations and discussion	Because data on the proportion of persons with *Pseudomonas* septicemia who have traveled outside the United States recently were not available, we used the proportion from Legionnaires' disease surveillance. Because a conservative estimate was desired, we included only hospitalizations and ED visits with a primary diagnosis of *Pseudomonas* septicemia, which could have excluded some hospitalizations and visits resulting from waterborne transmission.		

Pathogen: *Salmonella,* nontyphoidal serotypes			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Incidence of *Salmonella* infections excluding serotype Typhi reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–	Empirical	By site and year (2012–2015); Appendix 1 Table 2

Pathogen: *Salmonella,* nontyphoidal serotypes			
Model input	Data source(s)	Distribution	Parameters
	2015) (*1*); scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period).		
Population adjustment (year)	Incidence of nontyphoidal *Salmonella* in each FoodNet site by year applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed nontyphoidal *Salmonella* illnesses were enumerated by FoodNet active surveillance.	–	–
Underdiagnosis (for number of illnesses)			
Percent severe	Proportion of cases reporting bloody diarrhea in FoodNet case-control studies of sporadic laboratory-confirmed *Salmonella* infections (*3*). We used uniform minimum variance unbiased (UMVU) estimators for lower and upper endpoints.	PERT	Low, modal, high values: 0.35, 0.45, 0.71
Medical care seeking (severe)	Proportion (and 95% confidence interval (CI)) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	100% of clinical laboratories reported routinely testing fecal samples for *Salmonella* in the FoodNet Laboratory Survey (*4*). As Scallan et al. did (*3*), we assumed a slightly lower rate of 97%; uncertainty with this proportion was based on a 50% relative increase/decrease from 0.97 on an odds scale.	PERT	Low, modal, high values: 0.94, 0.97, 1.00
Laboratory test sensitivity	We assumed a laboratory test sensitivity rate of 70% based on studies of *Salmonella* (*7,8*). We assumed a lower bound of 60% and an upper bound of 90%.	PERT	Low, modal, high values: 0.60, 0.70, 0.90
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 003 (salmonellosis) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 003. This proportion was multiplied by the number of FoodNet case-patients with nontyphoidal *Salmonella* infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 1,769, 1,554, 1,742 HCUP hospitalizations (2012–2014): 10,255, 9,470, 10,260 Proportion by year, 2012–2014: 0.17, 0.16, 0.17
Proportion hospitalized	Proportion of FoodNet case-patients with nontyphoidal *Salmonella* infection who were hospitalized (2012–2015).	Empirical	By site and year (2012–2015), Appendix 1 Table 3
Proportion who died	Proportion of FoodNet case-patients with nontyphoidal *Salmonella* infection who died (2012–2015).	Empirical	By site and year (2012–2015), Appendix 1 Table 4
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of FoodNet case-patients with nontyphoidal *Salmonella* infection who reported travel outside the United States within 7 days of illness onset (2012–2015). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.06, 0.096, 0.14
Proportion waterborne	Structured expert judgment estimate for nontyphoidal *Salmonella* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0, 0.04, 0.06, 0.22
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM code 003 (salmonellosis), in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,230 (161–4,500)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 003 (salmonellosis), in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 14,900 (4,300–46,900)

Pathogen: *Salmonella,* nontyphoidal serotypes			
Model input	Data source(s)	Distribution	Parameters
Pathogen-specific limitations and discussion	Emergency department visits used ICD-9-CM codes, which might not fully capture all diagnosed nontyphoidal *Salmonella* infections. The proportion of persons with bloody and non-bloody diarrhea was based on data collected during 2000–2007. Healthcare-seeking behaviors might have changed over time.		

Pathogen: Shiga toxin-producing (STEC) *Escherichia coli* infection, serotype O157			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by STEC O157 infection reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–2015) (*1*); scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period).	Empirical	By site and year (2012–2015), Appendix 1 Table 2
Population adjustment (year)	Incidence of STEC O157 infection in each FoodNet site by year applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed STEC O157 illnesses were enumerated by FoodNet active surveillance.	–	–
Underdiagnosis (for number of illnesses)			
Percent severe	Proportion of case-patients by site reporting bloody diarrhea from FoodNet case-control study of sporadic laboratory-confirmed STEC O157 infections (*37*). We used the same lower and upper endpoints derived from Scallan et al. (*3*).	PERT	Low, modal, high values: 0.85, 0.90, 1.00
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Among clinical laboratories that performed on-site testing, proportion that used a method that would isolate STEC O157 in 2014, FoodNet Laboratory Survey (B.B. Bruce, pers. comm. Methods for the FoodNet Laboratory Survey were described by Hoefer et al. [*38*]). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.78, 0.84, 0.89
Test sensitivity	We used a laboratory test sensitivity rate of 70% based on studies of *Salmonella* (*7,8*). We assumed a lower bound of 60% and an upper bound of 90%.	PERT	Low, modal, high values: 0.60, 0.70, 0.90
Proportion with treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 041.41 (STEC O157 infection) compared to hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 041.41. This proportion was multiplied by the number of FoodNet case-patients with STEC O157 infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 118, 134, 124 HCUP hospitalizations (2012–2014): 770, 880, 695 Proportion by year, 2012–2014: 0.15, 0.15, 0.18
Proportion hospitalized	Proportion of FoodNet case-patients with STEC O157 infection who were hospitalized.	Empirical	By site and year (2012–2015), Appendix 1 Table 3
Proportion who died	Proportion of FoodNet case-patients with STEC O157 infection who died.	Empirical	By site and year (2012–2015), Appendix 1 Table 4

Pathogen: Shiga toxin-producing (STEC) *Escherichia coli* infection, serotype O157			
Model input	Data source(s)	Distribution	Parameters
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of FoodNet case-patients with STEC O157 infection who reported travel outside the United States within 7 d of illness onset (2012–2015). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.05, 0.10, 0.21
Proportion waterborne	Structured expert judgment estimate for STEC O157 infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.01, 0.05, 0.05, 0.13
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM codes 041.41 and 041.42, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases. Costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,070 (109–2,350)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 041.41, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 19,000 (3,790–85,000)
Pathogen-specific limitations and discussion	Scallan et al. (*3*) used the proportion of laboratories routinely testing for STEC O157, but we used the proportion of laboratories that could perform a test that would isolate STEC O157, whether they tested fecal samples routinely or upon physician request. We did this because a conservative estimate was desired, and because laboratory testing capability could have changed over time. Infections caused by STEC O157 have decreased in the past 10 y (*1*). The increasing use of culture-independent diagnostic tests (CIDTs) makes interpretation of trends in STEC infections difficult because CIDTs do not indicate which STEC serogroup caused the infection. The number of CIDT positive–only infections reported to FoodNet has been increasing markedly since 2013, as more clinical laboratories adopt CIDTs. Initially, increases were primarily limited to *Campylobacter* and STEC.		

Pathogen: Shiga toxin-producing *Escherichia coli* (STEC) infection, serotype non-O157			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by STEC non-O157 infection reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–2015) (*1*); scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period).	Empirical	By site and year (2012–2015), Appendix 1 Table 2
Population adjustment (year)	Incidence of STEC non-O157 infection in each FoodNet site by year, applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed non-O157 STEC illnesses were enumerated by FoodNet active surveillance.	–	–
Underdiagnosis (for number of illnesses)			
Percent severe	Proportion of non-O157 STEC cases of infection with bloody diarrhea from published studies in FoodNet sites (*39,40*). Uncertainty with this proportion (54%) was based on a 50% relative increase/decrease from 0.54 on an odds scale.	PERT	Low, modal, high values: 0.44, 0.54, 0.64
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–7) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25

Pathogen: Shiga toxin-producing *Escherichia coli* (STEC) infection, serotype non-O157			
Model input	Data source(s)	Distribution	Parameters
Laboratory testing	Among clinical laboratories that performed on-site testing, proportion that used a method that would isolate STEC non-O157 in 2014, from a FoodNet Laboratory Survey (B.B. Bruce, pers. comm.). Methods for the FoodNet Laboratory Survey were described by Hoefer et al. (*38*). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.45, 0.55, 0.65
Test sensitivity	We used a laboratory test sensitivity rate of 70% based on studies of *Salmonella* (*7,8*). We assumed a lower bound of 60% and an upper bound of 90%.	PERT	Low, modal, high values: 0.60, 0.70, 0.90
Proportion with treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 041.42 (STEC O157 infection) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 041.42. This proportion was multiplied by the number of FoodNet case-patients with STEC non-O157 infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 48, 38, 25 HCUP hospitalizations (2012–2014): 160, 305, 255 Proportion by year, 2012–2014: 0.30, 0.12, 0.10
Proportion hospitalized	Proportion of FoodNet case-patients with non-O157 STEC infection who were hospitalized.	Empirical	By site and year (2012–2015), Appendix 1 Table 3
Proportion who died	Proportion of FoodNet case-patients with non-O157 STEC infection who died.	Empirical	By site and year (2012–2015), Appendix 1 Table 4
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of FoodNet case-patients with non-O157 STEC infection who reported travel outside the United States within 7 d of illness onset (2012–2015). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.05, 0.095, 0.21
Proportion waterborne	Structured expert judgment estimate for non-O157 STEC infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0, 0.05, 0.06, 0.17
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release ED visits for ICD-9-CM codes 041.41 and 041.42, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases. Costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,070 (109–2,350)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 041.42, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 24,200 (4,780–138,000)
Pathogen-specific limitations and discussion	The increase in STEC incidence is driven by the increase in STEC non-O157, which is not typically included in routine fecal culture testing because it requires specialized methods (*1*). Routine fecal cultures performed in clinical laboratories typically include methods that identify only *Salmonella*, *Campylobacter*, *Shigella*, and, for some laboratories, STEC O157. The increased use of the syndrome panel tests might increase identification, and, thus, improve incidence estimates of pathogens for which testing was previously limited.		

Pathogen: *Shigella* spp.			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by *Shigella* spp. infection reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by FoodNet site (n = 10) and year (2012–2015) (*1*); scaled up to the US population (the FoodNet catchment area covers 10 sites around the United States and represented 15.3% of the US population in the study time period).	Empirical	By site and year (2012–2015), Appendix 1 Table 2
Population adjustment (year)	Incidence of *Shigella* spp. infection in each FoodNet site by year applied to 2014 US Census population estimates (*2*).	Degenerate	Adjustment by year (2012–2015): 1.01, 1.0, 1.0, 0.99

Pathogen: *Shigella* spp.			
Model input	Data source(s)	Distribution	Parameters
Underreporting	No underreporting multiplier; we assumed that all laboratory-confirmed *Shigella* spp. illnesses were enumerated by FoodNet active surveillance.	–	–
Underdiagnosis (for number of illnesses)			
Percent severe	Percent of laboratory-confirmed cases of *Shigella* spp. infection with bloody diarrhea reported to FoodNet surveillance in Minnesota and New York (*3*). We used uniform minimum variance unbiased (UMVU) estimators for lower and upper endpoints.	PERT	Low, modal, high values: 0.17, 0.35, 0.53
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Shigella* spp., from the FoodNet Laboratory Survey (*4*). We assumed a slightly lower rate of 97%; uncertainty with this proportion was based on a 50% relative increase/decrease from 0.97 on an odds scale.	PERT	Low, modal, high values: 0.94, 0.97, 1.00
Test sensitivity	We used a laboratory test sensitivity rate of 70% based on studies of *Salmonella* (*7,8*). We assumed a lower bound of 60% and an upper bound of 90%.	PERT	Low, modal, high values: 0.60, 0.70, 0.90
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 004 (shigellosis) compared with hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for ICD-9-CM code 004. This proportion was multiplied by the number of FoodNet case-patients with *Shigella* spp. infection who were hospitalized.	Empirical ratio	HCUP ED visits by year (2012–2014): 867, 652, 935 HCUP hospitalizations (2012–2014): 1,650, 1,405, 2,075 Proportion by year, 2012–2014: 0.53, 0.46, 0.46
Proportion hospitalized	Proportion of FoodNet case-patients with *Shigella* spp. infection who were hospitalized (2012–2015).	Empirical	By site and year (2012–2015), Appendix 1 Table 3
Proportion who died	Proportion of FoodNet case-patients with *Shigella* spp. infection who died (2012–2015).	Empirical	By site and year (2012–2015), Appendix 1 Table 4
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Proportion of FoodNet case-patients with *Shigella* spp. infection who reported travel outside the United States within 7 d of illness onset (2012–2015). Uncertainty with this proportion was based on a 50% relative increase/decrease on an odds scale.	PERT	Low, modal, high values: 0.05, 0.078, 0.11
Proportion waterborne	Structured expert judgment estimate for *Shigella* spp. infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.01, 0.03, 0.04, 0.21
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release emergency department visits for ICD-9-CM code 004 (shigellosis), in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported in Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 952 (115–3,980)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM code 004, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 14,200 (4,130–48,000)
Pathogen-specific limitations and discussion	The majority of *Shigella* spp. transmission in the United States is fecal–oral, transmitted person to person or through contaminated food.		

Pathogen: *Vibrio* spp., all			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Sum of illnesses caused by *Vibrio spp.* including *V. alginolyticus, V. vulnificus*, *V. parahaemolyticus*, and other species reported to CDC's Cholera and Other Vibrio Illness Surveillance (COVIS) System (2008–2014) (*41*). Because of an apparent trend over time, linear regression was used to estimate the projected illness for reference year 2014. The uncertainty around the estimated illness was based on the residuals from linear regression (see Appendix 2 for more information).	Empirical	By year (2008–2014): 599, 825, 927, 853, 944, 1176, 1252
Population adjustment (year)	Population ratios applied to each year during 2008–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*).	PERT	Low, modal, high values: 0.9, 1.1, 1.3
Underdiagnosis (for number of illnesses)			
Percent severe	Assumed to be a similar illness to non-typhoidal *Salmonella* infection.	PERT	Low, modal, high values: 0.35, 0.45, 0.71
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.10, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with a non-bloody diarrhea who sought medical care from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Vibrio spp.,* from the FoodNet Laboratory Survey (4).	PERT	Low, modal, high values: 0.41, 0.51, 0.61
Test sensitivity	Proportion of clinical laboratories using appropriate diagnostic tests to test fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.21, 0.28, 0.37
Proportion with a treat-and-release ED visit	Proportion of treat-and-release ED visits (in which the person was not admitted to the hospital) in the 2012–2014 Healthcare Cost and Utilization Project's National Emergency Department Sample (HCUP NEDS) for International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code 001.0 (cholera due to *Vibrio cholerae*), 001.1 (cholera due to *Vibrio cholera* El Tor), 001.9 (cholera, unspecified), 005.4 (food poisoning due to *Vibrio parahaemolyticus*), and 005.81 (food poisoning due to *Vibrio vulnificus*) compared to hospitalizations in the 2012–2014 HCUP National Inpatient Sample (HCUP NIS) for the same ICD-9-CM codes.	Empirical ratio	HCUP ED visits by year (2012–2014): 155, 197, 191 HCUP hospitalizations (2012–2014): 100, 175, 80 Proportion by year, 2012–2014: 1.55, 1.13, 2.39
Proportion hospitalized	Proportion of case-patients with *Vibrio spp.* infection reported to COVIS who were hospitalized (2008–2014).	Empirical	By year (2008–2014): 0.40, 0.36, 0.32, 0.34, 0.35, 0.35, 0.27
Proportion who died	Proportion of case-patients with *Vibrio spp.* infection reported to COVIS who died (2008–2014).	Empirical	By year (2008–2014): 0.06, 0.06, 0.06, 0.06, 0.06, 0.04, 0.04
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Based on proportion of case-patients with *Vibrio spp.* infection reported to COVIS who acquired the infection while traveling outside the United States in the 7 d before illness onset (2008–2014).	PERT	Low, modal, high values: 0.0992, 0.1339, 0.2275
Proportion waterborne	Structured expert judgment estimate for *Vibrio spp.* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.07, 0.24, 0.24, 0.38
Cost of treat-and-release ED visits	Sum of insurer and out-of-pocket payments for treat-and-release emergency department visits for ICD-9-CM codes 001, 005.4, and 005.81, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases, as reported by Adam et al. (*10*).	Empirical	Mean (2.5th percentile, 97.5th percentile): 1,030 (293–3,330)
Cost of hospitalizations	Sum of insurer and out-of-pocket payments for hospitalizations for ICD-9-CM codes 001, 005.4, and 005.81, in 2014 US dollars, in 2012–2013 IBM Watson Health MarketScan research databases.	Empirical	Mean (2.5th percentile, 97.5th percentile): 16,000 (3,780–39,900)

Pathogen: *Vibrio* spp., all			
Model input	Data source(s)	Distribution	Parameters
Pathogen-specific limitations and discussion	*Vibrio spp.* infection manifests in many different ways (e.g., acute gastrointestinal illness, wound infection, bacteremia). Medical care-seeking proportions likely differ for different manifestations, but the medical care-seeking proportions for acute gastrointestinal illness were used, because data were not available for other manifestations.		

Pathogen: *Vibrio alginolyticus*			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by *V. alginolyticus* reported to CDC's Cholera and Other Vibrio Illness Surveillance (COVIS) System (2008–2014) (*41*). Because of an apparent trend over time, linear regression was used to estimate the projected illness for reference year 2014. The uncertainty around the estimated illness was based on the residuals from linear regression (see Appendix 2 for more information).	Empirical	By year (2008–2014): 103, 129, 152, 157, 188, 205, 241
Population adjustment (year)	Population ratios applied to each year during 2008–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*).	PERT	Low, modal, high values: 0.9, 1.1, 1.3
Underdiagnosis (for number of illnesses)			
Percent severe	Assumed to be a similar illness to nontyphoidal *Salmonella* infection.	PERT	Low, modal, high values: 0.35, 0.45, 0.71
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.41, 0.51, 0.61
Test sensitivity	Proportion of clinical laboratories using appropriate diagnostic tests to test fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.21, 0.28, 0.37
Proportion with a treat-and-release ED visit	Could not calculate because there is no *V. alginolyticus*-specific International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) code.		
Proportion hospitalized	Proportion of case-patients with *Vibrio alginolyticus* infection reported to COVIS who were hospitalized (2008–2014).	Empirical	By year (2008–2014): 0.25, 0.13, 0.14, 0.11, 0.13, 0.21, 0.14
Proportion who died	Proportion of case-patients with *Vibrio alginolyticus* reported to COVIS who died (2008–2014).	Empirical	By year (2008–2014): 0.02, 0.02, 0.01, 0.00, 0.01, 0.01, 0.00
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of hospitalizations and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Based on proportion of case-patients with *Vibrio alginolyticus* infection reported to COVIS who acquired the infection while traveling outside the United States in the 7 d before illness onset (2008–2014).	PERT	Low, modal, high values: 0.0367, 0.0667, 0.0838
Proportion waterborne	Structured expert judgment estimate for *Vibrio alginolyticus* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.13, 0.36, 0.37, 0.71
Cost of treat-and-release ED visits	Could not calculate because there is no *V. alginolyticus*-specific ICD-9-CM code.		
Cost of hospitalizations	Could not calculate because there is no *V. alginolyticus*-specific ICD-9-CM code.		
Pathogen-specific limitations and discussion	Could not calculate costs because of poor ICD-9 code fit.		

Pathogen: *Vibrio parahaemolyticus*			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses due to *Vibrio parahaemolyticus* infection reported to CDC's Cholera and Other Vibrio Illness Surveillance (COVIS) System (2008–2014) (*41*). Because of an apparent trend over time, linear regression was used to estimate the projected illness for reference year 2014. The uncertainty around the estimated illness was based on the residuals from linear regression (see Appendix 2 for more information).	Empirical	By year (2008–2014): 270, 386, 421, 334, 431, 594, 605
Population adjustment (year)	Population ratios applied to each year during 2008–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*).	PERT	Low, modal, high values: 0.9, 1.1, 1.3
Underdiagnosis (for number of illnesses)			
Percent severe	Assumed to be a similar illness to nontyphoidal *Salmonella* infection.	PERT	Low, modal, high values: 0.35, 0.45, 0.71
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with a non-bloody diarrhea who sought medical care from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.41, 0.51, 0.61
Test sensitivity	Proportion of clinical laboratories using appropriate diagnostic tests to test fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.21, 0.28, 0.37
Proportion with a treat-and-release ED visit	Could not calculate because of a poor fit between International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) codes and infections by individual *Vibrio* spp.		
Proportion hospitalized	Proportion of case-patients with *Vibrio parahaemolyticus* infection reported to COVIS who were hospitalized (2008–2014).	Empirical	By year (2008–2014): 0.260, 0.230, 0.220, 0.240, 0.250, 0.210, 0.150
Proportion who died	Proportion of case-patients with *Vibrio parahaemolyticus* infection reported to COVIS who died (2008–2014).	Empirical	By year (2008–2014): 0.020, 0.010, 0.010, 0.020, 0.020, 0.007, 0.010
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of ED visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Based on proportion of case-patients with *Vibrio parahaemolyticus* infection reported to COVIS who acquired the infection while traveling outside the United States in the 7 d before illness onset (2008–2014).	PERT	Low, modal, high values: 0.0512, 0.0627, 0.1007
Proportion waterborne	Structured expert judgment estimate for *Vibrio parahaemolyticus* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.07, 0.24, 0.24, 0.38
Cost of treat-and-release emergency visits	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Cost of hospitalizations	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Pathogen-specific limitations and discussion	Could not calculate costs because of poor ICD-9 code fit.		

Pathogen: *Vibrio vulnificus*			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses caused by *Vibrio vulnificus* infection reported to CDC's Cholera and Other Vibrio Illness Surveillance (COVIS) System (2008–2014) (*41*). Because of an apparent trend over time, linear regression was used to estimate the projected illness for reference year 2014. The uncertainty around the estimated illness was based on the residuals from linear regression (see Appendix 2 for more information).	Empirical	By year (2008–2014): 85, 107, 133, 113, 119, 137, 124
Population adjustment (year)	Population ratios applied to each year during 2008–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*).	PERT	Low, modal, high values: 0.9, 1.1, 1.3
Underdiagnosis (for number of illnesses)			
Percent severe	Almost all cases assumed to be severe.	PERT	Low, modal, high values: 0.95, 1, 1
Medical care seeking (severe)	Assumed to have a high rate of medical care seeking.	PERT	Low, modal, high values: 0.80, 0.90, 1.00
Medical care seeking (mild)	Assumed to have a high rate of medical care seeking.	PERT	Low, modal, high values: 0.80, 0.90, 1.00
Specimen submission (severe)	Assumed to have a high rate of specimen submission.	PERT	Low, modal, high values: 0.70, 0.80, 0.90
Specimen submission (mild)	Assumed to have a high rate of specimen submission.	PERT	Low, modal, high values: 0.70, 0.80, 0.90
Laboratory testing	We assumed that most persons with *Vibrio vulnificus* who submitted a specimen for testing would be tested.	PERT	Low, modal, high values: 0.94, 0.97, 1.00
Test sensitivity	Based on sensitivity of blood cultures (*42,43*).	PERT	Low, modal, high values: 0.70, 0.85, 1.00
Proportion with a treat-and-release ED visit	Could not calculate because of a poor fit between International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) codes and infections by individual *Vibrio* species		
Proportion hospitalized	Proportion of case-patients with *Vibrio vulnificus* infection reported to COVIS who were hospitalized (2008–2014).	Empirical	By year (2008–2014): 0.86, 0.90, 0.75, 0.87, 0.87, 0.94, 0.79
Proportion who died	Proportion of case-patients with *Vibrio vulnificus* infection reported to COVIS who died (2008–2014).	Empirical	By year (2008–2014): 0.30, 0.32, 0.31, 0.31, 0.32, 0.28, 0.18
Underdiagnosis (ED visits, hospitalizations, deaths)	Underdiagnosis/reporting for hospitalizations and deaths (UDR H/D) were set to be the product of underdiagnosis for illness and under-reporting for illness. Underdiagnosis/ reporting for ED visit was set using a PERT distribution with parameters of (1, 2, 3).	Empirical	UDR H/D: 2.5%, median and 97.5%: 1.483, 1.855, 2.321
Proportion travel-related	Based on proportion of case-patients with *Vibrio vulnificus* infection reported to COVIS who acquired the infection while traveling outside the United States in the 7 d before illness onset (2008–2014).	PERT	Low, modal, high values: 0, 0.0111, 0.045
Proportion waterborne	Structured expert judgment estimate for *Vibrio vulnificus* infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0.4, 0.8, 0.77, 0.91
Cost of treat-and-release ED visits	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Cost of hospitalizations	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Pathogen-specific limitations and discussion	Could not calculate costs because of poor ICD-9 code fit.		

Pathogen: *Vibrio* spp., other			
Model input	Data source(s)	Distribution	Parameters
Reported illnesses	Number of illnesses due to *Vibrio spp.* other than *V. alginolyticus, V. vulnificus*, and *V. parahaemolyticus* reported to CDC's Cholera and Other Vibrio Illness Surveillance (COVIS) System (2008–2014) (*41)*. Because of an apparent trend over time, linear regression was used to estimate the projected illness for reference year 2014. The uncertainty around the estimated illness was based on the residuals from linear regression (see Appendix 2 for more information).	Empirical	By year (2008–2014): 141, 203, 221, 249, 206, 240, 282
Population adjustment (year)	Population ratios applied to each year from 2008–2014 based on US Census population estimates (*2*).	Degenerate	Adjustment by year (2008–2014): 1.05, 1.04, 1.03, 1.02, 1.01, 1.0, 1.0

Pathogen: *Vibrio* spp., other			
Model input	Data source(s)	Distribution	Parameters
Underreporting	Passive surveillance multiplier used to adjust for underreporting (*3*).	PERT	Low, modal, high values: 0.9, 1.1, 1.3
Underdiagnosis (for number of illnesses)			
Percent severe	Assumed to be a similar illness to non-typhoidal *Salmonella* infection.	PERT	Low, modal, high values: 0.35, 0.45, 0.71
Medical care seeking (severe)	Proportion (and 95% CI) of survey respondents with bloody diarrhea who sought medical care ,from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*)	PERT	Low, modal, high values: 0.19, 0.35, 0.51
Medical care seeking (mild)	Proportion (and 95% CI) of survey respondents with non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.15, 0.18, 0.20
Specimen submission (severe)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with bloody diarrhea who sought medical care from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).,	PERT	Low, modal, high values: 0.11, 0.36, 0.62
Specimen submission (mild)	Proportion (and 95% CI) of survey respondents who submitted a fecal specimen among persons with a non-bloody diarrhea who sought medical care, from FoodNet Population Surveys (2000–2001, 2002–2003, 2006–2007) (*3*).	PERT	Low, modal, high values: 0.12, 0.19, 0.25
Laboratory testing	Proportion of clinical laboratories routinely testing fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.41, 0.51, 0.61
Test sensitivity	Proportion of clinical laboratories using appropriate diagnostic tests to test fecal samples for *Vibrio* spp., from the FoodNet Laboratory Survey (*4*).	PERT	Low, modal, high values: 0.21, 0.28, 0.37
Proportion with a treat-and-release ED visit	Could not calculate because of a poor fit between International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) codes and infections by individual *Vibrio* species		
Proportion hospitalized	Proportion of case-patients with *Vibrio,* other infection reported to COVIS who were hospitalized (2008–2014).	Empirical	By year (2008–2014): 0.48, 0.45, 0.38, 0.36, 0.44, 0.46, 0.41
Proportion who died	Proportion of case-patients with *Vibrio,* other infection reported to COVIS who died (2008–2014).	Empirical	By year (2008–2014): 0.04, 0.05, 0.03, 0.03, 0.04, 0.03, 0.04
Underdiagnosis (ED visits, hospitalizations, deaths)	Number of emergency department visits, hospitalizations, and deaths doubled to account for underdiagnosis.	PERT	Low, modal, high values: 1, 2, 3
Proportion travel-related	Based on proportion of case-patients with *Vibrio,* other infection reported to COVIS who acquired the infection while traveling outside the United States in the 7 d before illness onset (2008–2014).	PERT	Low, modal, high values: 0.0992, 0.1339, 0.2275
Proportion waterborne	Structured expert judgment estimate for *Vibrio,* other infection (*9*).	Empirical	2.5th percentile, median, mean, 97.5th percentile: 0, 0.01, 0.02, 0.23
Cost of treat-and-release ED visits	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Cost of hospitalizations	Could not calculate because of a poor fit between ICD-9-CM codes and infections by individual *Vibrio* species.		
Pathogen-specific limitations and discussion	Could not calculate costs because of poor ICD-9 code fit.		

* A note on the descriptions of the distributions used here: The term “empirical” used here (as in Empirical Cumulative Density Function [ECDF]) refers to using a “finite sample” to construct a distribution to approximate the true underlying distribution/theoretical distribution. In this sense, bootstrapping observed data by simulation and simulating pseudodata for the burden outcomes are both empirical. “Degenerate” in probability terms means a constant here, in contrast to a random variable. In other words, it refers to a random variable that has a single possible value (a constant with probability 1). NA, not applicable; PERT, Program Evaluation and Review Technique.

Appendix 1 Table 2. Number of cases of illness reported to CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by pathogen, year, and FoodNet site

		FoodNet site									
Pathogen	Year	CA	CO	CT	GA	MD	MN	NM	NY	OR	TN
Campylobacter spp.	2012	1189	414	600	1058	662	1192	399	614	907	660
Campylobacter spp.	2013	1076	344	694	983	708	1190	415	673	870	741
Campylobacter spp.	2014	1040	330	812	946	729	1082	431	708	906	679
Campylobacter spp.	2015	1245	451	783	1090	772	1411	463	636	884	759
Cryptosporidium spp.	2012	48	26	41	275	83	340	94	50	230	71
Cryptosporidium spp.	2013	46	51	38	302	65	324	47	79	177	88
Cryptosporidium spp.	2014	32	26	44	269	76	337	80	88	113	124
Cryptosporidium spp.	2015	63	69	82	406	103	319	54	99	197	266
E. coli, STEC O157	2012	39	37	19	34	33	123	15	69	95	69
E. coli, STEC O157	2013	64	26	32	48	28	144	11	42	105	54
E. coli, STEC O157	2014	51	19	17	25	20	128	14	29	72	69
E. coli, STEC O157	2015	47	38	27	27	24	114	7	27	108	47
E. coli, STEC non-O157	2012	23	42	31	91	37	110	41	43	72	50
E. coli, STEC non-O157	2013	26	70	36	66	34	127	18	45	58	66
E. coli, STEC non-O157	2014	57	67	40	64	44	164	33	48	86	72
E. coli, STEC non-O157	2015	114	69	53	76	53	110	26	57	107	116
Salmonella spp.	2012	484	264	455	2681	906	781	327	501	387	1057
Salmonella spp.	2013	586	323	446	2288	829	811	350	451	364	859
Salmonella spp.	2014	618	332	464	2247	897	722	327	503	376	953
Salmonella spp.	2015	601	316	450	2113	935	974	429	486	518	897
Shigella spp.	2012	215	56	44	666	181	391	96	211	78	203
Shigella spp	2013	193	90	59	907	105	133	61	68	52	665
Shigella spp	2014	345	55	65	1038	248	93	63	42	45	780
Shigella spp	2015	299	66	60	1301	198	292	72	43	106	208

Appendix 1 Table 3. Proportion of case-patients hospitalized, from CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by pathogen, year, and FoodNet site

		FoodNet sites									
Pathogen	Year	CA	CO	CT	GA	MD	MN	NM	NY	OR	TN
Campylobacter spp.	2012	0.1490	0.1418	0.1760	0.2375	0.1755	0.2097	0.2532	0.1800	0.0907	0.2931
Campylobacter spp.	2013	0.1157	0.1462	0.1879	0.2810	0.2193	0.1630	0.2029	0.1985	0.0820	0.3175
Campylobacter spp.	2014	0.1360	0.1311	0.2145	0.2804	0.1886	0.1867	0.2266	0.2201	0.1199	0.3002
Campylobacter spp.	2015	0.1165	0.1496	0.1826	0.2922	0.2011	0.1979	0.2078	0.2208	0.1017	0.3225
Cryptosporidium spp.	2012	0.1795	0.2000	0.1220	0.3187	0.4691	0.1088	0.2903	0.1000	0.0437	0.2941
Cryptosporidium spp.	2013	0.1282	0.1765	0.0263	0.3199	0.3860	0.1296	0.3043	0.1899	0.0739	0.3125
Cryptosporidium spp.	2014	0.2069	0.2308	0.1591	0.3529	0.2917	0.1335	0.1125	0.1494	0.0545	0.1933
Cryptosporidium spp.	2015	0.2931	0.1159	0.1481	0.2926	0.2059	0.0909	0.1296	0.1429	0.0663	0.1587
E. coli, STEC O157	2012	0.2821	0.4167	0.3158	0.4706	0.4242	0.3171	0.4000	0.3676	0.3158	0.4478
E. coli, STEC O157	2013	0.3548	0.3077	0.3438	0.2766	0.3571	0.3542	0.3636	0.5476	0.4571	0.4118
E. coli, STEC O157	2014	0.3265	0.2632	0.5882	0.3200	0.4500	0.2969	0.4286	0.3793	0.2917	0.4559
E. coli, STEC O157	2015	0.3696	0.3421	0.4074	0.2800	0.4583	0.3158	0.4286	0.6296	0.4206	0.4419
E. coli, STEC non-O157	2012	0.1500	0.1220	0.2581	0.0769	0.2162	0.1455	0.3171	0.2326	0.1389	0.1042
E. coli, STEC non-O157	2013	0.0833	0.0571	0.1714	0.0606	0.1250	0.1654	0.3333	0.2667	0.0877	0.1563
E. coli, STEC non-O157	2014	0.0800	0.0758	0.1282	0.0702	0.1905	0.1707	0.2121	0.1250	0.1279	0.3676
E. coli, STEC non-O157	2015	0.1273	0.1471	0.1698	0.1757	0.1132	0.2545	0.1923	0.1754	0.1028	0.1415
Salmonella spp.	2012	0.2249	0.2727	0.2539	0.2986	0.3464	0.2586	0.3137	0.3353	0.2506	0.3834
Salmonella spp.	2013	0.2246	0.2755	0.2320	0.2896	0.3350	0.2762	0.2607	0.3073	0.2149	0.3522
Salmonella spp.	2014	0.2147	0.2515	0.3218	0.3169	0.3546	0.2645	0.2936	0.3153	0.2139	0.3297
Salmonella spp.	2015	0.2255	0.2283	0.2978	0.2938	0.2971	0.2710	0.3380	0.2934	0.2058	0.3184
Shigella spp.	2012	0.2100	0.1964	0.2727	0.2606	0.2652	0.1432	0.3053	0.2559	0.1538	0.3094
Shigella spp	2013	0.2640	0.1778	0.2712	0.1674	0.4043	0.2556	0.2131	0.2794	0.2885	0.1866
Shigella spp	2014	0.3526	0.3091	0.2462	0.2133	0.2544	0.2151	0.3016	0.1190	0.1778	0.1397
Shigella spp	2015	0.2955	0.2576	0.2167	0.2311	0.2974	0.2158	0.1806	0.3256	0.3113	0.2402

Appendix 1 Table 4. Proportion of case-patients who died, from CDC's Foodborne Diseases Active Surveillance Network (FoodNet) by pathogen, year, and FoodNet site

		FoodNet sites									
Pathogen	Year	CA	CO	CT	GA	MD	MN	NM	NY	OR	TN
Campylobacter spp.	2012	0.0000	0.0024	0.0000	0.0042	0.0016	0.0034	0.0026	0.0016	0.0000	0.0016
Campylobacter spp.	2013	0.0000	0.0000	0.0000	0.0083	0.0015	0.0042	0.0000	0.0045	0.0011	0.0014
Campylobacter spp.	2014	0.0000	0.0000	0.0000	0.0012	0.0000	0.0046	0.0023	0.0028	0.0033	0.0030
Campylobacter spp.	2015	0.0082	0.0022	0.0013	0.0080	0.0013	0.0064	0.0043	0.0016	0.0011	0.0040
Cryptosporidium spp.	2012	0.0000	0.0000	0.0000	0.0000	0.0366	0.0029	0.0108	0.0000	0.0043	0.0000
Cryptosporidium spp.	2013	0.0000	0.0196	0.0000	0.0066	0.0000	0.0031	0.0000	0.0000	0.0000	0.0000
Cryptosporidium spp.	2014	0.0000	0.0000	0.0000	0.0040	0.0000	0.0059	0.0000	0.0000	0.0000	0.0082
Cryptosporidium spp.	2015	0.0000	0.0145	0.0000	0.0076	0.0000	0.0000	0.0000	0.0000	0.0051	0.0038
E. coli, STEC O157	2012	0.0000	0.0000	0.0000	0.0323	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
E. coli, STEC O157	2013	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0190	0.0000
E. coli, STEC O157	2014	0.0000	0.0000	0.0000	0.0000	0.0000	0.0078	0.0000	0.0000	0.0139	0.0145
E. coli, STEC O157	2015	0.0000	0.0000	0.0370	0.0000	0.0000	0.0000	0.1429	0.0000	0.0093	0.0000
E. coli, STEC non-O157	2012	0.0476	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
E. coli, STEC non-O157	2013	0.0000	0.0000	0.0000	0.0000	0.0000	0.0079	0.0000	0.0000	0.0000	0.0000
E. coli, STEC non-O157	2014	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0208	0.0000	0.0000
E. coli, STEC non-O157	2015	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0093	0.0000
Salmonella spp.	2012	0.0022	0.0038	0.0066	0.0035	0.0034	0.0038	0.0031	0.0080	0.0103	0.0030
Salmonella spp.	2013	0.0036	0.0093	0.0090	0.0026	0.0062	0.0012	0.0000	0.0044	0.0055	0.0061
Salmonella spp.	2014	0.0051	0.0091	0.0043	0.0049	0.0033	0.0042	0.0061	0.0020	0.0027	0.0043
Salmonella spp.	2015	0.0018	0.0032	0.0044	0.0059	0.0053	0.0010	0.0140	0.0000	0.0039	0.0023
Shigella spp.	2012	0.0000	0.0000	0.0000	0.0017	0.0055	0.0026	0.0000	0.0000	0.0000	0.0000
Shigella spp	2013	0.0000	0.0000	0.0000	0.0011	0.0000	0.0000	0.0000	0.0000	0.0000	0.0032
Shigella spp	2014	0.0032	0.0000	0.0000	0.0031	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Shigella spp	2015	0.0000	0.0000	0.0000	0.0008	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

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Estimate of Burden and Direct Healthcare Cost of Infectious Waterborne Disease in the United States

Appendix 2

Model Types Used to Make Estimates

The process of estimating the burden of waterborne illness requires the use of disparate data sources and making subjective decisions on how to combine them. Briefly, after we identified our illnesses of interest, we combined data from available data sources (surveillance data systems, administrative data, or data from the literature) and applied multipliers to account for population standardization, underreporting, underdiagnosis, proportion domestically acquired, and proportion attributable to waterborne transmission. For pathogens with surveillance data, we adapted an approach laid out previously to estimate the burden of foodborne illness (*1*), with some modifications and differences, detailed in this appendix. For pathogens with administrative or literature data only, we developed new models to estimate the burden of waterborne illness. The summary statistics are based on distributions constructed from Monte Carlo simulation records. We report the mean and 95% credible interval (CrI), a range that covers 95% of the sample.

Burden Outcomes

We used the estimated annual total number of illnesses, hospitalizations, deaths, emergency department (ED) visits, total health care cost for hospitalizations, and total health care cost for ED visits to measure the burden of waterborne diseases in the United States.

Model Structures

We used 3 broad model types to estimate the burden outcomes, except health care cost burdens, for 17 known waterborne pathogens. Variations exist within each model type depending

on the pathogen, the diagnostic test type, severity of the disease, availability of input data, and choices made on multiplier values. Details on the variations by pathogen are available in Appendix 1.

Model type A was used for surveillance data. This model scales counts of laboratory-confirmed (reported) illnesses up to an estimated number of illnesses, accounting for both underreporting and underdiagnosis factors that contribute to illnesses not being reported to surveillance systems. This model was applied to both active and passive surveillance data (Appendix 2 Table).

Model type B was used for administrative data. This model scales hospitalization counts reported in administrative datasets up to an estimated number of illness, accounting for both hospitalization rate and underreporting and underdiagnosis factors that contribute to an illness not being seen in a hospital or reported to hospital discharge databases (Appendix 2 Table).

Model type C was used for publication-based data. This model scales populations at risk down to an estimated number of illnesses using publication reported incidence rates (Appendix 2 Table).

Model Type A: Burden Estimate for Pathogens Reported from Surveillance Systems

Model inputs (illnesses, hospitalizations, and deaths) were assigned distributions using previously defined methods (*1*). For pathogens reported in the active surveillance system (FoodNet) (*2*), data from different sites or years were treated as representatives from distinct populations. We chose to treat, for example, FoodNet confirmed case counts from 10 sites over 4 years (2012–2015) as representing 40 distinct population means. Each population contributes to the empirical distribution with equal probability. For pathogens reported in the passive surveillance systems, linear regression was applied to fit multiyear (2008–2014) national data and to estimate the average burden count for the reference year 2014. Residuals from all 7 years were randomly sampled with equal chance and then used in the calculation of the uncertainty of the predicted count, simulating the distribution of reported count.

All model inputs are multiplicative. Each multiplier either expands or contracts the observed/reported burden counts to produce the final burden estimate. We assume all multipliers in model type A to be mutually independent except for the ones associated with the

underdiagnosis of illness, where the multipliers associated with care-seeking and specimen submission rate depend on the severity of cases.

The distributions of model outputs were obtained via Monte Carlo simulation. During each simulation run, a random sample was drawn from the theoretical/empirical distribution of each model input; then they were multiplied sequentially depending on their positions in the model. The final product of all factors yielded the burden estimate. The empirical distribution pooled from a large number of simulated records (100,000 iterations) allowed us to estimate the uncertainty of the burden outcomes.

Only a fraction of cases whose records passed a series of stages in the reporting process could be seen in our surveillance system. Each multiplier value refers to the proportion of case records advancing to the next stage (e.g., the proportion of patients seeking medical care), and these multiplier values are all <1. To estimate the burden of illness, we use the reciprocal of these multiplier values, called expansive factors, to scale up the number of reported cases from the surveillance system (Appendix 2 Figure 1 and Figure 2, panel B). Appendix 2 Figure 1 describes the modeling process of scaling up reported confirmed cases by surveillance system up (model type A) in a mathematical format. The order of the multiplication does not matter, as the factors are commutative. The diagram shows 9 primary model outputs, identified in the box in the middle and obtained by inclusion of elements from vectors (column [1 or H or D] and row [1 or Dom or W]). For example, a combination of choosing D, Dom, and W yields the output for domestic waterborne deaths. Each of these factors is either a random variable, following an empirical distribution constructed from observed or estimated data or a parametric distribution, or a constant, such as the year adjustment factor to the 2014 population size. As illustrated in Appendix 2 Figures 2 and 3, the central location and spread of each model output reflects not only the multiplicative effect of its components but also the cumulative and joint effect of their uncertainties.

For all multipliers except the water attribution rate, we assumed the same distribution properties as those in the foodborne burden paper (*1*). We updated the distribution parameters whenever new data or information were available. For the waterborne attribution proportion, a calibrated and synthesized distribution for each pathogen was obtained from elicitation results of a panel of experts (*3*). The same assumptions about multiplier distributions were made among all

model types (A, B, and C). The underdiagnosis/underreporting factors for ED visits, hospitalizations, and deaths were set as beta/PERT distributions (*4*) with values of (min, mode, max)= (1, 2, 3). This rule was applied to all pathogens in the surveillance systems unless otherwise stated. Details of the choices made to define the distributions of model inputs by pathogen are available in Appendix 1.

Appendix 2 Figures 2 and 3 demonstrate the distributions involved in constructing estimates for *Shigella*, including the annual illness estimate (Appendix 2 Figure 2, panel A), the underdiagnosis multiplier (Appendix 2 Figure 2, panel B) and the hospitalization estimate (Appendix 2 Figure 3). The empirical and discrete nature of the source data is apparent in the first panel of Appendix 2 Figure 2, panel A. The right skewness in the water attribution rate dominates the distribution of the domestic waterborne illness. As shown in Appendix 2 Figure 2, panel B, a series of multipliers contributed to illnesses not being seen or verified or reported. These multipliers expanded the laboratory reported case counts in a multiplicative fashion and their impacts were passed onto the combined underdiagnosis multiplier in the main model (Appendix 2 Figure 2, panel A). The hospitalization estimate, as shown in Appendix 2 Figure 3, was similar to the illness estimate.

Model Type B: Burden Estimate for Pathogens/Data Reported from Administrative Systems and ED Visits for All Pathogens

Pathogens for which model type B was used did not have data available from national surveillance systems. Instead, data from the Agency for Healthcare Research and Quality Health Care Utilization Project's National Inpatient Sample (HCUP NIS) (*5*) and National Emergency Department Sample (HCUP NEDS) (*6*) were used. The NIS is the largest publicly available US hospital discharge database that includes all sources of payment (i.e., private insurance, public insurance, and the uninsured). HCUP NIS is a complex sample survey that produces weighted national estimates from a stratified sample of about 20% of hospital stays from community hospitals in the United States. Similarly, HCUP NEDS is a complex sample survey that produces weighted national estimates of emergency department visits. Appendix 2 Figure 4 shows the estimation steps for model type B pathogens. Each of these factors is either a random variable, following a parametric distribution (e.g., normal distribution or beta/PERT distribution), or a constant (year adjustment factor). Unlike pathogens in surveillance systems (model type A), here

hospitalization counts served as the initial model input. They were scaled up to estimate the number of illnesses by dividing by the hospitalization rate.

For ED visits, hospitalizations, and death counts reported in HCUP datasets, we assumed a mixture of 3 normal distributions with equal probability, with each year of data providing the parameters of a mixture component. Each individual year represented 1 normal population. The associated parameter mean was taken from the weighted nationwide frequency count and the standard deviation was calculated from the lower and upper limits assuming a normal distribution was used in the confidence interval construction.

The death counts were derived from 2 sources. The total death count is the sum of in-hospital deaths and out-of-hospital deaths, as described by Gargano et al. (*7*). In-hospital deaths were obtained using the number of hospitalizations for a particular illness in the HCUP NIS database that ended in death. Out-of-hospital deaths were obtained from out-of-hospital deaths reported for a particular illness in the National Vital Statistics System (NVSS) (*8*), which contains information on all death certificates filed in the United States. No uncertainty was reported for the out-of-hospital death count. Here we used it as a constant rather than a distribution. The model outputs and the distributions were quantified via Monte Carlo simulation.

Special treatments were employed in the simulation algorithms to ensure that the biological or clinical constraints of the model outputs were met. First, when a negative number occurred in the simulation under a normal distribution, it was replaced with zero. Second, for pathogens with high hospitalization rates ($\geq$75%), the 3 underdiagnosis factors (for illnesses, hospitalizations, and deaths) were set to be the same for each simulated record. This treatment ensured that the number of illness was greater than the number of hospitalizations and the number of deaths, true not only for the mean value but also for each simulated individual record.

The multiplicative impact of each factor on the final burden estimate was illustrated in Appendix 2 Figure 5. Details of the choices made on the multipliers and their parameters are provided in Appendix 1.

Appendix 2 Figure 5 demonstrates the distributions involved in constructing estimates of annual illnesses for *Pseudomonas* pneumonia. As shown previously, the hospitalization was a mixture of 3 normal distributions with variable mean values. Although the annual illness was

multimodal, the other multipliers followed 1-mode beta/PERT-distribution, spreading narrowly around their modes. The resulting smoothed distribution of domestically acquired waterborne illness was unimodal. The estimations for hospitalizations, deaths, and ED visits were modeled in a similar way except that the hospitalization rate component (the third panel) was removed from the equation.

Model Type C: Burden Estimate for Pathogen Reported from Literature Data

Model type C was used for 1 pathogen, norovirus. For norovirus, instead of using acute gastrointestinal illness (AGI) as a starting point for the estimate (*1*), we used incidence estimates (already adjusted for underdiagnosis) from 2 studies (*9,10*). The Hall et al. study (*9*) was conducted at 1 site of the Kaiser Permanente health care system. The Grytdal et al. study (*10*) was conducted at 2 additional sites of the Kaiser Permanente health care system. To combine the studies, the reported 3-number summary statistics (mean, lower, and upper limit) for incidence rate at each site were fit to a 4-parameter PERT distribution with the variation parameter fixed, while minimizing the overall distance between the 3 summary statistics and the model predicted values. The process was repeated for different values of the variation parameter. The corresponding parameter combination under the best fit, verified by subject matter experts via visual examinations, was assigned as the PERT distribution parameters for that site. The sampling distribution for the annual incidence rate was a mixture of the 3 beta distributions with 1 distribution representing 1 site. Each site had an equal probability of being drawn. We chose beta/PERT distribution to describe the incidence rate for the following reasons. First, the reported confidence intervals were asymmetric, making the normal distribution not immediately applicable. Second, the original datasets used to produce CIs in the publications were not available to us. Third, the beta distribution family has the capacity to accommodate left-skewed, right-skewed, and symmetric confidence intervals or distributions. Fourth, incidence rate takes values on a range with an upper and lower bound. The generalized beta/PERT distribution has the flexibility to set a range on incidence rates. In addition, we selected a different value from the default setup for the variation parameter of the PERT distribution, the same strategy used in the previous foodborne burden paper (*11*) because it gave us a fit with a narrower range and a more realistic distribution spread than the fit under the default value.

The most recent published norovirus hospitalization rate estimates were obtained by fitting a complex statistical model to multiyear (1996–2007) HCUP data (*12*). Although the data

showed a trend of increase in hospitalization rates during 1996–2007, we cannot say whether this trend continued or not, nor can we estimate the hospitalization rate in the reference year 2014 without additional data. Instead, we assumed that the reported multiyear hospitalization rates were a random sample from 1 homogeneous population following a beta/PERT distribution. The minimum, maximum, and mode of the multiyear rates were assigned as the input parameters for the PERT distribution. The same strategy was applied to death rates (*13*) and ED visits (*14*).

Appendix 2 Figure 6 describes the modeling process for norovirus for which populations at risk of illness were scaled down to estimate burden outcomes. As in model type A and B, all model inputs are assumed to be independent and multiplicative.

Appendix 2 Figures 7 and 8 demonstrate the distributions involved in constructing estimates for norovirus including the annual illness estimate (Appendix 2 Figure 7) and the annual hospitalization estimation (Appendix 2 Figure 8). The deaths and ED visits were estimated in the same way as hospitalizations. The norovirus model estimates start with population size and incidence rate. As shown in Appendix 2 Figure 7, a mixture of 3 beta/PERT-distributions from 3 sites of the Kaiser studies was used to describe the incidence rate for illnesses. Consequently, the multimodal feature was presented in the annual illness estimate (second panel in Appendix 2 Figure 7). There was no underdiagnosis adjustment for illness, as the publication already took that into account. Although the estimated annual illness distribution was multimodal, the long tail of the water attribution rate dominated in the final output. The resulting distribution of domestic waterborne illness was right-skewed with an extended right tail. The only difference in the estimation equation between hospitalizations (Appendix 2 Figure 8), deaths, or ED visits and the illnesses was that the incidence rate consisted of only 1 beta/PERT distribution instead of a mixture of PERT distributions.

Discussion

In selecting data sources for the burden estimate, we chose an active surveillance system over a passive one when both were available, as there is a greater nonstatistical uncertainty around passive estimates. In the case of *Vibrio* estimates, we used data reported in Cholera and Other *Vibrio* Illness Surveillance (COVIS) (*15*) instead of FoodNet because most *Vibrio* cases occur in Gulf states, and FoodNet sites do not include any of those states.

Previously, 90% CrIs were reported in the foodborne burden paper (*1*,*11*). A 90% CrI adds less uncertainty in more extreme quantile distributions, is a more robust estimate, and is narrower compared with a 95% CrI. Here, we chose to report 95% CrIs to be consistent with the coverable probability (95%) commonly used in publications. In all models, we assumed that the factors are stochastically independent. In some circumstances, this assumption may not hold.

In the determination of distribution parameters for multipliers, we relied on statistics reported in previous publications or statistics calculated based on updated data. In the absence of new data, we applied the same parameter values as those used in the foodborne burden paper (*1*). When only a point estimate was available for PERT distribution (e.g., international travel rate), we estimated the range based on a 50% relative increase/decrease from the mode/point estimate on an odds scale for proportion parameters. In general, the information on underdiagnosis/underreporting for hospitalizations, deaths, and ED visits is lacking. A factor of 2 was assumed in previous publications on burden estimation (*1*,*16*). We applied the factor of 2 and expanded the range by 1 (i.e., 2 ± 1). There are alternatives of modeling uncertainty, such as using multiplicative models or/and applying different magnitudes of variability. We chose the aforementioned strategies because, overall, the approach produced reasonable estimates.

In model B, we treated the out-of-hospital death count as a constant because the variability associated with the point estimate was not available. Because the number of out-of-hospital deaths is much smaller than number of in-hospital deaths, the contribution of its uncertainty to the uncertainty of total number of deaths is negligible. During the simulation of all 4 burden outcomes, we took special measures to ensure the counts to be nonnegative by assigning zeros to negative values. Most of the simulated counts were >0, with a few exceptions that occurred in the ED visit simulation. Overall, the proportion of negative values was very small (<0.81%). Therefore, the impact of truncating a normal distribution is considered negligible.

In this study, we took a different approach for norovirus from the one employed in the foodborne disease burden study (*1*) by modeling the incidence rates, hospitalization rates, death rates, and ED rates as following a PERT distribution. The distribution parameters were extracted from statistics reported in recent publications. Despite the differences in the modeling process,

data sources, time coverage, population coverage of the data, and the nonstatistical uncertainties (*11*) compared with our estimate, the burden estimates for norovirus illnesses were comparable.

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Appendix 2 Table. Model types for burden estimate of waterborne diseases, by pathogen

Model	Burden outcomes			
Pathogen	Illness	Hospitalization	Death	ED visits
Campylobacter spp.	Model type A	Model type A	Model type A	Model type B
Cryptosporidium spp.	Model type A	Model type A	Model type A	Model type B
Shiga toxin-producing *Escherichia coli* (STEC) O157	Model type A	Model type A	Model type A	Model type B
Shiga toxin-producing *E. coli* (STEC), non-O157	Model type A	Model type A	Model type A	Model type B
Giardia duodenalis	Model type A	Model type A	Model type A	Model type B
Legionella	Model type A	Model type A	Model type A	Model type B
Norovirus	Model type C	Model type C	Model type C	Model type C
Nontuberculous mycobacteria	Model type B	Model type B	Model type B	Model type B
Otitis externa	Model type B	Model type B	Model type B	Model type B
Pseudomonas pneumonia	Model type B	Model type B	Model type B	Model type B
Pseudomonas septicemia	Model type B	Model type B	Model type B	Model type B
Salmonella, nontyphoidal	Model type A	Model type A	Model type A	Model type B
Shigella spp.	Model type A	Model type A	Model type A	Model type B
Vibrio alginolyticus	Model type A	Model type A	Model type A	Model type B
Vibrio parahaemolyticus	Model type A	Model type A	Model type A	Model type B
Vibrio spp., other	Model type A	Model type A	Model type A	Model type B
Vibrio vulnificus	Model type A	Model type A	Model type A	Model type B

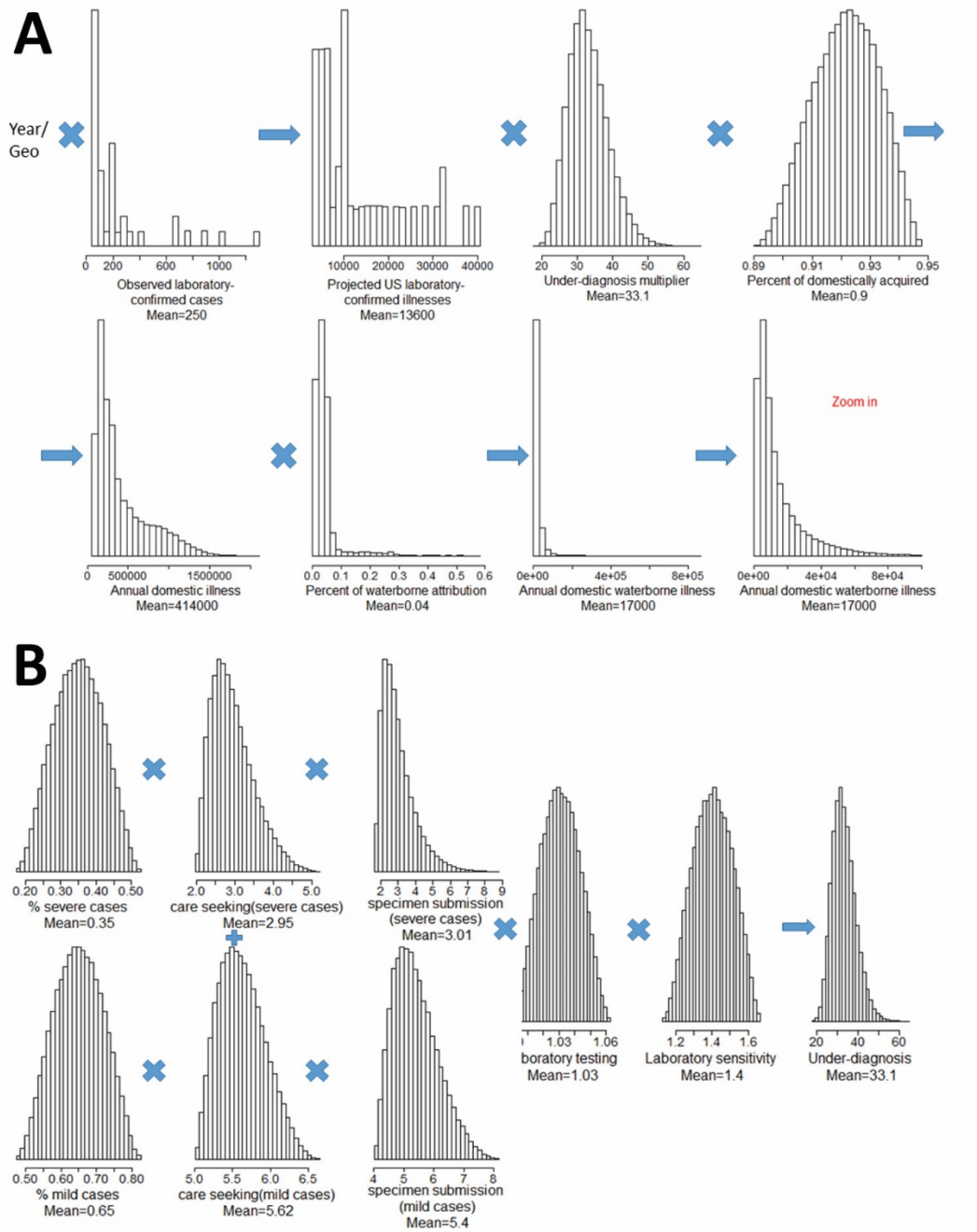
$$Count \times \begin{bmatrix} \boldsymbol{Year} \\ \&/or \\ \boldsymbol{Geo} \end{bmatrix} \times UR \times UD^{\dagger} \times \begin{bmatrix} 1 \\ or \\ H \\ or \\ D \end{bmatrix} \times [1 \quad or \quad Dom \quad or \quad W] \Longrightarrow$$

Illnesses	*Domestic Illnesses*	*Domestic Waterborne Illnesses*
Hospitalizations	*Domestic Hospitalizations*	*Domestic Waterborne Hospitalizations*
Deaths	*Domestic Deaths*	*Domestic Waterborne Deaths*

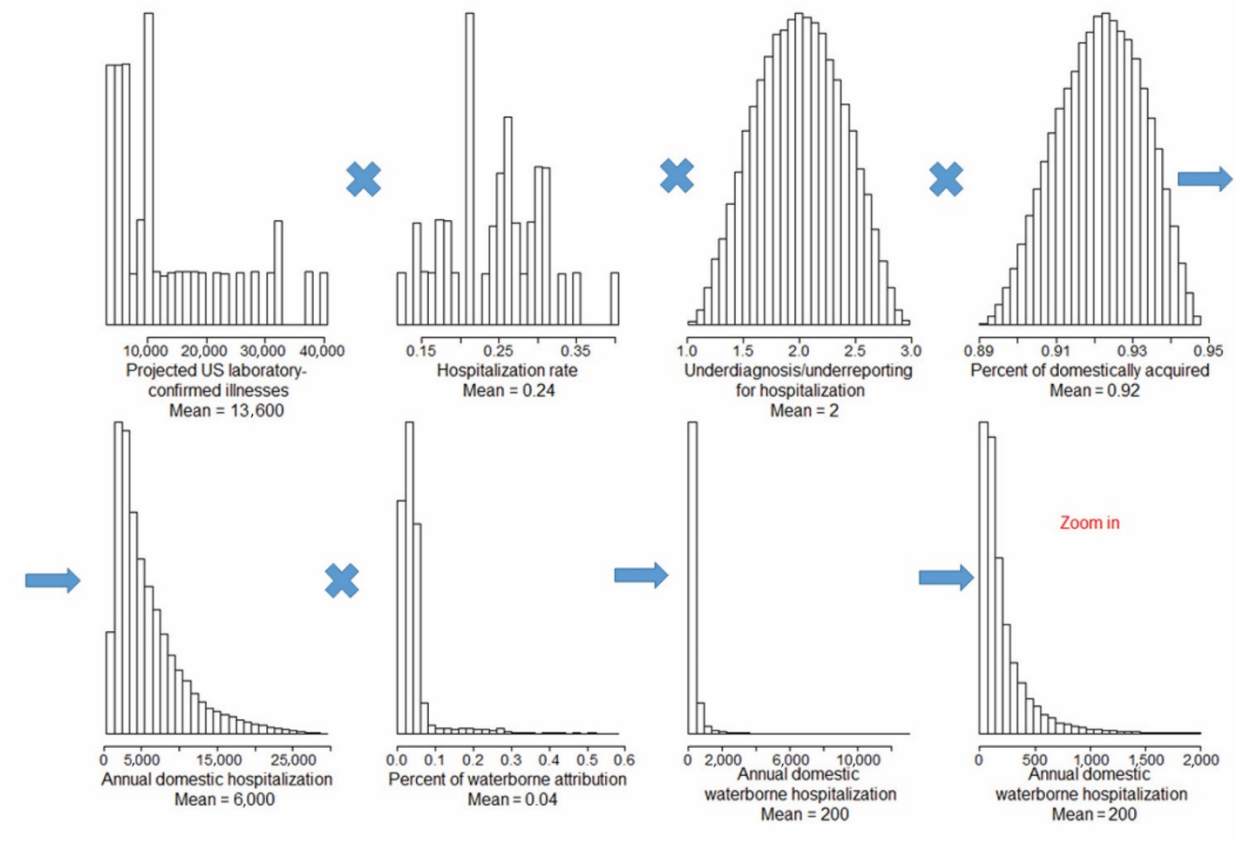
Underdiagnosis (UD) for Illnesses

$$\left\{ \begin{matrix} CS(Severe) \times SS(Severe) \times P(S) \\ + \\ CS(Mild) \times SS(Mild) \times (1 - P(S)) \end{matrix} \right\} \times LT \times LS$$

Appendix 2 Figure 1. Schematic illustration of model type A, which scales case counts up, and is based on surveillance data (*11*). *Count* refers to data in the form of cases of reported illnesses. *Year* is a deterministic factor to standardize non-2014 counts to 2014 (applied as needed). *Geo* is a deterministic expansive factor to scale FoodNet counts up to the entire US population (applied as needed). *UR* is an expansive factor to scale passive surveillance case counts up to active surveillance counts to account for underreporting (applied as needed). *UD* is an expansive factor to scale laboratory-confirmed cases to illnesses not being reported to the surveillance system to account for underdiagnosis. †*UR and UD*: for hospitalization or death or ED visits, there was only 1 factor accounting for both underreporting and underdiagnosis. This multiplier follows PERT distribution with mode 2. *CS* is an expansive factor to scale care seekers up to all ill, with severe and mild illness versions. It is the reciprocal of the proportion of cases seeking care. *SS* is an expansive factor to scale submitted samples up to all ill visits, with severe and mild illness versions. It is the reciprocal of the proportion of specimen submitted for laboratory testing. *P(S)* is the proportion of actual illness that is severe. *LT* is an expansive factor to scale tests performed up to samples submitted. It is the reciprocal of the proportion of specimen being tested. *LS* is an expansive factor to scale positive tests up to true positive specimens. It is the reciprocal of sensitivity. *H* is a contractive factor to scale illnesses down to hospitalized illnesses. *D* is a contractive factor to scale illnesses down to deaths. *Dom* is a contractive factor to scale total counts down to counts that are domestically acquired (applied as needed). *W* is a contractive factor to scale overall counts down to counts that are waterborne.



Appendix 2 Figure 2. A) Schematic diagram of the estimation of annual illnesses for *Shigella. X* axes show the relative frequency of observed or simulated values for each input or multiplier. *Year* is a deterministic factor to standardize non-2014 counts to 2014 (applied as needed). *Geo* is a deterministic expansive factor to scale FoodNet counts up to the entire U.S. population (applied as needed). B) Schematic diagram of underdiagnosis of illnesses for *Shigella. X* axes show the relative frequency of observed or simulated values for each input or multiplier.

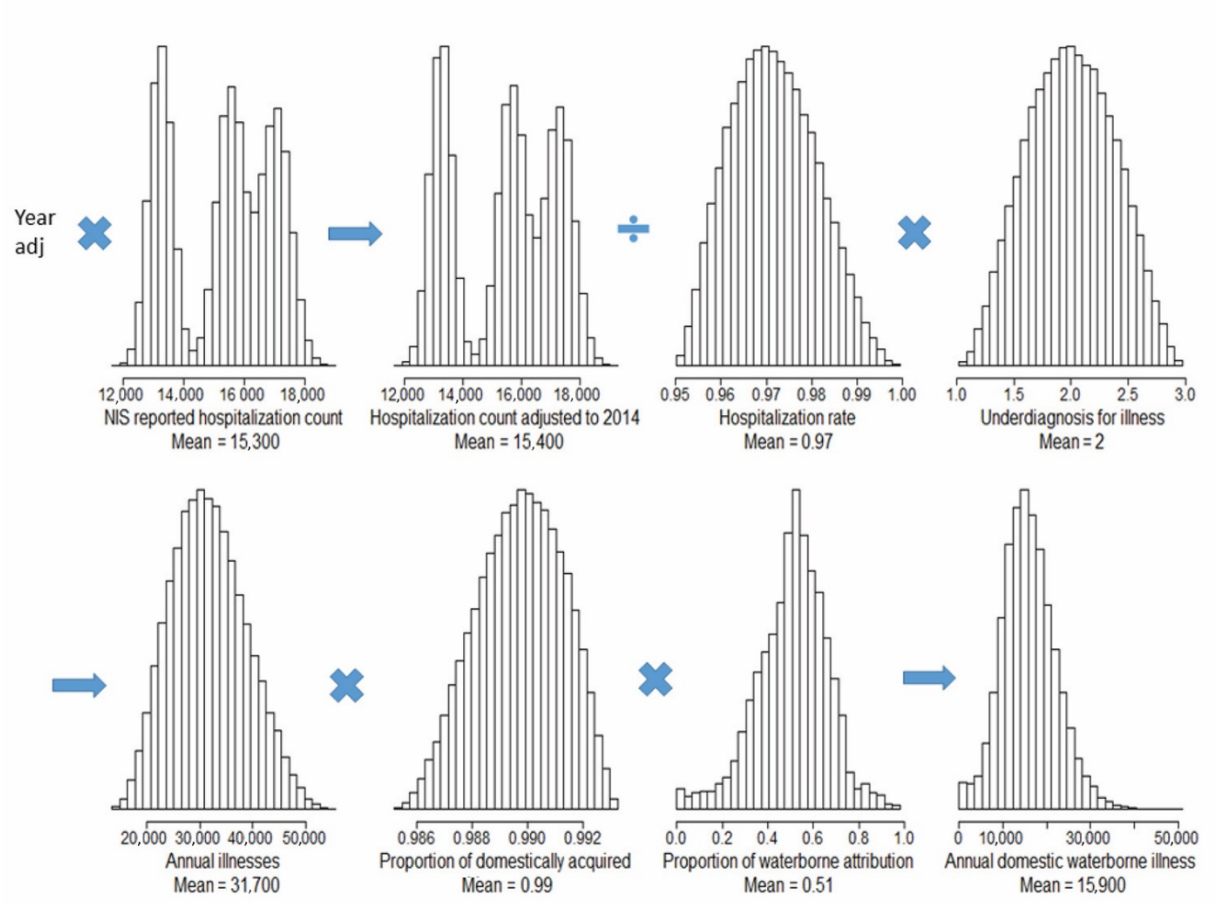


Appendix 2 Figure 3. Schematic diagram of the estimation of hospitalizations for *Shigella. X* axes show the relative frequency of observed or simulated values for each input or multiplier.

$$\begin{bmatrix} Hospitalization\ count \\ Hospitalization\ count \\ Death\ count \\ ED\ visit\ count \end{bmatrix} \times Year \times \begin{bmatrix} \frac{1}{Hospitalization\ rate} \\ 1 \\ 1 \\ 1 \end{bmatrix} \times UR \times UD \times [1 \quad or \quad Dom \quad or \quad W] \Longrightarrow$$

Illness	*Domestic Illness*	*Domestic waterborne illness*
Hospitalization	*Domestic hospitalization*	*Domestic waterborne hospitalization*
Death	*Domestic death*	*Domestic waterborne death*
ED visits	*Domestic ED visits*	*Domestic waterborne ED visits*

Appendix 2 Figure 4. Schematic illustration of model type B, which scales hospitalization counts up, and is based on administrative data. *Hospitalization count, death counts,* and *ED visit counts* refer to counts reported in HCUP NIS or HCUP NEDS datasets. *Year* is a deterministic factor to standardize non-2014 counts to 2014 (applied as needed). *1/Hospitalization rate* is an expansive factor to scale the hospitalization count up to the illness count. *UR* is an expansive factor to scale passive surveillance case counts up to active surveillance counts to account for underreporting (applied as needed). *UD* is an expansive factor to scale laboratory-confirmed cases to illnesses not being reported to the surveillance system to account for underdiagnosis. *UR and UD*: for hospitalization or death or ED visits, only 1 factor accounted for both underreporting and underdiagnosis. This multiplier follows PERT distribution with mode 2. *Dom* is a contractive factor to scale total counts down to counts that are domestically acquired (applied as needed). *W* is a contractive factor to scale overall counts down to counts that are waterborne.

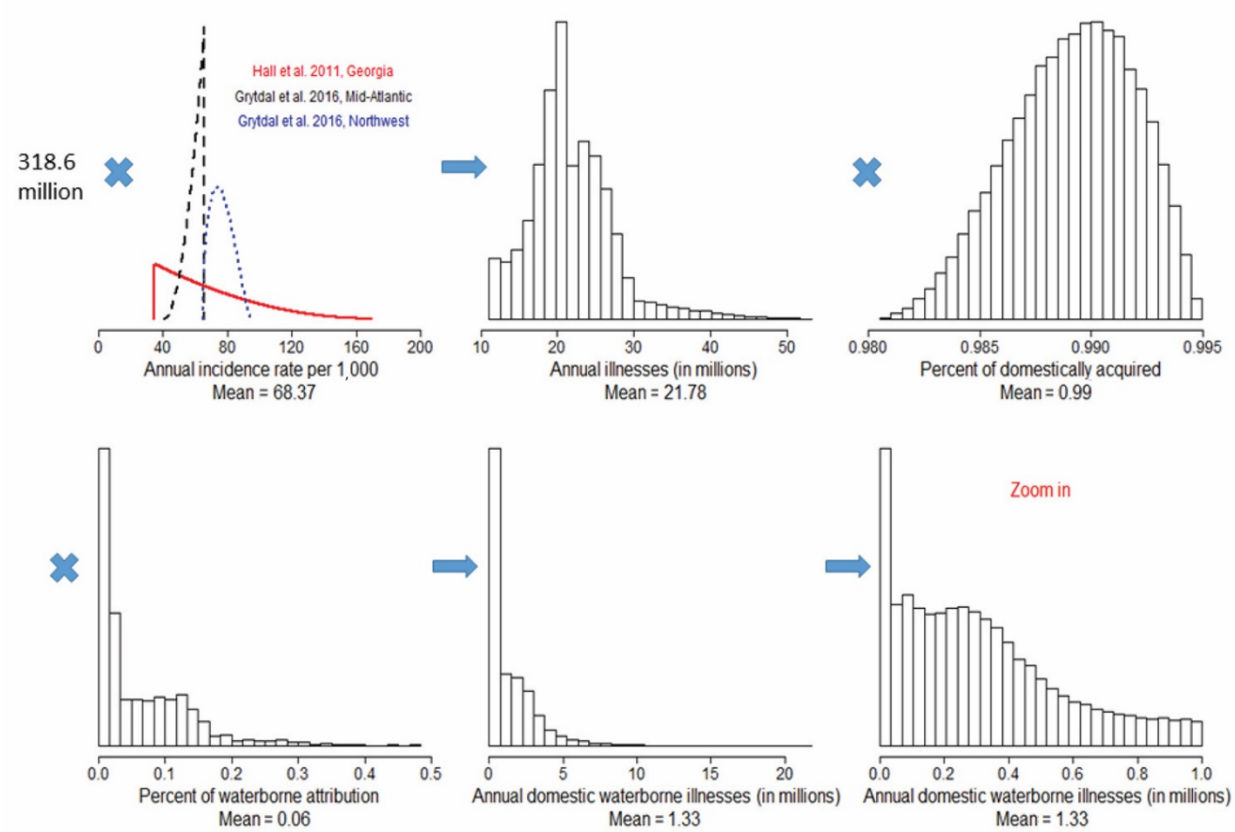


Appendix 2 Figure 5. Schematic diagram of the estimation of annual illness for *Pseudomonas* pneumonia. *X* axes show the relative frequency of observed or simulated values for each input or multiplier. *Year adj* is a deterministic factor to standardize non-2014 counts to 2014 (applied as needed).

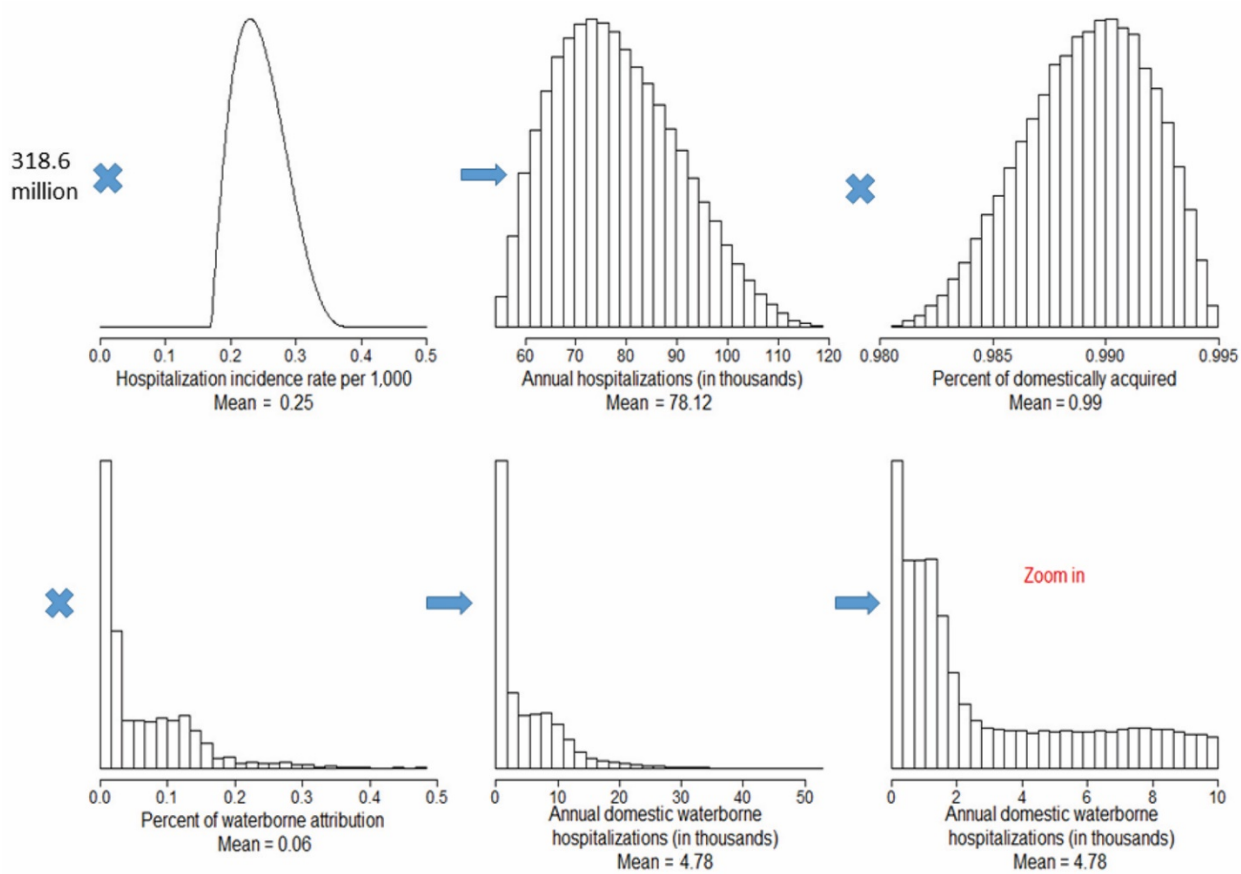
$$US\ Population\ 2014 \times \begin{bmatrix} Illness\ incidence\ rate \\ Hospitalization\ incidence\ rate \\ Death\ incidence\ rate \\ ED\ visit\ incidence\ rate \end{bmatrix} \times [1 \quad or \quad Dom \quad or \quad W] \Longrightarrow$$

Illness	*Domestic Illness*	*Domestic waterborne illness*
Hospitalization	*Domestic hospitalization*	*Domestic waterborne hospitalization*
Death	*Domestic death*	*Domestic waterborne death*
ED visits	*Domestic ED visits*	*Domestic waterborne ED visits*

Appendix 2 Figure 6. Schematic illustration of model type C, which scales the population at risk down, and is based on literature reported summary statistics. *Illness incidence rate:* the proportion of ill persons relative to the whole population at risk. *Hospitalization incidence rate and Death incidence rate* are the proportion of patients who were hospitalized or died relative to the whole population at risk. *ED visit incidence rate* is the proportion of patients who had ED visits (including both treated-and-released and admitted) relative to the whole population at risk. *Dom* is a contractive factor to scale total counts down to counts that are domestically acquired (applied as needed). *W* is a contractive factor to scale overall counts down to counts that are waterborne.



Appendix 2 Figure 7. Schematic diagram of the estimation of annual illnesses for norovirus. *X* axes show the relative frequency of observed or simulated values for each input or multiplier.



Appendix 2 Figure 8. Schematic diagram of the estimation of hospitalizations for norovirus. *X* axes show the relative frequency of observed or simulated values for each input or multiplier.

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Estimate of Burden and Direct Healthcare Cost of Infectious Waterborne Disease in the United States

Appendix 3

Additional Tables

Appendix 3 Table 1. Total annual cost to commercial insurers (sum of insurer payments, in 2014 US dollars) of emergency department visits and hospitalizations from waterborne transmission of selected infections, 2014, United States

	Treat-and-release ED visit			Hospitalization			Total
Disease	Mean insurer payment per visit (95% CrI)	Annual number of commercial visits paid due to waterborne transmission (95% CrI)	Total insurer cost of treat-and-release ED visits because of waterborne disease (95% CrI)	Mean insurer payment per stay (95% CrI)	Total annual number of stays because of waterborne transmission (95% CrI)	Total insurer cost of hospitalizations for waterborne disease (95% CrI)	Total annual insurer cost for waterborne disease (95% CrI)
Campylobacteriosis	2,120 (21–8,730)	190 (19–577)	402,000 (2,190–2,200,000)	14,100 (1,250–47,100)	944 (84–3,030)	13,000,000 (354,000–57,400,000)	13,400,000 (589,000–57,800,000)
Cryptosporidiosis	1,910 (16–9,280)	310 (105–603)	593,000 (5,050–2,800,000)	16,900 (1,560–82,700)	522 (48–1,650)	8,830,000 (217,000–47,000,000)	9,420,000 (588,000–47,500,000)
Giardiasis	1,800 (43–9,280)	365 (119–722)	656,000 (10,100–3,210,000)	24,100 (1,320–167,000)	503 (167–999)	12,100,000 (553,000–81,000,000)	12,800,000 (979,000–81,300,000)
Legionnaires' disease	1,230 (79–2,960)	275 (120–495)	338,000 (20,700–991,000)	44,900 (1,500–293,000)	4,610 (3,110–5,590)	207,000,000 (7,280,000–1,340,000,000)	208,000,000 (7,640,000–1,340,000,000)
Nontuberculous mycobacterial (NTM) infection	1,480 (34–6,460)	1,460 (739–2,240)	2,170,000 (40,600–9,380,000)	43,600 (1,320–243,000)	13,500 (7,030–19,400)	587,000,000 (16,400,000–3,340,000,000)	589,000,000 (18,900,000–3,340,000,000)
Otitis externa	517 (12–2,030)	324,000 (193,000–470,000)	167,000,000 (3,660,000–682,000,000)	13,100 (1,300–57,600)	8,750 (5,230–12,700)	114,000,000 (9,700,000–522,000,000)	282,000,000 (44,500,000–994,000,000)
Pseudomonas pneumonia	1,710 (34–8,890)	81 (21–153)	138,000 (2,240–819,000)	44,400 (1,300–192,000)	2,980 (795–5,420)	132,000,000 (2,750,000–640,000,000)	132,000,000 (2,870,000–640,000,000)
Pseudomonas septicemia	2,590 (161–11,800)	9 (1–26)	23,300 (228–169,000)	62,900 (1,330–385,000)	1,020 (131–2,540)	64,000,000 (732,000–397,000,000)	64,000,000 (742,000–397,000,000)
Salmonellosis, nontyphoidal	1,520 (56–7,900)	107 (8–372)	165,000 (1,540–977,000)	16,200 (1,360–74,100)	661 (44–2,470)	10,600,000 (173,000–59,100,000)	10,700,000 (276,000–59,300,000)
Shiga toxin-producing *E. coli* infection, O157	1,570 (3–5,390)*	5 (1–14)	7,870 (15–37,300)	24,800 (1,700–148,000)	69 (7–250)	1,720,000 (36,600–11,400,000)	1,730,000 (43,500–11,400,000)

	Treat-and-release ED visit			Hospitalization			Total
Disease	Mean insurer payment per visit (95% CrI)	Annual number of commercial visits paid due to waterborne transmission (95% CrI)	Total insurer cost of treat-and-release ED visits because of waterborne disease (95% CrI)	Mean insurer payment per stay (95% CrI)	Total annual number of stays because of waterborne transmission (95% CrI)	Total insurer cost of hospitalizations for waterborne disease (95% CrI)	Total annual insurer cost for waterborne disease (95% CrI)
Shiga toxin-producing *E. coli* infection, non-O157	1,570 (3–5,390)*	2 (0–06)	2,650 (00–15,600)	22,900 (1,140–95,700)	19 (0–77)	431,000 (00–2,990,000)	433,000 (644–3,000,000)
Shigellosis	1,960 (09–12,400)	24 (2–115)	46,600 (124–289,000)	17,700 (1,220–84,100)	113 (6–524)	1,920,000 (31,100–12,100,000)	1,960,000 (50,900–12,100,000)
Vibrio spp. infection	1,280 (300–4,440)	51 (10–112)	65,300 (4,150–262,000)	16,400 (399–49,200)	110 (67–158)	1,790,000 (37,300–6,290,000)	1,860,000 (134,000–6,380,000)
Total cost			172,000,000 (7,840,000–686,000,000)			1,160,000,000 (268,000,000–4,210,000,000)	1,330,000,000 (361,000,000–4,440,000,000)

*For emergency department (ED) visits only, costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.

Appendix 3 Table 2. Total annual cost to Medicare (sum of Medicare payments, in 2014 US dollars) of emergency department visits and hospitalizations from waterborne transmission of selected infections, 2014, United States

	Treat-and-release ED visit			Hospitalization			Total
Disease	Mean insurer payment per visit (95% CrI)	Annual number of commercial visits paid because of waterborne transmission (95% CrI)	Total insurer cost of treat-and-release ED visits for waterborne disease (95% CrI)	Mean insurer payment per stay (95% CrI)	Total annual number of stays because of waterborne transmission (95% CrI)	Total insurer cost of hospitalizations for waterborne disease (95% CrI)	Total annual insurer cost for waterborne disease (95% CrI)
Campylobacteriosis	1,190 (92–9,290)	51 (5–155)	60,500 (959–519,000)	13,700 (404–57,400)	842 (75–2,700)	11,500,000 (154,000–61,000,000)	11,500,000 (212,000–61,000,000)
Cryptosporidiosis	4,110 (129–18,000)	58 (20–113)	238,000 (4,250–1,270,000)	16,900 (00–155,000)	339 (31–1,080)	5,750,000 (9–39,400,000)	5,990,000 (142,000–39,500,000)
Giardiasis	1,040 (51–2,640)	76 (25–150)	78,800 (2,390–274,000)	22,900 (388–118,000)	341 (113–677)	7,790,000 (186,000–38,600,000)	7,870,000 (286,000–38,600,000)
Legionnaires' disease	626 (135–2,160)	43 (19–78)	27,200 (3,160–131,000)	32,800 (1,080–181,000)	4,930 (3,330–5,980)	162,000,000 (5,750,000–908,000,000)	162,000,000 (5,770,000–908,000,000)
Nontuberculous mycobacterial (NTM) infection	1,960 (47–10,000)	2,800 (1,420–4,280)	5,490,000 (81,200–33,400,000)	26,800 (647–159,000)	28,700 (15,000–41,400)	771,000,000 (17,200,000–4,440,000,000)	777,000,000 (19,500,000–4,440,000,000)
Otitis externa	421 (34–2,500)	43,600 (25,900–63,300)	18,400,000 (1,330,000–111,000,000)	13,500 (632–63,800)	8,740 (5,230–12,700)	118,000,000 (5,130,000–605,000,000)	136,000,000 (13,700,000–644,000,000)
Pseudomonas pneumonia	411 (54–1,970)	166 (43–315)	68,200 (4,490–393,000)	26,500 (572–145,000)	10,500 (2,790–19,000)	278,000,000 (3,880,000–1,530,000,000)	278,000,000 (3,940,000–1,530,000,000)
Pseudomonas septicemia	213 (67–529)	23 (1–68)	4,920 (188–20,100)	32,800 (768–179,000)	4,000 (516–9,990)	131,000,000 (1,410,000–783,000,000)	131,000,000 (1,410,000–783,000,000)
Salmonellosis, nontyphoidal	1,470 (79–8,960)	24 (2–82)	34,700 (391–257,000)	17,100 (474–80,900)	515 (34–1,920)	8,870,000 (64,400–50,300,000)	8,900,000 (84,500–50,300,000)
Shiga toxin-producing *E. coli* infection, O157	555 (84–1,510)*	5 (1–14)	2,790 (124–13,500)	16,600 (291–88,200)	42 (4–153)	700,000 (866–4,320,000)	702,000 (2,760–4,320,000)
Shiga toxin-producing *E. coli* infection, non-O157	555 (84–1,510)*	2 (0–06)	940 (0–5,710)	33,200 (1,040–243,000)	40 (0–167)	1,320,000 (0–11,000,000)	1,320,000 (274–11,000,000)
Shigellosis	297 (139–570)	3 (0–15)	892 (49–3,900)	10,200 (194–38,200)	54 (3–252)	546,000 (2,690–3,320,000)	547,000 (3,380–3,320,000)
Vibrio spp. infection	374 (269–479)	8 (2–18)	3,090 (528–7,690)	21,600 (5,280–76,300)	106 (65–153)	2,290,000 (457,000–8,750,000)	2,290,000 (461,000–8,750,000)
Total cost			24,400,000 (2,710,000–121,000,000)			1,500,000,000 (319,000,000–5,820,000,000)	1,520,000,000 (338,000,000–5,840,000,000)

*For emergency department (ED) visits only, costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.

Appendix 3 Table 3. Total annual cost to Medicaid (sum of Medicaid payments, in 2014 US dollars) of emergency department visits and hospitalizations from waterborne transmission of selected infections, 2014, United States

	Treat-and-release ED visit			Hospitalization			Total
Disease	Mean insurer payment per visit (95% CrI)	Annual number of commercial visits paid because of waterborne transmission (95% CrI)	Total insurer cost of treat-and-release ED visits for waterborne disease (95% CrI)	Mean insurer payment per stay (95% CrI)	Total annual number of stays because of waterborne transmission (95% CrI)	Total insurer cost of hospitalizations for waterborne disease (95% CrI)	Total annual insurer cost for waterborne disease (95% CrI)
Campylobacteriosis	436 (13–1,480)	77 (08–234)	33,600 (383–170,000)	5,710 (43–29,000)	363 (32–1,160)	2,050,000 (4,870–11,600,000)	2,080,000 (16,100–11,700,000)
Cryptosporidiosis	511 (1–3,420)	124 (42–241)	63,200 (161–405,000)	10,700 (16–64,200)	258 (24–817)	2,730,000 (3,300–15,300,000)	2,790,000 (29,200–15,400,000)
Giardiasis	555 (1–2,000)	126 (41–249)	69,600 (146–278,000)	14,300 (79–88,000)	254 (84–506)	3,630,000 (22,100–21,500,000)	3,700,000 (75,900–21,600,000)
Legionnaires' disease	*	111 (48–199)	65,600 (16,600–174,000)	18,600 (17–99,300)	1,260 (846–1,520)	23,300,000 (21,000–130,000,000)	23,400,000 (78,600–130,000,000)
Nontuberculous mycobacterial (NTM) infection	699 (4–3,130)	807 (407–1,230)	565,000 (3,520–2,490,000)	14,900 (45–70,300)	9,250 (4,830–13,300)	138,000,000 (361,000–687,000,000)	138,000,000 (811,000–689,000,000)
Otitis externa	194 (24–545)	200,000 (119,000–290,000)	38,700,000 (4,440,000–115,000,000)	6,530 (25–36,900)	5,740 (3,430–8,310)	37,400,000 (143,000–203,000,000)	76,200,000 (11,400,000–270,000,000)
Pseudomonas pneumonia	301 (20–1,710)	44 (11–84)	13,300 (556–77,400)	11,500 (18–53,500)	2,020 (540–3,680)	23,200,000 (26,800–115,000,000)	23,200,000 (40,200–115,000,000)
Pseudomonas septicemia	535 (51–2,470)	4 (0–12)	2,210 (25–17,100)	19,600 (46–113,000)	576 (74–1,440)	11,300,000 (12,900–72,200,000)	11,300,000 (14,300–72,200,000)
Salmonellosis, nontyphoidal	415 (17–2,090)	63 (5–218)	26,100 (302–173,000)	6,820 (32–26,300)	340 (23–1,270)	2,360,000 (4,580–13,500,000)	2,380,000 (13,300–13,500,000)
Shiga toxin-producing *E. coli* infection, O157	165 (10–672) †	2 (0–6)	368 (8–2,110)	4,270 (03–30,200)	27 (3–100)	116,000 (46–773,000)	116,000 (210–774,000)
Shiga toxin-producing *E. coli* infection, non-O157	165 (10–672) †	1 (0–3)	125 (0–832)	4,660 (41–32,000)	16 (0–64)	73,200 (0–524,000)	73,300 (28–524,000)
Shigellosis	294 (15–1,480)	37 (3–181)	10,900 (221–57,400)	7,620 (37–51,300)	78 (4–362)	611,000 (1,370–3,510,000)	622,000 (7,360–3,520,000)
Vibrio spp. infection	260 (30–1,010)	16 (3–36)	4,230 (361–15,400)	4,600 (13–46,000)	35 (22–51)	162,000 (445–1,350,000)	167,000 (1,550–1,360,000)
Total cost			39,600,000 (5,200,000–116,000,000)			245,000,000 (35,100,000–860,000,000)	284,000,000 (62,700,000–906,000,000)

*N<5, costs not reported.
†For emergency department (ED) visits only, costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.

Appendix 3 Table 4. Total annual cost (in 2014 US dollars) of emergency department visits and hospitalizations from all transmission routes of selected diseases, 2014, United States

	Treat-and-release ED visit			Hospitalization			Total
Disease or syndrome	Cost per visit (95% CrI)	Total annual number of treat-and-release ED visits because of all transmission routes (95% CrI)	Total cost of treat-and-release ED visits for selected diseases (95% CrI)	Cost per stay (95% CrI)	Total annual number of stays because of all transmission routes (95% CrI)	Total cost of hospitalizations for selected diseases (95% CrI)	Total annual direct healthcare cost of selected diseases (95% CrI)
Campylobacteriosis	1,710 (137–5,810)	2900 (1620–4630)	4,950,000 (398,000–18,700,000)	13,600 (3,850–35,800)	19,300 (8790–34,900)	261,000,000 (56,800,000–790,000,000)	266,000,000 (61,500,000–794,000,000)
Cryptosporidiosis	1,960 (238–6,270)	1260 (742–1880)	2,460,000 (257,000–8,150,000)	16,100 (4,360–55,400)	2,860 (439–8,060)	45,900,000 (3,710,000–195,000,000)	48,400,000 (5,670,000–197,000,000)
Giardiasis	1,620 (196–7,510)	1460 (902–2,090)	2,360,000 (284,000–9,880,000)	21,800 (6,160–99,200)	2,830 (1760–4,070)	61,800,000 (14,300,000–265,000,000)	64,200,000 (16,200,000–267,000,000)
Legionnaires' disease	691 (288–1,390)	691 (316–1,220)	477,000 (137,000–1,160,000)	37,100 (7,950–149,000)	11,200 (8,750–13,300)	416,000,000 (84,800,000–1,740,000,000)	416,000,000 (85,400,000–1,740,000,000)
Nontuberculous mycobacterial (NTM) infection	1,610 (129–6,430)	7,150 (5110–9,620)	11,500,000 (892,000–46,100,000)	29,600 (6,350–120,000)	72,400 (57,300–89,700)	2,140,000,000 (436,000,000–8,720,000,000)	2,160,000,000 (448,000,000–8,730,000,000)
Norovirus*	1,140	429,000	491,000,000	6,080	78,100	475,000,000	966,000,000
Otitis externa	494 (120–1,430)	726,000 (466,000–994,000)	358,000,000 (79,600,000–1,070,000,000)	12,200 (3,320–42,400)	29,700 (19,200–40,600)	365,000,000 (89,900,000–1,330,000,000)	723,000,000 (250,000,000–1,990,000,000)
Pseudomonas pneumonia	856 (89–4,190)	580 (321–902)	496,000 (45,500–2,440,000)	29,300 (5,910–114,000)	30,800 (18,700–44,700)	901,000,000 (164,000,000–3,710,000,000)	901,000,000 (165,000,000–3,710,000,000)
Pseudomonas septicemia	923 (95–3,190)	164 (36–326)	151,000 (9140–731,000)	38,200 (6,340–172,000)	25,300 (16300–34,800)	968,000,000 (149,000,000–4,240,000,000)	968,000,000 (149,000,000–4,240,000,000)
Salmonellosis, nontyphoidal	1,230 (161–4,500)	3400 (2100–4900)	4,200,000 (510,000–16,000,000)	14,900 (4,300–46,900)	26,600 (11400–52,800)	395,000,000 (79,500,000–1,410,000,000)	400,000,000 (83,300,000–1,420,000,000)
Shiga toxin-producing *E. coli* infection, O157†	1,070 (109–2,350)	252 (92–465)	269,000 (16600–794,000)	19,000 (3,790–85,000)	2640 (487–7630)	50,400,000 (4,270,000–244,000,000)	50,700,000 (4,530,000–244,000,000)
Shiga toxin-producing *E. coli* infection, non-O157†	1,070 (109–2,350)	75 (12–171)	79,600 (3090–274,000)	24,200 (4,780–138,000)	1420 (264–3810)	34,500,000 (2490000–223,000,000)	34,600,000 (2,570,000–223,000,000)
Shigellosis	952 (115–3,980)	1650 (540–2860)	1,570,000 (123,000–7,420,000)	14,200 (4,130–48,000)	6380 (929–20,300)	90,700,000 (8,170,000–398,000,000)	92,300,000 (9,280,000–400,000,000)
Vibrio spp. infection	1,030 (293–3,330)	366 (122–700)	376,000 (53,700–1,270,000)	16,000 (3,780–39,900)	782 (567–1030)	12,500,000 (2,620,000–32,300,000)	12,900,000 (3,010,000–32,800,000)
Total cost			878,000,000 (596,000,000–1,590,000,000)			6,220,000,000 (2,980,000,000–15,400,000,000)	7,100,000,000 (3,770,000,000–16,300,000,000)

*For norovirus only, costs were derived from previously published estimates that did not include uncertainty intervals. In addition, the number of emergency department visits includes visits in which the patient was admitted to the hospital.

†For emergency department (ED) visits only, costs for STEC O157 and STEC non-O157 were combined and payer proportion was derived from all ED visits instead of treat-and-release visits because of small sample size.